

Variation in hospital cost trajectories at the end of life by age, multimorbidity and cancer type

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Abstract

Background

Approximately thirty thousand people in Scotland are diagnosed with cancer annually, of whom a third live less than one year. The timing, nature and value of hospital-based healthcare for patients with advanced cancer are not well understood. The study's aim was to describe the timing and nature of hospital-based healthcare use and associated costs in the last year of life for patients with a cancer diagnosis.

Methods

We undertook a Scottish population-wide administrative data linkage study of hospital-based healthcare use for individuals with a cancer diagnosis, who died aged 60 and over between 2012 and 2017. Hospital admissions and length of stay (LOS), as well as the number and nature of outpatient and day case appointments were analysed. Generalised linear models were used to adjust costs for age, gender, socioeconomic deprivation status, rural-urban (RU) status and comorbidity.

Results

The study included 85,732 decedents with a cancer diagnosis. For 64,553 (75.3%) of them, cancer was the primary cause of death. Mean age at death was 80.01 (SD 8.15) years. The mean number of inpatient stays in the last year of life was 5.88 (SD 5.68), with a mean LOS of 7 days. Admission rates rose sharply in the last month of life. One year adjusted and unadjusted costs decreased with increasing age. A higher comorbidity burden was associated with higher costs. Major cost differences were present between cancer types.

Conclusions

People in Scotland in their last year of life with cancer are high users of secondary care. Hospitalisation accounts for a high proportion of costs, particularly in the last month of life. Further research is needed to examine triggers for hospitalisations and to identify influenceable reasons for unwarranted variation in hospital use among different cancer cohorts.

Keywords

healthcare use; end of life care; secondary care; costs; cancer

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Background

Approximately thirty thousand people in Scotland are diagnosed with cancer each year, of whom 10,000 live less than one year [1]. It is estimated that two out of five people will develop cancer in their lifetime. Over the last decade, cancer incidence has risen in Scotland, whilst the mortality rate has fallen. This trend can be explained by improvements in diagnosis and the development of newer anti-cancer therapies, the ageing population and the fact that cancer incidence increases with age [2].

In 2018 there were 16,153 cancer deaths registered in Scotland, excluding non-melanoma skin cancers [3]. A quarter of all deaths from cancer ($n = 3,980$) were attributed to lung cancer, followed by colorectal ($n = 1,743$), breast ($n = 1,001$), prostate ($n = 923$), and oesophageal ($n = 873$) cancers. These five cancer types were responsible for more than half of the Scottish cancer deaths.

People who are nearing the end of life are high users of secondary care services [4]. Currently around 50% of people in Scotland die in hospital [5–7]. A recent paper describing trends in place of death in Scotland between 2004 and 2016, found a reduction in hospital deaths from 58% to 50.1%, during the study period along with a corresponding increase in deaths in community settings including care homes [8]. Within the cancer population, a reduction in hospital deaths was observed between 2009 and 2016, with the percentage of deaths falling from 49% to 41% [3].

Hospitalisation of patients in the last year of life may be recommended and necessary for some people with complex clinical needs and increasing proximity to death. Nevertheless, evidence suggests that clinical interventions close to the end of life may also represent a clinical culture of ‘over-medicalisation’, with limited or no meaningful benefit to individuals [8–10]. The ‘Realistic Medicine’ report by the Scottish Chief Medical Officer recommends aligning clinical intervention with individual patients’ needs and preferences and moving away from the historic ‘doctor knows best’ culture [11].

The rising costs of cancer treatment, driven by new therapeutic options, is important context and necessitates that the true value of clinical interventions is understood. This is a crucial step ensuring that scarce resources can be directed appropriately [12, 13].

A systematic review, which included all English language retrospective studies looking at costs in cancer care using administrative data, showed that costs were influenced by a range of sociodemographic, clinical and health system characteristics. Further outcomes presented in the review, reported an exponential cost increase with proximity to death and showed inpatient care as the main driver of this [14]. A systematic review of Scotland-based palliative care research published in 2018 revealed a lack of health economic considerations applied to palliative and end of life matters [15].

Our recent study of secondary care costs for end of life care included the Scottish population who died between 2012 and 2017. We showed that intensity of healthcare use and costs were highest in cancer patients, mainly due to inpatient stays [4]. Similar results were found in our English parallel study [16]. Furthermore, in both studies the cancer cohort demonstrated

a particularly steep cost-increase in the final three months of life, again largely as a result of inpatient hospitalisation.

In the present study, we sought to understand more about the timing and nature of secondary healthcare use and associated costs for patients with cancer in their last year of life in Scotland and to identify factors associated with any variation identified (e.g. between cancer types, multimorbidity, age at death and socioeconomic status).

Methods

The study population in this retrospective cohort analysis included everyone with a recorded cancer diagnosis in Scotland who died between 2012 and 2017 and was over 60 years of age on their date of death. Hospital-based healthcare use over the last twelve months of life was examined via the linkage of cancer records (SMR06) to data from Scottish hospital records. The final dataset included cancer registry data, inpatient, outpatient and day-case activity (SMR00 and SMR01) and the National Records of Scotland (NRS) death registration data.

Ethics and consent

Approval for the study was obtained from the Scottish Public Benefit and Privacy panel (Ref: 1617-0100) for analysis within the Scottish National Research Data Safe Haven.

Data sources

Data were obtained via the Scottish Research Data Safe Haven from Public Health Scotland, who manage all health related data connected to NHS Scotland. Linkage was established using the Community Health Index (CHI) number as the primary key [17]. The Scottish Morbidity Record (SMR) outpatient (SMR00), inpatient and day case (SMR01) and the National Records of Scotland (NRS) record of deaths were linked to cancer registry data (SMR06). SMR01 includes episode-based patient records that relate to all acute inpatient and day cases. SMR00 relates to all outpatient activity including new and follow-up appointments. NRS manages the official register for deaths in Scotland, which includes all deaths with details on causes of death from a death certificate. All patient identifiers including the CHI were removed from the datasets prior to release in the National Safe Haven. Data quality control followed the well-established internal protocols of Public Health Scotland, undertaken prior to receiving the anonymised research extract.

Inclusion and exclusion criteria

Data linkage and detailed eligibility criteria are reported in Supplementary Figure 1 (Supplementary Material). Major inclusion criteria were:

- Death registered between January 1st 2012 and December 31st 2017
- Age at death ≥ 60 years

- Healthcare data available for a minimum of 365 days prior to death
- A linked record available in the cancer registry between January 1st 2011 and December 31st 2017

In the selection process of the study population, the NRS death dataset of the eligible cohort of decedents was merged with the outpatient (SMR00) and the inpatient and day-case (SMR01) dataset. Inpatient and outpatient resource-use data was excluded if resource use occurred outside the study period. Following this, SMR06 data was merged onto the existing clean dataset and decedents who did not have a cancer diagnosis were excluded. Data of decedents with a cancer diagnosis, fulfilling all other criteria for inclusion, were retained for the final analysis.

Patient characteristics

Patient characteristics included gender, age and primary cause of death, with a subsequent division into cancer as the primary cause of death and an “others” category. Cancer types were grouped based on number of patients and/or using the first two digits of the ICD-10 code. Comorbidity was estimated using the Charlson Comorbidity Index (CCI), based on secondary care coding, which entailed a 5 year look back from patients’ first contacts with secondary care using ICD-10 code lists developed by Public Health Scotland [18]. A rural-urban indicator was included, as was the Scottish Index of Multiple Deprivation (SIMD) [19, 20].

Outcome measures

Inpatient and day care

Hospital inpatient care in the last year of life was captured as the number of hospital admissions, the timing of these in relation to death, the mean number of bed days per inpatient stay and the total number of bed days over the twelve-month period.

Scottish health service costs (Scottish cost book) were used to estimate the cost of inpatient care, mainly specialty group costs including inpatient data for: (i) all specialties excluding long stays (code R040), (ii) long stay specialties (R040LS), and (iii) specialty group costs for day cases (R042) [21]. Costs related to critical care stays were included within the specialty group costs (i) and (ii). Scottish health service costs include all direct and indirect costs for each care episode within a specific specialty. Direct costs include all bed days, theatre hours, staff (medical, nursing, and pharmacy), therapy (radio-, physio and occupational), laboratory charges and others. Indirect costs include administration, catering, uniforms, laundry, waste disposal, heat, light, power, rent, furniture and more.

Outpatient care

Hospital outpatient data included the number of outpatient visits per patient in their last year of life, as well as the reasons for each individual appointment. Costs for outpatient

appointments were derived from the Scottish health service costs documents for; (i) specialty group costs for consultant led outpatient appointments (R044), (ii) specialty group costs for nurse led clinics (R045) and (iii) specialty group costs for Allied Health Professionals services (R046). The costs were based on national average unit costs for each service code.

Statistical analysis

Descriptive statistics were used to characterise the study population. Means and standard deviations (SD) were calculated for service use and costs. Aggregated results and results split by cancer type are presented. Gamma generalised linear models (GLM) with log-link, as recommended by Glick et al. (2014) were used to model costs as they are robust to the skewed distributions and the heteroscedasticity typical for healthcare related cost data. Known important predictors of costs are age, gender, primary cause of death, deprivation, urban-rural indicator and comorbidity. [22–24] The effects of age, primary cause of death and CCI were estimated in isolation, with the other predictors included as covariates in the GLM. Potential interactions between age and gender and between age and cause of death were also assessed. Analysis was carried out using Stata version 16 (StataCorp, College Station, TX, USA).

Results

Patient characteristics

Table 1 displays the patient characteristics for the final cohort comprising 85,732 decedents with a cancer diagnosis. Slightly over half of the study population was male (52.24%). The greatest proportion of decedents were aged between 70 and 79 years at time of death. The most common cancer type as a primary cause of death was lung cancer, making up over 20% of the included population.

Cancer was recorded as the primary cause of death in 64,553 (75.3%) patients. Patients who had a cancer diagnosis and died from cancer tended to be younger and had a higher resource use compared to those with another cause of death. For more details see Supplementary Figures 2 and 3.

