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Age, sex, and socioeconomic differences in multimorbidity measured in four ways: UK primary care cross-sectional analysis

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Abstract

Background: Multimorbidity poses major challenges to healthcare systems worldwide. Definitions with cut-offs of more than ≥ 2 long-term conditions (LTCs) might better capture populations with complexity but are not standardised.

Aim: This study examined variation in prevalence using different definitions of multimorbidity.

Design and setting: Cross-sectional study of 1168620 people in England.

Methods: Comparison of multimorbidity prevalence using four definitions: MM2+ (≥ 2 LTCs), MM3+ (≥ 3 LTCs), MM3+ from 3+ (≥ 3 LTCs from ≥ 3 ICD-10 chapters), and mental-physical MM (≥ 2 LTCs where ≥ 1 mental and ≥ 1 physical). Logistic regression was used to examine patient characteristics associated with multimorbidity under all four definitions.

Results: MM2+ was most common (40.4%) followed by MM3+ (27.5%), MM3+ from 3+ (22.6%), and mental-physical MM (18.9%). MM2+, MM3+, and MM3+ from 3+ were strongly associated with oldest age (aOR 58.09 [56.13-60.14]), aOR 77.69 [75.33-80.12]), and aOR 102.06 [98.61-105.65] respectively), but mental-physical MM was much less strongly associated (aOR 4.32 [4.21-4.43]). People in the most deprived decile had equivalent rates of multimorbidity at a younger age than those in the least deprived. This was most marked in mental-physical MM at 40-45 years younger, followed by MM2+ at 15-20 years, and MM3+ and MM3+ from 3+ at 10-15 years. Women had higher prevalence of multimorbidity under all definitions, which was most marked for mental-physical MM.

Conclusion: Estimated prevalence of multimorbidity depends on the definition used, and associations with age, sex, and socioeconomic position vary between definitions. Applicable multimorbidity research requires consistency of definitions across studies.

How this fits in

Multimorbidity poses major challenges to healthcare systems worldwide because of associated health service utilisation and mortality.

Definitions with cut-offs of more than ≥ 2 long-term conditions might better capture populations with complexity; however, these definitions are not standardised.

Estimated prevalence of multimorbidity depends on the definition used, and associations with age, sex, and socioeconomic position vary between definitions.

People in the most deprived decile had equivalent rates of multimorbidity at a younger age than those in the least deprived, and this difference was very large in mental-physical multimorbidity.

Introduction

Multimorbidity is usually defined as the presence of two or more long-term conditions (LTCs).¹ It is common in high-income countries, and is becoming more common in low- and middle-income countries.¹ Multimorbidity poses major challenges to health care systems worldwide, and is associated with higher health service utilisation² and mortality,³ but health services are usually designed to prioritise the management of single diseases.⁴ Definitions of multimorbidity are used inconsistently in research,⁵ and prevalence estimates vary widely across studies.^{6,7} This variation in prevalence is likely to relate to multiple factors, such as population demographics and study location, but also study methodology including the definitions of multimorbidity used.⁸ Multimorbidity is known to be more prevalent in older people, in women, and in people of lower socioeconomic position (SEP),^{2,9} but whether the strength of these associations depends on the definition used is uncertain.¹⁰

Some researchers have proposed that the conventional definition of multimorbidity as the presence of two or more long-term conditions does not capture those with the most complexity, disability, or functional impairment, and recommend using a higher cut-off, for example three or more LTCs.^{8 11} Others suggest that complexity of management is better captured by defining multimorbidity in terms of multiple LTCs from multiple body systems (defined in terms of International Classification of Diseases 10th version [ICD-10] chapters).¹² Co-existence of mental and physical health LTCs is also commonly suggested as a marker of complexity and need, and has been shown to be associated with higher levels of unplanned hospital admissions,¹³ and with faster functional decline than physical-only multimorbidity.¹⁴ However, there has been little comparison of how the prevalence of multimorbidity in different population groups varies under different definitions.¹⁵

The aim of this study was to examine how prevalence of multimorbidity defined in four ways varied by age, sex, and SEP in a large primary care population in England.

Methods

Study design and data sources

This study used a cross-sectional design to examine variation in prevalence when measuring multimorbidity using four different definitions. The study population included people who were alive

and registered with 149 Clinical Practice Research Datalink (CPRD)¹⁶ GOLD participating general practices in England on 30/11/15, with two years of GP registration prior to study index date.¹⁷ The study compared multimorbidity prevalence using four distinct definitions of multimorbidity, with the same 80 LTCs considered in the morbidity count for every analysis. Data were extracted from CPRD Gold practices, including linked primary care and hospital data from electronic health records.

Definition of outcomes and variables

For every individual, we defined the presence of 80 LTCs (10 of which were mental-health conditions), categorised into ICD-10 chapters. The 80 conditions were chosen because they featured in phenotyping algorithms in the HDR-UK Phenotype Library,¹⁸ and/or were recommended by a recent Delphi consensus study,¹⁹ and deemed to be relevant by clinical authors (CM, SWM, BG). All the codes used to identify individuals with each condition were mutually exclusive, therefore double counting of conditions was not possible. LTCs were defined using any code ever recorded in an individual's record. This approach was applied to all 80 LTCs because the purpose of the study was to compare different cut-offs therefore we chose to keep the method for defining the LTCs uniform. To do this, a set of existing code-lists^{18,20} were used that combined Read codes (version 2) applied to GP electronic health record data, laboratory results recorded in the GP electronic health record, and also International Classification of Diseases 10th version (ICD-10) codes applied to hospital admission data to identify those at risk of poor outcomes²¹ (Supplementary Table 1).

