

Commentary

Open Access

## Inappropriate prescribing and adverse drug events in older people

Hilary J Hamilton\*, Paul F Gallagher and Denis O'Mahony

Address: Department of Geriatric Medicine, Cork University Hospital, Wilton, Cork, Ireland

Email: Hilary J Hamilton\* - hilaryjane@yaho.com; Paul F Gallagher - pfgallagher@eircom.net; Denis O'Mahony - denis.omahony@hse.ie

\* Corresponding author

Published: 28 January 2009

Received: 13 October 2008

BMC Geriatrics 2009, 9:5 doi:10.1186/1471-2318-9-5

Accepted: 28 January 2009

This article is available from: <http://www.biomedcentral.com/1471-2318/9/5>

© 2009 Hamilton et al; licensee BioMed Central Ltd.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

### Abstract

Inappropriate prescribing (IP) in older patients is highly prevalent and is associated with an increased risk of adverse drug events (ADEs), morbidity, mortality and healthcare utilisation. Consequently, IP is a major safety concern and with changing population demographics, it is likely to become even more prevalent in the future. IP can be detected using explicit or implicit prescribing indicators. Theoretically, the routine clinical application of these IP criteria could represent an inexpensive and time efficient method to optimise prescribing practice. However, IP criteria must be sensitive, specific, have good inter-rater reliability and incorporate those medications most commonly associated with ADEs in older people. To be clinically relevant, use of prescribing appropriateness tools must translate into positive patient outcomes, such as reduced rates of ADEs. To accurately measure these outcomes, a reliable method of assessing the relationship between the administration of a drug and an adverse clinical event is required. The Naranjo criteria are the most widely used tool for assessing ADE causality, however, they are often difficult to interpret in the context of older patients. ADE causality criteria that allow for the multiple co-morbidities and prescribed medications in older people are required. Ultimately, the current high prevalence of IP and ADEs is unacceptable. IP screening criteria need to be tested as an intervention to assess their impact on the incidence of ADEs in vulnerable older patients. There is a role for IP screening tools in everyday clinical practice. These should enhance, not replace good clinical judgement, which in turn should be based on sound pharmacogeriatric training.

### Background

Older patients often have numerous co-morbidities for which they are prescribed multiple medications, thereby increasing the risk of adverse drug events (ADEs) [1]. This risk is compounded by age-related changes in physiology and body composition, which influence drug handling and response [2]. Furthermore, there is marked heterogeneity in health status and functional capacity in older people, often making prescribing decisions complex and challenging [2-4]. Evidence suggests that suboptimal or inappropriate prescribing (IP) is highly prevalent in older people and is associated with an increased risk of ADEs,

increased morbidity, mortality and healthcare utilisation [5-9]. With changing worldwide population demographics and an aging population, IP in older people is becoming a global healthcare concern [5].

IP encompasses the use of medicines that pose more risk than benefit, particularly where safer alternatives exist. IP also includes the misuse of medicines (inappropriate dose or duration), the prescription of medicines with clinically significant drug-drug and drug-disease interactions, and importantly, the under-use of potentially beneficial medications [5]. IP can be detected using explicit (criterion-

based) or implicit (judgement-based) prescribing indicators. Beers' criteria are the most widely cited explicit tool and have dominated the international literature since their development in the U.S. in 1991 [10]. They consist of two lists of medications to be avoided in older people, (a) independent of diagnosis, and (b) considering diagnosis, and do not address under-prescribing, drug-drug interactions or drug class duplication. They were originally designed for older nursing home residents, but were revised in 1997 [11] and 2002 [12] to be universally applicable to older patients. More recently, the STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions) criteria were validated in a European setting [13]. STOPP criteria (see additional file 1) are arranged according to physiological systems for ease of use and include reference to drug class duplication, drug-drug and drug-disease interactions. They are uniquely designed for use alongside the START (Screening Tool to Alert doctors to the Right Treatment) criteria, which highlight under-prescription or omission of clinically indicated, evidence-based medications [14], thereby addressing more domains of prescribing appropriateness than Beers' criteria alone. Explicit criteria have been criticised for having limited transferability between countries due to variations in regional prescribing patterns and drug availability [5]. Explicit criteria must also be regularly updated in line with evolving clinical evidence.

The Medication Appropriateness Index (MAI) [15] is an implicit tool which measures prescribing appropriateness according to ten criteria including indication, effectiveness, dose, administration, drug-drug and drug-disease interactions and cost. It does not address under-prescribing. Clinical expertise is required to apply some of the criteria, resulting in variable inter-rater reliability. Consequently, the MAI is predominantly used as a research tool.

