Clinical Epidemiology

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

# 10-Year Multimorbidity Trajectories in Older People Have Limited Benefit in Predicting Short-Term Health Outcomes in Comparison to Standard Multimorbidity Thresholds: A Population-Based Study

Marc Simard[1–4], Elham Rahme[5], Marjolaine Dubé[1], Véronique Boiteau[1], Denis Talbot[2,3], Miceline Mésidor[2,3], Yohann Moanahere Chiu[1,4,6], Caroline Sirois[1,3,4,6]

[1]Institut national de santé publique du Québec, Québec, QC, Canada; [2]Department of Social and Preventive Medicine, Faculty of Medicine, Université Laval, Québec, QC, Canada; [3]Centre de recherche du CHU de Québec, Québec, QC, Canada; [4]VITAM-Centre de recherche en santé durable, Québec, QC, Canada; [5]Department of Medicine, Division of Clinical Epidemiology, McGill University, and Centre for Outcomes Research and Evaluation, Research Institute of the McGill University Health Centre, Montréal, QC, Canada; [6]Faculty of de Pharmacy, Université Laval, Québec, QC, Canada

Correspondence: Marc Simard, Institut national de santé publique du Québec, 945, Wolfe, 5e étage, Québec, QC, G1V 5B3, Canada, Tel +1 418 650 5115 #5522, Fax +1 418 643 5099, Email marc.simard@inspq.qc.ca

**Purpose:** To identify multimorbidity trajectories among older adults and to compare their health outcome predictive performance with that of cross-sectional multimorbidity thresholds (eg, ≥2 chronic conditions (CCs)).

**Patients and Methods:** We performed a population-based longitudinal study with a random sample of 99,411 individuals aged >65 years on April 1, 2019. Using health administrative data, we calculated for each individual the yearly CCs number from 2010 to 2019 and constructed the trajectories with latent class growth analysis. We used logistic regression to determine the increase in predictive capacity (*c-statistic*) of multimorbidity trajectories and traditional cross-sectional indicators (≥2, ≥3, or ≥4 CCs, assessed in April 2019) over that of a baseline model (including age, sex, and deprivation). We predicted 1-year mortality, hospitalization, polypharmacy, and frequent general practitioner, specialist, or emergency department visits.

**Results:** We identified eight multimorbidity trajectories, each representing between 3% and 25% of the population. These trajectories exhibited trends of increasing, stable, or decreasing number of CCs. When predicting mortality, the 95% CI for the increase in the *c-statistic* for multimorbidity trajectories [0.032–0.044] overlapped with that of the ≥3 indicator [0.037–0.050]. Similar results were observed when predicting other health outcomes and with other cross-sectional indicators.

**Conclusion:** Multimorbidity trajectories displayed comparable health outcome predictive capacity to those of traditional cross-sectional multimorbidity indicators. Given its ease of calculation, continued use of traditional multimorbidity thresholds remains relevant for population-based multimorbidity surveillance and clinical practice.

**Keywords:** multimorbidity, trajectories, prevalence, health outcome prediction, population-based

## Introduction

In the last decades, the rise in life expectancy and the increasing prevalence of many chronic conditions have contributed to a heightened number of individuals coping with multiple chronic conditions, constituting a growing global public health challenge.[1,2] Multimorbidity, the coexistence of two or more chronic conditions within the same individual, exerts adverse effects both on individual health and the healthcare system.[3] It is indeed associated with higher risks of psychological distress, poor quality of life, polypharmacy, mortality, and heightened healthcare utilization, including hospitalization, outpatient visits and emergency department (ED) visits.[3]

Received: 24 January 2024
Accepted: 8 May 2024
Published: 22 May 2024

Public health authorities and health agencies utilize multimorbidity indicators, based on the prevalence of multiple chronic conditions, to monitor the burden of multimorbidity and allocate resources for the management and prevention of chronic diseases.[4] These indicators rely on cross-sectional count of chronic conditions, with most of them assessing the prevalence of individuals with at least two (≥2) or at least three (≥3) chronic conditions.[5] Indicators that capture the cooccurrence of multiple chronic conditions are also useful for clinical practice where treatment guidelines account for multimorbidity.[6]

Longitudinal approaches to assess multimorbidity, such as multimorbidity trajectories, are an emerging research area.[7] A multimorbidity trajectory identifies a subgroup of the population characterized by the number and the speed of onset of chronic conditions. Individuals in multimorbidity trajectories with a rapid onset or a high number of chronic conditions face an increasing risk of disability, mortality, and healthcare utilization.[8–10] While some studies have evaluated the effectiveness of multimorbidity trajectories in predicting health outcomes, only a few have directly compared their performance with cross-sectional indicators.[10–13] Chang et al conducted the sole population-based study, in which multimorbidity trajectories predicted healthcare costs as effectively as diseases count over a three-year period.[10] Other studies conducted in subpopulations (outpatients or individuals with ≥3 chronic conditions) in the US or the UK yielded conflicting results when predicting mortality, cognitive decline and healthcare utilization.[11–13] These studies were either constrained by a short follow-up duration or focused on a restricted number of health outcomes. A longer follow-up period is required due to the slow progression of many chronic diseases, which increases the probability of detecting the diagnosis of these diseases. For instance, cardiovascular events were observed between 6 and 10 years following the diagnosis of arterial hypertension in approximately 5% of individuals with higher blood pressure.[14] Additionally, it is important to consider a wide range of health outcomes, as the impact of multimorbidity varies across different outcomes.[3] Previous studies do not allow for determining whether multimorbidity trajectories predict health outcomes more effectively than traditional indicators at the population-level. However, this information is essential to determine whether clinicians should investigate the speed of onset of chronic diseases in their patients and to justify the development of new multimorbidity indicators for surveillance.

## Objectives

Our study aimed to 1) identify 10-year multimorbidity trajectories within the general population aged over 65 years, 2) evaluate the capacity of these trajectories to predict health outcomes, and 3) compare the predictive performance of multimorbidity trajectories with that of traditional cross-sectional multimorbidity indicators.

