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Novel Systemic Anticancer Treatments and Health Services Use at the End of Life Among Adults With Cancer

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Abstract

Purpose

Use of chemotherapy at the end of life (EOL) is discouraged, but evidence to guide decisions on the use of novel systemic anticancer treatment (SACT) agents is lacking. We examined trends of use among SACT types and association with health services use at the EOL.

Materials and Methods

We analyzed Canadian Ontario Cancer Registry data for adults diagnosed with solid tumors or hematologic malignancies within 5 years of death who received SACT between March 2015 and March 2021. Receipt of SACT in the last 30 days of life was categorized as chemotherapy alone, chemotherapy and immunotherapy, immunotherapy alone, and targeted therapy alone. Outcomes included high health services use, including multiple (≥2) emergency department (ED) visits, multiple (≥2) hospitalizations, or any (≥1) intensive care unit admission, and hospital deaths. Segmented linear regression estimated monthly trends; multivariable logistic regression estimated adjusted odds ratios (aORs) of outcomes for various SACT types.

Results

Among 68,963 patients, 18,337 (26.6%) received SACT at the EOL. From March 2015 to March 2020, use of SACT at the EOL increased (0.072% per month; $P < .001$), mainly driven by increased use of immunotherapy alone (0.064% per month; $P < .001$). Adjusted odds of high health services use and hospital death were more than two-fold greater among patients receiving SACT at the EOL (vs. none); individual aORs of high health services use and hospital death were 2.20 and 2.72 for chemotherapy alone, 2.36 and 3.10 for chemotherapy and immunotherapy, 1.92 and 2.27 for immunotherapy alone, and 1.75 and 2.37 for targeted therapy alone, respectively.

Conclusion

Use of SACT at the EOL increased significantly over time, driven by increased use of immunotherapy. SACT use at the EOL, regardless of its type, was associated with high health services use and hospital death. Guidelines on the use of SACT at the EOL should include novel cancer treatments.

Introduction

Receipt of chemotherapy at the end of life (EOL) has been associated with outcomes signaling poor-quality EOL care, such as death in a hospital, high health services use at the EOL, and a shorter duration between hospice admission and death.[1-4] Consequently, in 2012, ASCO and the National Quality Forum (NQF) developed an indicator, NQF 0210: "percentage of patients who died from cancer while receiving chemotherapy in the last 14 days of life."[5] The goal of NQF 0210 is to improve the quality of EOL care among patients with cancer by avoiding aggressive EOL treatment.[5] The National Comprehensive Cancer Network endorses NQF 0210, stating that high rates of chemotherapy use in the last 14 days of life should be examined for dosing safety and clinical appropriateness.[6] The Cancer Quality Council of Ontario in Canada has a similar quality metric with a 30-day time window,[7] and the European Society of Medical Oncology also advises against use of chemotherapy in the last month of life.[8]

Context

Key Objective

To examine trends in the use of novel systemic anticancer treatments (SACTs) at the end of life (EOL) and their association with high health services use at the EOL.

Knowledge Generated

In over 68,000 adult patients with cancer, trends of SACT at the EOL increased over time, driven by the use of immunotherapy. Receiving any type of SACT at the EOL, including immunotherapy and targeted therapy, was associated with high health services use at the EOL and hospital death.

Relevance *(J.W. Friedberg)*

Ultimately, the use of SACT at EOL should be guided by precision studies demonstrating reasonable risk/benefit ratios. In the meantime, these sobering results emphasize an urgent need for guidelines around SACT at EOL.*

*Relevance section written by *JCO* Editor-in-Chief Jonathan W. Friedberg, MD.

Two critical knowledge gaps related to the use of systemic anticancer treatment (SACT) at the EOL remain. First, several US studies have reported an increasing use of novel SACT (ie, immunotherapy and targeted therapy) and a concomitant decrease in the use of cytotoxic chemotherapy at the EOL in recent years.[9-12] It is unknown whether these trends also exist in countries with universal public health insurance, such as Canada. Second, and more importantly, little is known about whether the use of novel SACT agents is associated with outcomes representing poor-quality EOL care. Data from small single-center studies[13-15] and a recent abstract reporting on data from the US SEER-Medicare linked database[16] suggest that the use of novel SACT at the EOL may be associated with high rates of health services use compared with patients not receiving SACT at the EOL. If novel SACT is indeed also associated with indicators of poor-quality EOL care compared with not receiving SACT at

the EOL, then this would provide evidence to expand NQF 0210 and similar metrics beyond chemotherapy to novel SACT.

To address these knowledge gaps, we examined trends over time in the receipt of various types of SACT agents at the EOL from 2015 to 2021 in Ontario, Canada, to determine the patterns of use of chemotherapy, immunotherapy, and targeted therapy, alone or in combination. We also examined associations between the receipt of these various therapies at the EOL and high health services use at the EOL, including death in hospital.

