Association Between Frailty and Time Alive and At Home After Cancer Surgery Among Older Adults: A Population-Based Analysis

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ABSTRACT

Background: Although frailty is known to impact short-term postoperative outcomes, its long-term impact is unknown. This study examined the association between frailty and remaining alive and at home after cancer surgery among older adults. **Methods:** Adults aged ≥70 years undergoing cancer resection were included in this population-based retrospective cohort study using linked administrative datasets in Ontario, Canada. The probability of remaining alive and at home in the 5 years after cancer resection was evaluated using Kaplan-Meier methods. Extended Cox regression with time-varying effects examined the association between frailty and remaining alive and at home. **Results:** Of 82,037 patients, 6,443 (7.9%) had preoperative frailty. With median follow-up of 47 months (interquartile range, 23–81 months), patients with frailty had a significantly lower probability of remaining alive and at home 5 years after cancer surgery compared with those without frailty (39.1% [95% CI, 37.8%–40.4%] vs 62.5% [95% CI, 62.1%–63.9%]). After adjusting for age, sex, rural living, material deprivation, immigration status, cancer type, surgical procedure intensity, year of surgery, and receipt of perioperative therapy, frailty remained associated with increased hazards of not remaining alive and at home. This increase was highest 31 to 90 days after surgery (hazard ratio [HR], 2.00 [95% CI, 1.78–2.24]) and remained significantly elevated beyond 1 year after surgery (HR, 1.56 [95% CI, 1.48–1.64]). This pattern was observed across cancer sites, including those requiring low-intensity surgery (breast and melanoma). **Conclusions:** Preoperative frailty was independently associated with a decreased probability of remaining alive and at home after cancer surgery among older adults. This relationship persisted over time for all cancer types beyond short-term mortality and the initial postoperative period. Frailty assessment may be useful for all candidates for cancer surgery, and these data can be used when counseling, selecting, and preparing patients for surgery.

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Background

Older adults have the highest incidence of cancer and represent the fastest growing group of individuals requiring cancer surgery.[1–3] Shared decision-making with older adults, in particular regarding surgery, has inherent complexity due to different risk/benefit balance attributable to more prevalent comorbidities, frailty, decreased life expectancy, and potentially different tumor biology.[4,5] Although improved perioperative care and surgical techniques have created an opportunity for more extensive and invasive procedures to be performed safely for broader groups of older adults, postoperative recovery for older patients can still be long and challenging and can have long-term repercussions for quality of life. Understanding these repercussions is crucial in delivering patient-centered care, because older adults place higher importance on long-term functional independence and quality of life than on short-term risk.[6–11] The ability to maintain independence is essential for older adults. However, there are few data on functional outcomes after cancer surgery, with most studies limited to 6- to 12-month time horizons.[12–19] Lack of data regarding these outcomes impacts the accuracy of prognostication and can result in care that is not aligned with patients' values and wishes.

Frailty is a key consideration in the care of older adults. It represents a state of vulnerability to stressors associated with multisystem decline in physiologic reserve and function.[20] The prevalence of frailty in the general

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See page 1276 for related commentary.

older adult population is 10% to 20%, and up to 40% in older adults with cancer.[21–27] Frailty has been associated with increased risks of falls, disability, hospitalization, and overall mortality in the general population.[20,28–32] In surgical patients, it has been associated with increased risks of complications, mortality, and institutional disposition immediately after surgery.[33–36] Although it can be suspected that frailty similarly impacts long-term functional outcomes, this relationship has not been examined.

The ability to remain in one's own home, a concept known as *aging in place*, is an important patient-centered, long-term outcome that has been used to examine outcomes after critical illnesses as well as orthopedic and vascular surgery.[37–41] In this study, we examined the association between preoperative frailty and remaining alive and at home in the 5 years after cancer surgery in patients aged ≥70 years. Understanding how frailty might influence the likelihood of patients remaining alive and at home after cancer surgery will help guide shared decision-making discussions, preparedness for surgery, and postoperative care for older adults.

Methods

Study Design

We conducted a population-based retrospective cohort study of adults aged ≥70 years with a new diagnosis of solid malignancy between January 1, 2007, and December 31, 2017, undergoing resection of the primary tumor site.[42–44] The study was approved by the Sunnybrook Health Sciences Centre Research Ethics Board, and conducted and reported following the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement.[45]

Patient and Public Involvement

Two caregivers and family members of older adults who underwent major cancer surgery were involved in developing the research question, defining outcome measures, and interpreting the results.

Data Sources

Administrative databases stored at ICES (formerly known as the Institute for Clinical Evaluative Sciences) in Ontario, Canada, were deterministically linked using unique patient identifiers. The Ontario population benefits from universally accessible and publicly funded healthcare through the Ontario Health Insurance Plan (OHIP).[46]

The Ontario Cancer Registry (OCR) includes all patients with a cancer diagnosis in Ontario.[47] The Registered Persons Database contains vital status and demographic data.[48] The Immigration, Refugees and Citizenship Canada Permanent Resident database includes immigration application records.[49] Information on health services received, such as hospitalizations (including surgery), emergency department visits, rehabilitation center admissions, physician visits, prescriptions, and nursing home care, were extracted from the Canadian Institute for Health Information (CIHI) Discharge Abstract Database and Same-Day Surgery Database, National Ambulatory Care Reporting System, Ontario Mental Health Reporting System, National Rehabilitation Reporting System, OHIP Claims Database, Ontario Drug Benefit database, and Continuing Care Reporting System database. Details are provided in supplemental eTable 1, available with this article at JNCCN.org.

Study Cohort

We identified individuals aged ≥70 years with a new diagnosis of oropharyngeal, breast, esophageal, gastrointestinal, colorectal, hepatobiliary, pancreatic, genitourinary, gynecologic, or bronchopulmonary cancer or melanoma between January 1, 2007, and December 31, 2017, using ICD-O-3 codes in the OCR. We included patients undergoing surgery for their cancer from 90 days before to 180 days after their cancer diagnosis, according to the Canadian Classification of Health Interventions codes in the CIHI Discharge Abstract Database (supplemental eTable 2). The time window before surgery ensured the capture of patients diagnosed as a result of surgical pathology.

Patients were excluded if their date of death preceded their date of diagnosis, their date of death was missing, they had a previous cancer diagnosis in the 5 years before the index cancer diagnosis, or had ≥2 cancer diagnoses recorded on the same index diagnosis date. We also excluded individuals living in nursing home facilities before surgery, because they did not have an opportunity to spend time at home.

Exposure

Preoperative frailty was the primary exposure of interest.[50] Frailty was characterized using the Johns Hopkins Adjusted Clinical Groups (ACG) system frailty marker.[51–54] This system contains 32 Aggregated Diagnosis Groups (ADGs).[52,55–57] This frailty marker identifies 12 clusters of frailty-defining diagnoses within important geriatric domains, including nutrition and weight loss, cognition, mobility and falls, and social impairments, to create a dichotomous frailty variable. The Vulnerable Elders Survey and comprehensive geriatric assessment have been used to externally validate this frailty marker, showing moderate correlation with clinical frailty scores, and the marker has previously been used to investigate the impact of frailty on postoperative resource use and outcomes.[52,58,59]

Outcome Measures

The outcome of interest was time spent alive and at home after cancer surgery, operationalized as time to death or admission to a nursing home. Admission to a nursing home in Ontario is funded by provincial health insurance for those

who need 24-hour nursing and personal care, frequent assistance with activities of daily living, or constant supervision, and when the need for such care can no longer be safely met through publicly funded community-based services. Thus, admission to a nursing home is an accurate measure of clinically significant functional decline.

Patients who survived the hospital stay were considered eligible for the outcome, and time to death or admission to a nursing home was computed for all of them. Patients were followed from the date of surgery to the date of death or admission to a nursing home, and censored at the date of last contact or the end-of-study date on December 31, 2018, allowing an opportunity of a minimum of 12 months of follow-up for all patients.

Covariates

Age and sex were obtained from the Registered Persons Database. Rural living was determined using the Rurality Index for Ontario, based on the postal code of the patient's primary residence.[60] Immigration status was defined as a record of immigration in the College of Immigration and Citizenship Consultants (CICC).[49] Socioeconomic status was captured using the Material Deprivation Index, a composite index of the inability of individuals or households to afford consumption goods and activities typical in a society at a given point in time, categorized into quintiles.[61,62] The comorbidity burden was measured using the Johns Hopkins ACG System score, with a cutoff of 10 for high burden, as previously described.[56,57] The surgical procedure intensity was divided into high and low intensity using a standardized classification.[63] Finally, receipt of home care support was captured via the home care database. Covariates are detailed in supplemental eTable 3.

