

REVIEW ARTICLE

Beers criteria: an up-to-date tool for detecting inappropriate prescription in elderly

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Summary

Potentially inappropriate medications (PIM) are drugs that can cause significant unnecessary harm to patients. Prescribing PIM can cause significant healthcare problems, especially if there is a safer, similar, or even more effective alternative for the treatment. They are the cause of significant health issues that lead to increased treatment costs and reduced life quality. The main problem when it comes to treating geriatric population is a lack of specific guidelines for the treatment. This is mainly because clinical trials which are the main pillars of clinical guidelines are usually aimed at people aged 18 to 65, leaving the geriatric population aside. For this reason, as well as to reduce the prescription of PIM in the geriatric population many guidelines have been created, among which the AGS Beers criteria were the first and have remained the leading and most comprehensive tool for this purpose. Since 1991, the Beers criteria have gone through several updates and changes in format, and in 2012 they came under control of the American Geriatric Society. The constant updates and work on these guidelines saved them the top position, compared to other guidelines in this field. Taking all this into consideration, it is imperative for every clinician who works with geriatric patients to be familiar with these guidelines and to utilize them properly as explained.

Keywords: AGS Beers criteria, potentially inappropriate medication, geriatric population

INTRODUCTION

Potentially inappropriate medication in the geriatric population

Potentially inappropriate medication (PIM) also known as potentially inappropriate prescribing (PIP) is defined as a medication prescribed to patients whose risk of harm outweighs its benefits (1). This is why PIMs are considered a significant healthcare problem, especially if there is a safer, similar, or even more effective alternative for the treatment (1-3). There is also a more basic definition of PIMs which defines PIMs as drugs that can cause significant unnecessary harm to patients. PIMs can endanger a patient's life, especially in elderly population where they significantly increase the risk of mortality (2-4). Several decades of intensive PIM research revealed the fact that in the geriatric population, PIMs can cause significant health issues that lead to increased treatment costs and impaired quality of life. In the next section of this paper, the focus will be on health and economic consequences of PIMs, as well as on the benefits of PIM reduction.

Health consequences of potentially inappropriate medication

Elderly patients, due to multiple simultaneously present conditions and diseases, are commonly prescribed more medications than the rest of the population. Polypharmacy, as this phenomenon is called, is one of the biggest health issues of the geriatric population (2,3). In this population, polypharmacy-related problems are more evident due to changes in physiological and cognitive function, as well as in pharmacokinetic and pharmacodynamic changes, that are consequences of aging. Studies in this field reported that in the elderly PIMs may increase the incidence of adverse drug reactions (ADR), hospitalization, poorer treatment outcomes, and death (5-8). A nationwide large-scale survey from Japan was conveyed to determine the prevalence of adverse drug reactions caused by PIMs; it showed that PIM was responsible for adverse drug reactions in at least 8% of patients (5). In another study that investigated the occurrence of ADR in elderly hospitalized patients, PIMs were detected in almost 24 % of patients with ADR (6). The study managed to find a correlation between PIMs and the occurrence of ADR, marking PIMs a significant risk factor for ADR development (6). Varalo et al., (7) performed a study intending to determine the prevalence of PIMs in hospitalized elderly patients and to determine the connection between ADRs and PIMs. The study revealed that in hospitalized elderly patients 5% of ADRs were developed as a consequence of PIMs. All this literature evidence implies that prescribed PIMs mean worse health outcomes in elderly patients and drug-related problems occur significantly more often when compared to elderly patients without prescribed PIMs (8).

