American Journal of Epidemiology

Vol. 190, No. 1
DOI: 10.1093/aje/kwaa160
Advance Access publication:
July 24, 2020

Original Contribution

Premature Mortality Due to Hodgkin Lymphoma, Non-Hodgkin Lymphoma, Multiple Myeloma, and Leukemia in Canada: A Nationwide Analysis From 1980 to 2015

Truong-Minh Pham*, Grace Shen-Tu, Khanh Hoa Nguyen, Shuang Lu, Douglas C. Dover, Peter Duggan, Lorraine Shack, and Winson Y. Cheung

* Correspondence to Dr. Truong-Minh Pham, Surveillance and Reporting, Cancer Care Alberta, Alberta Health Services, Suite 1400, Sun Life Building, 10123-99 Street, Edmonton, Alberta T5J 3H1, Canada (e-mail: truongminh.pham@ahs.ca).

Initially submitted February 19, 2020; accepted for publication July 21, 2020.

Recently, we introduced a novel measure of "average life span shortened" (ALSS) to improve comparability of premature mortality over time. In this study, we applied this novel measure to examine trends in premature mortality caused by hematological cancers in Canada from 1980 to 2015. Mortality data for Hodgkin lymphoma, non-Hodgkin lymphoma, multiple myeloma, and leukemia were obtained from the World Health Organization mortality database. Years of life lost was calculated according to Canadian life tables. ALSS was defined as the ratio between years of life lost and expected life span. Over the study period, age-standardized rates of mortality decreased for all types of hematological cancers. Our new ALSS measure showed favorable trends in premature mortality for all types of hematological cancers among both sexes. For instance, men with non-Hodgkin lymphoma lost an average of 23.7% of their life span in 1980 versus 16.1% in 2015, while women with non-Hodgkin lymphoma lost an average of 21.7% of their life span in 1980 versus 15.5% in 2015. Results from this study showed that patients with hematological cancers experienced prolonged survival over a 35-year period although the magnitude of these life span gains varied by types of hematological cancers.

average life span shortened; average years of life lost; hematological cancers; premature mortality; years of life lost

Abbreviations: ASR, age-standardized rate; ALSS, average life span shortened; AYLL, average years of life lost; ICD-9, *International Classification of Diseases*, *Ninth Revision*; ICD-10, *International Classification of Diseases*, *Tenth Revision*; YLL, years of life lost.

Hematological cancers consist of a heterogeneous group of malignancies that arise from hematopoiesis, such as of the bone marrow, or lymphatic system. They are also called blood cancers and generally include 4 main cancer types: Hodgkin lymphoma, non-Hodgkin lymphoma, multiple myeloma, and leukemia (1–4). A recent report based on Canadian cancer statistics estimated that approximately 18,000 people were diagnosed with one of the 4 types of hematological cancers in 2017, and about 7,000 people died from it (5).

The age-standardized rate (ASR) has been a useful tool to characterize the burden of chronic conditions. The concept of premature mortality was more recently introduced to describe the impact of early deaths attributable to a particular health condition. To date, the most frequently used metrics for premature mortality include years of life lost (YLL) and average years of life lost (AYLL). However, these metrics are imperfect, particularly when attempting to compare results between studies, because there are 2 different algorithms for calculating YLL, and life expectancy of the general population often improves with time. Recent publications (6–10) from our group have discussed some of these challenges, which have compelled us to develop a novel measure called average life span shortened (ALSS) in order to improve comparability over time. Briefly, the ALSS is expressed as the ratio of YLL in relation to the expected life span among patients who died from a given health condition. We have subsequently applied the ALSS measure in estimating

long-term trends of premature mortality due to malignancies of the breast (6), central nervous system (7), head and neck (8), and prostate and testis (9) in the Canadian population, as well as kidney and bladder cancers in the Japanese population (10).

Given that little is known about premature mortality due to hematological cancers, the present study applied the novel measure of ALSS to evaluate trends in premature mortality due to the 4 main types of hematological cancers in the Canadian population between 1980 and 2015.

METHODS

Study population

We obtained mortality data from the World Health Organization mortality database (11). During the study period, causes of death for Canadians were coded according to the *International Classification of Diseases, Ninth Revision* (ICD-9), from 1980–1999 and the *Tenth Revision* (ICD-10) from 2000 onwards. Deaths due to Hodgkin lymphoma were coded as 201 in ICD-9 and C81 in ICD-10. Deaths due to non-Hodgkin lymphoma were coded as 200 and 202 in ICD-9 and C82, C83, C84, C85, C86, and C96 in ICD-10. Deaths due to multiple myeloma were coded as 203 in ICD-9 and C88 and C90 in ICD-10. Deaths due to leukemia were coded as 204–208 in ICD-9 and C91, C92, C93, C94, C95 in ICD-10. We were able to conduct only a subanalysis of the different types of non-Hodgkin lymphoma and leukemia for the recent period of 2000–2015 because the disease types are not compatible between ICD-9 and ICD-10.

Statistical analyses

We calculated the ASRs per 100,000 people for deaths due to hematological cancers using the direct method of standardization according to the World Standard Population (12). We calculated YLL according to the life-table method, which was described in the Global Burden of Disease Project (13, 14). Briefly, YLL is calculated by multiplying the number of deaths with the sex- and age-specific life expectancy obtained from respective Canadian life tables, which are based upon 3 years of data centered on census years (15). Seven versions of life tables were used to calculate the YLL in this study: the 1980–1982 life tables for 1980–1984, the 1985–1987 life tables for 1985–1989, the 1990–1992 life tables for 1990–1994, the 1995–1997 life tables for 1995–1999, the 2000–2002 life tables for 2000–2004, the 2005–2007 life tables for 2005–2009, and the 2010–2012 life tables for 2010–2015. During the study period, life expectancy at any given age increased in both men and women. Life expectancy at birth at the beginning of the study was 79 years among women and increased to 83 years at the end of the period. Similarly, life expectancy at birth increased from 72 to 79 years among men over the same period. The adjusted YLL rate per 1,000 people was calculated using the direct method of standardization according to the World Standard Population. The AYLL per decedent was estimated by dividing the total YLL by the total number of deaths (16). We calculated the ALSS, which provided an average percentage of life span shortened in relation to the expected life span among all decedents from hematological cancer. Details of the ALSS measure and its utility have been described previously (6–10). A general formula for the ALSS measure can be expressed as:

$$\mathrm{ALSS} = \frac{100 \times \sum d_i \times e_i}{\sum d_i \times (a_i + e_i)}$$

where d_i is number of deaths at age i; e_i is normative life expectancy at age i; a_i is age at death.

All statistical analyses were performed using SAS, version 9.3 (SAS Institute Inc., Cary, North Carolina). Trends in ASR and ALSS over time were depicted by the PROC SGPLOT with LOESS (locally estimated scatterplot smoothing) statement using a smoothing parameter of 0.2.

RESULTS

Tables 1 and 2 show the number of deaths and percentage of deaths according to age group for Hodgkin lymphoma, non-Hodgkin lymphoma, multiple myeloma, and leukemia from 1980 to 2015 among men and women, respectively. Over the study period, we observed that the number of deaths for all types of hematological cancers, except for Hodgkin lymphoma, increased among both sexes. Results also show a shift in distribution toward an older age of death for each type of hematological cancer. For instance, 9.8% of male deaths due to Hodgkin lymphoma occurred at 75 years of age or older in 1980, while this increased to 35.4% in 2015 (Table 1). Similarly, 37.5% of female deaths due to multiple myeloma occurred at 75 years of age or older in 1980, and this increased to 59.3% in 2015 (Table 2). Figure 1 shows the trends in ASRs over the study period. Although the ASRs fluctuated, there was a decrease in mortality rates at the end of the study period for all types of hematological cancers among both sexes. For men, the ASRs decreased from 0.9 to 0.2 per 100,000 men for Hodgkin lymphoma (Figure 1A); from 5.1 to 4.3 for non-Hodgkin lymphoma (Figure 1C); from 2.4 to 2.1 for multiple myeloma (Figure 1E); and from 7.3 to 4.2 for leukemia (Figure 1G). For women, the ASRs decreased from 0.5 to 0.1 per 100,000 women for Hodgkin lymphoma (Figure 1B); from 3.3 to 2.6 for non-Hodgkin lymphoma (Figure 1D); from 1.6 to 1.3 for multiple myeloma (Figure 1F); and from 4.3 to 2.4 for leukemia (Figure 1H).

