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ADMISSION TO PALLIATIVE CARE AND INDICATORS OF END-OF-LIFE INTENSITY OF CARE IN CANCER PATIENTS FROM THE LOMBARDY REGION, ITALY

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ADMISSION TO PALLIATIVE CARE AND INDICATORS OF END-OF-LIFE INTENSITY OF CARE IN CANCER PATIENTS FROM THE LOMBARDY REGION, ITALY

Subtitle: Palliative care and end-of-life intensity of care

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ABSTRACT

Objectives: Hospital-based and home palliative care have been associated to a reduction of aggressive treatments in the end-of-life, but data in the Italian context are scanty. We aim therefore investigate the role of palliative care on indicators of end-of-life intensity of care among cancer patients in Lombardy, the largest Italian region.

Methods: Within a retrospective study using the healthcare utilization databases of Lombardy, we selected all residents who died in 2019 with a diagnosis of cancer. We considered as exposure variables admission to palliative care and time at palliative care admission, and as indicators of aggressive care hospitalizations, diagnostic/therapeutic procedures, in-hospital death, emergency department visits, and chemotherapy over a time-window of 30 days before death; chemotherapy in the last 14 days was also considered.

Results: Our cohort included 26,539 individuals; of these, 14,320 (54%) were admitted to palliative care before death. Individuals who were admitted to palliative care had an odds ratio of 0.27 for one hospitalization, 0.14 for ≥2 hospitalizations, 0.25 for hospital stay ≥12 days, 0.38 for minor diagnostic/therapeutic procedures, 0.18 for major diagnostic/therapeutic procedures, 0.02 for in-hospital death, 0.35 for one emergency department visit, 0.29 for ≥2 emergency department visits, and 0.66 for chemotherapy use in the last 30 days; the odds ratio was 0.56 for chemotherapy use in the last 14 days.

Conclusions: This large real-world analysis confirms and further support the importance of palliative care assistance for cancer patients in the end-of-life; this is associated to a significant reduction in unnecessary treatments.

Keywords. cancer, end-of-life, epidemiology, Italy, palliative care, quality indicators.

KEY MESSAGES BOX

1. What is already known on this topic

- Hospital-based and home palliative care have been associated to a reduction of aggressive treatments in the end-of-life.
- Evidence indicate that earlier the admission to palliative care the less aggressive end-of-life care.
- Most of the evidence, however, comes from North America and Northern European countries, whereas data in the Italian context are scanty.

2. What this study adds

- This article further investigates the role of palliative care on indicators of end-of-life intensity of care among cancer patients in the Italian context.
- The study includes the analysis of several indicators of aggressive treatments in the end-of-life, providing a comprehensive picture of the impact on palliative care on the management of oncologic patients.

3. How this study might affect research, practice or policy

- This large real-world analysis confirms and further support the importance of palliative care assistance for cancer patients in the end-of-life. This work can support the progress in PC at regional and national level to further increase the number of cancer patients assisted, for a better management of the patients' end-of-life and significant reduction in unnecessary treatments and expensive health care resources.

INTRODUCTION

Cancer patients' care in the end-of-life (EOL) should be mainly focused to improve the quality of life (QOL) and alleviating symptoms due to the advancing disease rather than to cure the disease. Continuation of active treatments until the very late stage of the disease, invasive surgical procedures, frequent admission to emergency department (ED), acute hospital wards, and intensive care unit (ICU), as well as in-hospital death, have been suggested as indicators of aggressive care in the EOL [1-4]. Such treatments have indeed been reported to unfavourably affect patients' QOL and have been associated to elevated and unnecessary burden and costs for the health system.

Hospital-based and home palliative care (PC) – that has been fostered during the last decades in many high-income countries in order to better care (cancer) patients in the EOL – have been associated to a reduction of aggressive treatments in the EOL [5-18]. Evidence also indicate that the earlier the admission to PC the less aggressive EOL care [14 19-22]. Most of the evidence, however, comes from North America and Northern European countries, whereas data in the Italian context are scanty [17 18 21].

In order to further investigate the role of PC on indicators of EOL intensity of care among cancer patients, we conducted a retrospective study of individuals who died with cancer in Lombardy, the largest Italian region, focusing also on the role of time at PC admission.

MATERIAL AND METHODS

Data source

Data for the present retrospective study derive from the healthcare utilization databases of Lombardy, a region of Italy with about 10 million residents (i.e., about 15% of the Italian population). These databases include information on demographic data of all residents covered by the Regional Health Service, admissions to public or private hospitals, reimbursable drugs

dispensed by regional pharmacies or administered directly in healthcare services, disease specific exemptions, out-patient visits, high-cost drugs [23]. Moreover, we also used data of the activity of the CP in Lombardy, available for all private and public hospice and home PC services from Lombardy since 2019 [24].

