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Multimorbidity among persons aged 25-64 years: a population-based study of social determinants and all-cause mortality.

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3 **Multimorbidity among persons aged 25-64 years: a population-based study of social determinants**
4 **and all-cause mortality.**
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ABSTRACT

Background

Despite increasing multimorbidity across the lifespan little is known about co-occurrence of conditions and risk factors among younger adults. This population-based study examines multimorbidity, social determinants and associated mortality among younger and middle-age adults.

Method

Analysis was based on the Northern Ireland population aged 25-64 years enumerated in the 2011 Census (n=878,345), with all-cause mortality follow-up to 2014 (8,659 deaths). Logistic regression was used to examine social determinants and Cox proportional hazards models in the analysis of associated mortality.

Results

Prevalence of multimorbidity was 13.7% in females and 12.7% in males. There was a strong association between multimorbidity that included mental/cognitive illness and deprivation. Among those never married, multimorbid physical conditions were less likely (RRR=0.92: 95%CI=0.88, 0.95 for males; and RRR=0.90: 0.87, 0.94 for females). Rurality was associated with lower physical multimorbidity (RRR=0.92: 0.89, 0.95) but higher mental/cognitive multimorbidity (RRR=1.35: 1.12, 1.64) among females. All multimorbid categories were associated with elevated risk of mortality.

Conclusion

The health and economic challenges created by multimorbidity should be addressed further 'upstream'. Future multimorbidity research should include younger adults to inform the development of preventative interventions and align health and social care services more closely with patients' needs.

INTRODUCTION

Life expectancy and improved childhood survival have increased the population at risk of living with both chronic conditions and persisting multimorbidity [1]. While multimorbidity affects around a third of the general population at any time [2], estimates vary substantially across settings [3-8]. Moreover, the economic costs of polypharmacy and fragmented care are significant [9-10]. Despite such problems, care management remains mainly focused on single conditions [1].

While there is an urgent need to develop policies and strategies to more effectively identify, treat and manage multimorbidity across the lifespan [10], we know little about the inter-relationships between different conditions, co-occurrence of condition combinations, and the socio-demographic determinants among younger and adults, who have been shown to have higher levels of multimorbidity in absolute terms [5]. Additionally, the co-ordination of care across mental and physical health conditions may add to the complexity. Building on earlier evidence focusing on long-term multiple conditions and their determinants in older age [11], we sought to examine prevalence and patterns of multimorbidity, and the association between multimorbidity and mortality in a population group aged 25-64 years.

METHODS

Data

This analysis is based on the Northern Ireland Mortality Study (NIMS) [12]. Briefly, it is a linkage of the enumerated 2011 Census population with subsequently occurring deaths, followed-up until the end of 2014, representing 3.75 years of follow-up mortality data (8,659 deaths). Adjusted linkage match rates (allowing for the level of completeness of the enumeration) for the 3.75 years of follow-up are 2011=97.8%, 2012=98.2%, 2013=98.4% & 2014=98.4%. All data is confidential and subject to strict controls: it is held in a secure setting by the NI Statistics and Research Agency (NISRA); is available only to accredited researchers; who access de-identified data. Use of the NI Census for research was approved by the Office for Research Ethics Committees NI (ORECNI).

Measures

Morbidity and multimorbidity

The 2011 Census included questions on eleven health conditions that '*have lasted, or are expected to last, at least 12 months*'. These included: *deafness/partial hearing loss; blindness/partial sight loss, communication difficulty; mobility/dexterity problems; learning or intellectual difficulty; emotional or mental health conditions; long-term pain; breathing difficulties; confusion or memory*

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3 *loss; chronic illness; and other conditions*. Estimates of morbidity were derived from self-reported
4 *yes/no* responses to each of the eleven conditions. A dichotomous variable was generated to
5 identify individuals reporting multimorbid states: (i) no multimorbidity (either no morbidity or a
6 reported single condition); and (ii) at least two of the self-reported conditions. Additionally,
7 conditions were identified as either *physical* (deafness, blindness, mobility difficulty, long-term pain,
8 breathing difficulty and chronic illness) or *mental/cognitive* (learning difficulty, mental health
9 condition and memory loss). *Communication difficulties* and *other disorders* were excluded as it was
10 not possible to distinguish these as having either a physical or mental base. Finally, a six-fold
11 classification of morbidity was generated: *none recorded; single physical condition; single*
12 *mental/cognitive condition; multimorbid physical conditions; multimorbid mental/cognitive*
13 *conditions; and lastly, multimorbid physical and mental/cognitive conditions*.

23 Mortality

24 All-cause mortality was determined by examining all recorded (and linked) deaths from the General
25 Registers Office from 2011 (subsequent to the Census) to the end of 2014.

30 Socio-demographic and socio-economic risk factors

31 Individual characteristics known to be associated with morbidity were drawn from the Census,
32 including: age group (five-year bands); sex; marital status (grouped as married, never married and a
33 single separated/divorced/widowed group); and area of residence (urban, intermediate and rural).
34 Three variables representing socio-economic circumstance (SEC) were included: (i) household car
35 availability (grouped as two or more cars, one car, no car access); (ii) educational attainment
36 (university level, intermediate level, no qualifications recorded) and (iii) a combination of housing
37 tenure and rateable value of the property. Rateable value had been derived as part of an exercise by
38 central government in 2010 to determine the level of local residential taxes and combined with
39 tenure to produce a meaningful eight-fold gradation: social renting; private renting; and, for owner-
40 occupiers, five categories ranging from less than £75,000 to over £200,000, with an additional
41 category comprising *properties as yet unvalued*.