Economic consequence of potentially inappropriate medication

From an economic point of view, it is interesting to know that a single PIM prescribed to an elderly patient significantly increases healthcare expenditures (9). One of the estimates, which was done at the beginning of this century, revealed the severity of the economic burden that PIMs brought on the healthcare system (9). This study showed that in the United States of America (USA) around 7.2 billion US \$ was spent on healthcare expenditures that had occurred as a consequence of prescribing PIMs to elderly patients (9). A study from Germany, which compared healthcare costs between the elderly with and without prescribed PIMs, showed that in the first quarter of the year since the beginning of the study, healthcare costs were significantly higher in PIM group. More precisely, in the first quarter health care costs were 1237 €/patient higher in the PIM group (10). Another finding in connection with PIM costs was obtained from the economic analysis performed in French nursing homes. This French study determined how much PIM cost per day, and how much would be saved if the number of prescribed PIMs would be reduced. The cost of a single PIM prescriber per resident per day was 2.8 €, which means that in France 25 million € could be saved per year, only by reducing the number of PIMs in nursing homes (11). A cost-utility analysis performed to determine the economic impact of three commonly prescribed PIMs in the elderly (i.e., non-steroid anti-inflammatory drugs, benzodiazepines, and proton-pump inhibitors) showed that in 2014, these three PIMs were associated with greater costs and reduced quality-adjusted life years (12). Out of these three drugs, benzodiazepines had the highest incremental costs, with 3470 € when compared to non-sedative medications (12). All these studies demonstrated that PIMs were not only associated with health problems but also with a significant economic burden for the healthcare system in every country and that significant effort should be invested in reducing PIMs for several reasons: prolonging life, increasing quality-adjusted life year (QALY), and reducing treatment costs.

GUIDELINES FOR THE REDUCTION OF PIMS IN THE ELDERLY

Clinical trials that include geriatric patients are rare. Mainly, the data that could be found in the literature is related to unwanted effects and therapeutic problems in this population. This is why the modest literature data related to the treatment of the geriatric population is used to create guidelines in a way in which we are focusing on what should be avoided when treating these patients instead of what should be a drug of choice for certain conditions or diseases.

Since the first guidelines created by Beers in 1990s, many new guidelines have been created with the same idea to reduce PIMs in the elderly population. The main reason for expansion and creation of different guidelines is the fact that each is regionally specific and focused on drugs sold in that specific market. Since its creation, the use of the Beers criteria have been evaluated in different countries, and apart from being created especially for the USA market it has been shown that this criteria is possible to use all over the world. Sometimes some minor changes were needed which led to the creation of new criteria like PIM-Taiwan which was based on the Beers criteria. This is why the Beers criteria are the most well-known and most widely used criteria for PIM reduction in older adults in the world (13). Nevertheless, after the Beers criteria there were a few specific criteria created with a different philosophy than the Beers criteria and for different geographic regions. Some of those criteria are STOPP/START criteria and EU (7)-pim criterion (2,3). All the above-mentioned criteria were created for the general geriatric population and were to be used mainly by medical doctors. By that time, there was a growing need for different guidelines, and this is why specific guidelines have been created for nursing home residences NORGE-PNH which are focusing on PIMs, and also there are now guidelines that could be used by pharmacists GheOP3S tool which facilitated pharmacists' inclusion in the struggle for PIMs reduction. All these guidelines enriched the field and helped medical professionals involved in the treatment of the elderly.

AMERICAN GERIATRIC SOCIETY BEERS CRITERIA

The American Geriatric Society (AGS) Beers criteria are widely used criteria by healthcare providers, researchers, educators, healthcare administrators, and regulators (14). These criteria are created as a list of medications that should be avoided by the elderly, always or in specific situations. The primary goal of these criteria is to manage and improve the pharmacotherapeutic part of healthcare for people older than 65 years (14). In clinical settings, the Beers criteria are used for all aspects of care, except for palliative and hospice care (1). The AGS Beers criteria are the most known and most widely used criteria for PIM reduction in older adults (> 65 years) (13). Apart from its purpose in reducing PIM in the elderly, AGS Beers criteria should be used for educating clinicians working in the field of geriatric medicine and for the evaluation of costs and quality of provided healthcare.