# Methods

## Data Sources and Population

Our population-based cohort study included 100,000 community-dwelling individuals aged over 65 years on March 31, 2019. We used the SURVEYSELECT procedure in SAS to randomly select these individuals without replacement from a population of over 1.5 million community-dwelling eligible individuals ages over 65 years on March 31, 2019, included in the Québec Integrated Chronic Disease Surveillance System (QICDSS) at that time point. The QICDSS links five health administrative databases, namely demographic, death registry, physician claims records, pharmaceutical claim records, and hospital discharge abstract records, utilizing a unique patient identifier.[15] These databases are obtained from the Provincial Health Insurance Board (Régie de l'assurance maladie du Québec) and the Québec Ministry of Health. Notably, the QICDSS comprises medical records for >99% of the population and pharmaceutical records for 90% of the population ages over 65 years.[15] We selected 100,000 individuals from the 1.5 million eligible population to ensure a sufficient statistical power for our statistical analyses while ensuring acceptable computational time for execution, given the time-consuming nature of modeling methods used to identify trajectories (see "Statistical analysis" section). Demographic data include neighbourhood-level social and material deprivation quintiles, age, and sex. Social deprivation considers the proportion of single-parent families and individuals living alone in the neighbourhood, as captured in the 2016 census, while material deprivation accounts for employment status, educational attainment, and income level.[16] Physician claim records include diagnoses coded using the International Classification of Disease, 9th Revision, Québec

adaptation (ICD-9-QC) and the ICD 10th Revision Canadian Coding Standard (ICD-10-CA). Hospital discharge records include the primary diagnosis and up to 29 secondary diagnoses, coded using ICD-9-QC system until March 31, 2006, and ICD-10-CA system thereafter. Given that some individuals may have resided outside the province during this decade (less than 1% of the population), we excluded individuals who lived in the province less than five years during this 10-year period.

## Longitudinal Count of Chronic Conditions Over a 10-Year Period

We identified trajectories by analysing the yearly count of chronic conditions for each individual over a 10-year period, spanning from March 31, 2010, to March 31, 2019. We estimated the yearly count of prevalent and incident chronic conditions at the end of each fiscal year (March 31). The count was based on a predefined list of 21 chronic conditions utilizing a previously validated multimorbidity measure. Briefly, this multimorbidity measure includes a core set of highly prevalent chronic conditions having the highest disability adjusted life-years (DALYs) or years of life lost (YLLs) in Canada. The case definition for each chronic condition has been previously validated (Table A1), and a 10-year lookback period in inpatient and outpatient data was used to identify chronic conditions. This 10-year lookback period strikes an optimal balance between achieving accurate prevalence estimates and enhancing the predictive capacity for health outcomes.[17]

## Cross-Sectional Multimorbidity Indicators

We estimated cross-sectional multimorbidity prevalence using the count of prevalent and incident chronic conditions at the conclusion of the 10-year period, specifically on March 31, 2019. We used this count of chronic conditions to derive three multimorbidity indicators (≥2, ≥3, and ≥4 chronic conditions). We also included the total count of chronic conditions (0, 1, 2, 3, …, ≥8) as an additional indicator.

## Outcomes

We predicted six health outcomes that have been associated with multimorbidity and were quantifiable within the QICDSS during the 1-year follow-up period (from April 1, 2019, to March 31, 2020): all-cause mortality, polypharmacy, hospitalization, frequent ED admissions, and frequent general practitioner (GP) and specialist physician (SP) visits. We defined polypharmacy as ≥10 distinct denomination codes (active ingredients) for acute or chronic condition claimed during the 1-year period. We used a threshold of ≥10 medications that identify the first quartile of higher users among the population. We defined frequent ED visits based on a widely accepted threshold of ≥3 visits in the 1-year period.[18] A single ED visit was defined as 1 or more ED-related claims up to 2 consecutive days.[19] Frequent visits to any GP (≥7 visits) or any SP (≥10 visits) in the 1-year period were defined using the 95$^{th}$ percentile in the annual number of visits in the Québec adult population.[18,20]

## Statistical Analysis

We identified multimorbidity trajectories using latent class growth analysis (LCGA) models with Poisson distribution. Briefly, LCGA is a semi-parametric approach that employs finite mixture modeling to identify clusters of individuals exhibiting similar trajectories over time.[21] Model parameters are estimated using maximum likelihood. Yearly count of chronic conditions during a 10-year period was used to model trajectories (Figure 1). LCGA model identified each trajectory by grouping individuals with similar speed of onset and/or count of chronic conditions during the 10-year period. We let the number of trajectories vary from 1 to 10 across models, then determined the appropriate number of trajectories by combining clinical relevance, parsimony rules, and statistical criteria, as recommended by several authors.[21,22] Statistical criteria took into account the model adequacy (favoring models with a low Bayesian information criteria [BIC] and a p-value <5% from the Lo-Mendell-Rubin test [LMRT] indicating that a model with K trajectories is better than one with K-1 trajectories) or the posterior classification assignment probability (where a relative entropy >0.8 implies less uncertainty; an average posterior probability [APP] >70% signifies adequate classification; and odds of correct classification [OCC] >5 suggest high accuracy in trajectory assignment). We used descriptive statistics to present the characteristics of individuals within each trajectory.