Statistical Analysis

Descriptive statistics evaluated characteristics of the overall cohort and stratified by frailty status. Continuous variables were reported as median with interquartile range (IQR) and categorical variables as absolute number (n) and percent (%). Standardized differences were used to compare groups, with differences of $<10\%$ representing a negligible difference.[64]

The probability of remaining alive and at home, measured as time to death or admission to a nursing home from the date of surgery to 5 years after surgery, was estimated by using Kaplan-Meier methods. The outcome was first described for the whole cohort and compared between patients with and without preoperative frailty using the log-rank test. Multivariable Cox regression models were constructed to estimate the association between preoperative frailty and remaining alive and at home. Relevant demographic and clinical characteristics were identified a priori as potential confounders. Variables were selected based on clinical relevance and existing literature: age (categorical: 75–79, 80–84, ≥85 years), sex, rural residence, material deprivation (quintiles), immigration status, cancer type, surgical procedure intensity, year of surgery, and receipt of perioperative therapy (neoadjuvant, adjuvant). All variables were included to adjust the estimate of the independent association between preoperative frailty and the outcome. Because of the increased risk for early mortality after cancer surgery, an extended Cox model with time-varying effects was used. This method partitions the duration of follow-up into mutually exclusive time intervals, fitting a model that assumes that the hazard function is constant within each interval but not across intervals.[65–67] An interaction term between frailty and time intervals was included to examine the potentially varying association between frailty and remaining alive and at home over time. The time intervals were determined by clinical reasoning and relevance as 0 to 30 days (immediate postoperative period); 31 to 90 days and 91 to 180 days (intermediate postoperative periods); 181 to 360 days (first postoperative year); and 361 days to 5 years (long-term beyond first operative year).[66] The model can then assess potentially changing hazards of being alive and at home over the immediate and long-term postoperative periods. We conducted an a priori subgroup analysis that stratified the results by primary cancer type. Results were reported as hazard ratios (HRs) with 95% confidence intervals. The analyses were conducted for the entire cohort and stratified by cancer type.

Statistical significance was set at $P \leq .05$. All analyses were conducted using SAS Enterprise Guide 7.1 (SAS Institute Inc).

Results

The cohort included 82,037 patients (Figure 1), with a median age of 76 years (IQR, 73–81 years). Overall, 34,044 patients died during the follow-up period, including 2,215 (2.7%) patients who died during their postoperative hospital stay. The median length of stay was 4 days (IQR, 0–8 days) for patients who survived the hospital stay, and 16 days (IQR, 7–32 days) for those who died in the hospital. The majority of patients (90.5%; n=73,713) were discharged home, whereas 6.8% (n=5,544) were discharged to institutions (2.3% inpatient rehabilitation centers, 3.5% nursing home, 1.0% institution not identified) (Figure 2). In-hospital mortality was highest for patients with bronchopulmonary (3.4%) and gastrointestinal cancers (5.3%), and lowest for those with breast cancer (0.1%) and melanoma (0.5%).

Data were missing for rural residency in 0.8% of the cohort and for material deprivation in 0.6%. We therefore used a complete-case analysis approach for the multivariable analysis, whereby cases with missing data were excluded.[68]

Preoperative frailty was present in 6,443 (7.9%) patients. The characteristics of patients with and without frailty are presented in Table 1. Patients with frailty were more likely to be older, have a high comorbidity burden,

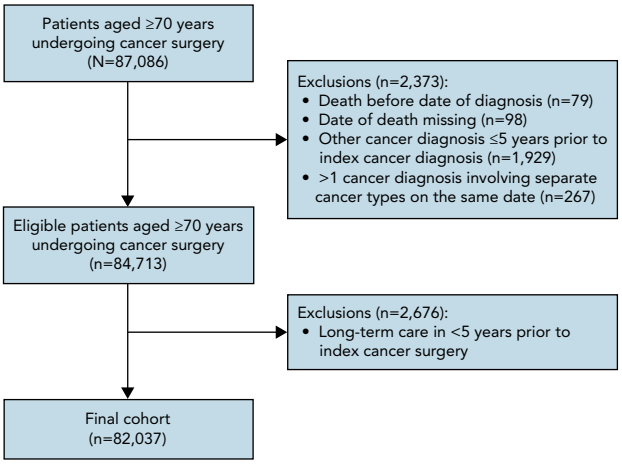


Figure 1. Flowchart of cohort creation.

and be diagnosed with gastrointestinal cancers. Discharge disposition differed for frail and nonfrail patients; frail patients more frequently died in the hospital, were discharged home with home care support, or were discharged to an institution (Figure 2).

Median follow-up was 47 months (IQR, 23–81 months). The 5-year probability of remaining alive and at home after cancer surgery for the entire cohort was 60.7% (95% CI, 60.3%–61.0%). The probability of being alive and at home after cancer surgery was overall lower for patients with preoperative frailty than for those without frailty (unadjusted log-rank $P<.001$) (Figure 3). This finding was consistent throughout the entire study period. At 1 year, the probability of remaining alive and at home was 75.5% (95% CI, 74.4%–76.5%) for patients with frailty compared with 87.6% (95% CI, 87.3%–87.8%) for those without, and at 5 years, it was 39.1% (95% CI, 37.8%–40.4%) compared with 62.5% (95% CI, 62.1%–62.9%), respectively.

After adjusting for potential confounders, frailty was associated with increased hazards of death or nursing home admission after cancer surgery (Figure 4, supplemental eTable 4). The hazards of death or nursing home admission associated with preoperative frailty changed over time. Although the hazards of death or nursing home admission for patients with frailty (vs nonfrail patients) was greatest between 31 and 90 days after surgery (HR, 2.44; 95% CI, 1.78–2.73), preoperative frailty remained associated with 56% increased hazards from 1 to 5 years after surgery (HR, 1.88; 95% CI, 1.80–1.97) (Figure 4).

Subgroup analyses by primary cancer type revealed similar patterns in the association between preoperative frailty and the probability of remaining alive and at home as the main analysis. The probabilities of remaining alive and at home were consistently lower for patients with frailty after surgery across most cancer types, including breast cancer and melanoma (supplemental eFigure 1). The changes in adjusted associations between frailty and remaining alive and at home over time varied by primary cancer type (Figure 5, supplemental eTable 5). There was no association between frailty and the probability of remaining alive and at home between 0 and 30 days for breast, bronchopulmonary, genitourinary, and head and neck cancers, and there also was no association between 31 and 90 days for breast cancer, head