Tables 3 and 4 summarize different metrics for premature mortality, including YLL (years), adjusted YLL rate (years per 1,000 people), and AYLL (years per decedent) for Hodgkin lymphoma, non-Hodgkin lymphoma, multiple myeloma, and leukemia from 1980 to 2015 among men and women, respectively. Overall, the total YLL increased for all types of hematological cancers over time, except Hodgkin lymphoma. For instance, there was an increase in YLL for leukemia among men from 19,020 years of life in 1980 to 22,224 in 2015 (Table 3) in accordance with the number of deaths increasing from 930 to 1,548 during that period (Table 1). We observed decreases in adjusted YLL rates with respect to any type of hematological cancers in

Table 1. Number of Deaths and Distribution According to Age Group for Hodgkin Lymphoma, Non-Hodgkin Lymphoma, Multiple Myeloma, and Leukemia among Men in Canada, 1980–2015

Year	Hodgkin				Non-Hodgkin				Multiple Myeloma				Leukemia			
	Distribution (%) of Deaths by Age Group, years			No. of Deaths	Distribution (%) of Deaths by Age Group, years			No. of Deaths	Distribution (%) of Deaths by Age Group, years			No. of Deaths	Distribution (%) of Deaths by Age Group, years			No. of Deaths
	<50	50–74	≥75		<50	50–74	≥75		<50	50–74	≥75		<50	50–74	≥75	
1980	51.2	39.0	9.8	123	20.9	54.2	24.9	670	5.7	62.2	32.1	315	23.9	45.6	30.5	930
1981	39.2	46.9	13.8	130	20.7	53.9	25.4	673	4.7	60.1	35.2	341	24.4	47.8	27.8	874
1982	45.8	38.1	16.1	118	14.3	56.8	28.8	676	3.7	62.8	33.5	352	22.1	47.7	30.1	926
1983	44.9	40.8	14.3	147	16.6	57.7	25.7	743	3.7	63.7	32.6	350	26.4	42.7	30.9	878
1984	51.9	31.8	16.3	129	13.7	57.4	28.8	721	4.4	59.9	35.7	367	23.0	44.9	32.1	952
1985	45.4	42.6	12.0	108	17.9	55.7	26.5	756	5.9	61.9	32.2	391	20.4	46.9	32.7	1,025
1986	44.9	43.2	11.9	118	16.5	54.5	29.0	829	4.8	60.2	35.1	442	21.3	47.6	31.1	983
1987	53.4	32.0	14.6	103	14.2	56.7	29.1	783	5.2	56.5	38.3	423	20.7	44.4	34.9	1,023
1988	44.9	48.0	7.1	98	16.4	56.8	26.7	894	4.0	58.0	38.0	421	18.1	45.3	36.6	1,041
1989	43.0	45.0	12.0	100	15.6	54.9	29.5	898	4.5	55.6	39.9	446	19.2	44.4	36.3	972
1990	34.7	39.8	25.5	98	14.9	53.1	32.0	940	3.8	57.3	38.9	499	16.8	47.4	35.8	1,005
1991	48.5	32.0	19.6	97	15.2	54.0	30.8	994	5.8	52.2	42.0	521	16.5	43.6	39.9	1,090
1992	50.5	35.8	13.7	95	16.8	54.7	28.5	1,032	3.5	57.2	39.2	451	16.4	46.1	37.5	1,018
1993	44.0	38.5	17.6	91	14.0	55.4	30.6	989	2.7	55.1	42.2	510	16.7	45.9	37.4	1,086
1994	37.3	47.0	15.7	83	14.2	54.2	31.6	1,106	5.4	55.6	39.1	558	15.7	46.0	38.3	1,050
1995	39.3	35.7	25.0	84	12.7	54.6	32.7	1,126	3.6	61.1	35.2	576	15.5	44.5	39.9	1,089
1996	40.3	43.3	16.4	67	13.8	54.6	31.6	1,161	5.0	55.9	39.1	562	13.5	46.0	40.6	1,186
1997	47.0	33.7	19.3	83	11.8	55.9	32.3	1,212	3.5	54.8	41.7	575	14.8	47.5	37.7	1,096
1998	40.6	39.1	20.3	69	12.6	53.9	33.5	1,282	4.5	54.4	41.2	605	16.0	46.4	37.6	1,178
1999	40.5	40.5	19.0	84	12.8	51.7	35.5	1,349	3.6	54.5	41.8	552	14.2	45.1	40.7	1,194
2000	35.9	51.3	12.8	78	11.3	55.0	33.7	1,350	2.2	50.7	47.1	580	14.5	45.0	40.5	1,190

Table continues

Table 1. Continued

Year	Hodgkin				Non-Hodgkin				Multiple Myeloma				Leukemia			
	Distribution (%) of Deaths by Age Group, years			No. of Deaths	Distribution (%) of Deaths by Age Group, years			No. of Deaths	Distribution (%) of Deaths by Age Group, years			No. of Deaths	Distribution (%) of Deaths by Age Group, years			No. of Deaths
	<50	50–74	≥75		<50	50–74	≥75		<50	50–74	≥75		<50	50–74	≥75	
2001	34.7	44.4	20.8	72	10.0	52.0	38.0	1,410	3.4	48.6	48.0	592	11.5	44.8	43.8	1,204
2002	33.9	42.4	23.7	59	9.1	54.1	36.9	1,354	3.6	48.8	47.7	646	11.7	41.7	46.6	1,201
2003	33.9	40.7	25.4	59	10.9	48.8	40.3	1,382	3.3	50.4	46.3	668	11.5	43.3	45.1	1,308
2004	30.1	50.7	19.2	73	9.2	51.4	39.4	1,399	4.0	49.7	46.3	668	11.3	41.7	47.0	1,309
2005	26.3	46.3	27.5	80	8.2	49.8	42.0	1,364	4.7	50.7	44.7	687	11.3	43.7	45.0	1,308
2006	36.5	41.9	21.6	74	8.1	49.4	42.5	1,335	3.4	49.1	47.5	638	9.0	45.8	45.2	1,282
2007	27.6	34.2	38.2	76	7.6	49.9	42.5	1,438	3.3	50.9	45.8	690	9.1	42.1	48.8	1,333
2008	37.3	39.0	23.7	59	7.4	48.7	44.0	1,397	3.7	52.1	44.2	629	9.6	43.2	47.3	1,360
2009	32.4	36.6	31.0	71	6.6	48.9	44.6	1,432	1.8	50.5	47.7	736	8.6	42.5	48.9	1,390
2010	33.3	44.0	22.6	84	7.7	46.1	46.2	1,385	2.0	44.2	53.8	697	8.0	42.1	49.9	1,358
2011	29.7	48.6	21.6	74	6.5	45.9	47.6	1,435	2.5	47.8	49.7	768	6.7	42.4	50.9	1,437
2012	28.6	51.9	19.5	77	5.2	46.2	48.6	1,454	2.9	48.9	48.2	824	7.2	42.5	50.3	1,500
2013	23.4	48.4	28.1	64	6.0	44.3	49.7	1,483	2.1	49.3	48.6	797	5.6	40.8	53.6	1,581
2014	22.9	48.6	28.6	70	5.6	43.5	50.9	1,531	3.4	48.4	48.2	851	6.0	41.0	53.0	1,623
2015	18.5	46.2	35.4	65	5.3	43.1	51.5	1,618	1.9	45.8	52.3	837	6.4	39.9	53.7	1,548

Table 2. Number of Deaths and Distribution According to Age Group for Hodgkin Lymphoma, Non-Hodgkin Lymphoma, Multiple Myeloma, and Leukemia among Women in Canada, 1980–2015

