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Predicting poorer health outcomes in older community-dwelling patients with multimorbidity: prospective cohort study assessing the accuracy of different multimorbidity definitions

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ABSTRACT

Purpose Multimorbidity is commonly defined and measured using condition counts. The UK National Institute for Health Care Excellence Guidelines for Multimorbidity suggest that a medication-orientated approach could be used to identify those in need of a multimorbidity approach to management.

Objectives To compare the accuracy of medication-based and diagnosis-based multimorbidity measures at higher cut-points to identify older community-dwelling patients who are at risk of poorer health outcomes.

Design A secondary analysis of a prospective cohort study with a 2-year follow-up (2010–2012).

Setting 15 general practices in Ireland.

Participants 904 older community-dwelling patients.

Exposure Baseline multimorbidity measurements based on both medication classes count (MCC) and chronic disease count (CDC).

Outcomes Mortality, self-reported health related quality of life, mental health and physical functioning at follow-up.

Analysis Sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) adjusting for clustering by practice for each outcome using both definitions.

Results Of the 904 baseline participants, 53 died during follow-up and 673 patients completed the follow-up questionnaire. At baseline, 223 patients had 3 or more chronic conditions and 89 patients were prescribed 10 or more medication classes. Sensitivity was low for both MCC and CDC measures for all outcomes. For specificity, MCC was better for all outcomes with estimates varying from 88.8% (95% CI 85.2% to 91.6%) for physical functioning to 90.9% (95% CI 86.2% to 94.1%) for self-reported health-related quality of life. There were no differences between MCC and CDC in terms of PPV and NPV for any outcomes.

Conclusions Neither measure demonstrated high sensitivity. However, MCC using a definition of 10 or more regular medication classes to define multimorbidity had higher specificity for predicting poorer health outcomes. While having limitations, this definition could be used for proactive identification of patients who may benefit from targeted clinical care.

Strengths and limitations of this study

► This study compares use of medication classes count with the more traditional method of chronic disease counts to define multimorbidity. This approach could be used proactively in the clinical setting to identify higher risk people.

► Our study used a large dataset with robust data collection from electronic health records combined with linked national pharmacy claims data and a patient questionnaire for self-reported outcomes.

► This study only included older patients with multimorbidity, further research would be needed to validate these results in other populations.

► This study is a secondary analysis and as such is limited to the data collected from the recruited population in the original cohort study.

INTRODUCTION

A high proportion of patients consulting in primary healthcare present with multimorbidity, defined generally as the presence of at least two chronic medical conditions.[1] Multimorbidity has a significant impact across the age ranges but is more common in older patients and is associated with poorer quality of life,[2 3] psychological distress,[4–6] loss of physical function,[7] polypharmacy and adverse drugs events[8] and care duplication and inconsistencies.[9 10] Within the broad multimorbidity population, outcomes are poorer in patients with more complex multimorbidity, which has been defined previously in terms of higher numbers of conditions or higher healthcare utilisation.

Even though associations with poorer health outcomes are clear, identifying older patients with multimorbidity who will benefit from a community-based intervention is difficult due to the heterogeneity of multimorbidity

definitions and measures, used in both public health and clinical interventions.[11] Existing trials have based inclusion on the number of conditions along with other markers of risk such as older age or high healthcare utilisation.[12] The UK National Institute for Health and Care Excellence (NICE) 2016 Guidance on Multimorbidity recommends that health practitioners should proactively identify patients that could benefit from a multimorbidity approach to clinical care. The NICE Guidance suggests considering a multimorbidity approach to care for adults of any age who are prescribed ≥10 medications with the advantage that this information can be retrieved from the electronic health record.[13] This approach to care is patient-centred as it follows patient goals and preference of care, focusing on quality of life by reducing treatment burden, adverse events, and unplanned care and improving services coordination. Polypharmacy is a marker of multimorbidity and patients identified this way can be regarded as having multimorbidity and offered broad interventions beyond medicines management. For condition count multimorbidity measurement, the literature suggests using ≥3 chronic conditions to identify patients with higher needs.[s14 15]

This study aimed to examine the accuracy of medication-based versus condition count-based definitions of multimorbidity in predicting poorer health outcomes for older community-dwelling patients.

