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Data Sharing statement: Data may be obtained from a third party and are not publicly available. A data request can be sent to ICES (formerly the Institute for Clinical Evaluative Sciences): https://www.ices.on.ca/About-ICES/ICES-Contacts-and-Locations/contact-form

Short title/Running head: Early palliative care in a cancer population
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ABSTRACT:

Objectives: To investigate whether cancer decedents who received palliative care early (i.e. >6 months before death) and not-early had different risk of using hospital care and supportive home care in the last month of life.

Design / Setting: We identified a population-based cohort of cancer decedents between 2004 and 2014 in Ontario, Canada using linked administrative data.

Participants: We propensity-score matched decedents on receiving early or not-early palliative care using billing claims. We created two groups of matched pairs: one that had Resident Assessment Instrument (RAI) home care assessments in the exposure period (Yes-RAI group) and one that did not (No-RAI group) to control for confounders uniquely available in the assessment, such as health instability and pain. The outcomes were the absolute risk difference between matched pairs in receiving hospital care, supportive home care, or hospital death.

Results: In the No-RAI group, we identified 36,238 pairs who received early and not-early palliative care. Those in the early palliative care group vs. not-early group had a lower absolute risk difference of dying in hospital (-10.0%) and receiving hospital care (-10.4%), and a higher absolute risk difference of receiving supportive home care (23.3%). In the Yes-RAI group, we identified 3,586 pairs, where results were similar in magnitude and direction.

Conclusions: Cancer decedents who received palliative care earlier than six months before death compared to those who did not had a lower absolute risk difference of receiving hospital care and dying in hospital, and an increased absolute risk difference of receiving supportive home care in the last month of life.

Strengths and limitations of this study

- This large population-based cohort study of all cancer decedents in Ontario, Canada from 2004-2014 uses consistent exposure and outcome definitions over a long period of time, which provides high external validity in real-world settings.
- The study used propensity scores to match decedents who received palliative care earlier than six months before death compared to those who did not, thereby reducing selection bias among those who receive early palliative care.
- Our study included and controlled for previously unmeasured confounders known to be associated with receipt of early palliative care (i.e. worse pain, ADL dependency, depression, cognitive decline, and health instability) derived from home care assessment data.
- The study matches those who have similar propensity to have received early palliative care, but this may not represent the entire population of cancer decedents.
- The study does not directly measure patient preferences, which is a confounder for use of early palliative care.

INTRODUCTION

Early palliative care is purported to improve quality of life and also avoid unnecessary acute care use, and thus reduce health system costs. There is a cancer clinical practice guideline that supports the early integration of palliative care with standard oncologic care.[1,2] Yet data shows palliative care is often applied very late in the disease trajectory or not at all. For example in Ontario, Canada, palliative care is used in 50% of all deaths for a median of 30 days before death.[3] US statistics are very similar.[4]

Several randomized trials on advanced cancer patients have shown that early palliative care reduced symptoms and some even had survival benefits.[5-7] However, the evidence is mixed as to whether it reduces health services utilization outcomes at end-of-life. There are trials that show that resource utilization at end of life is not different from "usual care." In particular, many of the trials implemented palliative care interventions close to diagnosis in controlled study settings, which is difficult to implement in the real-world. For example, the US Medicare Hospice Benefit uses an expected death within six months.[8] Additionally, many observational studies have found positive associations between early palliative care and reduced likelihood to receive aggressive care at end of life (e.g. reduced hospitalizations and hospital deaths).[9-14] However, observational studies are limited by selection bias, namely those who get early palliative care may be different from those who do not (e.g. sicker or more symptomatic in ways that are unmeasured). This is summarized in a large systematic review on early palliative care interventions, which found mixed evidence of benefits and noted key methodological issues of selection bias, as well as when 'early' began, the interventions, and usual care definitions varied.[15] Thus the evidence that early palliative care reduces late-life acute care use (particularly when it does not begin at diagnosis) is unclear. This gap has important health resource planning and economic implications.

This study investigated the impact of receiving palliative care early (at least six months before death) vs. not-early on outcomes in the last 30 days of life. By examining cancer patients in the universal health system of Ontario, Canada, we are able to address prior limitations, namely standardizing definitions for 'early' palliative care, usual care, and the palliative care

intervention. We used propensity-score matching to reduce selection bias in observational cohorts around receipt of early palliative care.

METHODS

Study Design and Data Sources

We performed a population-based, retrospective cohort study of all cancer decedents in Ontario, Canada from 2004-2014. We utilized propensity score matching to match decedents having received palliative care early (i.e., between 12 and six months before death) to those who did not (i.e. received palliative care late or not at all). We linked administrative databases housed at ICES (formally known as the Institute for Clinical Evaluative Sciences) including the: Ontario Cancer Registry (cancer diagnosis), Vital Statistics Registry (death date), Discharge Abstract Database (hospitalizations), National Ambulatory Care Reporting System (Emergency Department use), physician billings, Statistics Canada (sociodemographic data like income and rurality), and the Home Care Database, which includes all Resident Assessment Instrument-Home Care (RAI-HC) assessments. Datasets were linked using unique encoded identifiers and analyzed at ICES.

Study Population

We included decedents who had a cancer diagnosis in the Ontario Cancer Registry and a death caused by cancer as per the provincial Vital Statistics registry.

Exposure

In the exposure period (i.e. between 12 and six months before death), access to early palliative care was defined as having received: homecare with an end-of-life intent, a physician consult for palliative care in an outpatient clinic or home visit setting, or a hospitalization where palliative care was listed as the main reason for admission, as per prior research.[3] Once a patient was identified as having received early palliative care, they remained in the exposed group for analysis.

Outcomes

Outcomes were death in an acute care bed, and the aggregate measures of aggressive care and supportive home care in the last 30 days of life respectively. Aggressive care was

defined as one or a combination of ≥1 Emergency Department visit, hospital admission or ICU admission.[16] Supportive home care was defined as one or a combination of physician house call for palliative care, end-of-life homecare nursing or end-of-life personal support at home.[17] Each outcome was handled as a binary variable (Yes/No).

Statistical Analysis

To reduce selection bias for decedents who were exposed to early palliative care, we used propensity score matching to create a similar comparison group of unexposed decedents (not-early). The propensity score is an individual's probability of receiving early palliative care, given the values of their baseline measured covariates. Matching on the propensity score can estimate the effect of the intervention, which is unbiased by differences in the distributions of measured baseline covariates.[18,19] Our methods matches two individuals who have the same propensity to receive early palliative care in the exposure period, though one got early palliative care and one did not.

A priori we decided to examine the group who received long stay home care (i.e., expected to receive at least 60 days of home care) and thus had a RAI-HC assessment in the exposure period separately. This allowed us to control for additional confounders associated with receipt of early palliative care that are uniquely available in the RAI-HC. Therefore, we created two mutually exclusive groups of matched pairs and each pair consists of an exposed and unexposed decedent. One group is called the No-RAI group; the other the Yes-RAI group.

For the No-RAI group, all pairs were hard matched before the exposure period on: age at death, sex, cancer type, cancer stage (where available) and the logit of the propensity score (calipers of width less than or equal to 0.2 of the standard deviation of the logit of the propensity score).[20,21] We estimated the propensity score using a logistic regression model with exposure to early palliative care as the independent variable. The predictor variables in the propensity score regression included: income quintile, rurality, health region, prior hospital utilization in months 24 to 12 before death, Deyo-modified Charlson comorbidity score in months 24 to 12 before death, index year of death, and having had radiation or cancer surgery.[22]

For the Yes-RAI group, we utilize additional data from the RAI-HC, which is a standardized assessment for all long stay home care patients in Ontario, corresponding to the Minimum Data Set in the US.[23] In addition to matching procedure noted above for the No-RAI group, pairs were hard matched on health instability using the *Changes in Health, End-stage Disease, Signs and Symptoms (CHESS) scale*.[24,25] The following items were also included in the propensity score regression: functional performance and dependency using the ADL Self-performance Hierarchy Scale;[26] depression using the Depression Rating Scale;[27] cognitive impairment using the Cognitive Performance Scale;[28] pain intensity using the Pain Scale;[29] and living with a primary or secondary caregiver (Yes/No).