Year	Hodgkin				Non-Hodgkin				Multiple Myeloma				Leukemia			
	Distribution (%) of Deaths by Age Group, years			Deaths	Distribution (%) of Deaths by Age Group, years			Deaths	Distribution (%) of Deaths by Age Group, years			Deaths	Distribution (%) of Deaths by Age Group, years			Deaths
	<50	50–74	≥75		<50	50–74	≥75		<50	50–74	≥75		<50	50–74	≥75	
1980	50.7	32.4	16.9	71	12.7	50.2	37.1	536	4.6	57.9	37.5	261	26.4	38.6	35.0	651
1981	45.1	40.8	14.1	71	11.6	50.5	38.0	545	3.7	57.4	38.9	296	24.7	39.2	36.2	661
1982	25.3	43.0	31.6	79	12.2	54.8	33.1	608	3.4	55.8	40.8	326	21.3	42.3	36.4	690
1983	51.9	28.4	19.8	81	10.9	56.6	32.5	624	3.4	55.1	41.5	325	24.5	41.1	34.4	721
1984	36.7	46.8	16.5	79	12.7	50.7	36.7	608	5.5	44.7	49.8	329	22.2	39.0	38.8	721
1985	31.4	47.1	21.4	70	7.6	52.0	40.4	671	2.1	54.4	43.5	384	22.0	39.2	38.8	783
1986	46.6	28.8	24.7	73	10.9	52.4	36.7	700	3.1	56.9	39.9	383	21.3	38.4	40.3	718
1987	43.8	34.4	21.9	64	9.2	47.8	43.0	740	2.3	51.3	46.3	341	17.5	38.7	43.8	771
1988	44.8	25.4	29.9	67	10.9	49.7	39.4	723	2.0	55.4	42.7	410	17.0	39.9	43.1	812
1989	37.3	37.3	25.4	67	9.6	47.9	42.6	827	4.2	47.3	48.6	383	19.7	37.1	43.2	792
1990	32.8	39.1	28.1	64	9.0	47.9	43.1	846	3.5	51.8	44.7	425	17.7	39.3	43.0	812
1991	49.4	24.7	26.0	77	8.6	47.9	43.5	912	3.6	50.5	45.9	394	17.5	40.0	42.5	788
1992	46.0	28.6	25.4	63	9.7	47.1	43.2	905	3.4	50.4	46.1	464	15.7	39.7	44.6	846
1993	43.1	33.3	23.6	72	7.8	48.8	43.4	918	4.3	47.5	48.1	486	16.5	39.9	43.6	860
1994	31.9	19.1	48.9	47	9.1	50.1	40.8	964	4.4	46.9	48.8	480	14.5	40.2	45.3	813
1995	31.7	33.3	34.9	63	10.8	47.3	41.9	1,026	3.2	49.4	47.5	476	12.5	38.6	48.9	798
1996	31.7	23.3	45.0	60	10.1	45.3	44.6	1,038	3.0	51.3	45.7	497	16.6	36.2	47.1	889
1997	48.0	34.0	18.0	50	9.7	45.2	45.1	1,047	3.4	43.4	53.3	475	13.4	38.6	48.1	876
1998	26.5	38.8	34.7	49	8.2	45.2	46.6	1,118	3.1	46.3	50.6	449	12.3	38.0	49.7	860
1999	36.2	25.9	37.9	58	7.4	41.2	51.4	1,105	2.1	42.7	55.2	560	12.6	38.4	48.9	895

Table continues

Table 2. Continued

Year	Hodgkin				Non-Hodgkin				Multiple Myeloma				Leukemia			
	Distribution (%) of Deaths by Age Group, years			Deaths	Distribution (%) of Deaths by Age Group, years			Deaths	Distribution (%) of Deaths by Age Group, years			Deaths	Distribution (%) of Deaths by Age Group, years			Deaths
	<50	50–74	≥75		<50	50–74	≥75		<50	50–74	≥75		<50	50–74	≥75	
2000	30.0	28.0	42.0	50	8.5	44.9	46.6	1,192	2.1	43.8	54.1	525	13.2	33.9	52.9	858
2001	28.8	39.0	32.2	59	7.9	42.1	50.0	1,155	2.4	42.6	55.0	544	11.6	36.1	52.3	889
2002	43.9	26.8	29.3	41	6.9	43.1	50.0	1,185	2.9	42.3	54.9	596	12.0	31.7	56.3	876
2003	22.9	27.1	50.0	48	6.1	42.3	51.6	1,172	1.8	40.9	57.3	611	9.7	36.8	53.5	995
2004	29.6	27.8	42.6	54	7.7	41.2	51.1	1,261	3.1	39.9	56.9	576	10.2	35.8	54.0	947
2005	33.3	42.1	24.6	57	6.1	38.8	55.2	1,138	2.6	42.2	55.2	585	10.3	33.4	56.3	947
2006	28.3	24.5	47.2	53	5.1	37.7	57.3	1,158	3.8	41.7	54.5	583	9.4	35.1	55.5	999
2007	24.6	41.0	34.4	61	4.8	41.6	53.6	1,233	3.1	41.1	55.8	577	8.9	33.2	57.9	967
2008	19.0	38.1	42.9	42	3.9	39.5	56.5	1,166	2.5	41.2	56.3	590	10.5	34.9	54.6	1,035
2009	29.1	45.5	25.5	55	5.2	37.3	57.5	1,185	2.3	42.9	54.9	616	8.6	35.9	55.5	1,073
2010	35.8	30.2	34.0	53	4.0	37.8	58.2	1,147	1.4	40.7	57.9	592	9.0	33.0	58.0	1,015
2011	20.8	32.1	47.2	53	4.3	37.8	58.0	1,149	1.4	37.9	60.7	636	9.5	36.0	54.4	1,069
2012	24.0	38.0	38.0	50	4.7	35.4	59.9	1,213	2.5	34.1	63.4	631	7.4	36.5	56.0	1,142
2013	25.5	51.1	23.4	47	4.1	36.2	59.7	1,232	1.7	41.1	57.2	642	8.2	36.9	54.9	1,133
2014	20.8	41.5	37.7	53	3.5	37.2	59.3	1,196	0.5	41.7	57.8	659	9.7	31.0	59.3	1,160
2015	22.9	31.3	45.8	48	3.5	35.2	61.3	1,258	0.6	40.1	59.3	624	6.4	34.0	59.7	1,098