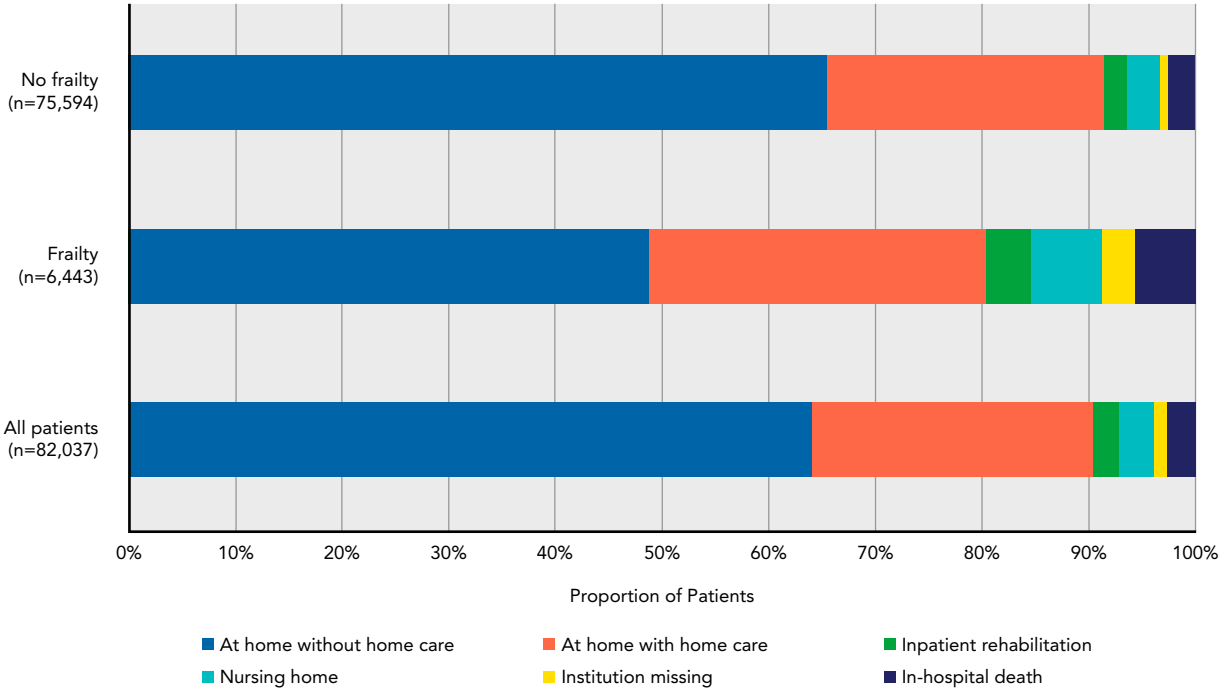


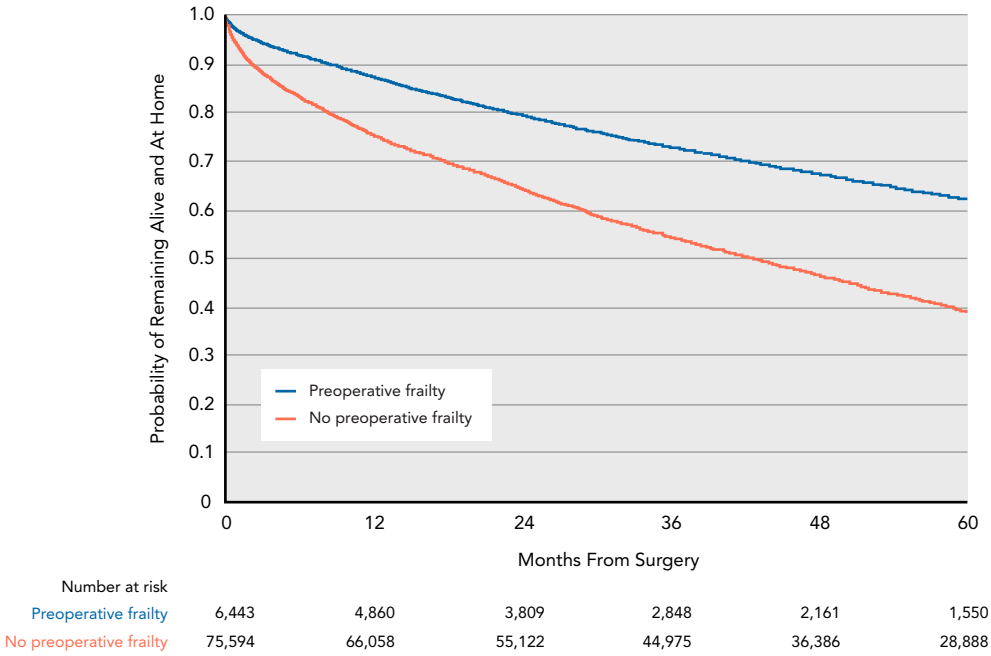
Figure 2. Discharge disposition for the entire cohort and stratified by preoperative frailty.

Table 1. Patient Characteristics, Stratified by Preoperative Frailty Status

Characteristic	All Patients n (%)	No Preoperative Frailty n (%)	Preoperative Frailty n (%)	Standardized Mean Difference[a]
Total, N	82,037	75,594	6,443	
Age group				
70–74 y	31,110 (37.9)	29,786 (39.4)	1,324 (20.5)	42%
75–79 y	23,439 (28.6)	21,815 (28.9)	1,624 (25.2)	8%
80–84 y	16,708 (20.4)	14,927 (19.7)	1,781 (27.6)	19%
≥85 y	10,780 (13.1)	9,066 (12.0)	1,714 (26.6)	38%
Sex				
Female	52,119 (63.5)	47,848 (63.3)	4,271 (66.3)	6%
Male	29,918 (36.5)	27,746 (36.7)	2,172 (33.7)	6%
Rural residence	8,380 (10.2)	7,791 (10.3)	589 (9.1)	4%
High comorbidity burden (ACG ≥10)	26,563 (32.4)	22,480 (29.7)	4,083 (63.4)	72%
Cancer type				
Breast	22,811 (27.8)	21,096 (27.9)	1,715 (26.6)	3%
Bronchopulmonary	7,429 (9.1)	6,902 (9.1)	527 (8.2)	3%
Gastrointestinal	32,036 (39.1)	29,131 (38.5)	2,905 (45.1)	13%
Genitourinary	8,483 (10.3)	8,008 (10.6)	475 (7.4)	11%
Gynecologic	6,658 (8.1)	6,246 (8.3)	412 (6.4)	7%
Head and neck	867 (1.1)	787 (1.0)	80 (1.2)	2%
Melanoma	3,753 (4.6)	3,424 (4.5)	329 (5.1)	3%
High-intensity surgical procedure	48,812 (59.5)	44,836 (59.3)	3,976 (61.7)	5%
Immigrant	4,639 (5.7)	4,367 (5.8)	272 (4.2)	7%
Material Deprivation Index[b] quintile				
First (least deprived)	14,896 (18.2)	13,843 (18.3)	1,053 (16.3)	5%
Second	15,941 (19.4)	14,726 (19.5)	1,215 (18.9)	2%
Third	16,351 (19.9)	15,068 (19.9)	1,283 (19.9)	0%
Fourth	17,662 (21.5)	16,243 (21.5)	1,419 (22.0)	1%
Fifth (most deprived)	16,673 (20.3)	15,249 (20.2)	1,424 (22.1)	5%
Time period of diagnosis				
2007–2011	36,344 (44.3)	33,643 (44.5)	2,701 (41.9)	5%
2012–2017	45,693 (55.7)	41,951 (55.5)	3,742 (58.1)	5%
Cancer stage				
I	19,431 (23.7)	18,060 (23.9)	1,371 (21.3)	6%
II	17,907 (21.8)	16,411 (21.7)	1,496 (23.2)	4%
III	10,912 (13.3)	10,014 (13.2)	898 (13.9)	2%
IV	3,451 (4.2)	3,176 (4.2)	275 (4.3)	0%
Unknown	30,336 (37.0)	27,933 (37.0)	2,403 (37.3)	1%
Neoadjuvant therapy	3,525 (4.3)	3,362 (4.4)	163 (2.5)	10%
Adjuvant therapy	24,423 (29.8)	23,252 (30.8)	1,171 (18.2)	30%

Abbreviation: ACG, Johns Hopkins Adjusted Clinical Group.
[a]Standardized mean difference >10% indicates significant difference.
[b]Composite index of the inability of individuals or households to afford consumption goods and activities typical in a society at a given point in time, categorized into quintiles.[61,62]

and neck cancers, and melanoma. For bronchopulmonary, gastrointestinal, genitourinary, and gynecologic cancers, the association between frailty and the probability of death or nursing home admission was greatest in the first 30 days after surgery. However, there was an independent association between frailty and death or nursing home admission from 1 to 5 years after surgery among patients for all cancer types. For cancer types with fewer patients (such



Number at risk						
Preoperative frailty	6,443	4,860	3,809	2,848	2,161	1,550
No preoperative frailty	75,594	66,058	55,122	44,975	36,386	28,888

Figure 3. Probability of being alive and at home from the time of surgery, stratified by preoperative frailty status for the entire cohort.

as head and neck cancers) and time intervals with fewer events (such as 0–30 days for breast cancer and melanoma), the confidence intervals were wide.

Discussion

In this population-based analysis of older adults undergoing cancer surgery, we compared the probability of remaining alive and at home in the 5 years after surgery for patients with and without preoperative frailty. Although the probability of remaining alive and at home postoperatively was high for all patients, it was significantly lower for those with frailty. The inverse association between frailty and remaining alive and at home was strongest in the first 3 months after surgery

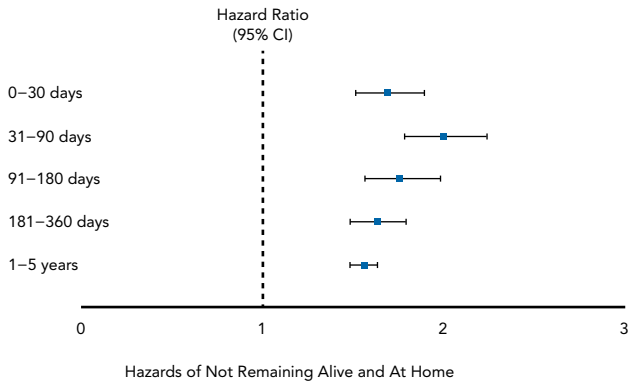


Figure 4. Adjusted hazard ratios of the association between preoperative frailty and remaining alive and at home for the entire cohort (multivariable extended Cox regression with time-varying effects). Adjusted for age (categorical), sex, rural residence, comorbidity burden, material deprivation, immigration status, stage at diagnosis, year of surgery, neoadjuvant therapy, adjuvant therapy, intensity of surgical procedure, and cancer type.

but persisted to 5 years after surgery. Furthermore, this association from years 1 to 5 was consistently observed across all cancer types, including those requiring lower-intensity or ambulatory surgery, such as breast cancer and melanoma.