The study outcome in all analyses was the presence of multimorbidity, defined in four different ways. "Multimorbidity 2+" was defined as the presence of ≥ 2 of the 80 LTCs and is the recommended definition.¹ "Multimorbidity 3+" was defined as ≥ 3 LTCs, "multimorbidity 3+ from 3+" as ≥ 3 LTCs from ≥ 3 different ICD-10 chapters, and "mental-physical multimorbidity" as the presence of ≥ 2 LTCs where at ≥ 1 was a mental health LTC and at ≥ 1 was a physical health LTC.

Statistical analysis

The prevalence of multimorbidity using the four definitions was calculated, and associations with patient demographic characteristics - age at study index date, sex, and SEP (defined by Index of Multiple Deprivation [IMD] deciles)²² - were examined. Data for the characteristics of the study population were represented as counts and proportions with 95% confidence intervals (95% CIs). No data were missing for age, sex, or IMD decile. Since age is very strongly associated with

multimorbidity, age-standardised prevalence in women, men, and each IMD decile was calculated using direct standardisation to the age-structure of the whole study population.²³ Logistic regression models were fitted to examine univariate (odds ratios [ORs]) and adjusted associations (adjusted odds ratios [aORs]), and 95% CIs of patient characteristics with the presence of multimorbidity using all four definitions. Multivariate models were adjusted for age, sex, and SEP. The large study size means that most comparisons were statistically significant, so clinical inference focused on the size and strength of associations rather than p values.

All analysis, modelling, and plotting was done in R version 3.6.2²⁴ in the ISO27001 and Scottish Government approved Health Informatics Centre Safe Haven environment.²⁵ The analysis was approved by the CPRD Independent Scientific Advisory Committee (reference 20_018).

Results

The study included 1168620 people with a median age of 44 years (IQR 23-60), of whom 587687 (50.3%) were women, and 88304 (7.6%) lived in the most deprived IMD decile areas (Table 1). There was substantial variation in the prevalence of multimorbidity using the four different definitions. Multimorbidity 2+ had highest prevalence (40.4%), followed by multimorbidity 3+ (27.5%), and multimorbidity 3+ from 3+ (22.6%). Mental-physical multimorbidity had the lowest prevalence (18.9%).

Multimorbidity became more prevalent with increasing age when using all four definitions and showed an S-shaped relationship between prevalence and advancing age: a relatively slow increase in the youngest, rapid increases in adulthood, and flattening in later life (Figure 1). Multimorbidity 2+ had the highest prevalence in all age-groups, and a faster rate of increase in early adulthood than multimorbidity 3+ and multimorbidity 3+ from 3+ (Table 1, Figure 1). Multimorbidity 2+, multimorbidity 3+, and multimorbidity 3+ from 3+ were strongly associated with oldest age (≥ 80 years versus 20-29 years); aOR 58.09 (95%CI 56.13-60.14), aOR 77.69 (95%CI 75.33-80.12), and aOR 102.06 (95%CI 98.61-105.65) respectively. Mental-physical multimorbidity was much less strongly associated with oldest age, aOR 4.32 (95%CI 4.21-4.43) (Table 2) but was present in more young- and middle-aged adults than multimorbidity 3+ and multimorbidity 3+ from 3+ (Figure 1).

Using all four multimorbidity definitions, prevalence (Table 1) and aORs (Table 2) of multimorbidity were higher in the most versus least deprived IMD decile: multimorbidity 2+ aOR 1.93 (95%CI 1.89-

1.97), multimorbidity 3+ aOR 2.23 (95%CI 2.18-2.28), multimorbidity 3+ from 3+ aOR 2.09 (95%CI 2.04-2.14), physical-mental multimorbidity aOR 2.14 (95%CI 2.10-2.19). Figure 2 shows multimorbidity prevalence in the most and least deprived IMD deciles by age: multimorbidity was more prevalent in the most deprived at all ages, with a widening of the gap starting at adolescence, widest in middle age, and converging in oldest age. There was a stepwise increase in multimorbidity prevalence with each IMD decile from least to most deprived for all definitions (Supplementary Figures 1 to 4).

Women had higher prevalence (Table 1) and aORs (Table 2) of multimorbidity versus men using all four definitions, although absolute differences were modest for multimorbidity 2+ (aOR 1.31 [95%CI 1.30–1.32]), and very small for multimorbidity 3+ (aOR 1.19 [95%CI 1.18-1.20]) and multimorbidity 3+ from 3+ (aOR 1.15 [1.14-1.16]). The largest differences were observed for mental-physical multimorbidity (prevalence of 22.9% in women and 14.9% in men; aOR 1.70 [95%CI 1.68-1.71] in women versus men) (Tables 1 and 2).

