International Journal of Epidemiology, 2019, 1340–1351
doi: 10.1093/ije/dyz052
Advance Access Publication Date: 3 April 2019
Original article

Miscellaneous

Socio-economic inequalities in life expectancy of older adults with and without multimorbidity: a record linkage study of 1.1 million people in England

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Editorial decision 27 February 2019; Accepted 13 March 2019

Abstract

Background: Age of onset of multimorbidity and its prevalence are well documented. However, its contribution to inequalities in life expectancy has yet to be quantified.
Methods: A cohort of 1.1 million English people aged 45 and older were followed up from 2001 to 2010. Multimorbidity was defined as having 2 or more of 30 major chronic diseases. Multi-state models were used to estimate years spent healthy and with multimorbidity, stratified by sex, smoking status and quintiles of small-area deprivation.
Results: Unequal rates of multimorbidity onset and subsequent survival contributed to higher life expectancy at age 65 for the least (Q1) compared with most (Q5) deprived: there was a 2-year gap in healthy life expectancy for men [Q1: 7.7 years (95% confidence interval: 6.4–8.5) vs Q5: 5.4 (4.4–6.0)] and a 3-year gap for women [Q1: 8.6 (7.5–9.4) vs Q5: 5.9 (4.8–6.4)]; a 1-year gap in life expectancy with multimorbidity for men [Q1: 10.4 (9.9–11.2) vs Q5: 9.1 (8.7–9.6)] but none for women [Q1: 11.6 (11.1–12.4) vs Q5: 11.5 (11.1–12.2)]. Inequalities were attenuated but not fully attributable to socio-economic differences in smoking prevalence: multimorbidity onset was latest for never smokers and subsequent survival was longer for never and ex smokers.

Conclusions: The association between social disadvantage and multimorbidity is complex. By quantifying socio-demographic and smoking-related contributions to multimorbidity onset and subsequent survival, we provide evidence for more equitable allocation of prevention and health-care resources to meet local needs.

Key words: Multimorbidity, inequalities, mortality, health expectancy, multi-state modelling

Key Messages

- By integrating temporal differences in multimorbidity onset, disease accumulation and survival, we quantified socio-economic and smoking-related differentials in life expectancy with and without multimorbidity at age 65.
- Compared with those living in the most deprived areas, the life expectancy advantage of the least deprived consisted of two components: delayed onset of multimorbidity (by 2 years for men and 3 years for women); and longer subsequent survival with multimorbidity (by 1 year for men but none for women).
- These differences were attenuated but not fully attributable to differences in smoker prevalence by neighbourhood deprivation. Giving up smoking appeared to have little impact on delaying the age of onset of multimorbidity compared with smokers; but served to extend years lived with multimorbidity.
- Neighbourhood deprivation is powerfully associated with the onset and subsequent survival with multimorbidity, independently of age, sex and smoking status.

Introduction

Life expectancy at age 65 in the most deprived fifth of the English population was 4 years shorter than in the least deprived fifth in 2010.[1,2] The inverse gradient between mortality and socio-economic position is well established; furthermore, deprivation affects age of multimorbidity onset and number of concurrent medical conditions.[3] However, it is uncertain how disease patterns and multimorbidity influence mortality: do disadvantaged groups acquire diseases more quickly and/or do they die earlier after becoming multimorbid? It also remains unclear how much risk factors such as smoking contribute to the inequality gaps in the years lived with and without multimorbity or whether the effects vary by sex. This is particularly relevant in ageing populations, given the trend of widening inequalities in relative mortality across several high-income countries.[4]

The prevalence of multimorbidity increases rapidly with age,[3,5–7] with multimorbidity being the norm rather than exception at very advanced ages.[5,8] Estimates vary across studies,[5,9] ranging from 55 to 98% for populations aged 60 or older, due in part to differences in the definition of multimorbidity, study setting and data-collection methods.[5] Across studies in high-income countries, prevalence is consistently higher in more disadvantaged groups.[5] Prevalence for individuals aged 30–34 in the most deprived areas was similar to those aged 45–49 in the least deprived areas in a Scottish study.[3]

Many aspects of individuals' health trajectories remain underexplored. The majority of previous studies of the association between social inequality and mortality assess rates of disease accumulation and subsequent mortality separately instead of jointly. For example, a longitudinal study characterized population subgroups with distinct differences in rates of disease accumulation,[10] whereas another study that controlled for deprivation compared baseline measures of multimorbidity for predicting mortality.[11] Studies of survival with and without multimorbidity generally report higher mortality in multimorbid individuals, and mortality rates are higher when multimorbidity is defined as the co-occurrence of at least three diseases.[12]

It is also rare that studies of health expectancies analyse disease accumulation trajectories in detail, across progressively severe disease states.[7] Previous studies focused on progressive decline in index conditions, e.g. cognitive function[13] and cardiovascular diseases,[14] without controlling for comorbidity. A recent study analysed these trajectories to develop projections of health expectancies with and without multimorbidity in an English population, but included socio-economic status as a predictor rather than reporting socio-economic differentials.[7]

This study quantifies socio-economic differences in age-specific rates of multimorbidity onset and subsequent mortality, in a cohort representative of the English population.[15,16] It also estimates socio-economic and health

behaviour differentials in years spent with one, two or at least three diseases.

Methods

Data sources

The study analyses linked electronic health records from 1.1 million English people aged 45 and over, followed up from 2001 to 2010. These individuals contribute data to the CALIBER (Clinical research using LInked Bespoke studies and Electronic health Records) programme[15] that links primary care [Clinical Practice Research Datalink (CPRD)], hospital [Hospital Episode Statistics (HES)], specialist disease registry (Myocardial Ischaemia National Audit Project) and national administrative (Office for National Statistics death registry and area deprivation) datasets. Electronic phenotypes of cardiovascular and several non-cardiovascular chronic diseases developed in previous studies were used (Supplementary Appendix A and B, available as Supplementary data at *IJE* online).[17]

Study population

This study has an open cohort design, with individuals becoming cohort members on the earliest date that they fulfilled all inclusion criteria: (i) registered with a participating primary-care practice that has agreed to data linkage; (ii) registered with a practice categorized as 'up-to-standard', based on CPRD data-quality criteria, for at least 1 year prior to study entry; (iii) aged 45 and over on 1 January 2001 or who turned 45 between 1 January 2001 and 25 March 2010.

Eligible individuals entered the study irrespective of initial health status. Approximately half (49%) of the individuals entered the study on 1 January 2001 and the remainder entered at a broadly constant rate in subsequent years. The start date was chosen such that there were sufficient observations of transitions between health states in the follow-up period, to investigate changes in health within a statistical analysis. The study end date was 25 March 2010—the latest date for which linked data were available when this study commenced. Individuals were followed up to the earliest of: death, deregistration from the practice, last data collection for the individual's practice or the study end date. The study included all 225 practices contributing linked data to CALIBER—approximately 40% of CPRD practices.[15]

The study protocol was approved by the UK Medicines & Healthcare products Regulatory Agency and registered on Clinicaltrials.gov (Identifier: NCT02609516). Further details on the dataset, its representativeness and exclusion criteria can be found in Supplementary Appendix A, available as Supplementary data at *IJE* online.

