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# The impact of multimorbidity on health care costs and utilisation: a systematic review of the UK literature

Soley-Bori Marina, Ashworth Mark, Bisquera Alessandra, Dodhia Hiten, Lynch Rebecca, Wang Yanzhong, Fox-Rushby Julia

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#### Authors

Marina Soley-Bori , Mark Ashworth, Alessandra Bisquera, Hiten Dodhia, Rebecca Lynch, Yanzhong Wang, and Julia Fox-Rushby

### Authors' affiliations

Marina Soley-Bori, PhD, Research Fellow in Health Economics, King's College London, School of Population Health Sciences, London, UK.

Mark Ashworth, DM, MRCP, FRCGP, Reader in Primary Care, King's College London, School of Population Health Sciences, London, UK.

Alessandra Bisquera, MSc, Research Fellow in Medical Statistics, King's College London, School of Population Health Sciences, London, UK.

Hiten Dodhia, MBChB, MSc, FFPH, Consultant in Public Health (Lambeth Council), Visiting Lecturer at King's College London; London, UK.

Rebecca Lynch, PhD, Research Fellow in Medical Anthropology, King's College London, School of Population Health Sciences, London, UK.

Yanzhong Wang, PhD, Reader in Medical Statistics, King's College London, School of Population Health Sciences, London, UK.

Julia Fox-Rushby, PhD, Professor of Health Economics, King's College London, School of Population Health Sciences, London, UK.

### **Corresponding author information**

Marina Soley-Bori King's College London, School of Population Health Sciences Guy's Campus, Addison House, Workspace AH 3.04 London SE1 1UL Marina.soley\_bori@kcl.ac.uk

#### 1 ABSTRACT 2 Background: Managing multimorbidity is complex for both patients and healthcare systems. 3 4 Multimorbid patients often use a variety of primary and secondary care services. Country-specific 5 research exploring the utilisation and cost consequences of multimorbidity may inform future 6 interventions and payment schemes in the UK. 7 Aim: To assess the relationship between multimorbidity, healthcare costs and utilisation. To determine how this relationship varies by disease combinations and health care components. 8 9 Design of study: Systematic literature review using Bidirectional Citation Search to Completion 10 (BCSC). References and citations from initial articles were iteratively reviewed until no further 11 sources were found. 12 Method: MEDLINE and grey literature were searched for UK studies since 2004. An iterative review 13 of references and citations was completed. Authors from all papers selected were asked to check 14 for completeness of UK evidence. A quality assessment tool was used to assess risk of bias (National 15 Institute of Health National Heart, Lung, and Blood Institute tool). Data were extracted, findings synthesized, and study heterogeneity assessed; meta-analysis was conducted when possible. 16 17 **Results**: Seventeen studies were identified, 7 predicting healthcare costs and 10 utilisation. 18 Multimorbidity is associated with increased total costs, hospital costs, care transition costs, primary care use, dental care use, emergency department use and hospitalisations. Several studies 19 20 demonstrated the high cost of depression and of hospitalisation associated with multimorbidity. 21 Conclusion: In the UK, multimorbidity increases utilisation and costs of primary, secondary and dental care. Future research is needed on whether integrated care schemes offer efficiencies in 22 23 health care provision for multimorbidity. 24

### 25 How this fits in

- 26 Multimorbidity, the presence of two or more conditions, is becoming the norm rather than the
- 27 exception in primary care. Our review of 17 UK studies has drawn attention to both the high service
- 28 utilisation and cost of providing health care to patients with multimorbidity, particularly when
- 29 depression is one of the conditions. One unanswered question is whether models of 'integrated
- 30 care' might mitigate the high cost of care.
- 31