Figure 2 shows the widest horizontal gap between multimorbidity prevalence by age between the most and least deprived IMD deciles for each definition of multimorbidity. In multimorbidity 2+, the widest age-gap (horizontal distance between the most and least deprived IMD deciles) was 15-20 years, i.e., people in the most deprived IMD decile had similar prevalence of multimorbidity 15-20 years younger than those in the least deprived IMD decile. For multimorbidity 3+ and multimorbidity 3+ from 3+ the widest age-gap in multimorbidity prevalence was 10-15 years. However, a much larger difference of 40-45 years was seen in mental-physical multimorbidity; 34.3% of 45–49-year-olds in the most deprived IMD decile had mental-physical multimorbidity versus 31.1% of 85–89-year-olds in the least deprived (Figure 2, Supplementary Table 3).

Discussion

Summary

This study finds substantial variation in the prevalence of multimorbidity using four different published definitions of multimorbidity. Multimorbidity 2+ had the highest prevalence, followed by multimorbidity 3+ and multimorbidity 3+ from 3+, and in all these definitions prevalence was considerably higher with increasing age. The prevalence was lowest using the mental-physical multimorbidity definition, with a flatter age distribution, and higher prevalence in younger to early middle-aged adults than using the multimorbidity 3+ and multimorbidity 3+ from 3+ definitions.

Multimorbidity prevalence was higher in people living in more deprived areas, and for all definitions, inequalities (the difference in prevalence between the most and least deprived groups for each definition) were largest in middle-age. At the point of greatest difference, people in the most deprived IMD decile would have the same prevalence of multimorbidity 40-45 years using the mental-physical multimorbidity definition, 15-20 years younger using the multimorbidity 2+ definition, and 10-15 years using the multimorbidity 3+ and multimorbidity 3+ from 3+ definitions. Prevalence of multimorbidity was higher in women than men using all four definitions, although adjusted associations were weak for all but mental-physical multimorbidity.

Strengths and Limitations

Strengths of this study include systematic analysis of multimorbidity prevalence rates using a large primary care population dataset. Multimorbidity prevalence calculations using each definition were based on counting 80 LTCs (compared to a median of 17 LTCs reported in the wider literature),¹⁰ including 10 mental health conditions, and almost all the conditions recommended by a recent international Delphi consensus study.¹⁹ The study has a number of limitations however. The dataset marginally under-represents people in the most deprived IMD decile (7.6% versus 10% of the population of England). A mitigating factor is the large population size which provides improved accuracy in the estimation of variance between associations with IMD deciles and stratification by SEP. All conditions were counted as equivalent, with no weighting based on severity, impact on quality of life, or clinical outcomes. However, unweighted counts are appropriate when the purpose is to measure prevalence,¹⁹ and future research could usefully explore associations of different multimorbidity measures with patient outcomes. The study uses routinely collected data and given that these data are not collected for research purposes, errors and biases can be introduced at the collection and cleaning stages due to issues such as underreporting, data-linkage problems, and misclassification bias.²⁶ However, because these data were collected under real-world conditions they maximise representativeness and generalisability of the population studied, and allow examination of a large population size.²⁶

Comparison with existing literature

Some existing literature exists that examines different definitions of multimorbidity. Storeng et al¹¹ used patient self-report of 38 conditions in people aged 60-69 years in Norway to examine multimorbidity defined as the presence of three or more LTCs from three or more ICD-10 chapters, termed “complex multimorbidity” (the same definition as multimorbidity 3+ from 3+ in the current study). Multimorbidity 3+ from 3+ was present in 47.8% of 60-69-year-olds, which is close to the

44.4% estimate in this study, although they found larger differences in prevalence between women and men. Multimorbidity 3+ from 3+ was strongly associated with the need for assistance with activities of daily living, and moderately associated with mortality.¹¹ Kato et al¹² performed a population-based study in Japan examining multimorbidity 2+ and multimorbidity 3+ from 3+ (also termed “complex multimorbidity”) in 38889 people who were both functionally independent and not receiving any nursing care when they completed a self-report questionnaire. Multimorbidity 2+ prevalence for people ≥ 65 years was 50.2%, which is lower than the estimates in this study (69.8% in 60-69 years rising to 93.4% in ≥ 80 years). Similarly, prevalence of multimorbidity 3+ from 3+ was lower in people aged ≥ 65 years, 19.5% in people aged ≥ 65 years, compared with this study (versus 44.4% aged 60-69 years rising to 80.3% aged ≥ 80 years). These differences are likely to reflect the selection of healthier people in the Japanese study, however significant associations were also observed between both multimorbidity 2+ and multimorbidity 3+ from 3+ with mortality.

Socioeconomic deprivation was significantly associated with multimorbidity in a Scottish study by Barnett et al,⁹ who reported prevalence rates of 11.0% in most deprived area versus 5.9% in the least deprived. Similarly, Payne et al¹³ performed a retrospective cohort study also in Scotland, and found that mental health morbidity was more prevalent in areas of deprivation and was independently associated with increased rates of unplanned hospital admission. Hauswaldt et al²⁷ examined prevalence of multimorbidity 2+ and multimorbidity 3+ from 3+ in German general practices. They found that women were more likely to be multimorbid than men and the gender ratio remained stable across both definitions, however they did not examine mental-physical multimorbidity which in the current study was more strongly associated with being a woman than the other definitions.