Materials and Methods

Study Design and Data Source

We conducted a population-based, retrospective observational cohort study using linked health administrative data from the ICES (formerly the Institute for Clinical Evaluative Sciences), Toronto, ON, Canada (Data Supplement, Table S1, online only). Ontario is Canada's most populous province, with over 13 million adults, and provides health insurance to all residents; the cost of approved intravenous cancer medicines is covered by the government.[17] Oral cancer medicines are funded by the government for people 65 years and older; younger patients access oral medicines via private insurance plans and/or alternative drug coverage programs. Although ICES data sets include intravenous and oral cancer medicines funded by public, private, and alternative programs, there is no indicator to identify the form of coverage.

The University Health Network Research Ethics Board approved the study and waived informed consent. We reported the study using the Strengthening the Reporting of Observational Studies in Epidemiology guidelines (Data Supplement, Table S2).[18]

Study Cohort

The study cohort included Ontario residents 18 years or older who died between March 16, 2015, and March 15, 2021; had been diagnosed within 5 years of death with any cancer except nonmelanoma skin cancer; and had received SACT (Data Supplement, Fig S1). The 5-year window between cancer diagnosis and death was specified to ensure that patients dying in later years of the study period would not be more likely to have survived longer than those dying in earlier years. Because the COVID-19 pandemic occurred during the last year of the study period, we classified the study period into March 16, 2015, to March 15, 2020, and March 16, 2020, to March 15, 2021. We extracted the sociodemographic and clinical information for all patients (Data Supplement, Table S1).

Independent Variables and Outcomes

Receipt of SACT at the EOL was measured as the proportion of patients in the study cohort who received their last dose of SACT within 30 days of death.[4,19] We identified SACT from ICES databases and categorized it as chemotherapy alone, combined chemotherapy and immunotherapy, immunotherapy alone, targeted therapy alone, hormonal therapy alone, combined chemotherapy and targeted therapy, and combined immunotherapy and targeted therapy; monoclonal antibodies were grouped with immunotherapy (Data Supplement, Table S3). Combinations of targeted therapy with chemotherapy (746 [1.1%]) or with immunotherapy (151 [0.2%]) constituted only 1.3% of all SACTs; therefore, we merged these two categories as other combinations.

Consistent with NQF-endorsed indicators developed by Earle et al to describe poor-quality EOL care,[1,2,20] and later used in other studies,[19,21-23] we used outcomes of multiple (≥2) ED visits, multiple (≥2) hospitalizations, and any (≥1) intensive care unit (ICU) admission within 30 days of death. Our primary outcome of high health services use at the EOL was a composite indicator of the proportion of patients in the study cohort who experienced one or more of these three outcomes (Data Supplement, Table S3). We identified deaths in hospital inpatients and emergency department and combined these as hospital deaths according to methods described in a previous study.[24]

Statistical Analysis

Descriptive statistics were used to summarize patient characteristics, health services use, and hospital death as percentages according to the receipt of SACT at the EOL. Given the large data set, we used standardized differences to compare patient characteristics. Unlike *P* values, standardized differences are not influenced by sample size and convey the magnitude of difference between groups (effect size).[25,26]

To examine trends in receipt of SACT at the EOL over time, we performed an interrupted time series (ITS) analysis using segmented linear regression to account for occurrence of the COVID-19 pandemic. The detailed methods of ITS analysis are presented in the Data Supplement (Table S4). We performed ITS analyses for health services use at the EOL and hospital death and stratified all analyses according to the type of SACT at the EOL, reporting results for chemotherapy alone, chemotherapy and immunotherapy, immunotherapy alone, and targeted therapy alone.

We performed univariable and multivariable logistic regression analyses, adjusting for all sociodemographic and clinical variables, to examine the association of SACT at the EOL with health services use at the EOL and with hospital death. Given that the intent of treatment and patterns of care may differ by cancer type and stage, we conducted exploratory subgroup analyses (after first performing tests for interaction) to test whether there were differences in the association between SACT at the EOL and high health services use at the EOL according to the cancer type (hematologic malignancies vs solid tumors) and cancer stage (stage I to III *v* stage IV). We considered the interaction statistically significant if the *P* value for the interaction term was <.05. We also performed a sensitivity analysis restricting the cohort to patients with stage IV solid tumors, who are most likely to have a foreseeably poor prognosis.

For ITS analyses, a *P* value of <.01 was statistically significant to account for multiple comparisons for each outcome. All analyses were performed using R v 4.2.2 (R Foundation for Statistical Computing).

