










# Factors associated with the aggressiveness of care at the end of life for patients with cancer dying in hospital: a nationwide retrospective cohort study in mainland Portugal

Diogo Martins-Branco <sup>1,2</sup>, Silvia Lopes <sup>3,4</sup>, Rita Canario <sup>1,5</sup>, Joao Freire,<sup>2</sup> Madalena Feio <sup>6</sup>, Jose Ferraz-Goncalves <sup>7</sup>, Gabriela Sousa <sup>5</sup>, Nuno Lunet <sup>8,9</sup>, Barbara Gomes <sup>1,10</sup>

**To cite:** Martins-Branco D, Lopes S, Canario R, *et al*. Factors associated with the aggressiveness of care at the end of life for patients with cancer dying in hospital: a nationwide retrospective cohort study in mainland Portugal. *ESMO Open* 2020;5:e000953. doi:10.1136/esmoopen-2020-000953

Received 29 July 2020  
Revised 27 August 2020  
Accepted 29 August 2020



Watch Video

esmoopen.bmj.com

© Author (s) (or their employer(s)) 2020. Re-use permitted under CC BY-NC. No commercial re-use. Published by BMJ on behalf of the European Society for Medical Oncology.

For numbered affiliations see end of article.

## Correspondence to

Dr Diogo Martins-Branco;  
diogo.mbranco@gmail.com

## ABSTRACT

**Introduction** There is growing concern about the aggressiveness of cancer care at the end of life (ACCEoL), defined as overly aggressive treatments that compromise the quality of life at its end. Recognising the most affected patients is a cornerstone to improve oncology care. Our aim is to identify factors associated with ACCEoL for patients with cancer dying in hospitals.

**Methods** All adult patients with cancer who died in public hospitals in mainland Portugal (January 2010 to December 2015), identified from the hospital morbidity database. This database provided individual clinical and demographic data. We obtained hospital and region-level variables from a survey and National Statistics. The primary outcome is a composite ACCEoL measure of 16 indicators. We used multilevel random effects logistic regression modelling ( $p < 0.05$ ).

**Results** We included 92 155 patients: median age 73 years; 62% male; 53% with metastatic disease. ACCEoL prevalence was 71% (95% CI 70% to 71%). The most prevalent indicators were >14 days in the hospital (43%, 42–43) and surgery (28%, 28–28) in the last 30 days. Older age ( $p < 0.001$ ), breast cancer (OR 0.83; 95% CI 0.76 to 0.91), and metastatic disease (0.54; 95% CI 0.50 to 0.58) were negatively associated with ACCEoL. In contrast, higher Deyo-Charlson Comorbidity Index ( $p < 0.001$ ), gastrointestinal and haematological malignancies ( $p < 0.001$ ), and death at cancer centre (1.31; 95% CI 1.01 to 1.72) or hospital with medical oncology department (1.29; 95% CI 1.02 to 1.63) were positively associated with ACCEoL. There was no association between hospital palliative care services at the hospital of death and ACCEoL.

**Conclusion** Clinical factors related to a better understanding of disease course are associated with ACCEoL reduction. Patients with more comorbidities and gastrointestinal malignancies might represent groups with complex needs, and haematological patients may be at increased risk because of unpredictable prognosis. Improvement of hospital palliative care services could help reduce ACCEoL, particularly in cancer centres and hospitals with medical oncology department, as those services are usually under-resourced, thus reaching few.

## Key questions

### What is already known about this subject?

- ▶ There is growing concern about the aggressiveness of cancer care at the end of life (ACCEoL), defined as overly aggressive treatments that compromise the quality of life.
- ▶ The end of life period most studied in relation to ACCEoL is the last month of life, for which Earle *et al*<sup>6</sup> identified key ACCEoL indicators, expanded by Luta *et al*.<sup>12</sup>
- ▶ Recognising the most affected patients is a cornerstone to improve this public health unmet need.

### What does this study add?

- ▶ Unchanged trend of high ACCEoL in a European country (Portugal)—7 out of 10 patients with cancer.
- ▶ Most prevalent indicators: >14 days in hospital and surgery in last 30 days of life.
- ▶ Older age, breast cancer and metastatic disease were associated with lower ACCEoL.
- ▶ Comorbidities, gastrointestinal and haematological cancers with higher ACCEoL.

### How might this impact on clinical practice?

- ▶ Clinicians should consider cancer type, disease stage, comorbidities, age and the influence of hospital oncology culture, to help patients with cancer to avoid ACCEoL.

## INTRODUCTION

Towards the end of life (EoL), patients with cancer wish to feel comfortable, be treated with dignity and achieve a sense of completion.<sup>1</sup> They also wish to avoid overly aggressive treatments, which can compromise symptom control and advance care planning.<sup>2</sup> Appropriate management of EoL care has been raised as a quality-of-care issue and indicators have been developed to identify health systems that apply overly intensive treatments



for terminal advanced cancer patients with very limited clinical benefit, defined as aggressiveness of cancer care at the EoL (ACCEoL).<sup>3</sup> As one component of EoL, the ACCEoL is interconnected with deleterious effects for patients and families such as worse quality of life and bereavement outcomes.<sup>4,5</sup> This led to growing concern across societies about the ACCEoL.<sup>6–11</sup>

Earle *et al*<sup>6</sup> reported one of the first ACCEoL studies, based on administrative data measuring key indicators within the last month of life, including overuse of chemotherapy (new regimen within 30 days, or any administration within 14 days before death), underuse of hospice care, and high rates of emergency room visits, hospitalisation or intensive care unit (ICU) admissions. They found that each indicator was present in less than one-third of patients but also that ACCEoL prevalence was increasing in the 90s in the USA.<sup>6</sup> Studies followed in other countries, interestingly with different findings.<sup>7–11</sup> Luta *et al*<sup>12</sup> proposed an expanded list of ACCEoL measures based on a systematic review.

