The use of Beers Criteria for safe medication prescription to older adults

O uso dos critérios de Beers para uma prescrição medicamentosa segura em pessoas idosas

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ABSTRACT

Older adults are more vulnerable to medication and polypharmacy effects, mainly when it comes to pharmacokinetics, pharmacodynamics and systemic interaction. Beers Criteria are internationally acknowledged standards aimed at identifying potentially inappropriate prescriptions, also known as PIPs. Four published versions of these criteria (2012, 2015, 2019 and 2023) were approached through narrative review, with emphasis on their main features and changes in them. The main results address recommendations to avoid antipsychotics prescription in case of behavioral disorders like those that take place in dementia; restriction to using anticoagulants; avoiding proton pump inhibitors for time equal to, or longer than, 8 weeks, as well as metoclopramide and sulfonylureas. Using benzodiazepines, which is a highlight in all 4 versions of the herein assessed criteria, must be avoided in case of delirium or cognitive impairment. Beers Criteria are a valuable method for clinical application to identify PIPs and to contribute to good clinical practices to endure effective assistance and correct drug prescriptions to older adults.

Keywords: Potentially Inappropriate Medication List; Inappropriate prescription; Polypharmacy; Aging health; Gerontology

RESUMO

As pessoas idosas são mais vulneráveis aos efeitos de medicamentos e da polifarmácia, principalmente no que diz respeito à farmacocinética, farmacodinâmica e interação sistêmica. Os Critérios de Beers são uma padronização de reconhecimento internacional que visam identificar prescrições potencialmente inapropriadas, também conhecidas como PPIs. Quatro versões publicadas desses critérios (2012, 2015, 2019 e 2023) foram abordadas por meio de revisão narrativa, com ênfase em suas principais características e alterações nelas ocorridas. Os principais resultados abordam recomendações para evitar a prescrição de antipsicóticos em caso de distúrbios comportamentais como os que ocorrem na demência; restrição ao uso de anticoagulantes; evitar inibidores da bomba de prótons por tempo igual ou superior a 8 semanas, bem como metoclopramida e sulfonylureas. O uso de benzodiazepínicos, destaque nas 4 versões dos critérios aqui avaliados, deve ser evitado em caso de delirium ou comprometimento cognitivo. Os Critérios de Beers são um valioso método de aplicação clínica para identificar PPIs e contribuir com boas práticas clínicas para garantir uma assistência eficaz e corretas prescrições de medicamentos para idosos.

Palavras-chave: Lista de medicamentos potencialmente inapropriados; Prescrição inadequada; Polimedicação; Saúde do Idoso; Gerontologia
INTRODUCTION

Increase in life expectancy broadens multi-morbidity prevalence due to association between aging, and systemic and degenerative diseases (GAGA et al., 2019).

Multi-morbidity is featured by the simultaneous existence of two or more diseases, and it is common at older ages (FRANCISCO et al., 2021). Moreover, it is overall associated with polypharmacy, which means simultaneously taking 5 or more medications (MASNOON et al., 2017).

Inappropriate drug use makes medication and medication-disease interactions reinforce the bidirectional association between multi-morbidity and functional damage (daily-life activities) in older adults (RAKESH et al., 2017).

Several factors contribute to nowadays situation, such as comorbidities typical of aging, chronic use of medication, physiological changes that increase sensitivity to medication effects and shortage of studies focused on the effectiveness and safety of proper drug use (MAHER; HANLON, 2014).

Potentially inappropriate prescriptions (PIPs) have straight influence on polypharmacy in older adults. This fact is related to cascading prescription, which is observed when medications’ adverse effects are mistakenly attributed to a new disease, a fact that leads to the prescription of a new drug to treat the adverse effect of other medications (RAKESH et al., 2017). This conduct increases the risk of adverse reactions to medications, and the degree of weakness, dependence, collateral effects and morbidity in the older population (SERRANO; COMELATO, 2019).