Because the distributions of covariates were well-balanced and not statistically different after matching the exposed and unexposed patients in both the No-RAI and Yes-RAI groups, we did not need to employ any regression methods for examining the exposure-outcomes relationship; thus for each outcome, we determined the absolute risk difference between the matched exposed and unexposed individuals in both Yes-RAI and No-RAI groups.[30] We used McNemar's test to determine statistical significance of the estimated risk difference.[31] Differences in risk between the exposure and control groups for each outcome were assessed using standardized differences. Standardized differences are more appropriate to use in this population-based study as they are not influenced by sample size (unlike p-values). Analysis was performed using SAS Enterprise Guide, version 7.1 (SAS Institute, Cary, NC).

As a sensitivity analysis, we divided the not-early group—i.e. unexposed group—into late palliative care (i.e., only received palliative care in the last six months of life) and never received palliative care. We then compared our outcomes by early vs. late and early vs. never separately. The study was approved by the Hamilton Integrated Research Ethics Board (#3039).

Patient and Public Involvement

Patients and the public were not involved this research.

RESULTS

Patients

In the overall cohort, there were 144,306 cancer decedents in Ontario between 2004 and 2014, of which 53,959 (37.4%) received early palliative care 12 to six months before death. Eighty-nine percent (n=128,248) of the overall cohort did not have a RAI-HC in the exposure period (No-RAI), who were matched separately than the 11% (n=16,058) who did have the assessment (Yes-RAI). (Figure 1) Baseline characteristics before propensity score matching are shown in Table S1 in the Supplementary Appendix, and those after propensity score matching are shown in Table 1.

In the No-RAI group, we matched 82.6% of patients who received early palliative care for a total of 36,238 matched pairs. After matching, the decedent covariate distributions were nearly identical between the two groups. For instance, average age was 69, 23.5% had lung cancer and 14.2% had stage IV disease. In the No-RAI group, the first initiation of early palliative care was about 300 days before death, of which half were initiated by homecare services and a third by outpatient physician billings. In the last 6 months of life, the early group received 91,321 palliative care services (30% home care, 33% physician consults and 24% hospital), whereas the late group received 63,994 palliative care services (25% home care, 35% physician consults and 29% hospital admissions).

In the Yes-RAI group, we matched 59.9% of patients who received homecare but without end-of-life intent in the exposure period for a total of 3,586 matched pairs. After matching, the decedent covariate distributions were nearly identical between the two groups. For instance, 11.8% had moderate to severe health instability using the CHESS score, 6.8% were fully dependent on their ADLs, and 11.0% had moderate-severe pain. In the Yes-RAI group, the first initiation of early palliative care was about 330 days before death, of which two-thirds were homecare services. In the last 6 months of life, the early group received 8,484 palliative care services (same distributions as No-RAI group) whereas the late group received 4,664 palliative care services (16% home care, 38% physician consults and 37% hospital admissions).

Aggressive Care

Among matched pairs in the No-RAI group, those who received early palliative care had lower risk difference of the aggressive care outcomes compared to the not-early group. (Table 2) 38.1% of the early palliative care decedents died in hospital, compared to 48.1% of the non-

early palliative care group, resulting in a lower absolute risk difference of 10.0%. Similarly, the aggregate measure of aggressive care was lower by 10.4% among early palliative care decedents. The early palliative care decedents have a lower absolute risk difference of an Emergency Department visit (9.7%), hospital admission (10.1%), and ICU admission (4.4%) in the last month of life compared to the not-early group.

Among matched pairs in the Yes-RAI groups, we found similar results in the direction and magnitude of the absolute risk differences favoring early palliative care. Note, McNemar's tests for matched pairs were significant ($p < 0.0001$ for all measures). Further, the sensitivity analyses in the Yes-RAI and No-RAI groups separately, looking at matched pairs of early vs. late palliative care and early vs. never palliative care respectively, showed that the early palliative care group consistently had lower absolute risk differences for all outcomes, in similar magnitudes. (Appendix S2)

Supportive Home Care

Among the matched pairs in the No-RAI group, those who received early palliative care had higher risk of receiving supportive home care outcomes compared to the not-early group. (Table 3) The aggregate measure of supportive home care was higher by 23% among early palliative care decedents vs. not-early decedents. 56.2% of the early palliative care decedents had any end-of-life home care nursing in the last 30 days, compared to 34.0% of the non-early palliative care group, resulting in a lower absolute risk difference of 22.2%. The early palliative care decedents have a higher absolute risk of having a physician house call (10.2%) and an end-of-life personal support worker in the last month of life (16.0%) vs. not-early decedents.

Among the matched pairs in the Yes-RAI groups, we found similar trends in direction, but at larger magnitudes: a 37.8% higher absolute risk difference of having any one of the three supportive home care outcomes. Note, McNemar's tests for matched pairs were significant ($p < 0.0001$ for all measures). Further the sensitivity analyses, examining early vs. late and early vs. never palliative care matched pairs separately, showed that early palliative care consistently had higher absolute risk differences for all outcomes. (Appendix S3)

DISCUSSION

In our population-based cohort of 114,306 cancer decedents, a propensity score matched cohort of those who received palliative care earlier than six months before death compared to those who did not had a lower absolute risk difference of receiving hospital care and dying in hospital, and an increased absolute risk difference of receiving supportive home care in the last month of life. While prior randomized trials provided high internal validity within controlled settings, our approach provides high external validity in real-world settings. Bolstering the credibility that early palliative care is beneficial is the consistency of our findings across 2004-2014, which predate the publication of seminal randomized trials;[5-7] and the use of a population-based cancer cohort, meaning the findings were not a result of a particular cancer centre, intervention program, or cancer type.

This study addressed some of the noted gaps in prior research: it uses consistent exposure and outcome definitions over a long period of time and uses a large population-based cohort of all cancer types. Moreover, by using data from the RAI-HC, our study was able to control for previously unmeasured confounders known to be associated with receipt of early palliative care, such as worse pain, ADL dependency, depression, cognitive decline, and health instability. This seeks to address selection bias in prior observational studies where those receiving palliative care might be different (e.g. worse symptoms or have worse health instability) than those who do not. Our results were consistent with and without matching for RAI-HC variables. To address patient preferences, we conducted a sensitivity analysis to examine early vs. late and early vs. never subgroups separately. The hypotheses were that the late subgroup were willing to receive palliative care but were offered it late and the never subgroup were more likely to refuse palliative care. In both subgroups, the findings were consistent with our overall study results, further supporting the benefits of early palliative care.

Our study has limitations. The propensity score matched design means we are comparing amongst those who are likely to have received early palliative care, but this may not represent the entire population of cancer decedents. We do not directly measure patient preferences, which would be useful to control for in future studies. As well, future research should examine outcomes of health system costs or patient and caregiver well-being.

In conclusion, across an 11-year population-based, cancer cohort, those who received early palliative care (before six months of death) compared to a matched cohort of those who did not, were more likely to receive supportive home care and less likely to receive hospital care in the last month of life.

Table 1. Demographics of Early vs. Not-Early Palliative Care

	After propensity score matching					
	No-RAI			Yes-RAI		
	Not Early Palliative Care (N = 36,238)	**Early Palliative Care (N = 36,238)**	**SD**	**Not Early Palliative Care (N = 3,586)**	**Early Palliative Care (N = 3,568)**	**SD**
Variables that were Hard Matched	**N (%)**	**N (%)**		**N (%)**	**N (%)**	
Female	17,702 (48.8)	17,702 (48.8)	0.00	1,826 (50.9)	1,826 (50.9)	0.00
Cancer Type at Diagnosis						
Breast	4,126 (11.4)	4,126 (11.4)	0.00	433 (12.1)	433 (12.1)	0.00
Colorectal	5266 (14.5)	5,266 (14.5)	0.00	722 (20.1)	722 (20.1)	0.00
Hematology	2,982 (8.2)	2,982 (8.2)	0.00	479 (13.4)	479 (13.4)	0.00
Lung	8,530 (23.5)	8,530 (23.5)	0.00	548 (15.3)	548 (15.3)	0.00
Prostate	3,053 (8.4)	3,053 (8.4)	0.00	486 (13.6)	486 (13.6)	0.00
Stage at Diagnosis						
Stage III	3,726 (10.3)	3,726 (10.3)	0.00	275 (7.7)	275 (7.7)	0.00
Stage IV	5,151 (14.2)	5,151 (14.2)	0.00	329 (9.2)	329 (9.2)	0.00
Unavailable	24,631 (68.0)	24,631 (68.0)	0.00	2,749 (76.7)	2,749 (76.7)	0.00
CHESS Score (when RAI-HC completed)						
No health instability	-	-	-	921 (25.7)	921 (25.7)	0.00
Low health instability	-	-	-	2,242 (62.5)	2,242 (62.5)	0.00
Moderate health instability	-	-	-	380 (10.6)	380 (10.6)	0.00
Severe health instability	-	-	-	43 (1.2)	43 (1.2)	0.00
Variables within the Propensity Score						
Lowest income quintile	7,058 (19.5)	7,146 (19.7)	0.01	776 (21.6)	790 (22.0)	0.01
Highest income quintile	7,102 (19.6)	7,130 (19.7)	0.00	626 (17.5)	622 (17.3)	0.00
Lives in Rural Community	5,206 (14.4)	5,236 (14.4)	0.00	579 (16.1)	568 (15.8)	0.01
Deyo-Charlson Comorbidity Score (>=1)	12,026 (33.2)	12,540 (34.6)	0.03	1,483 (41.4)	1,426 (39.8)	0.08
Had Radiation since diagnosis	22,337 (61.6)	21,982 (60.7)	0.02	1,894 (52.8)	1,950 (54.4)	0.03
Had Cancer Surgery since diagnosis	16,339 (45.1)	15,701 (43.3)	0.04	1,780 (49.6)	1,716 (47.9)	0.04
InterRAI Scales (When RAI-HC completed)						
Dependent on Activities of Daily Living	-	-	-	241 (6.7)	247 (6.9)	0.01
Minor-major depression	-	-	-	496 (13.8)	429 (10.0)	0.06

