Lung cancer deaths (England 2001–2017)—comorbidities: a national population-based analysis

Lesley A. Henson ,^{1,2} Emeka Chukwusa,¹ Clarissa Ng Yin Ling ,³ Shaheen A. Khan,⁴ Wei Gao ¹

¹Cicely Saunders Institute, Florence Nightingale Faculty of Nursing, Midwifery and Palliative Care, King's College London, London, UK

²St Ann's Hospice, Cheadle, Cheshire, England, UK

³King's College London, GKT School of Medicine, London, UK

⁴Department of Palliative Care, Guy's and St Thomas' NHS Foundation Trust, London, UK

Correspondence to

Lesley A. Henson, Cicely Saunders Institute, Florence Nightingale Faculty of Nursing, Midwifery and Palliative Care, King's College London, London SE5 9PJ, UK; lesley.henson@kcl.ac.uk

Received 9 April 2021

Accepted 28 June 2021

ABSTRACT

Background The presence of comorbidities in people with lung cancer is common. Despite this, large-scale contemporary reports describing patterns and trends in comorbidities are limited.

Design and methods Population-based patterns and trends analysis using Office for National Statistics Mortality Data. Our cohort included all adults who died from lung cancer (ICD-10 codes C33–C34) in England between 2001 and 2017. We describe decedents with 0, 1 or ≥2 comorbidities and explore changes overtime for the six most common comorbidities identified: chronic respiratory disease; diabetes; cardiovascular disease; dementia; cerebrovascular disease and chronic kidney disease. To determine future trends, the mean annual percentage change between 2001 and 2017 was calculated and projected forwards, while accounting for anticipated increases in lung cancer mortality.

Results There were 472 259 deaths from lung cancer (56.9% men; mean age 72.9 years, SD: 10.7). Overall, 19.0% of lung cancer decedents had 1 comorbidity at time of death and 8.8% had ≥2. The proportion of patients with comorbidities increased over time—between 2001 and 2017 decedents with 1 comorbidity increased 54.7%, while those with ≥2 increased 294.7%. The most common comorbidities were chronic respiratory disease and cardiovascular disease, contributing to 18.5% (95% CI: 18.0 to 18.9) and 11.4% (11.0 to 11.7) of deaths in 2017. Dementia and chronic kidney disease had the greatest increase in prevalence, increasing 311% and 289% respectively.

Conclusion To deliver high-quality outcomes for the growing proportion of lung cancer patients with comorbidities, oncology teams need to work across traditional boundaries of care. Novel areas for development include integration with dementia and chronic kidney disease services.

Key messages

What was already known?

- The presence of comorbidities in people with lung cancer is increasing over time.
- Current disease-focused models of care fail to meet the needs and preferences of patients with comorbidities.

What are the new findings?

- By 2032, we anticipate that >25% of all lung cancer patients will have ≥2 comorbidities at the end of life.
- Dementia and chronic kidney disease are the comorbidities expected to have the greatest increase in prevalence.

What is their clinical significance?

- To provide high-quality holistic care to future lung cancer patients, new integrated models of care are urgently needed.
- Innovative areas for service development include collaboration with dementia and chronic kidney disease services.

BACKGROUND

As our population ages, mortality from lung cancer—the most common cause of cancer-related deaths worldwide—is increasing. Between 2020 and 2040, lung cancer deaths are predicted to increase 37.3% in the UK and 63.8% globally.¹ The demographics of lung cancer patients are also changing over time with the average patient becoming older and more likely to be living with one or more long-term health conditions at time of diagnosis.^{2,3}

The negative impact of ageing and multimorbidity (defined as the presence of two or more long-term health conditions)⁴ on outcomes for lung cancer patients has been widely reported.⁵ Studies have found older patients are less likely to receive recommended anticancer therapies at diagnosis⁶ and throughout their illness,⁷ while the presence of

© Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY. Published by BMJ.

