Letter to the Editors

Assessing the harms of polypharmacy requires careful interpretation and consistent definitions

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The article by Payne and colleagues [1] concludes 'Assumptions that polypharmacy is always unsafe or harmful, ... need to be reconsidered in the clinical context of the conditions for which those drugs are being prescribed'. Given the large body of evidence that polypharmacy is associated with many harms, especially in older populations [2], the conclusion can be misinterpreted when translating to clinical practice, and the contribution of polypharmacy to hospitalization, and other clinical outcomes, should not be dismissed. This study demonstrates that use of ≥10 medications (or 'hyperpolypharmacy' [3]) was consistently associated with an increased risk of hospitalization across patient groups with any number of comorbidities. For those with multimorbidity, the relative effects of medications on hospitalization may be diminished by the effects of the diseases themselves [4]. This study adds to the evidence that in those with multimorbidity, following clinical guidelines for all of a patient's comorbidities has undesirable effects [5].

Moreover, although we agree with the authors that the term 'polypharmacy' is not well defined in the current literature, we question the methodology used by authors to define polypharmacy exposure. In their study of people aged ≥20 years (median age 49 years), Payne and colleagues defined polypharmacy as the prescription count 'none, 1–3, 4–6, 7–9 and 10 or more'. While, polypharmacy can refer to the prescribing of many drugs (appropriately) or too many drugs (inappropriately) [6], most polypharmacy definitions use cut-offs for defining the impact of medications use on adverse outcomes across different healthcare systems. For example, there is evidence that the use of \geq 5 medications as a definition of polypharmacy is associated with poor outcomes, such as frailty, disability, mortality and falls, in older adults [7–9]. These are clinically relevant outcomes and are associated with higher rates of hospitalization among older people. In addition, there are

limited studies which demonstrate conflicting evidence when investigating associations of polypharmacy among adults <60 years [10]. This highlights the need to establish clinically relevant cut-offs for polypharmacy in various age groups. For the comparison of polypharmacy between different studies, settings and countries, we propose that future studies define polypharmacy more consistently, specific to the population studied. Clinically important cutoffs for polypharmacy, whether it is use of ≥ 5 or ≥ 10 medications, must be measured and interpreted according to the clinical context, age, morbidity and other population characteristics. If the data presented by Payne and colleagues was further analyzed to determine clinically relevant polypharmacy cut-offs in the population studied, this would enable comparison with a substantial evidence base on polypharmacy which has uniformly shown that polypharmacy is harmful, particularly in older and more vulnerable patients, and help determine clearer polypharmacy trends in younger populations.

Competing Interests

All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare no support from any organization for the submitted work, no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years and no other relationships or activities that could appear to have influenced the submitted work.

REFERENCES

1 Payne RA, Abel GA, Avery AJ, Mercer SW, Roland MO. Is polypharmacy always hazardous? A retrospective cohort

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analysis using linked electronic health records from primary and secondary care. Br J Clin Pharmacol 2014; 77: 1073–82.

- 2 Hilmer SN, Gnjidic D. The effects of polypharmacy in older adults. Clin Pharmacol Ther 2009; 85: 86–8.
- **3** Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Cumming RG, Handelsman DJ, McLachlan AJ, Abernethy DR, Banks E, Le Couteur DG. High-risk prescribing and incidence of frailty among older community-dwelling men. Clin Pharmacol Ther 2012; 91: 521–8.
- **4** Payne RA, Abel GA, Guthrie B, Mercer SW. The effect of physical multimorbidity, mental health conditions and socioeconomic deprivation on unplanned admissions to hospital: a retrospective cohort study. CMAJ 2013; 185: E221–8.
- **5** Boyd CM, Darer J, Boult C, Fried LP, Boult L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. JAMA 2005; 294: 716–24.
- **6** Patterson SM, Hughes C, Kerse N, Cardwell CR, Bradley MC. Interventions to improve the appropriate use of polypharmacy for older people. Cochrane Database Syst Rev 2012; (5): CD008165.
- **7** Nobili A, Licata G, Salerno F, Pasina L, Tettamanti M, Franchi C, Vittorio L, Marengoni A, Corrao S, Iorio A, Marcucci M, Mannucci P. Polypharmacy, length of hospital stay, and in-hospital mortality among elderly patients in internal medicine wards. The REPOSI study. Eur J Clin Pharmacol 2011; 67: 507–19.
- 8 Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Waite L, Seibel MJ, McLachlan AJ, Cumming RG, Handelsman DJ, Le Couteur DG. Polypharmacy cutoff and outcomes: five or

more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. J Clin Epidemiol 2012; 65: 989–95.

- **9** Strehblow C, Smeikal M, Fasching P. Polypharmacy and excessive polypharmacy in octogenarians and older acutely hospitalized patients. Wien Klin Wochenschr 2014; 126: 195–200.
- 10 Calderon-Larranaga A, Gimeno-Feliu LA, Gonzalez-Rubio F, Poblador-Plou B, Lairla-San Jose M, Abad-Diez JM, Poncel-Falco A, Prados-Torres A. Polypharmacy patterns: unravelling systematic associations between prescribed medications. PLoS One 2013; 8: e84967.

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