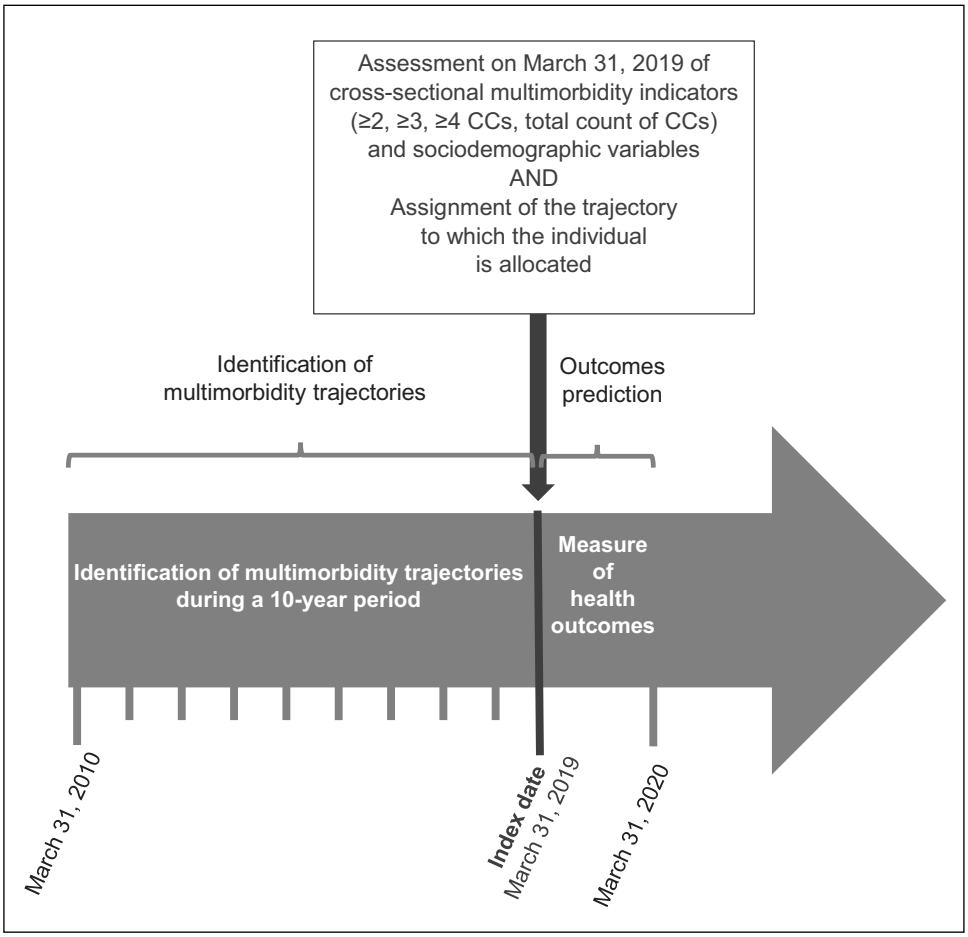


**Figure 1** Illustration of the study periods used to identify multimorbidity trajectories and to perform outcome prediction.
**Abbreviations**: ≥2 CCs, ≥3 CCs, ≥4 CCs: Multimorbidity indicators of the presence of at least 2, 3 or 4 chronic diseases; CCs: Chronic conditions.

For each health outcome, we assessed the predictive performance of multimorbidity trajectories over a 1-year follow-up using logistic regression models (Figure 1). To evaluate this performance, we calculated Wald 95% confidence interval of the difference in discrimination capacity (*c-statistic*) between the baseline model (comprising sociodemographic covariates: age group [66–70, …, ≥86], sex, material and social deprivations) and a second model including both baseline covariates and multimorbidity trajectories. Age was categorized into five-year intervals to align with the level of stratification used in our multimorbidity surveillance InfoBase. In order to verify if trajectories are better predictors than traditional cross-sectional multimorbidity indicators, we also calculated *c-statistic* differences between the baseline model and models including baseline covariates and, in turn, a cross-sectional multimorbidity indicator (≥2, ≥3, and ≥4 chronic conditions) or the total count of chronic conditions (0, 1, 2, 3, …, ≥8). We also estimated the overall performance of each model using the scaled Brier score which value ranges from 0 to 1; higher value indicates better performance. In the models for polypharmacy and healthcare utilization outcomes, we excluded deceased patients, as end-of-life healthcare utilization is not representative of the general population.[23]

## Sensitivity and Supplementary Analyses

As part of our sensitivity analysis, we estimated the predictive performance of multimorbidity trajectories using a smaller number of trajectories. Additionally, we repeated all the analyses using an alternative multimorbidity measure that used a wider list of 31 medical conditions combining conditions from both Elixhauser and Charlson indexes.[24,25] We also estimated the predictive performance of the multimorbidity measures when predicting polypharmacy using a different

threshold (≥5 medications). In supplementary analysis, we estimated the association between each multimorbidity trajectories and each health outcome.

Analyses were performed using SAS 9.4 (SAS Institute, Cary, NC) and Mplus (version 8.7).[26] We used the RECORD[27] and GRoLTS[28] checklists for reporting results (Tables A2 and A3).

## Results

Our study included 99,411 individuals, randomly selected from a population of 1.5 million individuals older than 65 years living in the province of Québec, Canada (Figure A1). On April 1, 2019, the mean age was 75 years, with 54% being female (Table 1). The prevalence of multimorbidity was 60.0%, 38.7%, and 23.1% for cross-sectional multimorbidity indicators of ≥2, ≥3, and ≥4 chronic conditions, respectively. During the one-year follow-up period, mortality occurred in 3% of the population. Other health outcomes were observed in proportions ranging from 5% to 36% (Table 1). We identified a total of 8 trajectories (Figure 2). As anticipated, the 8-trajectory model included trajectories with increasing, decreasing and stable longitudinal patterns (Figure 2). Nearly a third of the population evolved in trajectories having an increasing count of chronic conditions. Less than 3% evolved in decreasing shape trajectory and the majority (66%) in stable shape trajectories (Table 1). The mean age and the prevalence of health outcomes increased within trajectories where the count of chronic conditions is higher at the end of the 10-year period. Notably, an LMRT p-value higher than 5% and entropy under 80% when the number of trajectories reached 10 or more indicated that further improvements in model fit were unlikely after 9 trajectories (Table 2). Furthermore, considering that the BIC values showed a "stabilization" around 8 trajectories, we adopted an 8 trajectories model in accordance with the parsimony principle (Figure A2).

**Table 1** Characteristic of Individuals in Each Multimorbidity Trajectory, and in the Total Study Population, Québec, Canada, n = 99,411