Moderate-severe cognitive impairment	-	-	-	373 (10.4)	363 (10.1)	0.01
Moderate-severe pain	-	-	-	391 (10.9)	398 (11.1)	0.01
Caregiver Present at Home	-	-	-	2,279 (63.6)	2,264 (63.1)	0.01

Table 2: Aggressive care measures in decedents with or without a RAI assessment

	NO-RAI				YES-RAI			
	Early Palliative Care N = 36,238 (%)	Not Early Palliative Care N = 36,238 (%)	Absolute Risk Difference (%) (Early vs. Not Early)	SD	Early Palliative Care N = 3,586 (%)	Not Early Palliative Care N = 3,586 (%)	Absolute Risk Difference (%) (Early vs. Not Early)	SD
Death in acute care hospital	13,823 (38.1)	17,434 (48.1)	-10.0	0.21	1,278 (35.6)	1,751 (48.8)	-13.2	0.21
Aggressive care (any one or combination of the following three)	18,822 (51.9)	22,586 (62.3)	-10.4	0.21	1,718 (47.9)	2,089 (58.3)	-10.4	0.21
At least 1 ED visits within last 30 days	15,550 (42.9)	19,075 (52.6)	-9.7	0.21	1,454 (40.5)	1,827 (50.9)	-10.4	0.21
Any hospital admission within last 30 days	16,286 (44.9)	19,918 (55.0)	-10.1	0.25	1,492 (41.6)	1863 (52.0)	-10.4	0.25
Any ICU admission within last 30 days	1,299 (3.6)	2,889 (8.0)	-4.4	0.85	83 (2.3)	274 (7.6)	-5.3	0.85

*McNemar's test was significant to <0.0001 for all measures

Table 3: Supportive home care measures in decedents with or without a RAI assessment

	NO-RAI				YES-RAI			
	Early Palliative Care N = 36,238 (%)	Not Early Palliative Care N = 36,238 (%)	Absolute Risk Difference (%) (Early vs. Not Early)	SD	Early Palliative Care N = 3,586 (%)	Not Early Palliative Care N = 3,586 (%)	Absolute Risk Difference (%) (Early vs. Not Early)	SD
Supportive home care (any one or combination of the following three)	22,191 (61.2)	13,736 (37.9)	23.3	0.39	2,012 (56.1)	656 (18.3)	37.8	0.39
Physician house call in last 30 days	9,754 (26.9)	6,061 (16.7)	10.2	0.86	859 (24.0)	341 (9.5)	14.5	0.86
Palliative homecare nursing at home in last 30 days	20,370 (56.2)	12320 (34.0)	22.2	0.73	1,822 (50.8)	494 (13.8)	37.0	0.73
Palliative personal support at home in last 30 days	13,728 (37.9)	7,954 (21.9)	16.0	0.27	1,449 (40.4)	374 (10.4)	30.0	0.27

*McNemar's test was significant to <0.0001 for all measures

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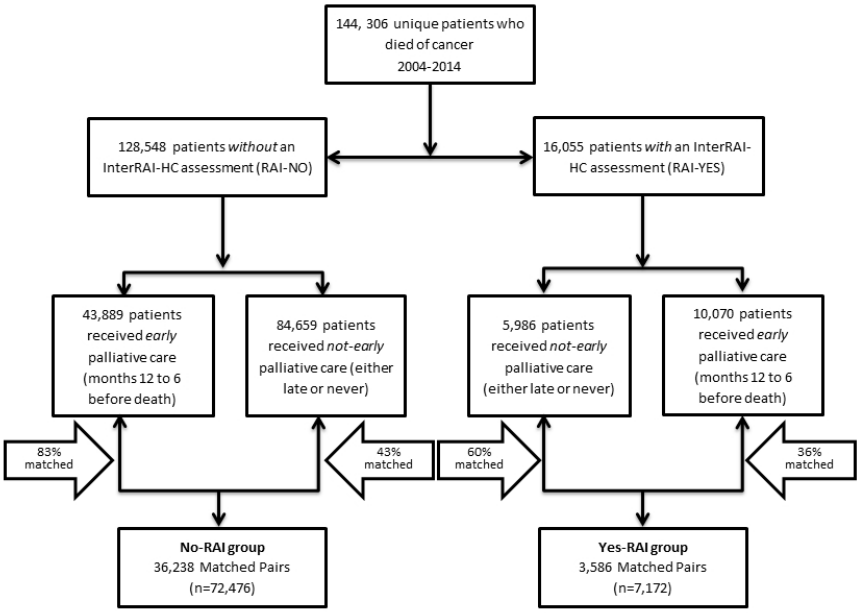
Figure 1. Consort Diagram



254x190mm (96 x 96 DPI)

Appendix S1. Demographics of Early vs. Not-Early before Propensity Score Matching

	Before Propensity Score matching		
	Not Early Palliative Care (N = 90,347)	**Early Palliative Care (N = 53,959)**	**SD**
Variables that were Hard Matched	**N (%)**	**N (%)**	
Female	41,994 (46.5)	27,113 (50.2)	0.59
Cancer Type at Diagnosis			
Breast	10,539 (11.7)	5,850 (10.8)	0.03
Colorectal	12,051 (13.3)	8,579 (15.9)	0.07
Hematology	10,546 (11.7)	4,150 (7.7)	0.13
Lung	17,444 (19.3)	13,050 (24.2)	0.12
Prostate	9,041 (10.0)	4,384 (8.1)	0.07
Stage at Diagnosis			
Stage III	6,222 (6.9)	5,858 (10.9)	0.14
Stage IV	7,347 (8.1)	10,832 (20.1)	0.35
Unavailable	70,351 (77.9)	32,731 (60.7)	0.38
CHESS Score (when RAI-HC completed)			
No health instability	1,704 (1.9)	2,221 (4.1)	0.13
Low health instability	3,433 (3.8)	5,458 (10.1)	0.25
Moderate health instability	714 (0.8)	1,761 (3.3)	0.18
Severe health instability	135 (0.1)	629 (1.2)	0.13
Variables within the Propensity Score			
Lowest income quintile	18,686 (20.7)	10,682 (19.8)	0.02
Highest income quintile	17,154 (19.0)	10,492 (19.4)	0.01
Lives in Rural Community	13,597 (15.0)	7,813 (14.5)	0.02
Deyo-Charlson Comorbidity Score (>=1)	13,728 (15.2)	9,553 (17.7)	0.10
Had Radiation since diagnosis	43,298 (47.9)	34,226 (63.4)	0.32
Had Cancer Surgery since diagnosis	37,369 (41.4)	23,917 (44.3)	0.59
InterRAI Scales (When RAI-HC completed)			
Dependent on Activities of Daily Living	433 (0.5)	684 (1.3)	0.08
Minor-major depression	809 (0.9)	1,797 (3.3)	0.17
Moderate-severe cognitive impairment	869 (1.0)	764 (1.4)	0.04
Moderate-severe pain	606 (0.7)	1,457 (2.7)	0.16
Caregiver Present at Home	3528 (3.9)	6,970 (12.9)	0.33