53 Analysis

54 Analysis for this study was restricted to persons aged between twenty-five and sixty-four years at
55 Census, living in private households and normally resident in NI (n=878,345). Descriptive statistics
56 report the prevalence of each self-reported health condition, any condition and multimorbidity.
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3 Logistic and multinomial logistic regression examined the association between socio-demographic
4 and socio-economic factors and multimorbidity, and logistic regression models report odds ratios
5 (OR) and multinomial models report relative risk ratios (RRR). Cox proportion hazards models
6 examined all-cause mortality. All analyses were completed using Stata version 15.0.
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RESULTS

Prevalence of morbidity and multimorbidity

The overall prevalence of *morbidity* (any self-reported health condition) among all adults aged 25-64 years was 31.8% (31.4% among males and 32.2% among females). The three most prevalent conditions for both males and females were long-term pain (10.4% for males, 12.1% for females), mobility problems (9.7% for males, 10.9% for females) and mental health problems (7.3% for males and 10.1% for females). *Multimorbidity* (presence of two or more conditions) was reported by 13.2% of all persons and was more prevalent in females (13.7%) compared to males (12.7%).

Socio-demographic and socio-economic associations with multimorbidity

Table 1 examines multimorbidity *per se* in comparison with a reference category comprising people reporting either no morbidity or a single morbid condition. Odds ratios (ORs) show the likelihood of multimorbidity associated with socio-demographic and socio-economic characteristics. Among all persons multimorbidity was higher in females when compared with males (OR=1.09: 95%CI=1.08, 1.11), and increasing with age (OR=8.40: 8.11, 8.71 for those aged 60-64). There was a strong protective effect associated with being married, and those living in intermediate and rural settings (when compared to their urban peers). Housing tenure/property value as a marker for SEC showed that those in social rented accommodation were at higher risk of multimorbidity (OR=3.26: 3.15, 3.38) compared to people living in the most expensive owner-occupied housing. These patterns are largely reflected in analysis stratified by sex, with the exception of area of residence, which was not associated with multimorbidity for males.

Socio-demographic and socio-economic associations with morbidity categories

As previously indicated, individuals were assigned to a mutually exclusive morbidity category based on the number and type of self-reported health conditions. Tables 2 and 3 show, in multinomial models stratified by sex, the likelihoods associated with the selected risk factors and the morbidity/multimorbidity outcomes. Relative risk ratios (RRR) are presented and are based on fully adjusted models. Minimally adjusted model results are available on request.

Age

Generally, for both males and females, relative risks associated with physical morbidities increased uniformly by age (for example, for multimorbid physical outcomes RRR=26.72: 95%CI=24.40, 29.26; and RRR=19.47: 17.94, 21.13 for males and females aged 60-64 respectively). Outcomes comprising

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3 mental/cognitive morbidities only are distributed more evenly through the age groups and peak in
4 middle-age before declining (for example, for multimorbid mental/cognitive outcomes RRR=1.95:
5 1.52, 2.48 for males aged 55-59; and RRR=2.27: 1.74, 2.96 for females aged 45-49).
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9 10 Marital status

11 When compared to their currently married peers, those widowed/separated or divorced had
12 increased risk across all morbidity outcomes, recording elevated likelihoods of multimorbid
13 mental/cognitive conditions (RRR=3.39: 95%CI=2.79, 4.12 for males and RRR=2.08: 1.70,2.53 for
14 females). While those never married recorded elevated odds associated with multiple
15 mental/cognitive conditions and generally show higher likelihoods over all morbidity outcomes, this
16 group shows some advantage with respect to physical health, with both males and females less likely
17 to report multimorbid physical conditions (RRR=0.92: 0.88, 0.95 for males and RRR=0.90: 0.87, 0.94
18 for females).
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26 27 Socio-economic circumstance (SEC)

28 The relative risks associated with SEC reflect the standard social-class gradients associated with
29 health outcomes. The risk of multimorbid outcomes with a mental health component is considerable
30 among the most disadvantaged. For example, the likelihoods of combined physical-mental/cognitive
31 morbidities for those in social rented accommodation was RRR=4.54: 4.16, 4.95 (males) and
32 RRR=4.92: 4.55, 5.32 (females), while the risk of multiple mental/cognitive health morbidities among
33 those with no educational qualifications was RRR=5.27: 4.37, 6.36 for males and RRR=6.21: 5.00,
34 7.72 for females.
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42 43 Area of residence

44 The analysis provides no evidence of an association between area of residence for males. However,
45 for females we found rurality associated with an increased likelihood of multimorbid
46 mental/cognitive outcomes (RRR=1.35: 1.12, 1.64) and decreased likelihood of multimorbid physical
47 outcomes (RRR=0.92: 0.89, 0.95). Additionally, multimorbid physical outcomes and multimorbid
48 physical-mental/cognitive outcomes were less likely among females living in intermediate settings
49 (RRR=0.93: 0.91, 0.96 and RRR=0.93: 0.90, 0.96 respectively).
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55 56 **All-cause mortality and morbidity**

57 Table 4 shows the mortality risks associated with each of the multimorbidity classifications: overall
58 there were 8,659 deaths during the follow-up period. Results show increased mortality across all five
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3 morbidity categories in the follow-up period compared to those with no morbidity, with highest risk
4 associated with the three *multimorbidity* categories for both males and females. Likelihoods were
5 notably elevated for both multimorbidity categories with a physical health component: multimorbid
6 physical (HR=3.20: 95%CI=2.95, 3.47 for males and HR=4.11: 3.74, 4.51 for females) and multimorbid
7 physical-mental/cognitive (HR=2.98: 2.73, 3.26 for males and HR=3.84: 3.47, 4.25) in fully adjusted
8 models.
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DISCUSSION

