

Onset and Progression of Multimorbidity over up to 19-year Follow-up: Sentinel Conditions, Accrual Patterns, and Timing in Older Europeans

Introduction

Non-communicable diseases are the leading causes of morbidity and mortality in middle- and high-income countries (World Health Organization, 2024). Multimorbidity, defined as the coexistence of multiple chronic or acute conditions in one individual, affects about one-third of adults globally and close to 40% in high-income settings (Van den Akker et al., 1996; Nguyen et al., 2019; Bezerra de Souza et al., 2021). Most multimorbidity research continues to emphasize prevalence, while incidence has been examined in relatively few studies. Yet incidence captures the dynamics and timing of disease accumulation, showing when people are most at risk of adding a new condition and when interventions could delay progression to multimorbidity (Kudesia et al., 2021; Shang et al., 2020).

Incidence estimates vary widely, from 1 to more than 300 new multimorbidity cases per 1,000, and cumulative incidence from 1% to 60% depending on follow-up and definition (Kudesia et al., 2021). These differences reflect methodological choices, but also the underlying distribution of age, deprivation, ethnicity and health behaviours in the populations studied. Despite this variation, the overall pattern is consistent: multimorbidity onset is highly age-dependent (Cezard et al., 2021). By contrast, sex differences are modest. Some studies report slightly higher incidence among women (Kudesia et al., 2021; St Sauver et al., 2015).

Beyond these demographic gradients, multimorbidity is also characterized by the way diseases progress and accumulate over time. The interval between successive conditions tends to shorten as more diseases appear, indicating acceleration in the process of accumulation (Shang et al., 2020). Certain conditions act as first - or sentinel - diagnoses that initiate the multimorbidity process. Hypertension, diabetes, and heart disease are frequent early diagnoses and are often followed by additional chronic conditions, especially other cardiometabolic disorders. Musculoskeletal conditions frequently appear in the early sequences, but in some cohorts cardiometabolic diseases tend to occur first and musculoskeletal conditions follow (Kudesia et al., 2021; Shang et al., 2020; Stannard et al., 2022).

In this study, we focus on the first onset of chronic diseases, identifying the first - or sentinel - diagnosed disease and health progressions thereafter. We map pathways of disease onset using the Survey of Health, Ageing and Retirement in Europe (SHARE), a cross-national longitudinal study of adults aged 50 years or older residing in Europe, followed for up to 19 years. We investigate which sentinel conditions most often initiate multimorbidity, how long it takes to move from the sentinel condition to multimorbidity, and how these onset pathways vary by sex and age.

Data and methods

Data comes from the Survey of Health, Ageing and Retirement in Europe (SHARE), a longitudinal study representative of adults aged 50 years or older living in Europe. SHARE began in 2004/05 and has since followed more than 140,000 participants through repeated, interviewer-administered, home-based surveys in the national language, tracing respondents who moved within the country. We used release 9.0.0 and restricted the analysis to participants from the 11 European countries present in wave 1 who were followed in subsequent waves up to wave 9. The study population was defined as individuals born in 1954 or earlier who did not have multimorbidity at baseline; that is, those with zero or one disease, yielding 15,573 adults. The sample included Austria (n=964), Germany (n=1,304), Sweden (n=1,902), the Netherlands (n=1,706), Spain (n=1,206), Italy (n=1,341), France (n=1,647), Denmark (n=968), Greece (n=1,813), Switzerland (n=622) and Belgium (n=2,100).

Chronic conditions were collected in the SHARE Physical Health module. At baseline, respondents were shown a list of doctor-diagnosed conditions and asked whether a doctor had ever told them they had any of them; at follow-up they were asked whether they currently had any of the listed conditions. Conditions included heart attack or other heart disease, hypertension, stroke, diabetes, peptic ulcer, chronic lung disease, arthritis, hip or femoral fracture, cancer, Parkinson's disease, Alzheimer's disease or dementia and cataract. We did not include asthma and osteoporosis, as these conditions were removed from the questionnaire after wave 4. Onset after baseline was dated to the midpoint between the last wave without the condition and the first wave with the condition. Dates of death came from end-of-life interviews.

Individuals were observed for up to 19 years. Those disease-free at baseline could remain disease-free, develop a first condition, or become multimorbid. Those with one condition at baseline could remain with one condition or become multimorbid. In both entry states, individuals could also die or be lost to follow-up. Our primary interest is the transition into a new morbid state, namely the first condition for those disease-free and multimorbidity for both groups. We assumed there were no remissions.

We estimated incidence separately for individuals disease-free at baseline and those with one baseline condition. For the former, we described progression to first condition and multimorbidity, including time from baseline to multimorbidity and from first to second condition. For the latter, we treated the baseline diagnosis as the sentinel condition and described progression to multimorbidity. Survival without multimorbidity, death and loss to follow-up were all tracked and reported. Cumulative incidence functions for multimorbidity were estimated by age and sex, with death treated as a competing risk. All estimates used calibrated cross-sectional weights supplied by SHARE and were conducted in R 4.2.2.

Preliminary results

Among adults aged 50 and older without multimorbidity at baseline, progression differed strongly by initial disease status. Over 19 years, about 59% of those who were disease-free at baseline developed multimorbidity, compared with about 81% of those who already had one chronic condition. This means that entering later adulthood disease-free was associated with a substantially lower probability of reaching multimorbidity during follow-up.

As expected, the timing of progression differed clearly between the two baseline groups. Among those who developed multimorbidity, the mean time from baseline to multimorbidity was about 9 years for individuals who were disease-free at baseline, compared with about 5 years for those who already had one chronic condition, a difference of more than 3 years. However, the conditions marking the beginning of disease accumulation were similar in both groups. Hypertension and arthritis were the dominant entry points and also the most common diagnoses at multimorbidity onset, suggesting that the main difference between groups was not the type of pathway observed, but the speed at which progression occurred.

Analyses of progression from sentinel conditions to multimorbidity were restricted to individuals who were disease-free at study entry and subsequently developed a first sentinel condition. This restriction allowed us to observe the pathway from first to second condition, including the timing of both events. Conditional on the sentinel condition, progression was concentrated in a limited number of empirically supported pathways rather than distributed evenly across all possible disease pairs. Hypertension and arthritis remained frequent second-condition destinations across several sentinel groups, but progression varied by sentinel condition in both probability and timing. Some pathways, particularly from cardiometabolic sentinels to common second diagnoses, occurred relatively soon after sentinel onset, whereas many disease-pair combinations were rare, weakly supported, or not estimable. Death before a second condition was also unevenly distributed, appearing more frequently after severe or later-life sentinel conditions, especially Alzheimer's disease.

This study can support more targeted monitoring and care planning by identifying the ages and sentinel conditions associated with higher progression to multimorbidity or death. By mapping common patterns of disease accumulation, the analysis shows where follow-up may need to be intensified. Rather than estimating causal effects of specific conditions, it provides a population-level map of where multimorbidity progression is concentrated, helping to guide hypotheses, risk stratification, and health-service planning.

References

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