### **Prevalence of inappropriate prescribing in the elderly**

IP is highly prevalent in older people, with up to 24% of community-dwelling patients [16] and 40% of nursing home residents in the United States [17] regularly receiving at least one potentially inappropriate medicine (PIM) according to Beers' criteria. IP prevalence is somewhat lower in Europe, though comparison between studies is limited by differing methodologies. Under-prescribing is even more widespread – a recent study found that 58% of older patients do not receive one or more clinically indicated medications according to START criteria [14]. Risk factors for IP include older age, polypharmacy and multiple attending physicians and pharmacists [5]. IP is associated with increased morbidity, mortality and healthcare cost, largely because of an increased prevalence of ADEs [5].

### **Adverse drug events and inappropriate prescribing**

ADEs are defined as any injury resulting from drug therapy – from appropriate care, or unsuitable or suboptimal care [18]. ADEs include adverse reactions during normal use of a medicine, and any harm due to medication error whether of omission or commission. Up to 35% of community-dwelling older people experience ADEs each year [19], the incidence being even higher amongst nursing home residents [8]. Up to 30% of hospital admissions in older people are related to ADEs [20]. The clinical relevance of IP relates to its association with negative outcomes including preventable ADEs. Therefore, regular application of IP screening criteria should, hypothetically, reduce the prevalence of ADEs and related morbidity. To accurately measure such outcomes, reliable assessment of the relationship between drug administration and adverse clinical event is required, both in terms of causality and preventability. The Naranjo criteria are often used to assess ADE causality (see additional file 2), with inter-rater agreement scores superior to subjective clinical judgement [21]. However, they can be difficult to interpret in the context of older patients with multiple co-morbidities and medications. ADEs in older patients often present with non-specific symptoms or geriatric syndromes such as cognitive impairment or falls e.g. a fall may be related to osteoarthritis or poor visual acuity as well as prescription of a medication that increases falls risk such as a benzodiazepine. The causal association can also be weakened as the Naranjo criteria evaluate drugs individually and do not address drug-drug interactions (see additional file 2).

The Hallas criteria classify ADEs as preventable, probably preventable, probably not preventable or definitely not preventable [22]. Preventable ADEs include those arising from the prescription of PIMs and suboptimal monitoring and dose adjustment. Non-preventable ADEs include allergic or idiosyncratic reactions.

The ultimate aim of IP screening tools is to optimise prescribing appropriateness and reduce negative outcomes including preventable ADEs. Therefore, the medications listed by explicit IP tools should be those most commonly associated with preventable ADEs in older people. Some studies have demonstrated no increased risk of ADEs in patients receiving Beers' criteria medications [23-25]. Some also conclude that Beers' criteria PIMs account for only a small proportion of ADEs in older patients [25,26]. However, interpretation of such studies is difficult as many were retrospective and lacked clinical detail, thereby resulting in incomplete application of Beers' criteria. Furthermore, many did not use rigorous ADE causality and preventability criteria. It is possible that Beers' criteria simply do not list those medications most commonly associ-

ated with preventable ADEs in older people, as suggested by a recent Irish study which reported that 12% of hospital admissions were related to ADEs resulting from STOPP criteria PIMs, with only 6% resulting from Beers' criteria PIMs [27].

Other interventions that optimise prescribing appropriateness include comprehensive geriatric assessment [28], clinical pharmacist intervention [29], prescriber education [30] and computerised decision support tools [31]. However, such interventions are resource intensive and not universally available. Consequently, there is a need for a simple, inexpensive and time-efficient screening tool which can be used routinely to guide prescribing practice and reduce the rate of IP in older patients. Such a tool should be sensitive, specific, include commonly encountered ADEs and have good inter-rater reliability. To be clinically relevant, use of such a screening tool must translate into positive clinical outcomes. Specific ADE causality assessment criteria for older people are also needed to measure the result of such interventions.

## Conclusion

Ultimately, the high prevalence of IP and preventable ADEs in older people is unacceptable, and represents a public health hazard likely to grow in tandem with ageing populations. Improved undergraduate and postgraduate training in geriatric pharmacotherapy is crucial. Though valid IP screening tools are desirable, they should enhance, not replace, clinical judgement. These screening tools need to be tested as an intervention in order to assess their impact on the incidence of ADEs in this vulnerable population.