Despite these advances in ACCEoL research, the issue remains neglected yet vital for clinical oncology, in face of the growing number of people dying with cancer.<sup>13</sup> Despite two-thirds of the population express a preference to die at home in a scenario of advanced cancer<sup>14</sup> and increases in several nations on the percentage of cancer patients dying at home rather than in hospital,<sup>15</sup> still many patients remain increasingly exposed to other ACCEoL indicators, such as ICU admission.<sup>16</sup> The rise of hospital deaths in other countries suggests a level of dependency on hospital resources and of ACCEoL which are contrary to people's preferences.<sup>14,17–19</sup>

Recognising the profile of patients at risk of receiving ACCEoL is critical for better understanding this public health unmet need and improving oncology care. Our study aims to identify factors associated with ACCEoL for cancer patients dying in hospitals.

## METHODS

### Study design and setting

This is a nationwide retrospective cohort study of adults who died with cancer in Portuguese hospitals. The study followed the REporting of studies Conducted using Observational Routinely-collected health Data statement.<sup>20</sup>

### Patients

We included all patients that: (1) died in a public hospital in mainland Portugal between January 2010 and December 2015; (2) were aged  $\geq 18$  years at the time of death and (3) had a diagnosis of cancer recorded in the episode leading to death, using International Classification of Diseases, ninth Revision, Clinical Modification (ICD-9-CM) codes from the chapter 'neoplasms' (codes 140–239), excluding benign neoplasms, carcinoma in situ, neoplasms of uncertain behaviour or unspecified nature (210–239).

### Primary outcome

Study outcome is a composite binary measure of ACCEoL, positive in the presence of at least one of 16 individual indicators (S1 - online supplemental file 1). The list of indicators from Earle *et al*<sup>6</sup> was expanded based on the systematic review by Luta *et al*.<sup>12</sup> A national expert panel assessed content validity. For all patients, all indicators were measured for the last 30 days of life, except the use of chemotherapy and immunotherapy/biological agents, which was shortened to the last 14 days of life, following Earle *et al*'s criteria.<sup>6</sup>

### Data sources

We used the hospital morbidity database (HMD) to identify patients and obtain individual-level data. The HMD contains routinely-collected data from all public hospitals in mainland Portugal for funding purposes, since 1989.<sup>21</sup> The dataset was anonymised by the Portuguese Health System Central Administration and included: (1) demographic data: sex, age at death and borough of residence; (2) clinical data coded by ICD-9-CM: metastatic disease status, procedures and main or secondary diagnoses used for the calculation of the Deyo-Charlson Comorbidity Index (DCCI)—used to predict mortality that derives from the sum of the score attributed to each comorbidity out of 17 chronic medical conditions<sup>22,23</sup> and (3) administrative data: date of admission, discharge or death, type of treatment (medical vs surgical) and hospital of death.

In September 2016, we surveyed all hospital administration boards and directors of palliative care services (PCS) created before January 2016. Following recommendations from a Cochrane Review on methods to increase response to postal and electronic questionnaires,<sup>24</sup> we obtained a 78% response rate. We used a semistructured questionnaire to obtain the following information: (1) hospital: hospital type (general vs cancer centre), hospital dimension (number of beds), existence of medical oncology department (MOD); (2) PCS: existence and creation date, existence of palliative care unit and number of beds. We made follow-up contacts and consulted the national directory of PCS to complete missing data. Hospital-level data were linked to individual-level data by hospital of death variable from HMD.

We obtained lists of boroughs classified by health region, urbanisation level (predominantly urban, mid-urban, predominantly rural) based on Census 2011 data and by deprivation level based on Census 2001 data (European Deprivation Index).<sup>25</sup> Region-level data were linked to individual and hospital-level data by borough of residence variable from HMD.

### Statistical analysis

We first described the study population, comparing the characteristics of patients who received ACCEoL with those that did not, using Pearson's  $\chi^2$  or Mann-Whitney tests. We then determined the prevalence of the composite measure of ACCEoL and each individual indicator for the whole population and by metastatic disease

status, primary cancer site and type of hospital of death. We examined trends in composite and individual indicators from 2010 to 2015, using  $\chi^2$  test for trend. We considered a difference of >5% as clinically meaningful.

Taking the composite ACCEoL measure as the dependent variable, unadjusted odds ratio (ORs) with 95% confidence interval (CI) were calculated for each independent variable. We used multilevel random effects logistic regression modelling (accounting for individual, hospital and region levels), including year of death and all independent variables that showed association with ACCEoL on unadjusted analysis. Finally, we conducted a subgroup analysis for patients with metastatic disease. All analyses were based on complete cases using STATA. IC12.1 ( $p < 0.05$ ).

## RESULTS

### Patient characteristics

We included 92 155 patients (S2 - online supplemental file 1), 62% male and median age of 73 years (interquartile range - IQR, 62–81). Fifty-three percent had metastatic disease and the most common primary solid tumour sites were lung (16%) and colorectal (10%). Twelve percent had haematological malignancies. The median DCCI score was eight points (IQR, 4–9). Only 15% died in a cancer centre but nearly all patients died in a hospital with MOD (93%). Most (66%) died in a hospital with hospital PCS (hPCS). The characteristics of the groups with and without ACCEoL were statistically different at: i) individual-level: all variables except year of death; ii) hospital-level: hPCS, MOD, hospital type, hospital dimension, health region; and iii) region-level: palliative care unit beds/100 deaths-year (table 1).

### PCS resources

Survey results showed that the percentage of hospital centres with hPCS increased from 42% (13/31) in 2010 to 74% (23/31) in 2015 ( $p < 0.05$ ), reflected in an increase of the percentage of patients who died in hospitals with hPCS (50% in 2010 to 82% in 2015,  $p < 0.001$ ) (S3 - online supplemental file 1).

### ACCEoL prevalence

The prevalence of the composite ACCEoL measure was 71% (95% CI 70% to 71%). The difference by metastatic disease status was only 3% (patients with metastatic disease: 70% vs others: 73%). ACCEoL also varied by primary cancer site (63% in breast cancer to 79% in haematological malignancies) and type of hospital of death (74% in cancer centre vs 69% in general hospital) (S4 - online supplemental file 1).