When discussing cancer surgery with patients, it is important to frame postoperative outcomes from the perspective of what they value most. Being able to remain in one's own home represents a key, long-term, patient-centered outcome for older adults.[38–42,69,70] The data herein help answer patients' questions, such as "How will I be living after surgery?" or "Will I be able to live independently after surgery?," and can be used in clinical practice to provide patient-centered information to support decision-making, counseling on and setting of expectations for life after surgery, and preparation for surgery. This understanding of the ability for patients to remain in their home after cancer surgery is crucial for counseling and preparing older adults for cancer surgery. Because patients who did not undergo surgery in our population would not have been representative of what would happen to patients selected for surgery who decided not to undergo surgery, we did not analyze that group. Even though we could not provide accurate information about what would happen to patients selected and offered surgery should they have declined it, the data herein are important. Telling patients what can be expected after surgery is valuable and fills a need in perioperative counseling. For example, if the long-term outcomes presented are not consistent with a patient's values and wishes, they may elect not to undergo surgery. If they undergo surgery, understanding the expected outcomes is also useful to have appropriate expectations after surgery and to prepare for expected needs.

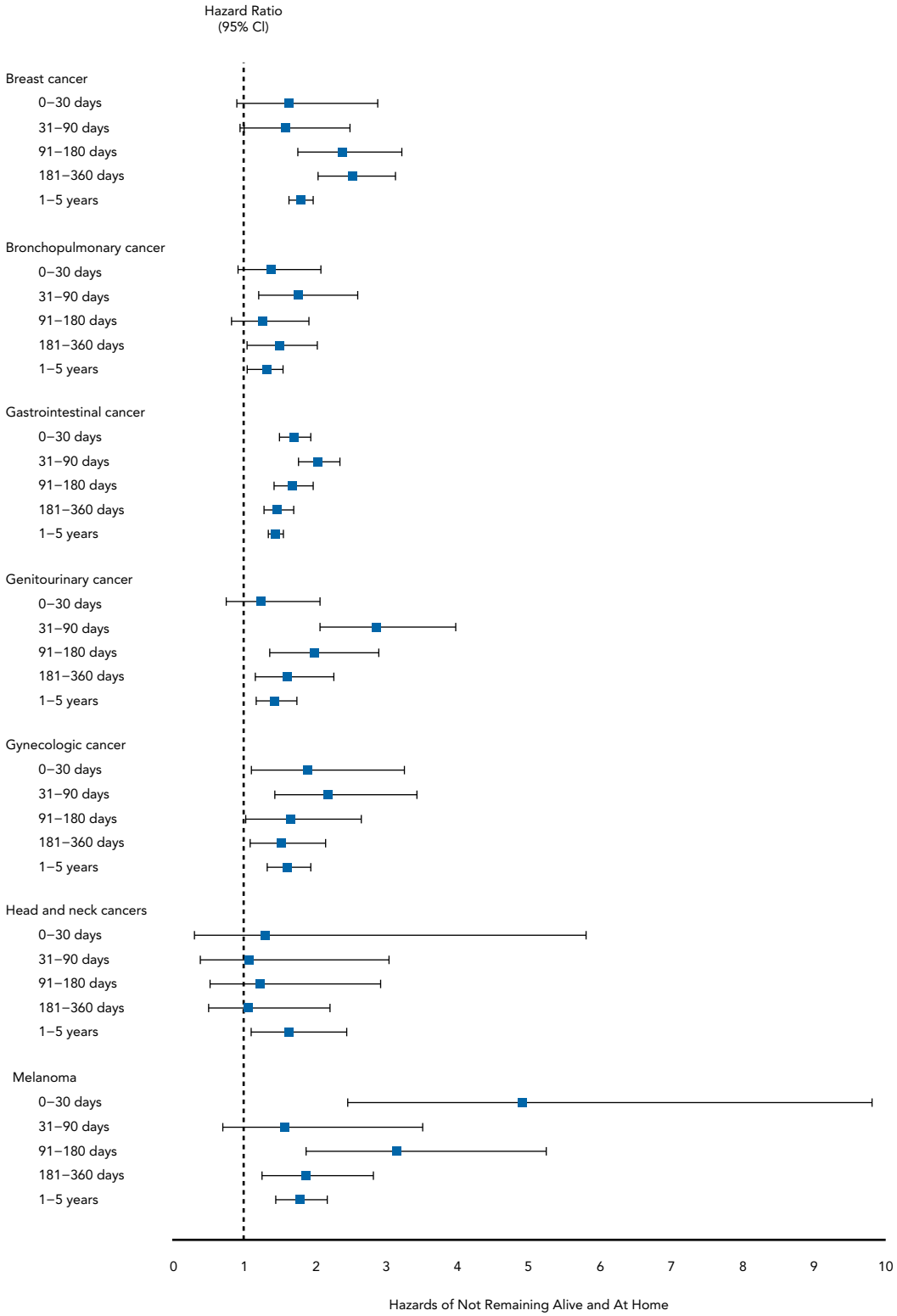


Figure 5. Adjusted hazard ratios of the association between preoperative frailty and remaining alive and at home, stratified by cancer type (multivariable extended Cox regression with time-varying effects).
Adjusted for age (categorical), sex, rural residence, comorbidity burden, material deprivation, immigration status, stage at diagnosis, year of surgery, neoadjuvant therapy, adjuvant therapy, and intensity of surgical procedure.

In surgical populations, frailty has been associated with increased risks of complications, readmission, prolonged length of stay, discharge to care facilities, costs, and mortality.[23,24,27,59] Frailty has also been linked to increased postoperative patient-reported disability and slower recovery.[59,71,72] However, these prior data have largely been limited to a 12-month postoperative time horizon and did not focus specifically on outcomes after cancer surgery.[59,71,72] Although such data are critical in understanding the role of frailty in patients' short-term outcomes, they do not represent the total burden of illness for older adults because of the limited scope and short time horizons. The data from this study regarding patients' ability to remain in their own home in the years after surgery, along with our prior data regarding the need for home care support after cancer,[42,43] provide an overall description for clinicians and patients of life in the years after cancer surgery for older adults.

We identified that patients with frailty had lower probability of remaining alive and at home over the 5 years after cancer surgery compared with those without frailty. Although the magnitude of this difference varied with the time period after surgery, it persisted beyond the first postoperative year. The initial hazards of death or admission to a nursing home were highest in the first 90 days after surgery, consistent with the traditional time window to optimally capture initial mortality after surgery.[73–75] These findings indicate that observed differences in the time spent alive and at home between patients with and without frailty are a result of not only higher short-term postoperative mortality or discharge to nursing homes but also an elevated baseline risk of physiologic and functional decline for patients with frailty. The observations were consistent across all surgical procedures, including lower-stress surgery, such as for breast cancer and melanoma. These findings complement prior data regarding higher morbidity and mortality in older adults with frailty undergoing both high- and low-intensity emergency and elective noncardiac surgery.[34–37,76] Our findings highlight the importance of assessing frailty in the preoperative period for all older adults considered for cancer surgery, regardless of the invasiveness of the procedure. Various frailty instruments that can be used at the point of care for screening are available and have been shown to be accurate, feasible, and easily integrated in routine clinical practice and workflow.[77–80]

Of note, the differences in long-term outcomes between patients with and without frailty should not lead to the conclusion that surgery is not indicated or is not worth the risk in the presence of frailty. Rather, acknowledgment of frailty-specific risks should allow an individualized, patient-centered discussion with patients to determine whether surgery is indicated and desired. To facilitate such discussions, validated prognostication tools to predict individualized probabilities of being alive and at home in the years after surgery should be the focus of future research. Such instruments would complement existing prognostication tools regarding short-term outcomes and would facilitate personalized counseling, decision-making, preparation for surgery, and postoperative monitoring.[81] Furthermore, preoperative interventions to mitigate the effect of frailty on postoperative outcomes are emerging, such as prehabilitation, and can be used if patients are assessed and identified.[82,83]