Implications for research and/or practice

There are several areas that require further research. Large studies examining the relationship between multimorbidity types with important outcomes (such as functional status and quality of life, and unscheduled hospital admission and death) are needed because different definitions may be appropriate to facilitate targeting of particular groups of patients for intervention. This might be particularly important for mental and physical health combinations where mental health inequalities are a large driver for the difference in multimorbidity prevalence rates between most and least deprived categories using that definition. Further exploration of problems experienced by people with each definition of multimorbidity is needed, including issues relating to access to and continuity

of care, so that services and interventions can be better designed to meet the needs of people with all definitions of multimorbidity.²⁸

This work builds understanding of disparities in the prevalence of multimorbidity based on age, sex, and, most strikingly, SEP, using different definitions. A key recommendation from a recent systematic review of systematic reviews of the definition and measurement of multimorbidity is that researchers need to be explicit about the definition used and rationale for this choice, so that comparisons can be made across studies from different settings.²⁹ Using a cut-off of two or more LTCs will allow researchers to be consistent with the majority of existing research,^{10,29} however, our study shows that a markedly different population group is identified when using the mental-physical multimorbidity definition compared with this most common definition. This is important because clinical judgement is required to adapt care accordingly for people with multimorbidity where the patient experience can involve difficulties managing competing treatment demands, especially seen in people with coexisting mental and physical health LTCs (for example, the additional difficulties experienced by people with schizophrenia and cardiovascular disease and/or diabetes where the condition itself can affect the ability to engage in lifestyle changes and treatment with antipsychotics additionally predispose to cardiovascular risk).³⁰ Therefore, alternative definitions of multimorbidity, such as mental-physical, might be used to redistribute allocation of resource to general practices in areas of higher deprivation, and within these practices, towards a markedly younger population than in areas of lower deprivation where the age-distribution of mental-physical multimorbidity is very different. Therefore, GPs can promote bespoke clinical judgements and reach shared care goals about a person's needs, preferences, and health priorities³¹ for this group who are known to have worse clinical outcomes than those with physical-only multimorbidity.^{13,14}

People living in the most deprived areas experience a greater burden of multimorbidity across all definitions, with a consistent dose response effect (Supplementary Figures 1-4), and this is most marked for mental-physical multimorbidity. Therefore, it is essential that policy and funding decisions support recommendations to tackle the inverse care law,³² coordinate services to target higher need populations, providing care delivered by multidisciplinary teams in these communities, with integration of health and social care services with particular focus on delivering combined care for mental and physical health conditions.³³ Additionally, continued work is needed to support GPs with appropriate clinical decision-making tools and models of care to support them in managing individuals with multiple conditions.³¹

In conclusion, this study finds that different definitions of multimorbidity have varying associations with age, sex, and SEP. Understanding which people in society have higher rates of different definitions of multimorbidity can help GPs and policy makers plan provision of care. Establishment of international consensus over which multimorbidity definitions should be used, in both research and clinical contexts, will improve translation of research findings across studies and provide clinical benchmarking to aid identification of individuals who are more likely to require additional support.