METHODS
The Strengthening The Reporting of Observational Studies in Epidemiology guidelines were used to guide the conduct and reporting of this study.[16]

Study design and population
This is a secondary analysis of a 2-year, prospective cohort study that was established to examine potentially inappropriate prescribing and adverse health outcomes in older community-dwelling patients.[17] The study population was recruited from 15 randomly selected general practices in Leinster, Ireland for a 2-year (2010–2012) prospective cohort study involving older community-dwelling patients. Proportionate stratified sampling was carried out based on the overall required sample size and the total number of eligible patients per practice assuming a 50% response rate and of 3070 eligible patients, a total of 1764 were invited to participate.[17 18] Of this group, 152 were ineligible on invitation based on eligibility criteria and 125 were not contactable resulting in 1487 patients eligible for participation.

Study inclusion criteria
1. Age ≥70 years on 1 January 2010.
2. in receipt of a valid general medical services card, which is means tested and entitles the holder to free public medical services including general practitioner (GP) care.

Exclusion criteria
1. Receiving palliative care.
2. Cognitive impairment at the level that would affect their ability to complete the outcome measure (defined as Mini Mental State Examination ≤20).
3. Significant hearing/speech/visual impairment.
4. Currently experiencing a psychotic episode.
5. Hospitalised long-term, in a nursing home, homeless or in sheltered accommodation.
6. Recent bereavement (within 4 weeks).

Of 1487 eligible and invited to participate at baseline (T0) a total of 904 (61%) agreed.[17 18] Two study populations are presented depending on the outcome of interest:
a. Patients who either completed a 2-year follow-up (T1) or died before T1 for mortality analysis (n=726).
b. Patients who completed T1 self-reported questionnaires for patient reported health outcomes analysis (n=673).

Demographic data collected
Sociodemographic variables collected included age, deprivation, gender, social class, education, marital status and living arrangements. Age and gender were collected from the GP electronic medical record. The deprivation score was obtained with the geocoded patients address based on the Small Area Health Research Unit which uses electoral division.[19] Education levels were classified as basic education (no formal education, primary education or lower secondary education only) or upper and postsecondary (all other higher levels of education). Social class was classified as unskilled (unskilled, gainfully occupied, unknown) or skilled (all other categories). Marital status was classified as married, separated/divorced, widowed and single/never married. Living arrangements were classified as living with husband/wife/life partner, family/relatives, living alone and other.

Exposure of interest: multimorbidity measures
Two measures of multimorbidity were selected based on current guidelines and literature.[14 15]

Medication classes count (MCC)
The number of regular prescribed medication classes was calculated by linkage to the national Health Services Executive-Primary Care Reimbursement Scheme pharmacy claims database. The number of medication classes prescribed to the patient were classified using the first three characters of the WHO-ATC classification system and the sample was divided using a cut-off definition of ≥10 prescribed medication classes.[20] The NICE guidelines indicate that a patient with ≥10 prescribed medicines and an additional risk factor would benefit from a multimorbidity approach.[21] As all cohort participants were ≥70 years, this population was considered as having an additional risk factor.

Chronic disease count (CDC)

At baseline, chronic diseases were collected from the GP electronic medical record by eight trained medical students using standardised data collection forms. A disease count proposed by Barnett *et al* which includes 40 chronic diseases on the basis of disease prevalence and severity was used to define multimorbidity.[22] A cut-off of ≥3 chronic diseases was used to identify multimorbidity.[14 15]

Primary outcomes

Mortality and patient reported outcome measures (PROM) were selected to identify patients with poorer health at follow-up. The study examined poorer self-reported health between T0 (baseline) and T1 (2 years). The PROMs were dichotomised, as described below to identify changes in outcome over the 2 years.

Mortality

Mortality was assessed by examining each participant's GP electronic medical record. Where there was any query regarding the date of death, it was double checked using a national repository of deaths in Ireland.