## Additional material

### Additional file 1

*Screening tool of older people's potentially inappropriate prescriptions. The following drug prescriptions are potentially inappropriate in persons aged  $\geq 65$  years of age.*

Click here for file

[<http://www.biomedcentral.com/content/supplementary/1471-2318-9-5-S1.doc>]

### Additional file 2

*The Naranjo adverse drug reaction probability scale; To assess the adverse drug reaction, please answer the following questionnaire and give the pertinent score. The Naranjo adverse drug reaction (ADR) probability scale. The Naranjo criteria classify the probability that an adverse event is related to drug therapy based on a list of weighted questions, which examine factors such as the temporal association of drug administration and event occurrence, alternative causes for the event, drug levels, dose – response relationships and previous patient experience with the medication. The ADR is assigned to a probability category from the total score as follows: definite if the overall score is 9 or greater, probable for a score of 5–8, possible for 1–4 and doubtful if the score is 0. The Naranjo criteria do not take into account drug-drug interactions. Drugs are evaluated individually for causality, and points deducted if another factor may have resulted in the adverse event, thereby weakening the causal association.*

Click here for file

[<http://www.biomedcentral.com/content/supplementary/1471-2318-9-5-S2.doc>]

## References

1. Lazarou J, Pomeranz BH, Corey PN: **Incidence of adverse drug reactions in hospitalised patients: a meta-analysis of prospective studies.** *JAMA* 1998, **279**:1200-5.
2. Mangoni AA, Jackson SH: **Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications.** *Br J Clin Pharmacol* 2004, **57**:6-14.
3. Nelson EA, Dannefer D: **Aged heterogeneity: fact or fiction? The fate of diversity in gerontological research.** *Gerontologist* 1992, **32**:17-23.
4. Woodhouse KW, O'Mahony MS: **Frailty and ageing.** *Age Ageing* 1997, **26**:245-46.
5. Spinewine A, Schmader KE, Barber N, Hughes C, Lapane KL, Swine C, Hanlon JT: **Appropriate prescribing in elderly people: how well can it be measured and optimised?** *Lancet* 2007, **370**:173-84.
6. Lindley CM, Tully MP, Paramsothy V, Tallis RC: **Inappropriate medication is a major cause of adverse drug reactions in elderly patients.** *Age Ageing* 1992, **21**:294-300.
7. Lau DT, Kasper JD, Potter DE, Lyles A, Bennett RG: **Hospitalization and death associated with potentially inappropriate medication prescriptions among elderly nursing home residents.** *Arch Intern Med* 2005, **165**:68-74.
8. Gurwitz JH, Field TS, Avorn J, McCormick D, Jain S, Eckler M, Benser M, Edmondson AC, Bates DW: **Incidence and preventability of adverse drug events in nursing homes.** *Am J Med* 2000, **209**:87-94.
9. Klarin I, Wimo A, Fastbom J: **The association of inappropriate drug use with hospitalisation and mortality: a population based study of the very old.** *Drugs Aging* 2005, **22**(1):69-82.
10. Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Beck JC: **Explicit criteria for determining inappropriate medication use in nursing home residents.** *Arch Intern Med* 1991, **151**:1825-32.
11. Beers MH: **Explicit criteria for determining potentially inappropriate medication use by the elderly. An update.** *Arch Intern Med* 1997, **157**:1531-36.
12. Fick DM, Cooper JW, Wade WE, Waller JL, MacLean JR, Beers MH: **Updating the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults – Results of a US Consensus Panel of Experts.** *Arch Intern Med* 2003, **163**:2716-24.
13. Gallagher P, Ryan C, Byrne S, Kennedy J, O'Mahony D: **STOPP (Screening Tool of Older Persons' Prescriptions) and START (Screening Tool to Alert Doctors to Right Treatment): Consensus Validation.** *Int J Clin Pharmacol Ther* 2008, **46**(2):72-83.
14. Barry PJ, Gallagher P, Ryan C, O'Mahony D: **START (Screening Tool to Alert doctors to the Right Treatment) – an evidence-**