Appendix S2. Aggressive Care Measures comparing Early vs. Late and Early vs. Never

	RAI NO				RAI YES			
Late PC vs. Early PC	Early Palliative Care N = 28,285 (%)	Late Palliative Care N = 28,285 (%)	Absolute Risk Difference (%) (Early vs Late Palliative Care)	SD	Early Palliative Care N = 2,323 (%)	Late Palliative Care N = 2,323 (%)	Absolute Risk Difference (%) (Early vs Late Palliative Care)	SD
Death in acute care hospital	10,788 (38.1)	13,109 (46.3)	-8.2	0.17	831 (35.8)	1,152 (49.6)	-13.8	0.28
Aggressive care (any one or combination of the following three)	14,763 (52.2)	17,379 (61.4)	-9.2	0.19	1,135 (48.9)	1,344 (57.9)	-9.0	0.18
At least 1 ED visits within last 30 days	12,232 (43.2)	14,552 (51.4)	-8.2	0.16	949 (40.9)	1,141 (49.1)	-8.2	0.17
Any hospital admission within last 30 days	12,750 (45.1)	15,492 (54.8)	-9.7	0.19	992 (42.7)	1,223 (52.6)	-9.9	0.20
Any ICU admission within last 30 days	1,022 (3.6)	1,379 (4.9)	-1.3	0.06	53 (2.3)	111 (4.8)	-2.5	0.14
Never PC vs. Early PC	Early Palliative Care N = 7,953 (%)	Never Palliative Care N = 7,953 (%)	Absolute Risk Difference (%) (Early vs Never Palliative Care)	SD	Early PC N = 1,263 (%)	Never Palliative Care N = 1,263 (%)	Absolute Risk Difference (%) (Early vs Never Palliative Care)	SD
Death in acute care hospital	3,035 (38.2)	4,325 (54.4)	-16.2	0.33	447 (35.4)	599 (47.4)	-12.0	0.25
Aggressive care (any one or combination of the following three)	4,059 (51.0)	5,207 (65.5)	-14.5	0.30	583 (46.2)	745 (59.0)	-12.8	0.26
At least 1 ED visits within last 30 days	3,318 (41.7)	4,523 (56.9)	-15.2	0.31	505 (40.0)	686 (54.3)	-14.3	0.29
Any hospital admission within last 30 days	3,536 (44.5)	4,426 (55.7)	-11.2	0.23	500 (39.6)	640 (50.7)	-11.1	0.22
Any ICU admission within last 30 days	277 (3.5)	1,510 (19.0)	-15.5	0.51	30 (2.4)	163 (12.9)	-10.5	0.40

*McNemar's test was significant to <0.0001 for all measures

Appendix S3. Supportive Home Care Measures comparing Early vs. Late and Early vs. Never

	RAI NO				RAI YES			
Late PC vs. Early PC	Early Palliative Care N = 28,285 (%)	Late Palliative Care N = 28,285 (%)	Absolute Risk Difference (%) (Early vs Late Palliative Care)	SD	Early Palliative Care N = 2,323 (%)	Late Palliative Care N = 2,323 (%)	Absolute Risk Difference (%) (Early vs Late Palliative Care)	SD
Supportive home care (any one or combination of the following three)	17,552 (62.1)	13,736 (48.6)	13.5	0.27	1,340 (57.7)	656 (28.2)	29.5	0.62
Physician house call in last 30 days	7,833 (27.7)	6,061 (21.4)	6.3	0.15	582 (25.1)	341 (14.7)	10.4	0.26
Palliative homecare nursing at home in last 30 days	16,083 (56.9)	12,320 (43.6)	13.3	0.27	1,213 (52.2)	494 (21.3)	30.9	0.68
Palliative personal support nursing at home in last 30 days	10,745 (38.0)	7,954 (28.1)	9.9	0.21	955 (41.4)	374 (16.1)	25.3	0.58
Never PC vs. Early PC	Early Palliative Care N = 7,953 (%)	Never Palliative Care N = 7,953 (%)	Absolute Risk Difference (%) (Early vs Never Palliative Care)	SD	Early Palliative Care N = 1,263 (%)	Never Palliative Care N = 1,263 (%)	Absolute Risk Difference (%) (Early vs Never Palliative Care)	SD
Supportive home care (any one or combination of the following three)	4,639 (58.3)	0	-	-	672 (53.2)	0	-	-
Physician house call in last 30 days	1,921 (24.2)	0	-	-	277 (21.9)	0	-	-
Palliative homecare nursing at home in last 30 days	4,287 (53.9)	0	-	-	609 (48.2)	0	-	-
Palliative personal support nursing at home in last 30 days	2,983 (37.5)	0	-	-	494 (39.1)	0	-	-

*McNemar's test was significant to <0.0001 for all measures

TRIPOD Checklist: Prediction Model Development

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	3
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	3
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	4
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	4
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	4+5
	5b	Describe eligibility criteria for participants.	4+5
	5c	Give details of treatments received, if relevant.	4+5
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	4+5
	6b	Report any actions to blind assessment of the outcome to be predicted.	4+5
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	4+5
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	4+5
Sample size	8	Explain how the study size was arrived at.	4
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	NA
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	5+6
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	4+5
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	4+5
Risk groups	11	Provide details on how risk groups were created, if done.	4+5
Results			
Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	6, figure1
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	6+7
Model development	14a	Specify the number of participants and outcome events in each analysis.	6+7
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	NA
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	NA
	15b	Explain how to the use the prediction model.	NA
Model performance	16	Report performance measures (with CIs) for the prediction model.	7+8,12, tables 2+3
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	9
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	8-9
Implications	20	Discuss the potential clinical use of the model and implications for future research.	9
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	1
Funding	22	Give the source of funding and the role of the funders for the present study.	1

We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

BMJ Open

End-of-life outcomes with or without early palliative care: A propensity-score matched, population-based cancer cohort study

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Short title/Running head: Early palliative care in a cancer population
W**ord count:** 3137 words; **Abstract:** 265 words

ABSTRACT:

Objectives: To investigate whether cancer decedents who received palliative care early (i.e. >6 months before death) and not-early had different risk of using hospital care and supportive home care in the last month of life.

Design / Setting: We identified a population-based cohort of cancer decedents between 2004 and 2014 in Ontario, Canada using linked administrative data. Analysis occurred between August 2017 to March 2019.

Participants: We propensity-score matched decedents on receiving early or not-early palliative care using billing claims. We created two groups of matched pairs: one that had Resident Assessment Instrument (RAI) home care assessments in the exposure period (Yes-RAI group) and one that did not (No-RAI group) to control for confounders uniquely available in the assessment, such as health instability and pain. The outcomes were the absolute risk difference between matched pairs in receiving hospital care, supportive home care, or hospital death.

Results: In the No-RAI group, we identified 36,238 pairs who received early and not-early palliative care. Those in the early palliative care group vs. not-early group had a lower absolute risk difference of dying in hospital (-10.0%) and receiving hospital care (-10.4%), and a higher absolute risk difference of receiving supportive home care (23.3%). In the Yes-RAI group, we identified 3,586 pairs, where results were similar in magnitude and direction.

Conclusions: Cancer decedents who received palliative care earlier than six months before death compared to those who did not had a lower absolute risk difference of receiving hospital care and dying in hospital, and an increased absolute risk difference of receiving supportive home care in the last month of life.

Strengths and limitations of this study

- This large population-based cohort study of all cancer decedents in Ontario, Canada from 2004-2014 uses consistent exposure and outcome definitions over a long period of time, which provides high external validity in real-world settings.
- The study used propensity scores to match decedents who received palliative care earlier than six months before death compared to those who did not, thereby reducing selection bias among those who receive early palliative care.
- Our study included and controlled for previously unmeasured confounders known to be associated with receipt of early palliative care (i.e. worse pain, ADL dependency, depression, cognitive decline, and health instability) derived from home care assessment data.
- The study matches those who have similar propensity to have received early palliative care, but this may not represent the entire population of cancer decedents.
- The study does not directly measure patient preferences, which is a confounder for use of early palliative care.

INTRODUCTION

Early palliative care is purported to improve quality of life and also avoid unnecessary acute care use, and thus reduce health system costs. Several randomized trials on advanced cancer patients have shown that early palliative care reduced symptoms and some even had survival benefits.[1-3] This evidence led to the oncology clinical practice guideline that supports the early integration of palliative care with standard oncologic care.[4,5] However, the evidence is mixed as to whether it reduces health services utilization outcomes at end-of-life. There are trials that show that resource utilization at end of life is not different from "usual care."

