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ABSTRACT

Background

Cancer survival estimates provide insights into the effectiveness of early detection and treatment. The stage of cancer at diagnosis is an important determinant of survival, reflecting the extent and spread at the time of disease detection. This work provides stage-specific, five-year survival results not previously available for Canada.

Data and methods

Data reflect the population-based Canadian Cancer Registry death-linked analytic file covering the period from 2010 to 2017. The stage at diagnosis was determined by the Collaborative Stage Data Collection System. Five-year net survival (NS) estimates for Canada excluding Quebec were derived using the Pohar Perme estimator for the five most commonly diagnosed cancers.

Results

Except for prostate cancer, NS decreased monotonically with increased stage at diagnosis. For example, female breast cancer NS estimates were 100% (stage I), 92% (stage II), 74% (stage III) and 23% (stage IV). Apart from lung cancer, stage I NS exceeded 90% for all cancers studied. The largest sex-specific difference in NS was for lung cancer stage I (female 66%; male 56%). Stage-specific NS generally decreased with age, particularly for early-stage lung cancer. Between the 2010-to-2012 and 2015-to-2017 periods, NS improved among stage IV prostate, female breast and lung cancer cases, as well as for stage I and III lung cancer cases; however, it did not improve at any stage for colon or rectal cancer cases.

Interpretation

The work highlights the importance of detecting cancer early, when treatment is most effective. It demonstrates some progress in stage-specific survival among top cancers in Canada and offers data to inform health policy, including screening, and clinical decisions regarding cancer treatment.

Keywords

malignant neoplasms; population surveillance; registries; stage; survival analysis

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What is already known on this subject?

- The stage of cancer at diagnosis is an important determinant of survival, reflecting the extent and spread at the time of disease detection.
- The staging of cancer cases is important at the population level because it helps health professionals evaluate the effectiveness of early detection. At the individual level, it guides clinical decisions regarding the most appropriate course of treatment.
- Five-year net survival (NS) estimates by stage at diagnosis were not previously available for Canada overall.

What does this study add?

- This study fills an important gap in providing Canadian, stage-specific, five-year NS estimates for the most commonly diagnosed cancers. It showcases the stage at diagnosis as a key predictor of prognosis and highlights the importance of detecting cancer at an early stage, when treatment is most effective.
- Apart from lung cancer, stage I five-year NS exceeded 90% for all cancers studied.
- Stage-specific, five-year NS generally decreased with age, particularly for early-stage lung cancer.
- Between the 2010-to-2012 and 2015-to-2017 periods, five-year NS improved among stage IV prostate, female breast and lung cancer cases, as well as for stage I and III lung cancer cases; however, it did not improve at any stage for colon or rectal cancer cases.

Cancer staging is a way of classifying cancer according to its extent and spread at the time of diagnosis. The staging of cancer cases is important at the population level because it helps health professionals evaluate the effectiveness of early detection, including screening programs.[1] For example, a shift in the stage distribution of cases towards lower stages at diagnosis after the initiation of a screening program provides some evidence for a successful program. The staging of cancer cases also helps with assessing trends in public health system demands and costs for cancer treatment. At the individual level, it guides clinical decisions regarding the most appropriate course of treatment.[2] Along with other potential predictive factors such as age, sex and the histology of the cancer, the stage at which a cancer is diagnosed often provides considerable prognostic insight.[2] It also permits the evaluation of treatment effectiveness.

The Canadian Cancer Registry (CCR) is a population-based database composed of cases diagnosed among Canadian residents since 1992.[3] The data originate from the provincial and territorial cancer registries that annually provide patient and tumour information to Statistics Canada, where the CCR is maintained. For the 2010-to-2017 data period, all Canadian provinces and territories except Quebec reported information on stage at diagnosis to the CCR for the most commonly diagnosed cancers in Canada. Stage-specific incidence data from the CCR have been the focus of several reports, including the 2018 Canadian Cancer Statistics special report on cancer incidence by stage.[4-7] In contrast, the publication of stage-specific survival figures using CCR data has, to date, been limited to three-year net survival (NS) estimates for lung and bronchus (lung) cancers.[8]

Short-term, stage-specific survival estimates have also been reported using data directly obtained from nine Canadian provinces. The International Cancer Benchmarking Partnership project has produced reports of one- and three-year lung[9] and colon[10] cancer NS based on cases diagnosed between 2010 and 2014 in seven high-income countries, including Canada. An additional study from this project reported on five-year colorectal cancer survival, though mortality follow-up for the province of Ontario was not available for the full five years.[11] An unrelated previous study examined two-year survival for colorectal and lung cancer.[12]

The recent extension of the CCR death-linked analytic file from 2014 to 2017 now offers an opportunity to provide more up-to-date NS figures and to profile, for the first time, five-year NS estimates for Canada (excluding Quebec). This study thus presents five-year, stage-specific cancer NS estimates for the most commonly diagnosed cancers in Canada—lung, breast, prostate, colon, and rectum and rectosigmoid junction (rectum)—which together constitute almost half of all annually diagnosed cancer cases.[13] NS estimates are compared across age groups and between biological sexes and two periods (2010-to-2012 vs. 2015-to-2017). The latter allows for the examination of potential short-term changes in stage-specific, five-year NS in Canada that could point to recent variations in screening behaviour or treatment modality.

Data and methods

Data sources and definitions

Canadian Cancer Registry death-linked analytic file

The data source was a pre-existing analytic file created by linking CCR cases diagnosed from 1992 to 2017 to mortality information complete through December 31, 2017, via Statistics Canada's Social Data Linkage Environment.[14] CCR cases originated from the version of the file released on January 29, 2020, which covered the period from 1992 to 2017. The mortality information was obtained from the CCR, the Canadian Vital Statistics Death database (CVSD)[15]—whose current scope is all deaths in Canada—and the T1 personal master file (as reported on tax returns). The use of death information on tax returns facilitated the identification of additional death events of patients in the CCR that may not have been included in the CVSD, such as out-of-country deaths. It was also used to validate the date of death when discrepancies between dates in the CCR and the CVSD were encountered.