- based screening tool to detect prescribing omissions in elderly patients. *Age Ageing* 2007, **36**:628-631.
15. Hanlon JT, Schmader KE, Samsa GP, Weinberger M, Uttech KM, Lewis IK, Cohen HJ, Feussner JR: **A method for assessing drug therapy appropriateness.** *J Clin Epidemiol* 1992, **45**:1045-51.
  16. Willcox SM, Himmelstein DU, Woolhandler S: **Inappropriate drug prescribing for the community-dwelling elderly.** *JAMA* 1994, **272**:292-296.
  17. Dhall J, Larrat EP, Laplane KL: **Use of potentially inappropriate drugs in nursing homes.** *Pharmacotherapy* 2002, **22**:88-96.
  18. Council of Europe. Committee of experts on management of safety and quality in health care (SP-SQS): **Expert group on safe medication practices. Glossary of terms related to patient and medication safety 2005.** [[http://www.who.int/patientsafety/highlights/COE\\_patient\\_and\\_medication\\_safety\\_gl.pdf](http://www.who.int/patientsafety/highlights/COE_patient_and_medication_safety_gl.pdf)].
  19. Hanlon JT, Schmader KE, Koronkowski MJ, Weinberger M, Landsman PB, Samsa GP, Lewis IK: **Adverse drug events in high risk older outpatients.** *J Am Geriatr Soc* 1997, **45**:945-948.
  20. Onder G, Pedone C, Landi F, Cesari M, Della Vedova C, Bernabei R, Gambassi G: **Adverse drug reactions as a cause of hospital admissions: results from the Italian Group of Pharmacoepidemiology in the Elderly (GIFA).** *J Am Geriatr Soc* 2002, **50**:1962.
  21. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, Janecek E, Domecq C, Greenblatt DJ: **A method for estimating the probability of adverse drug reactions.** *Clin Pharmacol Ther* 1981, **30**:239-45.
  22. Hallas J, Harvald B, Gram LF, Grodum E, Brøsen K, Haghfelt T, Damsbo N: **Drug related hospital admissions: the role of definitions and intensity of data collection and the possibility of prevention.** *J Intern Med* 1990, **228**:83-90.
  23. Rask KJ, Wells KJ, Teitel GS, Hawley JN, Richards C, Gazmararian JA: **Can an algorithm for inappropriate prescribing predict adverse drug events?** *Am J Manag Care* 2005, **11**:145-51.
  24. Page RL, Ruskin JM: **The risk of adverse drug events and hospital-related morbidity and mortality among older adults with potentially inappropriate medication use.** *Am J Geriatr Pharmacother* 2006, **4**:297-305.
  25. Laroche ML, Charnes JP, Nouaille Y, Picard B, Merle L: **Is inappropriate medication use a major cause of adverse drug reactions in the elderly?** *Br J Clin Pharmacol* 2007, **63**:177-86.
  26. Budnitz DS, Shehab N, Kegler SR, Richards CL: **Medication use leading to emergency department visits for adverse drug events in older adults.** *Ann Intern Med* 2007, **147**:755-65.
  27. Gallagher P, O'Mahony D: **STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions) application to acutely ill elderly patients and comparison with Beers' criteria.** *Age Ageing* 2008, **37**:673-9.
  28. Schmader KE, Hanlon JT, Pieper CF, Sloane R, Ruby CM, Twersky J, Francis SD, Branch LG, Lindblad CI, Artz M, Weinberger M, Feussner JR, Cohen HJ: **Effects of geriatric evaluation and management on adverse drug reactions and suboptimal prescribing in the frail elderly.** *Am J Med* 2004, **116**:394-401.
  29. Hanlon JT, Weinberger M, Samsa GP, Schmader KE, Uttech KM, Lewis IK, Cowper PA, Landsman PB, Cohen HJ, Feussner JR: **A randomised, controlled trial of a clinical pharmacist intervention to improve inappropriate prescribing in elderly outpatients with polypharmacy.** *Am J Med* 1996, **100**:428-37.
  30. Pimlott NJ, Hux JE, Wilson LM, Kahan M, Li C, Rosser WW: **Educating physicians to reduce benzodiazepine use by elderly patients: a randomised controlled trial.** *CMAJ* 2003, **168**:835-39.
  31. Tamblin R, Huang A, Perreault R, Jacques A, Roy D, Hanley J, McLeod P, Laprise R: **The medical office of the 21<sup>st</sup> century (MOXXI): effectiveness of computerized decision-making support in reducing inappropriate prescribing in primary care.** *CMAJ* 2003, **169**:549-56.

### Pre-publication history

The pre-publication history for this paper can be accessed here:

<http://www.biomedcentral.com/1471-2318/9/5/prepub>

Publish with **BioMed Central** and every scientist can read your work free of charge

"BioMed Central will be the most significant development for disseminating the results of biomedical research in our lifetime."

Sir Paul Nurse, Cancer Research UK

Your research papers will be:

- available free of charge to the entire biomedical community
- peer reviewed and published immediately upon acceptance
- cited in PubMed and archived on PubMed Central
- yours — you keep the copyright

Submit your manuscript here:

[http://www.biomedcentral.com/info/publishing\\_adv.asp](http://www.biomedcentral.com/info/publishing_adv.asp)