A previous study (SAN-JOSÉ et al., 2014) has shown that the prescription of ten or more medications (hyper-polypharmacy) is the strongest independent risk factor associated with inappropriate prescription and PIPs. Medication interactions happening among them are additional risk factors that can broaden PIPs’ inappropriate profile (BORIES et al., 2021). According to Hines and Murphy (2011, p. 365), “medication interaction is defined as significant clinical changes in the effect of a given drug (targeted drug) due to the co-administration of another one (precipitant drug)”.

Beers Criteria are one of the first validated tools to detect medications whose risks exceed their benefits (ABDELWAHED et al., 2021), since they identify medications that must be avoided by people over 65 years old, either in general terms or in case of specific diseases and conditions.
They were firstly developed by Mark Beers and collaborators in 1991 (BEERS et al., 1991) to feature drugs based on their adverse effects in older adults living in long-stay institutions; later on, it was expanded and reviewed, in 1997 and 2003, to cover all geriatric fields. The elaborated list aimed at contributing to medications’ correct prescription, as well as to monitor their effects. Such organization was accredited to the responsibility of the AGS (American Geriatrics Society) back in 2010; since then, it has produced new reviews every 03 years. In May 2023, it launched its last update, the so-called “AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults” (AGS, 2023).

It is important highlighting that this standardization is not applied to older adults who are in asylums and under palliative care (AGS, 2023).

The updated reviews are substantiated by scientific evidence and its methodological quality is highlighted by the GRADE tool (Grading of Recommendations Assessment, Development and Evaluation), which is seen as a universal, transparent and sensitive system developed by a group of researchers to grade the accuracy of evidences and strength of medication recommendations for a given case. Nowadays, several international institutions use GRADE, among them one finds the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC) and the Cochrane collaboration (KIRMAYR et al., 2021).

Beers Criteria must not define the right prescription, because medications in their list are not ultimately inappropriate or forbidden, but they have the potential to cause damage to health and interactions among medications. However, in some situations, their benefits can overcome their risks (STEINMAN; FICK, 2019).

Although the list does not provide on all inadequate therapeutics, the Beers Criteria describe specific medications, and advise about those that should not be administered, or about the ones that must be used with caution in older adults who present specific features due to the potential of impairing drug effects (FICK et al., 2019).

The aim of the present review is to analyze Beers Criteria recommendations by approaching the main changes and recommendations for proper drug prescriptions to older adults, as observed in their four published versions.
METHODS

A narrative and comparative analysis was applied to Beers Criteria published in 2012, 2015, 2019 and 2023 (last update) by the American Geriatrics Society, with emphasis on the main evidences of proper drug prescription to elderly individuals, as well as on changes made in their four versions.

A search was carried out in the PubMed database to find articles about the herein addressed topic, published from 2012 onwards, based on the following keywords (in separate and/or in combination), in English: Beers Criteria OR Beers’ Criteria; Inappropriate prescribing; Aged; Polypharmacy; Drug interactions; Gerontology – it totaled 40 articles.

RESULTS AND DISCUSSION

Recommendations and adverse effects described in the Beers Criteria aim over 65-year old individuals. It is worth emphasizing that in Brazil a person is featured as old person from the age of 60 years onwards. Since 2012 (FICK et al., 2012), the quality of these criteria has been enhanced by the American Geriatrics Society, based on an approach supported by scientific evidences and on rigorous systematic reviews carried out by a group of selected experts (CAMPANelli et al., 2012).

The Criteria were divided into three categories of medications and classes to “be avoided” in older adults, potentially inappropriate medications (PIPs) and classes to “be avoided” for certain diseases and syndromes, and a third list of potentially noxious medications that must be used with “caution” in older adults. Beers Criteria published in the first version presented quality evidence to allow correct prescribing recommendation, as well as focused on the list of medications that were potentially inadequate to all older adults (regardless of the diagnosis and clinical condition). It is seen as a broader list, whose items are recommended to be avoided.