Table 2 presents patient characteristics split by cancer type. The first column presents the cohort of patients who had a cancer diagnosis regardless of the main cause of death. The second column consists solely of those with cancer as the main cause of death. Compared to the whole cohort, patients in this category were slightly younger, from more deprived areas and had a higher level of comorbidity. Despite the study population being limited to older adults (60+), we observed differences in age at death across cancer types, with breast and prostate cancer patients being oldest at their time of death. The highest comorbidity burden was detected in those dying from ovarian cancer. There were noticeable differences in the socioeconomic status (SIMD) of patients by cancer type. Patients who died from lung cancer as their main cause of death were found to have the lowest SIMD with a mean value of 2.53 (1.33) whilst those dying from ovarian-, prostate-, brain- or hematologic cancers were typically less socioeconomically deprived, with

Table 1: Descriptive characteristics of Scottish decedents (2012 to 2017) with a cancer diagnosis

	Frequency	Percent
Sex		
Male	44787	52.24
Female	40945	47.76
Age category		
60–64	11937	13.92
65–69	14640	17.08
70–74	17279	20.15
75–79	17594	20.52
80–84	14173	16.53
85–89	7817	9.12
90+	2292	2.67
Cancer type/ group		
Cancer not main cause of death	21179	24.70
Bronchus/Lung	18372	21.43
Colon/Rectosigmoideum/Rectum	6342	7.40
Oesophagus/Stomach	5540	6.46
Kidney/Bladder	3555	4.15
Liver/Intrahepatic	2398	2.80
Pancreas	3334	3.89
Haematological	2342	2.73
Brain	1158	1.35
Breast	2136	2.49
Ovary	1331	1.55
Prostate	2846	3.32
“other” cancer	15199	17.73
Charlson Comorbidity Index (CCI)		
CCI 0 or not recorded	20325	23.71
CCI 1 - CCI 3	53412	62.30
CCI 4 - CCI 6	5143	6.00
CCI 7 - CCI 12	6852	7.99
Scottish Index of Multiple Deprivation (SIMD)		
SIMD 1st quintile (Most deprived)	19393	22.64
SIMD 2 nd quintile	19649	22.94
SIMD 3 rd quintile	17876	20.87
SIMD 4 th quintile	15260	17.82
SIMD 5th quintile (Least deprived)	13462	15.72
Urban-rural indicator		
1 - Large urban area	37967	44.29
2 - Other Urban Areas	30263	35.30
3 - Accessible Small Towns	8194	9.56
4 - Remote Small Towns	2258	2.63
5 - Accessible Rural Areas	1288	1.50
6 - Remote Rural Areas	5762	6.72

Percentages have been round to 2.d.p and therefore may not add up to 100%

a mean SIMD category value of 3 or more, indicating less deprived areas.

Inpatient, outpatient and day case use

Of the 85,732 patients included in the final analysis, 78,919 (92.05%) patients had at least one inpatient stay or day

case activity during their last year of life, whilst 75,863 (88.49%) had at least one outpatient attendance. The number of patients with no in- or outpatient appointment was less than 0.1%. The average number of inpatient stays, length of stay per inpatient stay, number of outpatient and day case appointments are presented in Supplementary Table 1. Results are split into cancer types and presented with regards to proximity to death. Over the last year of life, patients with

Table 2: Average age at death, comorbidity burden (measured using the Charlson Comorbidity Index [CCI]) and socioeconomic status (measured using the Scottish Index of Multiple Deprivation [SIMD]) of Scottish decedents (2012 to 2017) with a cancer diagnosis presented by cancer type

	All	Cancer	Bron./Lung	Col/Rec	Esoph/Sto.	Liver/Intr.	Pancreas	Kidney/Bl.	Breast	Ovary	Prostate	Brain	Hematolo
	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)
age death	80.01	78.85	77.32	80.15	78.56	78.20	77.99	80.01	81.16	78.61	80.87	75.61	79.66
age death	(8.15)	(7.82)	(7.35)	(7.86)	(7.76)	(7.48)	(7.67)	(7.67)	(8.57)	(7.78)	(7.84)	(6.89)	(7.57)
CCI	2.42	2.70	2.66	2.76	2.39	2.61	2.39	2.66	3.39	3.56	3.01	2.16	2.02
CCI	(2.17)	(2.24)	(2.16)	(2.28)	(1.55)	(1.92)	(1.79)	(2.22)	(2.93)	(2.87)	(2.71)	(1.30)	(1.34)
SIMD	2.81	2.79	2.53	2.93	2.83	2.81	2.95	2.84	2.96	3.00	3.04	3.11	3.05
SIMD	(1.38)	(1.38)	(1.33)	(1.39)	(1.38)	(1.41)	(1.38)	(1.37)	(1.38)	(1.40)	(1.38)	(1.36)	(1.38)

Bron./Lung: Bronchus and Lung cancer; Col/Rec: Colon, Rectosigmoideum and Rectum cancer; Esoph/Sto.: Esophagus/Stomach; Liver/Intr.: Liver and Intrahepatic cancer; Kidney/Bl.: Kidney and Bladder cancer; Hematolo.: Hematologic cancer; CCI: Charlson Comorbidity Index; SIMD: Scottish Index of Multiple Deprivation.

haematological cancers had the most inpatient appointments, with an average of 11.8 stays; but with a comparably shorter mean length of stay (LOS) of 6.1 days per stay. The longest average LOS was recorded for brain cancer patients followed by prostate cancer patients, with 9.07 and 7.94 days per stay, respectively. Haematological cancer patients had the highest number of outpatient appointments in their last year of life (mean 9.9 appointments), followed by ovary and breast cancer patients, with 6.6 and 6.3 appointments respectively. Relatively low resource use was captured for day cases, with haematological and ovarian cancer patients being most frequent day case attenders.

Patterns of healthcare use and associated costs by cancer type

Figure 1 demonstrates significant variation in patterns of healthcare use across cancer types. For a translation into costs, please see Supplementary Figure 4. Inpatient hospitalisation rates increased with proximity to death for all cancer types, though at very different rates. Varying degrees of use were observed between patients with cancer as the main cause of death and those who died from other causes, with the latter utilising fewer resources in their last year of life in all three categories (inpatient, outpatient and day case use). Once again, different patterns emerged depending on cancer type. Patients with haematological cancers were consistently high users of secondary care, with associated high costs. Considering the solid tumours only, ovarian cancer patients accessed considerably more outpatient and day care over the last year of life. Patients with certain other cancer types, for example those with brain cancer, recorded a high use of inpatient care whilst other resource use remained low. Conversely, patients with other types of cancer, such as cancers of the lower gastrointestinal tract, showed a high frequency of outpatient use whilst their use of inpatient services was minimal. Overall, frequency of outpatient care remained relatively constant over the last year of life for most cancer groups, except for those who died from haematological cancers. This patient cohort showed a steep increase in outpatient use up to the last month prior to death, followed

by a sizeable drop in the last month prior to death. When comparing resource use patterns of decedents with a cancer diagnosis who died from any other cause to those with cancer as their identified main cause of death, higher resource use can be observed for the latter across inpatient, outpatient and day case activity. Whilst patterns were similar for inpatient use with a steep increase especially in the last three month of life, day case and outpatient activity were more frequently recorded in those dying from cancer. For more information, see Supplementary Table 3.

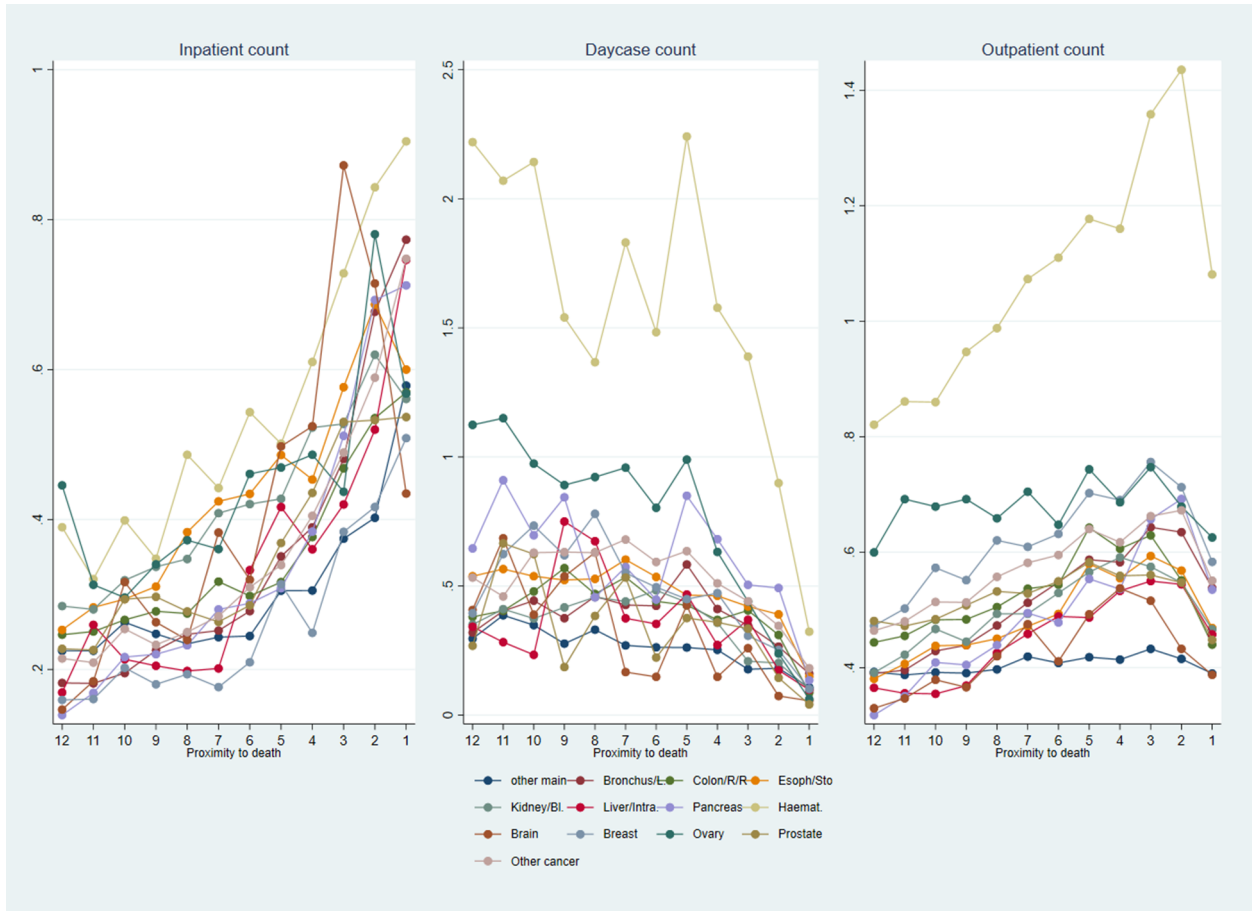
The results showing the frequency (presented in absolute numbers) of resource use are in line with the corresponding costs shown in Table 4 (and Supplementary Graph 4) which confirms the outlier position of haematological cancers in terms of costs. Costs for inpatient stays in the last year of life followed a clear and consistent pattern across all cancer types, with a steep rise over the last three months of life.

Univariate analysis and multivariate analysis

Results from the univariate analysis (Supplementary Tables 2–7) reveal significantly lower costs associated with increased age, female gender and residing in the 3rd and 4th SIMD decile categories (some of the less deprived postcode areas). Costs were observed to be slightly higher for those in SIMD quintile five (least deprived category) and for those living in the most urban areas. However, the majority of the variation in costs was explained by the clinical profiles of decedents, age and their level of comorbidity.