The most prevalent indicators were >14 days of length of stay in hospital (43%, 95% CI 42 to 43) and surgery (28%, 95% CI 28 to 28) within the last 30 days, with no clinically meaningful differences between patients with versus without metastatic disease except for ICU admission (4% vs 10%, respectively), mechanical ventilation

(2% vs 8%) and insertion of endotracheal tube (15% vs 22%) (figure 1).

The primary outcome remained stable overtime (from 71% in 2010 to 72% in 2011) and despite some indicators showing statistically significant changes from 2010 to 2015, none were considered clinically meaningful (S5 - online supplemental file 1).

### Factors associated with ACCEoL

In multivariate analysis, older age ( $p < 0.001$ ), breast cancer (OR 0.83; 95% CI 0.76 to 0.91), and metastatic disease (OR 0.54; 95% CI 0.50 to 0.58) were negatively associated with ACCEoL. In contrast, higher DCCI ( $p < 0.001$ ), gastrointestinal and haematological malignancies ( $p < 0.001$ ), and death at a cancer centre (OR 1.31; 95% CI 1.01 to 1.72) or at a hospital with MOD (OR 1.29; 95% CI 1.02 to 1.63) were positively associated with ACCEoL. Adjusting for confounders, there was no association between existence of hPCS and ACCEoL. There was a contextual effect of hospital-level with a median OR of 1.20 (95% CI 1.15 to 1.27), but no effect of region (S6 - online supplemental file 1). The subgroup analysis of patients with metastatic disease showed also a negative association with ACCEoL for male sex (OR 0.93, 95% CI 0.88 to 0.98) and cancer as main diagnosis of last hospital admission (OR 0.88, 95% CI 0.83 to 0.94), and a positive association for year of death (OR 1.03, 95% CI 1.01 to 1.05) (table 2).

## DISCUSSION

Our study showed an unchanged trend of high prevalence of ACCEoL in a European country. Seven out of 10 adult cancer patients dying in Portuguese public hospitals between 2010 and 2015 received ACCEoL, more than in other Western countries (71% vs 22%–65%).<sup>6 7 10 26</sup>

The high rate of hospitalisation may reflect not only the intensity of clinical care, but also the extent of social and clinical support in community and home settings. Free access to the National Health Service for cancer patients facilitates hospitalisation in a context of scarce community support. This should be considered when establishing comparisons with different health systems, where the prevalence of the most common individual indicator of our study, >14 days in hospital within the last month of life, was lower (43% vs 11%–30%).<sup>6 9</sup> On the other hand, we found ICU admission prevalence at the bottom of the previously reported range (6% vs 3%–25%)<sup>5–9</sup> and less prevalent in patients with metastatic disease (4% vs 10%), suggesting that the reduced use of limited and merely clinically driven hospital resources may reflect an adequate intensity of clinical care, despite the high rate of ACCEoL mainly due to hospitalisation.

However, more than one-fourth of the patients were submitted to a surgical intervention at the EoL, the most common procedure and the second most prevalent individual indicator. Although palliative surgical interventions in advanced stages and complications from a