To cite: Henson LA, Chukwusa E, Ng Yin Ling C, et al. *BMJ Supportive & Palliative Care* Epub ahead of print: [please include Day Month Year]. doi:10.1136/bmjspcare-2021-003107

comorbidities is associated with greater use of acute hospital services,⁸ lower health-related quality-of-life⁹ and increased mortality.^{10 11}

Present-day healthcare systems, where individual diseases determine models of service delivery, often results in care that is fragmented, unsafe and inefficient for those with comorbidities.^{12–14} For patients and their families, attending the hospital multiple times for different conditions can be burdensome, result in polypharmacy and the receipt of contradictory medical advice.¹⁵ For healthcare professionals, caring for multimorbid patients can be overwhelming, including for oncologists who lack sufficient time to provide high-quality holistic care that incorporates broader health maintenance activities alongside anti-cancer treatment and monitoring.^{14 16}

With the increasing prevalence of multimorbidity, oncology services need to urgently adapt to meet the changing needs of their patient population as well as address current inequities in care. Understanding patterns and trends in comorbidities is important for healthcare planning and policy. Despite this, large-scale contemporary reports describing comorbidities in people with lung cancer are lacking. We therefore conducted the following study, the aim of which was to determine the patterns as well as actual and projected trends in comorbidities for lung cancer decedents in England.

METHODS

Our study is reported according to the RECORD statement.¹⁷

Approval for the study and access to the data was received from the UK's Office for National Statistics (ONS).¹⁸ As per ONS procedures, a Data Access Agreement was signed with requisites for data management and protection. In addition, all researchers accessing the data (LAH, WG and EC) were individually assessed and approved by ONS. As all data were fully anonymised, no additional approvals were required to complete the analysis according to the Information Commissioner's Office guidelines, ONS procedures and those of King's College London Research Ethics Committee.

Study design and datasets

We conducted a population-based patterns and trends analysis using ONS Mortality Data for England. The ONS is the UK's largest independent producer of official statistics and is the recognised national statistical institute of the UK.¹⁸ Its Mortality Database holds information on all UK deaths including the 'underlying cause of death' and up to 15 'contributing' causes of death. Coding is carried out according to internationally agreed rules and using the WHO's Tenth Revision of the International Classification of Diseases and Related Health Problems (ICD-10).¹⁹ The ONS Mortality Database also contains basic demographic

information such as the decedent's age at death, gender and marital status.

National government statistics reporting the relative deprivation between neighbourhoods in England were used to derive information on decedents' socioeconomic status.^{20 21} The English Indices of Multiple Deprivation (IMD) version 2010 was linked to ONS Mortality data 2001 to 2010 and the IMD version 2015 was linked to data for 2011 to 2017.

Participants and variables

Our cohort included all adults (≥ 18 years at time of death) who died from lung cancer (underlying cause of death listed as ICD-10 codes C33 or C34) in England between 2001 and 2017. Descriptive variables were categorised as follows: age at death (< 55 ; 55–64; 65–74; 75–84; 85+ years); gender (male; female); marital status (divorced/separated; married; single; widowed; unknown); socioeconomic status (IMD quintiles, 1, most deprived; 5, least deprived).²⁰

Analysis/statistical methods

For each lung cancer decedent, we examined all contributing causes of death listed on their death certificate. We excluded the following contributing causes from our analysis: accidents; minor ailments; acute and/or self-limiting conditions such as infections; conditions related to cancer, for example, bone metastases; as these were not considered comorbidities—a comorbidity being defined as a co-occurring chronic condition or disease expected to impair a patient's long-term survival.²² All remaining contributing causes of death were conditions recognised as comorbidities—these were counted, and decedents categorised into those with zero, one or two plus comorbidities. Based on the findings of recent studies,^{12 23 24} we next considered six commonly recorded comorbidities and explored how their prevalence changed over time. These were: chronic respiratory disease (ICD-10 codes J4, J6, J7, J82 and J84); diabetes (E10–E14); cardiovascular disease including hypertension (I1, I20, I25, I7 and I8); dementia (F00, F01, F02, F03, G30–G32 and R54); cerebrovascular disease (I6) and chronic kidney disease (N11, N18 and N19). For future projections, we calculated the mean annual percentage change in comorbidities between 2001 and 2017 and projected this forward to 2040 while accounting for anticipated increases in lung cancer mortality.¹

All data were analysed using Microsoft Excel for Office 365 and Stata/IC 13 (STATA, College Station, TX).