References

1. Multimorbidity: a priority for global health research. The Academy of Medical Sciences. Available at <https://acmedsci.ac.uk/policy/policy-projects/multimorbidity> [accessed 18 April 2022] [
2. Cassell A, Edwards D, Harshfield A, et al. The epidemiology of multimorbidity in primary care: a retrospective cohort study. *Br J Gen Pract* 2018;68(669):e245. doi: 10.3399/bjgp18X695465
3. Willadsen TG, Siersma V, Nicolaisdóttir DR, et al. Multimorbidity and mortality. *J Comorb* 2018;8(1) doi: 10.1177/2235042X18804063
4. Moffat K, Mercer SW. Challenges of managing people with multimorbidity in today's healthcare systems. *BMC Fam Pract* 2015;16 doi: 10.1186/s12875-015-0344-4
5. Almirall J, Fortin M. The coexistence of terms to describe the presence of multiple concurrent diseases. *J Comorb* 2013;3(1):4-9. doi: 10.15256/joc.2013.3.22
6. Fortin M, Hudon C, Haggerty J, et al. Prevalence estimates of multimorbidity: a comparative study of two sources. *BMC Health Serv Res* 2010;10(1):111-11. doi: 10.1186/1472-6963-10-111
7. Ho IS-S, Azcoaga-Lorenzo A, Akbari A, et al. Variation in the estimated prevalence of multimorbidity: systematic review and meta-analysis of 193 international studies. *BMJ open* 2022;12(4):e057017-e17. doi: 10.1136/bmjopen-2021-057017
8. Fortin M, Stewart MP, Poitras M-ERNM, et al. A Systematic Review of Prevalence Studies on Multimorbidity: Toward a More Uniform Methodology. *Ann Fam Med* 2012;10(2):142-51. doi: 10.1370/afm.1337
9. Barnett K, Mercer SW, Norbury M, et al. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012;380(9836):37-43. doi: 10.1016/S0140-6736(12)60240-2
10. Ho IS-S, Azcoaga-Lorenzo A, Akbari A, et al. Examining variation in the measurement of multimorbidity in research: a systematic review of 566 studies. *Lancet Public health* 2021;6(8):e587-e97. doi: 10.1016/S2468-2667(21)00107-9
11. Storeng SH, Vinjerui KH, Sund ER, et al. Associations between complex multimorbidity, activities of daily living and mortality among older Norwegians. A prospective cohort study: the HUNT Study, Norway. *BMC Geriatr* 2020;20(1):21-21. doi: 10.1186/s12877-020-1425-3
12. Kato D, Kawachi I, Saito J, et al. Complex multimorbidity and mortality in Japan: a prospective propensity-matched cohort study. *BMJ open* 2021;11(8):e046749-e49. doi: 10.1136/bmjopen-2020-046749
13. Payne RA, Abel GA, Guthrie B, et al. The effect of physical multimorbidity, mental health conditions and socioeconomic deprivation on unplanned admissions to hospital: a retrospective cohort study.(Research)(Report). *CMAJ* 2013;185(5):E221. doi: 10.1503/cmaj.121349
14. Vetrano DL, Rizzuto D, Calderón-Larrañaga A, et al. Trajectories of functional decline in older adults with neuropsychiatric and cardiovascular multimorbidity: A Swedish cohort study. *PLoS Med* 2018;15(3):e1002503-e03. doi: 10.1371/journal.pmed.1002503
15. Harrison C, Britt H, Miller G, et al. Examining different measures of multimorbidity, using a large prospective cross-sectional study in Australian general practice. *BMJ open* 2014;4(7):e004694-e94. doi: 10.1136/bmjopen-2013-004694
16. Clinical Practice Research Datalink (CPRD): UK driving real-world evidence. Available at <https://cprd.com/primary-care-data-public-health-research> [accessed 15 June 2022].
17. Lewis JD, Bilker WB, Weinstein RB, et al. The relationship between time since registration and measured incidence rates in the General Practice Research Database. *Pharmacoepidemiol Drug Saf* 2005;14(7):443-51. doi: 10.1002/pds.1115
18. Kuan V, Denaxas S, Gonzalez-Izquierdo A, et al. A chronological map of 308 physical and mental health conditions from 4 million individuals in the English National Health Service. *Lancet Digital health* 2019;1(2):e63-e77. doi: 10.1016/S2589-7500(19)30012-3

19. Ho ISS, Azoaga-Lorenzo A, Akbari A, Davies J, Khunti K, Kadam U, Lyons RA, McCowan C, Mercer SW, Nirantharakumar K, Staniszezwska S, Guthrie B. Measuring multimorbidity in research: a Delphi consensus study. *BMJ Medicine* July 2022 doi: <http://dx.doi.org/10.1136/bmjmed-2022-000247>
20. HDR-UK CALIBER Phenotype Library. Available at <https://portal.caliberresearch.org> [accessed 8 June 2022].
21. Robertson L, Ayansina D, Johnston M, et al. Measuring multimorbidity in hospitalised patients using linked hospital episode data: comparison of two measures. *Int J Popul Data Sci* 2019;4(1):461-61. doi: 10.23889/ijpds.v4i1.461
22. The English Indices of Deprivation 2019; Ministry of Housing, Communities and Local Government. Available at https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/853811/loD2019_FAQ_v4.pdf [accessed 27 March 2022] [
23. RDocumentation. ageadjust.direct: Age standardization by direct method. Available at <https://www.rdocumentation.org/packages/epitools/versions/0.09/topics/ageadjust.direct> [accessed 14 June 2022].
24. R-Core-Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing. Vienna, Austria. Available from: <http://www.R-project.org>. [accessed 27 March 2021] [
25. University of Dundee Health Informatic Centre - Trusted Research Environment. Available at <https://www.dundee.ac.uk/hic/>. Accessed on 24 November 2020 [
26. Hemkens LG, Contopoulos-Ioannidis DG, Ioannidis JPA. Routinely collected data and comparative effectiveness evidence: promises and limitations. *CMAJ* 2016;188(8):E158-E64. doi: 10.1503/cmaj.150653
27. Hauswaldt J, Schmalstieg-Bahr K, Himmel W. Different definitions of multimorbidity and their effect on prevalence rates: a retrospective study in German general practices. *Prim Health Care Res Dev* 2022;23:e25-e25. doi: 10.1017/S146342362200010X
28. Salisbury C, Johnson L, Purdy S, et al. Epidemiology and impact of multimorbidity in primary care: A retrospective cohort study. *Br J Gen Pract* 2011;61(582):e12-e21. doi: 10.3399/bjgp11X548929
29. Johnston MC, Crilly M, Black C, et al. Defining and measuring multimorbidity: a systematic review of systematic reviews. *Johnston , M C , Crilly , M , Black , C , Prescott , G J & Mercer , S 2018 , ' Defining and measuring multimorbidity: a systematic review of systematic reviews ' , Eur J Public Health* <https://doi.org/10.1093/eurpub/cky098> 2018 doi: <https://doi.org/10.1093/eurpub/cky098>
30. Skou, S.T., Mair, F.S., Fortin, M. et al. Multimorbidity. *Nat Rev Dis Primers* 8, 48 (2022). <https://doi.org/10.1038/s41572-022-00376-4> [
31. NICE. Multimorbidity: clinical assessment and management. NICE guideline [NG56]. Available at <https://www.nice.org.uk/guidance/ng56> [accessed 06 June 2022]
32. Mercer SW, John P, Robson JP, et al. The inverse care law and the potential of primary care in deprived areas. 2021 *Lancet*
33. How should health policy respond to the growing challenge of multimorbidity? Policy Report 39: October 2018. Available at <https://www.bristol.ac.uk/media-library/sites/policybristol/PolicyBristol-Report-Oct18-health-challenge-multimorbidity.pdf> [accessed 06 June 2022] [

Tables and Figures.