**Table 1** Patients characteristics

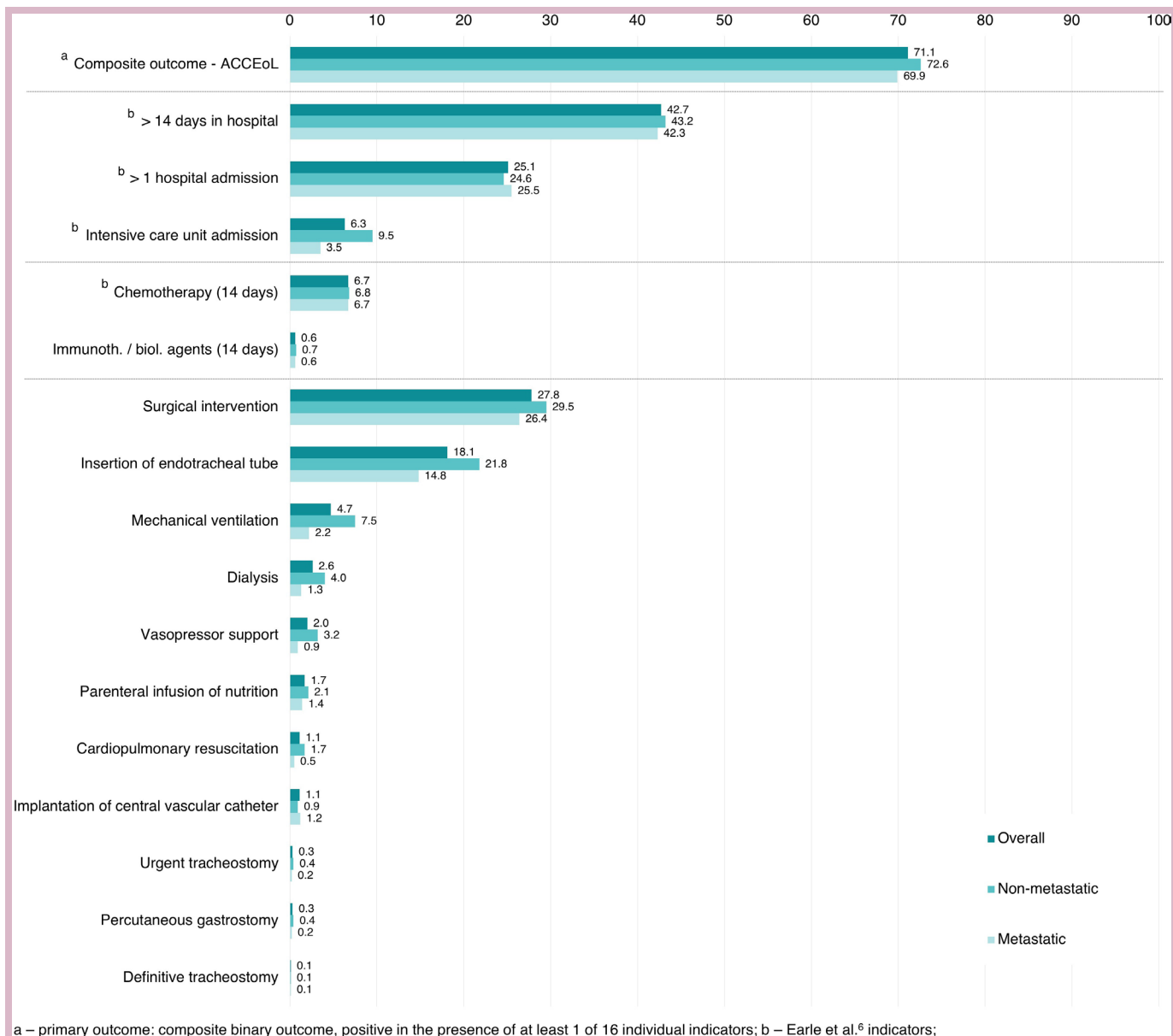
Characteristics		All patients (n=92 155)	Patients who died with ACCEoL (n=65 564)	Patients who died without ACCEoL (n=26 591)	Tests ( $\chi^2$ /Mann-Whitney (M-W))	
<b>Patient and health condition</b>	<b>Sex</b> (% male)	61.9	62.2	61.2	$\chi^2$ p=0.004	
	<b>Age at death</b>	Median in years (IQR)	73 (62–81)	72 (61–80)	75 (65–83)	M-W p<0.001
		18–39 (%)	2.0	2.3	1.1	M-W p<0.001
		40–49 (%)	5.2	5.7	4.0	
		50–59 (%)	13.1	13.9	11.1	
		60–69 (%)	21.4	22.5	18.7	
		70–79 (%)	29.5	29.8	28.6	
		80–89 (%)	24.7	22.5	29.9	
		≥90 (%)	4.3	3.3	6.6	
	<b>Primary cancer type</b>	Lung (%)	15.9	14.4	16.5	$\chi^2$ p<0.001
		Colorectal (%)	10.2	9.5	8.6	
		Gastric (%)	8.7	8.5	6.7	
		Prostate (%)	8.5	6.7	9.8	
		Breast (%)	5.8	4.7	7.1	
		Haematological (%)	11.9	12.4	8.0	
		Other (%)	41.3	43.7	43.4	
	<b>Deyo-Charlson Comorbidity Index, median score (IQR)</b>		8 (4–9)	8 (4–9)	8 (4–9)	M-W NS
		Less than mild: 2 (%)	11.6	10.4	14.3	M-W p<0.001
		Mild: 3–4 (%)	16.1	15.9	16.7	
		Moderate: 5–6 (%)	8.2	8.8	6.9	
	Severe: >6 (%)	64.1	64.9	62.1		
<b>Cancer as main diagnosis of last hospital admission (%)</b>		65.9	66.8	63.6	$\chi^2$ p<0.001	
<b>Metastatic disease (%)</b>		53.0	52.1	55.4	$\chi^2$ p<0.001	
<b>Year of death (%)</b>	2010	16.0	15.9	16.1	M-W NS	
	2011	16.4	16.5	16.2		
	2012	16.4	16.4	16.3		
	2013	16.8	16.9	16.7		
	2014	17.0	17.0	17.1		
	2015	17.4	17.3	17.5		

Continued

Table 1 Continued

Characteristics		All patients (n=92 155)	Patients who died with ACCEoL (n=65 564)	Patients who died without ACCEoL (n=26 591)	Tests ( $\chi^2$ /Mann-Whitney (M-W))
<b>Hospital where patient died</b>	<b>Hospital palliative care service</b> (% yes)	65.8	67.2	62.5	$\chi^2$ p<0.001
	Median years of existence (IQR)	4.6 (2.3–8.6)	4.6 (2.4–8.4)	4.6 (2.2–9.0)	M-W NS
	Quartile 1 (0.003–2.3 years) (%)	16.5	16.5	16.5	$\chi^2$ p<0.001
	Quartile 2 (2.3–4.6 years) (%)	16.4	17.1	14.8	
	Quartile 3 (4.6–8.6 years) (%)	16.5	17.0	15.2	
	Quartile 4 (8.6–23.0 years) (%)	16.4	16.7	15.9	
	<b>Medical oncology department</b> (% yes)	92.9	93.5	91.6	$\chi^2$ p<0.001
	<b>Hospital type</b> (% cancer centre)	14.7	15.2	13.4	$\chi^2$ p<0.001
	<b>Hospital dimension</b> , median no. beds (IQR)	380 (319–568)	380 (319–570)	380 (319–565)	M-W p=0.011
	Quartile 1 (6–319 beds) (%)	29.7	30.3	28.3	M-W p<0.001
	Quartile 2 (320–380 beds) (%)	21.0	20.2	22.8	
	Quartile 3 (381–568 beds) (%)	24.5	23.6	26.5	
	Quartile 4 (568–1299 beds) (%)	24.8	25.8	22.4	
	<b>Health region (HR)</b>	Lisbon and Tagus Valley (%)	40.8	41.4	39.4
North (%)		31.4	30.5	33.8	
Centre (%)		19.1	19.7	17.7	
Alentejo and Algarve (%)		8.6	8.4	9.2	
<b>Region where patient lived</b>	<b>Palliative care unit beds</b> , median no of palliative care unit beds/100 deaths-year, per HR (IQR)	1.00 (0.81–1.22)	1.00 (0.81–1.22)	1.00 (0.80–1.22)	M-W NS
	Quartile 1 (0–0.8) (%)	29.8	29.5	30.4	$\chi^2$ p<0.001
	Quartile 2 (0.8–1.0) (%)	22.4	22.2	23.2	
	Quartile 3 (1.0–1.2) (%)	23.5	24.1	22.1	
	Quartile 4 (1.2–19.4) (%)	24.3	24.2	24.4	
	<b>Home palliative care services</b> (% yes)	11.6	11.5	11.8	NS
	Median years of existence (IQR)	5.3 (2.3–15.8)	5.5 (2.3–15.8)	4.9 (2.2–15.6)	NS
	Quartile 1 (0.003–2.3 years) (%)	2.9	2.8	3.0	NS
	Quartile 2 (2.3–5.4 years) (%)	2.9	2.8	3.0	
	Quartile 3 (5.4–15.9 years) (%)	2.9	2.9	2.9	
	Quartile 4 (15.9–59.8 years) (%)	2.9	3.0	2.7	
	<b>European Deprivation Index</b> , median score (IQR)	–1.24 (–2.34–(–0.01))	–1.24 (–2.34–0.00)	–1.24 (–2.34–(–0.02))	NS
	Quartile 1 (least deprived: –7.31 to –2.34) (%)	25.5	25.6	25.2	NS
	Quartile 2 (–2.34 to –1.24) (%)	24.5	24.5	24.6	
	Quartile 3 (–1.24 to –0.01) (%)	25.0	24.8	25.4	
	Quartile 4 (most deprived: –0.01 to 13.47) (%)	25.0	25.1	24.8	
	<b>Urbanisation level</b>	Predominantly urban (%)	69.0	69.0	68.8
Mid-urban (%)		15.2	15.0	15.6	
Predominantly rural (%)		15.8	15.9	15.6	