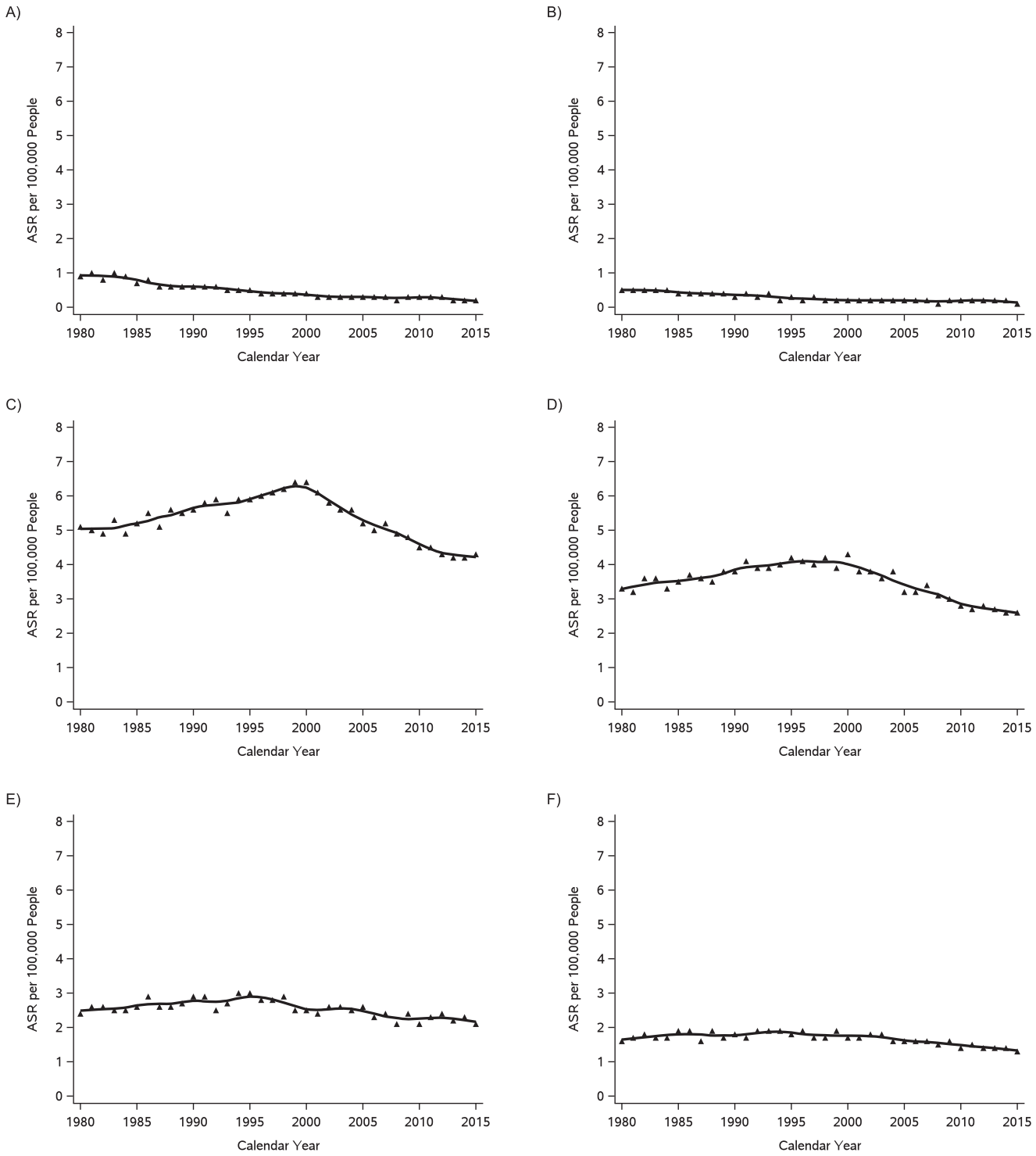

Figure 1 Continues

both sexes. For instance, YLL rates adjusted to the World Standard Population for Hodgkin lymphoma among women decreased from 0.17 to 0.05 years of life per 1,000 people (Table 4). AYLL also decreased over time for all types of hematological cancers in both sexes. Specifically, men with non-Hodgkin lymphoma lost an average of 19.1 years of life in 1980, which decreased to 14.1 years of life in 2015 (Table 3). Similarly, women with multiple myeloma lost an

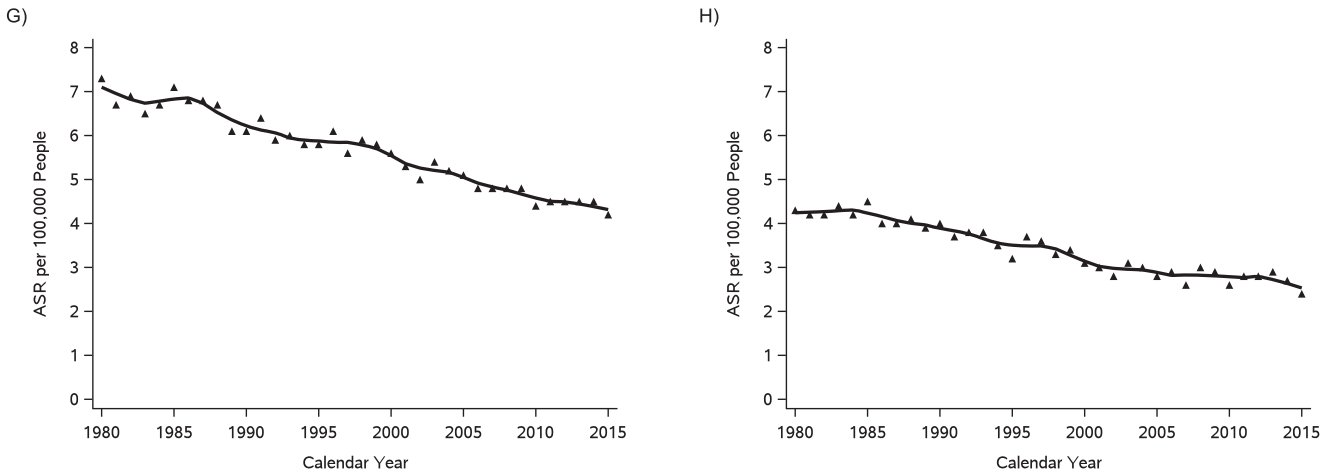

Figure 1. Trends of age-standardized rates (ASRs) for deaths due to Hodgkin lymphoma in men (A) and women (B); non-Hodgkin lymphoma in men (C) and women (D); multiple myeloma in men (E) and in women (F); and leukemia in men (G) and women (H) in Canada, 1980–2015.

average of 16.2 years of life in 1980, which decreased to13.7 years of life in 2015 (Table 4).

Trends of ALSS among decedents are depicted in Figure 2. In general, ALSS decreased over time for all types of hematological cancers in both sexes. Men with non-Hodgkin lymphoma lost an average of 23.7% of their life span in 1980, which decreased to 16.1% in 2015 (Figure 2C). Likewise, the life span of women with multiple myeloma was shortened by 18.7% in 1980, which decreased to 15.2% in 2015 (Figure 2F).

Table 5 shows the number of deaths, ASR of death, AYLL, and ALSS for the different types of non-Hodgkin lymphoma and leukemia in the years 2000, 2005, 2010, and 2015. From 2000 to 2015, we observed decreases in the ASR and AYLL values among most types. Results from the ALSS measure indicate steadily decreasing trends for all types of non-Hodgkin lymphoma and leukemia in both sexes. The greatest improvement in ALSS was observed in acute lymphocytic leukemia which improved by about 10 percentage points from 45.3% to 34.2% among men, and 37.3% to 28.6% among women, over the 15-year period. We observed smaller improvement for other types of leukemia. Likewise, the life span of patients with follicular lymphoma was prolonged by about 4 percentage points among men and 8 percentage points among women, whereas patients with nonfollicular lymphoma gained about 5 percentage points (men) and >3 percentage points (women). Patients with natural killer/T-cell lymphoma gained about 2 percentage points (both sexes) over the same period.

DISCUSSION

This study represents a comprehensive characterization of long-term premature mortality trends from hematological cancers in the Canadian population from 1980 to 2015. We observed decreasing trends in premature mortality, suggesting that the life span of hematological cancer patients is improving when compared with the life span of the general population. Results based on our new ALSS measure indicate that patients with leukemia lost an average of one-fourth of their life span at the beginning of the study period, whereas they lost less than one-fifth of their life span at the end of the study period (Figure 2). Comparing across all types, patients with Hodgkin lymphoma lost the largest portion of their life span, over 25% at the end of the study versus approximately 14%–17% caused by 3 other types in the same year (Figure 2). This observation was likely due to the tendency for Hodgkin lymphoma to occur in teenagers or young adults. The deceasing trends in ALSS for Hodgkin lymphoma from 36.9% to 25.0% in men (Figure 2A) and from 38.0% to 27.2% in women (Figure 2B) imply that life span of patients improved by about 11 percentage points over the course of the study.

Hematological malignancies mainly include lymphoma (Hodgkin and non-Hodgkin disease), multiple myeloma, and various forms of leukemia, such as acute lymphocytic leukemia, acute myelogenous leukemia, chronic lymphocytic leukemia, and chronic myelogenous leukemia. These diseases differ in terms of clinical characteristics, biological features, treatment approaches, and prognosis. Some occur more frequently among children while others are more common among adults. In the present study, we performed an analysis for all age groups. Accordingly, any survival gains from both childhood and adult hematological malignancies were all reflected in the ALSS calculation.