Results

Patient Characteristics According to Receipt of SACT at the EOL

We identified 68,963 patients who died within 5 years of a cancer diagnosis and received SACT between March 16, 2015, and March 15, 2021 (Data Supplement, Fig S1). Overall, 18,337 (26.6% [95% CI, 26.3% to 26.9%]) patients received SACT at the EOL, of whom 11,342 (61.9% [61.2-62.6]) received chemotherapy alone, 1,811 (9.9% [9.4-10.3]) received chemotherapy and immunotherapy, 2,506 (13.7% [13.2-14.2]) received immunotherapy alone, 1,407 (7.7% [7.3-8.1]) received targeted therapy alone, 954 (5.2% [4.9-5.5]) received hormonal therapy alone, and 317 (1.7% [1.5-1.9]) received other combinations. For the entire study period, patients who received SACT (*v* no SACT) at the EOL were more likely to have stage IV cancer at diagnosis, high

comorbidity burden in the last year of life, a hematologic malignancy, and treatment at a nonacademic institution (Table 1). Associations of patient characteristics across SACT types are shown in the Data Supplement (Table S5).

Table 1. Patient Characteristics According to Receipt of SACT at the EOL

Patient Characteristic[a]	All Patients (N = 68,963), No. (%)	Receipt of SACT at the EOL[b]		Standardized Difference
		No SACT (n = 50,626), No. (%)	Any SACT (n = 18,337), No. (%)	
Calendar year of (potential) 30-day EOL treatment				

EXPAND TABLE

NOTE. Bold entries show statistically significant standardized difference.

Abbreviations: EOL, end of life; NA, not applicable; Q, quintile; SACT, systemic anticancer treatment.

a At the index date (date of death): calendar year of (potential) 30-day EOL treatment, age group (years), sex, material deprivation quintile, and place of residence; at diagnosis: cancer stage and cancer site; last year of life: comorbidity burden; at last documented dose of SACT: institution type.

b Any SACT category includes the following: chemotherapy alone, chemotherapy and immunotherapy, immunotherapy alone, targeted therapy alone, hormonal therapy alone, and other combinations (targeted therapy in combination with chemotherapy or immunotherapy).

c Percentages do not account for unknown data.

d Unknown cancer stage includes patients whose disease could not be staged (eg, for leukemia).

Trends in Receipt of SACT at the EOL

From March 16, 2015, to March 15, 2020, the rate (percent receipt) of SACT at the EOL increased by 0.072% per month (95% CI, 0.049 to 0.096; $P < .001$; Fig 1, Data Supplement, Table S6). This increase was mainly driven by an increase of 0.064% per month (0.051-0.078; $P < .001$) in the rate of immunotherapy alone and also by a marginal increase in the rate of chemotherapy and immunotherapy (0.013% per month; 0.003-0.023; $P = .013$). There were no significant changes in these rates during the COVID-19 pandemic.