Main finding of this study

Our study indicates that multimorbidity is a pertinent health issue across the lifespan, echoing findings by Barnett *et al* [5]. Consistent with results on older age adults in NI [11] we found elevated risks of premature mortality associated with all categories of multi-morbidity amongst those aged 25-64 years. Some noteworthy findings also emerged from analysis of social determinants of multimorbidity and morbidity among younger adults. Our study found a high risk of multimorbidity with a mental/cognitive component among the most disadvantaged. While marriage was protective against multimorbidity *per se*, the study points to some advantage with respect to physical health among people who were never married. Females living in more rural settings were also less likely to have multimorbidity with a physical component, but more likely to have mental/cognitive multimorbidity.

What is already known on this topic

Governments and healthcare systems acknowledge the urgent need to re-orientate management of care away from traditional single condition models. However, Navickas *et al* [13] suggest that progress towards more sustainable care models is hampered by limited evidence on the prevalence, risks and aetiology of multimorbidity, particularly in younger age groups [14-15]. Taylor *et al* [14] found multimorbidity prevalence of approximately 4% in adults aged 20–39 years and 15% at 40–59 years compared to 39% in those aged sixty or more. McLean *et al.* [15] found a varying profile of conditions among younger and older adults with multimorbidity more likely comprising of mixed mental and physical conditions among younger adults. More evidence is required on the types of chronic conditions that commonly occur, their risk factors and their impact on impairment, service use and mortality among younger and middle age adults to better inform a lifespan approach to multimorbidity and allow targeting of scarce resources.

Violan *et al* [16] concluded that multimorbidity is consistently associated with increasing age, lower socio-economic status (SES) and female gender. A cross-sectional study, Asfar *et al* [17], across twenty-eight countries supports these broad findings. The study also noted a negative gradient associated with multimorbidity and socioeconomic circumstance which was more marked among younger age groups. Our findings are consistent with increased risk of multimorbidity with age but suggest a stronger gradient between age and morbidity combinations that include physical conditions for both males and females. All three indicators of socio-economic circumstance were also consistently predictive of multimorbidity. Importantly, our study showed an elevated risk of

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3 morbidity for outcomes with a mental health component among the most socially deprived, echoing
4 previous research in Scotland [5]. In a review of evidence on the link between SEC and mental
5 health, Muntaner *et al* [18] consider potential mechanisms underpinning this relationship, focusing
6 on the causal direction of the link between SEC and depression and the effect of early life course
7 influences amongst more deprived population groups on mental health problems in adulthood.
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13 Beyond age, gender and SEC, little is known about other social characteristics associated with
14 multimorbidity, particularly among younger adults. A population-based approach affords the
15 opportunity to conduct a fine-grained analysis with respect to multimorbidity, exploring a wider
16 range of social determinants than has been previously considered.
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20 21 22 23 What this study adds

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25 Our findings are derived from whole population Census data and include rich and robust socio-
26 economic data on individual and household circumstance. The study strengthens the evidence base
27 on the importance of examining multimorbidity in younger age groups. Additionally, few studies
28 have been able to examine the combinations of disorders and their social determinants. Thus, while
29 multimorbidity *per se* is consistently predictive of mortality [19-22], we found higher mortality risks
30 associated with all three multimorbidity categories, with risk most elevated for profiles that included
31 a physical condition. That said, the elevated risk of mortality associated with multimorbid
32 mental/cognitive conditions also raises important questions for research and service planning.
33 Higher mortality among multimorbid individuals may reflect complex mechanisms and interactions,
34 including the association of multimorbidity with frailty, functional impairment and disability [20-
35 21,23], the role of social support [22], and the impact of fragmented care [19]. Further in-depth
36 analysis on cause-specific mortality and multimorbidity clusters, particularly among younger and
37 middle-aged adults, would enhance the evidence base and inform the management and targeting of
38 resources for combinations of multimorbid conditions.
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50 As with other studies [24-26] we found females were more likely to report multimorbidity, *per se*.
51 Further sex-specific analysis of profiles of morbidity and multimorbidity however, suggest some
52 differences between males and females in relation to other characteristics associated with different
53 profiles of morbidity, which are discussed below.
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3 Marriage is known to be protective against morbidity [27-28] and we confirmed that those
4 widowed/separated or divorced had an elevated risk of multimorbidity *per se* and all profiles of
5 morbidity. For both males and females however, those never married were less likely to report
6 multimorbid physical health outcomes, but more likely to report multimorbid outcomes with a
7 mental/cognitive component. Further exploration of the association of marital status and the
8 influence of lifestyle factors and social support/networks may be useful to untangle these complex
9 associations.
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16 People living in urban communities have been found to have higher risk of poorer physical and
17 mental health and premature mortality [29-32]. While urban-rural inequalities with respect to
18 multimorbidity is less well evidenced, Garin et al [33] reported similar findings in a cross-national
19 study. However, while we noted lower risk of physical multimorbidity among females resident in
20 intermediate and rural settings, the same group had an increased risk of mental/cognitive
21 multimorbidity, not found in other studies [30, 32]. While further research and potential refinement
22 of multimorbid categories is required, urban/rural disparities may be explained by other factors
23 including social environment, isolation, stigma, access to services, access to green spaces [34] and
24 experience of life events [35].
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33 Limitations of this study