## 32 **1. INTRODUCTION**

With improvements in public health and access to good quality care, people are living longer but 33 34 frequently with multimorbidity. Multimorbidity—often defined as the coexistence of two or more 35 conditions(1)—challenges quality improvement and cost-containment efforts. In 2015, 54% of 36 England's over-65 population exhibited multimorbidity; this percentage is projected to increase to 37 68% by 2035(2). The current single disease-oriented model of care delivery struggles to address the 38 needs of multimorbid patients, who often experience care fragmentation, difficulty in managing 39 their treatments, and poor health outcomes(3-6). The Quality and Outcomes Framework (QOF), a 40 quality improvement programme available to all GP practices in England since 2004, links payments 41 to 77 indicators reflecting public health and clinical targets(7). However, as it takes no account of 42 multimorbidity(8–10), GPs are not incentivised through this significant mechanism to focus on 43 multimorbidity.

- 44 Besides quality of care shortfalls, multimorbidity may also result in higher healthcare utilisation and
- 45 costs compared with single health conditions(11). Lehnert and colleagues systematically reviewed 35
- 46 studies of the relationship between multimorbidity, costs and utilisation. They showed that costs

- 1 and utilisation (including physician visits, hospitalisations, and medication use) tend to increase with
- 2 the number of conditions. Lehnert's review, conducted in 2010, did not find any UK studies on this
- 3 topic. The relationship between multimorbidity and costs and utilisation, particularly its magnitude,
- 4 may vary not only by person-specific and environmental factors (e.g. frailty, income deprivation,
- 5 availability of social care services), but also across health systems (12,13).
- 6 This article summarizes findings on the relationship between multimorbidity, costs and utilisation in
- 7 the UK, with additional focus on the definition of multimorbidity, analytic methods used, study
- 8 limitations and research gaps. Implications for research and policy are also identified.

### 9 **2. METHODS**

- 10 This systematic search of literature followed the Bidirectional Citation Search to completion (BCSC)
- 11 method. BCSC starts by selecting an initial set of relevant papers ('pearls'), based on expert
- 12 knowledge or a systematic literature review, followed by a review of references and citations of the
- 13 'pearls' to gather further appropriate literature. After excluding irrelevant papers from the reference
- 14 and citation search, this process is repeated until no further sources are found. BCSC mirrors
- 15 snowballing of citation searches forward and backward, and iteratively repeats this process until no
- 16 further studies are identified. Although rarely used as the primary method of systematic searching,
- 17 BCSC may be an equally effective technique to comprehensively gather studies than a conventional
- 18 systematic literature review (14,15).
- 19 To identify the initial list of pearls, the authors' initial knowledge of papers was supplemented by a
- 20 Boolean logic search on Medline. The query (Appendix 1) combined terms used in the NICE
- 21 multimorbidity guidelines(16), Medline UK filter(17), and two systematic literature reviews on
- 22 multimorbidity(1,18). The NICE Evidence Search catalogue(19), SIGN (20), and the website of the
- 23 International Research Community on Multimorbidity(21) were also used to identify additional
- 24 publications and grey literature.
- 25 Two authors independently reviewed the first 100 titles and abstracts. The study inclusion and
- 26 exclusion criteria (**Table 1**) were further refined after discussing discrepancies and a second double
- 27 review of 100 sources was conducted. The first author screened the remaining articles. To target
- 28 original research testing the relationship between multimorbidity and costs and utilisation,
- 29 descriptive cost-of-illness, economic burden, or cost-effectiveness studies were excluded, along with
- 30 literature reviews, meta-analyses, and study protocols. Results of the search and selection are
- reported in accordance with PRISMA guidelines(22) (**Figure 1**, *Panel a*). The final list of selected
- 32 articles was shared with the corresponding author of each paper to check for comprehensiveness.
- 33 Data extraction and analysis focused on the study aims, definition of multimorbidity, justification of
- 34 analytic framework and econometric techniques to estimate cost and utilisation models, findings,
- 35 stated limitations, and research gaps. Risk of bias was assessed with the National Institute of
- 36 Health's Heart, Lung, and Blood Institute quality assessment tools for observational cohort and
- 37 cross-sectional studies(23). Following piloting of the data extraction form, two authors extracted
- 38 data on a randomly selected 10% of papers to check for consistency, the first author extracted the
- **39** remainder. The results were grouped by cost or utilisation study type, tabulated (**Table S1**), and
- 40 reported narratively. Multimorbidity parameter estimates, which quantify its relationship with costs
- 41 and utilisation, were gathered and systematically presented for analysis. The heterogeneity among
- 42 studies was assessed with  $I^2$  and data were pooled in a meta-analysis when possible.
- 43 **3. RESULTS**