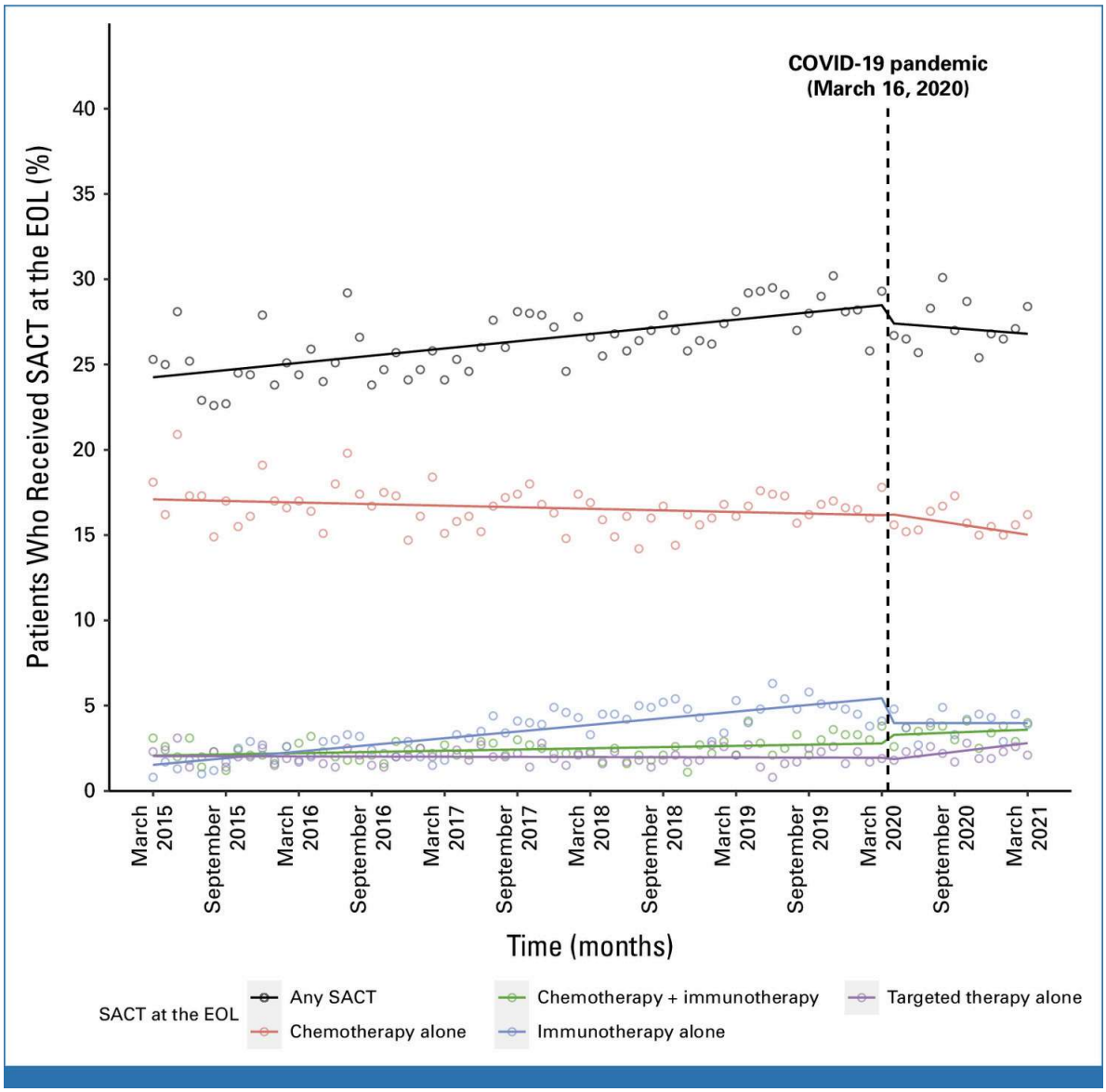


Fig 1. Trends of SACT at the EOL. Solid dots represent the observed rates. Solid lines represent the fitted estimates from interrupted time series analysis without seasonal variation to reveal the underlying trend. SACT, systemic anticancer treatment; EOL, end of life.

Health Services Use at the EOL and Hospital Death According to Receipt of SACT at the EOL

During the entire study period, patients who received SACT (*v* no SACT) at the EOL were significantly more likely to have high health services use (42.4% *v* 24.2%; standardized difference = 0.394), including ≥2 ED visits (23.5% *v* 13.0%; standardized difference = 0.272), ≥2 hospitalizations (16.3% *v* 9.3%; standardized difference = 0.211), ≥1 ICU admission (19.1% *v* 9.7%; standardized difference = 0.271), and more likely to die in a hospital (62.0% *v* 37.1%; standardized difference = 0.514; Table 2). When compared with patients who did not receive SACT at the EOL, the association between SACT at the EOL and health services use at the EOL was present across all SACT subtypes although it was slightly lower among those receiving immunotherapy (38.5% had high health services use) and targeted therapy alone (38.0%) than among those receiving chemotherapy alone (43.6%) and chemotherapy and immunotherapy (45.6%).

Table 2. Health Services Use at the EOL and Hospital Death According to Receipt of SACTs at the EOL

All Patients	Type of SACT at the EOL[a]					
	No SACT at the EOL	Any SACT	Chemotherapy Alone	Chemotherapy and Immunotherapy	Immunotherapy Alone	Targe Thera Alo

EXPAND TABLE

Abbreviations: ED, emergency department; EOL, end of life; ICU, intensive care unit; SACT, systemic anticancer treatment.

a Any SACT category includes the following: chemotherapy alone, chemotherapy and immunotherapy, immunotherapy alone, targeted therapy alone, hormonal therapy alone, and other combinations (targeted therapy in combination with chemotherapy or immunotherapy).

b Standardized difference: No SACT at the EOL versus any SACT (A), versus chemotherapy alone (B), versus chemotherapy and immunotherapy (C), versus immunotherapy alone (D), versus targeted therapy alone (E).

Adjusted Odds of Health Services Use at the EOL and Hospital Death According to Receipt of SACT at the EOL

In the multivariable analysis, receipt of SACT (*v* no SACT) at the EOL was associated with increased odds of high health services use at the EOL (adjusted odds ratio [aOR] = 2.12; 95% CI, 2.04 to 2.20) and hospital death (aOR, 2.61; 95% CI, 2.52 to 2.71; Fig 2, Data Supplement, Table S7). Specifically, the aORs of high health services use at the EOL by SACT types were 2.20 (2.11-2.30) for patients who received chemotherapy alone, 2.36 (2.13-2.61) for patients who received chemotherapy and immunotherapy, 1.92 (1.75-2.09) for patients who received immunotherapy alone, and 1.75 (1.56-1.96) for patients who received targeted therapy alone. The aORs of ≥2 ED visits and ≥2 hospitalizations at the EOL were similar across different SACT types. However, patients who received chemotherapy and immunotherapy had the highest odds of ≥1 ICU admission at the EOL (aOR = 2.63; 2.33-2.96) and hospital death (aOR = 3.10; 2.80-3.44).