The analytic file followed the multiple primary coding rules of the International Agency for Research on Cancer (IARC).[16] Cases were defined based on the International Classification of Diseases for Oncology, Third Edition,[17] and classified using Surveillance, Epidemiology, and End Results (SEER) Program grouping definitions.[18] The specific definitions are as follows: colon (C18.0 to C18.9, C26.0), rectum (C19.9, C20.9), lung (C34), breast (C50) and prostate (C61.9) cancers. Each definition includes only invasive cases (behaviour code of 3) and excludes cases with histology types 9590 to 9992 (leukemia, lymphoma and multiple myeloma), 9050 to 9055 (mesothelioma) and 9140 (Kaposi sarcoma).

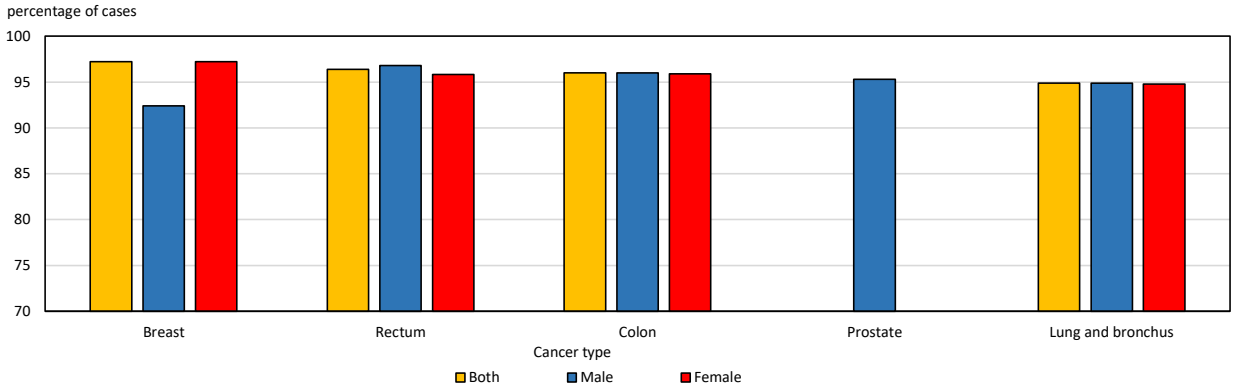
Stage data

Using the seventh edition of the American Joint Committee on Cancer's *Cancer Staging Manual*, the stage at diagnosis was determined by the Collaborative Stage Data Collection System, which incorporates the tumour, node and metastasis (TNM) staging system. Based on the TNM staging system, cancers are usually assigned an overall stage grouping categorized as either 0, I, II, III, IV or unknown.[19] As the size and spread of the cancer increase, the corresponding stage grouping increases. A detailed description of each stage grouping can be found elsewhere.[4] The unknown stage category is restricted to cases where staging was attempted but the collected information was insufficient to determine a specific stage (e.g., not all diagnostic workups necessary to determine a stage were performed or the workup record was incomplete). In contrast, missing stage refers to cases for which staging was not attempted (i.e., unstaged). Cancer-specific stage distributions by sex and age group are provided in Appendix Table A.1.

Inclusion and exclusions

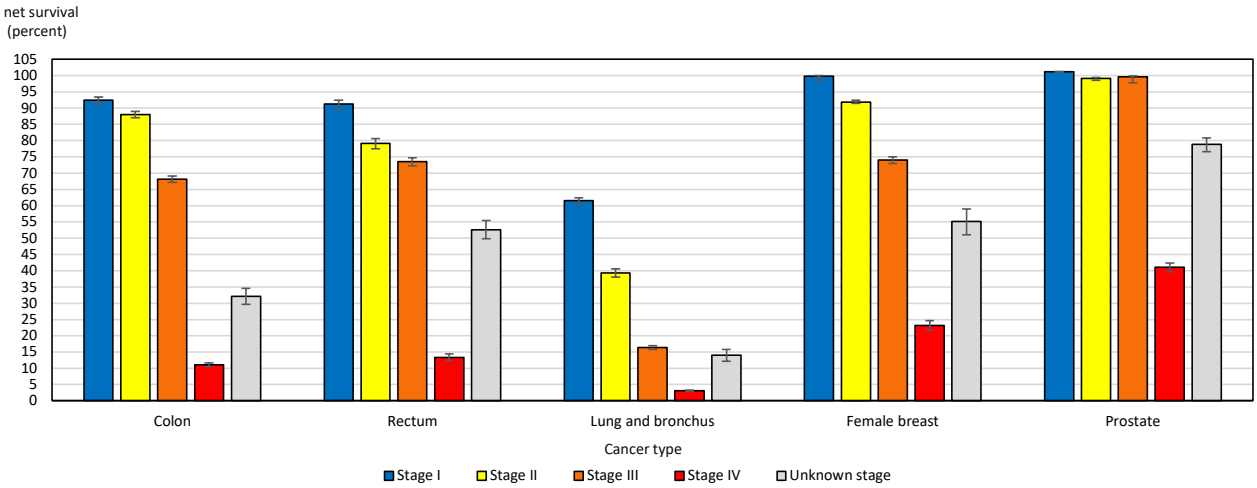
All new primary cancers of the colon, rectum, lung, breast and prostate diagnosed in individuals aged 15 to 99 years in the period from 2010 to 2017 were initially included. Cases from the province of Quebec were not available to be included. Of the cases that were originally included, those with an undefined survival time—specifically, cases for which the diagnosis had been established through an autopsy or a death certificate only or for which a death had been established but the year of death was unknown—were excluded (1.0%). The restriction of the dataset to first primary cancers per person, per individual cancer[20-23] resulted in a further rejection of 0.5% of cases. Of the remaining cases, 0.3% were excluded based on stage data, because they were either considered out of scope for survival analysis (i.e., non-invasive stage 0 cases or lung cancer cases

Figure 1
Percentage of cases for which stage data were available for selected cancers, by sex, Canada excluding Quebec, 2010-to-2017 period



Notes: Quebec is excluded because cases diagnosed in that province from 2011 onward had not been submitted to the Canadian Cancer Registry. Stage completeness was defined as the percentage of cases assigned a stage value (including those staged as 0 or occult) among cases considered stageable. Calculations exclude cases with undefined survival time and non-first primary cancers per person, per individual cancer.
Sources: Statistics Canada, Canadian Cancer Registry death linked file (1992 to 2017) and life tables.