- 1 This review identified 1,304 articles from the electronic searches, excluding duplicates. A total of 9
- 2 articles (initial "pearls") met our inclusion criteria after title, abstract, and full-text review (Figure 1,
- 3 *Panel a*). By inspecting the references and citations of the initial pearls, 8 more papers were selected
- 4 (Figure 1, Panel b), producing 17 papers for synthesis (3,13,24–38) (Appendix 3). Contact with study
- 5 authors (65% response) produced no further papers.

# 6 **3.1. Study aims and data**

7 The relationship between multimorbidity and healthcare utilisation was explored in ten studies,

8 while seven papers tackled multimorbidity and costs. Six studies covered the UK, nine focused on

9 England and two on Scotland. Both cross-sectional and longitudinal study designs were used, with up

- 10 to 8 years of participant follow up. The average sample size was 210,495 individuals (range 419(24)
- 11 to 819,590(25)) among the utilisation studies and 109,746 individuals (range 39,381(26) to
- 12 282,887(27)) for the cost studies.

# 13 **3.2. Definition of Multimorbidity**

14 Large variability in the type of diseases considered to create the multimorbidity or condition count

- 15 indicators was observed (Figure S1). All studies included conditions pertaining to the endocrine, and
- 16 cardiovascular and circulatory systems. However, only a few (n=5) considered the reproductive
- 17 system or infectious diseases. QOF conditions were used in 5 studies. The number of diseases
- 18 included in the multimorbidity or disease count measures ranged from 4 to any (see Appendix 4).
- 19 For example, Charlton and colleagues only considered CHD, stroke, colorectal cancer, and
- diabetes(27), while Payne and colleagues included 40 conditions covering almost all body
- 21 systems(28). Most studies did not provide an explicit definition of multimorbidity; six studies
  22 formally defined multimorbidity as two as more participant. Two studies as he can be as a formally defined multimorbidity.
- formally defined multimorbidity as two or more conditions. Two studies only considered long term
- 23 conditions to build their multimorbidity measures, while six studies focused on chronic conditions.

# 24 **3.3.** Characteristics of the studies on multimorbidity and utilisation

- 25 Some focal points of multimorbidity and utilisation studies included the interplay among
- 26 multimorbidity, deprivation and utilisation, the combination of mental and physical conditions, the
- 27 effect of multimorbidity among individuals with a long-term condition, and the comparison of
- 28 alternative multimorbidity measures (**Table S1**, Panel a).
- 29 Most studies (6 out of 10) explored the determinants of unscheduled care use, including emergency
- 30 department visits and hospital visits. Three studies aimed to explain primary care utilisation, while
- 31 one study explored dental care use. Seven studies applied a retrospective cohort study design, while
- 32 cross-sectional (n=2) and prospective cohort study designs were used in the remaining papers. Six
- 33 studies presented a justification for their analytic framework, including a study hypothesis (n=6) or a
- 34 reasoning behind the utilisation model specification (n=3). Most utilisation models were calibrated
- 35 using binary (use/non-use) logistic regression (n=7). Other multivariate regression techniques
- 36 included OLS with a log-transformed dependent variable, GLM with a log-link and a negative
- 37 binomial distribution, and a negative binomial regression. The most common predictors were age,
- gender, and deprivation. Other less common independent variables were education level, smoking
   status, distance to nearest hospital, and patient satisfaction. Three papers assessed the goodness of
- 40 fit of the utilisation models (29–31).
- 41 Multimorbidity contributes to higher healthcare utilisation, except for prolonged hospital stay
- 42 among the oldest patient group (90+ years) (**Table 2**). Patients with 4 or more conditions have
- 43 almost 15 times the odds of experiencing an unplanned potentially preventable hospitalisation