To date, mortality rate is one of the primary metrics in quantifying the health of populations. However, interests have expanded beyond whether or not a death has occurred. Researchers and decision makers are asking when or how early a death occurs ("premature mortality") in order to estimate the number of years a patient would have lived if death due to a specific condition did not take place. Such information can have societal and health-care policy

Table 3. Years of Life Lost, Adjusted Years of Life Lost Rate[a], and Average Years of Life Lost Due to Hodgkin Lymphoma, Non-Hodgkin Lymphoma, Multiple Myeloma, and Leukemia Among Men in Canada, 1980–2015

Year	Hodgkin			Non-Hodgkin			Multiple Myeloma			Leukemia		
	YLL	Adjusted YLL Rate	AYLL Per Decedent	YLL	Adjusted YLL Rate	AYLL Per Decedent	YLL	Adjusted YLL Rate	AYLL Per Decedent	YLL	Adjusted YLL Rate	AYLL Per Decedent
1980	3,517	0.25	28.6	12,818	1.01	19.1	4,284	0.33	13.6	19,020	1.56	20.5
1981	3,138	0.23	24.1	12,476	0.96	18.5	4,347	0.33	12.7	17,949	1.47	20.5
1982	3,152	0.22	26.7	11,414	0.85	16.9	4,503	0.34	12.8	18,183	1.43	19.6
1983	3,963	0.28	27.0	13,265	1.00	17.9	4,484	0.32	12.8	18,724	1.50	21.3
1984	3,624	0.26	28.1	11,646	0.84	16.2	4,705	0.33	12.8	18,628	1.43	19.6
1985	3,024	0.21	28.0	13,525	0.99	17.9	5,308	0.37	13.6	19,601	1.50	19.1
1986	3,184	0.21	27.0	14,289	0.99	17.2	5,687	0.39	12.9	19,283	1.45	19.6
1987	2,948	0.19	28.6	12,927	0.89	16.5	5,395	0.35	12.8	19,618	1.49	19.2
1988	2,665	0.17	27.2	15,640	1.04	17.5	5,217	0.33	12.4	18,544	1.34	17.8
1989	2,747	0.17	27.5	15,241	0.99	17.0	5,563	0.35	12.5	17,572	1.24	18.1
1990	2,355	0.15	24.0	15,812	1.00	16.8	6,604	0.40	13.2	18,399	1.26	18.3
1991	2,640	0.16	27.2	16,940	1.06	17.0	6,868	0.40	13.2	18,916	1.25	17.4
1992	2,658	0.17	28.0	18,007	1.09	17.4	5,971	0.35	13.2	17,748	1.16	17.4
1993	2,440	0.15	26.8	16,463	0.98	16.6	6,508	0.37	12.8	19,242	1.23	17.7
1994	2,038	0.12	24.6	18,525	1.07	16.7	7,465	0.41	13.4	18,128	1.16	17.3
1995	2,081	0.12	24.8	18,740	1.07	16.6	7,724	0.42	13.4	18,508	1.14	17.0
1996	1,759	0.10	26.2	19,803	1.11	17.1	7,595	0.41	13.5	19,496	1.17	16.4
1997	2,331	0.14	28.1	19,847	1.08	16.4	7,421	0.38	12.9	18,527	1.09	16.9
1998	1,756	0.11	25.5	20,922	1.12	16.3	7,901	0.40	13.1	20,518	1.20	17.4
1999	2,193	0.13	26.1	21,544	1.12	16.0	7,136	0.35	12.9	19,642	1.11	16.5
2000	2,118	0.12	27.1	22,330	1.14	16.5	7,311	0.34	12.6	20,642	1.17	17.3
2001	1,773	0.10	24.6	22,647	1.11	16.1	7,662	0.35	12.9	19,147	1.05	15.9
2002	1,501	0.08	25.4	21,338	1.02	15.8	8,248	0.36	12.8	18,797	1.00	15.7
2003	1,426	0.08	24.2	22,012	1.03	15.9	8,598	0.37	12.9	20,726	1.09	15.8
2004	1,681	0.09	23.0	21,887	0.98	15.6	8,671	0.37	13.0	20,084	1.01	15.3

Table continues

Table 3. Continued

Year	Hodgkin			Non-Hodgkin			Multiple Myeloma			Leukemia		
	YLL	Adjusted YLL Rate	AYLL Per Decedent	YLL	Adjusted YLL Rate	AYLL Per Decedent	YLL	Adjusted YLL Rate	AYLL Per Decedent	YLL	Adjusted YLL Rate	AYLL Per Decedent
2004	1,681	0.09	23.0	21,887	0.98	15.6	8,671	0.37	13.0	20,084	1.01	15.3
2005	1,764	0.09	22.1	21,432	0.93	15.7	9,464	0.39	13.8	21,149	1.03	16.2
2006	2,000	0.11	27.0	20,857	0.90	15.6	8,682	0.35	13.6	20,046	0.95	15.6
2007	1,640	0.08	21.6	22,256	0.92	15.5	9,507	0.37	13.8	20,314	0.95	15.2
2008	1,455	0.07	24.7	21,607	0.89	15.5	8,952	0.34	14.2	21,224	0.99	15.6
2009	1,745	0.09	24.6	20,914	0.81	14.6	9,670	0.35	13.1	21,291	0.98	15.3
2010	2,264	0.11	27.0	21,818	0.83	15.8	9,242	0.32	13.3	21,256	0.89	15.7
2011	1,904	0.09	25.7	21,750	0.80	15.2	10,400	0.35	13.5	21,575	0.85	15.0
2012	2,015	0.09	26.2	21,470	0.76	14.8	11,413	0.38	13.9	22,774	0.90	15.2
2013	1,442	0.06	22.5	21,695	0.75	14.6	10,908	0.35	13.7	22,368	0.82	14.1
2014	1,540	0.07	22.0	22,303	0.77	14.6	11,732	0.37	13.8	23,096	0.83	14.2
2015	1,383	0.06	21.3	22,868	0.75	14.1	10,841	0.32	13.0	22,224	0.82	14.4

Abbreviations: AYLL, average years of life lost; YLL, years of life lost.
[a] Adjusted YLL rate per 1,000 population, to the World Standard Population (12).

Table 4. Years of Life Lost, Adjusted Years of Life Lost Rate[a], and Average Years of Life Lost Due to Hodgkin Lymphoma, Non-Hodgkin Lymphoma, Multiple Myeloma, and Leukemia Among Women in Canada, 1980–2015

Year	Hodgkin			Non-Hodgkin			Multiple Myeloma			Leukemia		
	YLL	Adjusted YLL Rate	AYLL Per Decedent	YLL	Adjusted YLL Rate	AYLL Per Decedent	YLL	Adjusted YLL Rate	AYLL Per Decedent	YLL	Adjusted YLL Rate	AYLL Per Decedent
1980	2,257	0.17	31.8	10,004	0.71	18.7	4,220	0.28	16.2	15,956	1.32	24.5
1981	2,228	0.16	31.4	10,094	0.69	18.5	4,639	0.29	15.7	15,925	1.23	24.1
1982	1,906	0.13	24.1	11,489	0.78	18.9	4,947	0.30	15.2	15,457	1.16	22.4
1983	2,676	0.18	33.0	11,471	0.74	18.4	4,818	0.28	14.8	17,180	1.29	23.8
1984	2,328	0.15	29.5	11,279	0.72	18.6	4,686	0.28	14.2	16,134	1.18	22.4
1985	1,852	0.12	26.5	11,453	0.71	17.1	5,694	0.32	14.8	18,060	1.34	23.1
1986	2,276	0.15	31.2	12,992	0.82	18.6	5,964	0.34	15.6	15,580	1.12	21.7
1987	1,992	0.13	31.1	12,625	0.74	17.1	5,089	0.27	14.9	15,602	1.07	20.2
1988	1,984	0.13	29.6	13,036	0.76	18.0	6,207	0.33	15.1	16,012	1.05	19.7
1989	1,934	0.12	28.9	13,840	0.75	16.7	5,685	0.29	14.8	16,191	1.05	20.4
1990	1,727	0.10	27.0	14,700	0.81	17.4	6,406	0.32	15.1	16,623	1.06	20.5
1991	2,448	0.15	31.8	15,671	0.83	17.2	6,014	0.31	15.3	15,954	0.98	20.2
1992	2,019	0.13	32.0	15,764	0.83	17.4	7,061	0.34	15.2	16,295	0.96	19.3
1993	2,150	0.13	29.9	15,543	0.78	16.9	7,261	0.34	14.9	17,178	1.01	20.0
1994	1,099	0.06	23.4	16,760	0.83	17.4	7,140	0.33	14.9	15,438	0.88	19.0
1995	1,610	0.09	25.6	18,062	0.91	17.6	6,876	0.31	14.4	13,980	0.75	17.5
1996	1,386	0.07	23.1	17,582	0.85	16.9	7,316	0.33	14.7	17,187	1.00	19.3
1997	1,610	0.10	32.2	17,784	0.84	17.0	6,587	0.28	13.9	16,316	0.92	18.6
1998	1,158	0.06	23.6	18,540	0.86	16.6	6,542	0.29	14.6	15,431	0.82	17.9
1999	1,535	0.08	26.5	17,132	0.74	15.5	7,627	0.31	13.6	16,012	0.86	17.9
2000	1,318	0.08	26.4	20,084	0.88	16.8	7,347	0.29	14.0	15,069	0.75	17.6
2001	1,519	0.09	25.7	18,729	0.80	16.2	7,421	0.28	13.6	15,135	0.76	17.0
2002	1,280	0.07	31.2	18,867	0.78	15.9	8,252	0.30	13.8	14,805	0.70	16.9
2003	1,105	0.06	23.0	18,372	0.75	15.7	8,128	0.29	13.3	15,996	0.71	16.1
2004	1,353	0.08	25.1	20,185	0.79	16.0	7,946	0.28	13.8	15,810	0.72	16.7