Our results should be interpreted with consideration of their limitations. The data used were not collected specifically for the purposes of the research question and were analyzed retrospectively. Some data were lacking, such that we could not account for performance status (such as ECOG), cognitive function, and burden of cancer. There are also risks of misclassification using administrative health datasets. For example, the tool used to measure frailty is based on frailty-defining diagnoses; although it has been externally validated against clinical frailty scores, its correlation with such scores was moderate.[52,58,59] This is an issue shared with other administrative data algorithms for identifying frailty.[84] Our frailty exposure is also a dichotomous variable that does not distinguish between different levels of frailty. In particular, those with the greatest degree of frailty may not have been offered surgery or may have declined surgery. Thus, the results are generalizable only to older adults who are selected for and offered cancer surgery. As such, it is important that our results be interpreted in the context of patients selected for cancer surgery. For instance, only 8% of our cohort had preoperative frailty compared with 10% to 20% in the general older adult population and up to 40% in older adults diagnosed with cancer, pointing toward the expected selection bias for cancer surgery.[21–27]

Overall, we acknowledge a risk of misclassification with our datasets and frailty measure; this would have led to underestimating the prevalence of frailty and underestimates of the risk of remaining alive and at home. We also examined outcomes after surgery over a prolonged time horizon of 5 years, focusing on the association between frailty and long-term outcomes after surgery. We did not aim to determine whether the differences in outcomes between patients with and without frailty were a result of cancer surgery. The goal of the study was rather to provide a real-life picture of the natural postoperative history of older adults after cancer surgery and how this differs based on preoperative frailty. Moreover, because comparisons with older adults without cancer, older adults with cancer not having surgery, or younger patients with cancer undergoing surgery bear selection bias and are not informative for decision-making in the individual older adult selected for cancer surgery, these analyses were not undertaken. Nevertheless, the population-based design of this study allowed a detailed real-world evaluation of older adults undergoing cancer surgery with data available across the entire continuum of care. We used high-quality data to create the cohort, define the exposure, and measure outcomes. We conducted this study with a population within a

universal healthcare system in which insurance status does not confound access to nursing home admission. Furthermore, input from patient and family advisors ensured the clinical relevance and usefulness of the results.

Conclusions

Preoperative frailty was associated with a reduced probability of older adults remaining alive and living in their own home in the 5 years after cancer surgery. The impact of preoperative frailty on a patient's likelihood of remaining alive and at home persisted beyond the effect of short-term postoperative mortality and discharge disposition. Moreover, frailty was associated with reduced probability of being alive and at home for all cancer types, including those requiring lower-intensity surgery. This information highlights the need for surgeons to routinely screen and assess older adults for frailty before cancer surgeries and to use frailty-specific probabilities of outcomes when counseling, selecting, and preparing patients for surgery.

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Supplemental online content for:

Association Between Frailty and Time Alive and At Home After Cancer Surgery Among Older Adults: A Population-Based Analysis

Julie Hallet, MD, MSc; Bourke Tillman, MD; Jesse Zuckerman, MDCM; Matthew P. Guttman, MD, PhD; Tyler Chesney, MD, MSc; Alyson L. Mahar, PhD; Wing C. Chan, MPH; Natalie Coburn, MD, MPH; and Barbara Haas, MD, PhD

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eFigure 1: Probability of Remaining Alive and At Home From the Time of Surgery

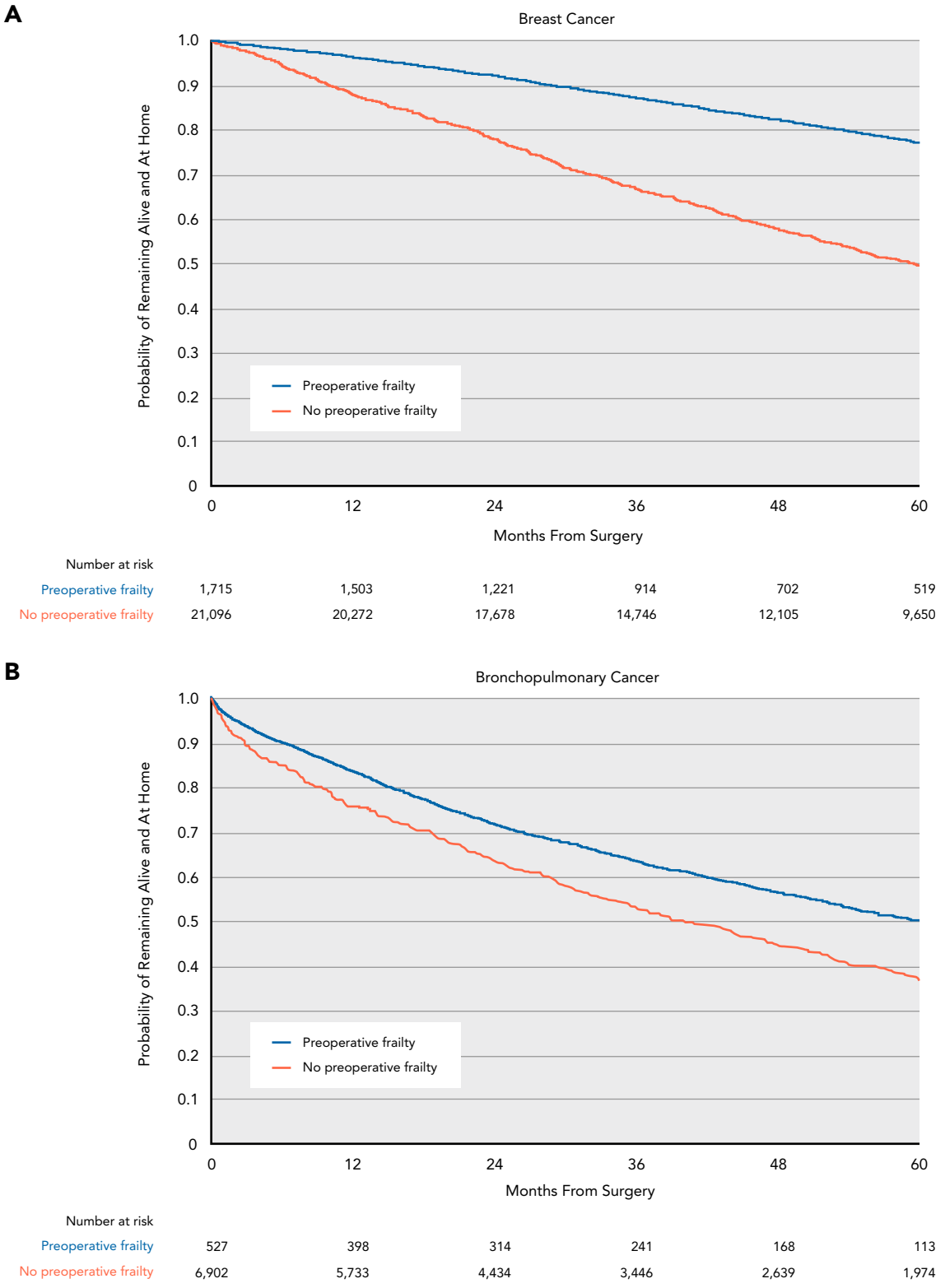
eTable 1: Data Sources

eTable 2: Strategy for Cohort Creation

eTable 3: Definition of Covariates

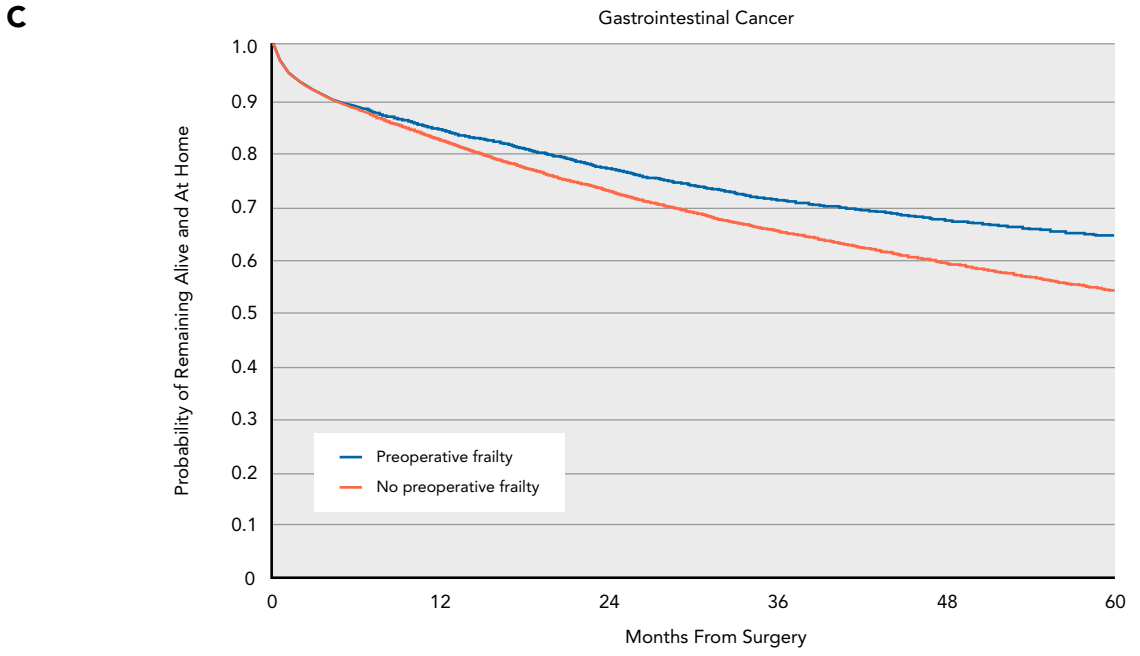
eTable 4: Unadjusted Association Between Preoperative Frailty and Remaining Alive and At Home

eTable 5: Adjusted HRs Showing Effect of Preoperative Frailty on Hazards of Remaining Alive and At Home After Cancer Surgery