- 1 (OR=14.38)(28). The combination of mental and physical conditions particularly increases the
- 2 probability of unplanned hospital care, between 58% and a 100% (28,31,36). In primary care,
- 3 multimorbidity—defined as 2 or more morbidities—more than doubles its expected use (OR=2.56)
- 4 compared to 0-1 morbidities (3). Adding a multimorbidity measure to a primary care utilisation
- 5 model already accounting for age, gender, deprivation, and GP practice fixed effects notably
- 6 improves goodness of fit (R-squared increased from 0.22 to 0.37 with ACG categories or 0.42 with
- 7 number of prescribed drugs)(30).
- 8 Review Manager 5 was used to calculate the overall effect of multimorbidity on healthcare
- 9 utilisation. Results from the random effects model (Appendix 6) suggest that people with
- 10 multimorbidity are expected to use health services 2.56 times more than people without
- 11 multimorbidty (OR=2.56, 95% 1.88-3.47). An I<sup>2</sup> =99% indicates considerable heterogeneity among
- 12 our studies, which highlights that the meta-analysis results should be considered with caution.
- 13

### 14 **3.4.** Characteristics of the studies on multimorbidity and costs

- 15 Exploration of multimorbidity and costs included the interplay between multimorbidity and
- 16 deprivation, the cost impact of specific disease combinations, the relationship between age, time-to-
- 17 death, and multimorbidity, and the comparison of alternative multimorbidity measures, among
- 18 others (Table S1, panel b).
- 19 Four main types of costs were assessed: total, primary care, hospital, and care transition costs. **Table**
- 20 3 shows that most studies (5 out of 7) included hospital costs. Among the three studies that explored
- 21 total costs (27,32,38), Kasteridis and colleagues generate total costs based on not only primary care
- and hospital care, but also mental health, community care, social care, and continuing care(38).
- 23 In most studies, costs were computed by multiplying the quantity of services used by standard unit
- costs. The main unit cost sources included the Personal Social Services Research Unit (PSSRU), the
- 25 General Practice Research Database (GPRD), NHS reference costs, and RESIP Gemscript Code
- 26 Dictionary and the First Data Bank Europe (FDBE) for drug unit costs. The papers predicting hospital
- 27 costs(26) and care transitions costs to hospitals(35) used Healthcare Resource Groups (HRGs).
- 28 Three papers used a longitudinal design, while cross-sectional and retrospective cohort study
- designs were used in three and one paper, respectively. Four studies presented a justification for
- 30 their analytic framework, including a study hypothesis (n=4) or a reasoning behind the cost model
- 31 specification (n=1).
- 32 Regarding the statistical techniques used to model costs, three papers chose a two-part
- 33 model(27,32,38). In the first stage, the probability of incurring positive costs is modelled. In the
- 34 second stage, costs are estimated using a GLM model with a log-link and Gamma distributed errors
- 35 or OLS regression with logged costs, conditional on costs being positive. Three other papers directly
- 36 calibrated cost models using OLS regression (with logged or unlogged costs)(13,26,29), and the
- 37 remaining paper compared OLS and a GLM model with a long-link and a Poisson distribution(33).
- 38 Besides clinical factors (e.g. indicators variables for certain medical conditions), cost models typically
- also adjusted for age, gender, and deprivation. Only one paper included a measure of functional
- 40 status or age-related impairments(32). Four papers assessed the goodness of fit of the cost
- 41 models(26,32,33,38).
- 42 Multimorbidity is positively associated with total costs, hospital costs, and care transition costs
- 43 (Table 3). Based on the results of two studies, patients with 1 to 3 conditions have between 1.55 and