In particular, many of the trials implemented palliative care interventions close to diagnosis in controlled study settings, which is difficult to implement in the real-world. For example, the United States' Medicare Hospice Benefit requires a physician to certify an expected death within six months.[6] Additionally, many observational studies have found positive associations between early palliative care and reduced likelihood to receive aggressive care at end of life (e.g. reduced hospitalizations and hospital deaths).[7-12] However, observational studies are limited by selection bias, namely those who get early palliative care may be different from those who do not (e.g. are sicker or more symptomatic in ways that are unmeasured). This is summarized in a large systematic review on early palliative care interventions, which found mixed evidence of benefits and noted key methodological issues of selection bias, as well as large variation in the definitions of when 'early' began, the interventions themselves, and usual care.[13] Thus the evidence that early palliative care reduces late-life acute care use (particularly when it does not begin at diagnosis) is unclear. This gap has important health resource planning and economic implications.

By examining cancer patients in the universal health system of Ontario, Canada, we are able to address prior limitations, namely standardizing definitions for 'early' palliative care, usual care, and the palliative care intervention. Usual care in Ontario means that cancer patients have access to publicly-subsidized palliative care in the form of: a palliative care outpatient clinic (e.g. multidisciplinary pain and symptom management clinic); palliative home care services by a nurse of personal care worker; or a family doctor providing palliative care via clinic or rarely via home-visit. Generally, these 3 services are independent of one another and

uncoordinated.[14] This contrasts the community-based, multidisciplinary team approach of palliative care delivery found in the United States via home hospice care[6] or in the United Kingdom via Macmillan cancer support program.[15] Although a small minority of patients might have access to a multidisciplinary, specialist palliative care team that makes home visits or a residential hospice, especially if they lived in a major city, this is haphazard and accessed typically in the last weeks of life.[16] If the patients were hospitalized, they could also receive a consult from a palliative care doctor individually or a multidisciplinary team (e.g. admitted to a palliative care unit) in the hospital. Unfortunately, data shows palliative care services are often used very late in the disease trajectory or not at all. For example in Ontario, Canada, palliative care services are used in 50% of all deaths for a median of 30 days before death.[17] In the United States, statistics are very similar, where palliative care via the Medicare Hospice Benefit is used in 45% of all deaths for a median of 17 days before death.[18]

Specifically this study investigated the impact of receiving palliative care early (at least six months before death) vs. not-early on outcomes in the last 30 days of life. We used propensity-score matching to reduce selection bias in observational cohorts around receipt of early palliative care.

METHODS

Study Design and Data Sources

We performed a population-based, retrospective cohort study of all cancer decedents in Ontario, Canada from 2004-2014. We utilized propensity score matching to match decedents having received palliative care early (i.e., between 12 and six months before death) to those who did not (i.e. received palliative care late or not at all). We linked administrative databases housed at ICES (formally known as the Institute for Clinical Evaluative Sciences) including the: Ontario Cancer Registry (cancer diagnosis), Vital Statistics Registry (death date), Discharge Abstract Database (hospitalizations), National Ambulatory Care Reporting System (Emergency Department use), physician billings, Statistics Canada (sociodemographic data like income and rurality), and the Home Care Database, which includes all Resident Assessment Instrument-

Home Care (RAI-HC) assessments. Datasets were linked using unique encoded identifiers and analyzed at ICES.

Study Population

We included decedents who had a cancer diagnosis in the Ontario Cancer Registry and a death caused by cancer as per the provincial Vital Statistics registry. Those whose cancer diagnosis was 6 months or less from death were excluded as they were not eligible for the exposure.

Exposure

In the exposure period (i.e. between 12 and six months before death),[19] access to early palliative care was defined as having received: homecare with an palliative care intent; a physician consult for palliative care in an inpatient admission (including complex continuing care), outpatient clinic, or a home visit setting; or a hospitalization where palliative care was listed as the main reason for admission, as per prior research.[17] Once a patient was identified as having received early palliative care, they remained in the exposed group for analysis.

Outcomes

Outcomes were death in an acute care bed, and the aggregate measures of aggressive care and supportive home care in the last 30 days of life respectively. Aggressive care was defined as one or a combination of ≥1 Emergency Department visit, hospital admission or ICU admission.[20] Supportive home care was defined as one or a combination of physician house call for palliative care, end-of-life homecare nursing or end-of-life personal support at home.[21] Each outcome was handled as a binary variable (Yes/No).

Statistical Analysis

To reduce selection bias for decedents who were exposed to early palliative care, we used propensity score matching to create a similar comparison group of unexposed decedents (not-early). The propensity score is an individual's probability of receiving early palliative care, given the values of their baseline measured covariates. Matching on the propensity score can estimate the effect of the intervention, which is unbiased by differences in the distributions of measured baseline covariates.[22,23] Our methods matches two individuals who have the same

propensity to receive early palliative care in the exposure period, though one got early palliative care and one did not.

A priori we decided to examine the group who received long-stay home care services (i.e., expected to receive at least 60 days of home care) and thus had a RAI-HC assessment in the exposure period separately. Of note, long-stay home care patients either received standard homecare (unexposed) or palliative homecare (exposed) services. This allowed us to control for additional confounders associated with receipt of early palliative care that are uniquely available in the RAI-HC. Therefore, we created two mutually exclusive groups of matched pairs and each pair consists of an exposed and unexposed decedent. One group is called the No-RAI group; the other the Yes-RAI group.

For the No-RAI group, all pairs were hard matched before the exposure period on: age at death, sex, cancer type, cancer stage (where available) and the logit of the propensity score (calipers of width less than or equal to 0.2 of the standard deviation of the logit of the propensity score).[24,25] We estimated the propensity score using a logistic regression model with exposure to early palliative care as the independent variable. The predictor variables in the propensity score regression included: income quintile, rurality, health region, prior hospital utilization in months 24 to 12 before death, Deyo-modified Charlson comorbidity score in months 24 to 12 before death, index year of death, and having had radiation or cancer surgery.[26]

For the Yes-RAI group, we utilize additional data from the RAI-HC, which is a standardized assessment for all long stay home care patients in Ontario, corresponding to the Minimum Data Set in the United States.[27] In addition to matching procedure noted above for the No-RAI group, pairs were hard matched on health instability using the *Changes in Health, End-stage Disease, Signs and Symptoms (CHESS) scale*.[28,29] The following items were also included in the propensity score regression: functional performance and dependency using the ADL Self-performance Hierarchy Scale;[30] depression using the Depression Rating Scale;[31] cognitive impairment using the Cognitive Performance Scale;[32] pain intensity using the Pain Scale;[33] and living with a primary or secondary caregiver (Yes/No).

Because the distributions of covariates were well-balanced and not statistically different after matching the exposed and unexposed patients in both the No-RAI and Yes-RAI groups, we did not need to employ any regression methods for examining the exposure-outcomes relationship; thus for each outcome, we determined the absolute risk difference between the matched exposed and unexposed individuals in both Yes-RAI and No-RAI groups.[34] We used McNemar's test to determine statistical significance of the estimated risk difference.[35] Differences in risk between the exposure and control groups for each outcome were assessed using standardized differences. Standardized differences are more appropriate to use in this population-based study as they are not influenced by sample size (unlike p-values). Analysis was performed using SAS Enterprise Guide, version 7.1 (SAS Institute, Cary, NC).

As a sensitivity analysis, we divided the not-early group—i.e. unexposed group—into late palliative care (i.e., only received palliative care in the last six months of life) and never received palliative care. We conducted a sensitivity analysis to examine early vs. late and early vs. never subgroups separately in an attempt to control for unmeasured patient preferences. The hypotheses were that some patients may refuse palliative care altogether (which would appear in our data as never receiving any palliative care services even near death); and other patients might have been willing to receive palliative care but were offered it late (which would appear in our data as receiving it in the final six months of life). Analyzing the late users to the early users specifically, was an attempt to separate out those patients who might have refused palliative care as per their preference. The study was approved by the Hamilton Integrated Research Ethics Board (#3039). The study is reported using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) framework for observational studies.[36]

Patient and Public Involvement

Patients and the public were not involved this research.