Knowledge about the published versions of Beers Criteria, based on an individual and comparative analysis, allows the best perception and awareness about medications. It contributes to correct drug prescription for older adults (Table 1).

Table 1 – Comparison of published Beers Criteria (2012-2015-2019-2023) and changes set to improve medication prescriptions to older people.
<table>
<thead>
<tr>
<th>Beers Criteria</th>
<th>Authors</th>
<th>Recommendations</th>
<th>Final considerations</th>
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| **2012**       | Panel of 11 experts in geriatric care and pharmacotherapy. CMS, NCQA and PQA representatives as members *ex officio.* | • Sliding scale insulin, megestrol and glyburide were added to the list of medications to be avoided.  
• Avoid glitazones – used to decrease resistance to insulin – in HF.  
• Avoid acetylcholinesterase inhibitors in older people with history of syncope.  
• Avoid SSRIs in older people with history of falls or fractures. | Based on rigorous systematic literature review, on using a consensus panel of experts, on evidence strength ranking, and on recommendations. They are destined to outpatient and institutional environments that provide care to over 65 years old individuals. |
| **2015**       | Panel with 13 experts in geriatric care and pharmacotherapy. CMS, NCQA and PQA representatives as members *ex officio.* | • Non-benzodiazepine hypnotics, previously accepted for up to 90 days, should be avoided.  
• The use of nitrofurantoin was made flexible if CrCl > 30 ml/min.  
• Only amiodarone remained as first-line antiarrhythmic drug for AF.  
• Avoid the prolonged use of proton pump inhibitors (risk of *C. difficile* infection and bone loss) and opioids in older people with history of falls or fractures, as well as the use of | A novelty was the list of medications that must be avoided or have their doses adjusted to kidney function and the list of impairing medication interactions. They apply to elderly ≥ 65 years old, except for those undergoing palliative care or suffering with terminal disease. |
antipsychotics in those with history of delirium.

2019 The panel included 13 clinicians and physicians, pharmacists and nurses; all of them attended to 2015 update process. CMS, NCQA and PQA representatives, *ex officio*, were also included in it.

- H2 antagonist antacids were allowed for dementia or cognitive impairment cases, but they should be avoided in case of delirium.
- Glimepiride has been warned as capable of causing risk of prolonged severe hypoglycemia.
- SNRIs should be avoided in patients with reports of falls/fractures.
- Quetiapine, clozapine and pimavanserin are antipsychotics nowadays allowed for Parkinson's disease. Cilostazol (used in peripheral vascular insufficiency) must be avoided in HF; calcium antagonists, such as verapamil and diltiazem, in IC with reduced ejection fraction; NSAIDs and cyclooxygenase-2 inhibitors in symptomatic HF.

The Final Criteria were released aimed at comments from the general public and sent to 39 organizations. In total, 244 individual comments were sent back from pharmaceutical companies and organizations. They were reviewed by panel co-chairs and shared with the panel for final approval, along with the proposed changes.

The panel encompassed 12 members from the nursing, medical and pharmaceutical

2023

- Avoid using ≥ 3 CNS-active drugs, including muscle relaxants.
- Do not use aspirin in the 1st prevention of cardiovascular disease.

The panel changed the order and wording of certain Criteria, recommendations and rationale.
fields who are experts in outpatient, home and hospital assistance, in houses of specialized nursing and in long-term care. CMS, NCQA and PQA representatives, *ex officio*, were included in it.

• Avoid prolonged use of rivaroxaban in non-valvular FA and TEV; use dabigatran “with caution” and do not use warfarin as initial therapy. Apixaban has been removed due to evidence of safety in case of kidney dysfunction.

• Avoid oral and transdermal estrogen in elderly women and deprescribe it; The vaginal type is accepted for vaginal atrophy or urinary tract infection prophylaxis.

• Avoid all sulfonylureas (heart failure risk, hypoglycemia); baclofen in case of kidney dysfunction (risk of encephalopathy) and avoid antipsychotics and opioids to treat behavioral disorders due to dementia and delirium.

