Discussions about the most appropriate methods for testing the effectiveness and safety of pharmacological intervention for older patients crowded the literature of the past decade, but little action has followed from such a wide discussion. The number of patients aged 65 years and older included in randomized controlled trials raised. However, epidemiological studies have generally demonstrated that the phenotypic emergence of the negative consequences of aging occur much later in life, in the eighth and ninth decade. Interestingly, this is the section of the population that is experiencing a steep demographic expansion, is often affected by severe comorbidity and disability, is the most eager consumer of drugs, and also the most likely to suffer from the iatrogenic consequences of chronic treatment and polypharmacy (1). In the United States, nearly 90% of patients over 75 years of age receive one or more medications, and the probability of having multiple prescription increases geometrically with age, severity of illness, and poor physical and cognitive function (2).

There are many reasons why frail older persons that assume multiple drugs are prone to develop iatrogenesis, including drug–drug interactions, reduced physiological reserve, changes in pharmacokinetics, and poor compliance (3).

The management of comorbid conditions with multiple medications is indeed one of the greatest challenges in geriatrics. The Hippocratic oath “primum non nocere” is translated into the “unchallenged principle” in geriatric medicine: The number of medications should be kept as low as possible. However, when facing the “brown bag full of pills” brought by your patient, deciding which treatment can stay and which ones should go is challenging. Of course, only drugs with proven efficacy should stay, but this is also not an easy decision. Elderly patients with comorbidity, disability, and polypharmacy are systematically excluded from clinical trials, even those trials that test drugs mostly used in those same elderly patients with comorbidity, disability, and polypharmacy. Due to those exclusion criteria, the findings of these trials cannot be extended to our typical patients: Therefore, we are left with an “unchallenged principle” and impossible decisions (4,5).

We are certainly not the first to denounce this difficult situation. Eminent geriatricians have voiced that the current practice produces an evidence-biased rather and evidence-based medicine and have called for the conduction of appropriately designed trials involving real geriatric patients (6,7).
These studies will be troublesome and hampered by the extraordinary heterogeneity of patients not only for health and functional status but also for extrinsic factors—such as income, formal or informal support, and functional and emotional profile—that strongly affect health status, especially in late life (8). The extreme complexity and soaring cost of these trials risk to hamper the development of new intervention that fail, older persons desperately need. An alternative strategy is required.

A recent article appeared in The Lancet by Spinewine and colleagues (9) claims that information technology has the potential to improve and rationalize drugs prescription. According to the authors, prescribing “in the future could use three cross-linked databases: the patient’s drug history, a scientific drug information reference and guideline database, and clinical information that is patient specific. Integrated prescribing systems offer promise, but tailoring such systems to the unique concerns of the geriatric patient population is warranted” (9). Indeed, this may represent a valuable alternative to randomized controlled trials. The possibilities are extraordinary, one can think of observational studies of the risk associated with use of potassium-sparing diuretics in patients with heart failure (10) or at studies elucidating the comparative safety of conventional and atypical antipsychotics for the treatment of behavioral disturbances in dementia (11).

Patients included in these observational studies are real, and remarkably older, sicker, and less functional than those traditionally enrolled in randomized controlled trials. As such, they provide invaluable information otherwise not available. Geriatric patients residing in the community, in hospital, and in long-term care facilities could be easily enrolled and drug treatment continuously assessed through electronic monitoring for the daily dispensing of medications. A standard set of information collected systematically in all geriatric patients will complement information on drug treatment and allow a continuous flow of data on virtually infinite numbers of patients, highlighting their most clinically relevant medical conditions and drug-related outcomes, over reliable periods of follow-up. Although this information is extremely valuable by itself, it may also lead to identifying questions that can be addressed in randomized controlled trials focusing on comorbidity and polypharmacy. Imagine a patients with arterial hypertension, atrial fibrillation, heart failure, and cerebrovascular disease (12). According to different guidelines, this patient should routinely receive an angiotensin converting enzyme-inhibitor (or an angiotensin-blocking agent), a diuretic, warfarin, and a statin, and a study could analyze the risk/benefit of further adding a beta-blocker for heart failure and/or heart rate control.

Based on this consideration, we would like to call for establishing networks of real and representative geriatric patients, studied with common assessment instruments and codified information on medication use. This appears the only feasible strategy to accrue the relevant information that can help in difficult decision about optimizing drug treatment in frail older patients while minimizing the risk of iatrogenesis. This new approach to pharmacoepidemiological research requires innovative methodologies and interdisciplinary integration of multiple experts, including geriatricians, pharmacologists, pharmacists, as well as epidemiologists, statisticians, and econometricians.

References