



Clinical appraisal of STOPP/START version 3 criteria

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Dear Editor,

A new version of the STOPP/START criteria for potentially inappropriate prescribing in older people was eagerly expected by many clinicians around the world. We were very pleased to read the 190 STOPP/START version 3 criteria (Appendix 1) recently published in the May 2023 issue of the *European Geriatric Medicine* journal by D O'Mahony and other European experts in geriatric pharmacotherapy [1]. As geriatricians and clinical pharmacists using STOPP/START criteria for daily clinical care, academic teaching and clinical research [2, 3], we wish to comment on the four steps followed by the authors in their approach to this third version.

The first step (i) was the consensus on the structure of the STOPP/START lists. The authors agreed on keeping the system-based classification of the previous versions, which makes them easy to compare but presents some limitations. On the one hand, the STOPP criteria most often classify criteria within specific systems based on the pharmacological class of medication, but sometimes—and less logically—on the system affected by the main side effect (B14, 15, 17–19; C10, 12, 15; D14, 24; F3–8; G4; J3). On the other hand, and more importantly in our opinion, the system-based classification is not user friendly in daily practice when clinicians face drugs classified in different STOPP system sections. For examples, β -blockers appear in the cardiovascular

(B3–5) and the endocrine (J3) systems, while digoxin is found in the cardiovascular (B1, 4, 21) and the renal (E1) sections. Benzodiazepines are included in central nervous (D8–10), respiratory (G4) and fall risk (K1) sections, while SSRI are in the central nervous system (D6–7), coagulation (C12) and fall-risk increasing (K8) sections. NSAIDs appear in four different sections (B17, 19; C10; E4; H2, 3, 6, 7). Until reliable software applications are available [4], it will be a challenge for clinicians to find all the criteria related to one drug scattered across different sections.

The second step (ii) was the revision of version 2 criteria for relevance and accuracy. In the results, the article reports the removal from version 2 of two STOPP criteria (C2; H7) and one START criterion (B1). Comparing version 3 to version 2, we identified the removal of two other STOPP criteria (G4: non-cardio-selective β -blockers in case of history of asthma requiring treatment; J6: androgens in the absence of hypogonadism) and one other START criterion (C4: topical treatment for primary open-angle glaucoma). We also note that STOPP C2 version 2 was logically changed in version 3 to START F3, but is now limited to the initiation of low-dose aspirin.

The third step (iii) of this update was a comprehensive although not systematic review of the literature by the two main authors to support existing and proposed new criteria. It is unclear whether the references (Appendix 2) were selected based on the population age (≥ 65 years). In contrast to the AGS criteria, we regret that no level of evidence and strength of recommendation were provided, as this is important information to support clinical decisions. Of the 298 references, only 78 (27%) were published after 2014 (including the 13 published in the 2021 issue of the British National Formulary), indicating a lack of new evidence for many criteria.

The consensus step (iv), achieved through a four-round Delphi validation process, is clearly described. We believe that—similar to the process followed for the AGS criteria—an interdisciplinary panel that would include pharmacists and a public consultation process could have further

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enhanced the validity of the criteria. The STOPP and START lists unfortunately do not distinguish between new, modified, and unchanged criteria, as pointed out in the editorial by North American colleagues [5]. Below, we highlight some important changes in this new version.

The STOPP list includes new drug groups, e.g. drugs prolonging the QTc interval (B15, which surprisingly include digoxin), and inhibiting G-glycoprotein drug efflux pump (C14). These clinically important classes are quite long and difficult to remember. Statin is a new STOPP criterion (B16), conservatively defined (primary cardiovascular prevention in adults ≥ 85 years with frailty and < 3 years of life expectancy). Some STOPP criteria include an important modification that is worth underlying, e.g. E1 (digoxin more than 90 days ≥ 125 $\mu\text{g/day}$ instead of > 125 $\mu\text{g/day}$), B19 (NSAIDs are no longer inappropriate in heart failure not requiring loop diuretic therapy) and C4 (antiplatelet agent in combination with anticoagulant agent in patients with atrial fibrillation in no more inappropriate in the presence of a coronary stent or a $> 50\%$ stenosis). Regarding the later, two important questions may be raised. First, should ischaemic events/stents outside the coronary artery system (peripheral or cerebral) be considered in the same way? Second, what would be the time limit applied to this exception?

As expected, new START criteria relate to evidence-based drugs in heart failure, such as spironolactone when $\text{eGFR} > 30$ ml/min (B7), SGLT-2 when symptomatic (B8), as well as sacubitril/valsartan when persisting in the presence of reduced ejection fraction (B9, with ACE inhibitor withdrawal). Several new START criteria appeared in the gastro-intestinal (G, $n = 6$), cardiovascular (B, $n = 5$) and renal (E, $n = 3$) sections. Of note, calcium is no more present in the drug therapy of osteoporosis (H3), except as prevention in patients with long-term systemic corticosteroid therapy (H2).

Importantly, the STOPP/START version 3 criteria address some major geriatric syndromes. STOPP criteria, besides the important the fall risk (K section, much longer in version 3), analgesic (L) and anti-muscarinic (M) groups, now include frailty (B16), non-cognitive symptoms of dementia (D5, 9, 15, 21), delirium (D14), dysphagia (F7), malnutrition (F8), chronic constipation (F3; I4), urinary incontinence (B10; I7) and insomnia (D10, 16, 25). The START criteria, after mentioning the importance of the patient's particular

clinical context (A1), now integrate frailty (B1–2), functional impairment (D1, 5, 7; F6; H1) and chronic constipation (F4–5).

We want to congratulate the Cork team for its pioneering work over the last two decades in creating and continuing updating the STOPP/START lists, which undoubtedly help clinicians improve prescribing appropriateness in older adults. Tools should be developed to support the implementation of these numerous criteria in daily clinical practice.

Declaration

Conflict of interest The authors declare that they have no conflict of interest.

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