ACCEoL, aggressiveness of cancer care at the end of life; NS, non-significant.



a – primary outcome: composite binary outcome, positive in the presence of at least 1 of 16 individual indicators; b – Earle et al.<sup>6</sup> indicators;

**Figure 1** Prevalence of composite and individual indicators of ACCEoL (%), overall and by disease stage. ACCEoL, aggressiveness of cancer care at the end of life; Immunoth, Immunotherapy; Biol, biological.

primary tumour resection procedure with curative intent might be causes, further studies should focus on this individual outcome. We found a relatively low prevalence of chemotherapy administration in the last 14 days of life, compared with previous reports (7% vs 2%–24%).<sup>6–9</sup> However, this indicator might be underestimated since it did not measure the administration of oral agents.

Breast cancer was the primary cancer type associated with the lowest rate of ACCEoL, probably due to better knowledge of clinical trajectories of disease subtypes. On the other hand, we found that patients with gastrointestinal and haematological malignancies are at increased risk of ACCEoL. In patients with gastrointestinal malignancies, it may be due to higher rate of postoperative complications in early stages and digestive haemorrhage or malignant obstructions in late stages.<sup>26</sup> Patients with

haematological malignancies represent a subgroup with more unpredictable prognosis and higher percentage of curative intent treatments, and therefore, as previously reported,<sup>7,10</sup> associated with higher ACCEoL. Also as previously reported,<sup>6,7</sup> patients with higher DCCI were at increased risk of ACCEoL, certainly related with higher complexity of care. As expected, patients with metastatic disease were less likely to experience ACCEoL, mainly when cancer was the main diagnosis of last hospital admission, suggesting that hospitalisation due to late stage disease progression is recognised. Despite trends remaining unchanged in the overall sample, ACCEoL is increasing over time in metastatic disease. This might be explained by the scientific advances on systemic antineoplastic treatments, mostly experienced in advanced stages. Aligned with literature,<sup>7,9</sup> age was the most influential

**Table 2** Factors associated with ACCEoL: multilevel logistic regression model

Factors	Unadjusted			Adjusted (n=57 683)		Adjusted (subgroup of patients with metastatic disease) (n=31 199)		
	N	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	
<b>Patient and health condition</b>	Sex (female—reference)	92 155						
	Male	57 071	1.04 (1.01 to 1.08)	<0.01	0.97 (0.93 to 1.01)	0.12	0.93 (0.88 to 0.98)	0.01
<b>Age at death (in years)</b>	18–39	1 800	Reference	<0.001	Reference	<0.001	Reference	<0.001
	40–49	4 790	0.71 (0.61 to 0.81)		0.81 (0.68 to 0.97)		0.78 (0.62 to 0.97)	
	50–59	12 038	0.61 (0.54 to 0.70)		0.70 (0.59 to 0.82)		0.65 (0.53 to 0.80)	
	60–69	19 745	0.59 (0.52 to 0.67)		0.65 (0.55 to 0.76)		0.57 (0.47 to 0.70)	
	70–79	27 147	0.51 (0.45 to 0.58)		0.54 (0.46 to 0.63)		0.48 (0.39 to 0.59)	
	80–89	22 718	0.37 (0.33 to 0.42)		0.40 (0.34 to 0.46)		0.36 (0.29 to 0.44)	
	≥90	3 917	0.25 (0.22 to 0.28)		0.27 (0.23 to 0.32)		0.23 (0.18 to 0.30)	
	<b>Primary cancer type</b>	92 155						
	Lung	14 695	Reference	<0.001	Reference	<0.001	Reference	<0.001
Colorectal	9 419	1.27 (1.19 to 1.34)		1.55 (1.44 to 1.67)		1.17 (1.07 to 1.28)		
Gastric	8 024	1.45 (1.36 to 1.54)		1.73 (1.60 to 1.87)		1.47 (1.33 to 1.62)		
Prostate	7 825	0.81 (0.77 to 0.86)		1.04 (0.97 to 1.13)		1.08 (0.97 to 1.20)		
Breast	5 346	0.77 (0.72 to 0.82)		0.83 (0.76 to 0.91)		0.72 (0.65 to 0.80)		
Haematological	11 013	1.77 (1.67 to 1.88)		1.73 (1.60 to 1.87)		·		
Other	38 046	1.13 (1.08 to 1.17)		1.29 (1.23 to 1.36)		1.12 (1.04 to 1.20)		
<b>Deyo-Charlson Comorbidity Index</b>	92 155							
Less mild: 2	10 646	Reference	<0.001	Reference	<0.001	·	·	
Mild: 3–4	14 864	1.31 (1.24 to 1.38)		1.31 (1.22 to 1.40)		·		
Moderate: 5–6	7 590	1.73 (1.62 to 1.84)		1.68 (1.54 to 1.84)		·		
Severe:>6	59 055	1.43 (1.37 to 1.49)		2.20 (2.02 to 2.38)		·		
<b>Cancer as main diagnosis of last hospital admission (no—reference)</b>	92 155							
Yes	60 732	1.15 (1.12 to 1.19)	<0.001	1.04 (0.99 to 1.08)	0.10	0.88 (0.83 to 0.94)	<0.001	
<b>Metastatic disease (no—reference)</b>	92 155							
Yes	48 870	0.88 (0.85 to 0.90)	<0.001	0.54 (0.51 to 0.58)	<0.001	·	·	
<b>Year of death (continuous)</b>	92 155	1.00 (0.99 to 1.01)	0.71	1.01 (1.00 to 1.03)	0.13	1.03 (1.01 to 1.05)	0.01	