Results of the multivariate analysis (including the sum of inpatient, outpatient and day case costs) (Table 3) confirmed the univariate results with the exception of the SIMD indicator, where only the findings related to the fifth quintile remained statistically significant. This may be due to its correlation with the rural-urban indicator. Adding in an interaction term between age and comorbidity in an attempt to unpick the effects and split the population by cause of death, it was observed that for decedents for whom cancer was the main

Figure 1: Inpatient, day case and outpatient resource use patterns, in cancer- patients' last 12 months of life. Proximity to death (in month) on the x-axis; average resource use within each month (counts) on the y-axis. Results are presented for each cancer type



Other main: cancer not main cause of death; Bronchus/L: Bronchus and Lung cancer; Colon/R/R: Colon, Rectosigmoideum and Rectum cancer; Esoph/Sto.: Esophagus/Stomach; Liver/Intra.: Liver and Intrahepatic cancer; Kidney/Bl.: Kidney and Bladder cancer; Hemat.: Hematologic cancer.

cause of death, age and comorbidity burden had a bigger impact on costs. (Supplementary Tables 8, 9)

Variation of secondary care use between cancer types (GLM for individual cancers)

Lung cancer secondary care pathways were associated with the lowest costs in the last year of life, followed by those for people with liver cancer (see Supplementary Table 4). Costs were adjusted for age, gender and comorbidity as well as RU and SIMD. Overall, the results presented in Table 4 confirmed the findings for all cancers. It was observed that increasing age was associated with lower costs for all cancer types, albeit that the magnitude of cost reduction with increasing age varied by cancer type. When dying from oesophageal, stomach or brain cancer, the last life year was significantly less costly for women than men. An increased number of comorbidities led to a cost increase. Deprivation and rurality did not have a significant effect on costs of secondary care, with the exception of lung cancer patients where the treatment for those residing in areas that are more rural was shown to be slightly less costly.

Looking at the costs in absolute terms, it becomes clear that certain cancer types were significantly more expensive than others. The GLMs for the individual cancer types are available upon request, though their translation into monetary values is presented in Table 4.

Interaction between age and comorbidity burden

In univariable and multivariable cost analyses for age and comorbidity, increasing age was associated with lower costs whilst an increasing number of comorbidities was associated with higher costs (Table 3).

Interaction terms between age and comorbidity showed considerable variation in their relationship between the cancer types, although these indicated a general tendency for comorbidities to have less impact on costs at older ages. Based on the negative coefficient on the interaction term, a higher comorbidity burden was associated with increased costs but less so with older age. Results supporting this finding are presented in Supplementary Table 10 and in the Supplementary Figures 5–7.

Table 3: Generalised linear model – multivariate Analysis, for patients with cancer as a primary cause of death

Category	Coefficient	CI [95%]
Age category		
60–64	0	[0,0]
65–69	−0.0845***	[−0.108,−0.0613]
70–74	−0.159***	[−0.182,−0.137]
75–79	−0.229***	[−0.252,−0.207]
80–84	−0.307***	[−0.331,−0.283]
85–89	−0.357***	[−0.385,−0.328]
90+	−0.396***	[−0.441,−0.352]
Charlson Comorbidity Index		
CCI 0 or not recorded	0	[0,0]
CCI 1- CCI 3	0.661***	[0.645,0.677]
CCI 4 - CCI 6	0.649***	[0.617,0.677]
CCI 7 - CCI 12	0.909***	[0.881,0.936]
Sex		
Male	0	[0,0]
Female	−0.0589***	[−0.0718,−0.0459]
Scottish Index of Multiple Deprivation		
SIMD 1st quintile (Most deprived)	0	[0,0]
SIMD 2 nd quintile	0.0323	[−0.0159,0.0224]
SIMD 3 rd quintile	−0.0193	[−0.0394,0.000707]
SIMD 4 th quintile	−0.0194	[−0.0401,0.0661]
SIMD 5th quintile (Least deprived)	0.0499***	[0.0237,0.0661]
Urban-rural indicator		
1 - Large urban area	0	[0,0]
2 - Other Urban Areas	−0.0454***	[−0.0601,−0.0308]
3 - Accessible Small Towns	−0.0736***	[−0.0966,−0.0506]
4 - Remote Small Towns	−0.0879***	[−0.129,−0.0469]
5 - Accessible Rural Areas	−0.149***	[−0.203,−0.0755]
6 - Remote Rural Areas	−0.103***	[−0.130,−0.0755]
Constant	9.069***	[9.041,9.096]
Observations	60728	

95% confidence intervals in brackets.

*p < 0.05, ** p < 0.01, ***p < 0.001.

Discussion

Main findings

There is a pervading myth that the escalating healthcare costs observed in developed nations worldwide are solely attributable to the ageing population. Instead of age, comorbidities and cancer diagnosis were identified as the main drivers of variation in cost at end of life for cancer patients over 65. However, patient age remained an important factor, with reduced costs evident for those who are the very oldest. This study's findings confirm the results of our recent studies, showing that patients with cancer dying at an older age use considerably less health care resources in their last year of life than their younger counterparts. [4, 16]

A 'Realistic Medicine' approach has been proposed as a response to a perception of excessive futile intervention in elderly cancer populations. Whilst previous studies have confirmed lower rates of healthcare utilisation at the end

of life for those with conditions such as dementia, our results show a high use of hospital-based care for the cancer population, albeit not for all types of cancer. However, clear interactions between age and tumour type are apparent, likely reflecting differential levels of treatment intensity in cancer types where the balance of harms and benefits may be more in favour of treatment. This might be complicated by differences in the composition or severity of comorbidities in different age groups, which may not be captured by the Charlson Comorbidity Index. Further studies with more detailed exploration of comorbidity data available in routine records are needed to unpick this complex relationship.

Variation in healthcare use between cancer types was most pronounced between those with haematological cancers compared with solid tumours. Within the group of patients who had solid tumours, those with ovarian cancer had the highest secondary care use and costs; an observation potentially explained by a practice of patients with advanced

Table 4: Generalised linear model results presented for “cancer not being the main cause of death” and all cancer types in- costs (£)

Category	Cancer NOT main cause †	Bronchus/ Lung	Colon/ Rectosig/ Rectum	Esophagus/ Stomach	Kidney/ Bladder	Liver/ Intrahepatic	Pancreas	Hematologic	Brain	Breast	Ovary	Prostate	Other cancers
Age category													
60-64	12489.7	12047.2	16924.9	15373.8	15498.8	13103.8	14551.3	36502.8	17527.5	14392.3	25440.8	15915	16773
65-69	12160.3**	11537***	14619.7**	14754	15325.6*	12189.1	13206	29082.8	16538.3	15148.2	21695.9	13341.6	14426.7***
70-74	10901.1**	10607.2***	12329.2***	12298.7	14011.7**	10270.1**	10829.2**	25428.1*	13991.7	11862.5**	18225	12835.1	13660.5***
75-79	10782.7***	9975.3***	11063.3***	11253.4	12704.5**	10707.5*	9178.4**	21420**	11066.5	10185.3***	13266.7**	12719.5	12420.5***
80-84	10027.5***	9421.6***	9933.5***	10570.2	11551.1**	8782.1***	8640.3*	15872.9**	8598.1*	8652.7***	11729.9*	10919.5	10639***
85-89	8993***	9250.1***	9562.1**	9505	10501.4**	8487.3**	7821.3*	14211.1**	9787.5	6697.4***	10232.9	9039.1	9666.4***
90+	8373.6***	9441.3***	8760.2**	8912.8	9132.9**	7073**	7554.5	11717.7*	10677.7	6010.5**	8576.4	8186.6	9133***
Sex													
Male	10926.3	10695.9	12680.2	13137.1	13783.7	10995.6	11282	24270.9	15424.5	12408.5	NA	12577.3	13599.5
Female	10171**	10941.8	12133.4	11808.5***	12778.1*	10952.6	11273.7	24425.3	13558.5**	11371.2	18065.1	NA	12699.8***
Charlson Comorbidity Index													
No Comorbidity	9856.7	7242.5	8526	8068.2	9640.1	8154.5	7683.9	15875.9	9029.6	10458.3	9301.8	10459	12262.5
CCI (1 to 3)	12846.6***	11209.6***	12779.3***	13017.8***	13811.7**	11121.1**	11832.1***	26158.1	15620.2*	12176.6*	17195.7	12900.6*	14841.5***
CCI (4 to 6)	17318.7***	12356.9*	12242.8	13913.8*	16209.1	12948.3*	11170.1	27551.2	12891.7	13698.8	11815.6**	14154.9	10405
CCI (7 to 12)	15971.3*	15886.2	17993*	16038.6	17362.4	17133*	15857.8	26107.2**	16307.7	15457.5	24681.6	17407.8	15771.6***
Scottish Index of Multiple Deprivation (SIMD)													
1st (most deprived)	11082.7	10864.9	12159.9	12906.9	14177.9	11405.7	11180.3	23633.3	13684.6	12077.5	18527.3	13212.6	12576.1
2nd	10948.3	10885.1	12423.7	12523.1	13267.6*	10874.3	10355.8*	25618	14444.4	10492.5	18008.7	12304.5	12813.7
3rd	10209***	10774.5	11944.4	12607.1	12963.1	11166.7	10589.8	22568	14943.2	11296.5	17754.3	12821.4	12957.6*
4th	10190.1***	10407.9	12879.5*	12528	13044.5	10221.8	12213.8	24531.9	15078.7	10266.7	17673.3	11710*	13205.5**
5th (least deprived)	10318.6**	11145.8	12810.7	12644.2	13491.2	11066.3	12329	25243.4	14813.9	12929.9	18376.4	12924.9	14644.6***
Urban- rural indicator													
Large Urban area	10834.5	11302.9	12937.8	13201.3	13815.5	11734.7	11488.4	25046.4	15258.6	11367.6	19223.5	12951	13335.6
Other Urban Areas	10658.9	10477.4***	12384.8	12338**	13053.7**	10301**	11137.7	24397.1	14276.1	11715.9	17468.1*	12431.4	13177.7
Access. Small Towns	10552.8*	10346.3***	11255.8***	12091.1**	13226.2	10939.4	11188.4	24969.7	15058.8	12755.7	16053.8*	12598.9	12952.9*
Remote Small Towns	9562.9	10728.8*	12451.2*	11298*	12287.6	8916.5	9634.7*	20620.8	13419.2	7955.4**	14700.6*	11011.5*	12273.4
Accessible Rural Areas	8760.5***	10138.2	10314.5*	14156	12960	9952.1	10383	16496.9*	13992.2	9834.7	20233.4	12057.9	11289.7*
Remote Rural Areas	9367.6***	9998.4***	11274.1***	11797.5**	13268.1	10079.8	11575.8	21420.6**	13291.1	9719.8**	16774.7	11793.1	12926.1
Observations	21071	18294	6297	5520	3542	2393	3320	2331	1154	2107	1322	2837	15050

* p > 0.05, ** p > 0.01, *** p > 0.001.

disease commonly receiving systemic treatment because of high response rates. This is contrasted with brain cancer decedents who had the lowest secondary care costs; and whose disease may be characterised by low rates of control, cure or response to intervention over the last year of life. It is important to note that this study included decedents only and therefore reflects pathways and outcomes for those who were not cured of their cancer by their treatment.