Table continues

Table 4. Continued

Year	Hodgkin			Non-Hodgkin			Multiple Myeloma			Leukemia		
	YLL	Adjusted YLL Rate	AYLL Per Decedent	YLL	Adjusted YLL Rate	AYLL Per Decedent	YLL	Adjusted YLL Rate	AYLL Per Decedent	YLL	Adjusted YLL Rate	AYLL Per Decedent
2005	1,602	0.09	28.1	17,239	0.64	15.1	8,251	0.29	14.1	15,784	0.72	16.7
2006	1,258	0.06	23.7	17,171	0.61	14.8	8,518	0.30	14.6	16,299	0.71	16.3
2007	1,453	0.07	23.8	18,718	0.66	15.2	8,347	0.28	14.5	15,032	0.60	15.5
2008	867	0.04	20.6	17,144	0.59	14.7	8,388	0.27	14.2	17,779	0.76	17.2
2009	1,458	0.07	26.5	17,478	0.60	14.7	8,838	0.29	14.3	17,235	0.68	16.1
2010	1,448	0.07	27.3	17,151	0.56	15.0	8,397	0.25	14.2	16,753	0.68	16.5
2011	1,161	0.05	21.9	17,118	0.54	14.9	8,996	0.26	14.1	18,230	0.74	17.1
2012	1,118	0.05	22.4	17,803	0.55	14.7	8,745	0.25	13.9	18,474	0.67	16.2
2013	1,204	0.05	25.6	18,107	0.56	14.7	9,259	0.26	14.4	19,417	0.80	17.1
2014	1,250	0.05	23.6	17,047	0.50	14.3	9,263	0.25	14.1	19,087	0.74	16.5
2015	1,155	0.05	24.1	17,701	0.50	14.1	8,566	0.22	13.7	17,151	0.60	15.6

Abbreviations: AYLL, average years of life lost; YLL, years of life lost.
[a] Adjusted YLL rate per 1,000 population, to the World Standard Population (12).

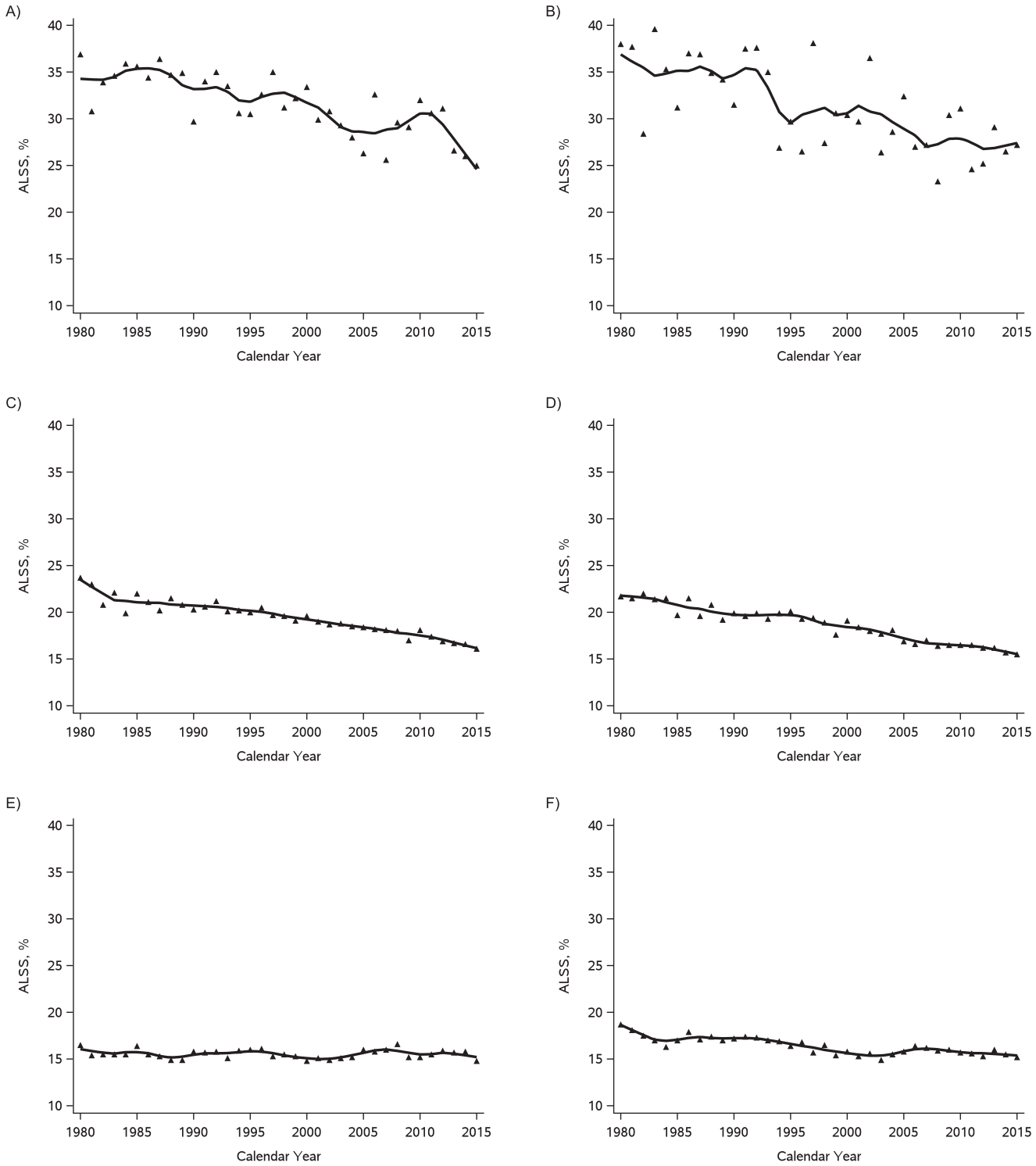

Figure 2 Continues

implications. In the present study, we provide several measures for premature mortality alongside the conventional mortality rate used to quantify the health of populations. YLL was calculated using the life-table method, which has been used within the Global Burden of Disease project (13, 17–19). However, comparability challenges persist even among studies applying the life-table method because life expectancy of the general population often improves with