• Use ticagrelor (risk of bleeding) and SGLT2 with caution (risk of urogenital infection; it increases glucose in the urine and diabetic ketoacidosis).

**Acronyms:** NSAIDs, non-hormonal anti-inflammatory drugs; CrCl, creatinine clearance; CMS, Centers for Medicare and Medicaid services; DOAC, direct-acting oral anticoagulants; eGFR, glomerular filtration rate; AF, Atrial fibrillation; HF, heart failure; SNRI, Serotonin and Norepinephrine Reuptake Inhibitors; SSRIs, selective serotonin reuptake inhibitors; PIP, potentially inappropriate medications; NCQA, National...
Committee for Quality Assurance; PQA, Pharmacy Quality Alliance; SGLT2, sodium-glucose cotransporter-2 inhibitors; CNS, central nervous system; VTE, venous thromboembolism.

Source: elaborated by the authors. Vargas DB; Miranda AF, 2023.

The Beers Criteria are updated to approach the evolution of medications available, as well as the understanding of action mechanisms, pharmacological interactions and adverse effects. Over the years, the profile of medications in the Beers’ list has changed, and it reflects the best understating of drugs prescribed to older people at the time to publish each new version of them. Continuous research has led to new recommendations and to guidelines for safe drug prescriptions (FICK et al., 2019).

Examples of medication interactions found in the list introduced in 2015, included both loop and potassium-sparing diuretics. Loop diuretics were included because they increased the risk of lithium toxicity and urinary incontinence in women. Potassium-sparing diuretics were included along with angiotensin converting enzyme inhibitors, because they are associated with risk of hyperkalemia. Moreover, they are recommended to be used with caution given their association with syndrome of inappropriate antidiuretic hormone secretion (SIADH) or hyponatremia (SAMUEL, 2015).

Strong scientific evidence recommended avoiding proton pump inhibitors for more than 8 weeks, since the 2015 version of the Criteria, because of risk of infection caused by C. difficile, osteoporosis and fractures, however, there are some exceptions to it. In 2023, pneumonia and gastrointestinal malignancies were added to the aforementioned risks. This is one of the most often used classes of medications worldwide, partly due to their free selling without medical prescription and because elderly individuals are particularly predisposed to be recommended for acidic suppression (BAIK; FUNG; MCDONALD, 2022).

Similarly, according to the panel, metoclopramide, which is often used to treat nausea and vomiting, must be avoided, because it can have extrapyramidal effects, mainly in older adults and after prolonged use (SALBU; FEUER, 2017).

The update also highlights the need of avoiding antipsychotics and other medications for behavioral disorders like dementia and delirium. The use of psychotropics must be the last option, and the decision about its administration must be shared with the aged patient and its caregivers (MÜHLBAUER et al., 2021).
It is worth pointing out that the Beers Criteria do not apply to older individuals under asylum and palliative care. However, these patients oftentimes have behavioral issues of high systemic complexity that cannot be controlled by any other means. Decision-making can demand other considerations within this context (MÜHLBAUER et al., 2021). The panel itself highlights that antipsychotics can be used if the non-pharmacological options fail. Nevertheless, it recommends the systematic attempt to deprescribe them and to use lower effective doses – it applies to all medications (PRAXEDES et al., 2021).

Benzodiazepines play key role in all 4 published versions. The most recent version (2023) presents strong recommendation for avoiding their use in older adults, mainly in delusional patients or in those with cognitive deficit. These drugs expose users to risk of drug abuse, inappropriate use and addiction, besides the risk of overdose due to slow metabolism observed in older adults (LOU; OKS, 2021). Seizure disorders and benzodiazepine withdrawal are among the indicated exceptions. The non-pharmacological approaches, such as sleep hygiene or psychotherapy, are seen as therapeutic options as effective as medication, and they have more sustainable outcomes in insomnia and depression (PARK et al., 2014).