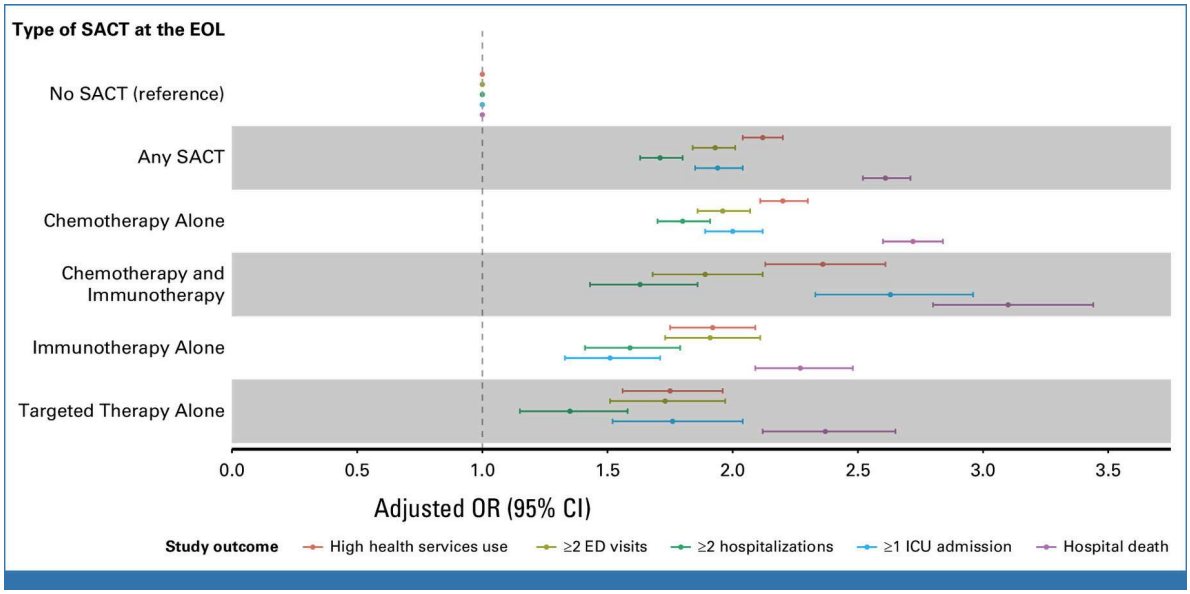


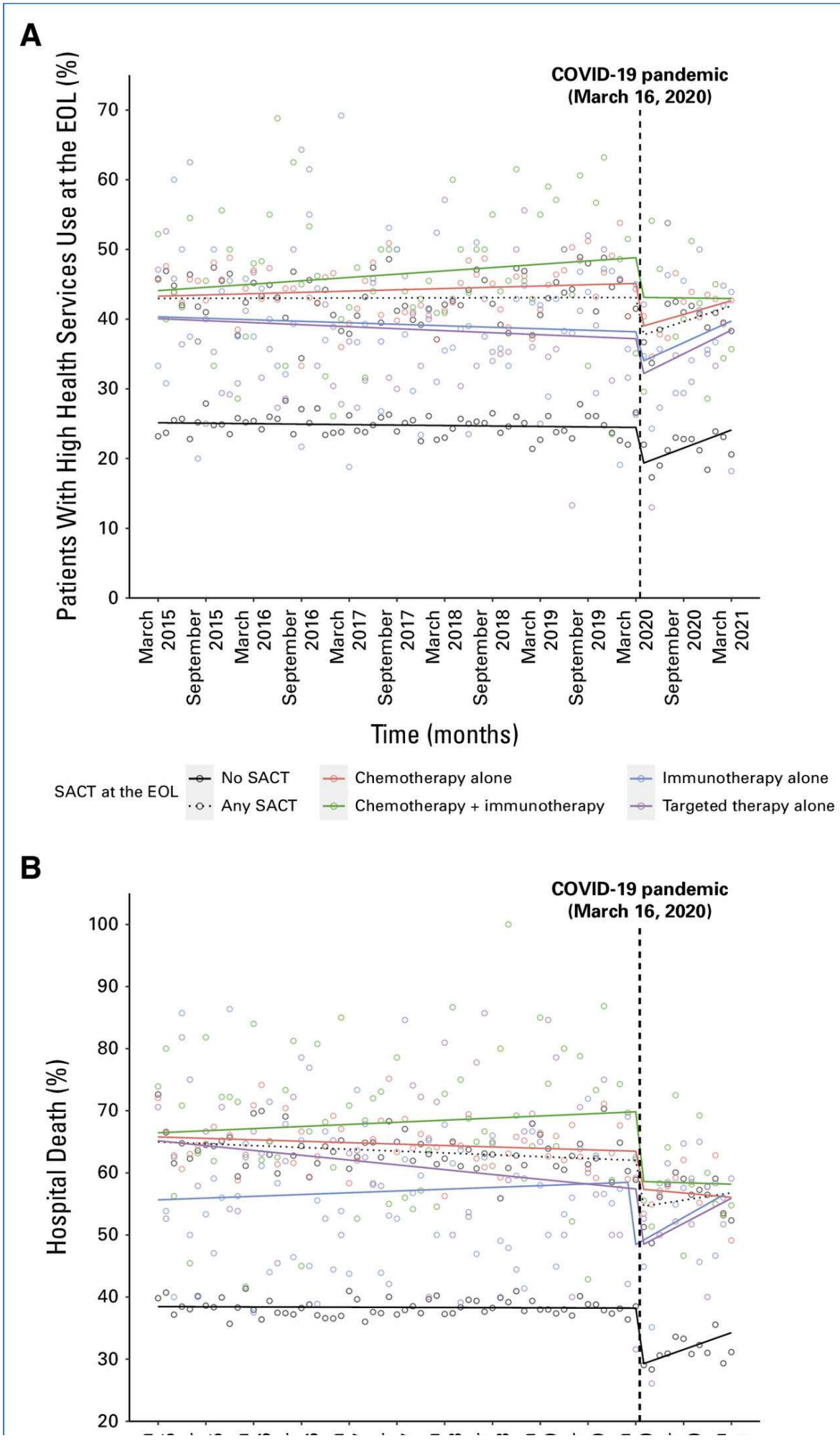
Fig 2. Forest plot of adjusted odds ratio of health services use at the EOL and hospital death by type of SACT at the EOL. ED, emergency department; ICU, intensive care unit; OR, odds ratio; SACT, systemic anticancer treatment; EOL, end of life.