Figure 2
Five-year, stage-specific net survival, selected cancers, ages 15 to 99 years, Canada excluding Quebec, 2010-to-2017 period



Notes: Quebec is excluded because cases diagnosed in that province from 2011 onward had not been submitted to the Canadian Cancer Registry. Follow-up of cases is available to the end of 2017.
Sources: Statistics Canada, Canadian Cancer Registry death linked file (1992 to 2017) and life tables.

staged as occult) or coded as "not applicable" (i.e., unstageable), and 4.1% were excluded because the stage variable was coded as a missing value (i.e., unstaged cases). A total of 531,732 cases were available for stage-specific survival analysis.

Statistical analysis

NS estimates were derived using an algorithm[24] that was augmented by Ron Dewar of the Nova Scotia Health Cancer Care Program[25] to include the Pohar Perme estimator of NS[26] using the hazard transformation approach.

The derivation of expected survival probabilities necessary for the calculation of NS has been described elsewhere.[27] While NS cannot exceed 100% in theory, in practice it is possible because of the relative survival framework in which it is estimated. However, confidence intervals for point estimates exceeding 100% were unavailable, because they are undefined for the log (-log) transformation approach used to construct them.

For each cancer type, patterns in overall five-year, stage-specific NS and stage-specific NS by sex and by age group were determined using cases diagnosed from 2010 to 2017 and the complete method of survival analysis. Apart from the analysis by sex, the focus of breast cancer was on females because of the rarity of cases among males. To provide the most up-to-date estimates and to facilitate the examination of changes in NS over time, the period method was used to determine predicted NS estimates for the 2015-to-2017 period and the cohort method was used to derive estimates for cases diagnosed from 2010 to 2012.[28]

The percentage point difference in five-year NS was used as the measure of differences in survival. Differences in NS were calculated before rounding the result. The Z-test was used to determine p-values for percentage point differences in NS; the standard errors of differences were estimated by the square root of the sum of the variances associated with the two NS estimates. P-values correspond to two-sided tests of the null hypothesis that the difference in NS is zero, with a significance level of 0.05.

Stage completeness was defined as the percentage of cases that were assigned a stage value (including those staged as 0 or occult) among the cases that were considered as stageable.[4] Estimates of stage completeness were calculated for each cancer type and sex, where applicable. For interpretational purposes, a separate analysis of cases with missing stage was also performed (see Appendix Table A.2).

Results

Stage completeness very high

Stage completeness refers to the percentage of cases not coded as unstaged. Stage completeness by cancer type ranged from 94.9% (lung) to 97.2% (breast) for the 2010-to-2017 period (Figure 1). Completeness was higher among females diagnosed with breast cancer than among males (97.2% versus 92.4%) and slightly higher among females for rectal cancer (96.8% versus 95.8%). For both lung and colon cancers, sex-specific stage completeness was virtually identical. Compared with cases that were staged, cases for which the stage was missing (unstaged) were more concentrated in the oldest age group for lung, breast and prostate cancers (Table A2). In contrast, for colon and rectal cancers, unstaged cases were more concentrated in the younger age groups. Of the unstaged cases overall, 98% were diagnosed in Ontario, a province that contributed 48% of the total cases to this study (data not shown).

Table 1
Five-year, stage-specific net survival by sex and differences in survival between sexes, selected cancers, ages 15 to 99 years, Canada excluding Quebec, 2010-to-2017 period

	Female			Male			Difference (female versus male)			
		95% Confidence interval			95% Confidence interval			95% Confidence interval		
Cancer type / Stage	Net survival (%)	from	to	Net survival (%)	from	to	Percentage points	from	to	p-value
Colon										
I	92	91	94	93	91	94	-0.3	-2.3	1.8	0.795
II	89	87	90	87	86	89	1.3	-0.8	3.3	0.227
III	67	66	69	69	67	70	-1.5	-3.6	0.5	0.148
IV	12	11	13	11	10	12	1.0	-0.2	2.3	0.108
Unknown	26	23	30	38	35	42	-12.0	-16.9	-7.1	< 0.001
Rectum										
I	92	90	94	91	89	92	1.2	-1.4	3.8	0.364
II	79	77	82	79	77	81	0.5	-2.7	3.8	0.747
III	75	73	77	73	71	74	2.7	0.2	5.1	0.034
IV	13	12	15	13	12	15	0.0	-2.2	2.2	0.999
Unknown	52	48	57	53	49	57	-0.3	-6.0	5.4	0.919
Lung and bronchus										
I	66	65	67	56	54	57	10.2	8.3	12.2	< 0.001
II	42	40	44	37	35	39	5.0	2.4	7.6	< 0.001
III	19	18	20	14	13	15	5.3	4.0	6.5	< 0.001
IV	4	3	4	3	2	3	1.2	0.8	1.6	< 0.001
Unknown	15	13	18	13	10	15	2.7	-0.9	6.4	0.138
Breast										
I	100	99	100	95	83	98	5.1	-1.3	11.4	0.121
II	92	91	92	87	78	92	5.4	-1.5	12.2	0.126
III	74	73	75	66 [E]	53	76	8.1	-3.5	19.6	0.171
IV	23	22	25	23 [E]	13	36	-0.2	-11.9	11.5	0.972
Unknown	55	51	59	F	F	F	F	F	F	0.315

E use with caution
F too unreliable to be published
Notes: Quebec is excluded because cases diagnosed in that province from 2011 onward had not been submitted to the Canadian Cancer Registry. Caution should be used in interpreting estimates associated with an unrounded standard error greater than 0.05 and smaller than or equal to 0.10; if the standard error was greater than 0.10, estimates were considered too unreliable to be published. Follow-up of cases is available to the end of 2017.
Sources: Statistics Canada, Canadian Cancer Registry death linked file (1992 to 2017) and life tables.