To retrieve data for our analysis, we performed a record linkage of all these healthcare utilization databases, through a unique anonymous subject identification code, in accordance with the European privacy regulations. By virtue of a specific agreement between the Mario Negri Institute and the Lombardy Region, it was not necessary to obtain approval from any ethics committee for the use of the regional healthcare utilization databases.

Study population

From the demographic database, we selected all the resident individuals registered in the Lombardy health system, who died in 2019. From this cohort, we selected those with a hospitalization or an out-patient visit for a malignant neoplasm (**Supplementary Table 1**) in the previous 5 years (between 2014 and 2019). We excluded individuals with less than 5 years enrollment in the Lombardy health system, those not resident in Lombardy or with erroneous attribution to the local health unit, those alive, and those with no date of death. Further, we identified individuals who have been admitted to PC assistance in 2019 and those who have not been admitted.

For each eligible individual, we retrieved demographic information (sex and age at death), site of neoplasm at cohort entry (**Supplementary Table 1**), and presence of advanced neoplasm. We also computed the Charlson's comorbidity index in the five years before death [25] and we assigned to each individual the quintile (on the regional distribution) of the deprivation index (DI) of the corresponding municipality of residence [26 27]. The latter index measures social and material deprivation in the presence of low educational level,

unemployment, living in rental property, living in a crowded house, and living in a single-parent family.

Exposure variables and outcomes

Exposure variable of interest was admission to PC. Moreover, we also considered time at PC as a secondary exposure variable, categorized into two classes, i.e., below 30 days and 30 days or more before death.

As indicators of EOL intensity of care, we selected the following variables over a time-window of 30 days before death: hospitalizations, number of hospitalizations, hospitalizations of 12 or more days, minor procedures (non-operating room procedures) or major procedures (all procedures considered valid operating room procedures) performed for diagnostic or therapeutic reasons following the Agency for Healthcare Research and Quality procedure class definitions [28], in-hospital death, ED visits, number of ED visits, and chemotherapy use; chemotherapy use in the last 14 days was also considered. These indicators were chosen among those proposed in the literature to measure aggressive care in the EOL [1 2] .

Statistical analysis

We used absolute and relative frequencies to describe categorical variables, and mean and standard deviation (SD) to describe continuous variables. P-values for the difference between study groups were tested with Chi-square test for categorical variables and non-parametric U test for continuous variables.

To investigate the association between PC admission and time at PC admission with the outcomes of interest, we used multivariable logistic regression models, adjusted for sex, age at death, patient's local health unit, deprivation index, tumor type, presence of advanced

neoplasm, and Charlson's comorbidity index. For ordinal outcome variables, multinomial logistic regression models were used, adjusted for the same confounding variables.

As a sensitivity analysis, we investigated the association between PC admission after a propensity score matched analysis to reduce the heterogeneity between individuals who have been admitted to PC and those who did not. A multivariable logistic regression was used to model the probability of having been referred to PC, given a set of covariates (i.e., patients' baseline characteristics). Each individual who have been admitted to PC (index case) was matched with one individual randomly selected from those have not been admitted to PC with a propensity score value within ±0.01 the corresponding index case's value [29]. All the analyses were performed using the SAS software Version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Figure 1 shows the flow-chart of individuals' selection. From 10,583,560 individuals registered in the Lombardy health system in 2019, we identified 26,539 residents in Lombardy, deceased in 2019 with a diagnosis of cancer between 2014 and 2019; of these, 14,320 (54%) had an admission to PC before death. Among those who had an admission to PC, 43.7% had assistance at home, 41.3% had assistance at hospice, and 14.9% had mixed assistance; mean duration of PC was 32.7 days (SD 43.7); 39.7% deceased at home and 52.7% deceased at hospice; 65.7% of individuals referred to PC <30 days before death, 17.5% 30 to <60 days before, and 16.8% ≥60 days before (data not shown).

Table 1 shows the characteristics of 26,539 individuals deceased in 2019 with a diagnosis of a malignant neoplasm, overall and according to PC admission. Forty-three percent of individuals were women, mean age was 76.2 (SD 11.3), most common neoplasms were those of the lung and respiratory system (15.2%), colorectum (9.7%), and bladder and urinary tract (9.0%), 12% of individuals had presence of advanced disease, and 16.2% had a high Charlson's

comorbidity index. Individuals who were admitted to PC were significantly more frequently women, were of a lower age, had more frequently pancreatic cancer and less frequently neoplasms of the lymphohematopoietic system, had more frequent advanced neoplasm, and had a higher Charlson's comorbidity index. No difference was found with reference to DI.