Subgroup and Sensitivity Analyses

The aORs of high health services use according to SACT at the EOL were similar or greater across types of health services use among patients with solid tumors compared with hematologic malignancies (Data Supplement, Table S8) and among patients with stage IV compared with stage I to III cancers (Data Supplement, Table S9). The results of sensitivity analysis limiting the cohort to stage IV solid tumors were similar to the main analysis (Data Supplement, Table S10).

Trends in Health Services Use at the EOL and Hospital Death According to Receipt of SACT at the EOL

Throughout the study period, monthly rates of high health services use at the EOL and of hospital death remained greater among patients who received SACT (*v* no SACT) at the EOL (Fig 3). Among patients who received both chemotherapy and immunotherapy at the EOL, there was a marginal monthly increase of 0.111% (95% CI, 0.006 to 0.216; $P = .042$) in the rate of high health services use and a statistically significant monthly increase of 0.088% (95% CI, 0.037 to 0.139; $P = .001$) in the rate of hospital death (Fig 3, Table 3). There was no significant change for any other type of SACT. During the first month of the pandemic, rates of high health services use and of hospital death decreased, regardless of receipt of SACT at the EOL, followed by a recuperative increase.


A
COVID-19 pandemic
(March 16, 2020)
Patients With High Health Services Use at the EOL (%)
0
10
20
30
40
50
60
70
March 2015
September 2015
March 2016
September 2016
March 2017
September 2017
March 2018
September 2018
March 2019
September 2019
March 2020
September 2020
March 2021
Time (months)
SACT at the EOL
No SACT
Any SACT
Chemotherapy alone
Chemotherapy + immunotherapy
Immunotherapy alone
Targeted therapy alone
B
COVID-19 pandemic
(March 16, 2020)
Hospital Death (%)
20
30
40
50
60
70
80
90
100

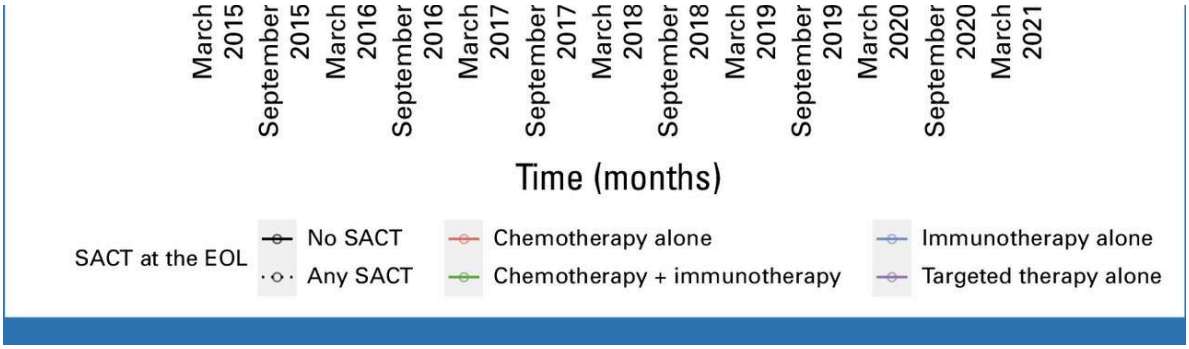


Fig 3. Trends of high health services use at the EOL and hospital death by type of SACT at the EOL. (A) Trend of high health services use by type of SACT at the EOL. (B) Trends of hospital death by type of SACT at the EOL. Solid dots represent the observed rates. Solid lines represent the fitted estimates from interrupted time series analysis without seasonal variation to reveal the underlying trend. SACT, systemic anticancer treatment; EOL, end of life.