34 The estimates of multimorbidity were derived from Census self-reports. While evidence on the
35 validity of self-reported chronic conditions obtained from Census data is limited, earlier validation
36 studies of self-reported chronic conditions point to reasonable accuracy for a range of conditions
37 [36-37] and conclude that self-reports are valid for effective use in population health management
38 interventions [37]. Secondly, the broad nature of questions relating to the range of conditions made
39 categorisation into morbidity categories (physical and mental/cognitive) and associated
40 *multimorbidity categories* problematic. Finally, it is likely that the prevalence of multimorbidity
41 (particularly multimorbid mental/cognitive conditions) is underestimated, given the broad nature of
42 the question: the question relating to mental health potentially encompasses a range of mood,
43 anxiety and behavioural conditions.
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52 Implications and future research

53 There are considerable benefits in using Census data to enhance basic knowledge of the prevalence
54 and risk of multimorbidity and associated mortality in the general population. Further work is
55 required in refining and validating census-based self-reported health indicators, particularly in
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3 relation to mental health. Our study affirms that multimorbidity poses a persisting challenge in
4 Western populations, where multimorbidity and complex multimorbidity are projected to rise [38].
5 While clinicians are aware of the association of multimorbidity, age and socio-economic
6 circumstances, they must also recognise patterns of multimorbidity and risk factors in younger and
7 middle-aged groups. Thus the evidence base on multimorbidity should include younger and middle-
8 aged adults and further studies are needed to explore the complex clustering of multiple conditions,
9 risk factors and how these change across the lifespan.
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36 **Conflict of interest**

37 None declared.
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REFERENCES

1. World Health Organisation. Multimorbidity: Technical Series on Safer Primary Care. Geneva: World Health Organization, 2016.
2. Nguyen H, Manolova G, Daskalopoulou C, Vitoratou S, Prince M, Prina AM. Prevalence of multimorbidity in community settings: A systematic review and meta-analysis of observational studies. *Journal of comorbidity*. 2019 Aug 20;9:2235042X19870934.
3. Allison F, Lix Lisa M, Kim R. Estimating multimorbidity prevalence with the Canadian Chronic Disease Surveillance System. *Health promotion and chronic disease prevention in Canada: research, policy and practice*. 2017 Jul;37(7):215.
4. de Carvalho JN, Roncalli ÂG, de Camargo Cancela M, de Souza DL. Prevalence of multimorbidity in the Brazilian adult population according to socioeconomic and demographic characteristics. *PloS one*. 2017 Apr 6;12(4):e0174322.
5. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *The Lancet*. 2012 Jul 7;380(9836):37-43.
6. Puth MT, Weckbecker K, Schmid M, Münster E. Prevalence of multimorbidity in Germany: impact of age and educational level in a cross-sectional study on 19,294 adults. *BMC public health*. 2017 Dec;17(1):826.
7. Prazeres F, Santiago L. Prevalence of multimorbidity in the adult population attending primary care in Portugal: a cross-sectional study. *BMJ open*. 2015 Sep 1;5(9):e009287.
8. Fortin M, Bravo G, Hudon C, Vanasse A, Lapointe L. Prevalence of multimorbidity among adults seen in family practice. *The Annals of Family Medicine*. 2005 May 1;3(3):223-8.
9. Picco L, Achilla E, Abdin E, et al. Economic burden of multimorbidity among older adults: impact on healthcare and societal costs. *BMC health services research*. 2016 Dec 1;16(1):173.
10. Salive ME. Multimorbidity in older adults. *Epidemiologic reviews*. 2013 Jan 1;35(1):75-83.
11. de Cock TP, Rosato M, Ferry F, Curran E, Leavey G. Patterns of long-term conditions in older age and subsequent mortality: a national study of inequalities in health. *European journal of public health*. 2019 Oct 26.
12. O'Reilly D, Rosato M, Catney G, Johnston F, Brolly M. Cohort description: The Northern Ireland Longitudinal Study (NILS). *International Journal of Epidemiology*. 2011 Feb 4;41(3):634-41.
13. Navickas R, Petric VK, Feigl AB, Seychell M. Multimorbidity: what do we know? What should we do?. *Journal of comorbidity*. 2016;6(1):4-11. Mair FS, Gallacher KL, Multimorbidity: what next?. *Br J Gen Pract*. 2017; 67 (659): 248-249.