| | Trajectories | | | | | | | | Study population |
|---|---|---|---|---|---|---|---|---|---|
| | Stable 0 CC | Decrease 0 CC | Increase 1 CC | Stable 1 CC | Stable 2 CCs | Fast increase 4 CCs | Increase 4 CCs | Increase 7 CCs | |
| Number of individuals | 10,510 | 3205 | 6907 | 26,818 | 28,426 | 3269 | 16,398 | 3878 | 99,411 |
| Number of CC at end of 10-year period, mean (SD) | 0.1 (0.3) | 0.1 (0.2) | 1.5 (0.9) | 1.3 (0.8) | 2.5 (1.0) | 4.1 (1.3) | 4.5 (1.4) | 6.9 (1.8) | 2.3 (1.9) |
| Increase in number of CC over the 10-year period[a], mean (SD) | 0.1 (0.3) | −0.9 (0.6) | 1.4 (0.9) | 0.3 (1.1) | 0.5 (1.5) | 3.7 (1.2) | 1.3 (2.1) | 1.8 (2.6) | 0.7 (1.7) |
| Age at end of 10-year period, mean (SD) | 71.2 (4.9) | 71.9 (5.5) | 72.3 (5.7) | 73.5 (6.3) | 75.9 (7.1) | 75.2 (7.1) | 78.1 (7.6) | 79.7 (7.7) | 74.8 (7.0) |
| Female (%) | 47.0 | 53.0 | 48.4 | 52.9 | 57.1 | 46.7 | 58.0 | 60.7 | 54.1 |
| Material deprivation quintile at end of 10-year period[b] (%) | | | | | | | | | |
| Q1: less deprived | 21.5 | 22.3 | 20.1 | 20.5 | 18.9 | 18.2 | 17.2 | 14.5 | 19.4 |
| Q2 | 19.5 | 18.0 | 19.1 | 19.6 | 18.2 | 19.3 | 16.9 | 15.9 | 18.5 |
| Q3 | 19.2 | 20.1 | 19.8 | 20.2 | 19.9 | 18.8 | 20.6 | 20.9 | 20.0 |
| Q4 | 20.1 | 19.5 | 20.0 | 20.1 | 21.3 | 20.7 | 21.5 | 22.7 | 20.7 |
| Q5: most deprived | 19.7 | 20.1 | 21.0 | 19.6 | 21.7 | 23.1 | 23.9 | 26.0 | 21.3 |
| Mortality (%) | 0.8 | 0.7 | 1.9 | 1.4 | 2.6 | 4.9 | 5.4 | 11.1 | 2.9 |
| Hospitalisation (≥1/year)[c] (%) | 4.4 | 5.3 | 8.2 | 7.6 | 11.7 | 17.0 | 19.6 | 32.5 | 11.6 |
| Emergency Unit (≥3/year)[c] (%) | 1.2 | 1.5 | 2.5 | 2.6 | 4.3 | 6.4 | 8.2 | 19.1 | 4.5 |
| Specialiste (≥10/year)[c] (%) | 4.1 | 4.5 | 8.6 | 8.2 | 13.0 | 18.9 | 21.9 | 32.7 | 12.5 |
| General practitioner (≥7/year)[c] (%) | 1.7 | 3.6 | 4.5 | 5.2 | 9.8 | 11.1 | 16.7 | 27.8 | 8.9 |
| Polypharmacy (≥10/year)[c] (%) | 4.5 | 9.7 | 15.2 | 21.1 | 43.3 | 47.7 | 70.4 | 89.1 | 36.3 |
| Number of drugs, mean (SD)[c] | 3.0 (3.2) | 4.4 (3.9) | 5.6 (4.2) | 6.6 (4.4) | 9.4 (5.0) | 10.0 (5.5) | 13.0 (6.0) | 17.8 (7.3) | 8.4 (6.0) |

**Notes**: [a]Proportion calculated among individuals without missing value on the number of chronic conditions in 2008 (Number of individuals included by trajectory: trajectory 1: n=10,106; 2: n=3193; 3: n=26,452; 4:n=6747; 5: n=28,426; 6: n=3221; 7: n=16,338; 8: n=3872). [b] Proportion calculated among individuals without missing value on material deprivation on April 1, 2019 (Number of individuals included by trajectory: trajectory 1: n=9801; 2: n=2989; 3: n=24,551; 4: n=6410; 5: n=25,252; 6: n=2901; 7: n=13,891; 8: n=3100). [c] Proportion calculated among individuals with complete drug insurance coverage during the one year follow-up (April 1, 2019 to March 31, 2020) (Number of individuals included by trajectory: trajectory 1: n=9319; 2: n=2805; 3: n=23,859; 4: n=6116; 5: n=25,433; 6: n=2853; 7: n=14,307; 8: n=3198).
**Abbreviations**: CC, chronic condition; Q1-Q5, First quintile - Fifth quintile; SD, standard deviation.

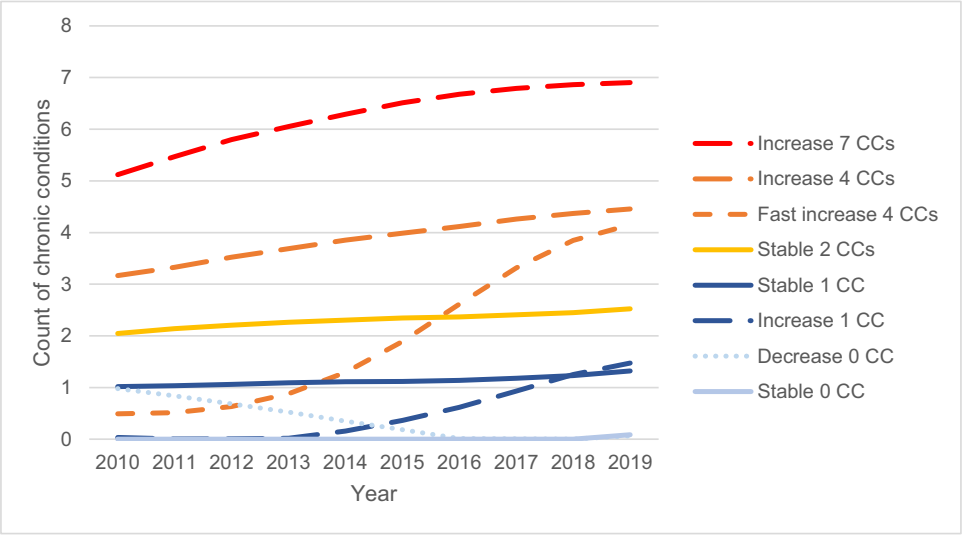


**Figure 2** Multimorbidity trajectories among individuals aged >65 years during a 10-year period, Québec, Canada, n = 99,411.
**Notes**: The year refers to the end of the fiscal year. For example, the count of prevalent chronic conditions (CCs) identified until March 31, 2010 was considered as the count for the year 2010.

Multimorbidity trajectories demonstrated the ability to predict all the health outcomes examined in the study. We observed an increase in the *c-statistic* value for each health outcome when multimorbidity trajectories were added to the baseline model. These increases in the *c-statistic* value ranged from 0.038 (95% CI: [0.032–0.044]) when predicting mortality to 0.162[0.158–0.166] when predicting polypharmacy (Figure 3, Table A4).