Continued



Table 2 Continued

Factors	Unadjusted			Adjusted (n=57 683)		Adjusted (subgroup of patients with metastatic disease) (n=31 199)	
	N	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
<b>Hospital where patient died</b>							
<b>Hospital palliative care service</b>	67 262						
No existence	23 001	Reference	<0.001	Reference	0.18	Reference	0.42
0.003–2.3 years of existence	11 075	1.15 (1.09 to 1.20)		1.02 (0.94 to 1.11)		1.02 (0.92 to 1.13)	
2.3–4.6 years of existence	11 038	1.32 (1.26 to 1.39)		1.10 (1.00 to 1.22)		1.09 (0.96 to 1.23)	
4.6–8.6 years of existence	11 076	1.28 (1.22 to 1.34)		1.05 (0.92 to 1.18)		1.02 (0.87 to 1.18)	
8.6–23.0 years of existence	11 063	1.20 (1.14 to 1.26)		0.97 (0.79 to 1.20)		1.01 (0.79 to 1.30)	
<b>Medical Oncology Department (no—reference)</b>	62 465						
Yes	58 055	1.31 (1.23 to 1.40)	<0.001	1.29 (1.02 to 1.63)	0.03	1.26 (0.98 to 1.62)	0.07
<b>Hospital type (General hospital—reference)</b>	92 155						
Cancer centre	13 536	1.16 (1.12 to 1.21)	<0.001	1.31 (1.01 to 1.72)	0.04	1.38 (1.04 to 1.83)	0.03
<b>Hospital dimension</b>	57 683						
6–319 beds	17 156	Reference	<0.001	Reference	0.20	Reference	0.10
320–380 beds	12 104	0.83 (0.79 to 0.87)		1.11 (1.00 to 1.24)		1.12 (0.99 to 1.28)	
381–568 beds	14 123	0.83 (0.79 to 0.87)		1.08 (0.96 to 1.24)		1.14 (0.98 to 1.32)	
568–1299 beds	14 300	1.08 (1.03 to 1.13)		1.03 (0.88 to 1.21)		1.10 (0.91 to 1.33)	
<b>Region where patient lived</b>							
<b>Palliative care unit beds*</b>	92 155						
0–0.8 beds/100 deaths, per HR	27 427	Reference	<0.01	Reference	0.24	Reference	0.13
0.8–1.0 beds/100 deaths, per HR	20 687	0.96 (0.91 to 1.00)		0.97 (0.92 to 1.02)		0.95 (0.88 to 1.02)	
1.0–1.2 beds/100 deaths, per HR	21 675	1.13 (1.08 to 1.18)		1.05 (0.97 to 1.12)		1.10 (1.00 to 1.21)	
1.2–19.4 beds/100 deaths, per HR	22 366	0.98 (0.94 to 1.02)		0.96 (0.88 to 1.04)		0.94 (0.84 to 1.05)	
<b>Home palliative care team</b>	92 155						
No existence	81 438	Reference	0.06	.	.	.	.
0.003–2.3 years of existence	2 662	0.93 (0.85 to 1.01)		.	.	.	.
2.3–5.4 years of existence	2 663	0.92 (0.85 to 1.00)		.	.	.	.
5.4–15.9 years of existence	2 662	1.00 (0.91 to 1.08)		.	.	.	.
15.9–59.8 years of existence	2 660	1.07 (0.98 to 1.17)		.	.	.	.
<b>European Deprivation Index</b>	85 688						
least deprived: –7.31 to –2.34	21 830	Reference	0.41	.	.	.	.
–2.34 to –1.24	21 024	0.98 (0.94 to 1.02)		.	.	.	.
–1.24 to –0.01	21 415	0.96 (0.92 to 1.00)		.	.	.	.
most deprived: –0.01 to 13.47	21 419	1.00 (0.95 to 1.04)		.	.	.	.
<b>Urbanisation level</b>	85 790						
Predominantly urban	59 170	Reference	0.32	.	.	.	.
Mid-urban	13 033	0.96 (0.92 to 1.00)		.	.	.	.
Predominantly rural	13 587	1.02 (0.97 to 1.06)		.	.	.	.

\*Median number of palliative care unit beds/100 deaths-year, per health region. ACCEoL, aggressiveness of cancer care at the end of life; HR, health region.

factor on ACCEoL, with the oldest patients having 73% lower odds of receiving ACCEoL compared with the youngest. Male sex in metastatic patients was associated with decreased risk of ACCEoL, a disparity not clearly

understood and the opposite of the reported in other continents,<sup>7 27</sup> maybe resulting from cultural differences.