Net survival inversely related to the stage at diagnosis

NS was observed to be inversely related to the stage at diagnosis for each cancer type, except for prostate cancer, for which there was little variation within the first three stage groups (Figure 2). For example, five-year NS for female breast cancer was 99.8% when diagnosed at stage I, dropping to 91.9% at stage II, then 74.0% at stage III and 23.2% at stage IV. Among cases diagnosed at stage I, five-year NS exceeded 90% for all cancer types except for lung cancer (62%). For lung cancer, estimates decreased by just over 20 percentage points from stage I to II and from stage II to III, and by 13 points from stage III to IV. For both female breast and colon cancers, smaller decreases were observed from stage I to II (8 and 4 percentage points, respectively) than from stage II to III (18 and 20 percentage points, respectively). For rectal cancer, conversely, NS decreased more from stage I to II (12 percentage points) than from stage II to III (6 percentage points). Sharp decreases in NS from stage III to IV were noted for each cancer type. Apart from lung cancer, for which NS at stage III was already quite low (16.3%), decreases from stage III to stage IV ranged from 51 percentage points for breast cancer to 60 percentage points for rectal cancer.

Stage-specific lung cancer net survival better among females than males

For lung cancer, five-year NS among females exceeded that among males at each known stage of diagnosis (Table 1). The largest difference, 10.2 percentage points, was observed among cases diagnosed at stage I. Differences of about 5 percentage points were seen at both stages II and III, while the difference at stage IV was smaller (1.2 percentage points). All noted differences were statistically significant ($p < 0.001$). For both colon and rectal cancers, there were no significant stage-specific differences in five-year NS between the sexes, except for a 2.7 percentage point advantage for females diagnosed with stage III rectal cancer ($p = 0.034$). Curiously, among colon cancer cases whose stage was recorded as unknown, NS for males exceeded that for females by 12 percentage points (38% versus 26%; $p < 0.001$). Relatively large sex-specific differences in survival point estimates in favour of females,

Table 2

Five-year, stage-specific net survival by age group, selected cancers, ages 15 to 99 years, Canada excluding Quebec, 2010-to-2017 period

	Cancer stage														
	I			II			III			IV			Unknown		
Cancer type / Age group (years)	Net survival (%)	95% Confidence interval from	to	Net survival (%)	95% Confidence interval from	to	Net survival (%)	95% Confidence interval from	to	Net survival (%)	95% Confidence interval from	to	Net survival (%)	95% Confidence interval from	to
Colon															
15 to 44	96	93	98	94	91	96	79	75	83	19	16	23	93	84	97
45 to 54	96	95	98	92	90	94	78	76	81	18	16	21	74	64	81
55 to 64	96	94	97	90	89	92	75	73	76	15	14	17	68	62	74
65 to 74	95	93	96	87	86	88	71	69	72	11	10	13	51	45	56
75 to 84	90	88	92	86	84	88	62	59	64	7	6	8	25	21	29
85 to 99	78	71	84	89	83	93	55	50	60	3	2	4	13	9	16
Rectum															
15 to 44	98	95	99	88	82	92	82	78	85	23	17	28	93	86	96
45 to 54	97	94	98	87	84	89	80	78	83	23	20	26	86	81	91
55 to 64	94	93	96	85	82	87	78	76	80	15	13	17	78	73	82
65 to 74	94	92	96	83	81	86	75	73	77	14	12	16	64	58	70
75 to 84	86	83	90	70	66	73	63	60	66	6	4	8	36	31	42
85 to 99	72	61	80	63	53	71	49	40	58	2	1	5	15	10	21
Lung and bronchus															
15 to 44	91	86	94	74 [E]	60	83	31	24	39	9	7	13	F	F	F
45 to 54	79	76	82	59	54	64	28	25	30	6	5	7	34 [E]	21	47
55 to 64	71	69	72	51	49	54	22	20	23	4	3	4	32	26	38
65 to 74	65	64	67	41	39	43	17	16	18	3	3	3	17	14	21
75 to 84	52	50	54	31	29	33	10	9	11	2	2	2	10	7	13
85 to 99	39	34	44	14	10	19	8	6	11	2	1	3	4	1	7
Female breast															
15 to 39	98	96	99	90	89	92	76	73	78	35	29	42	95	84	98
40 to 49	99	99	99	95	94	96	80	78	81	36	32	40	87	78	92
50 to 59	99	99	99	94	93	94	79	77	80	27	24	30	75	67	81
60 to 69	99	99	100	94	93	94	76	74	78	22	20	25	69	61	75
70 to 79	101	..	..	90	88	91	70	67	72	20	17	23	54	46	61
80 to 99	104	..	..	86	83	88	56	51	60	12	9	16	39	32	46
Prostate															
15 to 54	100	97	100	100	97	100	100	96	100	51	46	56	96	90	98
55 to 64	101	..	..	100	99	100	100	98	100	57	54	59	96	93	97
65 to 74	102	..	..	100	90	100	102	..	..	49	47	51	89	86	92
75 to 84	101	..	..	100	71	100	92	86	95	32	30	35	74	70	78
85 to 99	97 [E]	10	100	80	73	85	F	F	F	20	16	24	47	39	54

.. not available for a specific reference period

E use with caution

F too unreliable to be published

Notes: Quebec is excluded because cases diagnosed in that province from 2011 onward had not been submitted to the Canadian Cancer Registry. Caution should be used in interpreting estimates associated with an unrounded standard error greater than 0.05 and smaller than or equal to 0.10; estimates associated with a standard error greater than 0.10 were considered too unreliable to be published. Follow-up of cases is available to the end of 2017. Confidence intervals are undefined for unrounded point estimates of 100% or greater.

