RESEARCH LETTER

The FORTA (Fit fOR The Aged) List 2021: Fourth Version of a Validated Clinical Aid for Improved Pharmacotherapy in Older Adults

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Multimorbidity and, consequently, polypharmacy are highly prevalent in older adults [1, 2]. As the number of older people is continually growing [2, 3], both the concurrent use of multiple medications and inappropriate drug treatment causing drug-related problems will become an increasing medical challenge around the world if no effective preventive measures are implemented into clinical practice [4–6]. In general, the simultaneous use of multiple medications is often indicated, but its appropriateness should be assessed through the critical evaluation of pharmacotherapy in older individuals [7]. Over the last three decades, various listing approaches/criteria have been developed to aid prescribers in addressing these issues [8]. Most, such as the Beers criteria® [9], are drug-oriented listing approaches (DOLA) [7, 8], mainly supporting prescribers to identify potentially inappropriate medications (PIMs) for deprescribing [4]. Such negative lists cannot clearly yield improvements in relevant clinical outcomes (e.g. mortality or functional status) [4, 7, 8, 10, 11]. Representing a more effective solution, the FORTA [Fit fOR The Aged] List addresses both over- and undertreatment, leading to patients' medical needs being comprehensively met [7]. Such lists are classified as patient-in-focus listing approaches (PILA) [8], detecting both PIMs and potentially omitted drugs (POMs) [4]. PILAs require intricate medical knowledge about patients and the majority of randomized trials with these tools have been clinically successful [7, 8]. The FORTA List 2012 and its updates in 2015 and 2018 for German-speaking countries have been published in *Drugs & Aging* [7, 12, 13], and represent the only PILA drug lists that combine positive and negative labeling of drugs used for long-term drug treatment of common diseases in older adults [7]. At the same time, START/STOPP [14] criteria include action points and drug recommendations. The FORTA classifications in the FORTA List range from A (indispensable) to B (beneficial), C (questionable) and D (avoid), based on evidence for their safety, efficacy and age appropriateness [7]. The clinical usefulness, implementability and teachability of the FORTA List has been validated in randomized controlled clinical trials [7, 15, 16]. In these trials, a significant positive impact on appropriateness of drug treatment and the occurrence of adverse drug reactions was shown [7, 15]. In addition, relevant clinical endpoints such as activities of daily living (ADL) were significantly improved [15, 17, 18]. As new evidence in the field of geriatric pharmacology has emerged since the publication of the 2018 FORTA List, an update based again on a two-step Delphi process [7, 12, 13] was performed to comply with the 3-year cycle of former updates. Twenty experts from Germany, Austria and Switzerland participated in the evaluations. The metrics of changes for this update compared with the FORTA 2018 List are depicted in Table 1. The FORTA List 2021 (Supplementary Data 1 in the electronic supplementary material; also available at: https://www.umm.uni-heidelberg.de/klinische-pharmakologie/forschung/forta-projekt/) now contains 299 entries in 30 indications relevant to geriatrics. The highest percentage of disease-related entries with changed FORTA classifications was observed for arterial hypertension (13.3%, Table 1). All other items with altered FORTA labels are also shown in Table 1. Besides, the top three indications with the highest increase in the mean consensus coefficient as compared with the FORTA 2018 List were nausea and vomiting, BPSD (behavioral and psychological symptoms of dementia): depression, and dementia (Table 1). Over 99.6% (294 items) of the proposed 295 items received a consensus

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Table 1 Metrics of changes between the 2018 and 2021 versions of the FORTA list

All indications ranked by changes of entries [%]	Number of entries with a new classification/total number [%]	Number of upgraded entries	Number of downgraded entries	Number of new entries	Examples of upgraded entries	Examples of downgraded entries
Arterial hypertension	2/15 [33.3]	1	1	1	Indapamide B → A	β-Blockers B → C
COPD	1/11 [9.1]	0	1	0		Theophylline C → D
Depression	1/18 [5.5]	0	1	0		Moclobemide C → D
Top 3 indications with the highest increase in the mean consensus coefficient	2018 Mean consensus coefficient (range)			2021 Mean consensus coefficient (range)		p value (t test)
Nausea and vomiting	0.946 (0.894–1.000)			0.987 (0.947–1.000)		$p > 0.05$
BPSD: Depression	0.863 (0.857–0.875)			0.900 (0.875–0.925)		$p > 0.05$
Dementia	0.931 (0.714–1.000)			0.962 (0.875–1.000)		$p > 0.05$

FORTA List labels: A = indispensable, B = beneficial, C = questionable, and D = avoid [7]

COPD chronic obstructive pulmonary disease, *BPSD* behavioral and psychological symptoms of dementia, *FORTA* Fit fOR The Aged

coefficient of ≥ 0.8 after the first round of the Delphi process; only metamizole (for the treatment of chronic pain) had to be re-evaluated in the second round. Moreover, seven items were added to the list, such as sodium-dependent glucose co-transporter 2 (SGLT2) inhibitors for the treatment of heart failure, reflecting recent studies and guidelines regarding the treatment of heart failure [19–21]. SGLT2 inhibitors were labeled as FORTA B for heart failure while their classification for type 2 diabetes remained FORTA C. Interestingly, aducanumab, though not yet approved in Europe, was labeled as FORTA D. The FORTA List 2021 update now reflects recent advances and new clinical data regarding drug therapy of older people. Moreover, the new list is supported by an even wider consensus (mean consensus coefficient for all items 0.968) among experts as compared with its 2018 version (0.962); this demonstrates its increasingly coherent assessment by a large number of experts from different areas reflecting its consolidated validity.

Declarations

Conflict of interest Martin Wehling was employed by AstraZeneca R&D, Mölndal, as director of discovery medicine (translational medicine) from 2003 to 2006, while on sabbatical leave from his professorship at the University of Heidelberg. Since returning to this position in January 2007, he has received lecturing and consulting fees from Bristol Myers, Bayer, Boehringer-Ingelheim, LEO, Mundipharma, Novartis, Pfizer, Polyphor, Helsinn, Allergan, Allecra, Novo-Nordisk, Heel, AstraZeneca, Roche, Santhera, Sanofi-Aventis, Shire, Berlin-Chemie and Daichii-Sankyo. Farhad Pazan and Christel Weiss have no conflicts of interest to declare.

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

Availability of data and materials Not applicable.

Code availability Not applicable.

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