- 1 2.85 times the mean expected total cost of individuals without any morbidity (27,32). The
- 2 relationship between multimorbidity and primary care costs, however, does depend on the specific
- 3 disease pairs that patients exhibit and their age. In other words, not all disease combinations result
- 4 in higher primary care costs than treating separate patients with each condition. Depression is the
- 5 main cost-increasing comorbidity across all ages, while hypertension tends to be mostly cost-
- 6 limiting(13). Goodness of fit analyses suggest that adding multimorbidity to the specification of total
- 7 or primary care cost models results in large R-squared gains—R-square increased from 0.14 to 0.32
- 8 when Expanded Diagnosis Clusters (114 chronically related groupings of diagnoses) were added to
- 9 an age, gender, and deprivation-only model(33).
- 10 Only 2/7 cost studies presented parameter estimates quantifying the relationship between
- 11 multimorbidity and costs. Thus, a meta-analysis of cost studies was not feasible.
- 12

### 13 **3.5. Risk of bias assessment**

- 14 Eight studies were considered to have the least amount of bias with valid results (good quality)
- 15 (13,25–28,30,32,33), while the remaining studies were susceptible to some biases but deemed
- 16 insufficient to nullify their results (fair quality) (3,24,29,31,34–38). A sample size justification was
- 17 rarely provided and the exposure (in this case, multimorbidity) was only assessed once in most
- 18 cases. Only five studies measured the exposure before the outcome (in this case, utilisation or
- 19 costs). Loss to follow-up only was reported in one out of the nine cohort studies (**Appendix 5**).

# 20 **3.6. Limitations and research gaps**

- 21 The main limitations discussed in the 17 studies cover issues on data, measurement of confounders,
- 22 and multimorbidity indicators. First, Hazra et al. underscore the need to incorporate social care data
- 23 into existing nationally representative datasets to create comprehensive total cost measures (32).
- 24 Second, small area level social deprivation measures, which were included in most selected papers
- and are considered an important confounder, may cover extensive variability in socioeconomic
- status within a given small area and, therefore, suffer from measurement error(25,34). Salisbury et
- al. (29) and Payne et al. (28) discuss the importance of accounting for disease severity. This oft-
- disregarded confounder can be important, as some diagnosed conditions may be inactive or have no
- 29 functional status implications. Third, Brilleman et al. caution against multimorbidity indicators based
- 30 on QOF conditions because the primary focus is quality of care rather than chronicity (30). They also
- 31 discuss the need to explore disease clusters of more than two conditions and to create new
- 32 measures of multimorbidity calibrated on UK data(13,33).
- Other research gaps identified include exploring more detailed outcomes such as reasons of
   hospitalisation, regular A&E use, or length of hospitalisation.

## 35 DISCUSSION

# 36 Summary

- 37 This literature review identified 17 studies exploring the costs and utilisation consequences of
- 38 multimorbidity in the UK. Findings suggest that multimorbidity translates to increased costs and
- 39 utilisation, including total costs, hospital costs, care transition costs, primary care use, dental care
- 40 use, emergency department use, and hospitalisations. The most sizeable effect of multimorbidity is
- 41 on unplanned, potentially preventable, hospitalisations, with up to 14.38 times increase in the odds
- 42 for those with 4 + conditions. This effect is independent of age (28). Depression is a particularly

- 1 important cost and utilisation-increasing condition (13,27,28) and total primary care cost of multiple
- 2 conditions are not purely additive, depending on specific disease combinations and age groups (13).
- 3