RESULTS

Patients

After excluding those with a cancer diagnosis within 6 months of death (n=84,673), our overall eligible cohort consisted of 144,306 cancer decedents in Ontario between 2004 and

2014, of which 53,959 (37.4%) received early palliative care 12 to six months before death. Eighty-nine percent (n=128,248) of the overall cohort did not have a RAI-HC in the exposure period (No-RAI) and they were matched separately than the 11% (n=16,058) who did have the assessment (Yes-RAI). (Figure 1) Baseline characteristics before propensity score matching are shown in Appendix S1, and those after propensity score matching are shown in Table 1.

In the No-RAI group, we matched 82.6% of patients who received early palliative care for a total of 36,238 matched pairs. After matching, the decedent covariate distributions were nearly identical between the two groups. For instance, average age was 69, 23.5% had lung cancer and 14.2% had stage IV disease. In the No-RAI group, during the exposure period the group received 53,787 palliative care services, of which approximately 40% of services were homecare and 40% were outpatient physician billings. The first initiation of early palliative care was about 300 days before death. In the last 6 months of life, the early group received 91,321 palliative care services (30% home care, 33% physician consults and 24% hospital), whereas the late group received 63,994 palliative care services (25% home care, 35% physician consults and 29% hospital admissions).

In the Yes-RAI group, we matched 59.9% of patients who received regular homecare in the exposure period to those who received palliative homecare services in the exposure period for a total of 3,586 matched pairs. After matching, the decedent covariate distributions were nearly identical between the two groups. For instance, 11.8% had moderate to severe health instability using the CHESS score, 6.8% were fully dependent on their ADLs, and 11.0% had moderate-severe pain. In the Yes-RAI group, during the exposure period the group received 5,468 palliative care services, of which nearly half were homecare services. The first initiation of early palliative care was about 330 days before death. In the last 6 months of life, the early group received 8,484 palliative care services (same distributions as No-RAI group) whereas the late group received 4,664 palliative care services (16% home care, 38% physician consults and 37% hospital admissions).

Aggressive Care

Among matched pairs in the No-RAI group, those who received early palliative care had lower risk difference of the aggressive care outcomes compared to the not-early group. (Table

2) 38.1% of the early palliative care decedents died in hospital, compared to 48.1% of the non-early palliative care group, resulting in a lower absolute risk difference of 10.0%. Similarly, the aggregate measure of aggressive care was lower by 10.4% among early palliative care decedents. The early palliative care decedents have a lower absolute risk difference of an Emergency Department visit (9.7%), hospital admission (10.1%), and ICU admission (4.4%) in the last month of life compared to the not-early group.

Among matched pairs in the Yes-RAI groups, we found similar results in the direction and magnitude of the absolute risk differences favoring early palliative care. Note, McNemar's tests for matched pairs were significant ($p < 0.0001$ for all measures). Further, the sensitivity analyses in the Yes-RAI and No-RAI groups separately, looking at matched pairs of early vs. late palliative care and early vs. never palliative care respectively, showed that the early palliative care group consistently had lower absolute risk differences for all outcomes, in similar magnitudes. (Appendix S2)

Supportive Home Care

Among the matched pairs in the No-RAI group, those who received early palliative care had higher risk of receiving supportive home care outcomes compared to the not-early group. (Table 3) The aggregate measure of supportive home care was higher by 23% among early palliative care decedents vs. not-early decedents. 56.2% of the early palliative care decedents had any end-of-life home care nursing in the last 30 days, compared to 34.0% of the non-early palliative care group, resulting in a lower absolute risk difference of 22.2%. The early palliative care decedents have a higher absolute risk of having a physician house call (10.2%) and an end-of-life personal support worker in the last month of life (16.0%) vs. not-early decedents.

Among the matched pairs in the Yes-RAI groups, we found similar trends in direction, but at larger magnitudes: a 37.8% higher absolute risk difference of having any one of the three supportive home care outcomes. Note, McNemar's tests for matched pairs were significant ($p < 0.0001$ for all measures). Further the sensitivity analyses, examining early vs. late and early vs. never palliative care matched pairs separately, showed that early palliative care consistently had higher absolute risk differences for all outcomes. (Appendix S3)

DISCUSSION

In our population-based cohort of 114,306 cancer decedents, a propensity score matched cohort of those who received palliative care earlier than six months before death compared to those who did not had a: lower absolute risk of dying in hospital by 10-13%, lower absolute risk of an aggressive care outcome in the last month of life by 10%, and higher absolute risk of having a supportive care outcome in the last month of life by 23-38%. While prior randomized trials provided high internal validity within controlled settings, our approach provides high external validity in real-world settings. Bolstering the credibility that early palliative care is beneficial is the consistency of our findings across 2004-2014, which predate the publication of seminal randomized trials;[1-3] and the use of a population-based cancer cohort, meaning the findings were not a result of a particular cancer centre, intervention program, or cancer type.

This study addressed some of the noted gaps in prior research: it uses consistent exposure and outcome definitions over a long period of time and uses a large population-based cohort of all cancer types. Moreover, by using data from the RAI-HC, our study was able to control for previously unmeasured confounders known to be associated with receipt of early palliative care, such as worse pain, ADL dependency, depression, cognitive decline, and health instability. This seeks to address selection bias in prior observational studies where those receiving palliative care might be different (e.g. worse symptoms or have worse health instability) than those who do not. Our results were consistent with and without matching for RAI-HC variables. Moreover in our sensitivity analysis, where we examined early vs. late subgroup separately (where the assumption was that both groups of patients were amendable to receiving palliative care), the findings were consistent with our overall study results, further supporting the benefits of early palliative care.

The results of this study support policies to enable earlier access to end-of-life homecare services and outpatient physician services for palliative care. In particular, policies that prohibit the access of palliative care services unless one forgoes curative treatments or is certified as expected to die within 6 months or less are disincentives to earlier and concurrent access to palliative care. For instance in the United States, the Medicare Hospice Benefit

provides access to community-based hospice care but requires a physician to certify a life expectancy of less than six months and a patient commitment to forgo curative treatment.[37] Besides policies, education is critical because research shows that patient preferences sometimes change over time,[38] and that clinicians play an important role in introducing and initiating palliative care (e.g. Serious Illness Conversations) and helping patients make informed treatment decisions about goals of care for end of life.[39]

Our study has limitations. The propensity score matched design means we are comparing amongst those who are likely to have received early palliative care, but this may not represent the entire population of cancer decedents. We did not directly measure patient, family or provider preferences, which would be useful to control for in future studies. We used administrative data and billing codes to determine access to palliative care, which does not always represent the true intent of care provided, and we did not include billings from long-term care settings. As well, future research should examine outcomes of health system costs, health resource utilization, or patient and caregiver well-being.

In conclusion, across an 11-year population-based, cancer cohort, those who received early palliative care (before six months of death) compared to a matched cohort of those who did not, were more likely to receive supportive home care and less likely to receive hospital care in the last month of life. Our findings suggest that policies and education strategies to support the delivery of early palliative care might reduce the risk of dying in hospital and receiving aggressive care at end-of-life in real-world settings.