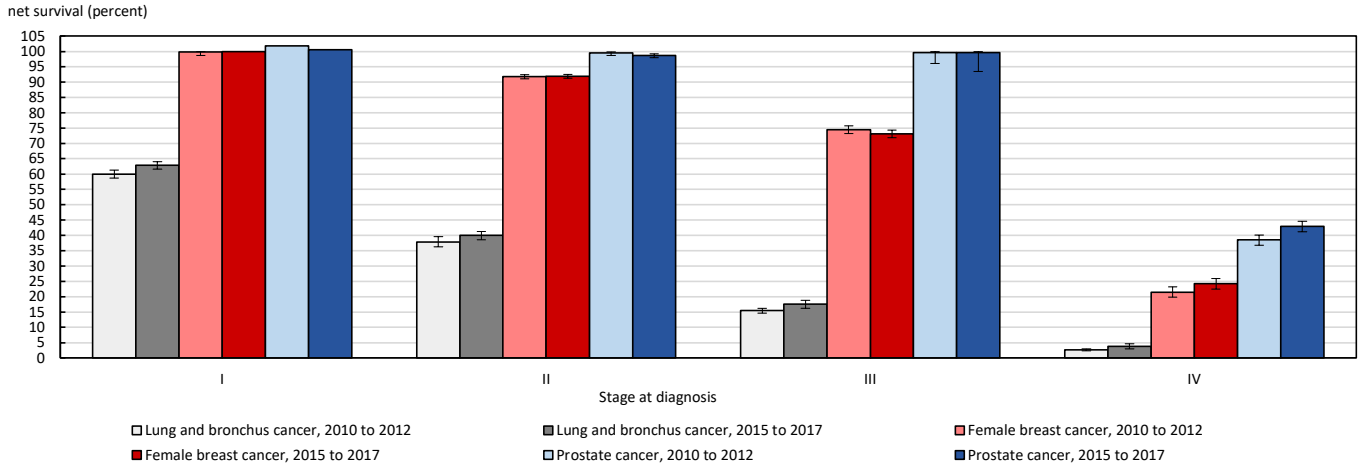
Sources: Statistics Canada, Canadian Cancer Registry death linked file (1992 to 2017) and life tables.

ranging from 5.1 to 8.1 percentage points, were observed for the first three stages of breast cancer. While individually these differences were not statistically significant, perhaps owing to the rarity of cases among males, the difference was significant for stages I through III combined (p = 0.001) (data not shown).

Stage-specific net survival generally decreases with age

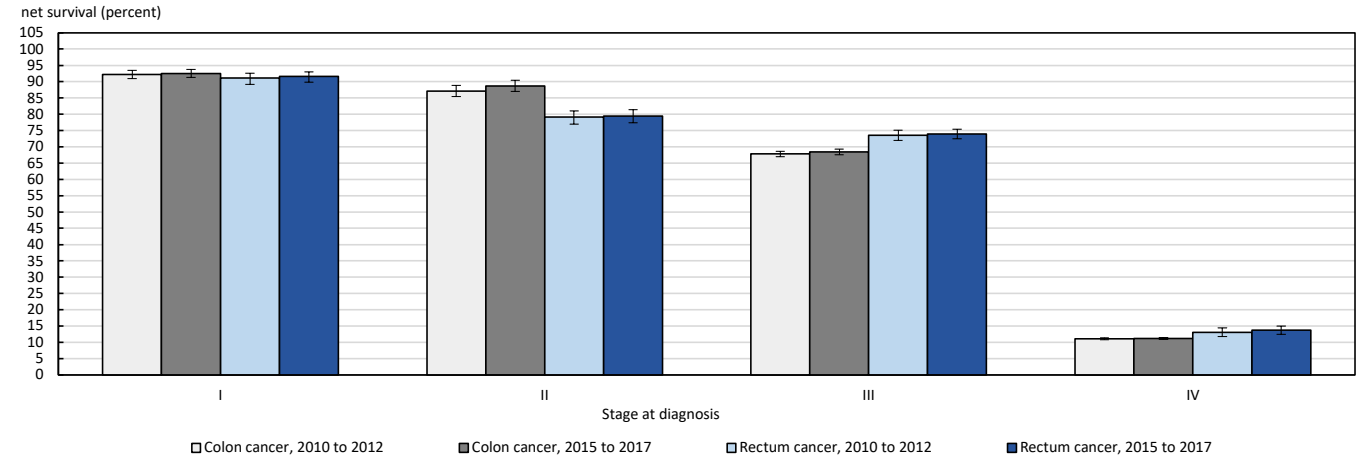
Stage-specific, five-year NS generally decreased with age (Table 2). The largest absolute decreases with age were observed for early-stage lung cancer. For cases diagnosed at stage II, five-year NS decreased by 60 percentage points, from 74% among those aged 15 to 44 years to 14% among those aged 85 to 99 years. A corresponding decrease of 52 percentage points was observed among those diagnosed with lung cancer at stage I. Lung cancer survival also declined considerably with age at advanced stages, but the absolute differences were attenuated by the relatively poor survival among the youngest group.

Figure 3A
Five-year, stage-specific net survival for lung and bronchus, female breast, and prostate cancers, ages 15 to 99 years, Canada excluding Quebec, 2010-to-2012 period versus 2015-to-2017 period



Notes: Quebec is excluded because cases diagnosed in that province from 2011 onward had not been submitted to the Canadian Cancer Registry.
Overlaid vertical bars denote 95% confidence intervals. Estimates for 2015 to 2017 are predicted.
Sources: Statistics Canada, Canadian Cancer Registry death linked file (1992 to 2017) and life tables.