During the last 30 days before death, 44.2% of individuals had at least one hospitalization, 5.6% had ≥2 hospitalizations, mean duration of hospitalization was 12.1 days (SD 7.5), 17% of individuals had ≥12 days of hospital stay, 45.7% received minor diagnostic/therapeutic procedures, 4.1% major diagnostic/therapeutic procedures, 28.2% died at hospital, 44.2% had at least one ED visit, 8.4% had ≥2 ED visits, and 8.9% received a chemotherapy treatment (2.4% in the last 14 days; **Table 2**). Individuals who were admitted to PC compared with those who have not been admitted had significantly less frequent hospitalizations and ED visits, shorter hospital stays, less minor or major diagnostic/therapeutic procedures, in-hospital deaths, and less use of chemotherapy in the last 30 days of life. Use of chemotherapy was also less frequent in the last 14 days of life. Individuals who were admitted to PC had an odds ratio (OR) of 0.27 for at least one hospitalization, 0.14 for ≥2 hospitalizations, 0.25 for hospital stay ≥12 days, 0.38 for minor diagnostic/therapeutic procedures, 0.18 for major diagnostic/therapeutic procedures, 0.02 for in-hospital death, 0.35 for at least one ED visit, 0.29 for ≥2 ED visits, and 0.66 for chemotherapy use in the last 30 days; the OR was 0.56 for chemotherapy use in the last 14 days. When we compared 9862 individuals who were admitted to PC and 9862 individuals who were not admitted to PC after propensity score matching (**Supplementary Table 2**), the results for the outcomes of interest were very similar to those in the unmatched study groups (**Supplementary Table 3**).

Individuals who were admitted to PC ≥30 days before death had similar baseline variables distribution compared to those who were admitted to PC <30 days before, except from the fact that were more frequently women and had more frequently a neoplasm of the brain (**Table 3**).

However, during the last 30 days before death they showed significant reductions in various outcome analysed, including reduced hospitalization (9% vs 42.9%, OR=0.13), lower number of hospitalizations (0.9% vs 3.6% with ≥2 hospitalizations, OR=0.14), less frequent long-term hospital stays (2.2% vs 16.6%, OR=0.08), less frequent minor (13.7% vs 46.9%, OR=0.18) or major (0.6% vs 1.9%, OR= 0.29) diagnostic/therapeutic procedures, more in-hospital deaths (4.1% vs 2.2%, OR=2.06), less ED visits (12.3% vs 43.7%, OR=0.18), lower number of ED visits (1.5% vs 7.8% with ≥2 ED visits, OR=0.13), and less frequent use of chemotherapy (5.8% vs 8.6%, OR=0.63), even 14 days before death (1.6% vs 1.9%, OR=0.80; **Table 4**).

DISCUSSION

Main findings and results of the study

In this real-world study from the largest Italian region, we found that about 45% of patients who died with cancer where hospitalized during the last 30 days of life, and about 30% died in hospital. Chemotherapy treatment was received by 8.5% and 2.3% of patients respectively in the last 30 days and 14 days. PC admission was associated with a significantly reduced risk of hospitalization, long-term hospital stays, (minor or major) diagnostic and therapeutic procedures, chemotherapy use during the last month of life; moreover, in-hospital death was extremely reduced in cancer patients who were admitted to PC. Further reductions in those indicators of aggressive EOL intensity of care were observed in patients who were admitted to PC 30 or more days before death, except for in-hospital death.

In our study, we found that about 54% of cancer patients were admitted to PC in the EOL. Such prevalence appears to be below the suggested standards, which indicates that at least 65% of cancer patients should have been admitted to PC; however, this data is in line with those reported in other areas from Italian and Europe [30 31].

With reference to the indicators of aggressive EOL care analysed in our study, we found that about 45% of patients were hospitalized during the last 30 days of life, a value that is within the range between 40% and 65% reported in previous investigations [14-18 32]. About 30% of cancer patients in Lombardy died in hospital, a value among the lowest reported in other studies (between 30% and 70%) [4 14 15 17-19 21 32]. Patients treated with chemotherapy in our population were 8.5% in the last 30 days and 2.3% in the last 14 days. Although there is some variability in the data reported in previous studies (with values between 5% and 20% in the last 30 days and between 2% and 10% in the last 14 days), chemotherapy exposure in our study appears quite low, particularly in the last 14 days [4 14-16 18 21 32 33]. Although it is possible that we had somehow underestimated chemotherapy use, this is a favourable indicator of the practice of EOL in cancer patients in this Italian region.