Health-related quality of life

The Euro-Qual 5 Dimensions (EQ-5D) is a generic instrument widely used to assess health-related quality of life by using ordinal scaling to assess fives domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Poorer self-reported health was defined using the Paretian principles method described by Devlin *et al*.[23] Following these principles, poorer health-related quality of life was operationalised as a decline in a greater number of domains scores compared with stable or improved domains scores.[23]

Mental health

The Hospital Anxiety and Depression Scale (HADS) is a measure assessing levels of anxiety and depression independently, which are then classified as normal, mild, moderate or severe.[24] Poorer self-reported mental health was defined as a higher score at follow up-compared with baseline according to the HADS.[24]

Physical functioning

The Vulnerable Elders Survey (VES-13) is a patient-reported outcome measure used to identify older patients at risk of functional decline.[25] In the derivation study for this tool, patients who scored ≥3 had four times the risk of death or functional decline over a 2-year period than patients who scored <3.[25] Accordingly, patients were classified as having poorer self-reported health if study participants who scored l<3 at baseline (T0) scored ≥3 at follow-up (T1).

Statistical analysis

Descriptive statistics are presented to describe patient characteristics. For categorical measures, the number of patients and percentage were calculated, and for continuous measures, the mean and SD. For continuous scales which showed evidence of, or were expected to show some skew, a median and interquartile range were presented. A X^2 test, t-test or Mann-Whitney test was used as appropriate, adjusting for clustering by practice, to examine possible associations between patient characteristics and multimorbidity measures (patients with ≥10 vs <10 prescribed medication classes and patients with ≥3 vs <3 chronic diseases).

The sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV), along with 95% CIs, were calculated adjusting for clustering by practice using Stata V.15 (StataCorp. 2017) for each outcome and using both exposures of interest (MCC and CDC). For our analyses, sensitivity is the probability of a patient who experiences the health outcome of interest (ie, death or decline in PROM at follow-up) having multimorbidity at baseline, specificity is the probability of a patient who does not experience the health outcome at follow-up not having multimorbidity at baseline, the PPV is the probability of a patient with multimorbidity at baseline having the health outcome at follow-up and the NPV is the probability of a patient without multimorbidity at baseline not having the health outcome at follow-up.

Risk of bias

The risk of bias was assessed in the cohort study using The Cochrane risk of bias tool for non-randomised studies.[26]

Patient and public involvement

This study is a secondary analysis of a cohort study which started enrolment in 2010. No patients or members of the public were involved in its design phase.

RESULTS

Participants

A total of 223 participants (30.7%) met the criteria for the CDC definition for multimorbidity, and 89 patients (12.3%) met the criteria for the MCC definition. Overall, 61 patients met both criteria. The median age of the total sample was 76.4 years, a total of 348 (47.9%) participants were men, 565 (77.8%) were classified as coming from the skilled social class and 433 (59.6%) reported a basic level of education. Descriptive characteristics of the patients identified by the CDC and the MCC cut-offs are presented in table 1. Patients with a disease count ≥3, compared with those with a disease count <3, were on average older and reported less formal education. Patients prescribed ≥10 medications classes were on average older, women and had less formal education compared with patients prescribed <10 medication classes.

OUTCOMES

The proportion of patients defined as having multimorbidity using both definitions who died or reported poorer health outcomes are presented in table 2. Patients with

Table 1 Study population descriptive characteristics at baseline (T0)