Defining multimorbidity

A chronic disease was defined as a 'health problem that requires ongoing management over a period of years or decades'[18] and which 'cannot be cured but can be controlled by medication or other therapies'.[19] A systematic literature review of the diseases included in multimorbidity studies was conducted and we received expert advice from primary-care clinicians and clinical epidemiologists on disease selection and definition (Supplementary Appendix B, available as Supplementary data at *IJE* online). Individuals concurrently having any 2 or more of a selected list of 30 major chronic diseases (Supplementary Appendix B Table 1, available as Supplementary data at *IJE* online), without any disease treated as an index or dominant condition,[20] were defined as multimorbid. Diagnosis dates of in-scope diseases were used, as estimates based on these are generally more relevant to clinicians, health-system planning and resource allocation than latent dates of disease onset. Those without any in-scope diseases were labelled 'healthy', regardless of whether they had any other diseases.

Cohort characteristics

The main unit of exposure for this study was the quintile of the English Index of Multiple Deprivation (IMD) 2007. The IMD is a composite index, combining multiple domains of relative deprivation calculated at small-area level, and the 2007 version was closest to the midpoint of the study period.[21] Based on residential addresses within small areas with an average population of 1500, eligible individuals were assigned to nationally derived quintiles, with the least deprived in quintile one (Q1) and most deprived in quintile five (Q5). The IMD has been a useful proxy for individual-level deprivation in an older population[22] and there has been little change in the geographical patterning of IMD quintiles at the small-area level for the preceding 25 years.[23]

The population was stratified by sex, IMD quintile and smoking status (never, ex and current) into 30 subpopulations, prior to analysis. The most recent smoking status recorded in primary care prior to the individual's entry into the study was used and, if unrecorded, was set to missing. Of the 1.3 million eligible individuals, 168 505 (13.1%) with missing smoking status were excluded (details in Supplementary Appendix A, available as Supplementary data at *IJE* online), as methods to treat missing values in the statistical model used have yet to be

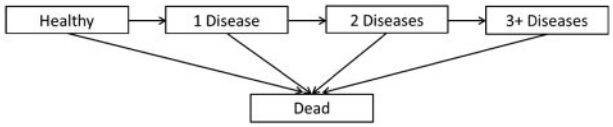

Figure 1. Structure of the multi-state model, with five health states (boxes) and seven allowable transitions (arrows) between states.

developed. Hence, 1.1 million individuals were included in the study.

Statistical methods

Age-specific multimorbidity prevalence, incidence rates and mortality rates were calculated using standard formulae,[24] by sex and IMD quintile (Supplementary Appendix D, available as Supplementary data at *IJE* online). To enable the use of parametric survival models, we verified that all transition rates changed exponentially with age (Supplementary Appendix C, available as Supplementary data at *IJE* online).

A prognostic multi-state survival model was used to analyse the non-recoverable disease progression of individuals between five health states—healthy, one disease, two diseases, at least three diseases and dead—over time. Separate models with the same structure were fitted to each of the 30 subpopulations. The health states and allowable transitions between states are shown in Figure 1, and further details on the model specification and the R package 'msm'[25] used in fitting these models are provided in Supplementary Appendix C, available as Supplementary data at *IJE* online.

The R 'ELECT' function[14] used the estimated transition rates from the multi-state model to estimate total life expectancies and partitioned them into life expectancies in each living state.

Since analyses were stratified by the risk factors (sex, IMD quintile and smoking status) rather than included as covariates, their effects on disease accumulation and mortality rates were not constrained to be proportional. We could therefore characterize state-specific life expectancies by each risk factor in detail. Within each strata, there were sufficient transitions of individuals between health states during the study to populate the model (Supplementary Table C1, available as Supplementary data at *IJE* online).

The state-specific life expectancies were estimated for the full age range of 45 and above, but are reported for the reference age of 65, in order to reflect patterns of disease accumulation and survival at older ages. Since individuals were generally healthy between ages 45 and 65 regardless of deprivation and smoking status, the use of an older reference age unmasks differential effects of these risk factors later in life.

The total life expectancies were validated against those estimated via period life table methods applied to the English population and the study cohort (Supplementary Table E3, available as Supplementary data at *IJE* online).

Results

Of the 1.1 million individuals in the study, 12.7% died during follow-up. At baseline, 47.5% were healthy, 28.3% had one disease and 24.1% were multimorbid. Individuals in the least deprived quintile (Q1) had a healthier baseline profile than those in the most deprived (Q5), with 10.9% more individuals who were healthy and 11.3% fewer individuals who were multimorbid (Table 1).

Multimorbidity prevalence, incidence rates and mortality rates

There was a clear social gradient and gap in multimorbidity prevalence between the least and most deprived quintiles between ages 45 and 80 (Figure 2). At ages 65–69, the gap in multimorbidity prevalence was 14.4% in men (Q1: 34.5%, Q5: 48.9%) and 16.7% in women (Q1: 34.1%, Q5: 50.8%) (Figure 2 and Supplementary Table D1a, available as Supplementary data at *IJE* online). The prevalences for Q1 men at ages 65–69 were comparable to those for Q5 men approximately 10 years younger, and those for Q1 women at ages 65–69 were comparable to Q5 women approximately 15 years younger.

Age-specific multimorbidity incidence rates were higher for Q5 compared with Q1 for all ages and both sexes (Figure 3 and Supplementary Table D1b, available as Supplementary data at *IJE* online). Mortality rates were on average six times as high for those with multimorbidity as those without multimorbidity, across ages and across deprivation quintiles (Figure 4 and Supplementary Tables D1c and d, available as Supplementary data at *IJE* online). All incidence and mortality rates, by sex and deprivation, displayed a broadly exponential and increasing age trend (Figures 3 and 4).

Higher incidence rates, coupled with higher mortality rates with and without multimorbidity, imply that individuals in Q5 spent less time without multimorbidity than individuals in Q1. A multi-state model was required to quantify average time spent with multimorbidity, taking into account rates of entry to and exits from each health state.