What this study adds

Our study supports the evidence from previous investigations that PC admission has a relevant role in reducing various indicators of EOL aggressive care [5-18]. In particular, we found that PC reduced hospitalizations by over 70%, long hospital stay by 75%, ED visit by 65%, and use of chemotherapy by 35% during the last month. Further, in-hospital death was extremely limited in cancer patients who were admitted to PC (2.8%) compared to those who were not admitted (58%; OR= 0.01). The results on the impact of PC on hospitalizations, long-term hospital stay, ED visits and chemotherapy use are in broad agreement with those found in previous studies. The hospital death prevalence in patients who referred to PC in our study was, however, much lower than those found in other investigations. It is also of interest to note that among patients admitted to PC about 53% died in hospice and 40% died at home. These findings indicate that assistance to PC in the Lombardy region allows to largely avoid in-hospital death, in line with the expectations of patients and their family, that have been reported to prefer home or other healthcare places rather than hospital as place of death [34-37].

Our data further confirm that earlier PC admission is associated to a further reduction in unnecessary hospitalizations, ED visits, and chemotherapy treatment in the EOL [14 19-22]. However, in our population in-hospital death increased by two-fold in patients with earlier admission to PC. This finding is quite unexpected and it is not easy to explain. Our findings add further evidence that early PC - as simultaneous care in the early phases of the disease, which are not considered in our analysis - is associated to a better cancer patient's care, with improved management of patient's symptoms and QOL, treatment of drug adverse effects, and possibly a prolonged survival [38-41].

Strengths and limitations of the study

Among the strengths of our study there is the fact that is a real-world study, conducted in a large, unselected population of patients died with cancer in the study area. While other studies considered only advanced or poor-prognosis neoplasms [17 42], we preferred to include all patients who were hospitalized for cancer in the last 5 years, therefore including also neoplasms with a longer prognosis. Moreover, we had access to various sources of health data from all the beneficiaries of the regional health system (such as the SDO, pharmaceutical, out-patient visits, and high cost neoplastic drug register). In addition, we could also link those databases with the informative data of all Lombardy residents who were admitted to PC [24]. Moreover, we could adjust our estimates for various socio-demographic and available health information within our databases. As a sensitivity analysis, we also matched patients who were admitted to PC with those who were not admitted to using propensity score, in order to make more comparable the study groups, since they may have different socio-economic and clinical characteristics at PC admission.

Our study has also a few limitations. First, this is a retrospective study, with some inherent weaknesses, including in particular the fact that we started from the time at death, that in actual care situation is unknown. However, previous data indicated that retrospective studies are as

good as prospective ones to investigate patterns in the EOL [43]. Second, we considered patients died with cancer and not of cancer, since in our databases there was no information on the cause of death. Therefore, we could have included some patients whose main cause of death was not cancer; however, their number should be small considering the long time-window for the identification of the study cohort (5 years) and that the number of cancer deaths identified in our study (N=26,539) was very similar to that reported by the official statistics (N=29,509) for the year 2019 [44]. Third, in our databases we had no information on various patients' clinical variables and patients reported outcomes; therefore, we could not adjust our estimates for those patients' characteristics, nor understand whether for each single patient potentially aggressive interventions at the EOL were indeed well justified. Finally, our data refer to a single Italian region and the findings cannot be considered generalizable to other Italian regions or countries, where PC practices can be different. Nonetheless, our findings are largely comparable with those reported in similar studies from other countries.

Conclusions

In conclusion, this large real-world analysis confirms and further support the importance of PC assistance for cancer patients in the EOL. Further progress in PC at regional and national level is therefore desirable in order to further increase the number of cancer patients assisted, for a better management of the patients' EOL and significant reduction in unnecessary treatments and expensive health care resources.

Contributors

MVC performed the statistical analyses and contributed in drafting the manuscript. OC and MP provided their clinical knowledge for the study design and interpretation of study results and contributed in drafting the manuscript. AN, GF, IF and OL gave access to data and contributed in the interpretation of study results. CB conceived the project and drafted the manuscript. All authors discussed the results and approved the final version of the manuscript.

Declaration of interests

The authors have no conflicts of interest to declare.

Ethical approval

By virtue of a specific agreement between the Mario Negri Institute and the Lombardy Region, it was not necessary to obtain approval from any ethics committee for the use of the anonymous administrative data extracted from the regional healthcare utilization databases.

Transparency statement

Cristina Bosetti (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported and that no important aspects of the study have been omitted.

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played no role in the study design, in the collection, analysis, and interpretation of data, in the writing of the report, and in the decision to submit the paper for publication.

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Data sharing

Research data cannot be shared because data ownership is of the Lombardy Region.

FIGURE LEGEND

Figure 1. Flowchart of individuals' selection.