14. Taylor AW, Price K, Gill TK et al. Multimorbidity-not just an older person's issue. Results from an Australian biomedical study. *BMC public health*. 2010 Dec 1;10(1):718
15. McLean G, Gunn J, Wyke S, Guthrie B, Watt GC, Blane DN, Mercer SW. The influence of socioeconomic deprivation on multimorbidity at different ages: a cross-sectional study. *Br J Gen Pract*. 2014 Jul 1;64(624):e440-7.
16. Violán C, Foguet-Boreu Q, Flores-Mateo G et al. Prevalence, determinants and patterns of multimorbidity in primary care: a systematic review of observational studies. *PLoS one*. 2014 Jul 21;9(7):e102149.
17. Afshar S, Roderick PJ, Kowal P, Dimitrov BD, Hill AG. Multimorbidity and the inequalities of global ageing: a cross-sectional study of 28 countries using the World Health Surveys. *BMC Public Health*. 2015 Dec;15(1):776.
18. Muntaner C, Eaton WW, Miech R, O'campo P. Socioeconomic position and major mental disorders. *Epidemiologic reviews*. 2004 Jul 1;26(1):53-62.
19. Nunes BP, Flores TR, Mielke GI, Thumé E, Facchini LA. Multimorbidity and mortality in older adults: a systematic review and meta-analysis. *Archives of gerontology and geriatrics*. 2016 Nov 1;67:130-8.
20. Wei MY, Mukamal KJ. Multimorbidity, Mortality, and Long-Term Physical Functioning in 3 Prospective Cohorts of Community-Dwelling Adults. *American journal of epidemiology*. 2017 Jun 1;187(1):103-12.
21. St John PD, Tyas SL, Menec V, Tate R. Multimorbidity, disability, and mortality in community-dwelling older adults. *Canadian family physician*. 2014 May 1;60(5):e272-80.
22. Olaya B, Domènech-Abella J, Moneta MV et al. All-cause mortality and multimorbidity in older adults: the role of social support and loneliness. *Experimental gerontology*. 2017 Dec 1;99:120-6.
23. Nguyen QD, Wu C, Odden MC, Kim DH. Multimorbidity patterns, frailty, and survival in community-dwelling older adults. *The Journals of Gerontology: Series A*. 2019 Jul 12;74(8):1265-70.
24. Abad-Díez JM, Calderón-Larrañaga A, Poncel-Falcó A et al. Age and gender differences in the prevalence and patterns of multimorbidity in the older population. *BMC geriatrics*. 2014 Dec;14(1):75.
25. Gorman BK, Read JN. Gender disparities in adult health: an examination of three measures of morbidity. *Journal of health and social behavior*. 2006 Jun;47(2):95-110.
26. Tsang A, Von Korff M, Lee S et al. Common chronic pain conditions in developed and developing countries: gender and age differences and comorbidity with depression-anxiety disorders. *The journal of pain*. 2008 Oct 1;9(10):883-91.

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27. Verbrugge LM. Marital status and health. *Journal of Marriage and the Family*. 1979 May 1:267-85.
28. Umberson D. Gender, marital status and the social control of health behavior. *Social science & medicine*. 1992 Apr 1;34(8):907-17.
29. Riva M, Curtis S, Gauvin L, Fagg J. Unravelling the extent of inequalities in health across urban and rural areas: evidence from a national sample in England. *Social science & medicine*. 2009 Feb 1;68(4):654-63.
30. Peen J, Schoevers RA, Beekman AT, Dekker J. The current status of urban-rural differences in psychiatric disorders. *Acta Psychiatrica Scandinavica*. 2010 Feb 1;121(2):84-93.
31. O'Reilly G, O'Reilly D, Rosato M, Connolly S. Urban and rural variations in morbidity and mortality in Northern Ireland. *BMC Public Health*. 2007 Dec;7(1):123.
32. Kovess-Masféty V, Alonso J, de Graaf R, Demyttenaere K. A European Approach to Rural—Urban Differences in Mental Health: The ESEMeD 2000 Comparative Study. *The Canadian Journal of Psychiatry*. 2005 Dec;50(14):926-36.
33. Garin N, Koyanagi A, Chatterji S, Tyrovolas S, Olaya B, Leonardi M, Lara E, Koskinen S, Tobiasz-Adamczyk B, Ayuso-Mateos JL, Haro JM. Global multimorbidity patterns: a cross-sectional, population-based, multi-country study. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*. 2016 Feb 1;71(2):205-14.
34. Mitchell R, Popham F. Effect of exposure to natural environment on health inequalities: an observational population study. *The Lancet*. 2008 Nov 8;372(9650):1655-60.
35. Prudo R, Brown GW, Harris T, Dowland J. Psychiatric disorder in a rural and an urban population: 2. Sensitivity to loss. *Psychological Medicine*. 1981 Aug;11(3):601-16.
36. Lee Y. The predictive value of self assessed general, physical, and mental health on functional decline and mortality in older adults. *Journal of Epidemiology & Community Health*. 2000 Feb 1;54(2):123-9.
37. Chapman, L. How valid is self-reported health data? A Chapman Institute white paper. Chapman Institute. 2012. <https://chapmaninstitute.com/resources/valid-self-reported-health-data/>. Accessed February 2018.
38. Kingston A, Robinson L, Booth H, Knapp M, Jagger C, MODEM project. Projections of multi-morbidity in the older population in England to 2035: estimates from the Population Ageing and Care Simulation (PACSim) model. *Age and ageing*. 2018 Jan 24;47(3):374-80.

Table 1. Socio-demographic and socio-economic characteristics associations with multimorbidity among persons aged 25-64. Findings represent odds ratios (OR) and 95% confidence intervals (CIs) from logistic regression models.