**Table 2** Statistical Assessment of the Optimal Number of Trajectories from Latent Class Growth Analysis Models Based on Counts of Chronic Conditions Across the 10 Periods

| Statistic | Number of trajectories | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| BIC | 3,021,335 | 2,843,389 | 2,783,447 | 2,767,115 | 2,749,090 | 2,740,220 | 2,735,442 | 2,732,890 | 2,731,395 |
| LMRT p-value | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | 1 |
| Entropy | 91.2% | 91.7% | 87.8% | 83.6% | 83.6% | 84.0% | 82.7% | 80.3% | 79.8% |
| APP of each trajectory | 0.973 | 0.979 | 0.962 | 0.863 | 0.846 | 0.856 | 0.720 | 0.870 | 0.881 |
| | 0.977 | 0.960 | 0.909 | 0.904 | 0.896 | 0.876 | 0.810 | 0.758 | 0.746 |
| | | 0.957 | 0.935 | 0.968 | 0.898 | 0.840 | 0.856 | 0.721 | 0.699 |
| | | | 0.934 | 0.860 | 0.859 | 0.974 | 0.892 | 0.890 | 0.824 |
| | | | | 0.909 | 0.974 | 0.896 | 0.865 | 0.861 | 0.906 |
| | | | | | 0.884 | 0.870 | 0.970 | 0.970 | 0.660 |
| | | | | | | 0.904 | 0.859 | 0.848 | 0.967 |
| | | | | | | | 0.898 | 0.791 | 0.873 |
| | | | | | | | | 0.838 | 0.781 |
| | | | | | | | | | 0.834 |
| OCC of each trajectory | 34.5 | 221.3 | 149.3 | 12.8 | 11.7 | 29.2 | 75.5 | 551.0 | 103.1 |
| | 44.6 | 21.5 | 15.8 | 175.2 | 174.7 | 207.0 | 10.6 | 9.5 | 14.8 |
| | | 52.4 | 99.8 | 193.8 | 104.1 | 11.9 | 30.3 | 75.7 | 90.6 |
| | | | 27.2 | 23.1 | 25.8 | 315.9 | 111.4 | 110.9 | 65.2 |
| | | | | 26.3 | 303.1 | 112.7 | 17.3 | 193.6 | 311.6 |
| | | | | | 22.3 | 17.6 | 272.6 | 272.7 | 90.5 |
| | | | | | | 232.0 | 184.2 | 16.9 | 247.1 |
| | | | | | | | 216.9 | 16.2 | 618.0 |
| | | | | | | | | 74.4 | 10.1 |
| | | | | | | | | | 15.2 |

(*Continued*)

**Table 2** (Continued).

| Statistic | Number of trajectories | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Fraction of study population in each trajectory | 0.512<br>0.488 | 0.174<br>0.528<br>0.298 | 0.145<br>0.387<br>0.126<br>0.342 | 0.329<br>0.051<br>0.134<br>0.210<br>0.275 | 0.319<br>0.047<br>0.078<br>0.191<br>0.110<br>0.255 | 0.169<br>0.033<br>0.307<br>0.106<br>0.071<br>0.275<br>0.039 | 0.033<br>0.286<br>0.164<br>0.069<br>0.270<br>0.106<br>0.032<br>0.039 | 0.012<br>0.248<br>0.033<br>0.068<br>0.031<br>0.106<br>0.248<br>0.189<br>0.065 | 0.067<br>0.166<br>0.025<br>0.067<br>0.030<br>0.021<br>0.106<br>0.011<br>0.261<br>0.249 |

**Abbreviations**: BIC, Bayesian information criteria; APP, Average posterior probability; LMRT, Lo-Mendell-Rubin test; OCC, Odds of correct classification.

For several health outcomes, multimorbidity trajectories were not better predictors than traditional cross-sectional multimorbidity indicators. For example, when predicting mortality, the 95% CI of the increase in *c-statistic* value for the ≥3 chronic condition indicator [0.037–0.050] overlapped a wide range of the 95% CI of the increase in *c-statistic* value observed when using multimorbidity trajectories [0.032–0.044] (Figure 3, Table A4). Similar results were observed when predicting hospitalizations and visits to the specialists. Multimorbidity trajectories seemed to perform better in predicting visits to GPs and polypharmacy than traditional cross-sectional multimorbidity indicators. Nevertheless, the increase in *c-statistic* value for multimorbidity trajectories consistently remained lower than the increase observed for the total count of chronic conditions. Observation of the scaled Brier score of each model led to the same findings (Table A4).

## Sensitivity and Supplementary Analyses

Performance of multimorbidity trajectories including only 4 trajectories was lower compared to the prediction of 8-trajectory model (Table A4, Figure A3 and Figure A4). The choice of 4 trajectories was made in this sensitivity analysis since the decrease in BIC value started to slow down at this point (Figure A2). The multimorbidity trajectories identified using a wider list of medical conditions (Figure A5), and the predictive performance of these trajectories was consistent with those observed in the main analyses (Table A5 and Figure A6). When defining polypharmacy using the ≥5 medication threshold, results remained consistent when compared to the ≥10 medication threshold (Table A4 and Figure A4). In supplementary analyses, we assessed the associations between multimorbidity trajectories and each health outcome. Unsurprisingly, the risk of developing each health outcome increased when the number of chronic conditions at the end of the 10-year period increased among trajectories.

# Discussion

In this population-based study, we identified eight distinct multimorbidity trajectories with increasing, stable, or decreasing shapes. Multimorbidity trajectories proved to be as effective as traditional cross-sectional multimorbidity indicators in predicting health outcomes. The only exception occurred when predicting polypharmacy, where multimorbidity trajectories exhibited superior predictive capacity than ≥2, ≥3, and ≥4 chronic conditions, but still remained below the predictive performance of the total count of chronic conditions.