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Table 1. Characteristics of 26,539 individuals deceased in 2019 with a diagnosis of a malignant neoplasm, overall and according to palliative care (PC) admission. Lombardy, Italy.

	All (N=26,539)	**PC (N=14,320)**	**No PC (N=12,219)**
	N (%)	**N (%)**	**N (%)**
Sex, female	11478 (43.3)	6456 (45.1)	5022 (41.1)
Age (years)			
<65	4234 (16.0)	2619 (18.3)	1615 (13.2)
65-74	6020 (22.7)	3539 (24.7)	2481 (20.3)
75-84	9709 (36.6)	5347 (37.3)	4362 (35.7)
≥85	6576 (24.8)	2815 (19.7)	3761 (30.8)
Mean (SD)	76.2 (11.3)	74.8 (11.1)	77.9 (11.2)
Deprivation index			
I	5207 (19.7)	2876 (20.1)	2331 (19.1)
II	5076 (19.2)	2741 (19.2)	2335 (19.1)
II	5456 (20.6)	2974 (20.8)	2482 (20.3)
IV	5416 (20.4)	2927 (20.5)	2489 (20.4)
V	5341 (20.2)	2772 (19.4)	2569 (21.1)
Missing	*43*	*30*	*13*
Mean (SD)	1.6 (2.1)	1.6 (2.1)	1.6 (2.1)
Malignant neoplasm			
Oesophagus, stomach and duodenum	1667 (6.3)	1043 (7.3)	624 (5.1)
Colorectum	2569 (9.7)	1435 (10.0)	1134 (9.3)
Liver and biliary tract	1731 (6.5)	1031 (7.2)	700 (5.7)
Pancreas	1521 (5.7)	1047 (7.3)	474 (3.9)
Lung/respiratory system	4037 (15.2)	2380 (16.6)	1657 (13.6)
Breast	1468 (5.5)	678 (4.7)	790 (6.5)
Female genital organs	834 (3.1)	531 (3.7)	303 (2.5)
Prostate and male genital organs	993 (3.7)	487 (3.4)	506 (4.1)
Bladder and urinary tract	2383 (9.0)	1113 (7.8)	1270 (10.4)
Brain	727 (2.7)	514 (3.6)	213 (1.7)
Lymphoematopoietic neoplasms	1802 (6.8)	690 (4.8)	1112 (9.1)
Other malignant neoplasms	6807 (25.7)	3371 (23.5)	3436 (28.1)
Presence of advanced neoplasm, yes	3193 (12.0)	2075 (14.5)	1118 (9.2)
Charlson's comorbidity index[a]			
0-2	7254 (27.3)	3507 (24.5)	3747 (30.7)
3-5	5423 (20.4)	2276 (15.9)	3147 (25.8)
6-8	9561 (36.0)	5987 (41.8)	3574 (29.3)
≥9	4301 (16.2)	2550 (17.8)	1751 (14.3)
Mean (SD)	5.6 (3.2)	6.0 (3.1)	5.1 (3.2)

SD: standard deviation. [a]During last five years of life.

Table 2. Indicators of end-of-life indicators of intensive care among 26,539 individuals deceased in 2019 with a diagnosis of a malignant neoplasm, overall and according to palliative care (PC) admission. Lombardy, Italy.

	All (N=26,539)	PC (N=14,320)	No PC (N=12,219)	OR (95% CI) for PC vs no PC[a]
	N (%)	N (%)	N (%)	
Hospitalizations in the last 30 days				
No	14813 (55.8)	9845 (68.8)	4968 (40.7)	1.00[b]
Yes	11726 (44.2)	4475 (31.3)	7251 (59.3)	0.27 (0.25-0.28)
N. of hospitalizations in the last 30 days				
0	14813 (55.8)	9845 (68.8)	4968 (40.7)	1.00[b]
1	10239 (38.6)	4093 (28.6)	6146 (50.3)	0.29 (0.27-0.31)
≥2	1487 (5.6)	382 (2.7)	1105 (9.0)	0.14 (0.12-0.16)
Duration of hospital stay in the last 30 days (days)				
0	14813 (55.8)	9845 (68.8)	4968 (40.7)	1.00[b]
>0-<12	7208 (27.2)	2807 (19.6)	4401 (36.0)	0.27 (0.26-0.29)
≥12	4518 (17.0)	1668 (11.7)	2850 (23.3)	0.25 (0.24-0.27)
Minor diagnostic/therapeutic procedures in the last 30 days				
No	14407 (54.3)	9231 (64.5)	5176 (42.4)	1.00[b]
Yes	12132 (45.7)	5089 (35.5)	7043 (57.6)	0.38 (0.36-0.40)
Major diagnostic/therapeutic procedures in the last 30 days				
No	25444 (95.9)	14117 (98.6)	11327 (92.7)	1.00[b]
Yes	1095 (4.1)	203 (1.4)	892 (7.3)	0.18 (0.15-0.21)
In-hospital death				
No	19068 (71.9)	13914 (97.2)	5154 (42.2)	1.00[b]
Yes	7471 (28.2)	406 (2.8)	7065 (57.8)	0.02 (0.01-0.02)
Emergency department visits in the last 30 days				