RESULTS

In England, between 2001 and 2017, there were 472 259 deaths from lung cancer (ICD-10 codes C33 and C34). Mean age at death was 72.9 years (SD: 10.7); 56.9% of deaths were in men. Table 1 presents the demographic characteristics of the study population.

Table 1 Cohort characteristics (n=472 259)

	Total sample		2001–2005		2006–2010		2011–2015		2016–2017	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Total	472 259	100	133 981	100	139 595	100	142 590	100	56 093	100
Age in years at time of death, mean (min;max)	73 (18;111)				72 (20;104)		73 (18;106)		73 (18;111)	
Age in years at time of death										
<55	25 243	5.3	8227	6.1	7520	5.4	6926	4.9	2570	4.6
55–64	75 498	16	22 267	16.6	23 775	17	21 697	15.2	7759	13.8
65–74	146 059	30.9	41 897	31.3	41 512	29.7	44 554	31.2	18 096	32.3
75–84	161 510	34.2	47 977	35.8	48 221	34.5	46 803	32.8	18 509	33
85+	63 949	13.5	13 613	10.2	18 567	13.3	22 610	15.9	9159	16.3
Gender										
Female	203 641	43.1	53 766	40.1	60 119	43.1	64 061	44.9	25 695	45.8
Male	268 618	56.9	80 215	59.9	79 476	56.9	78 529	55.1	30 398	54.2
Number of comorbidities										
0	340 764	72.2	1,07,229	80	1,03,653	74.3	94 904	66.6	34 978	62.4
1	89 894	19	20 577	15.4	25 576	18.3	30 947	21.7	12 794	22.8
2+	41 601	8.8	6 175	4.6	10 366	7.4	16 739	11.7	8321	14.8
Marital status										
Divorced/separated	59 262	12.5	13 109	9.8	16 809	12	20 598	14.4	8746	15.6
Married	239 150	50.6	70 544	52.7	71 209	51	70 327	49.3	27 070	48.3
Single	33 150	7	8896	6.6	9357	6.7	10 473	7.3	4424	7.9
Widowed	137 802	29.2	40 585	30.3	41 362	29.6	40 384	28.3	15 471	27.6
Unknown	2895	0.6	847	0.6	858	0.6	808	0.6	382	0.7
Socioeconomic status (IMD quintile)										
1 (most deprived)	125 190	26.5	36 968	27.6	37 061	26.5	36 931	25.9	14 230	25.4
2	103 205	21.9	29 706	22.2	30 591	21.9	30 760	21.6	12 148	21.7
3	92 998	19.7	26 088	19.5	27 638	19.8	28 120	19.7	11 152	19.9
4	82 061	17.4	22 740	17	24 511	17.6	25 013	17.5	9797	17.5
5 (least deprived)	68 805	14.6	18 479	13.8	19 794	14.2	21 766	15.3	8766	15.6
IMD, Index of Multiple Deprivation.										

Table 2 Proportion of lung cancer decedents with 0, 1 and 2+ comorbidities by age group (A) and socioeconomic status (B)

A					
Age in years at time of death N (%)					
Number of comorbidities	<55	55–64	65–74	75–84	85+
0	22 001 (87.2)	60 804 (80.5)	106 998 (73.3)	110 199 (68.2)	40 687 (63.6)
1	2560 (10.1)	10 988 (14.6)	27 131 (18.6)	33 727 (20.9)	14 868 (23.3)
2+	682 (2.7)	3706 (4.9)	11 930 (8.2)	17 584 (10.9)	8394 (13.1)
B					
Socioeconomic status (IMD quintile) N (%)					
Number of comorbidities	1, most deprived	2	3	4	5, least deprived
0	87 461 (69.9)	73 766 (71.5)	67 596 (72.7)	60 475 (73.7)	51 391 (74.7)
1	25 323 (20.2)	19 891 (19.3)	17 299 (18.6)	14 750 (18.0)	12 011 (17.5)
2+	12 406 (9.9)	9548 (9.3)	8103 (8.7)	6836 (8.3)	5403 (7.9)

IMD, Index of Multiple Deprivation.