Life expectancies

Total life expectancies at age 65 by IMD quintile ranged from 18.1 years [95% confidence interval (CI): 17.5–18.4] for the least deprived (Q1) to 14.5 years (13.9–14.7) for the

Table 1. Socio-demographic and health profile of individuals aged 45 and over, by IMD 2007 quintile. England, CALIBER 2001–10

	All quintiles	Q1 (least deprived)	Q2	Q3	Q4	Q5 (most deprived)
Cohort population (*n*)	1 114 563	289 328	277 591	222 901	196 953	127 790
Deaths (*n*)	141 951	28 758	32 839	29 815	28 857	21 682
Person-years (millions)	6.34	1.70	1.60	1.27	1.08	0.68
Females (%)	53.4	52.9	53.4	53.6	54.0	53.1
Age at baseline, years						
Mean (SD)	58.8 (13.0)	58.0 (12.6)	59.0 (12.9)	59.4 (13.1)	59.2 (13.2)	58.8 (13.1)
45–54 (%)	48.8	51.7	48.0	46.8	47.8	49.4
55–64 (%)	21.4	21.2	22.2	22.0	20.9	19.9
65–74 (%)	15.8	14.9	16.0	16.4	16.3	15.9
75–84 (%)	10.3	9.0	10.2	10.7	11.2	11.3
85+ (%)	3.7	3.3	3.7	4.0	3.9	3.4
Health status at baseline						
Healthy (%)	47.5	51.8	49.0	46.7	44.4	40.9
1 disease (%)	28.3	28.3	28.2	28.5	28.5	27.8
2 diseases (%)	13.6	12.0	13.0	14.0	14.9	16.2
3+ diseases (%)	10.5	7.9	9.7	10.9	12.2	15.0
Smoking status at baseline						
Never smoker (%)	62.0	69.2	64.8	61.3	56.1	50.3
Ex smoker (%)	21.8	20.1	21.7	22.4	22.7	22.9
Current smoker (%)	16.2	10.6	13.5	16.3	21.2	26.8

most deprived (Q5) in men (Table 2) and 20.3 years (19.9–20.5) (Q1) to 17.4 years (17.0–17.6) (Q5) in women (Table 3).

For each deprivation quintile, life expectancy was separated into years spent healthy and with successively higher counts of concurrent diseases (Tables 2 and 3). For men, there was a 2.3-year gap in life expectancy without multimorbidity between Q1 and Q5 [Q1: 7.7 years (95% CI: 6.3–8.5) vs Q5: 5.4 years (4.3–6.0)], followed by a further 1.3-year gap in life expectancy with multimorbidity [Q1: 10.4 years (9.9–11.2) vs Q5: 9.1 years (8.7–9.7)]. Across quintiles, there were gradients in life expectancy in each state (Figure 5A and Supplementary Table E1, available as Supplementary data at *IJE* online). For women, there was a 2.7-year gap in life expectancy without multimorbidity [Q1: 8.6 years (7.3–9.4) vs Q5: 5.9 years (4.8–6.4)], but no additional gap in life expectancy with multimorbidity [Q1: 11.6 years (11.0–12.5) vs Q5: 11.5 years (11.1–12.2)]. Across quintiles, there were gradients in life expectancy only prior to multimorbidity onset, as women survived for approximately 11.6 years regardless of quintile after becoming multimorbid (Figure 6A and Supplementary Table E2, available as Supplementary data at *IJE* online).

To investigate whether these patterns were attributable to socio-economic differences in smoking status, Figures 5 and 6B–D each displays state-specific life expectancies stratified by smoking status. For each sex, life expectancy without multimorbidity was highest for never smokers and similar for ex and current smokers. In contrast, life expectancy with multimorbidity was similar for never and ex smokers and lowest for current smokers. This pattern was more marked for men than for women.

More generally, total life expectancies at age 65 were highest for never smokers and lowest for current smokers across ages (Tables 2 and 3). When split by smoking status, the gap in life expectancies between Q1 and Q5 persisted but narrowed slightly, from 3.6 (overall) to 2.9–3.3 years for men and from 2.9 (overall) to 2.0–2.6 years for women.

We then focused on the middle quintile (Q3) to examine life expectancies with and without multimorbidity by smoking status for ages 65–90. We have used Q3 as an exemplar because of the five population strata (by deprivation quintile) and its life-expectancy and multimorbidity accumulation patterns were closest to those for the overall England population. Furthermore, smoking-status differentials were broadly similar across all deprivation quintiles, for both sexes (Figures 7 and 8), and were thus generalizable across quintiles. For Q3 individuals aged 65, never smokers had the highest total life expectancy [men: 17.8 years (95% CI: 16.8–18.3), women: 20.0 years (19.5–20.3)], whereas life expectancy was lowest for current smokers [men: 13.4 years (12.4–14.0), women: 15.0 years (14.1–15.6)] (Tables 2A and 2B). Smoking-status differentials were decomposed into two effects: never smokers spent more remaining years

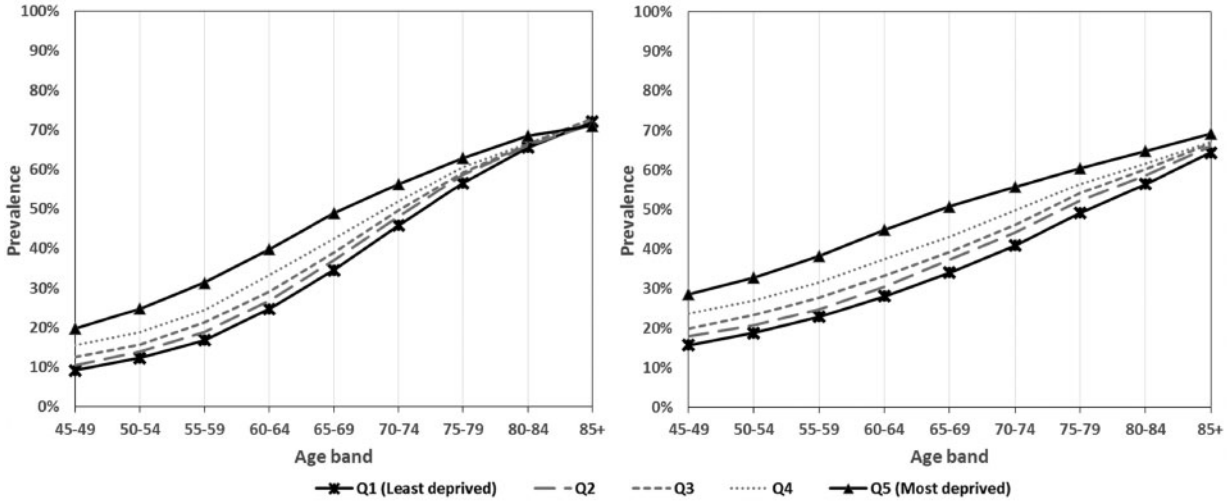

Figure 2. Prevalence of multimorbidity for adults aged 45 and over, by deprivation quintile, 2001–10, England, in men (left) and women (right).

