# Effect of Mental Health on Multimorbidity Onset and Outcomes

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## Introduction

Multimorbidity, defined as the co-existence of multiple chronic conditions, is an increasingly pressing global public health challenge. Its prevalence is rising, with evidence indicating that younger cohorts are developing and accumulating chronic conditions at an accelerated rate compared to older generations (Bishop et al., 2022; Rhee et al., 2024; The Lancet, 2024). This coincides with an increase in life expectancy that is not necessarily accompanied by gains in healthy life expectancy (World Health Organization, , leading to significant implications for healthcare systems. Understanding the causes and risk factors leading to multimorbidity is therefore a public health priority.

Alongside this rise in multimorbidity and longevity, mental health diagnoses are also increasing globally (Wu et al., , with mounting evidence on their impact on mortality and quality of life (Co ok . These trends suggest that a substantial proportion of individuals will experience both physical multimorbidity and mental health conditions, underscoring the need to explore their interrelationship and mutual impact.

A growing body of research highlights the close relationship between mental and physical health, particularly in the context of multimorbidity. Individuals with mental health conditions frequently experience multiple chronic diseases, with mental illness acting as both a risk factor for physical morbidity and a modifier of health outcomes (Momen et al., 2022; Prina et al., 2019). Studies consistently show that individuals with mental health disorders have a higher mortality risk, largely attributed to co-existing physical conditions (De Hert et al., 2011; Feng et al., 2023; McIntyre et al., . For instance, comorbid physical illnesses contribute significantly to the personal and societal burden of bipolar disorder (McIntyre et al., . Furthermore, research has demonstrated that depression serves as a precipitating factor for cardiovascular disease, increasing risk through associated behaviours such as (Rugulies, 2002; Sandhi et al., 2021; Vancampfort et al., 2015). Conversely, in conditions such as cancer, the onset of mental health disorders often follows a physical diagnosis, suggesting a complex bidirectional relationship (Breitbart et al., 2000; Feng et al., .

Beyond its impact on disease onset, mental illness may also amplify the adverse outcomes of multimorbidity. Depression, for example, has been shown to mediate the negative effects of frailty on chronic disease accumulation among older adults (Feng et al., . Additionally, mental health conditions are linked to increased healthcare utilization among multimorbid

patients, often leading to greater disparities in care quality (Circelli et al., 2022; Zhu et al., 2020). Despite these associations, individuals with mental illness may receive suboptimal healthcare compared to those without psychiatric diagnoses (Thornicroft et al., 2009).

## Rationale:

Existing research clearly indicates a strong interplay between mental health conditions and chronic disease burden, with studies showing that mental health conditions can accelerate the onset and exacerbate the impact of multimorbidity (Momen et al., 2020; Scott et al., . However, there remains a critical gap: the effect of mental health diagnoses on the transitions from a healthy state to single physical morbidity, from single to multimorbidity and or complex multimorbidity. Additionally, while prior work suggests that co-occurring mental health conditions can worsen clinical outcomes and increase healthcare use, the specific mortality risk associated with mental health disorders in different physical morbidity and multimorbidity groups—and how this might vary by age and sex—has yet to be studied. Addressing these gaps is essential to guide the development of targeted interventions and care pathways that recognize mental health conditions as key contributors to multimorbidity onset and progression and its adverse outcomes. By clarifying how mental health diagnoses influence disease accumulation trajectories and mortality risk, this research will provide evidence to help clinicians and policymakers design more holistic, patient-centered strategies that improve both mental and physical health outcomes.

Specific Objectives:

- Does a mental health diagnosis effect the onset and/or timing of progression from health to morbidity, multimorbidity and complex multimorbidity?
- Does a mental health diagnosis effect the mortality risk among different morbidity groups?
- Is the effect of mental health diagnoses on morbidity progression different based on age and sex of the patient at diagnosis?

## Proposed methods:

### *Data:*

We use the HEALIN cohort, a population-based dataset that follows a random sample of 1,551,126 individuals (accounting for 22% of the total Catalan population) from 2005 up to 2021 (Solé-Auró et al., . This sample is representative in terms of age, sex, and region. Potential to include other data sources

### *Definitions:*

We use a list of conditions recommended in a Delphi consensus studies as to be always included in multimorbidity research (Ho et al., . Individuals free of any index conditions will be classified as “Healthy”. A diagnosis with one condition the list classifies a patient as having “Morbidity.” Having “Multimorbidity” will be defined as having two or more conditions affecting only one organ system, while “Complex Multimorbidity” will require two or more conditions affecting multiple organ systems.
Mental health conditions will be identified using ICD-10/ICD-11 (F00–F99) codes for Mental and Behavioral Disorders. All but two mental health conditions recommended to be included in the above mentioned Delphi study on multimorbidity (Ho et al., will be included; dementia will be excluded and instead categorized here as neurodegenerative conditions.

Individuals will be included if they were healthy for at least six months of the start of the observation period. They will be considered to have a mental health condition if they developed one at least six months before receiving a diagnosis of any of the conditions listed in the multimorbidity index.

### *Study design:*

We constructed a retrospective cohort study using electronic health records from the HEALIN cohort. Eligible individuals were those with at least one healthcare contact recorded in the visites dataset in 2005 or later, ensuring they were actively observed during the period when data quality is reliable. The date of cohort entry (index date) was defined as the first year of observed contact (January 1 of that year). Diagnoses were mapped to condition groups, with mental health conditions flagged separately. Individuals with a record of the outcome condition B before their index date were excluded to focus on incident cases. Each participant was followed from index date until the earliest of: first diagnosis of condition B (the primary event), death (treated as a competing event), or administrative censoring at the end of follow-up (December 31, 2022). Time-to-event was calculated in years from index to exit. Mental health exposure was defined as having a mental health diagnosis recorded at least six months before the outcome event. Baseline sociodemographic characteristics and comorbidity status (excluding mental health) were summarised by mental health exposure status, and outcomes were described using a competing risks framework distinguishing incident B, death before B, and censoring.

Statistical methods (preliminary):

1- Descriptive analysis:
    a. Calculate incidence of morbidity, multimorbidity and complex multimorbidity in the general population and by age and sex, stratified by whether the person has a mental health condition
2- Survival analysis
    a. Calculate mortality rate in the general population and by age and sex among the three morbidity groups, stratified by presence or absence of a mental health diagnosis at baseline
    b. Cox-proportional hazards ratio to estimate the effect of mental health diagnosis on mortality, adjusting for age and sex and mental health condition category

## Expected results

We expect to observe that individuals with a diagnosed mental health condition have a higher and earlier risk of progressing from a healthy state to single morbidity, multimorbidity, and complex multimorbidity compared to those without a mental health diagnosis. These trajectories are likely to differ by mental health diagnosis category and by age at onset, with older adults potentially experiencing more rapid disease accumulation. We also anticipate that mortality rates will be significantly elevated among multimorbid individuals with co-occurring mental health conditions, consistent with previous evidence showing excess mortality among those with mental illness, mostly attributable to physical comorbidities.

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