	All (N=26,539) N (%)	PC (N=14,320) N (%)	No PC (N=12,219) N (%)	OR (95% CI) for PC vs no PC[a]
No	14801 (55.8)	9611 (67.1)	5190 (42.5)	1.00[b]
Yes	11738 (44.2)	4709 (32.9)	7029 (57.5)	0.35 (0.34-0.37)
N. of emergency department visits in the last				
0	14801 (55.8)	9611 (67.1)	5190 (42.5)	1.00[b]
1	9510 (35.8)	3898 (27.2)	5612 (45.9)	0.37 (0.35-0.39)
≥2	2228 (8.4)	811 (5.7)	1417 (11.6)	0.29 (0.27-0.32)
Chemotherapy in the last 30 days				
No	24179 (91.1)	13232 (92.4)	10947 (89.6)	1.00[b]
Yes	2360 (8.9)	1088 (7.6)	1272 (10.4)	0.66 (0.58-0.70)
Chemotherapy in the last 14 days				
No	25910 (97.6)	14063 (98.2)	11847 (97.0)	1.00[b]
Yes	629 (2.4)	257 (1.8)	372 (3.0)	0.56 (0.47-0.66)

95% CI: 95% confidence interval; OR: odds ratio; SD: standard deviation.
[a]Estimates adjusted for sex, age, local health unit, deprivation index, tumor type, presence advanced neoplasm, and Charlson's comorbidity index.
[b]Reference category.

Table 3. Characteristics of 14,320 individuals deceased in 2019 with a diagnosis of a malignant neoplasm and admitted to palliative care (PC) according to time at admission. Lombardy, Italy.

	PC admission <30 days before death (N=9406)	PC admission ≥30 days before death (N=4914)
	N (%)	N (%)
Sex, female	4023 (42.8)	2433 (49.5)
Age (years)		
<65	1671 (17.8)	948 (19.3)
65-74	2388 (25.4)	1151 (23.4)
75-84	3502 (37.2)	1845 (37.6)
≥85	1845 (19.6)	970 (19.7)
Mean (SD)	74.9 (11.0)	74.6 (11.4)
Deprivation index		
I	1892 (20.2)	984 (20.1)
II	1808 (19.3)	933 (19.0)
II	1950 (27.8)	1024 (20.9)
IV	1947 (20.7)	980 (20.0)
V	1790 (19.1)	982 (20.0)
Missing	*19*	*11*
Mean (SD)	1.6 (2.1)	1.6 (2.2)
Malignant neoplasm		
Oesophagus, stomach and duodenum	688 (7.3)	355 (7.2)
Colorectum	874 (9.3)	561 (11.4)
Liver and biliary tract	717 (7.6)	314 (6.4)
Pancreas	701 (7.5)	346 (7.0)
Lung/respiratory system	1596 (17.0)	784 (16.0)
Breast	415 (4.4)	263 (5.4)
Female genital organs	354 (3.8)	177 (3.6)
Prostate and male genital organs	318 (3.4)	169 (3.4)
Bladder and urinary tract	773 (8.2)	340 (6.9)
Brain	266 (2.8)	248 (5.1)
Lymphoematopoietic neoplasms	493 (5.2)	197 (4.0)
Other malignant neoplasms	2211 (23.5)	1160 (23.6)
Presence of advanced neoplasm, yes	1331 (14.2)	744 (15.1)
Charlson's comorbidity Index[a]		
0-2	2258 (24.0)	1249 (25.4)
3-5	1508 (16.0)	768 (15.6)
6-8	3944 (41.9)	2043 (41.6)
≥9	1696 (18.0)	854 (17.4)
Mean (SD)	6.0 (3.1)	6.0 (3.1)

IQR: interquartile range; SD: standard deviation. [b]During last five years of life.

Table 4. Time at palliative care (PC) admission and end-of-life indicators among 14,320 individuals deceased in 2019 with a diagnosis of a malignant neoplasm. Lombardy, Italy.