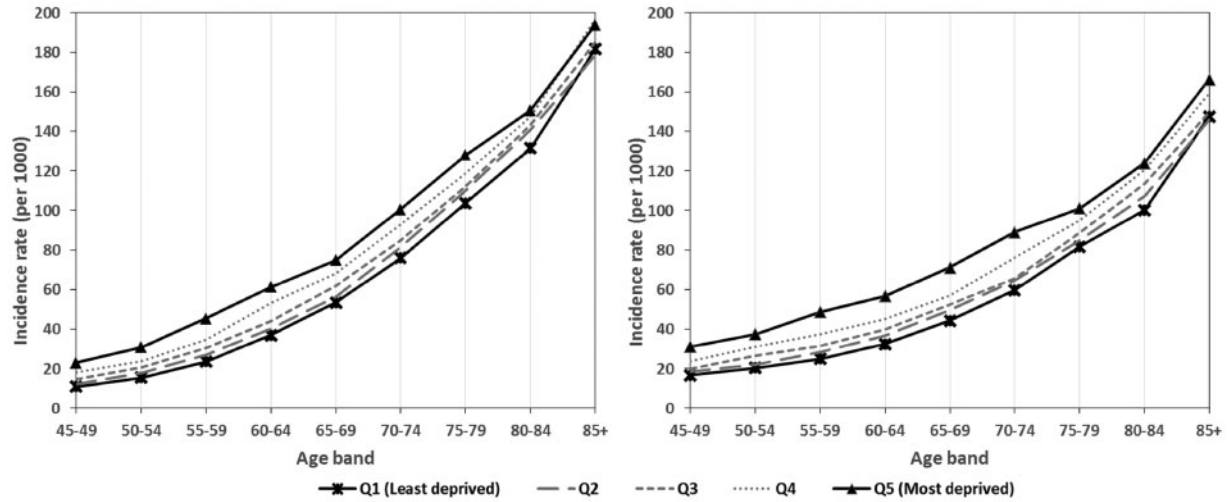

Figure 3. Incidence rates of multimorbidity for adults aged 45 and over, by deprivation quintile, 2001–10, England, in men (left) and women (right).

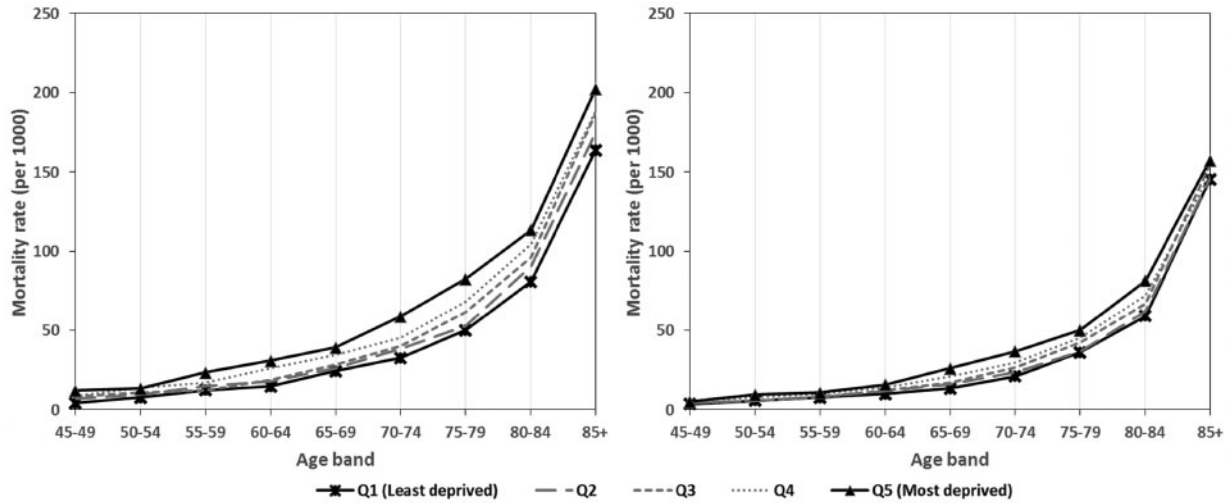

Figure 4. Mortality rates for multimorbid adults aged 45 and over, by deprivation quintile, 2001–10, England, in men (left) and women (right).

Table 2. Life expectancies for men with and without multimorbidity at age 65, by IMD 2007 quintile, smoking status and health state

		Years spent without multimorbidity (95% CI)	Years spent with multimorbidity (95% CI)	Total (95% CI)	Time spent with multimorbidity (%)
Overall	Q1 (least deprived)	7.7 (6.3, 8.5)	10.4 (9.9, 11.2)	18.1 (17.5, 18.4)	57
	Q2	7.3 (6.0, 7.9)	10.0 (9.7, 10.8)	17.4 (16.8, 17.7)	58
	Q3	6.9 (5.4, 7.6)	9.8 (9.4, 10.7)	16.7 (16.2, 17.0)	59
	Q4	6.2 (5.2, 6.8)	9.5 (9.1, 10.1)	15.7 (15.2, 16.0)	61
	Q5 (most deprived)	5.4 (4.3, 6.0)	9.1 (8.7, 9.7)	14.5 (13.9, 14.7)	63
Never smokers	Q1 (least deprived)	8.6 (6.2, 9.5)	10.3 (9.7, 11.8)	18.9 (18.0, 19.3)	54
	Q2	8.1 (5.9, 9.0)	10.1 (9.6, 11.5)	18.3 (17.5, 18.7)	55
	Q3	7.8 (5.3, 8.7)	10.0 (9.4, 11.5)	17.8 (16.8, 18.3)	56
	Q4	7.2 (5.2, 8.2)	9.8 (9.3, 11.1)	17.1 (16.3, 17.5)	58
	Q5 (most deprived)	6.6 (3.4, 7.5)	9.4 (8.8, 11.2)	16.0 (14.8, 16.5)	59
Ex smokers	Q1 (least deprived)	6.8 (4.0, 7.8)	11 (10.2, 12.7)	17.8 (16.7, 18.2)	62
	Q2	6.5 (3.8, 7.5)	10.6 (10, 12.3)	17.1 (16.0, 17.6)	62
	Q3	6.2 (3.3, 7.1)	10.5 (9.8, 12.1)	16.6 (15.4, 17.1)	63
	Q4	5.6 (3.0, 6.5)	10.0 (9.5, 11.6)	15.7 (14.6, 16.1)	64
	Q5 (most deprived)	4.9 (2.2, 5.8)	9.6 (9.1, 11.2)	14.6 (13.6, 15.1)	66
Current smokers	Q1 (least deprived)	6.3 (3.2, 7.2)	8.6 (8, 10.3)	14.9 (13.1, 15.5)	58
	Q2	5.9 (3.3, 6.8)	8.3 (7.8, 9.7)	14.3 (13.1, 14.8)	58
	Q3	5.5 (3.4, 6.3)	7.9 (7.4, 9.1)	13.4 (12.4, 14.0)	59
	Q4	4.9 (3.3, 5.6)	7.6 (7.1, 8.5)	12.6 (11.7, 12.9)	61
	Q5 (most deprived)	4.2 (2.8, 4.8)	7.4 (7.0, 8.2)	11.6 (10.9, 12.0)	64

This table is based on figures in Supplementary Appendix E, available as Supplementary data at *IJE* online.

without multimorbidity than ex and current smokers (Figures 7B and 8B); and never and ex smokers spent equal numbers of years with multimorbidity and more years than current smokers (Figures 7C and 8C). This 5-year difference between never and current smokers' total life expectancies was much larger than the overall Q3 sex differential of 2.5 years (Supplementary Tables E1 and E2, available as Supplementary data at *IJE* online).

