

APPENDIX 1 – Supplementary Material

Supplementary Table S1. Cancer definitions using ICD-O-3

Cancer type	ICD-O-3 code
All cancers	C00.0–C80.9
Anus ^{2,5}	C21
Bladder	C67
Brain	C70-C72
Breast	C50
Cervix ^{1,5}	C53
Colorectal	C18–C20, C26.0
Esophagus	C15
Hodgkin lymphoma ^{3,4}	Histologies 9650-9667
Kaposi sarcoma ^{1,3}	Histology 91403
Kidney	C64 - C65
Larynx ⁸	C32
Leukemia	C42
Liver ^{2,6}	C22
Lung	C34
Malignant neoplasm of other and unspecified male genital organs ^{2,5,9}	C63
Melanoma of the skin	C44 with histologies 8720–8790
Multiple myeloma	Histologies 9731–9732, 9734
Nasopharynx ^{2,4}	C11
Non-Hodgkin lymphoma ^{1, 4}	Histologies 9590–9597, 967-972, 9735, 9737, 9738
Oral cavity & pharynx ^{2,5}	C00–C00.9, C01.9-C02.9, C03-C11, C12.9, C13, C14.0, C14.2, C14.8
Ovary	C56.9
Pancreas	C25
Penis ^{2,5}	C60
Prostate	C61.9
Stomach ^{2,7}	C16
Testis	C62
Thyroid	C73.9
Uterus	C54-C55
Vagina ^{2,5}	C52
Vulva ^{2,5}	C51

ICD-O-3=International Classification of Disease for Oncology, Third Edition ICD-10=International Statistical Classification of Diseases and Related Health Problems, Tenth Version 2016. All cancer types exclude basal cell and squamous cell skin cancers. Classification of infection-related cancer groupings was based on the IARC monograph volume 100B, and then selected those sites where IARC deemed there was sufficient epidemiological evidence in humans. (IARC Monograph Volume 100B. Biological Agents. 2012; Bouvard et al. Lancet Oncology. 2009)

Acronyms: HBV/HCV – hepatitis B and C viruses; HPV – human papillomavirus; EBV – Epstein-Barr virus; HHV-8 – human herpesvirus-8

¹AIDS-defining cancers. Cervical cancer was not included in the infection-related NADC classification as it is part of the ADC classification.

²Infection-related non-AIDS defining cancers

³HHV-8-associated cancer

⁴EBV-associated cancer

⁵HPV-associated cancers

⁶HBV/HCV-associated cancer

⁷H. Pylori-associated cancer

⁸The IARC Working Group considered that the epidemiological evidence was inconclusive to confirm the role of HPV in cancer of the larynx (IARC Monograph Volume 100B. Biological Agents. 2012)

⁹Considered part of HPV-related anogenital classification

Supplementary Table S2. Site-specific incident cancers diagnosed among people with and without HIV in Ontario, Canada, 1996-2020

Specific cancer site, n (%)	Cancers diagnosed among people with HIV	Cancers diagnosed among people without HIV	Total
Any cancer	1534 (100)	903 (100)	2437 (100)
Non-Hodgkin lymphoma ³	305 (19.9)	37 (4.1)	342 (14.0)
Kaposi sarcoma ³	235-241	<6	241 (9.9)
Lung	121 (7.9)	98 (10.8)	219 (9.0)
Prostate	116 (7.6)	186 (20.6)	302 (12.4)
Anus ³	106-112	<6	112 (4.6)
Colorectal	80 (5.2)	106 (11.7)	186 (7.6)
Liver ³	49 (3.2)	19 (2.1)	68 (2.8)
Hematopoietic and reticuloendothelial System (Leukemia)	49 (3.2)	46 (5.1)	95 (3.9)
Oral cavity and pharynx ³	49 (3.2)	20 (2.2)	69 (2.8)
Hodgkin lymphoma ³	46-52	<6	52 (2.1)
Breast	45 (2.9)	47 (5.2)	92 (3.8)
Melanoma of the skin	38 (2.5)	45 (5.0)	83 (3.4)
Kidney and renal pelvis	36 (2.3)	36 (4.0)	72 (2.9)
Thyroid	33 (2.2)	53 (5.9)	86 (3.5)
Male genitalia (penis ³ , testis)	19 (1.2)	12 (1.3)	31 (1.3)
Stomach ³	18 (1.2)	23 (2.5)	41 (1.7)
Cervix ³	15-21	<6	21 (0.9)
Brain/Central Nervous System	17 (1.1)	20 (2.2)	37 (1.5)
Female upper genital tract (corpus uteri, uterus, ovary, placenta)	17 (1.1)	14 (1.5)	31 (1.3)
Multiple myeloma	17 (1.1)	17 (1.9)	34 (1.4)
Bladder	16 (1.0)	21 (2.3)	37 (1.5)
Pancreas	15 (1.0)	18 (2.0)	33 (1.3)
Esophagus	13 (0.8)	9 (1.0)	22 (0.9)
Other connective and soft tissue ¹	10 (0.7)	8 (0.9)	18 (0.7)
Female lower genital tract (vulva, vagina) ³	7-13	<6	13 (0.5)
Biliary tract	9 (0.6)	8 (0.9)	17 (0.7)
Larynx	9 (0.6)	8 (0.9)	17 (0.7)
Lymph nodes	3-9	<6	9 (0.4)
All other cancer sites ²	16-33	22-40	55 (2.3)

