Optimization of Medication by Pharmacists in Older People With Multimorbidity for Improved Outcomes—Mirage or Reality?

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Multimorbidity commonly leads to polypharmacy in old age, and polypharmacy in turn engenders inappropriate prescribing, which is a major risk factor for adverse drug events (ADEs). Medication-related morbidity is increasingly a public health problem in most countries where aging populations are now presenting the predominant challenge to health services provision and funding. Not surprisingly, interventions that are seen as potential moderators of medication-related morbidity have been the subject of a variety of studies over the last decade, including large-scale randomized clinical trials. Interventions that are shown to attenuate hard end points, such as unscheduled hospitalization, hospital length of stay, and overall health care use in the community, have the potential to be highly important for older people with multimorbidity by reducing avoidable morbidity. The same interventions, if effective, also represent a transferrable and internationally relevant means of reducing health care expenditures. The importance of such interventions is reflected in the 2017 World Health Organization Medication Without Harm initiative, with its target of reducing medication-related harm internationally by 50% by 2022.

The results of the Medication Reviews Bridging Healthcare (MedBridge) trial by Kempen et al are interesting and important for several reasons. The trial team went to considerable lengths to examine the effects of 2 well-constructed pharmacist interventions designed to optimize medication of older patients with multimorbidity in 4 Swedish hospitals in 1 region compared with usual pharmaceutical care. The first intervention was a comprehensive medication review (CMR), the second was CMR with detailed and structured postdischarge follow-up. The trial design was appropriately cluster-randomized and adequately powered to properly test the impact of the extended CMR among older adults admitted to the 4 hospitals. The primary end point, unplanned hospital visits (emergency department [ED] attendances and admissions) within 12 months of randomization, was highly relevant. Secondary end points were also important: medication-related admissions, primary care physician visits, time to first unscheduled hospital visit, all-cause mortality, and hospitalization care costs. The MedBridge trial was sufficiently large scale, randomizing 2644 older people with multimorbidity with associated polypharmacy to 1 of 3 trial arms. The drop-out rate was very small—only 7 patients. Results showed no significant difference among the 2 intervention groups and control group in terms of the composite primary outcome; counterintuitively, the CMR with postdischarge follow-up group showed a significant 29% increase in ED visits in isolation compared with the usual care group. None of the secondary outcomes showed significant difference among the 2 intervention groups and the control group. That is, neither of the pharmacist-delivered CMR interventions significantly reduced any of the primary or secondary outcomes.

The MedBridge trial results align with another US randomized clinical trial by Gurwitz et al examining a multifaceted pharmacist intervention focused on particularly high-risk medications (ie, anticoagulants, antidiabetic drugs and opioids) in older patients with multimorbidity (ie, aged >50 years, mean age, 68.9 years). The 2 end points in the study by Gurwitz et al were adverse drug-related incidents and clinically important medication errors, including actual ADEs and potential ADEs. The pharmacist intervention encompassed detailed assessment of the patients and their medications at home, education of the patients using evidence-based teaching resources, focused communication of actual and potential problems with patients' primary care teams, and telephone follow-up with the patients (and caregivers, when necessary). Once again, the carefully designed
pharmacist intervention failed to significantly attenuate either of the end points. However, the trial by Gurwitz et al\(^4\) was of substantially smaller scale than the MedBridge trial\(^3\) and involved only 1 single-group community-based practice in Massachusetts.

In contrast, the Odense Pharmacist Trial Investigating Medication Interventions at Sector Transfer (OPTIMIST) trial,\(^5\) published in 2018, found that an extended pharmacist-delivered medication review and optimization intervention conferred significant benefit compared with a limited version of the same intervention or standard (routine) pharmaceutical care. The primary end points in the OPTIMIST trial\(^5\) were readmission within 30 days and readmission within 180 days; the composite primary end point was readmission or ED attendance within 180 days. Like the trial by Gurwitz et al,\(^4\) OPTIMIST trial\(^5\) patients were spread across a broad age range, with a median age of 72 years, and were significantly younger than the patients in the MedBridge trial,\(^3\) who had a median age of 81 years. In the OPTIMIST trial,\(^5\) patients recruited in 4 different Danish hospitals were randomized to 1 of 3 trial arms: usual pharmaceutical care (control), basic intervention, or extended intervention. Both basic and extended interventions were designed around a core structured pharmacist-delivered medication review, the basic intervention being conducted once shortly after admission, after baseline medical assessment and medication adjustment. The pharmacist medication review examined whether any conditions were left untreated, treatment goals were reached, and prescribed pharmacotherapy was in line with national treatment guidelines. There was particular focus on drug classes most commonly implicated in drug-related acute admissions, ie, low-dose aspirin, diuretics, anticoagulants, and nonsteroidal anti-inflammatory drugs. The extended intervention had additional elements of medication reconciliation at discharge, a structured motivational interview with the patient including detailed discussion of the medication changes made during admission and maintained in the discharge prescription, a comprehensive report on all medication changes for the patient’s primary care physician plus telephone follow-up within 3 days of discharge with patients’ primary care physicians, community pharmacists, and (when relevant) the principal caregivers. While the finding of significant benefit from the extended intervention on the 2 primary end points and the composite end point is important, subgroup analysis is interesting in relation to its efficacy in older patients who were more frail and more similar to MedBridge trial\(^3\) participants. Patients aged 65 years and older receiving the extended intervention had a significant 20% lower risk of experiencing the primary composite end point than patients receiving usual pharmaceutical care, compared with patients younger than 65 years. Similarly, patients receiving more than 8 daily drugs on admission had a significant 27% reduction in experiencing the primary composite end point compared with patients receiving usual pharmaceutical care; patients using 8 or fewer daily drugs did not have a significant reduction in the primary composite end point. Finally, patients with more comorbidity (Charlson comorbidity index scores \(\geq 3\)) fared worse than other patients with less comorbidity (Charlson scores ranging 0-2), the latter experiencing a significant 31% reduction in the primary composite end point.

The bulk of medication adjustment for people with multimorbidity aged older than 80 years is done by people who are not specialists in geriatric medicine or clinical pharmacology. Therefore, it makes theoretical sense to seek to involve pharmacists appropriately trained in medication surveillance and optimization in this rapidly increasing patient population. A 2019 overview of systematic reviews,\(^6\) most of which were published since 2010, concluded that medication appropriateness was improved by applying interventions to tackle polypharmacy in older people with multimorbidity. Most of these medication optimizing interventions could be applied by pharmacists. However, a 2021 systematic review of the impact of practice-based pharmacists on medication optimization in older people with multimorbidity and polypharmacy\(^7\) found that most studies meeting inclusion criteria were of poor quality and difficult to assess for risk of bias; therefore, the systematic review was inconclusive. The recent MedBridge\(^3\) and OPTIMIST\(^5\) trials neither prove or disprove the potential benefit of pharmacist-driven medication review and optimization for older patients with multimorbidity. A head-to-head randomized clinical trial comparison of physician-delivered vs pharmacist-delivered structured medication review and optimization interventions...
could usefully answer the question of whether physicians and pharmacists get similar or different results from the same intervention. Only then will we understand more clearly the role of pharmacists in medication optimization of older people with multimorbidity exposed to polypharmacy.

**ARTICLE INFORMATION**


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