		All persons aged 25-64	Males aged 25-64	Females aged 25-64
	% of Group	Fully Adjusted † OR (95%CI)	Fully Adjusted † OR (95%CI)	Fully Adjusted † OR (95%CI)
Age				
25-29	4.31	1.00	1.00	1.00
30-34	5.19	1.37 (1.32, 1.43) ***	1.31 (1.23, 1.39) ***	1.43 (1.35, 1.51) ***
35-39	7.36	2.04 (1.97, 2.12) ***	1.90 (1.80, 2.01) ***	2.16 (2.06, 2.27) ***
40-44	11.32	2.91 (2.81, 3.02) ***	2.65 (2.52, 2.80) ***	3.12 (2.97, 3.27) ***
45-49	14.77	3.89 (3.76, 4.03) ***	3.61 (3.43, 3.80) ***	4.11 (3.91, 4.31) ***
50-54	17.22	5.21 (5.03, 5.40) ***	4.97 (4.72, 5.23) ***	5.38 (5.12, 5.65) ***
55-59	18.39	6.90 (6.66, 7.15) ***	6.85 (6.51, 7.21) ***	6.86 (6.53, 7.20) ***
60-64	21.44	8.40 (8.11, 8.71) ***	8.99 (8.54, 9.47) ***	7.80 (7.42, 8.20) ***
Sex				
Male	12.66	1.00		
Female	13.67	1.09 (1.08, 1.11) ***		
Marital status				
Married	11.23	1.00	1.00	1.00
Never married	11.32	1.21 (1.18, 1.23) ***	1.24 (1.21, 1.28) ***	1.17 (1.14, 1.20) ***
Widowed/Separated/Divorced	24.46	1.28 (1.25, 1.30) ***	1.26 (1.23, 1.30) ***	1.29 (1.26, 1.32) ***
Tenure/ property value¥				
£200+	6.56	1.00	1.00	1.00
£150-£199	8.62	1.25 (1.21, 1.30) ***	1.24 (1.18, 1.30) ***	1.26 (1.21, 1.33) ***
£100-£149	10.77	1.46 (1.41, 1.50) ***	1.36 (1.30, 1.42) ***	1.55 (1.48, 1.62) ***
£75-£99	13.31	1.61 (1.56, 1.67) ***	1.50 (1.43, 1.58) ***	1.72 (1.64, 1.80) ***
<£75	14.77	1.57 (1.52, 1.63) ***	1.46 (1.39, 1.54) ***	1.68 (1.59, 1.76) ***
privately rented	13.98	2.07 (2.00, 2.14) ***	1.89 (1.80, 1.99) ***	2.24 (2.13, 2.34) ***
social renting	30.53	3.26 (3.15, 3.38) ***	3.16 (3.00, 3.32) ***	3.34 (3.18, 3.50) ***
value not assigned	6.81	1.18 (1.13, 1.24) ***	1.11 (1.04, 1.18) **	1.26 (1.19, 1.34) ***
Household car access				
Two or more	8.08	1.00	1.00	1.00
One	15.83	1.47 (1.45, 1.50) ***	1.56 (1.52, 1.60) ***	1.40 (1.37, 1.43) ***
None	26.08	1.84 (1.79, 1.88) ***	2.02 (1.95, 2.09) ***	1.69 (1.64, 1.75) ***
Area				
Urban	14.59	1.00	1.00	1.00

Intermediate	13.66	0.97 (0.95, 0.98) ***	1.00 (0.98, 1.02)	0.94 (0.92, 0.96) ***
Rural	10.67	0.97 (0.95, 0.99)**	0.98 (0.96, 1.01)	0.96 (0.93, 0.98)**
Education				
Degree	6.64	1.00	1.00	1.00
Intermediate level	10.89	1.49 (1.46, 1.52) ***	1.53 (1.49, 1.58) ***	1.46 (1.42, 1.49) ***
No qualifications	27.10	2.43 (2.39, 2.48) ***	2.48 (2.41, 2.55) ***	2.42 (2.35, 2.48) ***

‡ models fully adjusted for all variables in the table. Age and sex adjusted models available on request.

¥ value measured in thousands of pounds sterling.

***: p<0.001; **: p<0.005; *: p<0.05

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Table 2. Males (25-64): socio-demographic and socio-economic variation across differing levels of multimorbidity. Results represent relative risk ratios (RRR) and 95% CIs derived from fully adjusted multinomial logistic regressions (reference group=no morbidity)

	Single physical RRR (95%CI)	Single mental/cognitive RRR (95%CI)	Multimorbid physical RRR (95%CI)	Multimorbid mental/cognitive RRR (95%CI)	Multi-morbid physical- mental/cognitive RRR (95%CI)
Age group					
25-29	1.00	1.00	1.00	1.00	1.00
30-34	1.18 (1.13, 1.24)***	1.33 (1.25, 1.43)***	1.52 (1.37, 1.69)***	1.69 (1.39, 2.05)***	1.30 (1.20, 1.42)***
35-39	1.48 (1.41, 1.54)***	1.66 (1.56, 1.78)***	2.61 (2.37, 2.89)***	1.76 (1.44, 2.14)***	1.99 (1.84, 2.15)***
40-44	1.80 (1.72, 1.88)***	1.86 (1.74, 1.99)***	4.00 (3.64, 4.40)***	1.89 (1.55, 2.30)***	2.85 (2.65, 3.07)***
45-49	2.26 (2.17, 2.36)***	1.95 (1.82, 2.08)***	5.99 (5.46, 6.57)***	1.90 (1.54, 2.33)***	4.00 (3.72, 4.30)***
50-54	2.92 (2.80, 3.05)***	2.12 (1.97, 2.28)***	9.84 (8.98, 10.79)***	1.89 (1.51, 2.36)***	5.29 (4.91, 5.69)***
55-59	3.91 (3.74, 4.09)***	2.11 (1.95, 2.28)***	16.35 (14.93, 17.91)***	1.95 (1.52, 2.48)***	6.66 (6.18, 7.17)***
60-64	5.40 (5.17, 5.65)***	1.92 (1.77, 2.10)***	26.72 (24.40, 29.26)***	1.60 (1.21, 2.10)**	7.58 (7.02, 8.17)***
Marital status					
Married	1.00	1.00	1.00	1.00	1.00
Never married	1.04 (1.02, 1.07)**	2.74 (2.62, 2.87)***	0.92 (0.88, 0.95)***	5.24 (4.42, 6.22)***	1.61 (1.55, 1.68)***
Widowed/Separated/Div	1.11 (1.08, 1.15)***	2.00 (1.90, 2.12)***	1.08 (1.04, 1.13)***	3.39 (2.79, 4.12)***	1.74 (1.67, 1.81)***
Tenure/ property value					
£200,000+	1.00	1.00	1.00	1.00	1.00
£150-£199,999	1.12 (1.08, 1.16)***	1.08 (0.98, 1.19)	1.30 (1.22, 1.39)***	1.12 (0.74, 1.72)	1.30 (1.18, 1.43)***
£100,000-£149,999	1.15 (1.11, 1.19)***	1.09 (1.00, 1.19)	1.49 (1.41, 1.58)***	1.00 (0.69, 1.46)	1.47 (1.35, 1.60)***
£75,000-£99,999	1.18 (1.13, 1.23)***	1.04 (0.95, 1.15)	1.69 (1.59, 1.80)***	0.98 (0.67, 1.45)	1.69 (1.55, 1.84)***
<£75,000	1.22 (1.16, 1.27)***	0.99 (0.90, 1.10)	1.75 (1.63, 1.87)***	0.89 (0.60, 1.33)	1.57 (1.44, 1.72)***
privately rented	1.15 (1.10, 1.20)***	1.31 (1.20, 1.44)***	1.95 (1.82, 2.09)***	1.48 (1.02, 2.16)*	2.39 (2.19, 2.60)***
social renting	1.64 (1.56, 1.72)***	2.07 (1.89, 2.27)***	3.63 (3.39, 3.88)***	2.78 (1.91, 4.04)***	4.54 (4.16, 4.95)***
no value assigned	1.05 (1.00, 1.10)	0.91 (0.81, 1.02)	1.25 (1.15, 1.36)***	0.94 (0.59, 1.50)	1.09 (0.97, 1.22)
Household Car access					
Two or more	1.00	1.00	1.00	1.00	1.00
One car	1.12 (1.10, 1.15)***	1.56 (1.49, 1.64)***	1.51 (1.46, 1.56)***	1.95 (1.64, 2.33)***	1.92 (1.85, 2.00)***
None	1.30 (1.26, 1.35)***	2.86 (2.70, 3.03)***	1.67 (1.59, 1.75)***	4.90 (4.05, 5.93)***	3.02 (2.87, 3.17)***