Table 1. Demographics of Early vs. Not-Early Palliative Care

	After propensity score matching					
	No-RAI			Yes-RAI		
	Not Early Palliative Care (N = 36,238)	**Early Palliative Care (N = 36,238)**	**SD**	**Not Early Palliative Care (N = 3,586)**	**Early Palliative Care (N = 3,568)**	**SD**
Variables that were Hard Matched	**N (%)**	**N (%)**		**N (%)**	**N (%)**	
Mean age ± Standard Deviation	69.43 ± 12.84	69.36 ± 12.87	0.01	76.63 ± 11.25	76.46 ± 11.19	0.01
Female	17,702 (48.8)	17,702 (48.8)	0.00	1,826 (50.9)	1,826 (50.9)	0.00
Cancer Type at Diagnosis						
Breast	4,126 (11.4)	4,126 (11.4)	0.00	433 (12.1)	433 (12.1)	0.00
Colorectal	5266 (14.5)	5,266 (14.5)	0.00	722 (20.1)	722 (20.1)	0.00
Hematology	2,982 (8.2)	2,982 (8.2)	0.00	479 (13.4)	479 (13.4)	0.00
Lung	8,530 (23.5)	8,530 (23.5)	0.00	548 (15.3)	548 (15.3)	0.00
Prostate	3,053 (8.4)	3,053 (8.4)	0.00	486 (13.6)	486 (13.6)	0.00
Stage at Diagnosis						
Stage III	3,726 (10.3)	3,726 (10.3)	0.00	275 (7.7)	275 (7.7)	0.00
Stage IV	5,151 (14.2)	5,151 (14.2)	0.00	329 (9.2)	329 (9.2)	0.00
Unavailable	24,631 (68.0)	24,631 (68.0)	0.00	2,749 (76.7)	2,749 (76.7)	0.00
CHESS Score (when RAI-HC completed)						
No health instability	-	-	-	921 (25.7)	921 (25.7)	0.00
Low health instability	-	-	-	2,242 (62.5)	2,242 (62.5)	0.00
Moderate health instability	-	-	-	380 (10.6)	380 (10.6)	0.00
Severe health instability	-	-	-	43 (1.2)	43 (1.2)	0.00
Variables within the Propensity Score						
Lowest income quintile	7,058 (19.5)	7,146 (19.7)	0.01	776 (21.6)	790 (22.0)	0.01
Highest income quintile	7,102 (19.6)	7,130 (19.7)	0.00	626 (17.5)	622 (17.3)	0.00
Lives in Rural Community	5,206 (14.4)	5,236 (14.4)	0.00	579 (16.1)	568 (15.8)	0.01
Deyo-Charlson Comorbidity Score (>=1)	12,026 (33.2)	12,540 (34.6)	0.03	1,483 (41.4)	1,426 (39.8)	0.08
Had Radiation since diagnosis	22,337 (61.6)	21,982 (60.7)	0.02	1,894 (52.8)	1,950 (54.4)	0.03
Had Cancer Surgery since diagnosis	16,339 (45.1)	15,701 (43.3)	0.04	1,780 (49.6)	1,716 (47.9)	0.04
Mean hospital days (between 2 and 1 years before death) ± SD	0.82 ± 1.12	0.84 ± 1.17	0.01	0.94 ± 1.21	0.91 ± 1.16	0.03
Disease duration						
0-5 years	28,084 (77.5)	29,115 (80.3)	0.07	2,347 (65.4)	2,515 (70.1)	0.10
6-11 years	4,918 (13.6)	4,581 (12.6)	0.03	656 (18.3)	636 (17.7)	0.01
12-17 years	2,018 (5.6)	1,618 (4.5)	0.05	324 (9.0)	249 (6.9)	0.08
18+ years	1,218 (3.4)	924 (2.5)	0.05	259 (7.2)	186 (5.2)	0.08
InterRAI Scales (When RAI-HC completed)						
Dependent on Activities of Daily Living	-	-	-	241 (6.7)	247 (6.9)	0.01
Minor-major depression	-	-	-	496 (13.8)	429 (10.0)	0.06
Moderate-severe cognitive impairment	-	-	-	373 (10.4)	363 (10.1)	0.01
Moderate-severe pain	-	-	-	391 (10.9)	398 (11.1)	0.01
Caregiver Present at Home	-	-	-	2,279 (63.6)	2,264 (63.1)	0.01

Table 2: Aggressive care measures in decedents with or without a RAI assessment

	NO-RAI				YES-RAI			
	Early Palliative Care N = 36,238 (%)	Not Early Palliative Care N = 36,238 (%)	Absolute Risk Difference (%) (Early vs. Not Early)	SD	Early Palliative Care N = 3,586 (%)	Not Early Palliative Care N = 3,586 (%)	Absolute Risk Difference (%) (Early vs. Not Early)	SD
Death in acute care hospital	13,823 (38.1)	17,434 (48.1)	-10.0	0.21	1,278 (35.6)	1,751 (48.8)	-13.2	0.21
Aggressive care (any one or combination of the following three)	18,822 (51.9)	22,586 (62.3)	-10.4	0.21	1,718 (47.9)	2,089 (58.3)	-10.4	0.21
At least 1 ED visits within last 30 days	15,550 (42.9)	19,075 (52.6)	-9.7	0.21	1,454 (40.5)	1,827 (50.9)	-10.4	0.21
Any hospital admission within last 30 days	16,286 (44.9)	19,918 (55.0)	-10.1	0.25	1,492 (41.6)	1863 (52.0)	-10.4	0.25
Any ICU admission within last 30 days	1,299 (3.6)	2,889 (8.0)	-4.4	0.85	83 (2.3)	274 (7.6)	-5.3	0.85

*McNemar's test was significant to <0.0001 for all measures

Table 3: Supportive home care measures in decedents with or without a RAI assessment

	NO-RAI				YES-RAI			
	Early Palliative Care N = 36,238 (%)	Not Early Palliative Care N = 36,238 (%)	Absolute Risk Difference (%) (Early vs. Not Early)	SD	Early Palliative Care N = 3,586 (%)	Not Early Palliative Care N = 3,586 (%)	Absolute Risk Difference (%) (Early vs. Not Early)	SD
Supportive home care (any one or combination of the following three)	22,191 (61.2)	13,736 (37.9)	23.3	0.39	2,012 (56.1)	656 (18.3)	37.8	0.39
Physician house call in last 30 days	9,754 (26.9)	6,061 (16.7)	10.2	0.86	859 (24.0)	341 (9.5)	14.5	0.86
Palliative homecare nursing at home in last 30 days	20,370 (56.2)	12320 (34.0)	22.2	0.73	1,822 (50.8)	494 (13.8)	37.0	0.73
Palliative personal support at home in last 30 days	13,728 (37.9)	7,954 (21.9)	16.0	0.27	1,449 (40.4)	374 (10.4)	30.0	0.27

*McNemar's test was significant to <0.0001 for all measures

[Title for Figures:]

Figure 1. CONSORT Diagram

Contributors: HS, LB and RS conceived the hypothesis, acquired the data, and designed the analysis plan. UEO performed the analyses. HS wrote the manuscript. All authors (HS, LB, RS, FB, KM, DG, BL, KC, SP, UEO) authors interpreted the data, critically revised the manuscript for important intellectual content, and approved the final manuscript. HS, UEO and RS had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Competing Interests Declaration: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Data Sharing statement: Data may be obtained from a third party and are not publicly available. A data request can be sent to ICES (formerly the Institute for Clinical Evaluative Sciences): https://www.ices.on.ca/About-ICES/ICES-Contacts-and-Locations/contact-form

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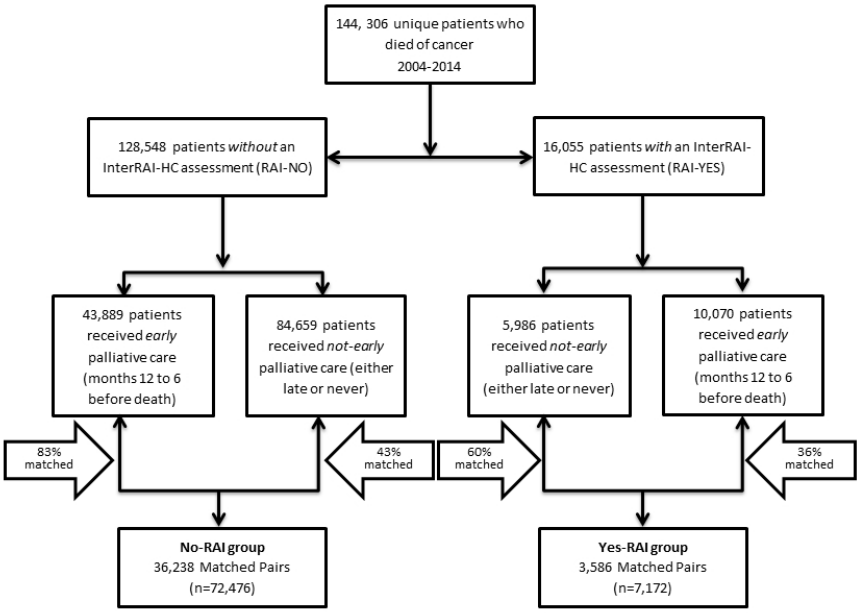
Figure 1. Consort Diagram



254x190mm (96 x 96 DPI)

Appendix S1. Demographics of Early vs. Not-Early before Propensity Score Matching