Discussion

This large, population-based study of inequalities in multimorbidity demonstrates that socially disadvantaged men become multimorbid 2 years earlier and, after becoming multimorbid, survive for 1 year less than advantaged men. Whilst disadvantaged women become multimorbid 3 years earlier than advantaged women, this does not lead to survival differences with multimorbidity. Thus, the lower life expectancy of disadvantaged men is due to both earlier multimorbidity onset and earlier death. Conversely, for disadvantaged women, it is mainly due to earlier multimorbidity onset. The social gradient in both age of onset and survival with multimorbidity were attenuated but not fully attributable to socio-economic differences in smoking prevalence: within each deprivation quintile, the onset of multimorbidity was delayed for never smokers and subsequent survival was extended for never and ex smokers. Giving up smoking appears to have little impact on multimorbidity onset but delays subsequent death, suggesting that interventions to change some health behaviours may be more effective earlier in life.

Sex differences in survival after multimorbidity onset may be due to differences in disease combinations and their associated fatality rates. The state definitions of this multimorbidity model can be modified to investigate inequalities in the onset and progression of specific diseases.

This novel longitudinal, multi-stage and multiple-outcome approach allows us to concurrently study rates of disease accumulation and death, to derive life expectancies with and without multimorbidity. Additionally, we can estimate socio-economic, demographic and health-behaviour impacts on these quantities.

The large-scale CALIBER dataset is nationally representative.[16,17] Linking longitudinal primary care and hospital records, including dates of disease diagnoses and death, enables investigation of a broad range of chronic diseases and disease trajectories of individuals over a long time period. The incidence and mortality rates of multimorbidity reported

Table 3. Life expectancies for women with and without multimorbidity at age 65, by IMD 2007 quintile, smoking status and health state

		Years spent without multimorbidity (95% CI)	Years spent with multimorbidity (95% CI)	Total (95% CI)	Time spent with multimorbidity (%)
Overall	Q1 (least deprived)	8.6 (7.3, 9.4)	11.6 (11.0, 12.5)	20.3 (19.9, 20.5)	57
	Q2	8.1 (7.0, 8.8)	11.8 (11.3, 12.5)	19.9 (19.5, 20.1)	59
	Q3	7.6 (6.5, 8.3)	11.6 (11.1, 12.4)	19.2 (18.8, 19.5)	60
	Q4	6.8 (5.9, 7.5)	11.7 (11.2, 12.3)	18.5 (18.2, 18.8)	63
	Q5 (most deprived)	5.9 (4.8, 6.4)	11.5 (11.1, 12.2)	17.4 (17.0, 17.6)	66
Never smokers	Q1 (least deprived)	9.2 (7.4, 10.1)	11.6 (11.0, 12.9)	20.9 (20.4, 21.2)	56
	Q2	8.7 (7.4, 9.6)	11.8 (11.3, 12.7)	20.6 (20.0, 20.9)	58
	Q3	8.3 (6.7, 9.2)	11.7 (11.1, 12.9)	20.0 (19.5, 20.3)	59
	Q4	7.7 (6.0, 8.6)	12.0 (11.3, 13.2)	19.7 (19.2, 20.0)	61
	Q5 (most deprived)	7.0 (4.9, 7.9)	12.0 (11.3, 13.3)	18.9 (18.2, 19.3)	63
Ex smokers	Q1 (least deprived)	7.2 (3.4, 7.2)	12.0 (8.9, 11.6)	19.3 (18.2, 19.7)	63
	Q2	6.8 (3.6, 6.8)	12.4 (9.2, 11.3)	19.2 (18.2, 19.7)	65
	Q3	6.3 (3.4, 6.5)	12.3 (8.7, 10.8)	18.6 (17.6, 19.1)	66
	Q4	5.6 (3.4, 5.8)	12.3 (8.5, 10.0)	18.0 (17.2, 18.5)	69
	Q5 (most deprived)	4.8 (2.8, 4.7)	12.0 (8.8, 10.3)	16.7 (15.8, 17.1)	71
Current smokers	Q1 (least deprived)	6.2 (4.0, 8.4)	9.8 (11.2, 14.3)	15.9 (14.8, 16.5)	61
	Q2	5.9 (4.1, 7.9)	9.8 (11.6, 14.2)	15.7 (14.8, 16.2)	62
	Q3	5.6 (3.5, 7.5)	9.4 (11.5, 14.2)	15.0 (14.1, 15.6)	63
	Q4	5.1 (3.4, 6.7)	9.1 (11.6, 13.9)	14.1 (13.4, 14.5)	64
	Q5 (most deprived)	4.0 (2.4, 5.6)	9.3 (11.3, 13.6)	13.3 (12.8, 13.7)	70

This table is based on figures in Supplementary Appendix E, available as Supplementary data at *IJE* online.

in this study result in prevalences similar to those reported in other studies,[3,5,6] despite different disease definitions and selection criteria. The exponential distribution of diseases and deaths across ages fits the model specifications well (Supplementary Appendix C, available as Supplementary data at *IJE* online). The six-fold difference in multimorbid and non-multimorbid mortality rates suggests that it is pertinent to analyse deaths at each stage in the disease-accumulation pathway separately (Figure 1) to more accurately estimate the impact of multimorbidity on lifespan.

The main study limitations were, first, electronic health records are designed to serve health services and cannot be assumed to provide complete, accurate and standardized measures of individuals' health status.[17] For example, diagnostic coding practices may vary between primary-care providers and over time. Although minimized through record linkage, some diagnoses might be under-recorded, particularly mental health and musculoskeletal disorders.[3] Second, standard and complete measures of disease severity, duration and interactions with acute diseases were not available. Third, unlike survey data, routine health-care datasets only record ecological measures of socio-economic status. We used the best available composite index of small-area deprivation as a proxy measure of compositional and contextual effects of social environments on individuals' health.[18,26] Many studies have shown that contextual measures have an independent effect on health outcomes after taking into account individual risk factor profiles.[27,28] Ideally, both individual and area-based measures should be used together in analysis. Accordingly, we have used smoking status as a marker of individual health behaviour and small-area deprivation as a marker of the contextual effects of more upstream risks of the living environment (such as barriers to access to services, unemployment and crime, which are included in the composite index of area deprivation[21]). Contextual effects may operate through several pathways, including material or infrastructural resources, shared norms and social cohesion.[29]