Table 1. Characteristics of the whole study population and cohorts defined by each definition of multimorbidity.

	Whole population, no. (% of whole population) N=1,168,620	Population with multimorbidity 2+ (No., and row %)	Population with multimorbidity 3+ (No., and row %)	Population with multimorbidity 3+ from 3+ (No., and row %)	Population with mental-physical multimorbidity (No., and row %)
Whole population		4726041 (40.4%)	321920 (27.5%)	264035 (22.6%)	220774 (18.9)
Age group, years					
0 – 9	113955 (9.7)	2741 (2.4%)	617 (0.5%)	527 (0.5%)	448 (0.4%)
10 - 19	137517 (11.8)	9132 (6.6%)	2437 (1.8%)	1681 (1.2%)	3432 (2.5%)
20 – 29	122237 (10.5)	24919 (20.4%)	9620 (7.9%)	5081 (4.1%)	13614 (11.1%)
30 - 39	143243 (12.3)	39875 (27.8%)	18809 (13.1%)	10560 (7.4%)	23154 (16.2%)
40 – 49	176061 (15.1)	66748 (38.0%)	36590 (20.8%)	24782 (14.1%)	38405 (21.8%)
50 - 59	173435 (14.8)	89267 (51.5%)	57029 (32.8%)	45043 (26.0%)	46731 (26.9%)
60 – 69	141041 (12.1)	98234 (69.8%)	72820 (51.6%)	62694 (44.4%)	42985 (30.5%)
70 - 79	97843 (8.4)	82596 (84.4%)	69649 (71.2%)	62824 (64.2%)	30101 (30.7%)
≥80	63288 (5.4)	59092 (93.4%)	54349 (85.8%)	50843 (80.3%)	21904 (34.6%)
IMD decile					
1 (least deprived)	167558 (14.3)	62032 (37.0%)	40593 (24.2%)	33343 (19.9%)	25820 (15.4%)
2	129704 (11.1)	51504 (39.7%)	34680 (26.7%)	28625 (22.1%)	22291 (17.2%)
3	128234 (11.0)	51794 (40.4%)	35047 (27.3%)	29,016 (23.0%)	22917 (17.9%)
4	109986 (9.4)	45681 (41.5%)	31143 (28.3%)	25822 (23.5%)	20588 (18.7%)
5	127816 (10.9)	53601 (41.9%)	36775 (28.8%)	30377 (23.8%)	24051 (18.8%)
6	104158 (8.9)	44279 (42.5%)	30545 (29.3%)	25325 (24.3%)	20753 (19.9%)
7	108782 (9.3)	44097 (40.5%)	30291 (27.8%)	24812 (22.8%)	21220 (19.5%)
8	103501 (8.9)	43102 (41.6%)	29717 (28.7%)	24295 (23.5%)	21813 (21.1%)
9	100577 (8.6)	40019 (39.8%)	27471 (27.3%)	24295 (22.0%)	20784 (20.7%)
10 (most deprived)	88304 (7.6)	36495 (41.3%)	25658 (29.0%)	20313 (23.0%)	20537 (23.3%)
Sex					
Men	580933 (49.7)	215555 (37.1%)	146552 (25.2%)	120159 (20.7%)	86328 (14.9%)
Women	587687 (50.3)	257049 (43.7%)	175368 (29.8%)	143876 (24.5%)	134446 (22.9%)

Figure 1. Prevalence of multimorbidity by age using four different definitions.