	Before Propensity Score matching		
	Not Early Palliative Care (N = 90,347)	**Early Palliative Care (N = 53,959)**	**SD**
Variables that were Hard Matched	**N (%)**	**N (%)**	
Mean Age ± Standard Deviation (SD)	72 ± 13	69 ± 14	0.21
Female	41,994 (46.5)	27,113 (50.2)	0.59
Cancer Type at Diagnosis			
Breast	10,539 (11.7)	5,850 (10.8)	0.03
Colorectal	12,051 (13.3)	8,579 (15.9)	0.07
Hematology	10,546 (11.7)	4,150 (7.7)	0.13
Lung	17,444 (19.3)	13,050 (24.2)	0.12
Prostate	9,041 (10.0)	4,384 (8.1)	0.07
Stage at Diagnosis			
Stage III	6,222 (6.9)	5,858 (10.9)	0.14
Stage IV	7,347 (8.1)	10,832 (20.1)	0.35
Unavailable	70,351 (77.9)	32,731 (60.7)	0.38
CHESS Score (when RAI-HC completed)			
No health instability	1,704 (1.9)	2,221 (4.1)	0.13
Low health instability	3,433 (3.8)	5,458 (10.1)	0.25
Moderate health instability	714 (0.8)	1,761 (3.3)	0.18
Severe health instability	135 (0.1)	629 (1.2)	0.13
InterRAI Scales (When RAI-HC completed)			
Dependent on Activities of Daily Living	433 (0.5)	684 (1.3)	0.08
Minor-major depression	809 (0.9)	1,797 (3.3)	0.17
Moderate-severe cognitive impairment	869 (1.0)	764 (1.4)	0.04
Moderate-severe pain	606 (0.7)	1,457 (2.7)	0.16
Caregiver Present at Home	3528 (3.9)	6,970 (12.9)	0.33
Variables within the Propensity Score			
Lowest income quintile	18,686 (20.7)	10,682 (19.8)	0.02
Highest income quintile	17,154 (19.0)	10,492 (19.4)	0.01
Lives in Rural Community	13,597 (15.0)	7,813 (14.5)	0.02
Deyo-Charlson Comorbidity Score (>=1)	13,728 (15.2)	9,553 (17.7)	0.10
Had Radiation since diagnosis	43,298 (47.9)	34,226 (63.4)	0.32

Had Cancer Surgery since diagnosis	37,369 (41.4)	23,917 (44.3)	0.59
Prior hospital utilization (Mean no. of visits in year 2 to 1 before death ± SD)	0.71 ± 1.09	0.96 ± 1.23	0.22
Disease Duration (Diagnosis to death)			
0-5 years	66,375 (73.5)	43,930 (81.4)	0.19
6-11 years	13,907 15.4)	6,467 (12.0)	0.10
12-17 years	5,848 (6.5)	2,249 (4.2)	0.10
18+ years	4,217 (4.7)	1,313 (2.4)	0.12
Health Region			
1	5,302 (5.9)	3,144 (5.8)	0.00
2	7,628 (8.4)	4,408 (8.2)	0.01
3	4,235 (4.7)	3,277 (6.1)	0.06
4	12,721 (14.1)	6,028 (11.2)	0.09
5	3,220 (3.6)	2,413 (4.5)	0.05
6	6,148 (6.8)	3,488 (6.5)	0.01
7	7,621 (8.4)	4,254 (7.9)	0.02
8	9,094 (10.1)	5,355 (9.9)	0.00
9	10,227 (11.3)	6,153 (11.4)	0.00
10	4,911 (5.4)	2,744 (5.1)	0.02
11	7,808 (8.6)	6,117 (11.3)	0.09
12	3,531 (3.9)	2,424 (4.5)	0.03
13	5,795 (6.4)	3,079 (5.7)	0.03
14	2,025 (2.2)	1,040 (1.9)	0.02

Appendix S2. Aggressive Care Measures comparing Early vs. Late and Early vs. Never

	RAI NO				RAI YES			
Late PC vs. Early PC	Early Palliative Care N = 28,285 (%)	Late Palliative Care N = 28,285 (%)	Absolute Risk Difference (%) (Early vs Late Palliative Care)	SD	Early Palliative Care N = 2,323 (%)	Late Palliative Care N = 2,323 (%)	Absolute Risk Difference (%) (Early vs Late Palliative Care)	SD
Death in acute care hospital	10,788 (38.1)	13,109 (46.3)	-8.2	0.17	831 (35.8)	1,152 (49.6)	-13.8	0.28
Aggressive care (any one or combination of the following three)	14,763 (52.2)	17,379 (61.4)	-9.2	0.19	1,135 (48.9)	1,344 (57.9)	-9.0	0.18
At least 1 ED visits within last 30 days	12,232 (43.2)	14,552 (51.4)	-8.2	0.16	949 (40.9)	1,141 (49.1)	-8.2	0.17
Any hospital admission within last 30 days	12,750 (45.1)	15,492 (54.8)	-9.7	0.19	992 (42.7)	1,223 (52.6)	-9.9	0.20
Any ICU admission within last 30 days	1,022 (3.6)	1,379 (4.9)	-1.3	0.06	53 (2.3)	111 (4.8)	-2.5	0.14
Never PC vs. Early PC	Early Palliative Care N = 7,953 (%)	Never Palliative Care N = 7,953 (%)	Absolute Risk Difference (%) (Early vs Never Palliative Care)	SD	Early PC N = 1,263 (%)	Never Palliative Care N = 1,263 (%)	Absolute Risk Difference (%) (Early vs Never Palliative Care)	SD
Death in acute care hospital	3,035 (38.2)	4,325 (54.4)	-16.2	0.33	447 (35.4)	599 (47.4)	-12.0	0.25
Aggressive care (any one or combination of the following three)	4,059 (51.0)	5,207 (65.5)	-14.5	0.30	583 (46.2)	745 (59.0)	-12.8	0.26
At least 1 ED visits within last 30 days	3,318 (41.7)	4,523 (56.9)	-15.2	0.31	505 (40.0)	686 (54.3)	-14.3	0.29
Any hospital admission within last 30 days	3,536 (44.5)	4,426 (55.7)	-11.2	0.23	500 (39.6)	640 (50.7)	-11.1	0.22
Any ICU admission within last 30 days	277 (3.5)	1,510 (19.0)	-15.5	0.51	30 (2.4)	163 (12.9)	-10.5	0.40

*McNemar's test was significant to <0.0001 for all measures

Appendix S3. Supportive Home Care Measures comparing Early vs. Late and Early vs. Never

	RAI NO				RAI YES			
Late PC vs. Early PC	Early Palliative Care N = 28,285 (%)	Late Palliative Care N = 28,285 (%)	Absolute Risk Difference (%) (Early vs Late Palliative Care)	SD	Early Palliative Care N = 2,323 (%)	Late Palliative Care N = 2,323 (%)	Absolute Risk Difference (%) (Early vs Late Palliative Care)	SD
Supportive home care (any one or combination of the following three)	17,552 (62.1)	13,736 (48.6)	13.5	0.27	1,340 (57.7)	656 (28.2)	29.5	0.62
Physician house call in last 30 days	7,833 (27.7)	6,061 (21.4)	6.3	0.15	582 (25.1)	341 (14.7)	10.4	0.26
Palliative homecare nursing at home in last 30 days	16,083 (56.9)	12,320 (43.6)	13.3	0.27	1,213 (52.2)	494 (21.3)	30.9	0.68
Palliative personal support nursing at home in last 30 days	10,745 (38.0)	7,954 (28.1)	9.9	0.21	955 (41.4)	374 (16.1)	25.3	0.58
Never PC vs. Early PC	Early Palliative Care N = 7,953 (%)	Never Palliative Care N = 7,953 (%)	Absolute Risk Difference (%) (Early vs Never Palliative Care)	SD	Early Palliative Care N = 1,263 (%)	Never Palliative Care N = 1,263 (%)	Absolute Risk Difference (%) (Early vs Never Palliative Care)	SD
Supportive home care (any one or combination of the following three)	4,639 (58.3)	0	-	-	672 (53.2)	0	-	-
Physician house call in last 30 days	1,921 (24.2)	0	-	-	277 (21.9)	0	-	-
Palliative homecare nursing at home in last 30 days	4,287 (53.9)	0	-	-	609 (48.2)	0	-	-
Palliative personal support nursing at home in last 30 days	2,983 (37.5)	0	-	-	494 (39.1)	0	-	-

*McNemar's test was significant to <0.0001 for all measures

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

	Item No	Recommendation	Page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6-7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	6-7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
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	6-8
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*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	8
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	9
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	Fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9, Table 1, Table S1
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) Summarise follow-up time (eg, average and total amount)	Table 1
Outcome data	15*	Report numbers of outcome events or summary measures over time	9-10, Table 2,

			Table 3, Table S2 Table S3
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	NA
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9-10, Table S2, Table 3
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10 Table S2 Table S3
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
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
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	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	2

*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.