Considering environmental factors, death at a cancer centre and death at a hospital with MOD were associated



with higher risk of receiving ACCEoL. These findings might be due to higher complexity of cases treated in cancer centres or easier access to antineoplastic treatments and clinical trials when MOD exists at the hospital of admission. On the other hand, and in contrast with what literature reports,<sup>28</sup> our study showed no association of availability of hPCS and reduction of ACCEoL. This result might be influenced by the fact that hospitals with hPCS are often those with a case mix of more complex patients, with higher risk of ACCEoL. It also may be because hPCS effect was measured at a hospital-level, since the HMD did not provide individual data on hPCS intervention (we could only measure the existence of hPCS at the hospital where a given patient died). Moreover, late referral or limited human resources in hPCS could hinder their impact on ACCEoL. There was no effect of region-level characteristics on ACCEoL, as opposed to other studies.<sup>7</sup>

This is a robust nationwide study that used multivariate methods to control for confounders at different levels. However, the use of routinely-collected data generated for administrative purposes does not allow to conclude to what extent the ACCEoL was adequate or inadequate for each individual, as the HMD does not contain the cause of death or the setting of the anticancer treatment (curative vs palliative). To overcome this limitation, we planned the subgroup analysis of metastatic disease as a sensitivity analysis, since the treatment intent in these patients is mostly palliative. We expanded the Earle *et al's* framework,<sup>6</sup> but emergency department visits were not included in this study, thus the prevalence of ACCEoL could be even higher than we estimated (measurement bias). In contrast, the study was restricted to people who died in hospital, who are likely to receive higher ACCEoL than those who died elsewhere (selection bias).

## CONCLUSIONS

This study unravelled important data on ACCEoL and associated risk factors, expanding the earlier framework for measuring ACCEoL. We confirmed that clinical factors related with a better understanding of disease course are associated with ACCEoL reduction. In contrast, we identified groups of patients at increased risk for ACCEoL such as patients with more comorbidities, gastrointestinal and haematological malignancies. Therefore, clinicians should seek for better integration of prognostic estimations with adequate timing for anticipated discussion of patients and families' preferences and expectations, particularly within the high-risk groups identified by our study. Efforts should be made for empowerment and reinforcement of the growing number of hospital and home PCS, with human resources, earlier referral and integration into a comprehensive cancer care plan, mainly in cancer centres and hospitals with MOD. The study recognised need for further research on the impact of the social and clinical community support on hospitalisation rates, determinants for surgery procedure, management of haematological malignancies at the EoL, and higher

ACCEoL in patients who deceased at cancer centres or hospitals with MOD.

### Author affiliations

<sup>1</sup>Cicely Saunders Institute of Palliative Care, Policy and Rehabilitation, King's College London, London, UK

<sup>2</sup>Medical Oncology Department, Instituto Português de Oncologia de Lisboa Francisco Gentil, Lisbon, Portugal

<sup>3</sup>NOVA National School of Public Health, Public Health Research Centre, Universidade NOVA de Lisboa, Lisbon, Portugal

<sup>4</sup>Comprehensive Health Research Centre, Universidade NOVA de Lisboa, Lisbon, Portugal

<sup>5</sup>Medical Oncology Department, Instituto Português de Oncologia de Coimbra Francisco Gentil, Coimbra, Portugal

<sup>6</sup>Hospital Palliative Care Support Team, Instituto Português de Oncologia de Lisboa Francisco Gentil, Lisbon, Portugal

<sup>7</sup>Palliative Care Service, Instituto Português de Oncologia do Porto Francisco Gentil, Porto, Portugal

<sup>8</sup>Department of Public Health and Forensic Sciences and Medical Education, University of Porto Medical School, Porto, Portugal

<sup>9</sup>EPIUnit, Institute of Public Health, University of Porto, Porto, Portugal

<sup>10</sup>Faculty of Medicine, University of Coimbra, Coimbra, Portugal

**Twitter** Diogo Martins-Branco @DMBranco and Barbara Gomes @B\_Gomes\_

**Acknowledgements** This project was performed as part of the DINAMO Project, which aims to enhance advanced training and research to optimise home palliative care in Portugal (Principal Investigator – Barbara Gomes, Scientific Director – Irene J. Higginson, other members – P.L. Ferreira, H. Aguiar, A.F. Lacerda, V.P. Sarmiento, D. Soares, R. Canário, M. de Brito, C. Ribeiro, D. Martins-Branco). HMD was provided by Portuguese Health System Central Administration. European Deprivation Index was obtained by courtesy of one of its authors – Ana Isabel Ribeiro. Scientific and institutional support from the Portuguese Society of Oncology. This study was possible also due to the participation of all the centres and teams who answered to the nationwide survey. The study was partly presented as a meeting/conference abstract at: American Society of Clinical Oncology, Palliative and Supportive Care in Oncology Symposium 2018, San Diego, California, USA; and European Society of Medical Oncology Annual Meeting 2017, Madrid, Spain.

**Contributors** All authors have participated in the development of the study, data collection, analysis, and interpretation of the results, writing and reviewing of the manuscript and approve the final text.

**Funding** This work was supported by the Calouste Gulbenkian Foundation as part of the DINAMO Project (grant number 127 988 to BG); and the Núcleo Regional do Sul – Liga Portuguesa Contra o Cancro (43/2015 and 35/2016 to DM-B).

**Competing interests** The first author declares honoraria from Merck Sharp & Dohme, Angelini, Pfizer, AstraZeneca, Novartis, and Bristol-Myers Squibb, and meeting/travel grants from Janssen, Roche, Laboratórios Vitória, Novartis, Gilead Sciences, Ipsen, Merck Sharp & Dohme, and Pierre Fabre.

**Patient consent for publication** Not required.

**Ethics approval** We used anonymised routinely collected data hence no ethical approval was required.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available on reasonable request. Data may be obtained from a third party and are not publicly available. All data relevant to the study are included in the article or uploaded as supplementary information. Raw data from HMD was provided by the Portuguese Health System Central Administration. Study protocol, programming code and data from the national survey to the hospital administration boards and directors of PCS is stored by the corresponding author. Lists of boroughs classified by health region and urbanisation level is based on Census 2011 data. European Deprivation Index was obtained by courtesy of one of its authors.