Alongside the treatment context differences between cancer types, there are many clinical differences in the symptoms and complications that patients experience and the consequences of these for secondary care use. For instance, patients with advanced ovarian cancer commonly experience bowel obstruction or require ascites to be drained, necessitating inpatient admission. Individuals with haematological cancers typically require regular blood product support alongside their treatment, also necessitating in- and/or outpatient care. Therefore, the cancer type and its clinical manifestations, as well as the typical treatment approaches, will necessarily inform the need for secondary care interventions.

Whilst acknowledging the valuable role that hospital-based care offers many patients with cancer in their last year of life, it is also important to consider that some secondary care interventions may not be beneficial. Perceived ‘over-medicalisation’ towards the end of life has been shown to have a negative impact on patients’ and relatives’ satisfaction with care and to be linked with a lower quality of life [25–27]. There is a clear need to elicit patient and family expectations and preferences for care and to aim for a meaningful shared decision-making approach [11], arguably at all stages of the cancer journey, but especially as the illness advances and the likelihood of benefit from acute medical care may be diminishing.

Alongside the need to align care with patients’ needs and preferences, it is also critical that only those treatments and interventions that offer a reasonable chance of benefit are offered, in order that our scarce health care resources are utilised efficiently. New, highly effective treatments for several cancer types have been very welcome, but we cannot ignore the additional financial burden of these on our already strained health care system. It is therefore ever more crucial to ensure that treatments are targeted to those who stand to benefit

the most [12, 13]. As costs at the end of life are frequently included in health economic models of new cancer drugs for reimbursement submissions, this study provides data that will be of direct use for this purpose. Furthermore, improving the quality and appropriateness of care for patients in the last phase of life is a national and international priority [28].

This study confirms recent research showing that secondary care costs typically rise steeply in the last months of life [4, 29, 32, 33]. These are important findings given that the majority of cancer deaths occur in hospital, despite expressed preferences ahead of time by the majority for end-of-life care at home [30]. Likelihood of dying in in-patient palliative or end-of-life care facilities are further dependent on the level of remoteness, with a higher chance of dying in an inpatient facility when driving time is less than ten minutes [34]. A recent trend for more community-based deaths of people with cancer has been observed, and this may reflect an increasing tendency towards advance care planning. An interesting finding in our study was the association between rurality and lower hospital costs, possibly reflecting proactive primary care for more rural populations, and alternative pathways to acute hospitalisation such as community hospital admission. Further lower costs for patients from rural areas could be associated to longer travel times and/or lower access to secondary care; considerations, which need to be taken into account when considering centralising specialist cancer care [35]. Another factor potentially influencing the level of secondary care use is the level of rurality; it was shown to influence cancer related self-efficacy, with an increase in self-efficacy in rural areas [36].

Strengths and limitations of the study

This study captures healthcare data for the entire Scottish decedent population. By including routine datasets covering the whole population, there was low risk of sampling errors and selection bias along with the inclusion of exact incidence and prevalence rates. Furthermore, the administrative datasets covered several years, supporting the inclusion of data from up to five years prior to death (informed the calculation of CCI) as well as decedents over several years. In addition, learning from routine electronic health and administrative records carried no burden for the study participants.

Although the breadth and depth of Scottish administrative data was a strength, there were some notable gaps in our data. We were restricted to deaths in over 60 year olds due to the availability of data which was part of a wider research programme. All data included originated in secondary care, albeit across inpatient, outpatient and daycase services. Primary care 'in hours' and 'out of hours' data was not available for this project, nor was data relating to social care and specialist palliative care and data on drugs. These are important parts of the care jigsaw, given that even with frequent hospitalisation, most patients spent most of their last year of life being cared for in the community. Furthermore, it did not allow for comparisons in secondary care use to be drawn between patients with differing degrees of primary care or specialist palliative care input; areas which are of great relevance and interest. A further limitation arose from the way the CCI was derived. CCI values were linked solely to inpatient datasets (92% had at least one inpatient appointment)

leaving 8% without a CCI value. The results relating to the CCI therefore might have excluded the 'better managed in the community' or 'relatively healthier' patients with a comorbid condition that did not lead to admission or secondary outpatient care. Further data gaps related to specialist cancer treatments such as chemotherapy or radiotherapy. Despite our data not providing detailed information on specialist cancer treatments, due to the underlying structure of the Scottish Health Service Costs it is highly likely that the costs are reflected in the analysis [21].

It should be noted that our parallel study in England encompassed primary care data, but only for a small sample of the English national population; thus, neither study has managed complete data capture [29]. Future regional studies may be more likely to achieve in-depth, near whole healthcare system examination. A further limitation of this study is that we did not hear from people with advanced cancer or those close to them about their experiences of healthcare and the extent to which the care they accessed offered them meaningful benefit. Future studies should arguably incorporate a mixed methods approach, whereby routine data provides objective data relating to clinical pathways and costs, and qualitative research alongside illuminates the subjective, lived experience. It is only by examining value from both the health system and personal perspectives that we can expect to make recommendations about how resources can be optimally targeted.

Conclusions

We have described patterns of secondary healthcare use and associated costs for all Scottish decedents with a cancer diagnosis who died between 2012 and 2017. Our headline finding is that inpatient hospitalisation accounted for the greatest proportion of costs across all cancer types, and particularly so over the last weeks of life. This end of life phase, when deteriorating health is inevitable, is a time when we might reasonably question the value of inpatient hospital care for many.

We recommend further research to identify enablers of a potential shift from secondary care to community care at the end of life. We do not know if the observed drop-off in in day-case and outpatient activity is replaced by community services such as GP contacts and community palliative care visits, or if it is simply replaced by inpatient hospital activity as people become too frail or sick to attend on an outpatient basis. It is not clear from this study, or indeed in others, whether community services are adequately resourced to meet cancer patients' needs as they deteriorate, or if they are potentially underused. It is likely that there are some cancer types which may be more readily supported in primary care than others. We require better insight into the value of the social care system and how community care can be a realistic alternative to hospital-based care if it is both resourced and accessible. We recommend to replicate this study in other health systems for additional learning. Integrated health and social care in Scotland is a new reality and provides opportunity for whole system learning [28]. Whether primary care can be seen as a substitute for secondary care or not is the rationale for a

planned research project that will delve into primary care and community data [31].

Declarations

Ethics

Approval was granted by the Scottish Public Benefit and Privacy panel (Ref: 1617-0100) for analysis within the Scottish National Research Data Safe Haven.

Conflict of interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Authors' contributions

KD and led the conception and design of the study supported by PH. KD led the data acquisition, conducted data management and analysis supported by EL, EG, JM and PH. KD led the data interpretation supported by EG, EL, GT, XL, JB, EL and PH. KD, EL, GT and JB drafted and revised the article supported PH. All authors critically reviewed and edited the paper and approved the final version to be published.

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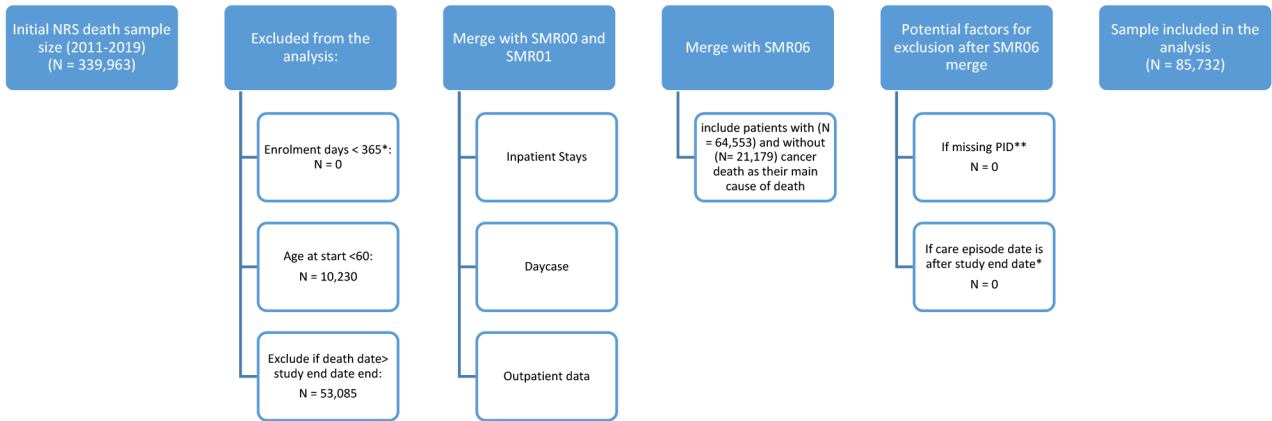
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Supplementary Figure 1: Flow chart of datalinkage & inclusion/exclusion criteria

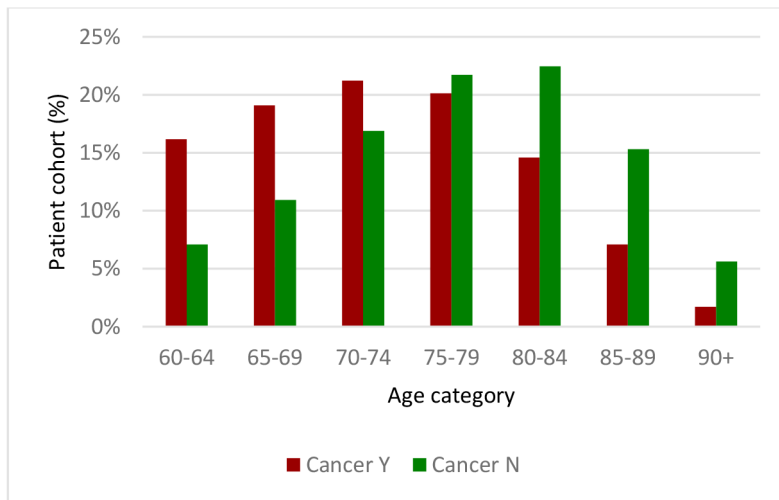


*No exclusions were necessary as the datasets included data for a longer time as the study period.

**PID = Person Identification Number.

NRS death: National Records of Scotland, Vital Events – Deaths; SMR00: Outpatient Attendance; SMR01: General/Acute Inpatient and Day Case; SMR06: Scottish Cancer Registry.