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Area					
Urban					
Intermediate	1.00	1.00	1.00	1.00	1.00
Rural	1.00 (0.98, 1.03)	1.03 (0.99, 1.07)	1.02 (0.98, 1.05)	1.03 (0.92, 1.16)	0.99 (0.95, 1.02)
	0.97 (0.95, 0.99)*	0.99 (0.94, 1.04)	1.00 (0.97, 1.04)	1.10 (0.94, 1.29)	0.97 (0.93, 1.01)
Education level					
Degree or higher					
Intermediate level	1.00	1.00	1.00	1.00	1.00
No qualifications	1.23 (1.20, 1.26)***	1.37 (1.31, 1.44)***	1.59 (1.54, 1.65)***	2.03 (1.68, 2.45)***	1.68 (1.60, 1.76)***
	1.32 (1.29, 1.36)***	2.43 (2.31, 2.56)***	2.19 (2.10, 2.28)***	5.27 (4.37, 6.36)***	3.55 (3.39, 3.72)***

***: p<0.001; **: p<0.005; *: p<0.05

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Table 3. Females (25-64): socio-demographic and socio-economic variation across differing levels of multimorbidity. Results represent relative risk ratios (RRR) and 95% CIs derived from a fully adjusted multinomial logistic regression (reference group=no morbidity)