Smoking is a modifiable behaviour that could be affected by disease onset. Smoking status changes in turn affect multimorbidity onset and subsequent survival. In our study, smoking status could not be incorporated as time-varying due to inconsistencies in recording practices and uncertainties in the timings of smoking-status changes. A validation study found that, whilst current smokers are likely to be correctly identified, the recording of ex and never smokers was inconsistent with prevalences from a national survey.[30]

Finally, we were unable to include other risk factors in the model because of high levels of missing data (Supplementary Table A1, available as Supplementary data

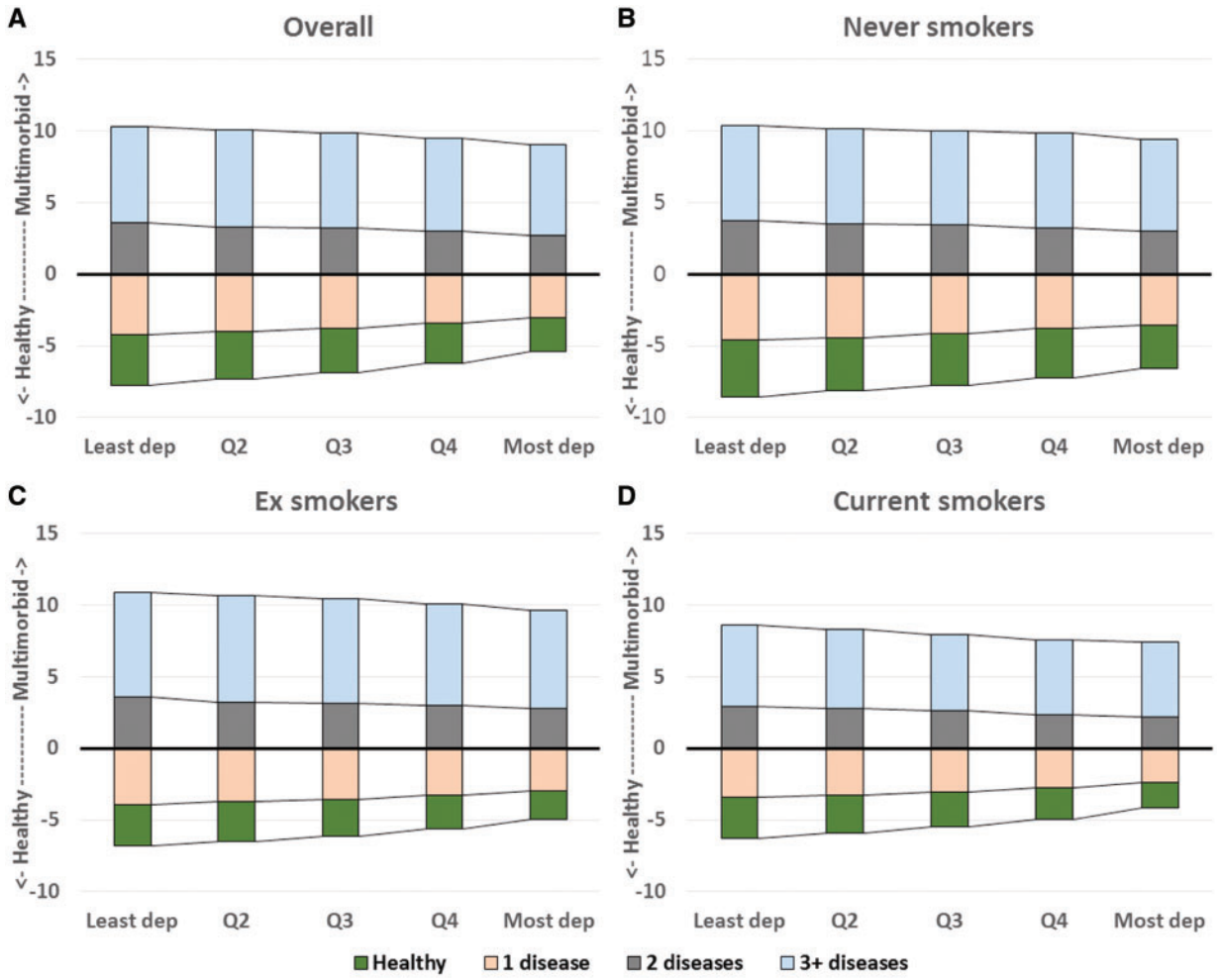

Figure 5. Life expectancies at age 65 for men—years spent with (positive) or without (negative) multimorbidity, by IMD 2007 quintile and smoking status.

The scale on the graphs has been aligned to the point of multimorbidity onset, to clearly illustrate the social gradients of both components, e.g. overall, Q1 men spend the first 7.7 years of their life without multimorbidity (–7.7 years below the line of onset) before spending the next 10.4 years with multimorbidity (+10.4 years above the line).

at *IJE* online) and the potential for model over-specification. However, health expectancies are presented in detail by sex, deprivation quintile, smoking status, age and health state, capturing the main drivers of socio-economic inequality in health outcomes.

The increasing burden of multimorbidity places strain on the National Health Service (NHS), which is a tax-funded, universal system. Our results provide compelling evidence for resource allocation that better reflects the needs of local populations. This should include not only higher levels of health-care resources and targeted interventions for prevention, but also the recruitment of a workforce with expertise in managing multimorbidity.

Supplementary data

Supplementary data are available at *IJE* online.

Funding

This work was supported by Legal & General Assurance Society Ltd and partially supported by the National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care North Thames at Bart's Health NHS Trust (NIHR CLAHRC North Thames). The views expressed in this article are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care. The funders had no role in the study design, data collection, data analysis, data interpretation or writing of the report. Mei Sum Chan and Madhavi Bajekal had full access to all the data in the study and final responsibility for the decision to submit for publication.