### 4 Strengths and Limitations

5 This study brings together UK literature on the statistical and econometric modelling of cost and 6 health service utilisation associated with multimorbidity. As part of BCSC, the identification of the 7 initial set of relevant papers included a systematic literature review to minimize bias in study choice. 8 This was supported by a clear set of inclusion and exclusion criteria throughout the search 9 methodology, from the systematic literature review to the citation and reference review of the 10 initial pearls. However, our choice to maximize the generalisability of findings across disease 11 conditions meant that papers focused on the effect of multimorbidity on a single disease patient 12 population were excluded. A second limitation is that, even though studies from a single country 13 were gathered, considerable heterogeneity across papers in their populations, conditions included in 14 the multimorbidity measures, and statistical techniques was observed; the utilisation meta-analysis 15 results should be considered with caution. Finally, the applicability of our results to other countries 16 may be limited, but their country-specific focus aims to better inform UK healthcare policy.

### 17 Comparison with existing literature

- 18 The results of this UK-focused review concur with Lehnert's study, which was based on 35 non-UK
- 19 international studies. Multimorbidity is positively associated with costs and utilisation, with a
- 20 particularly large effect on hospital stays. However, a shift in the conceptualisation of multimorbidity
- 21 from purely disease counts to specific disease combinations/clusters and the focus on specific age
- 22 groups are trends noted in this review. This review, by using a less conventional search strategy,
- 23 brings together 17 new UK-specific studies and comprehensively summarises the magnitude of the
- 24 relationship between multimorbidity and utilisation and costs.

### 25 Implications for research and practice

- 26 Conceptual frameworks describing how multimorbidity affects healthcare costs and utilisation 27 considering clinical, behavioral, and environmental factors—such as the one developed by Zulman 28 and colleagues on comorbidity interrelatedness and quality of care(6)—should more often guide 29 statistical and econometric modeling of these outcomes. The impact of disease severity, diagnosis 30 sequence, and quality of care on costs of multimorbid patients remains mostly unexplored, as well 31 as polypharmacy and risk of medication adverse events. Identifying the most common disease 32 clusters has also been recognised by Whitty and colleagues as essential to advance towards a 33 cluster-medicine model that successfully combines specialist and generalist care(39). Multimorbidity 34 often worsens quality of life and disability, which are only partially captured by primary and 35 secondary healthcare data. A comprehensive measurement of multimorbidity utilisation and costs 36 requires integrating social care data into existing nationally representative datasets.
- 37 NHS England policy(40) supports expansion of integrated care schemes, particularly those with
- 38 better coordinate community health, mental health and hospital services. This review, identifying
- 39 depression as the main cost-increasing condition and highlighting the substantial contribution of
- 40 multimorbidity to unplanned hospitalisations, provides evidence in support of this policy goal.
- 41
- 42

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-18

### TABLES

Table 1. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria			
<ul> <li>Original research</li> </ul>	Non-human research			
<ul> <li>UK study</li> </ul>	<ul> <li>Descriptive cost-of-illness or economic burden</li> </ul>			
<ul> <li>Focused on assessing the relationship between multimorbidity and costs/utilisation as stated in the title or the study goal in the abstract</li> <li>Published after 2004*</li> </ul>	<ul> <li>studies, literature reviews or meta- analyses (unless meets inclusion criteria**), cost-effectiveness studies, or study protocols</li> <li>Study population is limited to a single condition, or a single condition with a procedure, risk factor, or complication of the single condition</li> </ul>			

\* The 2004 threshold corresponds to the year when QOF was implemented and the NHS began the deployment of improved computerized applications for clinical records and diagnoses.\*\* In this case, references were searched for additional primary studies.