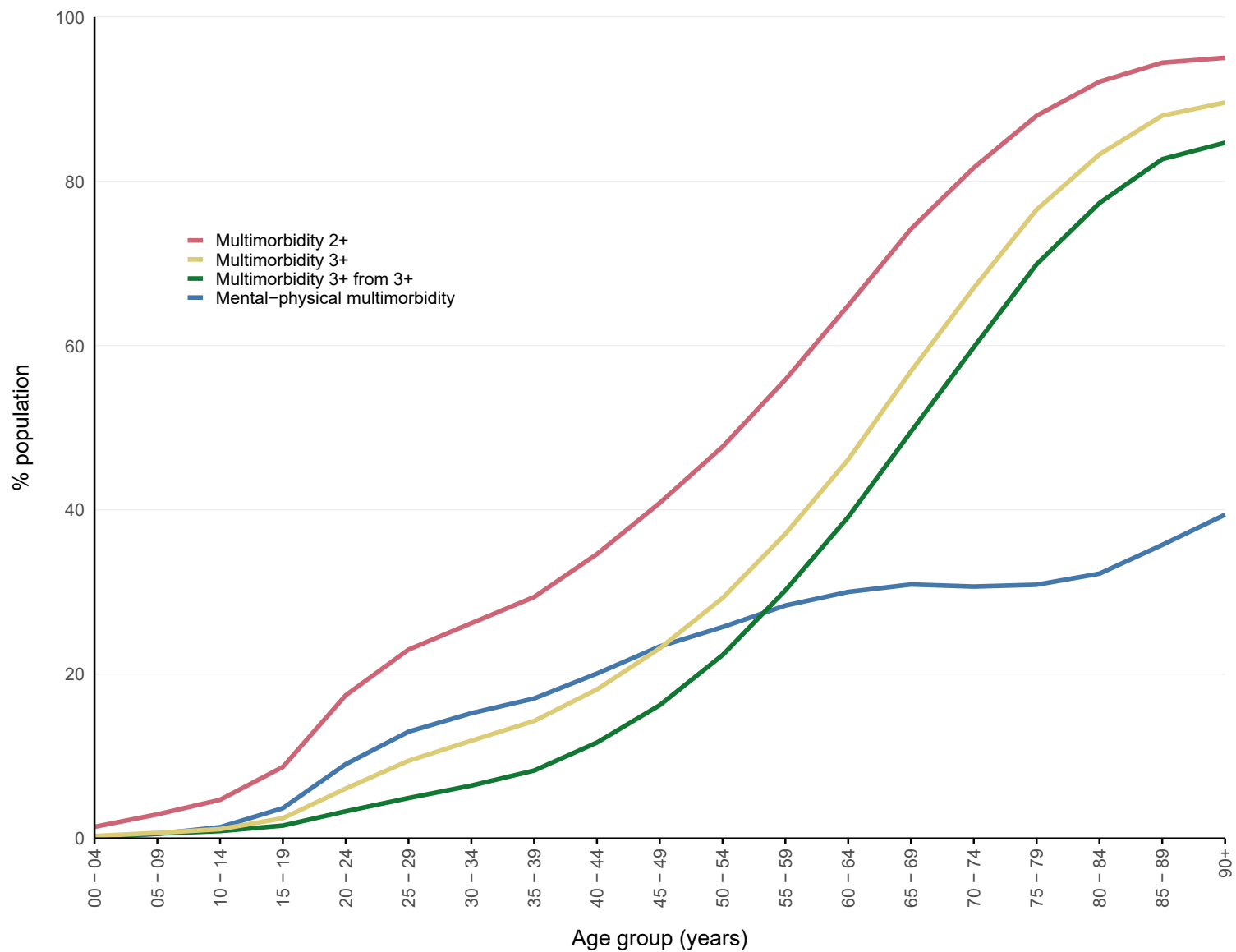
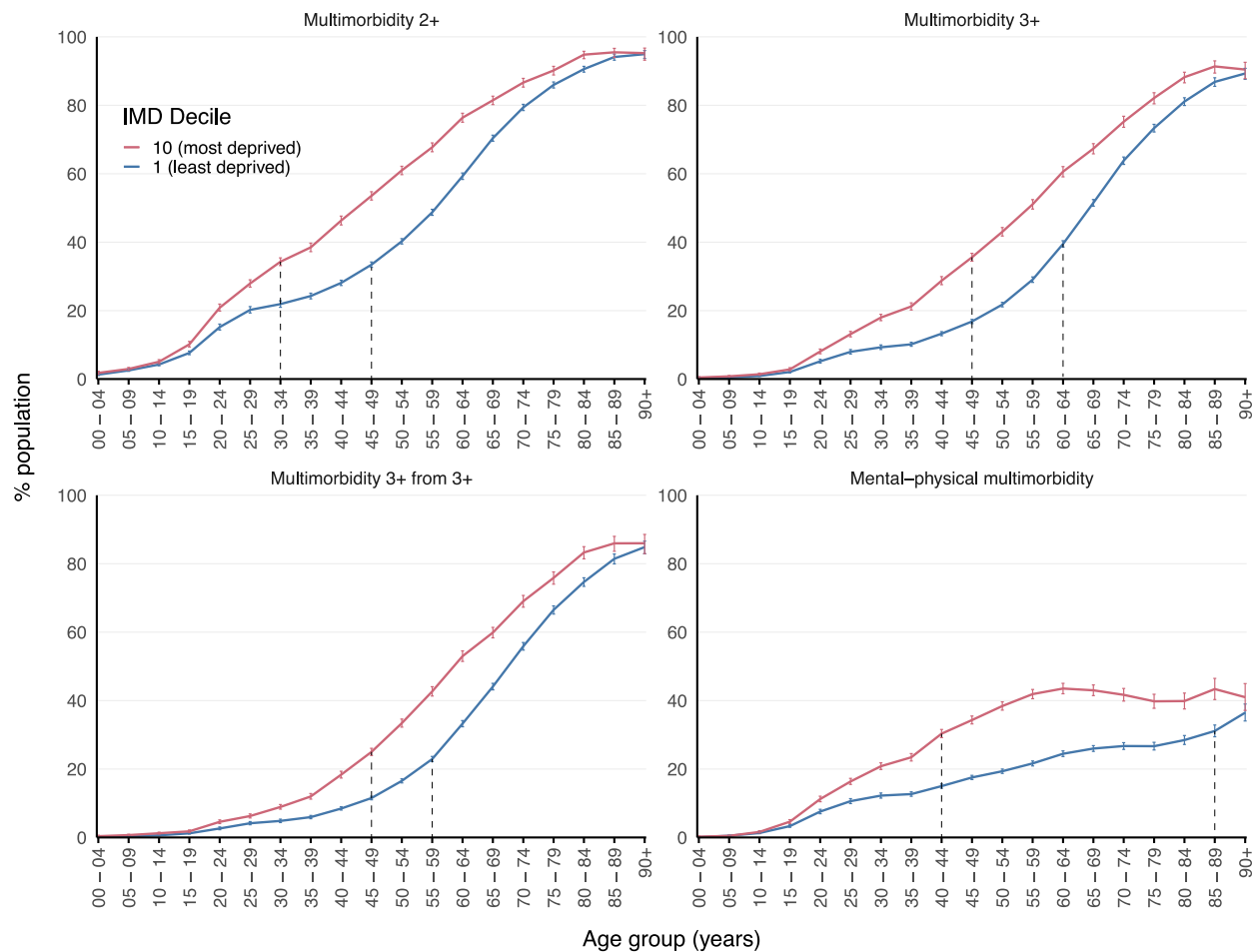