Among all lung cancer decedents, 39.5% (n=186 696) had at least one other illness/condition listed on their death certificate as contributing to the cause of death. This reduced to 27.8% (n=131 495), once conditions and illnesses not considered to be comorbidities (accidents; minor ailments; acute and/or self-limiting illnesses; those related to cancer) were excluded. 19.0% (n=89 894) of all lung cancer decedents had one comorbidity at time of death and 8.8% (n=41 601) had two or more (table 1).

The proportion of decedents with comorbidities increased with age. For those <55 years, 2.7% (95% CI: 2.5 to 2.9) had two plus comorbidities at time of death compared with 13.1% (95% CI: 12.9 to 13.4) of those aged ≥85 years. The proportion of lung cancer decedents with comorbidities was also higher in more deprived areas of England (table 2).

The number of lung cancer decedents with comorbidities increased over time (figure 1). Between 2001 and 2017, the proportion of decedents with one comorbidity increased 54.7% (from 14.8% in 2001 to 22.9% in 2017), while those with two or more comorbidities increased 294.7% (from 3.8% to 15.0%). If current trends continue, by 2032, more than a quarter of all lung cancer patients will be living with two or more comorbidities at the end of life.

Figure 1 Actual (2001–2017) and projected (2018–2040) proportion of lung cancer decedents in England with 0, 1 and 2+ comorbidities.

The most common comorbidities identified were chronic respiratory disease and cardiovascular disease including hypertension. In 2017, chronic respiratory disease contributed to 18.5% (95% CI: 18.0 to 18.9) of deaths from lung cancer and cardiovascular disease including hypertension to 11.4% (11.0 to 11.7). Diabetes contributed to 4.9% (95% CI: 4.7 to 5.2), cerebrovascular disease to 2.6% (95% CI: 2.4 to 2.8), chronic kidney disease 2.3% (95% CI: 2.1 to 2.5) and dementia 4.2% (95% CI: 4.0 to 4.5). The prevalence of all six comorbidities increased significantly during the study period but was greatest for dementia (311%) and chronic kidney disease (289%) (figure 2). Based on our future projections, by 2045, 10% of all lung cancer patients will be living with dementia at the end of life, 11% with diabetes and 6% with chronic kidney disease.

DISCUSSION

Using population-level data over a 17-year period (2001–2017) this study determined actual and predicted patterns and trends in comorbidities for lung cancer decedents in England, UK. Our findings provide valuable information for healthcare professionals, managers and policymakers when planning and delivering future cancer services.

We found the proportion of lung cancer decedents with two or more comorbidities increased 294.7% between 2001 and 2017. Comorbid conditions are known to affect older patients disproportionately and our study suggests that if current trends continue, by 2032 more than 25% of lung cancer patients will be living with multiple comorbidities at the end of life. While this increase is not unexpected given the broader context of population growth and ageing, our findings highlight the scale of these changes and emphasise the urgency with which oncology services need to adapt. Understanding the association between age, comorbidity type and severity is important as this has the potential to impact cancer patients' treatment and prognosis.^{25 26} Furthermore, the prevalence of some comorbidities, such as HIV/AIDS and obesity,

Figure 2 Actual (2001–2017) and projected (2018–2040) number and type of comorbidities for lung cancer decedents in England.

decrease with age.²⁷ By understanding current and future patterns and trends, policymakers can plan future services that are able to meet the needs and preferences of their patients and reduce inequities in care.

Currently in England, most oncology services remain single-disease focused in their approach to care—a model that fails most multimorbid cancer patients. Greater integration between specialties has the potential to improve outcomes for cancer patients and their caregivers, while also reducing strain on National Health Service resources.²⁸ Research exploring the impact of integrated care models for individuals with non-cancer conditions have shown mostly positive outcomes, however, these studies have focused primarily on older and/or frail populations, and few have been extended beyond the demonstration phase.²⁹ Evidence for the effectiveness of integrated care models beyond the experimental phase is much more limited, and when present, the impact has often taken years to be realised. Hebert and colleagues evaluated the impact of a coordination-type integrated care model on health, satisfaction, empowerment and the service utilisation of people aged ≥ 75 years at risk of functional decline in Quebec, Canada.³⁰ Key components of the intervention included a case manager, single entry point, single assessment instrument coupled with a case-mix management system and coordination between decision makers and managers at regional and local levels. The quasi experimental study found greater satisfaction and patient empowerment in the intervention group along with a lower

number of emergency department visits and hospitalisations. However, there was no significant difference in functional decline and unmet need between groups until year 4 of the study when the intervention group showed fewer cases of functional decline ($p < 0.001$) and less unmet need ($p < 0.001$).³⁰