**Supplemental material** This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability



of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, any changes made are indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

#### ORCID iDs

Diogo Martins-Branco <http://orcid.org/0000-0002-7214-4818>

Silvia Lopes <http://orcid.org/0000-0002-6048-396X>

Rita Canario <http://orcid.org/0000-0002-3563-7752>

Madalena Feio <http://orcid.org/0000-0003-4597-2578>

Jose Ferraz-Goncalves <http://orcid.org/0000-0002-9506-7106>

Gabriela Sousa <http://orcid.org/0000-0002-1563-5522>

Nuno Lunet <http://orcid.org/0000-0003-1870-1430>

Barbara Gomes <http://orcid.org/0000-0001-8149-1806>

#### REFERENCES

- Steinhauser KE, Christakis NA, Clipp EC, *et al.* Factors considered important at the end of life by patients, family, physicians, and other care providers. *JAMA* 2000;284:2476–282.
- Heyland DK, Dodek P, Rocker G, *et al.* What matters most in end-of-life care: perceptions of seriously ill patients and their family members. *CMAJ* 2006;174:627–33.
- Earle CC, Park ER, Lai B, *et al.* Identifying potential indicators of the quality of end-of-life cancer care from administrative data. *J Clin Oncol* 2003;21:1133–8.
- Wright AA, Zhang B, Ray A, *et al.* Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. *JAMA* 2008;300:1665–73.
- Ersek M, Miller SC, Wagner TH, *et al.* Association between aggressive care and bereaved families' evaluation of end-of-life care for veterans with non-small cell lung cancer who died in Veterans Affairs facilities. *Cancer* 2017;123:3186–94.
- Earle CC, Neville BA, Landrum MB, *et al.* Trends in the aggressiveness of cancer care near the end of life. *J Clin Oncol* 2004;22:315–21.
- Ho TH, Barbera L, Saskin R, *et al.* Trends in the aggressiveness of end-of-life cancer care in the universal health care system of Ontario, Canada. *J Clin Oncol* 2011;29:1587–91.
- Choi Y, Keam B, Kim TM, *et al.* Cancer treatment near the end-of-life becomes more aggressive: changes in trend during 10 years at a single Institute. *Cancer Res Treat* 2015;47:555–63.
- Hassan AA, Mohsen H, Allam AA, *et al.* Trends in the aggressiveness of end-of-life cancer care in the state of Qatar. *J Glob Oncol* 2016;2:68–75.
- Henson LA, Gomes B, Koffman J, *et al.* Factors associated with aggressive end of life cancer care. *Support Care Cancer* 2016;24:1079–89.
- Tang ST, Wu S-C, Hung Y-N, *et al.* Determinants of aggressive end-of-life care for Taiwanese cancer decedents, 2001 to 2006. *J Clin Oncol* 2009;27:4613–8.
- Luta X, Maessen M, Egger M, *et al.* Measuring intensity of end of life care: a systematic review. *PLoS One* 2015;10:e0123764.
- Global Burden of Disease Cancer Collaboration, Fitzmaurice C, Dicker D, *et al.* The global burden of cancer 2013. *JAMA Oncol* 2015;1:505–27.
- Gomes B, Higginson IJ, Calanzani N, *et al.* Preferences for place of death if faced with advanced cancer: a population survey in England, Flanders, Germany, Italy, the Netherlands, Portugal and Spain. *Ann Oncol* 2012;23:2006–15.
- Teno JM, Gozalo PL, Bynum JPW, *et al.* Change in end-of-life care for Medicare beneficiaries: site of death, place of care, and health care transitions in 2000, 2005, and 2009. *JAMA* 2013;309:470–7.
- Teno JM, Gozalo PL, Bynum JPW, *et al.* Change in end-of-life care for Medicare beneficiaries. *JAMA* 2013;309:470–7.
- Sarmento VP, Higginson IJ, Ferreira PL, *et al.* Past trends and projections of hospital deaths to inform the integration of palliative care in one of the most ageing countries in the world. *Palliat Med* 2016;30:363–73.
- Gomes B, Sarmento VP, Ferreira PL, *et al.* [Epidemiological study of place of death in Portugal in 2010 and comparison with the preferences of the Portuguese population]. *Acta Med Port* 2013;26:327–34.
- Gomes B, Calanzani N, Gysels M, *et al.* Heterogeneity and changes in preferences for dying at home: a systematic review. *BMC Palliat Care* 2013;12:7.
- Benchimol EI, Smeeth L, Guttmann A, *et al.* The reporting of studies conducted using observational Routinely-collected health data (record) statement. *PLoS Med* 2015;12:e01001885.
- Urbano J, Bentes M. Definição da produção do hospital : os grupos de diagnósticos homogêneos. *Rev Port Saúde Pública* 1990;8:49–60.
- Charlson ME, Pompei P, Ales KL, *et al.* A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.
- Quan H, Sundararajan V, Halfon P, *et al.* Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005;43:1130–9.
- Edwards PJ, Roberts I, Clarke MJ, *et al.* Methods to increase response to postal and electronic questionnaires. *Cochrane Database Syst Rev* 2009:MR000008.
- Ribeiro AI, Mayer A, Miranda A, *et al.* The Portuguese version of the European deprivation index: an instrument to study health inequalities. *Acta Med Port* 2017;30:17–25.
- Merchant SJ, Lajkosz K, Brogly SB, *et al.* The final 30 days of life: a study of patients with gastrointestinal cancer in Ontario, Canada. *J Palliat Care* 2017;32:92–100.
- Chang C, Wu C, Yin W, *et al.* Low socioeconomic status is associated with more aggressive End-of-Life care for Working-Age terminal cancer patients. *Oncologist* 2014.
- Triplett DP, LeBrett WG, Bryant AK, *et al.* Effect of palliative care on aggressiveness of end-of-life care among patients with advanced cancer. *J Oncol Pract* 2017;13:e760–9.