Figure 3B
Five-year, stage-specific net survival for colon and rectum cancers, ages 15 to 99 years, Canada excluding Quebec, 2010-to-2012 period versus 2015-to-2017 period



Notes: Quebec is excluded because cases diagnosed in that province from 2011 onward had not been submitted to the Canadian Cancer Registry.
Overlaid vertical bars denote 95% confidence intervals. Estimates for 2015 to 2017 are predicted.
Sources: Statistics Canada, Canadian Cancer Registry death linked file (1992 to 2017) and life tables.

Decreases in five-year NS between the youngest and oldest age groups for rectal cancer ranged from 33 percentage points among those diagnosed at stage III to 21 percentage points among stage IV cases. At each stage, most of the overall decrease occurred in the older age groups (i.e., from 65 to 74 years to 85 to 99 years). Similar, but less pronounced, decreases in NS with age were observed among those diagnosed with colon cancer, especially at stage II. For prostate and female breast cancers, the largest decreases between the youngest and oldest age groups were observed at stage IV (31 and 23 percentage points, respectively) with a steeper decline between older age groups for prostate cancer.

Net survival generally worse for unknown stage and unstaged cases

Cancer-specific, five-year NS estimates among cases with unknown stage tended to be intermediate to those observed for stages III and IV, but closer to stage III (Figure 2). These cases were most frequently diagnosed at an advanced age, when NS is typically poorest (Table A.1; Table 2). Among unstaged cases, five-year NS was lower for all cancers apart from rectal cancer, for which there was no overall difference (Table A.2). Differences were greatest in the oldest age groups (75 years and older) for each cancer type. For breast cancer, much higher NS among staged versus unstaged cases was observed in

individuals as young as 50 years. The age group-specific survival for unstaged cases generally tended to approximate most closely that of corresponding estimates for stage III for each cancer (Table A.2; Table 2).

Recent increases in lung cancer net survival across most stages

Significant increases in five-year lung cancer NS from the 2010-to-2012 period to the 2015-to-2017 period were observed for each stage group ($p \leq 0.001$) except for stage II (Figure 3a). Increases ranged from 1.1 percentage points among cases diagnosed at stage IV to 2.9 percentage points among cases diagnosed at stage I. While the 2.1 percentage point increase among stage II cases was not statistically significant ($p = 0.098$), a relatively small proportion of lung cancer cases (8%) were diagnosed at this stage, resulting in diminished statistical power.

Significant stage-specific increases in five-year NS from the 2010-to-2012 period to the 2015-to-2017 period were observed only among stage IV cases for both prostate (4.4 percentage points, $p < 0.001$) and female breast (2.7 percentage points, $p = 0.031$) cancers. In contrast, there was a significant decrease in NS of 0.9 percentage points ($p = 0.003$) among prostate cancer cases diagnosed at stage I and II combined (data not shown). For cancers of the colon and rectum, no significant differences in five-year NS were observed between the reported periods for known stages of diagnosis (Figure 3b).

Discussion

This study presents the first Canadian (excluding Quebec) estimates of five-year survival by stage at diagnosis. An inverse relationship between five-year NS and stage at diagnosis was observed for each cancer, with the notable exception of prostate cancer, for which NS was consistently approximately 100% for the first three stages but declined substantially for stage IV. Sex differences were most pronounced for lung cancer, where NS among females exceeded that among males at each stage. Age was also an important predictor of survival as stage-specific NS generally decreased with advancing age, particularly for early-stage lung cancer. From the 2010-to-2012 period to the 2015-to-2017 period, significant increases in NS were observed among stage IV prostate and female breast cancer cases, and among both early- and late-stage disease for lung cancer.

Apart from lung cancer, stage I NS exceeded 90% for all cancers studied. This finding underscores the importance of detecting cancer at an early stage, when treatment is most effective. The recent recommendation to introduce lung cancer screening programs for individuals at high risk for lung cancer because of cigarette smoking history[29] may be a positive step in this direction. Organized screening programs already exist for breast and colorectal cancers. Individuals diagnosed with breast cancer through mammography screening typically have their cancer detected earlier in disease progression than those diagnosed through other means. As a result, they tend to benefit more from therapy and have a reduced risk of dying from their diagnosis.[30,31] Screening is similarly important for the early detection and treatment of colorectal cancer, because symptoms for this disease typically develop later in its progression.[32]

In contrast to patients diagnosed with colon cancer, many rectal cancer patients clinically identified as having late-stage disease would have received neoadjuvant therapy during the time of this study.[33] The shrinkage of tumours prior to surgery and pathological assessment would have likely led to the downstaging of some stage III rectal cancer cases to pathological stage II, resulting in a somewhat artificial decrease of the stage II NS estimate. Additionally, a small percentage of patients would likely have had a complete clinical response, no longer needing surgery.[33] Absent of a pathological report, and with only partial stage information available, these patients would have contributed to the unknown stage category; therefore, they may have artificially increased its estimated NS relative to the corresponding estimate for colon cancer.

Prostate cancer tends to be slow growing, and treatment is such that average survival outcomes are excellent and comparable among males diagnosed at stages I through III. Nonetheless, curative treatments can have repercussions that can diminish quality of life, including urinary incontinence and sexual dysfunction.[34] The substantial decline in five-year NS from stage III to stage IV prostate cancer observed in this study has been reported elsewhere[35] and reflects historical difficulties in treating this disease once it has reached this stage.