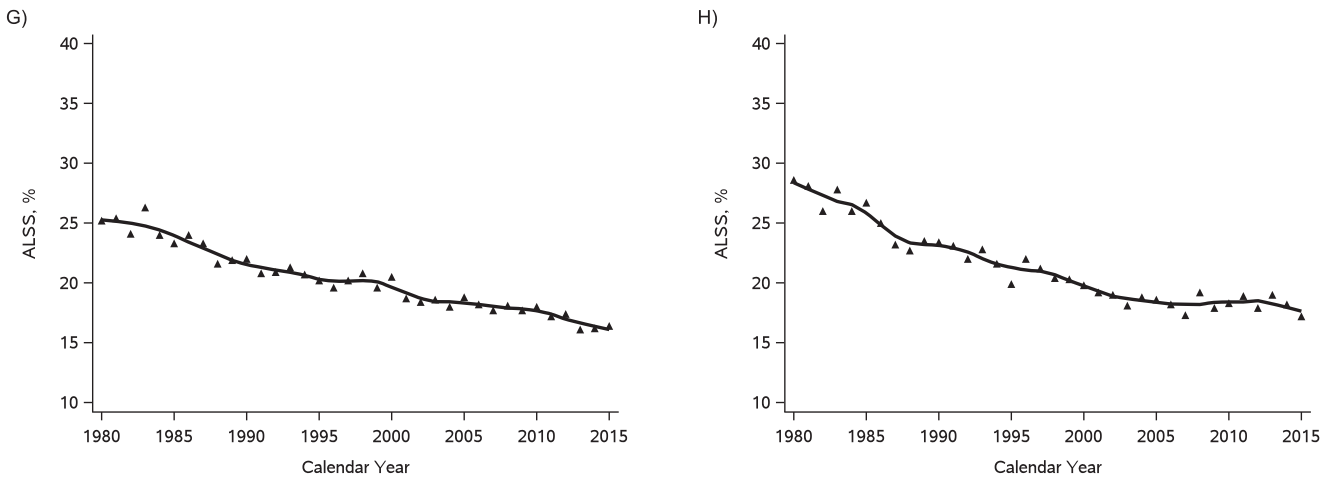

Figure 2. Trends of average life span shortened (ALSS) among decedents for Hodgkin lymphoma in men (A) and women (B); non-Hodgkin lymphoma in men (C) and women (D); multiple myeloma in men (E) and women (F); and leukemia in men (G) and women (H) in Canada, 1980–2015.

time. For instance, our study showed that men in 1980 died of non-Hodgkin lymphoma approximately 19.1 years before expectation, whereas men in 2015 died approximately 14.1 years before expectation, as the AYLL measure indicated (Table 3). These numbers suggest an absolute survival gain of about 5 years; however, the gain might be about 12 years of life because life expectancy at birth increased by 7 years over the same period of time, from 72 to 79 years, according to the Canadian life tables for men. Therefore, interpretation of trends in AYLL over time often requires a consideration of changes in the national life tables. In contrast, ALSS was calculated as a ratio of life lost in relation to the expected life span for each calendar year. In this way, the ALSS inherently takes into account changes in life tables when estimating expected life span of patients and uses it as the denominator in the ALSS calculation. Therefore, a health-decision maker does not need to consider changes in the national life tables when interpreting the ALSS results.

In the present study, we were able to conduct subanalyses of the different types of non-Hodgkin lymphoma and leukemia only for recent years, from 2000 through 2015, because of incompatibility between ICD-9 and ICD-10. In general, we observed decreasing trends in ALSS for all types of non-Hodgkin lymphoma and leukemia. In particular, the largest improvement, by about 10 percentage points of life span, was observed for acute lymphocytic leukemia. We also noted a limitation of the data regarding documentation practices on death certificates. Specifically, a large proportion of unspecified non-Hodgkin lymphoma likely reflected the inability to determine the underlying cause of death in some cases and consequently resulted in a smaller proportion of deaths due to follicular lymphoma and nonfollicular lymphoma.

Favorable trends in premature mortality observed in the present study could be a result of multiple factors. These include advances in diagnosis and treatment, as well as the impact of demographic changes over the entire Canadian population. First, innovations in diagnostic methods have allowed for more refined definition of the types of hematological malignancies. The incorporation of flow cytometry and molecular and genetic studies, as well as clinical presentation with traditional morphological and immunohistochemical features have identified types of these cancers with specific presentations. These changes were first described in the REAL (20) classification and have been further updated in the *World Health Organization Classification of Tumours of Hematopoietic and Lymphoid Tissues* (21). These improvements have resulted in more accurate diagnosis, which in turn allows for specific and more effective treatments to be developed for these entities. Second, we hypothesized that advances in treatments over the past several decades might contribute to the gain in life span of patients with hematological malignancies. Specifically, the treatment of hematological malignancies has evolved to include a combination of modalities and targeted therapies with new effective agents. Examples consist of tyrosine kinase inhibitors for chronic myelogenous leukemia (22), monoclonal antibodies for non-Hodgkin lymphoma and myeloma (23, 24), and proteasome inhibitors and immunomodulatory drugs for myeloma. A UK study of long-term survival after treatment of Hodgkin lymphoma showed that 15-year survival has increased from 57% to 74% between 1983–1992 and 1993–2002 (23). This improvement in survival was likely due to the introduction of doxorubicin in the early 1980s, as well as better approaches to the management of toxicities, such as neutropenic sepsis (23). Further advances in the survival of Hodgkin disease are seen from the application of more aggressive chemotherapy regimens for advanced disease, the routine use of stem-cell transplantation for relapses, and the introduction of novel agents such as brentuximab vedotin and checkpoint inhibitors. Last, the aging of the entire population over recent decades could play a role in the long-term trends of premature mortality. With the increasing life span of the entire Canadian population, more

Table 5. Number of Deaths, Age-Standardized Rate, Average Years of Life Lost, and Average Life Span Shortened Among Deaths Caused by Types of Non-Hodgkin Lymphoma and Leukemia in Canada in 2000, 2005, 2010, and 2015

Cancer Type	ICD- 10 Code	No. of Deaths				ASR per 100,000[a]				AYLL, years[b]				ALSS, %[c]			
		2000	2005	2010	2015	2000	2005	2010	2015	2000	2005	2010	2015	2000	2005	2010	2015
Among Men																	
Non-Hodgkin lymphoma																	
Follicular lymphoma	C82	16	34	32	57	0.07	0.14	0.11	0.16	16.8	18.8	17.5	14.2	20.2	22.3	20.5	16.3
Nonfollicular lymphoma	C83	143	162	261	338	0.70	0.62	0.87	0.93	18.9	16.5	16.6	15.5	22.7	19.4	19.2	17.8
NK/T-cell lymphoma[d]	C84, C86	38	68	58	110	0.19	0.28	0.22	0.33	19.3	18.7	22.6	18.3	23.0	22.1	26.6	21.3
Other non-Hodgkin lymphoma		1,153	1,100	1,034	1,113	5.41	4.16	3.28	2.86	16.1	15.3	15.1	13.3	19.2	17.9	17.3	15.1
Leukemia																	
Acute lymphocytic leukemia	C91.0	81	74	67	76	0.49	0.43	0.34	0.32	36.5	35.7	33.5	28.8	45.3	43.4	39.8	34.2
Chronic lymphocytic leukemia	C91.1	275	327	370	325	1.20	1.20	1.11	0.78	11.2	12.6	12.2	11.0	12.9	14.5	13.8	12.3
Acute myelogenous leukemia	C92.0	314	380	464	611	1.53	1.53	1.57	1.73	18.9	17.8	17.3	15.7	22.7	21.1	20.1	18.1
Chronic myelogenous leukemia	C92.1	125	65	57	77	0.60	0.25	0.18	0.20	19.8	15.1	15.5	13.7	23.7	17.6	17.8	15.4
Other leukemia		395	462	400	459	1.82	1.71	1.23	1.16	15.6	14.4	14.0	12.6	18.4	16.5	15.9	14.3
Among Women																	
Non-Hodgkin lymphoma																	
Follicular lymphoma	C82	17	31	33	47	0.06	0.10	0.09	0.09	19.5	17.3	15.8	13.2	22.4	19.6	17.6	14.5
Non-follicular lymphoma	C83	108	105	185	204	0.42	0.33	0.50	0.45	18.2	16.6	16.8	15.5	20.8	18.7	18.7	17.2
NK/T-cell lymphoma[d]	C84, C86	28	39	50	66	0.11	0.12	0.16	0.18	21.9	17.3	21.2	20.1	25.1	19.4	24.0	22.6
Other non-Hodgkin lymphoma		1,039	963	879	941	3.68	2.68	2.07	1.86	16.5	14.8	14.2	13.4	18.7	16.6	15.6	14.7
Leukemia																	
Acute lymphocytic leukemia	C91.0	43	47	51	62	0.23	0.23	0.23	0.21	32.2	33.9	32.2	25.5	37.3	39.2	36.9	28.6
Chronic lymphocytic leukemia	C91.1	178	231	186	220	0.53	0.51	0.35	0.35	10.8	10.0	10.6	10.2	11.9	10.8	11.5	11.0
Acute myelogenous leukemia	C92.0	238	279	411	443	0.96	0.97	1.22	1.13	21.7	20.8	19.3	18.7	24.9	23.7	21.7	20.9
Chronic myelogenous leukemia	C92.1	78	53	49	48	0.27	0.17	0.11	0.09	16.6	17.4	13.8	13.3	18.7	19.5	15.1	14.4
Other leukemia		321	337	318	325	1.08	0.94	0.74	0.66	16.5	15.3	14.2	13.6	18.6	17.1	15.6	14.8

Abbreviations: ALSS, average life span shortened; ASR, age-standardized rate; AYLL, average years of life lost; ICD-10, *International Classification of Diseases*, *Tenth Revision*.