Table 3. Segmented Linear Regression Analysis of High Health Services Use at the EOL According to Receipt of SACT at the EOL

Health Services Use at the EOL	Type of SACT at the EOL[a]	Parameter Estimates,[b] % Change Per Month (95% CI); *P*		
		Trend Before the COVID-19 Pandemic (March 16, 2015, to March 15, 2020)	Level Change After the Start of the COVID-19 Pandemic (March 16, 2020, to April 15, 2020)	Trend Change After the Start of the COVID-19 Pandemic (April 16, 2020, to March 15, 2021)

EXPAND TABLE

Abbreviations: ED, emergency department; EOL, end of life; ICU, intensive care unit; SACT, systemic anticancer treatment.

a Any SACT category includes the following: chemotherapy alone, chemotherapy and immunotherapy, immunotherapy alone, targeted therapy alone, hormonal therapy alone, and other combinations (targeted therapy in combination with chemotherapy or immunotherapy).

b The trend before the COVID-19 pandemic estimates the change in mean number of a specific outcome per patient for each month before the pandemic. Level change after the start of the COVID-19 pandemic estimates the level change in mean number of a specific outcome per patient immediately after the start of the COVID-19 pandemic. Trend change after the start of the COVID-19 pandemic estimates the change in the trend in the mean number of a specific outcome per patient after the start of the COVID-19 pandemic, compared with the monthly trend before the pandemic. The sum of trend before the COVID-19 pandemic and trend change after the start of the COVID-19 pandemic will estimate the overall slope during the first year of the pandemic.

c Data point 1 for immunotherapy alone and data point 74 for any SACT, chemotherapy alone, and immunotherapy alone removed from segmented regression analysis to avoid the outlier effect.

Discussion

In this population-based study of over 68,000 adults with cancer, the rate of SACT at the EOL increased significantly between March 2015 and March 2020, driven mainly by the increased receipt of immunotherapy. Receiving SACT at the EOL was associated with high health services use at the EOL and increased hospital deaths, even after accounting for patients' medical and demographic characteristics. This association persisted across all types of SACTs, including immunotherapy and targeted therapy. These findings have important

implications for clinical practice and initiatives to improve the quality of EOL care for patients with advanced cancer.

Unlike a recent US study that reported stable rates of SACT at the EOL at approximately 39% from 2015 to 2019,[9] we observed an increase in our Canadian cohort from approximately 25% in 2015 to almost 29% in 2020, with no significant impact by the COVID-19 pandemic. Receipt of immunotherapy at the EOL increased in both countries, albeit more so in the US cohort; EOL chemotherapy decreased in the United States and remained constant in our study. The smaller (though still three-fold) increase in the receipt of immunotherapy and persistence of chemotherapy at the EOL in Canada may reflect less access to novel SACT, because of a complex and often lengthy public funding process.[27,28] In both countries, however, SACT use at the EOL has persisted or increased, despite the existence of quality criteria discouraging this use in both countries for more than a decade.[5,7]

There may be several reasons for increasing rates of SACT and immunotherapy use at the EOL. Physicians may find it more difficult and emotionally demanding to discuss stopping SACT than to continue treatment, resulting in missed opportunities for EOL discussions.[21,29-32] Physicians may believe that there is little harm in continuing immunotherapy and targeted therapy, with their generally more favorable side effect profiles,[33] or may prescribe them at the EOL as a last resort.[9,11,12] Patients might have a poor understanding of the severity of their disease or choose to pursue treatment for marginal gains.[32] Oncology training programs may also not place sufficient emphasis on communication skills and palliative care.[34,35]

Other factors at practice and health care system levels might have an important impact on SACT use at the EOL. In our study, as well as in a recent US study,[36] patients treated at academic centers were less likely to receive SACT at the EOL than those at nonacademic centers. Although reasons for this association are unclear, academic centers tend to have greater access to supportive care resources, including specialized palliative care. In turn, specialized palliative care has been shown in randomized controlled trials to increase EOL discussions and decrease SACT use at the EOL for patients with solid tumors and hematologic malignancies.[37-39] Although methods of reimbursement have been associated with SACT use in the United States[36,40] and Europe,[41] these incentives may be less prevalent in ON, where oncologists are predominantly paid by salary through the Ministry of Health.[42,43]

Compared with patients receiving no SACT at the EOL, those receiving SACT were more than twice likely to have high health services in the last month of life and to die in a hospital. These associations persisted across SACT types, including in the analysis restricted to patients with stage 4 solid tumors, indicating that NQF 0210 is relevant regardless of the SACT type and should also be applied to patients receiving immunotherapy and targeted therapies. In addition, our findings provide support for extending NQF 0210 from 14 days to 30 days, as is under discussion and is already the case for ESMO and CQCO guidelines.[6-8] Most importantly, our findings support national guidelines recommending that physicians initiate iterative discussions about goals of care as early as possible after the diagnosis of incurable cancer,[44,45] regardless of the type of SACT.