Patient characteristic	All patients	Patients with ≥10 prescribed medication classes			Patients with ≥3 chronic diseases		
	n (%)*	Yes n (%)*	No n (%)*	P value†	Yes n (%)*	No n (%)*	P value†
N	726 (100%)	89 (12.3%)	637 (87.7%)		223 (30.7%)	503 (69.3%)	
Median age (IQR), years	76.4 (72.9–80.3)	78.8 (73.8–83.2)	76.1 (72.9–79.8)	0.013	77.6 (74.1–81.1)	76.0 (72.8–79.8)	0.002
Mean deprivation score (SD)	1.4 (2.6)	1.8 (2.3)	1.4 (2.6)	0.075	1.6 (2.4)	1.3 (2.6)	0.272
Gender							
Male	348 (47.9%)	33 (37.1%)	315 (49.5%)	0.038	112 (50.2%)	236 (46.9%)	0.246
Female	378 (52.1%)	56 (62.9%)	322 (50.6%)		111 (48.8%)	267 (53.1%)	
Social class							
Unskilled	161 (22.2%)	29 (32.6%)	132 (20.7%)	0.064	55 (24.7%)	106 (21.1%)	0.636
Skilled	565 (77.8%)	60 (67.4%)	505 (79.3%)		168 (75.3%)	397 (78.9%)	
Education							
Basic	433 (59.6%)	66 (75%)	367 (57.9%)	0.014	155 (70.1%)	278 (55.5%)	0.006
Higher	293 (40.4%)	22 (25.0%)	267 (42.1%)		66 (29.9%)	223 (44.5%)	
Marital status‡							
Married	342 (47.1%)	35 (39.3%)	307 (42.3%)	0.127	94 (42.3%)	248 (49.3%)	0.296
Separated/divorced	34 (4.7%)	2 (2.3%)	32 (5.0%)		12 (5.4%)	22 (4.4%)	
Widowed	224 (30.9%)	39 (43.8%)	185 (29.1%)		81 (36.5%)	143 (28.4%)	
Single/never married	125 (17.2%)	13 (14.6%)	112 (17.6%)		35 (15.8%)	90 (17.9%)	
Living arrangement‡							
Husband/wife/life partner	333 (45.9%)	33 (37.1%)	300 (47.2%)	0.246	92 (41.4%)	241 (47.9%)	0.508
Family/relatives	90 (12.4%)	12 (13.5%)	78 (12.3%)		27 (12.2%)	63 (12.5%)	
Living alone	266 (36.6%)	37 (41.6%)	229 (36.0%)		91 (41.0%)	175 (34.8%)	
Other	36 (5.0%)	7 (7.9%)	29 (4.6%)		12 (5.4%)	24 (4.8%)	

*Unless otherwise stated.
†Cluster adjusted Mann-Whitney test (age), t-test (deprivation score) or χ^2 test for categorical variables.
‡Missing for two people.

Table 2 Patients with multimorbidity according to MCC or CDC and outcomes of death, decline in health-related quality of life, decline in physical functioning and decline in psychological well-being

Outcome	MCC			CDC		
	Patients with <10 medications	Patients with ≥10 medications	Cluster adjusted χ^2 p value	Patients with <3 chronic diseases	Patients with ≥3 chronic diseases	Cluster adjusted X^2 p value
Death (n=724)						
No	598 (94.0%)	73 (83.0%)	<0.001	472 (94.0%)	199 (89.6%)	0.054
Yes	38 (6.0%)	15 (17.0%)		30 (6.0%)	23 (10.4%)	
Decline in health-related quality of life (EQ-5D) (n=636)						
No	393 (68.3%)	39 (63.9%)	0.443	310 (68.0%)	122 (67.8%)	0.820
Yes	182 (31.7%)	22 (36.0%)		146 (32.0%)	58 (32.2%%)	
Decline in physical functioning (VES-13) (n=673)						
No	525 (87.7%)	66 (89.2%)	0.622	418 (88.4%)	173 (86.5%)	0.768
Yes	74 (12.4%)	8 (10.8%)		55 (11.6%)	27 (13.5%)	
Decline in psychological well-being (HADS) (n=649)						
No	501 (86.7%)	56 (78.9%)	0.116	401 (88.3%)	156 (80.0%)	0.017
Yes	77 (13.3%)	15 (21.1%)		53 (11.7%)	39 (19.5%)	

CDC, chronic disease count; EQ5D, Euro-Qual 5 Dimensions; HADS, Hospital Anxiety and Depression Scale; MCC, medication classes count; VES-13, Vulnerable Elders Survey.

≥10 medication classes had a significantly higher mortality rate compared with patients with <10 medication classes (17% vs 6%, p<0.001). There was no difference in the other outcomes measured. Patients with a disease count of ≥3, compared with those with a disease count of <3, had a significantly higher decline in psychological well-being (19.5% vs 11.7%, p=0.017) but there was no difference in any of the other outcomes.