## Implication

The limited improvement in predicting health outcomes with multimorbidity trajectories in comparison with traditional cross-sectional multimorbidity indicators implies the continued relevance of traditional indicators. For stakeholders, it suggests that introducing longitudinal information into new multimorbidity indicators may not be urgently needed, as it could add complexity without substantially improving their effectiveness. Multimorbidity indicators based on the prevalence of chronic

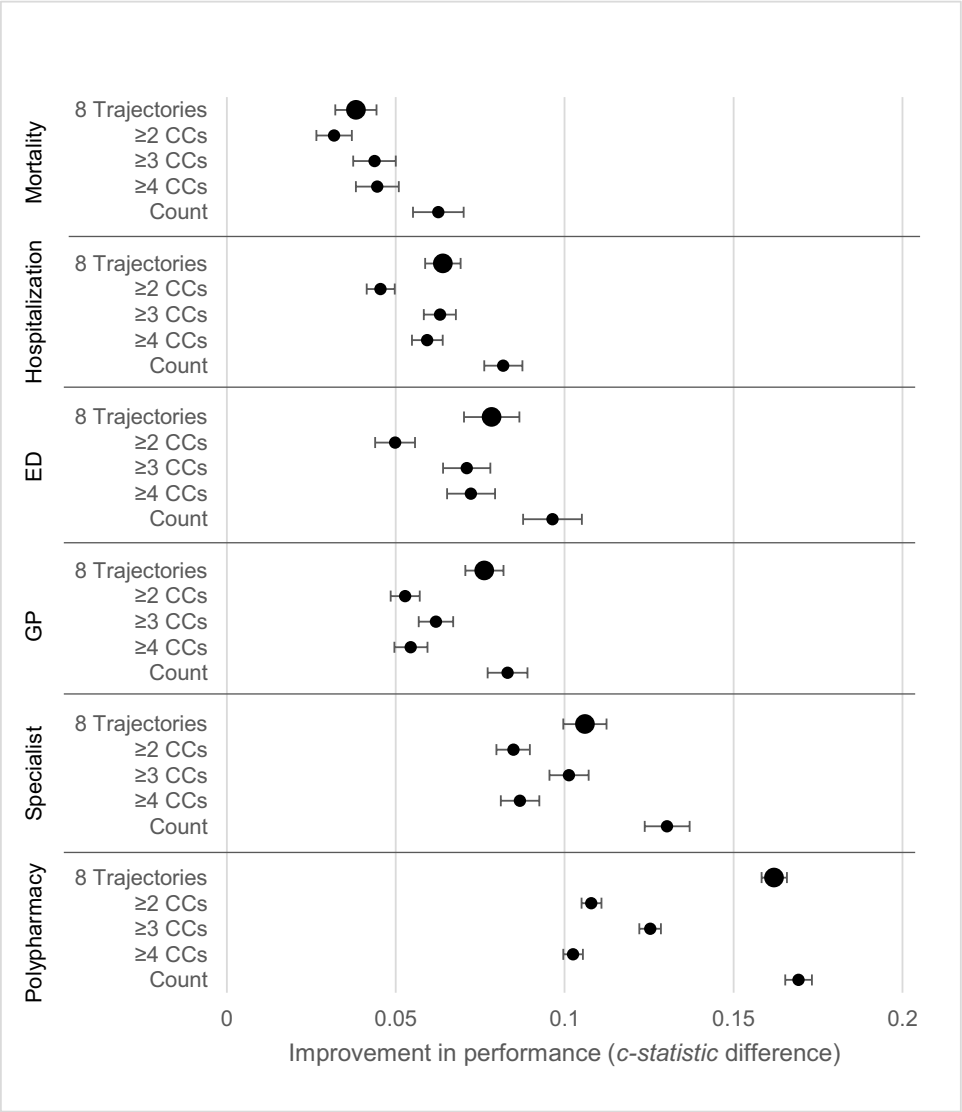


**Figure 3** Improvement in performance (*c-statistic*) for multimorbidity trajectories and each cross-sectional multimorbidity indicator (≥2, ≥3, ≥4 CCs, total count of chronic conditions) in comparison with the baseline model (which includes age, sex, deprivation) to predict 1-year mortality, polypharmacy, hospitalization, frequent ED admissions and frequent visits to the specialist or the GP, Québec, Canada, n = 99,411.

**Abbreviations**: ≥2 CCs, ≥3 CCs, ≥4 CCs: Multimorbidity indicator of the presence of at least 2, 3 or 4 chronic diseases; Count: Total count of chronic conditions; ED: Emergency department visits; GP: General practitioner.

conditions, such as ≥2, ≥3, and ≥4 chronic conditions, remain valid and relevant. For clinicians, it implies that in certain situations, investigating the chronological history of a patient's chronic conditions may not be necessary; knowing the current number of chronic conditions may suffice for effective patient care. This could translate in more time for doctor-patient dialogues regarding treatment and prevention choices—an important consideration given that workload and time constraints can hinder shared decision-making in primary care.[29,30]

## Interpretation Within the Context of Literature

The shapes of multimorbidity trajectories identified in our study, with mostly stable (3 trajectories) or increasing (4 trajectories) patterns, are similar to what has been observed in previous studies using latent growth models.[7] For example, Strauss et al identified three increasing and two stable trajectories among 27,410 primary care patients aged 50 and over in UK between 2003 and 2005.[31] In a random sample of 1705 people aged 65 years and over in South Korea, Lee et al identified 2 increasing and 2 stable trajectories.[32] As observed in our study, the speed of onset of chronic conditions varied across trajectories with increasing

shapes in both previous studies. For example, in the Lee et al, the count of chronic conditions increased from 2 during a 10-year period in the first trajectory and from 1 in the second.[32] Although less common, decreasing shape trajectories have also been identified among 121,733 hospitalized patients aged 60 years and over in South Korea between 2002 and 2008.[33]

Our study provides additional evidence supporting the relevance and validity of cross-sectional multimorbidity indicators compared to longitudinal trajectories when predicting health outcomes among adults aged over 65 years. Our findings confirmed those of the Chang et al[10] while addressing the key limitations of their study, namely: the limited trajectory follow-up duration (only three years); the prediction of a single health outcome (healthcare cost); and the a priori empirically determined trajectory creation that did not account for the identification of latent subgroups with similar speed of onset of chronic conditions. However, our results do not preclude the possibility that multimorbidity trajectories would perform better than traditional cross-sectional multimorbidity indicators in predicting health outcomes that we did not consider in our study. Exploring whether similar findings emerge in populations under 65 and in pediatric groups would be of interest. Additionally, expanding research by including frailty, quality of life and social vulnerability characteristics of individuals in the identification of multimorbidity trajectories and the evaluation of their predictive capacity presents an exciting avenue for future research. Considering additional geriatric condition markers for disease severity and disease–disease interactions may also be of interest. However, a recent study conducted in a population-based setting using the US Medicare database concluded that incorporating such information had limited potential to enhance multimorbidity measures.[34]