[a] Age-standardized rate per 100,000 population, to the World Standard Population (12).

[b] AYLL in years per decedent.

[c] ALSS in percentage among decedents.

[d] Natural killer/T-cell lymphoma.

patients are diagnosed with hematological malignancies in the older age groups because of a larger proportion of elderly people. This change in demographics will contribute less to an overall YLL while the number of deaths could rise with time. As expected, upon adjustment to the World Standard Population, decreasing trends in YLL rates were observed in both sexes. Furthermore, we observed steadily decreasing trends in AYLL and ALSS measures for all types of hematological cancers (see Tables 3 and 4).

The strength of this study was the use of the novel ALSS measure in assessing premature mortality. This novel measure provides a strategy to examine changes in premature mortality over time. Indeed, interpretation of ALSS results is rather straightforward. According to Figure 2C, health-decision makers can state something like that life span of men with non-Hodgkin lymphoma was prolonged by approximately 8 percentage points at the end of the study as the ALSS decreased from 23.7% to 16.1%. Another strength of this study is that it represents the first comprehensive analysis of long-term trends in premature mortality for all types of hematological cancers in the Canadian population. Conversely, there are several limitations. This is largely a descriptive analysis given that the study design did not allow us to investigate potential factors associated with changes in premature mortality. Another limitation is that description of new entities for non-Hodgkin lymphoma were primarily responsible for the discrepancy between ICD-9 and ICD-10 editions over the entire study period.

In conclusion, results from this study show that patients with hematological cancers have had their lives prolonged over a 35-year period, although life span gains varied slightly by types of hematological cancers. The favorable trend in premature mortality might be a proxy indicator of how effectively the health-care system has improved with respect to diagnosis and treatment of these cancers in Canada.

ACKNOWLEDGMENTS

Author affiliations: Surveillance and Reporting, Cancer Research & Analytics, Cancer Care Alberta, Alberta Health Services, Edmonton and Calgary, Canada (Truong-Minh Pham, Shuang Lu, Lorraine Shack); Alberta's Tomorrow Project, Cancer Research & Analytics, Cancer Care Alberta, Alberta Health Services, Calgary, Canada (Grace Shen-Tu); Department of Pharmacology, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Canada (Khanh Hoa Nguyen); Canadian VIGOUR Centre, Department of Medicine, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Canada (Douglas C. Dover); Department of Medicine, Cumming School of Medicine, University of Calgary, Calgary, Canada (Peter Duggan); and Department of Oncology, Cumming School of Medicine, University of Calgary, Calgary, Canada (Lorraine Shack, Winson Y. Cheung).

We are grateful to the World Health Organization and sincerely thank their staff for their efforts in collecting and monitoring the mortality database.

The content in this article is solely responsibility of the authors and the views of authors do not necessarily represent those of their affiliated organizations.

Conflict of interest: none declared.

REFERENCES

1. Yung L, Linch D. Hodgkin's lymphoma. *Lancet*. 2003; 361(9361):943–951.
2. Armitage JO, Gascoyne RD, Lunning MA, et al. Non-Hodgkin lymphoma. *Lancet*. 2017;390(10091):298–310.
3. Palumbo A, Anderson K. Multiple myeloma. *N Engl J Med*. 2011;364(11):1046–1060.
4. Grigoropoulos NF, Petter R, Van 't Veer MB, et al. Leukaemia update. Part 1: diagnosis and management. *BMJ*. 2013;346:f1660.
5. Canadian Cancer Society. Canadian Cancer Statistics 2017. Toronto, Canada: Canadian Cancer Society; 2017. http://www.cancer.ca/~/media/cancer.ca/CW/cancer%20information/cancer%20101/Canadian%20cancer%20statistics/Canadian-Cancer-Statistics-2017-EN.pdf. Accessed April 15, 2020.
6. Pham TM, Sikdar KC, Kaposhi B, et al. Premature mortality due to breast cancer among Canadian women: an analysis of a 30-year period from 1980 through 2010. *Eur J Public Health*. 2018;28(2):348–352.
7. Pham TM, Sikdar KC, Cheung WY, et al. Premature mortality due to malignancies of the central nervous system in Canada, 1980–2010. *Neuroepidemiology*. 2018;50(3–4): 195–200.
8. Atchison KM, Pham TM, Sikdar KC, et al. Premature deaths due to head and neck cancers in Canada: a nationwide analysis from 1980 to 2010. *Laryngoscope*. 2020;130(4): 911–917.
9. Pham TM, Shack L, Cheung WY. Introduction of a novel measure of premature mortality caused by chronic conditions: real-world examples from prostate and testis cancers in Canada, 1980–2015. *Ann Epidemiol*. 2019;37:81–83.
10. Pham TM, Kubo T, Fujino Y, et al. Premature mortality due to malignancies of the kidney and bladder in Japan, 1980–2010. *J Epidemiol*. 2019;29(12):464–470.
11. World Health Organization. WHO statistical information system. WHO mortality database. http://www.who.int/healthinfo/mortality_data/en/. Accessed March 25, 2020.
12. Segi M. *Cancer Mortality for Selected Sites In 24 Countries*. Nagoya, Japan: Department of Public Health, Tohoku University School of Medicine; 1960.
13. Murray CJ, Lopez AD. *The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability From Diseases, Injuries, and Risk Factors in 1990 and Projected to 2020*. Boston, MA: Harvard School of Public Health on behalf of the World Health Organization and World Bank; 1996.
14. Feigin VL, Roth GA, Naghavi M, et al. Global burden of stroke and risk factors in 188 countries, during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet Neurol*. 2016;15(9):913–924.
15. Statistics Canada. Life tables, Canada, provinces and territories. https://www150.statcan.gc.ca/n1/en/catalogue/84-537-X. Accessed on June 10, 2019.
16. Burnet NG, Jefferies SJ, Benson RJ, et al. Years of life lost (YLL) from cancer is an important measure of population burden—and should be considered when allocating research funds. *Br J Cancer*. 2005;92(2):241–245.

17. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. *Lancet*. 1997;349(9064):1498–1504.
18. Global Burden of Disease Study Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2015; 386(9995):743–800.
19. Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. *Lancet*. 1997; 349(9061):1269–1276.
20. Harris NL, Jaffe ES, Stein H, et al. A revised European-American classification of lymphoid neoplasms: a proposal from the International Lymphoma Study Group. *Blood*. 1994; 84(5):1361–1392.
21. Werdlow SH, Campo E, Harris NL, et al. *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues*. 4th ed. Vol. 2. Lyon, France: WHO Press; 2017.
22. Shah A, Andersson TM, Rachet B, et al. Survival and cure of acute myeloid leukaemia in England, 1971–2006: a population-based study. *Br J Haematol*. 2013;162(4):509–516.
23. Bessell EM, Bouliotis G, Armstrong S, et al. Long-term survival after treatment for Hodgkin's disease (1973–2002): improved survival with successive 10-year cohorts. *Br J Cancer*. 2012;107(3):531–536.
24. DeVita VT Jr, Chu E. A history of cancer chemotherapy. *Cancer Res*. 2008;68(21):8643–8653.