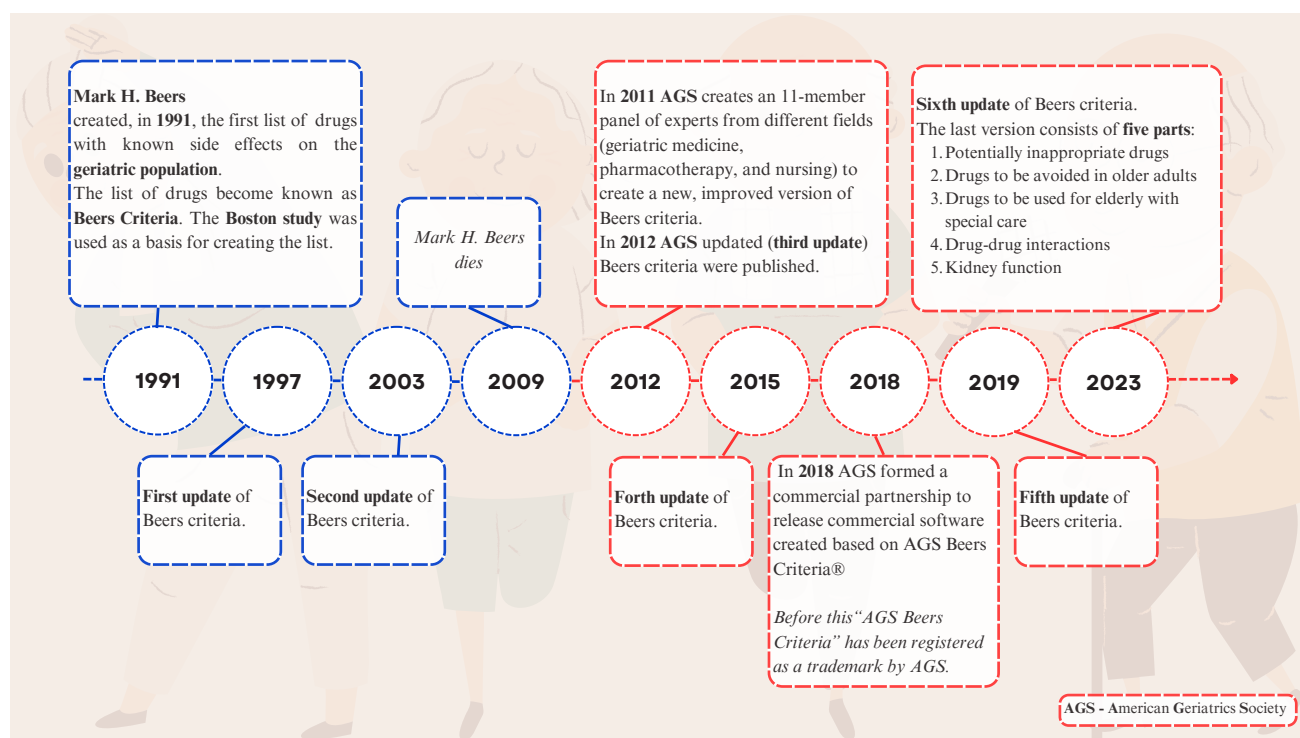
History of the AGS Beers criteria

The American geriatric society (AGS) Beers criterion was first created in 1991 by Mark H. Beers, a geriatrician whose research was focused on drug interaction in

geriatric patients which led to the creation of the Beers guidelines. Beers deserves great credit for his criteria influenced a wave of much-needed innovation in geriatric pharmacology. The criteria were initially updated in 1997 and 2003. After Beer died in 2011, AGS became responsible for revisions and updates of the Beers criteria. The first criteria update under the supervision of AGS was published in 2012 (15). For this revision, AGS organized an eleven-member panel. The panel consisted of experts in different fields of geriatric medicine (medical doctors, nurses, pharmacists, and researchers). The panel created an update using the modified Delphi method. In the review process, the experts' panel decided whether new criteria, derived from literature data, should be added to the existing list of criteria, or if the existing criteria should be removed or revoked. The newly updated Beers criteria were based on experts' knowledge and literature review. Since 2012, the year when the first Beers criteria were updated under the supervision of AGS, there have been three more updates. Currently, AGS is trying to provide updates on the Beers criteria every 3 years. The last AGS Beers criteria update was published in May 2023. The detailed timeline of Beers criteria was presented in **Figure 1**.