Improvement in survival for lung cancer has been shown to have played a leading role in recent improvements in the survival for all cancers combined in Canada.[27] The current study further revealed that recent progress in lung cancer survival is apparent in most, if not all, stage groups. Improvements in survival for this disease are attributable to advances in treatment and early diagnosis.[36] In addition, the accuracy of staging—fundamental for the selection of treatment—has improved.[37] Surgery is most often considered for early-stage lung cancer and usually leads to the best outcomes. While the proportion of patients eligible for surgery is still relatively small, it has increased recently with the introduction of less invasive surgical techniques.[36] Radiotherapy can be used in all stages of disease. Technological advancements have improved the radiotherapy targeting of tumours and allowed this treatment to be used more often and with greater success.[38] A third example is that advances in systemic therapies for non-small cell lung cancer have led to improved survival for patients diagnosed with late-stage disease.[37,39] In the United Kingdom, early diagnosis efforts, such as increasing awareness through national media campaigns, have led to more lung cancer cases being diagnosed at earlier stages of the disease.[40]

Similarly, the significant increase in five-year NS observed among stage IV prostate cancer cases from the 2010-to-2012 period to the 2015-to-2017 period likely reflects recent transformational breakthroughs in treatment.[34,41] These include the approval of several new chemotherapeutic agents since 2010, such as new hormone and antibody therapies, as well as

new targeted therapies (e.g., androgen receptor blockers). Further improvement in survival for stage IV prostate cancer may be forthcoming as the optimal use and sequencing of these agents have yet to be determined.[42] Improvements in systemic therapies have also been reported to prolong life in females diagnosed with advanced breast cancer,[43] likely accounting for the recent increase in stage IV breast cancer survival observed in this study. However, as treatment goals remain restricted to extending life and reducing symptoms, metastatic breast cancer continues to be virtually incurable.[43]

For lung cancer, the results reported suggest a clear five-year survival advantage among females at each stage relative to males. The findings support previous research indicating stage-specific advantages in shorter-term lung cancer survival among females, both in Canada and internationally.[9] For breast cancer, higher five-year survival among females has been reported for Canada and elsewhere.[44-47] In the United States, this advantage has been demonstrated to exist at each stage of disease.[45] The current results indicate that this may also be true in Canada for stages I to III as the magnitude of sex stage-specific survival differences was comparable with that in the United States. However, differences in Canada were not significant, possibly because of low statistical power (i.e., over 125 times more cases in the U.S. study). Furthermore, in contrast to the U.S. results, stage IV five-year breast cancer survival was virtually identical among males and females. The reason underlying these disparities in survival is not well understood.[45] For colon and rectal cancers, the absence of significant sex differences in survival could indicate that screening may provide similar benefits for both sexes.

Strengths and limitations

This study was conducted using incidence data from the CCR, one of the highest-quality national population-based cancer registries in the world.[48] Mortality follow-up was determined using three sources of death information, increasing the likelihood of capturing not only deaths occurring in the jurisdiction of diagnosis, but also those occurring in other jurisdictions, including those in and outside Canada. Thus, the file used in this study should be considered more complete than other files created by compiling data directly from provincial cancer registries.[49]

The results of this study pertain to Canada excluding Quebec, as the CCR has not received data from this jurisdiction since the 2010 data year. Additionally, some cases were not staged or, if they were, were staged as unknown. While the overall percentage of such cases was relatively low, in both situations the cases were skewed towards older age groups, for which NS was typically poorest. As such, there may be some slight overestimation of stage-specific survival estimates for all ages combined. Given that the survival among cases with missing or unknown stage most closely resembled that seen among stage III cases, this effect may be more pronounced for later stages of disease. Finally, while NS may differ by histologic subtype within the cancers presented herein (e.g., small cell lung cancer versus non-small cell lung cancer[8]), the examination of these differences, whether overall or by stage, was beyond the scope of this study.

Conclusion

This study fills an important gap in providing Canadian, stage-specific, five-year NS estimates. The work showcases the stage at diagnosis as a key predictor of prognosis and highlights the importance of detecting cancer at an early stage, when treatment is most effective. It is also a good example of the use of low-cost data linkage to produce valuable evidence that informs health care delivery. The findings can be used by Canadian health professionals to better inform health policy and treatment evaluation. In addition, while these population-based results reflect average outcomes rather than individual prognoses, they may also be used to educate cancer patients on their disease and treatment options. Routine capture of the stage at diagnosis for an expanded list of cancer types would facilitate analyses to provide further valuable insights into cancer survival in Canada. Future studies should focus on stage-specific analyses by histologic subtype and geographical jurisdiction across Canada.

Appendix Table A.1
Stage distribution by sex and age group, selected cancers, ages 15 to 99 years, Canada excluding Quebec, 2010-to-2017 period