	PC admission <30 days before death (N=9406)	PC admission ≥30 days before death (N=4914)	OR (95% CI) for PC admission ≥30 days vs <30 days before death[a]
	N (%)	N (%)	
Hospitalizations in the last 30 days			
No	5374 (57.1)	4471 (91.0)	1.00[b]
Yes	4032 (42.9)	443 (9.0)	0.13 (0.11-0.14)
N. of hospitalizations in the last 30 days			
0	5374 (57.1)	4471 (91.0)	1.00[b]
1	3692 (39.3)	401 (8.2)	0.13 (0.11-0.14)
≥2	340 (3.6)	42 (0.9)	0.14 (0.10-0.19)
Duration of hospital stay in the last 30 days (days)			
0	5374 (57.1)	4471 (91.0)	1.00[b]
>0-<12	2470 (26.3)	337 (6.9)	0.16 (0.14-0.18)
≥12	1562 (16.6)	106 (2.2)	0.08 (0.07-0.10)
Minor diagnostic/therapeutic procedures in the last 30 days			
No	499 (53.1)	4241 (86.3)	1.00[b]
Yes	4416 (46.9)	673 (13.7)	0.18 (0.16-0.19)
Major diagnostic/therapeutic procedures in the last 30 days			
No	9231 (98.1)	4886 (99.4)	1.00[b]
Yes	175 (1.9)	28 (0.6)	0.29 (0.19-0.44)
In-hospital death			
No	9203 (97.8)	4711 (95.9)	1.00[b]
Yes	203 (2.2)	203 (4.1)	2.06 (1.68-2.52)
Emergency department visits in the last 30 days			
No	5300 (56.4)	4311 (87.7)	1.00[b]
Yes	4106 (43.7)	603 (12.3)	0.18 (0.16-0.20)
N. of emergency department visits in the last			
0	5300 (56.4)	4311 (87.7)	1.00[b]
1	3370 (35.8)	528 (10.7)	0.19 (0.17-0.21)
≥2	736 (7.8)	75 (1.5)	0.13 (0.10-0.16)
Chemotherapy in the last 30 days			
No	8602 (91.5)	4630 (94.2)	1.00[b]
Yes	804 (8.6)	284 (5.8)	0.63 (0.55-0.73)
Chemotherapy in the last 14 days			

	PC admission <30 days before death (N=9406) N (%)	PC admission ≥30 days before death (N=4914) N (%)	OR (95% CI) for PC admission ≥30 days vs <30 days before death[a]
No	9227 (98.1)	4836 (98.4)	1.00[b]
Yes	179 (1.9)	78 (1.6)	0.80 (0.61-1.06)

95% CI: 95% confidence interval; OR: odds ratio; SD: standard deviation.
[a]Estimates adjusted for sex, age, local health unit, deprivation index, tumor type, presence advanced neoplasm, and Charlson's comorbidity index. [b]Reference category.

Supplementary Table 1. List of malignant neoplasms.

Neoplasm	ICD-9-CM code
All malignant neoplasms	140-208
Oesophagus, stomach and duodenum	150-152
Colorectum	153-154
Liver and biliary tract	155-156
Pancreas	157
Lung/respiratory system	160-165
Breast	174-175
Female genital organs	179-184
Prostate and male genital organs	185-187
Bladder and urinary tract	188-189
Brain	191
Lymphohematopoietic neoplasms	200-208
Other malignant neoplasms	140-149, 158, 159, 166-173, 176-178, 190, 192-199
Advanced neoplasms	196.0-196.2, 196.5-196.6, 196.8-196.9, 197.0-197.8, 198.0-198.7, 198.81-198.82, 198.89, 199.0

ICD9-CM International Classification of Diseases, 9th revision, clinical modifications.

Supplementary Table 2. Characteristics of 19,724 individuals deceased in 2019 with a diagnosis of a malignant neoplasm according to palliative care (PC) admission after propensity score matching. Lombardy, Italy.