Some parallels can be drawn between the limited value of multimorbidity trajectories to predict short-term health outcomes, and previous studies that have compared predictive performance of multimorbidity patterns and with cross-sectional multimorbidity measures based on the count of chronic diseases. For example, Xu et al identified five multimorbidity patterns in a nationwide representative survey of nearly 17,000 Chinese individuals aged 50 and over, and assessed their performance in predicting disability.[35] The performance of these patterns in a nationwide representative survey of nearly 17,000 Chinese individuals aged 50 and over in predicting disability (*c-statistic*=0.735) was found to be comparable to that of the count of diseases (*c-statistic*=0.736). Similar results were observed in another survey among over 13,000 Chinese individuals aged 65 and above.[36] These findings support the notion that multimorbidity measures based on the count of chronic diseases remain a valuable tool in population surveillance, while ongoing research is needed to explore new alternative approaches.

## Strengths and Limitations

To the best of our knowledge, our study was the first population-based investigation to compare the predictive performance of long-term trajectories with traditional cross-sectional multimorbidity indicators. Our use of latent class growth model is another strength, as it does not require prior knowledge of individuals' group membership and allows the assignment of individual subgroups based on similar count of chronic conditions and onset speed.[21] From a public health perspective, this is highly relevant as it provides insights into subgroup sizes, risks estimation for specific outcomes, and aids in identifying high-risk individuals and planning resource allocation in chronic disease management and prevention. Finally, we performed sensitivity analyses using different numbers of trajectories and a broader list of chronic conditions, further confirming our main findings.

Some limitations arise due to the nature of administrative health data. First, the lack of validation for ICD codes in outpatient data is a concern, although we addressed it by using validated case definitions that typically required at least two codes within a specified time frame. Second, the limited granularity of four-digit ICD codes in outpatient data may reduce precision in identifying conditions such as stroke and renal diseases. Additionally, latent class growth model may fail to identify rare but real patterns, as the classification of each trajectory cannot be independently verified. Exclusion of 589 individuals who lived in the province of Québec for less than five years during the 10-year period used to identify multimorbidity trajectories may have introduced bias into the results. However, this bias is considered minimal, as the characteristics of the sample used to identify the trajectories are virtually the same as those of the initial n=100,000 random sample (Table A6).

## Conclusion

Our study reveals that nearly one-third of the population older than 65 had experienced multimorbidity trajectories marked by an increasing number of chronic conditions over the previous 10-year period. However, multimorbidity trajectories did not improve the prediction of health outcomes when compared to traditional cross-sectional multimorbidity indicators. This suggests that prevalence-based multimorbidity indicators, such as ≥2, ≥3, and ≥4 chronic conditions, and the total count of chronic conditions remains relevant for clinical practice and population-level multimorbidity surveillance. There is no imperative need to modify these indicators to account for the speed of chronic condition onset.

## Data Sharing Statement

The datasets generated and/or analysed during the current study are not publicly available due to data confidentiality requirements from the QICDSS. Code lists are available in supplementary data or in published papers.

## Ethics Approval

The use of QICDSS for population health surveillance and methodological development has received approval from the custodians of the databases, the provincial Public Health Research Ethics Board and the Québec Commission responsible for safeguarding privacy and regulating access to information (Commission d'accès à l'information du Québec).

## Acknowledgments

The authors are grateful to all QICDSS team members for their support. The abstract of this paper was presented at the 39th International Conference on Pharmacoepidemiology & Therapeutic Risk Management as an oral presentation with preliminary findings.

## Funding

There is no funding to report.

## Disclosure

DT is supported by a research career award from the Fonds de recherche du Québec – Santé. YC is part of the Canadian Institutes of Health Research – postdoctoral fellowship. CS reports grants from Fonds de recherche du Québec - Santé, during the conduct of the study. The authors report no other conflicts of interest in this work.

## References

1. World Health Organisation. Multimorbidity: Technical series on safer primary care; 2016:Available from: https://apps.who.int/iris/bitstream/handle/10665/252275/9789241511650-eng.pdfAccessed may 13, 2024
2. Lancet T, The Lancet. Making more of multimorbidity: an emerging priority. *Lancet*. 2018;391(10131):1637. doi:10.1016/S0140-6736(18)30941-3
3. Marengoni A, Angleman S, Melis R, et al. Aging with multimorbidity: a systematic review of the literature. *Ageing Res Rev*. 2011;10(4):430–439.
4. Betancourt MT, Roberts KC, Bennett T-L, Driscoll ER, Jayaraman G, Pelletier L. Monitoring chronic diseases in Canada: The chronic disease indicator framework. *Chronic Diseases and Injuries in Canada*. 2014;34(Suppl Supplement 1):1–30. doi:10.24095/hpcdp.34.S1.01
5. Johnston MC, Crilly M, Black C, Prescott GJ, Mercer SW. Defining and measuring multimorbidity: a systematic review of systematic reviews. *Eur J Public Health*. 2019;29(1):182–189. doi:10.1093/eurpub/cky098
6. Wise J. NICE issues guidance to tackle multimorbidity. *BMJ*. 2016;353:i1864. doi:10.1136/bmj.i1864
7. Cezard G, McHale CT, Sullivan F, Bowles JKF, Keenan K. Studying trajectories of multimorbidity: a systematic scoping review of longitudinal approaches and evidence. *BMJ Open*. 2021;11(11):e048485. doi:10.1136/bmjopen-2020-048485
8. Hsu HC. Trajectories of multimorbidity and impacts on successful aging. *ExpGerontol*. 2015;66(1873–6815 (Electronic)):32–38.
9. Calderón-Larrañaga A, Santoni G, Wang HX, et al. Rapidly developing multimorbidity and disability in older adults: does social background matter? *J Intern Med*. 2018;283(5):489–499. doi:10.1111/joim.12739
10. Chang HY, Clark JM, Weiner JP. Morbidity trajectories as predictors of utilization: multi-year disease patterns in Taiwan's national health insurance program. *Med Care*. 2011;49(10):918–923. doi:10.1097/MLR.0b013e31821b344f
11. Zeng C, Ellis JL, Steiner JF, Shoup JA, McQuillan DB, Bayliss EA. Assessment of morbidity over time in predicting health outcomes. *Med Care*. 2014;52(Suppl 3):S52–59. doi:10.1097/MLR.0000000000000033
12. Fraccaro P, Kontopantelis E, Sperrin M, et al. Predicting mortality from change-over-time in the Charlson Comorbidity Index: a retrospective cohort study in a data-intensive UK health system. *Medicine*. 2016;95(43):e4973. doi:10.1097/MD.0000000000004973
13. Fabbri E, An Y, Zoli M, et al. Association between accelerated multimorbidity and age-related cognitive decline in older Baltimore longitudinal study of aging participants without Dementia. *J Am Geriatr Soc*. 2016;64(5):965–972. doi:10.1111/jgs.14092