	Both sexes						Male						Female					
		Cancer stage						Cancer stage						Cancer stage				
Cancer type / Age group (years)	Number of cases	I (%)	II (%)	III (%)	IV (%)	Unk (%)	Number of cases	I (%)	II (%)	III (%)	IV (%)	Unk (%)	Number of cases	I (%)	II (%)	III (%)	IV (%)	Unk (%)
Colon	83,441	22	27	26	21	4	43,213	23	27	25	21	4	40,228	21	28	26	20	5
15 to 44	3,217	30	20	24	23	3	1,562	27	22	24	24	2	1,655	32	18	24	22	4
45 to 54	7,072	22	23	28	26	2	3,646	23	23	28	24	2	3,426	22	22	28	27	2
55 to 64	15,885	24	24	27	23	2	8,959	25	24	26	23	2	6,926	22	24	29	23	2
65 to 74	23,253	24	27	26	20	2	13,129	25	26	26	20	3	10,124	23	29	27	19	2
75 to 84	22,857	21	31	26	18	4	11,501	21	30	25	19	4	11,356	21	31	26	18	4
85 to 99	11,157	15	30	23	20	12	4,416	15	31	22	20	12	6,741	15	30	24	19	12
Rectum	42,118	24	19	33	18	6	26,363	23	19	33	19	5	15,755	25	19	32	17	7
15 to 44	2,094	20	13	39	21	7	1,096	16	13	41	23	7	998	24	13	37	20	6
45 to 54	5,745	22	15	38	20	5	3,396	21	15	39	21	4	2,349	24	15	36	19	5
55 to 64	10,620	23	18	36	18	5	7,000	22	18	36	19	4	3,620	25	18	35	16	6
65 to 74	11,675	26	19	33	17	4	7,877	26	19	34	17	4	3,798	27	20	32	17	5
75 to 84	8,555	24	23	29	17	7	5,294	24	23	29	18	7	3,261	24	22	30	17	7
85 to 99	3,429	22	22	21	18	17	1,700	22	23	22	18	15	1,729	23	21	20	18	18
Lung and bronchus	134,390	20	8	19	51	2	68,695	17	8	20	53	2	65,695	22	8	19	49	2
15 to 44	1,279	22	6	16	54	1	585	20	6	16	56	1	694	24	6	16	53	1
45 to 54	8,272	16	6	20	58	1	3,720	12	6	20	61	1	4,552	19	6	19	55	1
55 to 64	28,848	18	8	20	53	1	14,495	15	8	21	55	1	14,353	21	8	20	50	1
65 to 74	45,865	21	8	20	49	1	23,815	18	9	20	51	2	22,050	24	8	20	47	1
75 to 84	38,047	21	8	19	49	2	20,066	19	9	20	51	3	17,981	24	8	19	47	2
85 to 99	12,079	17	7	16	54	5	6,014	16	8	17	54	5	6,065	18	7	16	54	5
Breast	142,104	44	37	13	5	1	1,148	30	43	17	9	1	140,956	44	37	13	5	1
15 to 39	6,340	24	47	22	6	1	22	23	36	27	14	0	6,318	24	47	22	6	1
40 to 49	20,355	35	42	17	4	1	49	41	29	20	8	2	20,306	35	42	17	4	1
50 to 59	33,738	45	37	13	5	1	184	28	43	17	11	1	33,554	45	37	13	5	1
60 to 69	38,142	52	32	10	5	1	330	31	42	16	10	1	37,812	52	32	10	5	1
70 to 79	26,700	50	34	10	6	1	355	31	45	16	8	1	26,345	50	33	10	6	1
80 to 99	16,829	30	43	14	8	5	208	26	46	18	9	1	16,621	30	43	14	8	5
Prostate	…	…	…	…	…	…	129,679	21	51	13	11	4	…	…	…	…	…	…
15 to 54	…	…	…	…	…	…	9,532	29	47	15	7	2	…	…	…	…	…	…
55 to 64	…	…	…	…	…	…	37,970	26	47	16	8	3	…	…	…	…	…	…
65 to 74	…	…	…	…	…	…	50,469	21	53	14	9	3	…	…	…	…	…	…
75 to 84	…	…	…	…	…	…	25,201	14	57	6	17	6	…	…	…	…	…	…
85 to 99	…	…	…	…	…	…	6,507	8	39	3	36	14	…	…	…	…	…	…

. . . not applicable

Notes: Unk = Unknown. Quebec is excluded because cases diagnosed in that province from 2011 onward had not been submitted to the Canadian Cancer Registry. Case counts and percentage distributions are based on cases included in survival analyses (see methods). Sex-specific row percentage totals may not sum to 100 because of rounding.
Source: Statistics Canada, Canadian Cancer Registry death linked file (1992 to 2017).

Appendix Table A.2

Distribution of cases and five-year net survival by staging status and age group, selected cancers, ages 15 to 99 years, Canada excluding Quebec, 2010-to-2017 period

	Distribution		Five-year net survival					
	Unstaged	Staged	Unstaged			Staged		
			NS	95% CI		NS	95% CI	
Cancer type / Age group (years)	%	%	(%)	from	to	(%)	from	to
Colon	...	...	58	56	60	65	65	66
15 to 44	5.7	3.9	83	76	88	73	71	75
45 to 54	11.7	8.5	71	65	77	70	69	71
55 to 64	21.4	19.1	68	63	72	69	68	70
65 to 74	25.0	27.9	64	59	68	68	68	69
75 to 84	22.4	27.4	48	42	53	63	62	65
85 to 99	13.9	13.3	30	22	38	53	51	55
Rectum	...	...	65	62	69	67	66	67
15 to 44	8.4	5.0	73[E]	62	82	74	72	76
45 to 54	19.9	13.6	82	75	87	74	72	75
55 to 64	24.2	25.2	78	72	83	72	70	73
65 to 74	24.6	27.8	66	58	72	70	69	71
75 to 84	15.2	20.3	36	27	46	58	57	60
85 to 99	7.7	8.1	33[E]	18	48	43	39	46
Lung and bronchus	...	...	16	15	17	20	20	20
15 to 44	1.6	1.0	45[E]	34	55	37	34	40
45 to 54	5.6	6.2	28	23	33	25	24	26
55 to 64	17.9	21.5	21	18	24	24	23	24
65 to 74	30.1	34.1	19	17	22	22	22	23
75 to 84	29.5	28.3	12	10	14	17	16	17
85 to 99	15.3	9.0	4	2	7	10	9	11
Breast	...	...	76	74	78	89	88	89
15 to 39	5.1	4.5	86	79	91	86	84	87
40 to 49	14.8	14.4	89	86	92	91	91	92
50 to 59	20.6	23.8	82	78	85	91	90	91
60 to 69	23.8	26.8	78	74	82	91	91	92
70 to 79	18.7	18.7	72	67	76	89	88	89
80 to 99	17.0	11.8	56	48	63	78	76	80
Prostate	...	...	82	80	84	93	92	93
15 to 54	7.4	7.4	95	91	97	96	96	97
55 to 64	25.8	29.3	94	92	96	97	97	97
65 to 74	33.3	38.9	94	91	95	96	96	97
75 to 84	22.9	19.4	73	68	76	87	86	88
85 to 99	10.6	5.0	32	25	40	56	53	60

... not applicable

[E] use with caution

Notes: NS = net survival. CI = confidence interval. Quebec is excluded because cases diagnosed in that province from 2011 onward had not been submitted to the Canadian Cancer Registry. Caution should be used in interpreting estimates associated with an unrounded standard error greater than 0.05 and smaller than or equal to 0.10. Distribution percentages are based on cases otherwise eligible for survival analysis (see methods). Staged cases include those staged as unknown. Cancer-specific column percentage totals may not sum to 100 because of rounding.

Sources: Statistics Canada, Canadian Cancer Registry death linked file (1992 to 2017) and life tables.

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