Acknowledgements

We wish to thank the Multimorbidity Advisory Group members: Carol Jagger (Chair), Chris Salisbury, Fiona Matthews, Brian Ridsdale and José Iparraguirre for their invaluable advice; Tim Riffe for methodological advice on the validation of health expectancies;

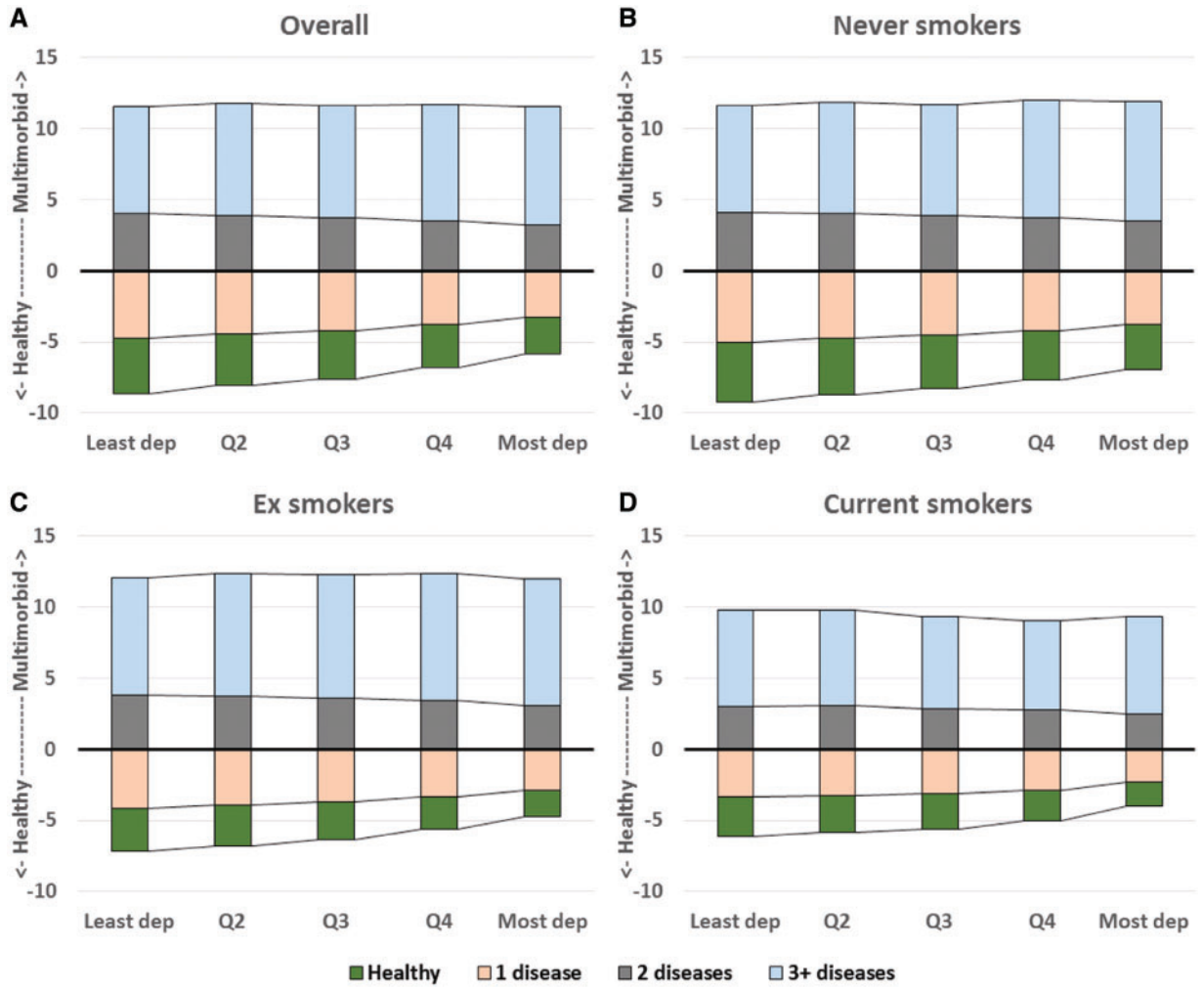

Figure 6. Life expectancies at age 65 for women—years spent with (positive) or without (negative) multimorbidity, by IMD 2007 quintile and smoking status.

The scale on the graphs has been aligned to the point of multimorbidity onset, to clearly illustrate the social gradients of both components.

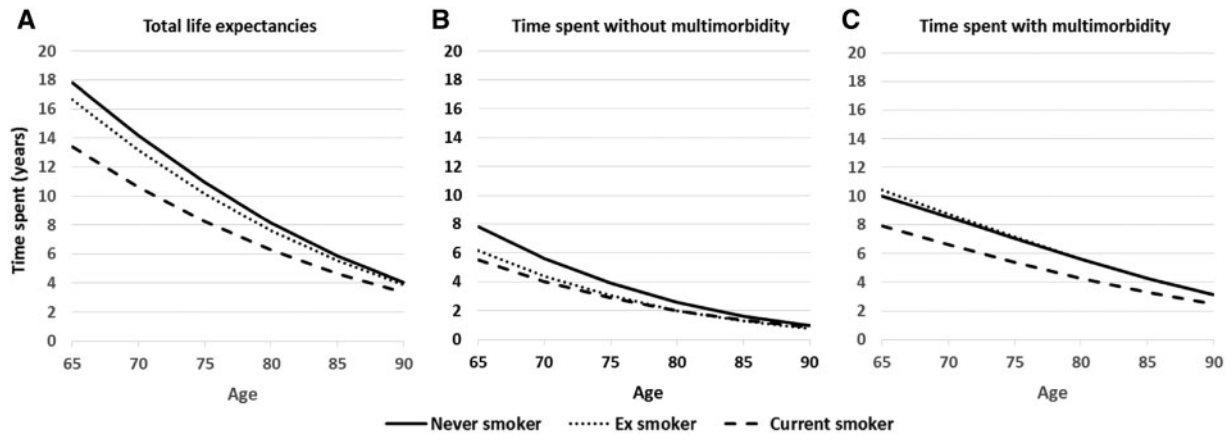

Figure 7. Total life expectancies (**A**), split into time spent without multimorbidity (**B**) and time spent with multimorbidity (**C**) at 5-year age intervals from 65 to 90, by smoking status, Q3 men.

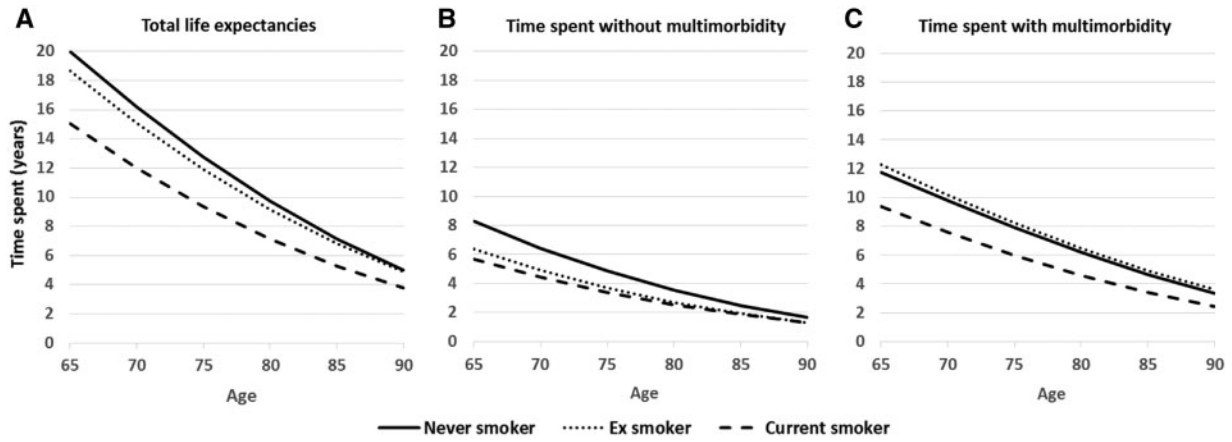

Figure 8. Total life expectancies (**A**), split into time spent without multimorbidity (**B**) and time spent with multimorbidity (**C**) at 5-year age intervals from 65 to 90, by smoking status, Q3 women.

and Joanna Cowan, Bruce Guthrie, Joseph Lu, Peter Martin and Chris Salisbury for advice on study design.

