In this issue of *JAMA Network Open*, Ie and colleagues evaluated the effect of a multidisciplinary team-based medication optimization program in older adult inpatients receiving 5 or more medications. Between 2019 and 2022, 442 participants were recruited from 8 internal medicine wards in a single hospital in Japan. The participants were medically complex; they were selected based on an expected length of hospital stay of at least 1 week, and they had an average of 4 diagnoses at baseline and approximately one-quarter died within 1 year. The intervention had no effect on the primary outcome of a composite of death, unscheduled hospital, and rehospitalization over 12 months. However, the intervention reduced medication burden and potentially inappropriate medication use; participants in the intervention group were prescribed 0.89 fewer medications compared with the usual care group ($P < .001$), and a lower proportion were receiving 1 or more potentially inappropriate medications (26.2% vs 33.0%; $P = .03$). Importantly, these differences were sustained throughout the follow-up period of 1 year.

Polypharmacy, or the use of multiple medications, is a growing public health problem. The prevalence of polypharmacy rises with age, compounded by disease-specific guidelines which often do not consider the presence of multiple chronic conditions. Thus, medications can accumulate over time in aging adults, with little or no plan of when to reduce or stop a medication. Polypharmacy is problematic for a number of reasons. First, polypharmacy is associated with adverse outcomes, including poor physical and cognitive function, nursing home admission, and death. The precise effects of polypharmacy are hard to quantify, owing to a heterogeneous definition of polypharmacy, the complexity of the population at risk, and confounding by indication. Second, polypharmacy puts an individual at risk for potentially inappropriate medication use. Potentially inappropriate medications are medications with known adverse effects among older adults, and in whom the potential benefits need to be weighed carefully against the harms. Third, polypharmacy is costly; both the direct costs of the medications and indirect costs of adverse events can result in substantial costs to patients and society. Cost estimates vary widely, but a study in 2018 estimated that the health care costs resulting from nonoptimized medication therapy exceeds half of a trillion dollars in the United States. Finally, polypharmacy is often at odds with patient preference and quality of life. A systematic review found that medication-related burden influences patients’ health and well-being.

To address these concerns, several tools have been developed to support medication optimization and deprescribing including the Beers criteria and STOPP/START criteria. Both tools provide explicit criteria regarding which medications to consider deprescribing. Deprescribing is part of good prescribing practice and involves stopping medications that are no longer needed and in which the potential benefits no longer outweigh the harms. It is important to note that medication optimization and deprescribing are not one-and-done tools. These practices are part of ongoing care as a patient ages, and potential benefits and harms, as well as patient goals of care, shift over time. Because these practices are relatively nascent, the optimal approach remains unclear.

The innovation of the approach by Ie and colleagues was to use a combined structured and team-based approach to reduce unnecessary medications. As a structured approach, they used a clinical decision support system to generate a list of potentially inappropriate medications as well as prescribing omissions consistent with the STOPP/START criteria version 2. As a secondary approach, the care team reviewed the medications and engaged in an organized discussion about the
indication, benefits and harms, and goals. This process took an average of 16 minutes. The prescribing optimization proposals were then presented to patient and attending physician.

Although the impact on the primary outcome was null, the impact on medication use is impressive. There are several reasons why the investigation may have underestimated the effect of the medication optimization protocol. For ethical reasons, the control group also received medication reconciliation conducted by ward-based pharmacists. Both intervention and control groups benefited from a reduction in medication count over time and a reduction in potentially inappropriate medication use. Second, although this population had a high medication burden (median of 8 medications), only 42% were prescribed 1 or more potentially inappropriate medication. Thus, the benefit of a similar intervention may be stronger in a group with more inappropriate medication use. Third, the use of a single center may have led to a spillover effect of the intervention into the control group. Moreover, patients were randomized, not clinicians, thus it is unclear whether the awareness of a potentially inappropriate medication in one patient may have affected clinician prescribing decisions in a subsequent patient. Future trials of medication optimization interventions may wish to randomize at the practice level to address this potential limitation.

Despite the null effect on the primary outcome, this investigation remains an important contribution to the literature. An intervention that is effective in reducing medication burden and potentially inappropriate medications is a win for patients and their clinicians. And at a population level, even small effect sizes could lead to important reductions in adverse effects, cost savings, and improvements in patient quality of life. There is an urgent need for more trials of deprescribing and medication optimization. We have spent decades of science and billions of dollars to build evidence-based medicine and better understand when and in whom to initiate medications. Now it is imperative that we provide the complementary science to better understand when and in whom to stop medications.