Clarity regarding the components that challenge and support integrated models of care in oncology is still needed. A systematic review of interventions to improve coordination between primary care and oncology found insufficient evidence for the effectiveness of nurse navigators, treatment care plans and the creation of multidisciplinary teams.³¹ However, these results should be interpreted with caution as the impact from integrated care initiatives may only be seen years later—beyond the follow-up period of most research studies.³² While simple measures, such as coordinating clinic times, can minimise the need for repeated investigations and reduce burden on hospital transport services,¹⁵ in-depth evaluation of complex integrated service delivery models is still needed to determine their effectiveness.³³

There is more conclusive evidence for the benefits of integrating oncology with palliative care.^{34 35} In their landmark study, Temel and colleagues showed that patients newly diagnosed with non-small cell lung cancer who received palliative care soon after diagnosis had better outcomes, including greater improvements in quality of life and mood, compared with controls.³⁶ The intervention arm of the randomised controlled trial involved patients receiving standard palliative care under ‘clinical practice guidelines for palliative care’

which include the management of comorbid conditions. This attention to patient's comorbidities is likely to be one of the active ingredients that led to patients being more stable and having better outcomes.³⁶

Understanding patterns and trends over time for different comorbidities provides healthcare professionals, managers and policymakers with opportunities to also consider novel approaches to service development. Our study found that the most common comorbidities for patients with lung cancer were chronic respiratory disease and cardiovascular disease including hypertension. However, the greatest increase in comorbidity prevalence was found for dementia and chronic kidney disease. When developing future cancer services, policymakers should consider models of care that involve collaboration and/or integration with healthcare professionals from dementia and renal support services. Not only do these comorbidities show the greatest increase in prevalence, they are also disciplines that oncologists are less likely to be familiar with and up-to-date with the latest investigative and management options.

Strengths and limitations

Strengths of our study include the use of ONS mortality data, allowing us to assess comorbidity patterns and trends at a population-level over time. The ONS Mortality Database uses information obtained from a patient's death certificate, which unfortunately also presents limitations, mostly relating to a degree of inaccurate recordings.³⁷ More recent evidence suggests that the overall accuracy of death certificate information has improved³⁸ and cause of death information is reported to be more sensitive and specific for cancer than other diseases.³⁹ However despite this, it is likely that our cohort included some patients whose cause of death and/or comorbidity data were inaccurately recorded. Furthermore, the increasing prevalence of comorbidities identified by our study may represent greater reporting over time rather than any actual increase in disease prevalence. Our data did not include information about the severity of any comorbidities listed or the amount and type of healthcare services accessed by patients prior to death. We were therefore unable to evaluate the impact of these factors. Finally, our future projections are simple and limited by assumptions that included a linear change over time.

CONCLUSIONS

The number of lung cancer decedents with multiple comorbidities is increasing over time. To deliver high-quality outcomes and positive experiences for this growing population, oncology services need to work across traditional boundaries of care. The most common comorbidities found in patients with lung cancer were chronic respiratory disease and cardiovascular disease including hypertension, however the

greatest increase in prevalence was found for dementia and chronic kidney disease. Novel areas for development of integrated service delivery models, therefore, include collaboration with dementia and chronic kidney disease specialists.

Contributors Conception and design: LAH, EC and WG. Checking and cleaning of data: LAH and EC supervised by WG. Data analysis and interpretation: all authors. Manuscript writing: LAH with critical revisions from all authors. Final approval of manuscript: all authors.