Utilisation/Cost type	MM specification		Magnitude	Parameter estimate type	Reference
Primary care visits (n=3)		_		countace type	
(11-5)	Number of QOF LTCs	•	<b>0.37</b> (0.36-0.38)	Marginal effect	(29)
	MM vs not	-	<b>2.56</b> (2.48-2.64)	Odds ratio	(3)
Dental visits (n=1)		_	. , ,		x /
	MM vs not		<b>1.23</b> (1.08-1.38)	Odds ratio	(37)
A&E visits (n=2)		_	, , , , , , , , , , , , , , , , , , ,		
	HADS score of 8 or		<b>1.58</b> (1.04-2.41)	Odds ratio	(36)
	more vs lower			$\mathbf{A}$	
	1 QOF LTC vs none		<b>1.12</b> (1.10-1.13)	Odds ratio	(25)
	2 QOF LTC vs none		<b>1.28</b> (1.25-1.31)	Odds ratio	(25)
	3 QOF LTC vs none		<b>1.65</b> (1.59-1.71)	Odds ratio	(25)
	≥4 QOF LTC vs none		<b>2.55</b> (2.44-2.66)	Odds ratio	(25)
Hospitalisations					
(n=4)					
All	1 LTC vs none		<b>1.77</b> (1.59-1.98)	Odds ratio	(34)
	2 LTC vs none		<b>2.41</b> (2.12-2.72)	Odds ratio	(34)
	3 LTC vs none		<b>3.53</b> (3.06-4.07)	Odds ratio	(34)
	≥4 QOF LTC vs none		<b>4.33</b> (3.63-5.17)	Odds ratio	(34)
	MM vs not		2.58 (2.48-2.69)	Yearly rate ratio	(3)
Unplanned all	1 PC vs none		<b>1.70</b> (1.59-1.82)	Odds ratio	(28)
	2 PC vs none		<b>2.69</b> (2.50-2.89)	Odds ratio	(28)
	3 PC vs none		<b>3.47</b> (3.21-3.76)	Odds ratio	(28)
	≥4 PC vs none		<b>5.87</b> (5.45-6.32)	Odds ratio	(28)
Unplanned	1 PC vs none		<b>2.50</b> (2.07-3.03)	Odds ratio	(28)
potentially	2 PC vs none		<b>4.93</b> (4.06-5.99)	Odds ratio	(28)
preventable	3 PC vs none	्र 🏦	<b>6.82</b> (5.55-8.37)	Odds ratio	(28)
	≥4 PC vs none		<b>14.38</b> (11.87-	Odds ratio	(28)
		)	17.43)		
Prolonged length of	MM vs not (90+		<b>0.61</b> (0.32-1.13)	Risk ratio	(24)
stay	population)				
Total Costs (n=3)					
	1-3 LTC vs none		<b>1.62</b> (1.28-2.03)	Mean ratio	(32)
	4-6 LTC vs none		<b>2.53</b> (2.01-3.19)	Mean ratio	(32)
	7-9 LTC vs none		<b>3.82</b> (3.01-4.85)	Mean ratio	(32)
	1 LTC vs none		<b>1.99</b> (1.95-2.03)	Mean ratio	(27)
	2 LTC vs none		<b>2.53</b> (2.46-2.58)	Mean ratio	(27)
	3 LTC vs none		<b>2.86</b> (2.72-3.03)	Mean ratio	(27)
Care transition costs	Comorbidity pairs vs	分	p<0.001	Increasing trend	(35)
(n=1)	index LTC	Ц		in association	
Primary care costs	Costs of 1 patient with		Increasing or	Estimated	(33)
(n=2)	2 LTC vs 2 separate	<u>л</u> к/	decreasing costs	prevalence-	
	patients with each LTC		when co-occurring	adjusted cost	
Hospital costs (n=1)	Individual LTC	分	p<0.01 for 90% of	Estimated	(26)
	Time to Death (TTD) as	_	the estimated	coefficient	
	a proxy for morbidity		coefficients		

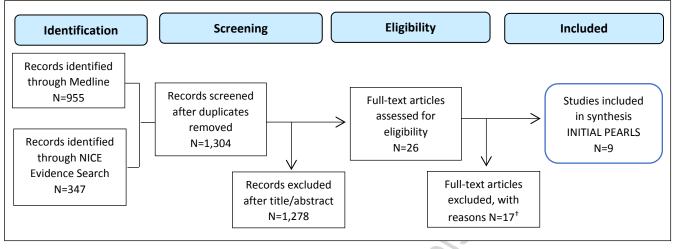
### Table 2. Summary of the relationship between multimorbidity, costs, and utilisation