Structure of AGS Beers Criteria

In this section, we will shortly present the most important parts of the AGS Beers criteria. The latest update is a product of a workgroup assembled of 12 experts with background in medicine, nursing, and pharmacotherapy. Ten members of this panel also worked on the 2019 update of AGS Beers criteria (16). The AGS Beers criteria 2023 is basically a list of medications that, if possible, should be always avoided, or should be avoided in certain situations (i.e. specific diseases or conditions) (14). The core of AGS Beers criteria are five parts that consist of several criteria. These parts are: (1) medications that are potentially inappropriate in most older adults; (2) medications that should typically be avoided in older adults with certain conditions (possible drug-disease or -syndrome interface); (3) medications that should be used by the elderly, but with special care; (4) drug-drug interactions that should be avoided in the elderly; (5) medication to avoid or adjust the dose based on kidney function. These five parts remained from the AGS Beers 2015 and AGS Beers 2019 versions of these criteria (14,15). In the last version, 38 drugs or medication classes were skipped when compared to the 2019 criteria (14,16). In total, 10 new criteria were added to AGS Beers 2023 criteria when compared to the last version (14,16). Also, 32 drugs/criteria from AGS Beers 2019 were modified in AGS Beers 2023 (i.e. switched from one part to another part of the guidelines based on new evidence, had clarified or modified language, were modified based on the newly discovered risks, etc.).



The first part of the criteria consists of the drugs which are potentially inappropriate in older adults, such as anticholinergic drugs (first-generation antihistamines, antiparkinsonian agents, and antispasmodics), antithrombotic drugs, anti-infective drugs, and drugs for pain; drugs affecting different organ systems (cardiovascular, endocrine, gastrointestinal, genito-urinary and central nervous system). The strength of recommendation for many elements of this part of criteria is marked as strong. The strength of the recommendation was weak only for androgens and estrogens (with or without progestins) for topical use. For this part of the guidelines, the quality of evidence was predominantly moderate to high.

The second part consists of the drugs that should be avoided in certain conditions or diseases since these drugs can aggravate the primary disease. For example, thiazolidinediones antidiabetic drugs with some pleiotropic effects (17) can promote fluid retention and thus are avoided in older adults with heart failure (16). The strength of recommendation for all criteria, except for alpha-1 blockers and antipsychotics in syncope (week), is marked as strong (16). The quality of evidence for this part of the criteria is predominantly moderate (16).

The third part of the AGS Beers 2023 criteria is dedicated to drugs that need to be used with caution in older adults. For example, prasugrel or ticagrelor should be used with caution due to a high risk of major bleeding in those 75 and older. Still, these drugs can have some benefits for selected patients. The strength of recommendation for all criteria of this part of the Beers criteria, except for SGLT2 inhibitors (week), is considered strong (16). The quality of evidence is moderate for all these criteria. The only exception is the trimethoprim-sulfamethoxazole combination for which the quality of evidence is low (16).

The fourth part of the criteria is dedicated to drug-drug interactions that are best to be avoided in the population older than 65 years (16). Most of the listed interactions are focused on the drugs that affect the central nervous system. For all the listed interactions, the strength of recommendation was marked as strong. The quality of evidence was moderate for all recommendations, while it was high only for criteria that considered a combination of CNS active drugs.

The fifth part considers drugs that should be avoided or drugs whose dosage should be adjusted regarding the kidney function. The kidney function is estimated based on creatinine clearance (mL/min). The strength of recommendation for this part of the criteria was strong for all, except for tramadol and duloxetine which should be avoided when creatinine clearance is under 30 mL/min. The quality of evidence for this part of the guidelines was moderate except for the mentioned tramadol criteria for which the quality of evidence was low.

EXAMPLES OF SUCCESSFUL UTILIZATION OF THE AGS BEERS CRITERIA AND THEIR LIMITATIONS IN PRACTICE

The AGS Beers criteria are created to be used in the USA. They may be used internationally, but still, a validation study needs to be performed. Previous versions were examined in different parts of the world and the results of these studies support the use of criteria outside of the USA. Also, these criteria are supposed to be used in any type of clinical care except hospice and end-of-life care such as nursing homes. Nevertheless, some data show that the AGS Beers criteria could be used in nursing homes as well

(3). The interpretation of the data from studies in nursing homes should be taken with special caution because in nursing homes there is a flaming issue of PIMs. This is why when using this guideline improperly it may seem that there are more PIMs than there really are. This is why it is always highlighted to use these guidelines properly, as explained in the AGS Beers criteria. Also, there are other guidelines specially created to address the most common problems in prescribing practice in nursing homes.