Funding Dr LAH, King's College London, received funding via a clinical lectureship from the National Institute for Health Research (NIHR). This study was also supported by the NIHR Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust. The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

Disclaimer The funders had no role in the study design, data analysis, decision to publish or preparation of the manuscript.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. Data supplied by the Office for National Statistics.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution 4.0 Unported (CC BY 4.0) license, which permits others to copy, redistribute, remix, transform and build upon this work for any purpose, provided the original work is properly cited, a link to the licence is given, and indication of whether changes were made. See: <https://creativecommons.org/licenses/by/4.0/>.

ORCID iDs

Lesley A. Henson <http://orcid.org/0000-0003-4799-7365>
Clarissa Ng Yin Ling <http://orcid.org/0000-0003-0873-5741>
Wei Gao <http://orcid.org/0000-0001-8298-3415>

REFERENCES

- 1 Ferlay J, Ervik M, Lam F. Global cancer Observatory: cancer tomorrow. Lyon, France: international agency for research on cancer, 2018. Available: <https://gco.iarc.fr/tomorrow> [Accessed 12 Aug 2019].
- 2 Aarts MJ, Aerts JG, van den Borne BE, *et al.* Comorbidity in patients with small-cell lung cancer: trends and prognostic impact. *Clin Lung Cancer* 2015;16:282–91.
- 3 Jørgensen TL, Hallas J, Friis S, *et al.* Comorbidity in elderly cancer patients in relation to overall and cancer-specific mortality. *Br J Cancer* 2012;106:1353–60.
- 4 NICE. Multimorbidity: clinical assessment and management. National Institute for health and care excellence, 2016. Available: <https://www.nice.org.uk/guidance/ng56>
- 5 Sarfati D, Koczwara B, Jackson C. The impact of comorbidity on cancer and its treatment. *CA Cancer J Clin* 2016;66:337–50.
- 6 Potosky AL, Saxman S, Wallace RB, *et al.* Population variations in the initial treatment of non-small-cell lung cancer. *J Clin Oncol* 2004;22:3261–8.
- 7 Earle CC, Venditti LN, Neumann PJ, *et al.* Who gets chemotherapy for metastatic lung cancer? *Chest* 2000;117:1239–46.
- 8 Henson LA, Higginson IJ, Gao W, *et al.* What factors influence emergency department visits by patients with cancer at the