	Single physical RRR (95%CI)	Single mental/cognitive RRR (95%CI)	Multimorbid physical RRR (95%CI)	Multimorbid mental/cognitive RRR (95%CI)	Multi-morbid physical- mental/cognitive RRR (95%CI)
Age					
25-29	1.00	1.00	1.00	1.00	1.00
30-34	1.13 (1.08, 1.18)***	1.37 (1.30, 1.45)***	1.49 (1.36, 1.64)***	1.56 (1.21, 2.02)**	1.50 (1.40, 1.62)***
35-39	1.37 (1.31, 1.43)***	1.74 (1.65, 1.84)***	2.35 (2.15, 2.57)***	2.23 (1.73, 2.86)***	2.50 (2.33, 2.68)***
40-44	1.65 (1.58, 1.72)***	1.71 (1.62, 1.81)***	3.77 (3.47, 4.11)***	2.22 (1.72, 2.86)***	3.60 (3.37, 3.85)***
45-49	2.03 (1.95, 2.12)***	1.76 (1.66, 1.86)***	5.61 (5.17, 6.10)***	2.27 (1.74, 2.96)***	4.67 (4.37, 4.99)***
50-54	2.58 (2.47, 2.69)***	1.50 (1.41, 1.60)***	8.59 (7.91, 9.32)***	2.20 (1.65, 2.92)***	5.78 (5.40, 6.19)***
55-59	3.26 (3.12, 3.41)***	1.41 (1.31, 1.51)***	13.42 (12.36, 14.57)***	1.84 (1.34, 2.53)***	6.56 (6.12, 7.03)***
60-64	4.29 (4.10, 4.48)***	0.88 (0.81, 0.95)**	19.47 (17.94, 21.13)***	1.34 (0.95, 1.90)	5.69 (5.30, 6.11)***
Marital status					
Married	1.00	1.00	1.00	1.00	1.00
Never married	1.06 (1.03, 1.09)***	1.55 (1.49, 1.61)***	0.90 (0.87, 0.94)***	3.22 (2.66, 3.90)***	1.43 (1.38, 1.49)***
Widowed/Separated/Div	1.07 (1.05, 1.10)***	1.72 (1.66, 1.79)***	1.06 (1.02, 1.09)**	2.08 (1.70, 2.53)***	1.78 (1.72, 1.84)***
Tenure/ property value					
£200,000+	1.00	1.00	1.00	1.00	1.00
£150,000-£199,999	1.14 (1.10, 1.19)***	1.24 (1.14, 1.34)***	1.28 (1.20, 1.36)***	1.30 (0.80, 2.11)	1.38 (1.27, 1.49)***
£100,000-£149,999	1.26 (1.21, 1.31)***	1.34 (1.25, 1.44)***	1.64 (1.55, 1.73)***	1.16 (0.74, 1.81)	1.74 (1.62, 1.88)***
£75,000-£99,999	1.37 (1.32, 1.43)***	1.40 (1.30, 1.51)***	1.83 (1.72, 1.95)***	1.44 (0.92, 2.26)	2.07 (1.91, 2.23)***
<£75,000	1.39 (1.33, 1.45)***	1.35 (1.24, 1.47)***	1.83 (1.71, 1.95)***	1.33 (0.83, 2.13)	2.02 (1.86, 2.19)***
privately rented	1.32 (1.27, 1.38)***	1.68 (1.55, 1.81)***	2.11 (1.98, 2.26)***	2.01 (1.29, 3.14)**	2.98 (2.76, 3.23)***
social renting	1.79 (1.71, 1.88)***	2.32 (2.14, 2.51)***	3.60 (3.37, 3.84)***	2.71 (1.74, 4.22)***	4.92 (4.55, 5.32)***
no value assigned	1.15 (1.09, 1.21)***	1.15 (1.04, 1.26)**	1.34 (1.24, 1.46)***	1.18 (0.68, 2.06)	1.31 (1.18, 1.45)***
Household Car access					
Two or more	1.00	1.00	1.00	1.00	1.00
One car	1.14 (1.11, 1.16)***	1.51 (1.45, 1.57)***	1.38 (1.33, 1.42)***	1.73 (1.40, 2.13)***	1.63 (1.57, 1.68)***
None	1.30 (1.25, 1.35)***	2.26 (2.15, 2.37)***	1.55 (1.47, 1.62)***	3.32 (2.62, 4.21)***	2.27 (2.17, 2.38)***
Area					
Urban	1.00	1.00	1.00	1.00	1.00
Intermediate	1.01 (0.99, 1.03)	1.01 (0.97, 1.04)	0.93 (0.91, 0.96)***	1.13 (0.97, 1.30)	0.93 (0.90, 0.96)***

Rural	0.98 (0.96, 1.00)	1.04 (1.00, 1.09)	0.92 (0.89, 0.95)***	1.35 (1.12, 1.64)**	0.99 (0.95, 1.03)
Education level					
Degree or higher	1.00	1.00	1.00	1.00	1.00
Intermediate level	1.16 (1.14, 1.19)***	1.63 (1.58, 1.70)***	1.37 (1.32, 1.41)***	1.78 (1.43, 2.21)***	1.84 (1.77, 1.91)***
No qualifications	1.40 (1.36, 1.44)***	2.56 (2.45, 2.67)***	2.09 (2.02, 2.17)***	6.21 (5.00, 7.72)***	3.79 (3.64, 3.95)***

***: p<0.001; **: p<0.005; *: p<0.05

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Table 4. All-cause mortality associated with categories of morbidity/multimorbidity. Results represent hazard ratios (HR) and 95% CIs from Cox Proportional Hazard models

Morbidity category	All persons aged 25-64			Males aged 25-64		Females aged 25-64	
	deaths (%)	Unadjusted HR (95% CI)	Fully adjusted HR (95% CI) †	Unadjusted HR (95% CI)	Fully adjusted HR (95% CI) †	Unadjusted HR (95% CI)	Fully adjusted HR (95% CI) †
No morbidity	0.45	1.00	1.00	1.00	1.00	1.00	1.00
Single Physical	1.67	3.74 (3.53, 3.96)***	2.31 (2.18, 2.45)***	3.33 (3.09, 3.60)***	2.07 (1.91, 2.24)***	4.30 (3.93, 4.71)***	2.71 (2.47, 2.98)***
Single Men/ Cog	1.09	2.44 (2.19, 2.71)***	1.77 (1.59, 1.97)***	2.93 (2.56, 3.36)***	1.82 (1.58, 2.09)***	2.10 (1.78, 2.49)***	1.72 (1.45, 2.04)***
Multi-morbid Physical	3.65	8.25 (7.79, 8.74)***	3.55 (3.34, 3.78)***	7.56 (7.01, 8.16)***	3.20 (2.95, 3.47)***	9.34 (8.55, 10.21)***	4.11 (3.74, 4.51)***
Multi-morbid Men/ Cog	2.06	4.62 (3.49, 6.13)***	2.62 (1.97, 3.48)***	4.62 (3.34, 6.40)***	2.52 (1.81, 3.50)***	3.74 (2.12, 6.61)***	2.49 (1.41, 4.40)***
Multi-morbid Phys-Men/ Cog	3.19	7.20 (6.77, 7.66)***	3.32 (3.10, 3.54)***	7.08 (6.52, 7.69)***	2.98 (2.73, 3.26)***	7.76 (7.07, 8.52)***	3.84 (3.47, 4.25)***

† models adjusted for all included indicators: sex (in model including 'all persons'), marital status, rateable value of property, household car access, educational attainment & area of residence.

***: p<0.001

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