Table 2. Associations between patient characteristics and the presence of multimorbidity under four definitions.

	aOR (95% CI) for multimorbidity 2+	aOR (95% CI) for multimorbidity 3+	aOR (95% CI) for multimorbidity 3+ from 3+	aOR (95% CI) for mental-physical multimorbidity
Age group (years)^a				
0 – 9	0.10 (0.09-0.10)	0.06 (0.06-0.07)	0.11 (0.10-0.12)	0.03 (0.03-0.03)
10 - 19	0.28 (0.28-0.29)	0.22 (0.21-0.23)	0.29 (0.28-0.31)	0.21 (0.20-0.22)
20 – 29	Reference	Reference	Reference	Reference
30 - 39	1.53 (1.50-1.55)	1.80 (1.76-1.85)	1.87 (1.80-1.93)	1.55 (1.52-1.59)
40 – 49	2.50 (2.46-2.54)	3.25 (3.18-3.33)	3.98 (3.86-4.10)	2.34 (2.29-2.39)
50 - 59	4.39 (4.32-4.47)	6.16 (6.02-6.31)	8.62 (8.37-8.89)	3.14 (3.08-3.21)
60 – 69	9.60 (9.43-9.78)	13.62 (13.31-13.95)	20.31 (19.71-20.94)	3.75 (3.67-3.83)
70 - 79	22.75 (22.25-23.27)	31.82 (31.03-32.63)	45.06 (43.68-46.50)	3.77 (3.69-3.86)
≥80	58.09 (56.13-60.14)	77.69 (75.33-80.12)	102.06 (98.61-105.65)	4.32 (4.21-4.43)
IMD decile^b				
1 (least deprived)	Reference	Reference	Reference	Reference
2	1.10 (1.08-1.12)	1.12 (1.09-1.14)	1.11 (1.09-1.13)	1.12 (1.10-1.14)
3	1.16 (1.14-1.18)	1.18 (1.15-1.20)	1.17 (1.15-1.20)	1.19 (1.16-1.21)
4	1.20 (1.18-1.22)	1.22 (1.20-1.25)	1.21 (1.19-1.24)	1.24 (1.21-1.27)
5	1.25 (1.22-1.27)	1.28 (1.25-1.30)	1.25 (1.23-1.28)	1.26 (1.24-1.29)
6	1.33 (1.31-1.36)	1.38 (1.36-1.41)	1.37 (1.34-1.40)	1.38 (1.35-1.41)
7	1.37 (1.34-1.39)	1.46 (1.43-1.49)	1.43 (1.40-1.47)	1.43 (1.40-1.46)
8	1.52 (1.50-1.55)	1.63 (1.59-1.66)	1.59 (1.56-1.63)	1.63 (1.59-1.66)
9	1.63 (1.60-1.66)	1.80 (1.76-1.84)	1.74 (1.70-1.78)	1.72 (1.69-1.76)
10 (most deprived)	1.93 (1.89-1.97)	2.23 (2.18-2.28)	2.09 (2.04-2.14)	2.14 (2.10-2.19)
Sex^c				
Men	Reference	Reference	Reference	Reference
Women	1.31 (1.30–1.32)	1.19 (1.18-1.20)	1.15 (1.14-1.16)	1.70 (1.68-1.71)

^a Adjusted for socioeconomic position (SEP) and sex, ^b Adjusted for age and sex, ^c Adjusted for age and SEP

Figure 2. Prevalence of each definition of multimorbidity in the most and least deprived IMD decile, by age.



Graphical representation of the estimated multimorbidity prevalence for each of the four definitions, comparing the most and least deprived IMD decile. 95% CIs are represented by coloured vertical lines. Dashed vertical grey lines represent the point at which the horizontal gap (difference in multimorbidity prevalence) between most and least deprived IMD deciles is largest (i.e., where there is greatest inequality in the age at which people have multimorbidity).