The association between SACT use at the EOL and high health services use at the EOL may stem from the same ethos of pursuing treatment rather than engaging patients in EOL discussions. If SACT is continued or initiated (too) late in the disease course, patients might have multiple hospitalizations because of their advanced disease. Toxicities resulting from SACT use at the EOL may also lead to high health services use; these toxicities

may differ by type of SACT, which may account for the observed differences in patterns of health services use. The increased prevalence of ICU visits among patients receiving chemotherapy and immunotherapy may be due to a relatively greater incidence of all grade and severe adverse events in patients receiving these combination therapies.[46] Although immunotherapies are generally associated with less toxicity than cytotoxic chemotherapy,[33,47] immune-related adverse events may nevertheless lead to repeated ED visits,[48,49] which were similar across all forms of SACT. A recent analysis found that practices with higher rates of SACT at the EOL did not have improved survival compared with those with lower rates.[50] Thus, there does not appear to be any meaningful benefit from SACT for patients with very advanced disease. Clinicians should carefully consider patient prognosis, toxicities, and likelihood of benefit from SACT, including immunotherapy and targeted therapy, and prioritize EOL discussions over commencing or continuing SACT in patients with far advanced cancer.

In some cases, it may be difficult to foresee that patients are approaching the EOL or death may occur suddenly in the context of treatment with curative intent. This is more likely in patients with early-stage disease and for those with hematologic malignancies; of note, the latter group had high use of both SACT and health services at the EOL, as has been shown in smaller studies.[51-53] However, in our study, patients with stage IV disease at diagnosis were more likely to receive SACT at the EOL than those with earlier-stage disease, and associations between SACT at the EOL and high health services use were similar or stronger in patients with stage IV disease (compared with stage I to III) and solid tumors (compared with hematologic malignancies). Moreover, all associations were maintained in the sensitivity analysis limited to patients with stage IV solid tumors. Thus, the association between EOL SACT and high health services use persisted even after excluding patients whose disease might have been unavoidable because of curative treatment.

Our study was unique in being conducted in a country with a single-payer national health system, with data coverage of the entire population of Ontario. Previous studies comparing the United States and Canada demonstrated that ICU admissions near the EOL were higher in the United States and hospital deaths were higher in Canada.[54,55] These differences may in part be due to higher per-day hospital costs and better availability of home-based hospice services in the United States and greater availability of ICU beds in that country. Despite these differences, costs at the EOL are similarly high in both countries[54] and data from a recent abstract using US SEER-Medicare data[16] indicate similar associations between SACT use and health services use at the EOL.

Our study had limitations. Our results demonstrate associations rather than direct causation, and there may be unmeasured confounding. We were unable to account for some potentially confounding factors, such as ethnicity/race and religious/cultural affiliation, because this information is not systematically collected in the public health data of Ontario. In addition, we were unable to assess patient preferences regarding care at the EOL, characteristics of individual prescribing clinicians, or the prevalence and content of EOL discussions. Although ICES data sets capture drug information of patients covered under private health insurance or alternate drug coverage plans, there is no indicator in the data sets to identify such coverage. Although we used the cancer site as a covariate in our analyses, there may be heterogeneity for diseases within these sites, particularly for hematologic malignancies. Despite these limitations, our study presents the most up-to-date information for assessing trends in SACT and health services use at the EOL, using robust population-based

data linked at the individual level for both solid tumors and hematologic malignancies, with full coverage of all adult deaths and health services use for the most populous province in Canada.

In conclusion, in this population-based cohort study, receipt of SACT at the EOL increased over time, particularly for immunotherapy. Receiving any type of SACT at the EOL—including immunotherapy and targeted therapy—was associated with increased rates of health services use at the EOL and hospital death. These findings provide support for the extension of quality criteria for the avoidance of SACT at the EOL beyond chemotherapy to immunotherapy and targeted therapies and for extending the time frame from 14 days to 30 days before death. Our results also challenge the widely held perception that prescribing immunotherapy or targeted therapy at the EOL is a benign intervention. Oncologists prescribing novel SACT at the EOL should bear in mind that its use in patients with advanced cancer is associated with indicators of a poor EOL experience and should instead prioritize timely goals-of-care discussions in this population.

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Data Supplement

- Data Supplement

Disclaimer

The analyses, conclusions, opinions, and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred.

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Authors' Disclosures of Potential Conflicts of Interest

Novel Systemic Anticancer Treatments and Health Services Use at the End of Life Among Adults With Cancer

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