One of the most expressive changes observed in criteria published in 2019 – and kept in the 2023 criteria – was related to sulfonylureas, whose recommendation was expanded to “to be avoided” under any situation. According to the panel, they can increase the risk of heart diseases, of death due to all causes and of stroke. If one has in mind that one of the goals to treat diabetes mellitus is to avoid heart complications (YUN; KO, 2021), it is possible stating that this is a quite remarkable statement.

Prolonged hypoglycemia is also a likely complication caused by these medications, mainly long-acting sulfonylureas (glimepiride) (SERRANO; COMELATO, 2019). Yet, about the 2019 Criteria, some uncommon drugs were removed from it (such as carboplatin, cyclophosphamide, cisplatin) and some specific drugs were added to the list (glimepiride, rivaroxaban, tramadol) – they are considered inappropriate for elderly individuals (COTILLAS; EGOCHEAGA, 2023).

One of the main changes in the 2023 Criteria lied on the inclusion of warfarin in the widest list. Its use must be avoided because new data in the literature about the use of anticoagulants prioritize direct-acting oral anticoagulants. It is important avoiding to use warfarin as initial therapy to treat venous thromboembolism or non-valvular atrial fibrillation, except if alternative choices are contraindicated. In case of older people who
have been using it for a longer time, recommendation lies on going on with it in case of well-controlled ISR (international standardized ratio) - > 70% of time in therapeutic range (AGS, 2023).

Warfarin increases the risk of intracranial bleeding the most, and their efficacy is equal to, or lower than, that of direct oral anticoagulants (COTILLAS; EGOCHEAGA, 2023). In same situations, the long-term use of rivaroxaban must be avoided in older people, and prioritize the use of safer anticoagulants.

Other remarkable change in Criteria published in 2023 was the recommendation to avoid using aspirin to primary prevention of heart diseases, due to significant increase in risk of bleeding in senility, as well as to assess deprescription for older adults who have already used it in primary prevention (AGS, 2023).

The most updated criteria in the list of medication interactions emphasized concern with lithium toxicity, which can happen to its combination to angiotensin-converting enzyme inhibitors, angiotensin receptor blockers or loop diuretics (AGS, 2023).

Oral and transdermal estrogen must be avoided for older women; its vaginal type seems appropriate to symptomatic vaginal atrophy or urinary tract infection prophylaxis. Deprescription must be taken into account for older women who already use non-vaginal estrogen replacement (COTILLAS; EGOCHEAGA, 2023).

Risks of menopausal hormone therapy (HT) are low in women who have started treatment within 10 years prior to menopause (or before turning 60 years old). In this case, there is benefit for overall survival, coronary heart disease and osteoporosis prevention in women recommended to treatment. However, there is strong evidence of increased risk of venous thromboembolism in HT started at any age: prior to, or after, the age of 60 years. There is no evidence that HT has benefited women who have started treatment 10 years, or more, after menopause or who started it after the age of 60 years old. Actually, there were higher risks of coronary heart disease and all-cause mortality. Furthermore, it is associated with risk of stroke, venous thromboembolism and pulmonary embolism (HMP; COSP; SANCHEZ, 2015; ROSSOUW et al., 2013).

It is worth highlighting that, phosphodiesterase-5 inhibitors, which are used to approach erectile dysfunction, are associated with several adverse effects, including arterial hypotension and circulatory shock with fatal outcome (GUL; SEREFOGLU, 2019). These medications were not yet taken into consideration and placed in any PIP list of Beers Criteria guidelines.
FINAL CONSIDERATIONS

Medications potentially inappropriate for prescription are still prescribed in a non-standardized way as first-line treatment for older adults, despite evidence of bad clinical outcomes when they are used.

Knowledge about the four editions of published Beers Criteria, their features and changes in them, overtime, allow a better analysis of, and improvements in, the prescription and interactions of medication inappropriate to older adults.

The Beers Criteria can contribute to good care provision practices aimed at older people, if they are properly used by prescribers. It is so, because they allow providing accurate instructions about the medications to be used, about their interactions and about their direct reflex on older adults health and quality of life.

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