This and the previous version of the criteria were evaluated and validated in different clinical settings and in different populations. The AGS Beers criteria were created for primary health care, and they were evaluated for this purpose in a cross-sectional study conducted in two primary health care centers in Brazil (18). These criteria were also evaluated in a specific subgroup of the geriatric population, in so-called very old people (80 years and above) (19). The use of AGS Beers criteria was also validated in older (> 65 years) cancer outpatients with multimorbidity (20). There is evidence that the AGS Beers criteria can be used with great success for finding PIMs in psychiatry and internal medicine (21, 22). Also, the use of these guidelines has been proven to be successful in detecting PIMs in patients with chronic kidney disease (23). The use of these criteria was, among others, validated in Brazil, China, India, Jordan, Korea, Lithuania, Nigeria, Portugal, Serbia, South Africa, Spain, the USA (3, 18-30).

The main problem with the AGS Beers criteria is that they are constantly, in each new update, skipping the part related to supplement use. Supplement use is becoming more and more pronounced in different age groups. We are currently witnessing an increasing interest in research in the field of supplements. On a daily basis, we are getting new insights into where the use of different supple-

ments could be useful (31 - 33). Still, their interaction with drugs and different diseases and conditions could be a serious health problem, especially in sensitive populations such as the geriatric population.

CONCLUSION

The AGS Beers criteria are certainly a powerful tool in reducing PIMs in the geriatric population, as well as in reducing the development of ADE and unintended consequences of inadequately prescribed drugs, while at the same time reducing the healthcare costs. Although initially created for the USA healthcare system, these criteria have been proven effective in various healthcare systems around the world. The most powerful feature of the AGS Beers criteria is their constant 3-year updates, based on the latest literature data. Considering all of these, it is imperative for every clinician who works with geriatric patients to know these criteria and to utilize them properly as explained in these criteria.

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Conflict of interest

None to declare.

Author Contributions

Both authors contributed significantly to the conception and design of this review article and to preparing the draft of the manuscript.

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BIRSOVI KRITERIJUMI: MODERNA ALATKA ZA OTKRIVANJE NEADEKVATNO PROPISANIH LEKOVA U GERIJATRIJSKOJ POPULACIJI

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Sažetak

Potencijalno neodgovarajući lekovi su lekovi koji pacijentima mogu nepotrebno da naruše zdravlje tokom njihove redovne primene u terapiji. Propisivanje potencijalno neodgovarajućih lekova može izazvati značajne zdravstvene probleme, što treba izbeći, posebno ako postoji bezbednija, po efikasnosti slična, ili čak efikasnija alternativa za lečenje. Potencijalno neodgovarajući lekovi su uzrok zdravstvenih problema, dovode do povećanja troškova lečenja i smanjenja kvaliteta života. Glavni problem u lečenju gerijatrijske populacije je izostanak specifičnih smernica za lečenje. Kako klinička ispitivanja, koja su glavni izvor informacija za kliničke smernice, obično obuhvataju ljude uzrasta od 18 do 65 godina, nedostaje dovoljno relevantnih informacija na osnovu kojih bi se kreirale terapijske smernice za gerijatrijsku

populaciju. Kako nema adekvatnih smernica za terapiju pacijenata u gerijatrijskoj populaciji, i kako bi se smanjio broj neadekvatno propisanih lekova, osmišljeni su vodiči sa tim ciljem. Prvi je ovakve vodiče osmislio Mark Birs 1991. godine. Nakon ovih vodiča osmišljen je veliki broj vodiča sa sličnom namenom. Međutim, Birsovi kriterijumi ostaju i do danas najkorišćeniji i najpoznatiji kriterijumi u svetu. Ovo je pre svega rezultat stalne dopune i osavremenjivanja ovih vodiča. Sam Birsov vodič je prošao kroz nekoliko dopuna i promenu formata, a od 2012. godine ovaj vodič uređuje Američko gerijatrijsko udruženje. Sve ovo čini Birsove kriterijume odličnom alatkom za pronalaženje neadekvatno propisanih lekova u gerijatrijskoj populaciji, a samim tim je od važnosti za sve lekare koji rade sa gerijatrijskom populacijom.

Ključne reči: Birsovi kriterijumi, neadekvatno propisani lekovi, gerijatrijska populacija

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