14. Lee JH, Kim SH, Kang SH, et al. Blood pressure control and cardiovascular outcomes: Real-world implications of the 2017 acc/aha hypertension guideline. *Sci Rep*. 2018;8(1):13155. doi:10.1038/s41598-018-31549-5
15. Blais C, Jean S, Sirois C, et al. Quebec integrated chronic disease surveillance system (QICDSS), an innovative approach. *Chronic Dis Inj Can*. 2014;34(1925–6523 (Electronic)):226–235. doi:10.24095/hpcdp.34.4.06
16. Pampalon R, Raymond G. A deprivation index for health and welfare planning in Quebec. *Chronic Dis Can*. 2000;21:104–113.
17. Simard M, Rahme E, Dubé M, Boiteau V, Talbot D, Sirois C. Multimorbidity prevalence and health outcome prediction: assessing the impact of lookback periods, disease count, and definition criteria in health administrative data at the population-based level. *BMC Med Res Methodol*. 2024 24 113 doi:10.1186/s12874-024-02243-0.
18. Gaulin M, Simard M, Candas B, Lesage A, Sirois C. Combined impacts of multimorbidity and mental disorders on frequent emergency department visits: a retrospective cohort study in Quebec, Canada. *CMAJ*. 2019;191(26):E724–E732. doi:10.1503/cmaj.181712
19. Belzile E, Sanche S, McCusker J, Vadeboncoeur A, Ciampi A, Levesque JF A measure of emergency department use based on Quebec's administrative data [technical report]; 2011.
20. Mbuya-Bienge C, Simard M, Gaulin M, Candas B, Sirois C. Does socio-economic status influence the effect of multimorbidity on the frequent use of ambulatory care services in a universal healthcare system? A population-based cohort study. *BMC Health Serv Res*. 2021;21(1):202. doi:10.1186/s12913-021-06194-w
21. Nagin DS. *Group-Based Modeling of Development*. Harvard University Press.; 2005.
22. van der Nest G, Lima Passos V, MJJM C, van Breukelen GJP. An overview of mixture modelling for latent evolutions in longitudinal data: modelling approaches, fit statistics and software. *Adv Life Course Res*. 2020;43:100323. doi:10.1016/j.alcr.2019.100323
23. Langton JM, Blanch B, Drew AK, Haas M, Ingham JM, Pearson SA. Retrospective studies of end-of-life resource utilization and costs in cancer care using health administrative data: a systematic review. *Palliat Med*. 2014;28(10):1167–1196.3. doi:10.1177/0269216314533813
24. Simard M, Sirois C, Candas B. Validation of the Combined Comorbidity Index of Charlson and Elixhauser to Predict 30-Day Mortality Across ICD-9 and ICD-10. *Med Care*. 2018;56(5):441–447. doi:10.1097/MLR.0000000000000905
25. Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. *J Clin Epidemiol*. 2011;64(7):749–759. doi:10.1016/j.jclinepi.2010.10.004
26. Muthén LK, Muthén BO *Mplus User's Guide*; 2011.
27. Benchimol EI, Smeeth L, Guttmann A, et al. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. *PLoS Med*. 2015;12(10):e1001885. doi:10.1371/journal.pmed.1001885
28. van de Schoot R, Sijbrandij M, Winter SD, Depaoli S, Vermunt JK. The GRoLTS-Checklist: Guidelines for Reporting on Latent Trajectory Studies. *Struct Equ Modeling*. 2017;24(3):451–467. doi:10.1080/10705511.2016.1247646
29. Rubio-Valera M, Pons-Vigués M, Martínez-Andrés M, Moreno-Peral P, Berenguera A, Fernández A. Barriers and facilitators for the implementation of primary prevention and health promotion activities in primary care: a synthesis through meta-ethnography. *PLoS One*. 2014;9(2):e89554. doi:10.1371/journal.pone.0089554
30. Légaré F, Witteman HO. Shared decision making: examining key elements and barriers to adoption into routine clinical practice. *Health Aff*. 2013;32(2):276–284. doi:10.1377/hlthaff.2012.1078
31. Strauss VY, Jones PW, Kadam UT, Jordan KP. Distinct trajectories of multimorbidity in primary care were identified using latent class growth analysis. *J Clin Epidemiol*. 2014:1878–5921. (Electronic))
32. Lee SA, Joo S, Chai HW, Jun HJ. Patterns of multimorbidity trajectories and their correlates among Korean older adults. *Age Ageing*. 2021;50(4):1336–1341. doi:10.1093/ageing/afab002
33. Kim JH, Rhee Y, Lee Y. Longitudinal changes in comorbidity patterns over time in relation to mortality in older Korean adults. *Arch Gerontol Geriatr*. 2018;79:63–68. doi:10.1016/j.archger.2018.08.004
34. Steinman MA, Jing B, Shah SJ, et al. Development and validation of novel multimorbidity indices for older adults. *J Am Geriatr Soc*. 2023;71(1):121–135. doi:10.1111/jgs.18052
35. Xu HW, Liu H, Luo Y, et al. Comparing a new multimorbidity index with other multimorbidity measures for predicting disability trajectories. *J Affect Disord*. 2024;346:167–173. doi:10.1016/j.jad.2023.11.014
36. SS Y, HW X, Han L, et al. Multimorbidity measures differentially predicted mortality among older Chinese adults. *J Clin Epidemiol*. 2022;146:97–105. doi:10.1016/j.jclinepi.2022.03.002