	PC (N=9862)	No PC (N=9862)	Absolute standardized difference
	N (%)	N (%)	
Sex, female	4233 (42.9)	4085 (41.4)	0.03
Age (years)			
<65	1537 (15.6)	1507 (15.3)	0.01
65-74	2319 (23.5)	2250 (22.8)	0.02
75-84	3590 (36.4)	3774 (38.3)	0.04
≥85	2416 (24.5)	2331 (23.6)	0.02
Mean (SD)	76.1 (11.0)	76.2 (10.9)	0.01
Deprivation index			
I	1989 (20.2)	1875 (19.0)	0.03
II	1969 (20.0)	1891 (19.2)	0.02
II	2033 (20.6)	2020 (20.5)	0.00
IV	2012 (20.4)	2018 (20.5)	0.00
V	1859 (18.9)	2058 (20.9)	-0.05
Mean (SD)	1.6 (2.1)	1.6 (2.1)	0.00
Malignant neoplasm			
Oesophagus, stomach, and duodenum	643 (6.5)	611 (6.2)	0.01
Colorectum	1070 (10.9)	1024 (10.4)	0.02
Liver and biliary tract	696 (7.1)	672 (6.8)	0.01
Pancreas	493 (5.0)	471 (4.8)	0.01
Lung/respiratory system	1559 (15.8)	1612 (16.4)	0.02
Breast	575 (5.8)	571 (5.8)	0.00
Female genital organs	306 (3.1)	294 (3.0)	0.01
Prostate and male genital organs	404 (4.1)	413 (4.2)	0.01
Bladder and urinary tract	950 (9.6)	979 (9.9)	0.01
Brain	235 (2.4)	211 (2.1)	0.02
Lymphoematopoietic neoplasms	673 (6.8)	687 (7.1)	0.01
Other malignant neoplasms	2258 (22.9)	2307 (23.4)	0.01
Presence of advanced neoplasm, yes	1012 (10.3)	1114 (11.3)	0.03
Charlson's comorbidity Index[a]			
0-2	2726 (27.6)	2671 (27.1)	0.01
3-5	2020 (20.5)	2063 (20.9)	0.01
6-8	3375 (34.2)	3459 (35.1)	0.02
≥9	1741 (17.7)	1669 (16.9)	0.02
Mean (SD)	5.6 (3.2)	5.6 (3.2)	0.00

SD: standard deviation. [a]During last five years of life.

Supplementary Table 3. Time at palliative care (PC) admission and end-of-life indicators among 19,724 individuals deceased in 2019 with a diagnosis of a malignant neoplasm after propensity score matching. Lombardy, Italy.

	PC (N=9862)	No PC (N=9862)	OR (95% CI) for PC vs no PC[a]
	N (%)	N (%)	
Hospitalizations in the last 30 days			
No	6808 (69.0)	3785 (38.4)	1.00[b]
Yes	3054 (31.0)	6077 (61.6)	0.28 (0.26-0.30)
N. of hospitalizations in the last 30 days			
0	6808 (69.0)	3785 (38.4)	1.00[b]
1	2799 (28.4)	5137 (52.1)	0.30 (0.20-0.33)
≥2	255 (2.6)	940 (9.5)	0.14 (0.11-0.17)
Duration of hospital stay in the last 30 days (days)			
0	6808 (69.0)	3785 (38.4)	1.00[b]
>0-<12	1911 (19.4)	3653 (37.0)	0.30 (0.28-0.33)
≥12	1143 (11.6)	2424 (24.6)	0.24 (0.22-0.27)
Minor diagnostic/therapeutic procedures in the last 30 days			
No	6329 (64.2)	4062 (41.2)	1.00[b]
Yes	3533 (35.8)	5800 (58.8)	0.39 (0.37-0.42)
Major diagnostic/therapeutic procedures in the last 30 days			
No	9727 (98.6)	9126 (92.5)	1.00[b]
Yes	135 (1.4)	736 (7.5)	0.17 (0.14-0.21)
In-hospital death			
No	9593 (97.3)	3895 (39.5)	1.00[b]
Yes	269 (2.7)	5967 (60.5)	0.02 (0.02-0.02)
Emergency department visits in the last 30 days			
No	6564 (66.6)	4109 (41.7)	1.00[b]
Yes	3298 (33.4)	5753 (58.3)	0.36 (0.34-0.38)
N. of emergency department visits in the last			
0	6564 (66.6)	4109 (41.7)	1.00[b]
1	2717 (27.6)	4570 (46.3)	0.36 (0.34-0.39)
≥2	581 (5.9)	1183 (12.0)	0.33 (0.29-0.38)
Chemotherapy in the last 30 days			
No	9117 (92.5)	8759 (88.8)	1.00[b]
Yes	745 (7.6)	1103 (11.2)	0.65 (0.59-0.72)
Chemotherapy in the last 14 days			
No	9678 (98.1)	9555 (96.9)	1.00[b]
Yes	184 (1.9)	307 (3.1)	0.59 (0.49-0.71)

95% CI: 95% confidence interval; OR: odds ratio; SD: standard deviation.

[a]Estimates adjusted for sex, age, local health unit, deprivation index, tumor type, presence advanced neoplasm, and Charlson's comorbidity Index. [b]Reference category.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
		Introduction	
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
		Methods	
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4,5
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	NA
		(*d*) If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7 and Supplementary Material
		(c) Consider use of a flow diagram	Supplementary Material
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7,8

		(b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	Tables and Supplementary Material NA
Outcome data	15*	Report numbers of outcome events or summary measures over time	8 and Tables
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9 Tables and Supplementary Material NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8,9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9,10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11,12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10,11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.