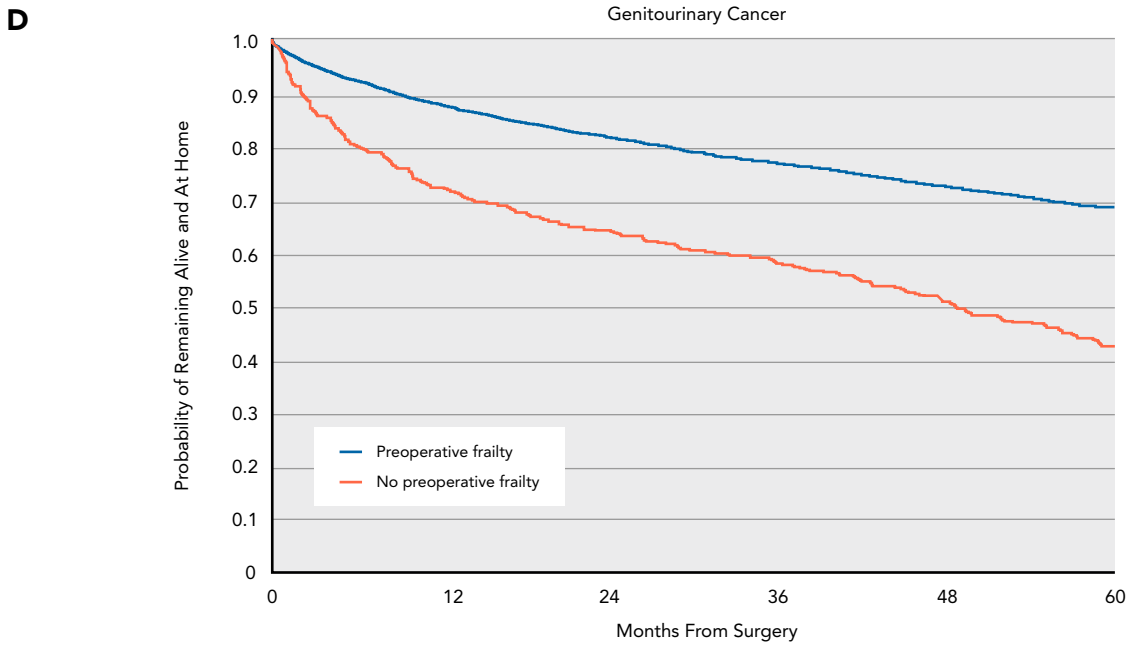


eFigure 1. Probability of remaining alive and at home from the time of surgery for **(A)** breast and **(B)** bronchopulmonary cancers.

(*continued on next page*)



Number at risk						
Preoperative frailty	2,905	1,978	1,525	1,141	886	632
No preoperative frailty	29,131	23,754	19,466	15,735	12,680	10,051

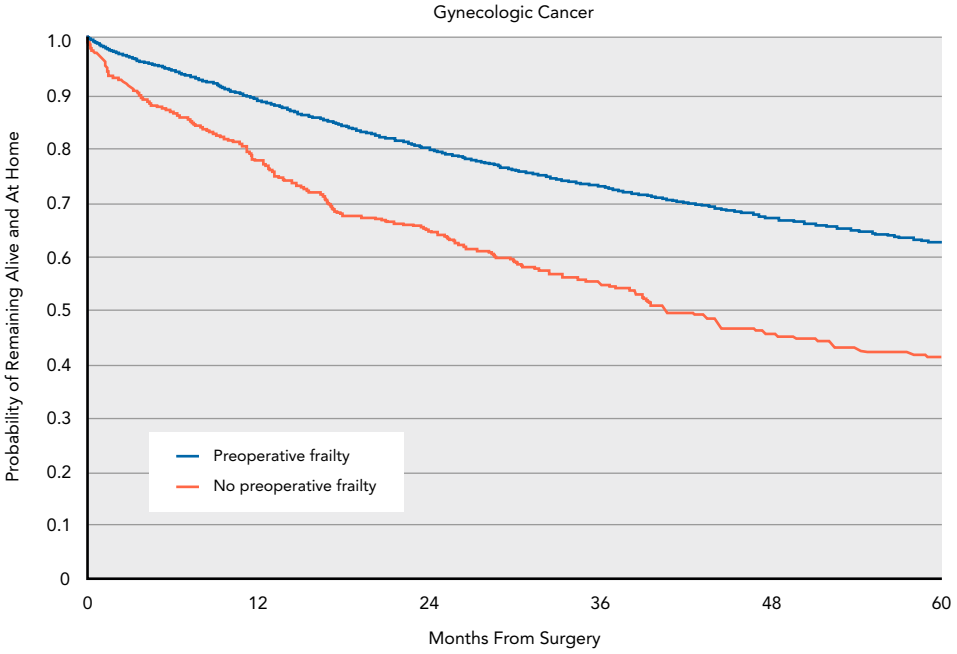


Number at risk						
Preoperative frailty	475	344	272	216	161	113
No preoperative frailty	8,008	7,008	5,962	5,008	4,137	3,369

eFigure 1 (cont.). Probability of remaining alive and at home from the time of surgery for **(C)** gastrointestinal and **(D)** genitourinary cancers.

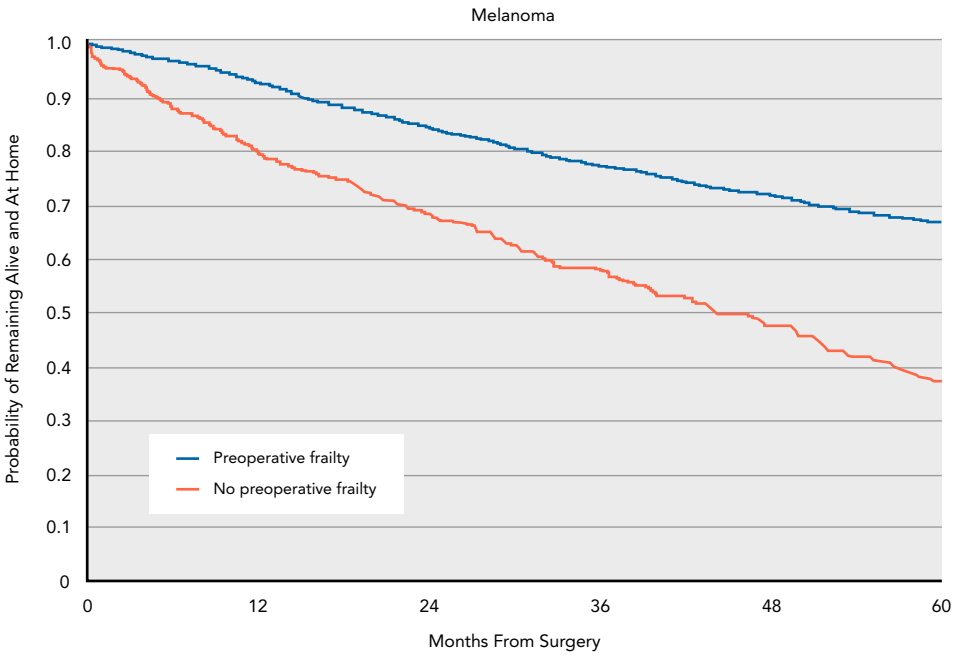
(continued on next page)

E



Number at risk						
Preoperative frailty	412	318	234	161	118	90
No preoperative frailty	6,246	5,489	4,489	3,579	2,856	2,314

