Dear Sir,

We have read with interest the systematic review article of Diederichs and colleagues (1), referring to the existing multimorbidity indexes. We fully agree with the authors in their opinions that clear and comprehensive criteria for the selection of chronic conditions, which qualify for multimorbidity, are still lacking. Accordingly, there is no agreement on the number and type of diseases to be included in multimorbidity indices, so these lack homogeneity, as well as external reproducibility in the case of prognostic multimorbidity tools. For this reason, most clinicians and investigators, usually, continue to use the Charlson–Deyo index as the gold-standard tool when referring to prognosis in patients with multiple chronic diseases (PMCD) (2,3). Nevertheless, the Charlson–Deyo index has been around for over 20 years; during this time, new diagnostic–therapeutic options have drastically changed the course of many of the included conditions (2,4).

Recently, the new notion of polypathological patient (PP) has been introduced in the management of these populations (5,6). This definition arose from the needs of clinicians to integrally approach the medical problems of patients with multiple diseases. In these patients, it is difficult to establish the protagonism of any of the comorbidities because of their similar complexity, their similar potential to become unstable, and their mutual relationships. A PMCD is considered a PP when suffering from chronic diseases from two or more of eight predefined categories; these categories were established by a panel of experts using criteria of end effect on function of key organs (independently of the primary disease), frequent chronic conditions with high mortality and/or potential of becoming unstable, or frequent comorbidities when mental and/or functional impairment thresholds were definitively reached (4–7). Therefore, the PP notion is globally centered on the patient and not on any “protagonist” disease nor on any professional health care worker who attends a PMCD. An increasing number of studies are determining that this emergent population is reasonably homogeneous, highly complex, clinically vulnerable, functionally impaired, dependent on caregivers, and socially fragile (7).

Additionally, the Polypathological Patient and Advanced Age Study Group, of the Spanish Society of Internal Medicine, has recently developed and validated a 1-year mortality predictive index on PP, by means of a multicenter prospective cohort-study recruiting 1,632 PP after hospital discharge, outpatient clinics, or home hospitalization, from 33 hospitals (8). The PROFUND index includes nine easy-to-achieve variables: one demographical (age ≥ 85 years, 3 points), four clinical (presence of active neoplasia, 6 points; dementia, 3 points; disabling dyspnea by means of III–IV functional class on New York Heart Association and/or Medical Research Council, 3 points; delirium during last hospital admission, 3 points), one laboratory (hemoglobinemia < 10 g/dL, 3 points), one functional (Barthel index < 60 points, 4 points), one sociofamilial (caregiver other than spouse or no caregiver; 2 points), and one care (number of hospital admissions in last 12 months ≥4, 3 points) variable. Mortality in the derivation/validation cohorts is detailed in Tables 1 and 2.

Calibration was good in derivation/validation cohorts, and discrimination power by area under the curve was 0.77/0.7, respectively. When comparing the PROFUND index with the Charlson–Deyo index, this last showed a good calibration but a lower discrimination power (area under the curve, 0.59).

We think, that this new notion of PP is in the way of solving this heterogeneity, because it comprises the 11 diagnosis cited by the authors, points toward advanced-age populations (mean age of PP in different studies ranged 74–78 years), and reflects an homogeneous, emergent (in-hospital prevalence of PP ranges 24%–40%), and high-risk population...
global 1-year mortality in the PROFUND study was 37%). Besides, interobserver reliability in detection of PP has also been tested, with good results in terms of kappa index (6).

Like the authors state (1), prognosis is specially important in high-risk populations in order to reassess care goals, redefine medically necessary therapies, focus on symptom control, assess other physical, psychosocial, and spiritual problems, and consider earlier palliative care. With the knowledge of a reasonable precise prognosis, clinicians can feel more comfortable raising important issues like care goals, treatment preferences, advanced planning, and clinical therapeutic options with patients and their families. For these reasons, we developed and validated the PROFUND index, specifically focused on PP, using nine simple measures of different clinical areas that can be easily determined with a routine patient overall evaluation. It effectively stratifies PP into groups at varying risks of death, and it can be used in a variety of different policy making, epidemiological, clinical, and research settings.

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**CONFLICT OF INTEREST**
The authors have no conflicts of interest to report.