The sensitivity, specificity, PPV and NPV along with 95% CIs adjusted for clustering by practice are presented in table 3 for both definitions of multimorbidity for each outcome of interest. For mortality, specificity was higher for MCC (89.0%; 95% CI 86.0% to 91.5%) compared with the CDC (70.3%; 95% CI 63.5% to 76.3%). For decline in health-related quality of life, both CDC and MCC measures had low sensitivity, however, the CDC (28.5%; 95% CI 22.1% to 35.9%) was higher than the MCC (10.5%; 95% CI 7.6% to 14.4%). In terms of specificity, MCC (90.9%; 95% CI 86.2% to 94.1%) was higher when compared with the CDC measure (71.9%; 95% CI 64.8% to 78.1%).

Similar patterns were reported for decline in physical functioning and psychological functioning as were seen for decline in health-related quality of life. Specificity was moderate for the CDC measure for both decline in physical functioning (71.9%; 95% CI 64.8% to 78.1%) and decline in psychological functioning (71.1%; 95% CI 64.6% to 76.9%). The MCC demonstrated higher specificity (decline in physical functioning: 88.8%; 95% CI 85.2% to 91.6% and decline in psychological functioning: 89.9%; 95% CI 86.2% to 92.7%).

Risk of bias
The risk of bias is reported fully in the primary cohort study previously.[17] Overall, the risk of bias was low regarding losses to follow-up. As this is a secondary analysis, exclusion of participants with cognitive impairment and the small sample of participants with ≥15 medication classes could reduce generalisability.[26]

DISCUSSION
Main results
In this population of community-dwelling older patients, sensitivity was low for both the MCC and CDC measures for all outcomes. However, for self-reported health-related quality of life, psychological well-being and physical functioning at follow-up, the CDC measure was more sensitive. There was no difference in sensitivity between measures for the outcome of death. In terms of specificity, the MCC approach was better for all outcomes with estimates varying from 88.8% (95% CI 85.2% to 91.6%) for physical functioning to 90.9% (95% CI 86.2% to 94.1%) for self-reported health-related quality of life.

With high specificity, the MCC definition has better potential to proactively 'rule-in' patients with multimorbidity who are more likely to have poorer health outcomes compared with the more widely used condition count approach. There are also fewer patients identified using the MCC definition, which is more manageable from a clinical or organisational perspective. However, both definitions had insufficient sensitivity, showing a limited potential to accurately 'rule out' patient at risk of poorer health outcomes in this population. Ideally a definition with both high sensitivity and specificity could be used to target multimorbidity interventions but existing risk stratification models have similar limitations.[27]

Table 3 Cluster-adjusted sensitivity, specificity, PPV and NPV of multimorbidity measures

Multimorbidity measure	Sample	Outcome	Sensitivity (%, 95% CI)	Specificity (%, 95% CI)	PPV (%, 95% CI)	NPV (%, 95% CI)
Patients with ≥10 prescribed medication classes	All patients (n=726)	Death	28.0% (18.7% to 39.8%)	89.0% (86.0% to 91.5%)	17.1% (9.9% to 28.5%)	94.1% (91.1% to 96.2%)
	Patients who completed follow-up questionnaire (n=673)	Decline in health-related quality of life (EQ-5D) (n=636)	10.5% (7.6% to 14.4%)	90.9% (86.2% to 94.1%)	36.9% (24.4% to 51.5%)	68.3% (65.1% to 71.3%)
		Decline in physical functioning (VES-13)	8.9% (5.5% to 14.3%)	88.8% (85.2% to 91.6%)	10.1% (5.4% to 18.0%)	87.7% (84.6% to 90.2%)
		Decline in physical functioning (VES-13) (n=673)	16.3% (10.4% to 24.5%)	89.9% (86.2% to 92.7%)	21.1% (13.0% to 32.4%)	87.3% (85.1% to 89.2%)
Patients with ≥3 chronic diseases	All patients (n=726)	Death	41.6% (33.9% to 49.7%)	70.3% (63.5% to 76.3%)	10.5% (6.6% to 16.1%)	94.0% (91.8% to 95.6%)
	Patients completing follow-up questionnaire (n=673)	Decline in health-related quality of life (EQ-5D) (n=636)	28.5% (22.1% to 35.9%)	71.9% (64.8% to 78.1%)	32.0% (28.8% to 35.3%)	67.9% (64.4% to 71.2%)
		Decline in physical functioning (VES-13)	35.3% (22.9% to 50.0%)	71.1% (64.6% to 76.9%)	12.7% (9.9% to 16.2%)	88.8% (84.4% to 92.0%)
		Decline in physical functioning (VES-13) (n=673)	42.8% (31.7% to 54.6%)	72.3% (66.0% to 77.9%)	19.9% (14.8% to 26.1%)	88.4% (85.6% to 90.7%)

EQ5D, Euro–Qual 5 Dimensions; HADS, Hospital Anxiety and Depression Scale; NPV, negative predictive value; PPV, positive predictive value; VES-13, Vulnerable Elders Survey.