F

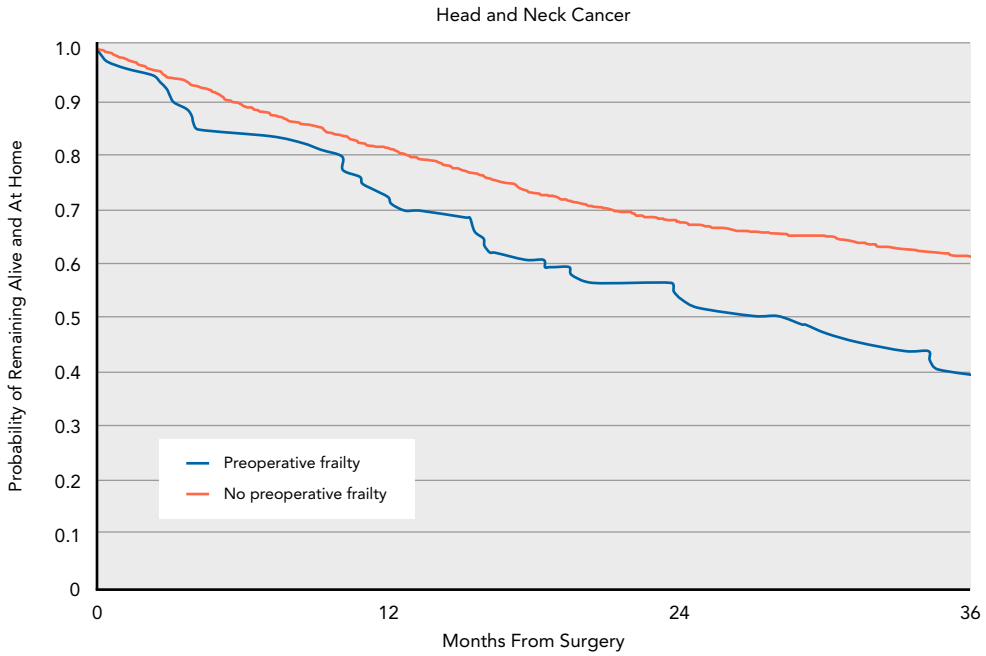


Number at risk						
Preoperative frailty	329	260	207	151	108	73
No preoperative frailty	3,424	3,161	2,610	2,060	1,659	1,292

eFigure 1 (cont.). Probability of remaining alive and at home from the time of surgery for **(E)** gynecologic cancer and **(F)** melanoma.

(*continued on next page*)

G



Number at risk				
Preoperative frailty	80	59	36	24
No preoperative frailty	787	640	483	401

eFigure 1 (cont.). Probability of remaining alive and at home from the time of surgery for **(G)** head and neck cancers. Data for head and neck cancers are reported up to 36 months due to small numbers at risk beyond that time point.

eTable 1. Data Sources

Database	Description
Ontario Cancer Registry (OCR)	The OCR is a passive, provincial registry of all incident cancer diagnoses in Ontario. It includes 96% of cancer diagnoses in the province. Information included in the registry: cancer topography and morphology/histology, and details of diagnosis (eg, types of contributing information to the diagnosis, dates).
Activity Level Reporting (ALR) of Cancer Care Ontario	Cancer Care Ontario maintains a database of cancer-specific services, including consultations, chemotherapy, and radiotherapy, provided by regional cancer centers in the province. Because all radiotherapy is delivered at regional cancer centers, this database is a complete source for this information. However, because not all patients with cancer who receive surgery or chemotherapy visit a regional cancer center, this database cannot be used as a population data source for those treatments.
Registered Persons Database (RPDB)	The RPDB is an ICES database derived from all administrative data sources and provides demographic data, including age, patient residence, vital status, date of last contact with the healthcare system, and Ontario Health Insurance Plan eligibility.
Ontario Office of the Registrar General (ORG)	The ORG contains gold standard vital status data for all Ontarians. According to the Vital Statistics Act, it is mandatory to register all deaths occurring in the province.
Ontario Marginalization Index (ON-Marg)	ON-Marg is a specialized database using census data to profile relative area-level marginalization dependency, deprivation, ethnic concentration, and instability at various geographic levels in Ontario.
Ontario Health Insurance Plan (OHIP)	The OHIP database contains all physician billing data, including information on diagnoses as well as services provided, such as receipt of surgery, chemotherapy, and radiotherapy.
National Ambulatory Care Reporting System (NACRS)	The NACRS collects data elements describing emergency health services provided by emergency departments in Ontario, including diagnoses, procedures, and administrative information such as wait times.
Ontario Drug Benefit (ODB) database	The ODB database contains all information for prescription drugs dispensed by community pharmacies and long-term care/nursing facilities. It covers all seniors (age ≥65 y) and individuals on social assistance for all prescriptions listed on the provincial formulary.
New Drug Funding Program (NDFP)	The NDFP contains information for high-cost drugs for all ages, including new and often expensive systemic therapies.
Assistive Devices Program (ADP)	The ADP captures amounts reimbursed to individuals based on claims for medical equipment (eg, walker, insulin pump).
Home Care Data (HCD)	The HCD includes information on home care services provided by Ontario's Community Care Access Centres (CCACs) established by the Ministry of Health to provide access to government-funded home and community services. It captures all information on services provided by or coordinated by CCACs, including type of services, service dates, and functional assessments.
Continuing Care Reporting System (CCRS)	The CCRS contains information on individuals receiving facility-based continuing care, including medical long-term care, rehabilitation, geriatric assessment, respite care, palliative care, and nursing home care.
Immigration, Refugees and Citizenship Canada Permanent Resident Database (IRCC-PD)	The IRCC-PD includes information on immigration, permanent residence, and citizenship since 1985.

eTable 2. Strategy for Cohort Creation

Cancer Site	Subtype	ICD-O-3 Code	Resection Codes (CIHI CCI Codes)
Breast		C50.0–C50.9	**Excision partial:** 1YM87^^, 1YM88^^ (with reconstruction) **Mastectomy:** 1YM89^^, 1YM90^^ (with reconstruction), 1YM91^^ (radical), 1YM92^^ (radical with reconstruction)
Melanoma		C44.2–C44.9	**Head and neck:** 1YF87^^, 1YG87^^ **Trunk and abdomen:** 1YS87^^ **Extremities:** 1YR87^^ (axilla), 1YT87^^ (arm), 1YU87^^ (hand), 1YV87^^ (leg), 1YW87^^ (foot) **Other:** 1YZ87^^ (NEC)
Gastrointestinal	Esophageal	C15.0–C15.9	1NA87^^, 1NA88^^, 1NA89^^, 1NA90^^, 1NA91^^, 1NA92^^ *Except: 1NA87BA^^, 1NA87DA^^, 1NA87LA^^*
	Gastric	C16.0–C16.9	1NF87^^, 1NF89^^, 1NF90^^, 1NF91^^, 1NF92^^ *Except: 1NF87BA^^, 1NF87DA^^, 1NF87LA^^*
	Hepato-pancreaticobiliary	**Liver:** C22.0, C22.1 **Biliary:** C23.9, C24.0, C24.1, C24.8, C24.9 **Pancreas:** C25.0–C25.9	**Liver:** 1OA87^^ **Bile ducts:** 1OE87^^, 1OE89^^ *Except: 1OE87BA^^, 1OE89BA^^* **Pancreas:** 1OJ87^^ (distal), 1OJ89^^ (distal), 1OK87^^ (Whipple), 1OK89^^ (Whipple), 1OK91^^ (Whipple)
	Colorectal and enteric	**Small bowel:** C17.0–C17.9 **Colon:** C18.0–C18.9 **Rectum:** C19.9, C20.9	**Small bowel:** 1NK87^^ *Except: 1NK87BA^^, 1NK87DA^^, 1NK87LA^^* **Colon:** 1NM87^^, 1NM89^^, 1NM91^^ *Except: 1NM87BA^^, 1NM87DA^^, 1NM87LA^^* **Rectum:** 1NQ87^^, 1NQ89^^ *Except: 1NQ87BA^^, 1NQ87DA^^, 1NQ87LA^^*
Genitourinary (excluding penis, seminal vesicle, urethra)	Kidney and ureter	C64.9, C65.9, C66.9	**Kidney:** 1PC87^^, 1PC89^^, 1PC91^^, 1PE87^^, 1PE89^^, 1PE91^^ **Ureter:** 1PG87^^, 1PG89^^ *Except: 1PG87BA^^, 1PG89BA^^*
	Bladder	C67.0–C67.9	1PL87^^, 1PM87^^, 1PM89^^, 1PM90^^, 1PM91^^, 1PM92^^ *Except: 1PL87BA^^, 1PL89BA^^, 1PM87BA^^, 1PM89BA^^*
	Prostate	C61.9	1QT87^^, 1QT91^^ *Except: 1QT87BA^^*
	Adrenal	C74.0, C74.1, C74.9	1PB87^^, 1PB89^^ *Except: 1PB87DA^^, 1PB89DA^^*
Gynecologic (excluding vulva)		**Vagina:** C52.9 **Cervix:** C53.0, C53.1, C53.8, C53.9 **Uterus:** C54.0, C54.1, C54.2, C54.3, C54.8, C54.9, C55.9 **Ovaries:** C56.9, C57.0, C57.1, C57.2, C57.3, C57.4 **Others:** C57.7, C57.8, C57.9	**Ovary and fallopian:** 1RB87^^, 1RB89^^, 1RF87^^, 1RF89^^ **Uterus:** 1RM87^^, 1RM89^^, 1RM91^^ *Except: 1RM87BA^^, 1RM89^^* **Cervix:** 1RN87^^, 1RN89^^, 1RN91^^ *Except: 1RN87CR^^, 1RN89CR^^* **Vagina:** 1RS87^^, 1RS89^^ *Except: 1RS87AA^^, 1RS89CR^^*
Bronchopulmonary		C30.0–C34.9, C38.1–C39.9	**Lobectomy:** 1GR87^^, 1GR89^^, 1GR91^^, 1GT87^^ **Pneumonectomy:** 1GT89^^, 1GT91^^
Oropharyngeal		C00.0–C14.8, C76.0	1ED87^^, 1ED91^^, 1FJ87^^, 1FX87^^