- end of life? analysis of a 124,030 patient cohort. *Palliat Med* 2018;32:426–38.
- 9 Grønberg BH, Sundstrøm S, Kaasa S, *et al.* Influence of comorbidity on survival, toxicity and health-related quality of life in patients with advanced non-small-cell lung cancer receiving platinum-doublet chemotherapy. *Eur J Cancer* 2010;46:2225–34.
 - 10 Janssen-Heijnen MLG, Houterman S, Lemmens VEPP, *et al.* Prognostic impact of increasing age and co-morbidity in cancer patients: a population-based approach. *Crit Rev Oncol Hematol* 2005;55:231–40.
 - 11 Asmis TR, Ding K, Seymour L, *et al.* Age and comorbidity as independent prognostic factors in the treatment of non small-cell lung cancer: a review of national cancer Institute of Canada clinical Trials Group trials. *J Clin Oncol* 2008;26:54–9.
 - 12 Barnett K, Mercer SW, Norbury M, *et al.* Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012;380:37–43.
 - 13 Stafford M, Steventon A, Thorlby R. *Briefing: understanding the health care needs of people with multiple health conditions.* The Health Foundation, 2018.
 - 14 Institute of Medicine, Committee on quality of health care in America. *Crossing the quality chasm: a new health system for the 21st century.* National Academies Press, 2001.
 - 15 Rosbach M, Andersen JS. Patient-experienced burden of treatment in patients with multimorbidity - a systematic review of qualitative data. *PLoS One* 2017;12:e0179916.
 - 16 Ritchie CS, Kvale E, Fisch MJ. Multimorbidity: an issue of growing importance for oncologists. *J Oncol Pract* 2011;7:371–4.
 - 17 Benchimol EI, Smeeth L, Guttman A, *et al.* The reporting of studies conducted using observational Routinely-collected health data (record) statement. *PLoS Med* 2015;12:ARTN e1001885.
 - 18 Office for national statistics, 2019. Available: <https://www.ons.gov.uk/> [Accessed 07 Nov 2019].
 - 19 World Health Organisation. ICD-10: International Statistical Classification of Diseases and Related Health Problems: 10th revision, 2016. Available: <https://icd.who.int/browse10/2016/en> [Accessed 18 Apr 2019].
 - 20 Ministry of Housing, Communities & Local Government - English indices of deprivation. GOV.UK, 2012. Available: <https://www.gov.uk/government/collections/english-indices-of-deprivation> [Accessed 12 Apr 2019].
 - 21 Abel GA, Barclay ME, Payne RA. Adjusted indices of multiple deprivation to enable comparisons within and between constituent countries of the UK including an illustration using mortality rates. *BMJ Open* 2016;6:e012750.
 - 22 Valderas JM, Starfield B, Sibbald B, *et al.* Defining comorbidity: implications for understanding health and health services. *Ann Fam Med* 2009;7:357–63.
 - 23 Obi J, Mehari A, Gillum R. Mortality related to chronic obstructive pulmonary disease and co-morbidities in the United States, a multiple causes of death analysis. *COPD* 2018;15:200–5.
 - 24 Salive ME. Multimorbidity in older adults. *Epidemiol Rev* 2013;35:75–83.
 - 25 Yancik R, Ganz PA, Varricchio CG, *et al.* Perspectives on comorbidity and cancer in older patients: approaches to expand the knowledge base. *J Clin Oncol* 2001;19:1147–51.
 - 26 Geraci JM, Escalante CP, Freeman JL, *et al.* Comorbid disease and cancer: the need for more relevant conceptual models in health services research. *J Clin Oncol* 2005;23:7399–404.
 - 27 Piccirillo JF, Vlahiotis A, Barrett LB, *et al.* The changing prevalence of comorbidity across the age spectrum. *Crit Rev Oncol Hematol* 2008;67:124–32.
 - 28 Daveson BA, Harding R, Shipman C, *et al.* The real-world problem of care coordination: a longitudinal qualitative study with patients living with advanced progressive illness and their unpaid caregivers. *PLoS One* 2014;9:e95523.
 - 29 Johri M, Beland F, Bergman H. International experiments in integrated care for the elderly: a synthesis of the evidence. *Int J Geriatr Psychiatry* 2003;18:222–35.
 - 30 Hébert R, Raïche M, Dubois M-F, *et al.* Impact of PRISMA, a coordination-type integrated service delivery system for frail older people in Quebec (Canada): a quasi-experimental study. *J Gerontol B Psychol Sci Soc Sci* 2010;65B:107–18.
 - 31 Tomasone JR, Brouwers MC, Vukmirovic M, *et al.* Interventions to improve care coordination between primary healthcare and oncology care providers: a systematic review. *ESMO Open* 2016;1:e000077.
 - 32 Bardsley M, Smith J, Car J. *Evaluation of the first year of the inner North West London integrated care pilot. research report.* Nuffield Trust and Imperial College London, 2015.
 - 33 Craig P, Dieppe P, Macintyre S, *et al.* Developing and evaluating complex interventions: the new medical Research Council guidance. *BMJ* 2008;337:a1655.
 - 34 Henson LA, Gao W, Higginson IJ, *et al.* Emergency department attendance by patients with cancer in their last month of life: a systematic review and meta-analysis. *J Clin Oncol* 2015;33:370–6.
 - 35 Zimmermann C, Swami N, Krzyzanowska M, *et al.* Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. *Lancet* 2014;383:1721–30.
 - 36 Temel JS, Greer JA, Muzikansky A, *et al.* Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med* 2010;363:733–42.
 - 37 Roulson J, Benbow EW, Hasleton PS. Discrepancies between clinical and autopsy diagnosis and the value of post mortem histology; a meta-analysis and review. *Histopathology* 2005;47:551–9.
 - 38 Office for National Statistics. *Death certification reform: a case study on the potential impact on mortality statistics, England and Wales. experimental statistics*, 2012: 1–16.
 - 39 Mieno MN, Tanaka N, Arai T, *et al.* Accuracy of death certificates and assessment of factors for misclassification of underlying cause of death. *J Epidemiol* 2016;26:191–8.