Supplementary Figure 2: Percentage of cancer patients with cancer as their main cause of death (Cancer = Y) and “other” main death diagnosis (Cancer = N) by age



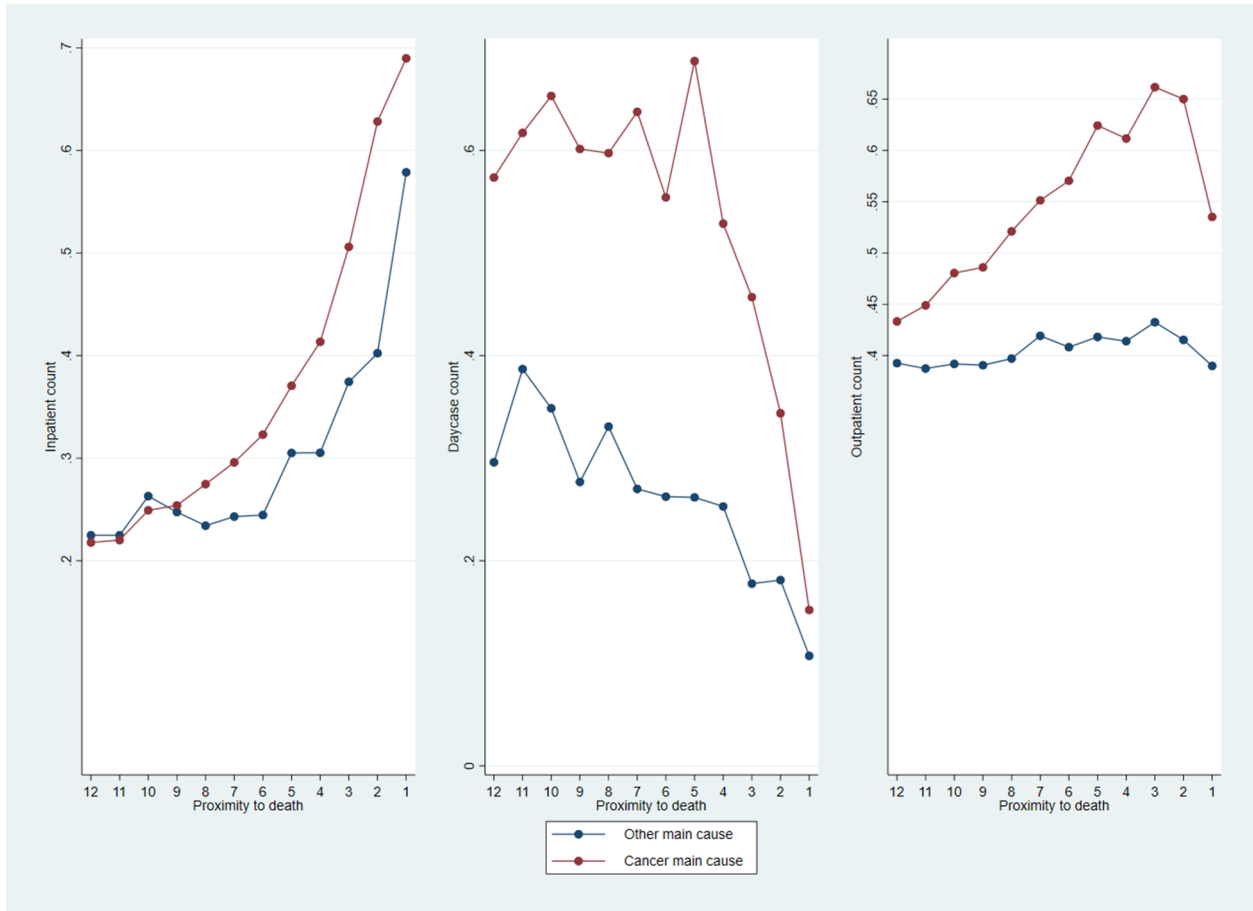
Supplementary Table 1: Resource use (Inpatient, Inpatient LOS, Outpatient appointments and daycase use) over proximity to death (last 12, 6, 3, 1 month) by cancer type

	All		Cancer main cause		Bronchus Lung		Col. Rect. Rectosig.		Esoph. Stomache		Liver. Intrahep.		Pancreas		Kidney Bladder		Breast		Ovary		Prostate		Brain		Haem.		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Proximity to Death: 12 months																											
Inpatient	5.88	5.68	5.99	5.88	5.30	4.11	5.75	4.68	6.15	4.93	5.21	4.41	5.68	5.60	6.36	4.57	5.60	5.19	8.41	8.33	5.72	4.23	5.27	3.42	11.80	14.99	
Average LOS	7.15	13.14	7.10	12.54	6.52	11.38	7.36	13.02	6.09	10.69	7.78	12.03	6.96	10.74	7.88	13.90	8.29	16.12	6.72	12.67	7.94	13.14	9.07	15.58	6.10	12.09	
Outpatient	5.01	6.00	5.31	6.28	5.08	5.04	5.09	6.35	4.97	4.64	4.29	4.65	4.78	5.86	4.86	5.00	6.25	7.34	6.59	7.08	5.24	5.14	3.94	3.87	9.92	14.31	
Day cases	1.15	4.76	1.36	5.19	0.97	3.19	1.19	3.89	1.45	4.33	0.64	2.85	1.52	5.07	0.92	3.37	1.40	4.61	3.20	8.18	0.83	2.92	0.30	1.73	6.45	15.33	
Proximity to Death: 6 months																											
Inpatient	3.47	3.70	3.55	3.77	3.40	3.12	3.20	3.20	3.55	3.42	3.32	3.15	3.48	3.44	3.64	3.39	3.15	3.33	4.07	4.84	3.37	3.38	3.49	2.98	6.01	8.32	
Average LOS	7.56	12.31	7.63	11.98	7.02	11.07	8.04	13.02	6.80	11.16	8.26	12.14	7.37	10.40	8.54	13.13	8.74	12.84	7.69	11.35	8.75	13.56	9.53	14.42	6.44	12.10	
Outpatient	2.79	3.52	3.01	3.69	2.98	3.07	2.77	3.67	2.83	2.85	2.47	2.90	2.84	3.54	2.69	2.92	3.48	4.26	3.42	4.11	2.72	3.01	2.21	2.27	5.67	8.26	
Day cases	0.47	2.45	0.56	2.68	0.44	1.84	0.43	1.88	0.63	2.28	0.28	1.65	0.64	2.63	0.35	1.69	0.50	2.25	1.12	4.08	0.30	1.57	0.12	0.91	2.73	7.99	
Proximity to Death: 3 months																											
Inpatient	2.05	2.50	2.08	2.50	2.11	2.31	1.85	2.28	2.00	2.45	2.02	2.32	2.09	2.31	2.03	2.45	1.85	2.24	2.07	2.67	1.89	2.39	1.94	2.36	2.98	4.40	
Average LOS	7.67	11.05	7.91	11.00	7.33	10.27	8.24	11.26	7.33	10.46	8.29	10.91	7.62	10.03	8.85	12.16	9.19	12.19	8.29	10.41	9.09	12.38	10.68	14.13	6.38	10.43	
Outpatient	1.19	1.22	1.28	1.24	1.34	1.20	1.13	1.20	1.25	1.19	1.12	1.15	1.27	1.24	1.17	1.15	1.38	1.31	1.40	1.25	1.12	1.17	1.01	1.06	1.82	1.66	
Day cases	0.17	1.13	0.19	1.24	0.16	0.91	0.14	0.90	0.24	1.16	0.11	0.92	0.23	1.24	0.12	0.81	0.17	1.09	0.31	1.64	0.09	0.67	0.03	0.37	0.98	3.72	
Proximity to Death: 1 month																											
Inpatient	0.79	1.39	0.76	1.35	0.82	1.38	0.66	1.27	0.67	1.28	0.80	1.34	0.74	1.26	0.63	1.30	0.73	1.29	0.63	1.26	0.63	1.22	0.46	1.15	0.90	1.63	
Average LOS	6.01	6.83	6.45	7.00	6.14	6.77	6.60	7.12	6.33	6.85	6.66	7.18	6.66	7.03	6.88	6.97	6.64	7.02	7.33	7.45	6.98	7.37	7.98	8.13	5.26	6.51	
Outpatient	0.46	0.85	0.50	0.88	0.52	0.84	0.41	0.77	0.46	0.80	0.43	0.78	0.53	0.96	0.43	0.76	0.56	0.92	0.56	0.97	0.39	0.74	0.37	0.76	0.87	1.47	
Day cases	0.03	0.33	0.03	0.34	0.03	0.30	0.02	0.22	0.04	0.37	0.02	0.28	0.03	0.34	0.02	0.21	0.03	0.31	0.03	0.34	0.02	0.25	0.00	0.00	0.12	0.77	

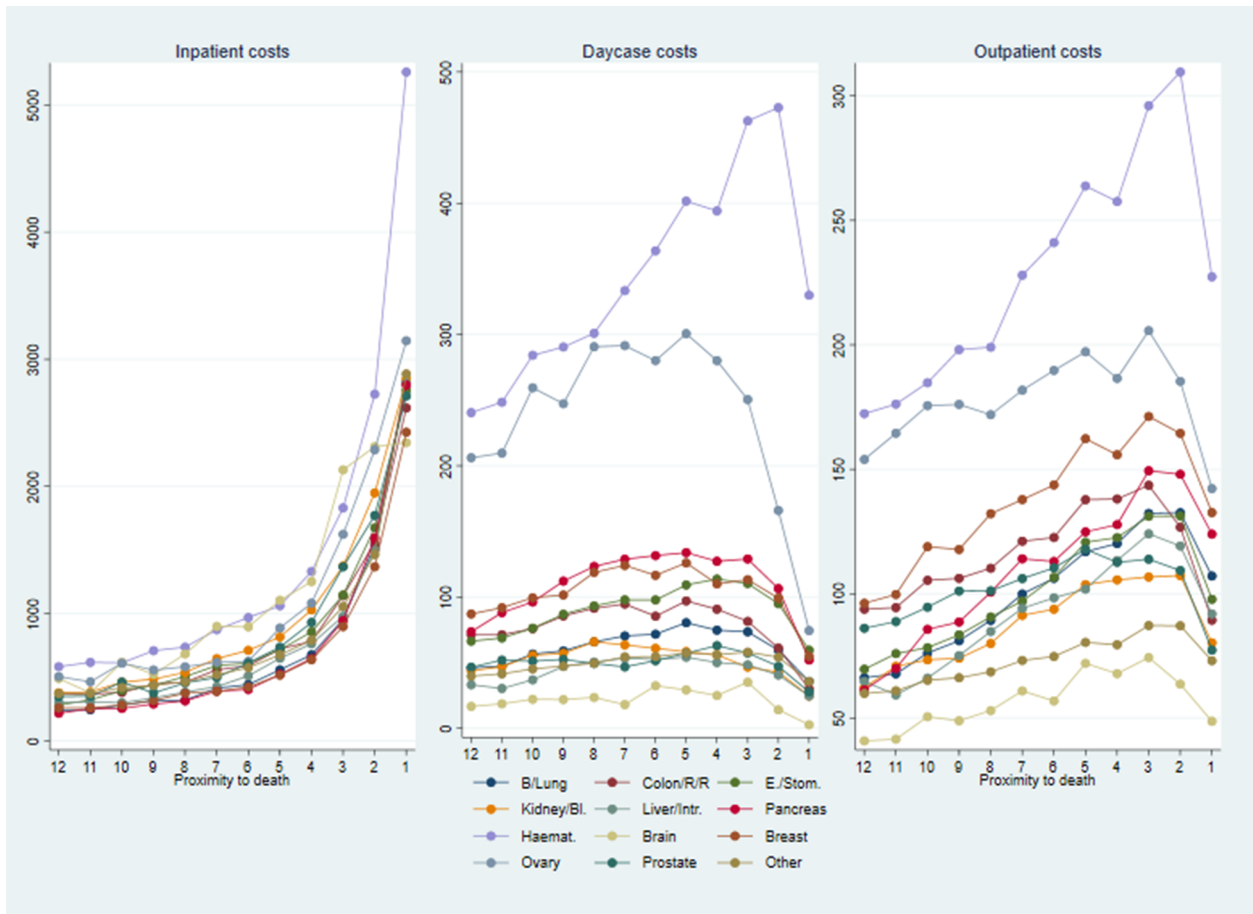
LOS: Length of stay.