Notes: The number of articles is indicated in parenthesis next to the cost or utilisation type. See **Appendix 3** for the complete 17 study references. Mean ratios can be obtained by exponentiating the parameter estimates from a GLM model with the log-link, they have an interpretation similar to an odds ratio. For example, individuals with 7-9 conditions have 3.82 times the mean expected total costs of individuals without comorbidities. QOF=Quality and Outcomes Framework. MM=multimorbidity. HADS score=Hospital Anxiety and Depression Scale. LTC=long-term condition. PC=physical condition. Prolonged length of stay is defined as 7 or more days in the hospital. Care transitions are defined as healthcare changes from general practice to Accident and Emergency (A&E) or hospital care.

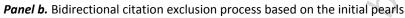
		Total cost			Primary care costs		Care transition costs
	Hazra,201 8(10)	Charlton, 2013 (4)	Kasteridis, 2014 (11)	Brilleman, 2014 (12)	Brilleman, 2013 (13)	Howdon, 2018 (3)	Kadam, 2013 (15)
Primary care					1	2	
Primary care episodes							
Clinic face-to-face visits							
Telephone contacts							
Out-of-hours encounters							
Investigations							
Medication							
Emergency consultations							
Home visits							
Hospital			-				
Acute inpatient							
Hospital admission		•				•	•
Outpatient visit			. O			•	
Day case visit		•	•			•	
Accident and emergency visit			•				
Mental health							
Community care							
Social care							
Continuing care		·X					

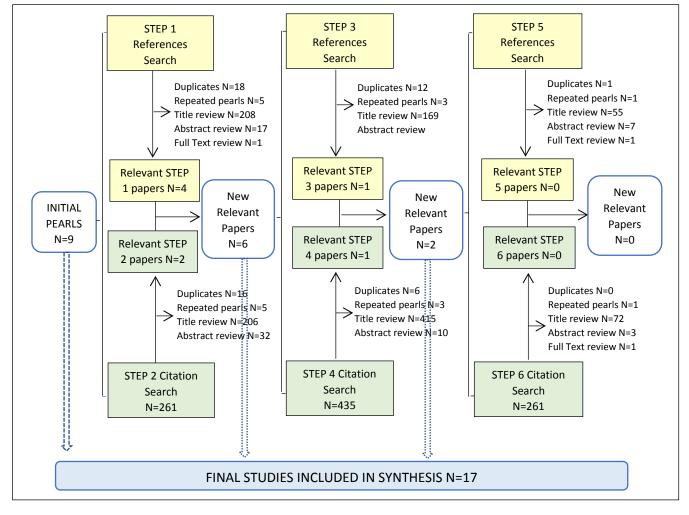
### FIGURES

### Figure 1. Flowchart illustrating the search process



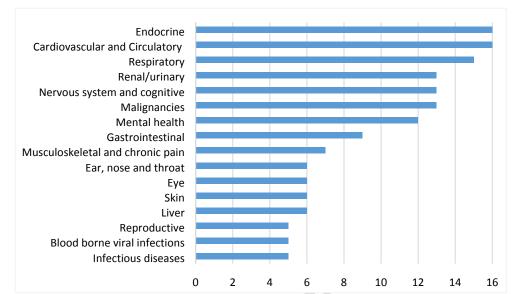
Panel a. Systematic literature review to identify the initial pearls





Notes: † Appendix 2 presents the list of these 17 excluded full-text articles with reasons.

Figure 2. Number of papers that included each body system in their multimorbidity measures



Note: Medical conditions were grouped into body systems to facilitate data display. See **Appendix 4** for more details. This graph excludes Kasteridis and colleagues' study as it did not detail the 49 conditions included in its multimorbidity measure.

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