Conflict of interest: Mei Sum Chan was, and Madhavi Bajekal remains, an honorary research staff member at University College London, on secondment from their employer Legal & General Assurance Society Ltd (L&G). Ardo van den Hout received a one-off payment from L&G for statistical advice to the project. L&G has no role in study design, data collection, data analysis, data interpretation or writing of the report. All other authors have no conflict of interest to disclose.

References

1. Office for National Statistics. *Number of Deaths by Age Group, Sex and Index of Multiple Deprivation (IMD) Quintile for Lower Super Output Areas (LSOA), Deaths Registered Between 1981 and 2012*. 2014. http://www.ons.gov.uk/ons/publications/all-releases.html? definition=tcm: 77–274752017 (4 November 2017, date last accessed).
2. Office for National Statistics. *Population Estimates for UK, England and Wales, Scotland and Northern Ireland*. 2017. https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/datasets/populationestimatesforukenglandandwalesscotlandandnorthernireland2017 (4 November 2017, date last accessed).
3. 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. *Lancet* 2012;**380**:37–43.
4. Mackenbach JP, Kulhánová I, Menvielle G *et al*. Trends in inequalities in premature mortality: a study of 3.2 million deaths in 13 European countries. *J Epidemiol Community Health* 2015;**69**:207–17.
5. Marengoni A, Angleman S, Melis R *et al*. Aging with multimorbidity: a systematic review of the literature. *Ageing Res Rev* 2011;**10**:430–39.
6. Melzer D, Tavakoly B, Winder RE *et al*. Much more medicine for the oldest old: trends in UK electronic clinical records. *Age Ageing* 2015;**44**:46–53.
7. Kingston A, Robinson L, Booth H, Knapp M, Jagger C. Projections of multi-morbidity in the older population in England to 2035: estimates from the Population Ageing and Care Simulation (PACSim) model. *Age Ageing* 2018;**47**:374–80.
8. Fortin M, Stewart M, Poitras ME, Almirall J, Maddocks H. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. *Ann Fam Med* 2012;**10**:142–51.
9. Diederichs C, Berger K, Bartels DB. The measurement of multiple chronic diseases—a systematic review on existing multimorbidity indices. *J Gerontol A Biol Sci Med Sci* 2011;**66**:301–11.
10. Strauss VY, Jones PW, Kadam UT, Jordan KP. Distinct trajectories of multimorbidity in primary care were identified using latent class growth analysis. *J Clin Epidemiol* 2014;**67**:1163–71.
11. Brilleman SL, Salisbury C. Comparing measures of multimorbidity to predict outcomes in primary care: a cross sectional study. *Fam Pract* 2013;**30**:172–78.
12. Nunes BP, Flores TR, Mielke GI, Thume E, Facchini LA. Multimorbidity and mortality in older adults: a systematic review and meta-analysis. *Arch Gerontol Geriatr* 2016;**67**:130–38.
13. van den Hout A. *Multi-State Survival Models for Interval-Censored Data*. Boca Raton: CRC/Chapman & Hall, 2014.
14. Asaria M, Walker S, Palmer S *et al*. Using electronic health records to predict costs and outcomes in stable coronary artery disease. *Heart* 2016;**102**:755–62.
15. Denaxas SC, George J, Herrett E *et al*. Data resource profile: cardiovascular disease research using linked bespoke studies and electronic health records (CALIBER). *Int J Epidemiol* 2012;**41**:1625–38.
16. Herrett E, Gallagher AM, Bhaskaran K *et al*. Data resource profile: Clinical Practice Research Datalink (CPRD). *Int J Epidemiol* 2015;**44**:827–36.
17. Pujades-Rodriguez M, George J, Shah AD *et al*. Heterogeneous associations between smoking and a wide range of initial presentations of cardiovascular disease in 1937360 people in England: lifetime risks and implications for risk prediction. *Int J Epidemiol* 2015;**44**:129–41.
18. World Health Organization. *Innovative Care for Chronic Conditions: building Blocks for Action: global Report*. Geneva: World Health Organization, 2002.

19. Department of Health. *2010 to 2015 Government Policy: Long Term Health Conditions*. London: Department of Health, 2015.
20. Salisbury CJ, Mercer SW, Fortin M (eds). *The ABC of Multimorbidity*. Oxford: Wiley-Blackwell, 2014.
21. Department for Communities and Local Government. *Indices of Deprivation 2007*. London: Department for Communities and Local Government, 2008.
22. Bajekal M, Scholes S, O'Flaherty M, Raine R, Norman P, Capewell S. Unequal trends in coronary heart disease mortality by socioeconomic circumstances, England 1982–2006: an analytical study. *PLoS One* 2013;**8**:e59608.
23. Gregory IN. Comparisons between geographies of mortality and deprivation from the 1900s and 2001: spatial analysis of census and mortality statistics. *BMJ* 2009;**339**:b3454.
24. Kirkwood BR, Sterne J. *Essential Medical Statistics*, 2nd edn. Oxford: Blackwell Science, 2003.
25. Jackson C. Multi-state models for panel data: the MSM package for R. *J Stat Softw* 2011;**38**:1–28.
26. Grundy E, Holt G. The socioeconomic status of older adults: how should we measure it in studies of health inequalities? *J Epidemiol Community Health* 2001;**55**:895–904.
27. Foster HME, Celis-Morales CA, Nicholl BI *et al*. The effect of socioeconomic deprivation on the association between an extended measurement of unhealthy lifestyle factors and health outcomes: a prospective analysis of the UK Biobank cohort. *Lancet Public Health* 2018;**3**:e576–85.
28. Silhol R, Zins M, Chauvin P, Chaix P. Investigating the spatial variability in incidence of coronary heart disease in the Gazel Cohort: the impact of area socioeconomic position and mediating role of risk factors. *J Epidemiol Community Health* 2011;**65**:137–43.
29. MacIntyre S, Ellaway A, Cummins S. Place effects on health: how can we conceptualise, operationalise and measure them? *Soc Sci Med* 2002;**55**:125–39.
30. Marston L, Carpenter JR, Walters KR *et al*. Smoker, ex-smoker or non-smoker? The validity of routinely recorded smoking status in UK primary care: a cross-sectional study. *BMJ Open* 2014;**4**:e004958.