Supplementary Figure 3: Inpatient, day case and outpatient resource use patterns in cancer- patients' last 12 months of life. Proximity to death (in month) on the x-axis; average resource use within each month on the y-axis. Results are presented for cancer patients with and without cancer as main cause of death



Supplementary Figure 4: Inpatient, day case and outpatient cost patterns in cancer- patients' last 12 months of life. Proximity to death (in month) on the x-axis; average costs (in £) within each month on the y-axis. Results are presented for each cancer type



Other main: cancer not main cause of death; Bronchus/L:Bronchus and Lung cancer; Colon/R/R: Colon, Rectosigmoideum and Rectum cancer; Esoph/Sto.: Esophagus/Stomach; Liver/Intra.: Liver and Intrahepatic cancer; Kidney/Bl.: Kidney and Bladder cancer; Hemat.: Hematologic cancer.



Supplementary Table 2: Univariate analysis GLM – Gender (margins for readability)

Sex	Costs	CI [95%]
Male	12562.7***	[12451.7,12673.7]
Female	11616.0***	[11508.5,11723.5]
Observations	85328	

*p < 0.05, **p < 0.01, ***p < 0.001.

Supplementary Table 3: Univariate Analysis GLM - Age in categories

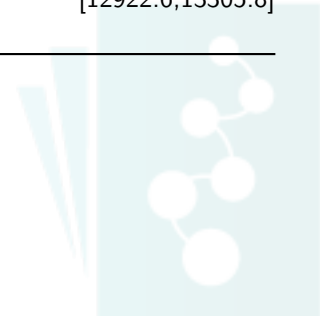
Age category	Costs	CI [95%]
60-64	15895.0***	[15632.4,16157.5]
65-69	14216.6***	[14004.5,14428.8]
70-74	12708.3***	[12533.8,12882.8]
75-79	11212.3***	[11059.6,11365.0]
80-84	9765.3***	[9617.2,9913.5]
85-89	8583.4***	[8407.8,8759.0]
90+	7738.8***	[7444.4,8033.3]
Observations	85328	

*p < 0.05, **p < 0.01, ***p < 0.001.

Supplementary Table 4: Univariate analysis GLM – Cancer type (grouped)

Cancer type/group	Costs	CI [95%]
Cancer NOT main cause [†]	10532.4***	[10402.3,10662.5]
Bronchus/Lung	10812.5***	[10669.2,10955.8]
Colon/Rectosig/Rectum	12395.4***	[12115.5,12675.3]
Esoph./Stomache	12639.3***	[12334.3,12944.2]
Kidney/Bladder	13347.2***	[12945.2,13749.3]
Liver/Intrahepatic	10947.7***	[10546.6,11348.8]
Pancreas	11312.9***	[10961.0,11664.7]
Haematologic	24358.4***	[23454.2,25262.7]
Brain	14617.4***	[13846.4,15388.4]
Breast	11089.2***	[10656.2,11522.3]
Ovary	18070.3***	[17179.4,18961.3]
Prostate	12501.9***	[12081.0,12922.8]
Other cancers	13114.2***	[12922.6,13305.8]
Observations	85328	

*p < 0.05, **p < 0.01, ***p < 0.001.



Supplementary Table 5: Univariate analysis GLM - Comorbidity (Charlson score 0 to 12)

Charlson comorbidity index	Costs	CI [95%]
0	9221.5***	[9086.7,9356.3]
1	11735.3***	[11498.0,11972.6]
2	13287.1***	[13171.3,13403.0]
3	15167.7***	[14886.0,15449.4]
4	18513.3***	[17736.1,19290.6]
5	19746.4***	[18124.5,21368.2]
6	9608.1***	[9313.8,9902.4]
7	13239.1***	[12293.6,14184.7]
8	18177.0***	[17755.0,18598.9]
9	19455.4***	[18254.7,20656.1]
10	21071.9***	[18012.9,24130.9]
11	18674.2***	[12057.9,25290.6]
12	22770.0***	[10535.0,35005.0]
Observations	78919	

*p < 0.05, **p < 0.01, ***p < 0.001.

Supplementary Table 6: Univariate analysis GLM - rural-urban indicator

Urban-rural indicator	Costs	CI [95%]
Large urban area	12605.0***	[12484.1,12725.9]
Other Urban Areas	11867.5***	[11740.0,11995.0]
Accessible Small Towns	11717.2***	[11475.1,11959.2]
Remote Small Towns	11194.5***	[10753.3,11635.7]
Accessible Rural Areas	11005.1***	[10431.8,11578.4]
Remote Rural Areas	11296.5***	[11017.6,11575.4]
Observations	85328	

*p < 0.05, **p < 0.01, ***p < 0.001.

Supplementary Table 7: Univariate analysis GLM - SIMD

Scottish index of multiple deprivation	Costs	CI [95%]
1st (most deprived)	12252.7***	[12088.3,12417.1]
2nd	12052.0***	[11891.3,12212.7]
3rd	11815.1***	[11649.9,11980.4]
4th	11876.8***	[11697.1,12056.5]
5th	12645.7***	[12442.0,12849.4]
Observations	85238	

*p < 0.05, **p < 0.01, ***p < 0.001.

Supplementary Table 8: Multivariate analysis GLM - Cancer MAIN cause of death

Age category	Coefficient	CI [95%]
60–64	0	[0,0]
65–69	–0.0991***	[–0.126,–0.0717]
70–74	–0.203***	[–0.241,–0.165]
75–79	–0.301***	[–0.352,–0.250]
80–84	–0.419***	[–0.484,–0.353]
85–89	–0.484***	[–0.565,–0.402]
90+	–0.529***	[–0.635,–0.422]
Comorbidity Index category		
CCI=0	0	[0,0]
CCI=1	0.302***	[0.266,0.339]
CCI=2	0.187***	[0.109,0.266]
CCI=3	0.488***	[0.371,0.604]
Age and Comorbidity		
age at death	0.00434*	[0.00100,0.00768]
Charlson (0-12)	0.0752***	[0.0382,0.112]
age # Charlson	–0.000866***	[–0.00130,–0.000435]
Sex		
Male	0	[0,0]
Female	–0.0366***	[–0.0502,–0.0230]
Scottish Index of Multiple Deprivation		
1 st (most deprived)	0	[0,0]
2nd	0.00811	[–0.0119,0.0281]
3rd	0.0216*	[0.000498,0.0426]
4th	0.0358**	[0.0141,0.0575]
5th	0.0983***	[0.0760,0.121]
Urban-rural indicator		
RU=1	0	[0,0]
RU=2	–0.0521***	[–0.0675,–0.0367]
RU=3	–0.0777***	[–0.102,–0.0535]
RU=4	–0.0914***	[–0.135,–0.0480]
RU=5	–0.0996***	[–0.156,–0.0437]
RU=6	–0.0789***	[–0.108,–0.0501]
Constant	9.080***	[8.844,9.316]
Observations	60728	

* p < 0.05, ** p < 0.01, *** p < 0.001.



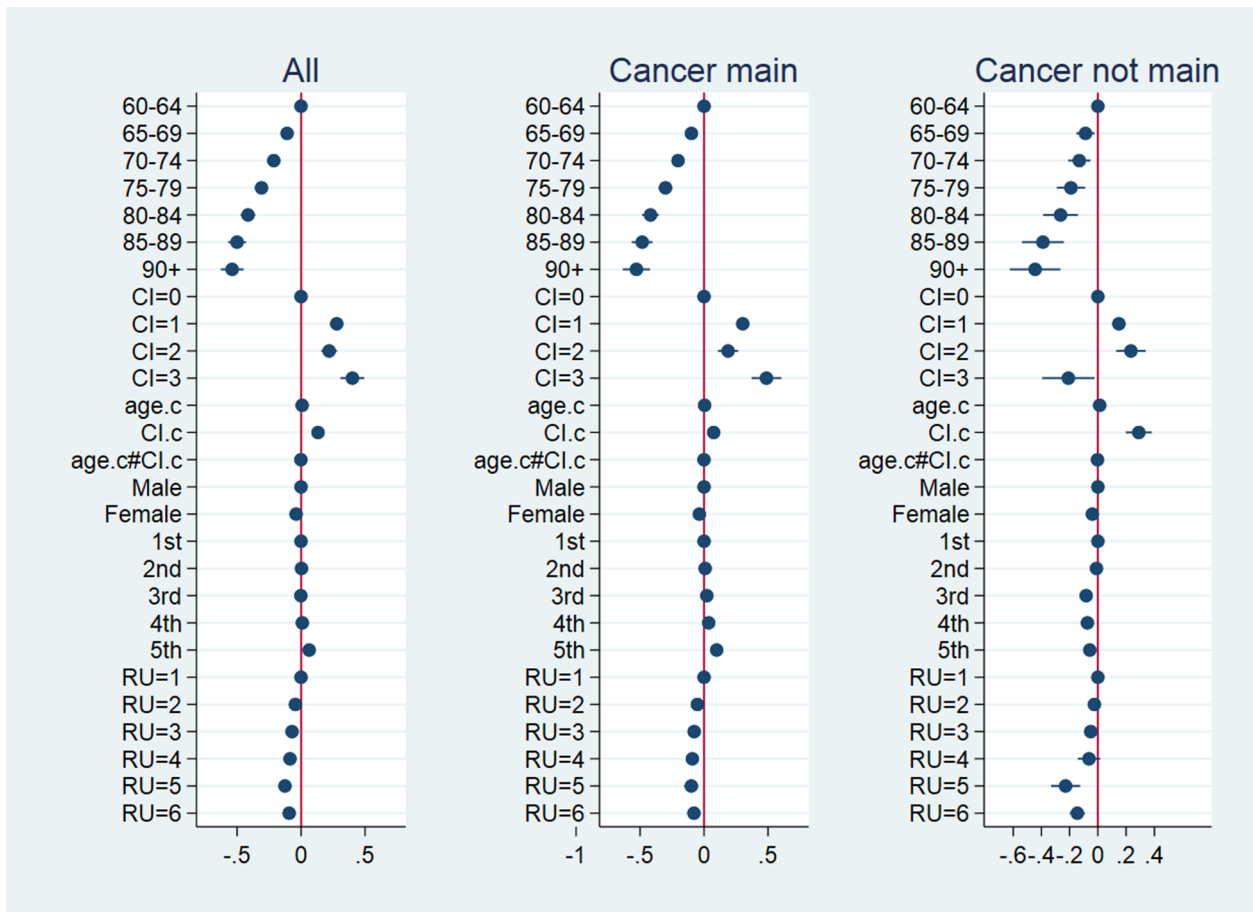
Supplementary Table 9: Multivariate analysis GLM - Cancer NOT main cause of death