Abbreviations: CCI, Canadian Classification of Health Interventions; CIHI, Canadian Institute for Health Information.

eTable 3. Definition of Covariates

Variable	Definition	Source	Type	Analysis Format
Age	Year of age at diagnosis	OCR	Categorical	70–74 y 75–79 y 80–84 y ≥85 y
Sex	Sex	OCR RPDB	Dichotomous	Male/Female
Material deprivation	Measure of the inability of individuals or households to afford goods or activities typical in a society at a given time[a]	Canadian Census RPDB ON-Marg	Categorical	First (least deprived) Second Third Fourth Fifth (most deprived)
Rural residence	Determined with postal code of residence as per national census definition of a community with <10,000 people[b]	RPDB	Dichotomous	Urban/rural
Immigration status	Immigrant defined as permanent residence granted or citizenship in 1985 or later[c]	IRCC-PD	Dichotomous	Immigrant Nonimmigrant (long-standing resident)
Year of diagnosis	Year of cancer diagnosis date	OCR	Ordinal	2007, 2008, 2009, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017
Comorbidity burden	Measured using the Johns Hopkins Adjusted Clinical Groups system score based on health service use with a 24-month look-back window before the date of cancer diagnosis whereby the 32 Aggregated Diagnosis Groups (ADGs) are summed to create a total score[d,e]	CIHI-DAD CIHI-SDS OHIP	Dichotomous	<10 ≥10
Preoperative frailty	Measured using the Johns Hopkins Adjusted Clinical Groups system frailty marker[f]	CIHI-DAD CIHI-SDS NACRS	Dichotomous	Frailty No frailty
Cancer type	Type of primary cancer based on ICD-O-3 codes (supplemental eTable 2)	OCR	Categorical	Breast Skin (melanoma) Gastrointestinal Genitourinary Gynecologic Bronchopulmonary Oropharyngeal
Intensity of surgery	Intensity of the surgical procedure in terms of baseline risk, using a consensus-validated definition[g]	CIHI-DAD CIHI-SDS	Dichotomous	Low High
Neoadjuvant therapy	Receipt of radiation therapy or chemotherapy from 180 days before date of surgery to date of surgery	OHIP ALR	Dichotomous	Yes No
Adjuvant therapy	Receipt of radiation therapy or chemotherapy with first treatment administered within 180 days from the date of surgery	OHIP ALR	Dichotomous	Yes No

Abbreviations: ALR, Activity Level Reporting; CIHI, Canadian Institute for Health Information; DAD, Discharge Abstract Database; IRCC-PD, Immigration, Refugees and Citizenship Canada Permanent Resident Database; NACRS, National Ambulatory Care Reporting System; OCR, Ontario Cancer Registry; OHIP, Ontario Health Insurance Plan; ON-Marg, Ontario Marginalization Index; RPDB, Registered Persons Database; SDS, Same-Day Surgery Database.

[a]Matheson FI, Dunn JR, Smith KL, et al. Development of the Canadian Marginalization Index: a new tool for the study of inequality. Can J Public Health 2012;103:S12–16.
[b]Du Plessis V, Beshiri R, Bollman R. Definitions of rural. Ottawa, Ontario, Canada: Statistics Canada, Agriculture Division; 2002.
[c]Chiu M, Lebenbaum M, Lam K, et al. Describing the linkages of the immigration, refugees and citizenship Canada permanent resident data and vital statistics death registry to Ontario's administrative health database. BMC Med Inform Decis Mak 2016;16:135.
[d]Reid RJ, Roos NP, MacWilliam L, et al. Assessing population health care need using a claims-based ACG morbidity measure: a validation analysis in the Province of Manitoba. Health Serv Res 2002;37:1345–1364.
[e]Reid RJ, MacWilliam L, Verhulst L, et al. Performance of the ACG case-mix system in two Canadian provinces. Med Care 2001;39:86–99.
[f]Sternberg SA, Wershof Schwartz A, Karunananthan S, et al. The identification of frailty: a systematic literature review. J Am Geriatr Soc 2011;59:2129–2138.
[g]Schwarze ML, Barnato AE, Rathouz PJ, et al. Development of a list of high-risk operations for patients 65 years and older. JAMA Surg 2015;150:325–331.

eTable 4. Unadjusted Association Between Preoperative Frailty and Remaining Alive and At Home by Postoperative Time Interval[a]

Postoperative Time Interval	HR[b] (95% CI)
0–30 days	2.10 (1.88–2.35)
31–90 days	2.44 (2.18–2.73)
91–180 days	2.10 (1.86–2.36)
181–360 days	1.99 (1.80–2.17)
1–5 years	1.88 (1.80–1.97)

Abbreviation: HR, hazard ratio.
[a]Univariable extended Cox regression with time-varying effects.
[b]Hazards of death or admission to nursing home (HR >1 indicates higher hazard of not being alive and at home).

eTable 5. Adjusted HRs Showing Effect of Preoperative Frailty on Hazards of Remaining Alive and At Home After Cancer Surgery, Stratified by Cancer Type[a]

Postoperative Time Interval	Breast Cancer HR[b] (95% CI)	Bronchopulmonary Cancer HR[b] (95% CI)	Gastrointestinal Cancer HR[b] (95% CI)	Genitourinary Cancer HR[b] (95% CI)	Gynecologic Cancer HR[b] (95% CI)	Head and Neck Cancers HR[b] (95% CI)	Melanoma HR[b] (95% CI)
0–30 days	1.61 (0.91–2.87)	1.37 (0.90–2.07)	1.69 (1.48–1.92)	1.23 (0.73–2.05)	1.88 (1.09–3.24)	1.29 (0.29–5.80)	4.90 (2.45–9.80)
31–90 days	1.57 (0.99–2.48)	1.76 (1.20–2.59)	2.02 (1.76–2.34)	2.85 (2.00–3.97)	2.23 (1.42–3.51)	1.06 (0.37–3.02)	1.56 (0.69–3.51)
91–180 days	2.36 (1.74–3.20)	1.24 (0.81–1.90)	1.66 (1.41–1.96)	1.98 (1.35–2.88)	1.63 (1.01–2.63)	1.22 (0.51–2.90)	3.12 (1.86–5.23)
181–360 days	2.52 (2.03–3.11)	1.49 (1.10–2.00)	1.46 (1.27–1.68)	1.60 (1.15–2.24)	1.51 (1.07–2.12)	1.04 (0.49–2.20)	1.87 (1.24–2.80)
1–5 years	1.78 (1.62–1.96)	1.31 (1.12–1.54)	1.43 (1.33–1.53)	1.42 (1.16–1.73)	1.59 (1.31–1.92)	1.63 (1.09–2.43)	1.76 (1.44–2.15)

Abbreviation: HR, hazard ratio.
[a]Multivariable extended Cox regression with time-varying effects.
[b]Hazard of death or admission to nursing care (HR <1 indicates higher probability of remaining alive and at home). Adjusted for age (categorical), sex, rural residence, comorbidity burden, material deprivation, immigration status, stage at diagnosis, year of surgery, neoadjuvant therapy, adjuvant therapy, and intensity of surgical procedure.