Strengths and limitations

In this cohort study, the MCC variable was obtained from linked national pharmacy claims data and the number of chronic diseases count was obtained via review of the participants' electronic medical record, which adds to the robustness to the data used in this analysis. A main strength of the study is that the dataset includes a variety of outcomes including mortality and patient-reported outcomes.

The first limitation of this study is inherent to the secondary analysis design. By using previously collected data, it is not possible to align data collection directly with the goals of the current study, however we did have a wide range of patient reported and chart data available for analysis. The cohort study sample was limited to a community-dwelling older people without cognitive, visual or hearing impairment. However, recent studies indicate that multimorbidity is not just a feature of ageing but is also prevalent in younger populations.[1 28 29] We limited the number of chronic conditions identified in the records to 40 prespecified conditions. Another potential limitation is the collection of data from medical records as there may have been some variation in recording of conditions. Medication classes were used as the predictor of interest as per the WHO-ATC classification system rather than individual medications. Further research is needed to validate our findings in larger samples

Comparison with existing literature

Previous studies have reported mixed results concerning the predictive power of multimorbidity definitions for different outcomes. Several studies have showed that a weighted diagnosis count, the Charlson index was an suitable measure to predict mortality[30–32] However, a large cohort study (n=95 372) comparing six measure of multimorbidity reported that the number of prescribed medications was the most accurate multimorbidity measurement to predict future GP and practice nurses consultations and that it was also the second most accurate measure to predict mortality, just behind the Charlson index.[33] A previous analysis of the current cohort study data compared five continuous count-based definitions of multimorbidity and reported poor discrimination in predicting hospital admissions and self-reported functional decline for all multimorbidity measures, with the medication class-based definition performing marginally better than diagnosis-based definitions.[34] A previous study reported that using a ≥10 medication class cut-off to measure multimorbidity performed similarly to another risk score with low sensitivity and high specificity, when applied in clinical settings to predict cardiovascular disease risk.[27] Our findings are build on this previous research, by comparing the predictive power of a medication class count definition against a disease count definition using pragmatic cut-off points and also examining a range of self-reported health outcomes in addition to mortality. Research to date has highlighted the limitations of multimorbidity measures in predicting adverse events and work in this area is now expanding to include biomarkers in an effort to address these limitations.[35 36]

Implications for future research and clinical practice

Further research should assess the accuracy of multimorbidity measures in a larger range of primary care populations, including middle-aged patients with multimorbidity and older patients with cognitive decline. Larger sample sizes are needed to test the ≥15 medications cut-off measure for multimorbidity also recommended as an alternative in the UK NICE Multimorbidity Guidance.[21] In our study, there was little difference in medication and condition count measures in identifying older people at higher risk of poor health outcomes but MCC demonstrated higher specificity showing a slight difference in age, suggesting that the medication definition might better identify older people at higher risk. While it shares some limitations with other multimorbidity measures, clinicians and researchers can follow the expert consensus in the UK NICE Multimorbidity Guidance recommendations by using MCC to identify higher risk patients with multimorbidity as it is easy to use and offers a pragmatic approach and potential for identification of patients through prescribing or electronic health records.

CONCLUSIONS

This study shows that using two measures of multimorbidity, a MCC cut-off of ≥10 and a CDC of ≥3 chronic diseases had low sensitivity in relation to predicting mortality, self-reported health-related quality of life, mental health and physical functioning, although the CDC was slightly more sensitive for the majority of outcomes. The MCC approach demonstrated higher specificity for mortality and decline in health status, making it possible to rule-in a small sample of patients identified with a risk of poorer health outcomes with a low rate of false positives. However, the low sensitivity means that some of those identified as low risk may also experience poorer health outcomes.

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