Age category	Coefficient	CI [95%]
60-64	0	[0,0]
65-69	-0.0880**	[-0.153,-0.0235]
70-74	-0.132**	[-0.210,-0.0528]
75-79	-0.191***	[-0.291,-0.0902]
80-84	-0.264***	[-0.387,-0.141]
85-89	-0.390***	[-0.538,-0.241]
90+	-0.445***	[-0.624,-0.266]
Comorbidity Index category		
CCI=0	0	[0,0]
CCI=1	0.149***	[0.105,0.193]
CCI=2	0.235***	[0.130,0.339]
CCI=3	-0.209*	[-0.395,-0.0230]
Age and Comorbidity		
age at death	0.0130***	[0.00716,0.0189]
charlson (0-12)	0.290***	[0.198,0.382]
age # charlson	-0.00250***	[-0.00361,-0.00140]
Sex		
Male	0	[0,0]
Female	-0.0386**	[-0.0633,-0.0138]
Scottish Index of Multiple Deprivation		
1st	0	[0,0]
2nd	-0.00966	[-0.0461,0.0268]
3rd	-0.0826***	[-0.120,-0.0448]
4th	-0.0741***	[-0.113,-0.0348]
5th	-0.0573**	[-0.0976,-0.0170]
Urban-rural indicator		
RU=1	0	[0,0]
RU=2	-0.0247	[-0.0523,0.00283]
RU=3	-0.0502*	[-0.0939,-0.00659]
RU=4	-0.0625	[-0.141,0.0161]
RU=5	-0.229***	[-0.332,-0.125]
RU=6	-0.145***	[-0.199,-0.0921]
Constant	8.377***	[7.962,8.792]
Observations	18093	

* p < 0.05, ** p < 0.01, *** p < 0.001.



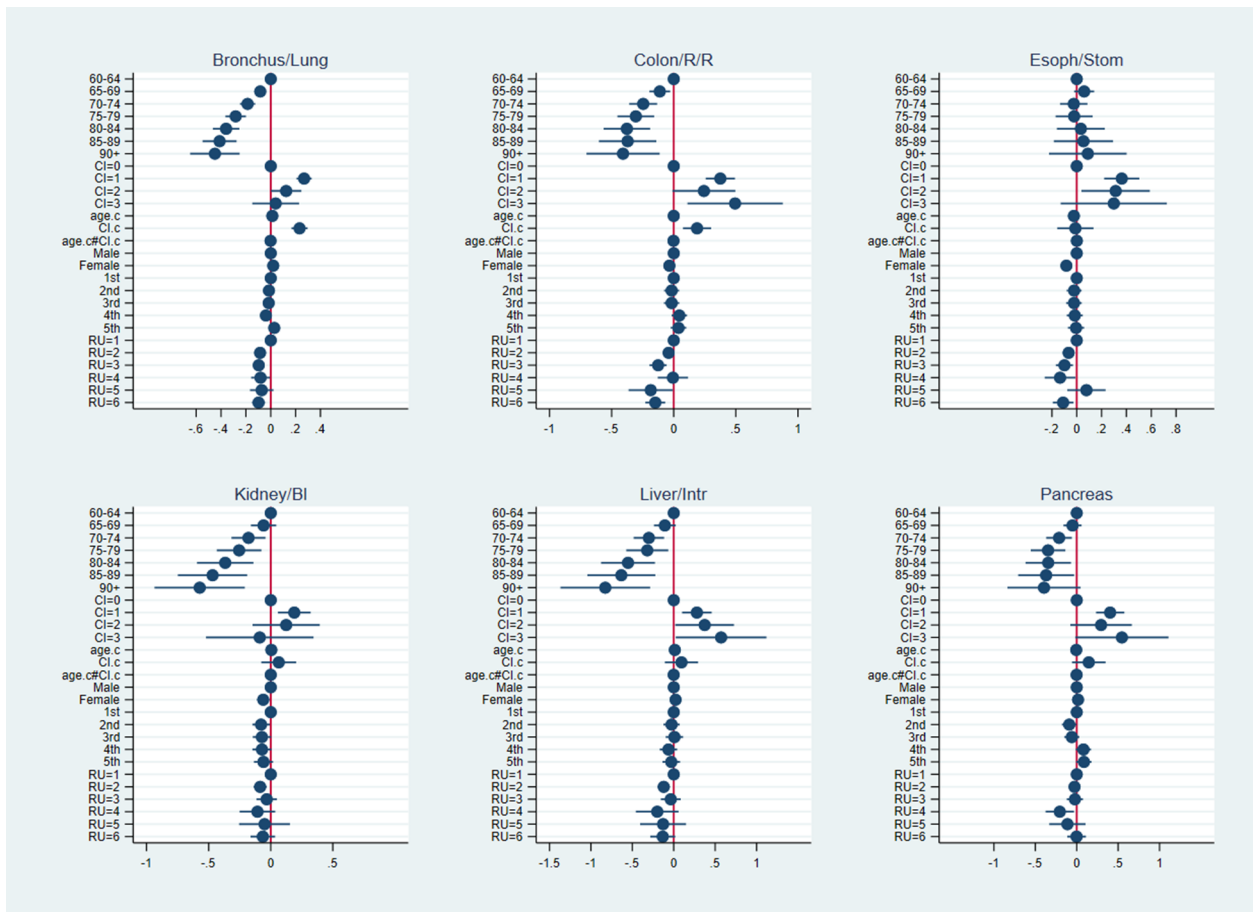
Supplementary Figure 5: Graphical representation of GLM results including interaction term (interaction between age and comorbidity burden) for all patients, and those with and without cancer as main cause of death



CI: Charlson Comorbidity Index; age.c: Age as a continuous variable; CI.c: Charlson Comorbidity Index as a continuous variable; age.c#CI.c: Interaction between age and Charlson Comorbidity Index (both as continuous variables); 1st to 5th: SIMD1 to SIMD 5 (Scottish index of multiple deprivation) in quintiles from most to least deprived areas; RU: Urban-rural indicator.



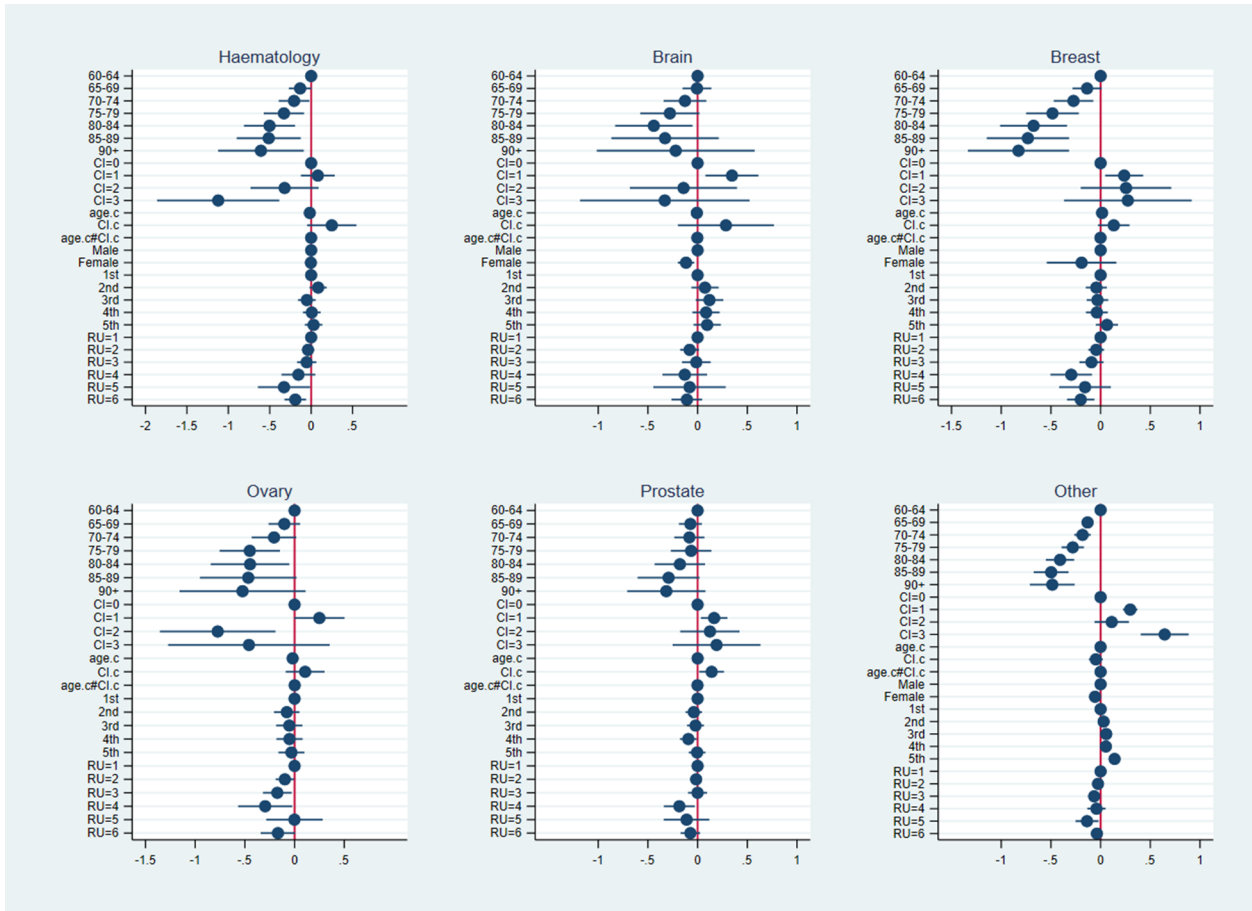
Supplementary Figure 6: Graphical representation of GLM results including interaction term (interaction between age and comorbidity burden) for the different cancer types 1/2



CI: Charlson Comorbidity Index; age.c: Age as a continuous variable; CI.c: Charlson Comorbidity Index as a continuous variable; age.c#CI.c: Interaction between age and Charlson Comorbidity Index (both as continuous variables); 1st to 5th: SIMD1 to SIMD 5 (Scottish index of multiple deprivation) in quintiles from most to least deprived areas; RU: Urban-rural indicator.



Supplementary Figure 7: Graphical representation of GLM results including interaction term (interaction between age and comorbidity burden) for the different cancer types 1/2



CI: Charlson Comorbidity Index; age.c: Age as a continuous variable; CI.c: Charlson Comorbidity Index as a continuous variable; age.c#CI.c: Interaction between age and Charlson Comorbidity Index (both as continuous variables); 1st to 5th: SIMD1 to SIMD 5 (Scottish index of multiple deprivation) in quintiles from most to least deprived areas; RU: Urban-rural indicator.



Supplementary Table 10: GLM results for decedents with cancer as their main cause of death and cancer not as their main cause and for individual cancer types

	Cancer main	Cancer not main	Bronchus/Lung	Colon/R/Rectum	Esophy/Stomache	Kidney/Bladder	Liver/Intrahep.
Age category							
60-64	0 [-0.126, -0.0717]	0 [-0.153, -0.0235]	0 [-0.127, -0.0418]	0 [-0.112, -0.0286]	0 [-0.0209, 0.141]	0 [-0.160, 0.0443]	0 [-0.239, 0.0249]
65-69	-0.0991** [-0.241, -0.165]	-0.132** [-0.210, -0.0528]	-0.186** [-0.247, -0.125]	-0.246** [-0.358, -0.133]	-0.237 [-0.134, 0.0865]	-0.179* [-0.316, -0.0428]	-0.107 [-0.484, -0.117]
70-74	-0.203** [-0.352, -0.250]	-0.191** [-0.291, -0.0902]	-0.282** [-0.365, -0.199]	-0.305** [-0.454, -0.157]	-0.209 [-0.170, 0.128]	-0.255** [-0.435, -0.0747]	-0.320** [-0.573, -0.0664]
75-79	-0.419** [-0.484, -0.353]	-0.264** [-0.367, -0.144]	-0.359** [-0.466, -0.253]	-0.377** [-0.565, -0.190]	0.0335 [-0.160, 0.227]	-0.366** [-0.594, -0.139]	-0.582** [-0.877, -0.227]
80-84	-0.484** [-0.565, -0.402]	-0.390** [-0.538, -0.241]	-0.412** [-0.548, -0.276]	-0.371** [-0.602, -0.140]	0.0542 [-0.184, 0.293]	-0.468** [-0.748, -0.189]	-0.633** [-1.044, -0.222]
85-89	-0.529** [-0.635, -0.422]	-0.445** [-0.624, -0.266]	-0.449** [-0.649, -0.250]	-0.408** [-0.703, -0.114]	0.0893 [-0.223, 0.402]	-0.572** [-0.935, -0.208]	-0.827** [-1.368, -0.285]
90+							
Comorbidity category							
CCI=0	0 [0.266, 0.339]	0 [0.105, 0.193]	0 [0.208, 0.329]	0 [0.258, 0.493]	0 [0.221, 0.504]	0 [0.0977, 0.321]	0 [0.101, 0.458]
CCI=1 (1 to 3)	0.149** [0.109, 0.206]	0.235** [0.130, 0.339]	0.124** [0.00170, 0.246]	0.243 [-0.00980, 0.496]	0.313* [0.0383, 0.898]	0.124 [-0.146, 0.395]	0.373* [0.0186, 0.728]
CCI=2 (4 to 6)	0.488** [0.371, 0.604]	-0.209* [-0.395, -0.0230]	0.0394 [-0.149, 0.228]	0.494* [0.110, 0.878]	0.298 [-0.129, 0.726]	-0.0884 [-0.522, 0.345]	0.572* [0.0243, 1.119]
CCI=3 (7 to 12)							
Age, comorbidity index (0 to 12) and interaction between age and comorbidity							
age at death	0.00434* [0.00100, 0.00768]	0.130*** [0.00716, 0.189]	0.0128** [0.00274, 0.0184]	-0.000326 [-0.0098, 0.0092]	-0.0231*** [-0.0333, -0.0128]	0.00498 [-0.0086, 0.0165]	0.0131 [-0.0041, 0.0304]
charlson	0.0752*** [0.0382, 0.112]	0.290*** [0.198, 0.382]	0.232*** [0.167, 0.297]	0.188*** [0.0741, 0.301]	-0.0108 [-0.157, 0.135]	0.0645 [-0.0760, 0.205]	0.0937 [-0.107, 0.294]
age #	-0.000866** [-0.0013, -0.0004]	-0.00250** [-0.0036, -0.001]	-0.00181*** [-0.0025, -0.001]	-0.00194** [-0.0032, -0.0006]	0.000742 [-0.00099, 0.0024]	0.00274 [-0.0013, 0.0018]	-0.000913 [-0.0034, 0.0015]
Sex							
Male	0 [0.0502, -0.0230]	0 [0.063, -0.0138]	0 [0.024, 0.0425]	0 [-0.0741, 0.0040]	0 [0.125, -0.0418]	0 [-0.108, -0.0128]	0 [-0.0464, 0.0909]
Female							
Scottish Index of Multiple Deprivation (SIMD)							
1st	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]
2nd	0.00811 [-0.0119, 0.0281]	-0.00966 [-0.0461, 0.0268]	-0.0145 [-0.0449, 0.0160]	-0.0168 [-0.0772, 0.0436]	-0.021 [-0.0810, 0.0389]	-0.0780* [-0.148, -0.00798]	-0.0262 [-0.124, 0.0719]
3rd	0.0216 [0.000498, 0.0426]	-0.0826** [-0.120, -0.0448]	-0.0166 [-0.0504, 0.0171]	-0.0167 [-0.0783, 0.0449]	-0.0222 [-0.0848, 0.0404]	-0.0713 [-0.145, 0.0206]	0.00838 [-0.0962, 0.113]
4th	0.0358** [0.0141, 0.0575]	-0.0741*** [-0.113, -0.0348]	-0.0387* [-0.075, -0.0024]	0.0449 [-0.0171, 0.107]	-0.016 [-0.0801, 0.0481]	-0.0705 [-0.147, 0.00602]	-0.0632 [-0.168, 0.0417]
5th	0.0983*** [0.0760, 0.121]	-0.0573 [-0.097, -0.0170]	0.0283 [-0.0117, 0.0683]	0.0383 [-0.0248, 0.101]	-0.00544 [-0.0709, 0.0600]	-0.0584 [-0.136, 0.0189]	-0.0302 [-0.137, 0.0765]
Urban - rural indicator							
RU=1	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]
RU=2	-0.0521*** [-0.0675, -0.0367]	-0.0247 [-0.052, 0.00283]	-0.0856*** [-0.111, -0.0604]	-0.0409 [-0.085, 0.00347]	-0.0652** [-0.111, -0.0195]	-0.0854** [-0.139, -0.0322]	-0.121** [-0.196, -0.0461]
RU=3	-0.0777** [-0.102, -0.0535]	-0.0502* [-0.094, -0.0066]	-0.0966*** [-0.137, -0.0565]	-0.126*** [-0.195, -0.0569]	-0.0990** [-0.168, -0.0298]	-0.0327 [-0.115, 0.0492]	-0.0355 [-0.156, 0.0846]
RU=4	-0.0914*** [-0.135, -0.0480]	-0.0625 [-0.141, 0.0161]	-0.0822 [-0.158, -0.0063]	-0.00631 [-0.128, 0.115]	-0.134* [-0.258, -0.0109]	-0.107 [-0.251, 0.0364]	-0.199 [-0.457, 0.0584]
RU=5	-0.0996*** [-0.156, -0.0437]	-0.229*** [-0.332, -0.125]	-0.0728 [-0.167, 0.0216]	-0.185* [-0.363, -0.00761]	0.0781 [-0.0764, 0.233]	-0.0499 [-0.285, 0.155]	-0.129 [-0.406, 0.148]
RU=6	-0.0789*** [-0.108, -0.0501]	-0.145*** [-0.199, -0.0921]	-0.0980*** [-0.151, -0.0450]	-0.148*** [-0.228, -0.0683]	-0.110** [-0.193, -0.0264]	-0.0637 [-0.163, 0.0354]	-0.133 [-0.283, 0.178]
Constant	8.080 [8.844, 9.316]	8.377 [7.962, 8.792]	8.090 [7.698, 8.482]	9.308 [8.626, 9.989]	10.88 [10.14, 11.62]	9.091 [8.263, 9.918]	8.287 [7.061, 9.512]
Observations	60728	18093	17345	5936	5364	3407	2286

95% confidence intervals in brackets.
* p < 0.05, ** p < 0.01, *** p < 0.001.



Supplementary Table 10: Continued.

	Pancreas	Hematologic	Brain	Breast	Ovary	Prostate	"other" cancer
Age category							
60-64	0	0	0	0	0	0	0
65-69	-0.0506	-0.133	-0.00586	-0.136	-0.104	-0.0725	-0.131**
70-74	-0.213**	-0.206*	-0.127	-0.272**	-0.207	-0.0825	-0.183**
75-79	-0.346**	-0.329**	-0.279	-0.484**	-0.451**	-0.0651	-0.280**
80-84	-0.344*	-0.503**	-0.441*	-0.674**	-0.448*	-0.178	-0.408*
85-89	-0.369*	-0.513**	-0.328	-0.732**	-0.466	-0.292	-0.497**
90+	-0.395	-0.607*	-0.22	-0.826**	-0.524	-0.315	-0.486**
Comorbidity category							
CCI=0	0	0	0	0	0	0	0
CCI=1	0.404**	0.0807	0.346*	0.238*	0.249	0.167*	0.298**
CCI=2	0.294	-0.321	-0.141	0.256	-0.774**	0.124	0.112
CCI=3	0.545	-1.123**	-0.33	0.274	-0.459	0.191	0.645**
Age, comorbidity index (0 to 12) and interaction between age and comorbidity							
age at death	-0.00572	-0.0166*	-0.00745	0.0154	-0.0196	0.000266	-0.00043
charlson (0-12)	0.145	0.249	0.285	0.133	0.106	0.141*	-0.0474
age # charlson	-0.00159	-0.000618	-0.00226	-0.00124	0.000899	-0.00119	0.00000274
Sex							
Male	0	0	0	0	NA	0	0
Female	0.0157	-0.00366	-0.116**	-0.191	NA	NA	-0.0659**
Scottish Index of Multiple Deprivation (SIMD)							
1st	0	0	0	0	0	0	0
2nd	-0.0905*	0.0849	0.0746	-0.0427	-0.0786	-0.038	0.03
3rd	-0.0592	-0.0521	0.12	-0.0314	-0.053	-0.0208	0.0568*
4th	0.0809	0.0797	0.0851	-0.0376	-0.0514	-0.0930*	0.0533*
5th	0.0872	0.0295	0.0963	0.0641	-0.032	-0.00487	0.141**
Urban- rural indicator							
RU=1	0	0	0	0	0	0	0
RU=2	-0.0266	-0.0381	-0.0801	-0.0439	-0.0979*	-0.0142	-0.0261
RU=3	-0.0219	-0.0543	-0.0129	-0.0917	-0.174*	0.0000123	-0.0850*
RU=4	-0.205*	-0.154	-0.129	0.295**	-0.296*	-0.183*	-0.0412
RU=5	-0.113	-0.328*	0.0805	-0.156	-0.0105	-0.11	-0.137*
RU=6	-0.00187	-0.192**	-0.108	-0.200**	-0.168	-0.0725	-0.0368
Constant	9.557	11.24	9.733	8.481	11.00	9.332	9.660
Observations	3185	2262	1117	1792	1276	2621	14133

95% confidence intervals in brackets.
 * p < 0.05, ** p < 0.01, *** p < 0.001.