¹ Includes blood vessel, bursa, cartilage, fascia, fat, ligament except uterine, lymphatic vessel, muscle, synovia, tendon (sheath). Excludes cartilage (of): articular (C40-C41), larynx (C32.3), nose (C30.0), connective tissue of

breast (C50.-), Kaposi sarcoma (C46.-), mesothelioma (C45.-), peripheral nerves and autonomic nervous system (C47.-), peritoneum (C48.-), retroperitoneum (C48.0)

²All other sites include: larynx (C32.-), other and unspecified parts of biliary tract (C24.-), other malignant neoplasms of skin (C44.-), lymph nodes (C77.-), nasal cavity and middle ear (C30.-), urethra (C68.-), retroperitoneum and peritoneum (C48.-), small intestine (C17.-), gallbladder (C23.-), heart (C38.-), adrenal gland (C74.-).

³Indicates cancers that have a known infectious cause

Note: Ranges are shown to suppress a small cell count (less than 6)

Supplementary Table S3. Cumulative incidence risk (%) by age 75 for people with and without HIV by calendar period, Ontario, Canada, 1996–2020

Cancer group	Cumulative risk, % (95% CI)					
	Calendar periods			Calendar periods		
	1996–2003	2004–2011	2012–2020	1996–2003	2004–2011	2012–2020
	People with HIV			People without HIV		
All cancers	34.1 (28.9-39.2)	35.5 (31.5-39.5)	28.0 (25.2-30.7)	32.8 (20.0-45.6)	28.8 (23.9-33.7)	26.4 (24.0-28.9)
Infection-unrelated cancer	18.7 (12.9-24.4)	19.4 (15.5-23.3)	18.6 (16.3-20.8)	28.4 (15.7-41.2)	26.5 (21.6-31.4)	23.2 (20.8-25.5)
Infection-related cancer	20.8 (16.7-24.9)	21.1 (17.5-24.6)	12.1 (9.8-14.4)	6.1 (0.0-12.8)	3.1 (1.4-4.9)	4.3 (3.1-5.6)
ADC	14.8 (11.9-17.7)	14.3 (11.1-17.5)	7.2 (5.1-9.4)	6.1 (0.0-12.8)	0.8 (0.0-1.6)	1.8 (1.0-2.7)
Infection-related NADC	7.4 (3.5-11.3)	8.1 (5.7-10.6)	5.3 (4.3-6.3)	0.0 (0.0-0.0)	2.3 (0.7-3.9)	2.6 (1.6-3.5)
<i>Most common site-specific NADCs among people with HIV</i>						
Prostate ¹	6.8 (2.7-10.9)	3.4 (1.5-5.2)	5.4 (3.9-6.9)	9.9 (2.8-17.0)	10.3 (6.7-13.9)	9.2 (7.2-11.2)
Lung	3.0 (0.6-5.5)	4.2 (2.4-6.1)	3.4 (2.3-4.6)	7.1 (0.0-14.7)	4.7 (2.0-7.4)	3.9 (2.7-5.1)
Colorectal	2.1 (0.3-3.9)	2.4 (0.8-3.9)	2.3 (1.5-3.2)	3.3 (0.1-6.4)	4.5 (1.9-7.0)	2.5 (1.6-3.4)
Anal	2.6 (0.7-4.5)	2.4 (1.0-3.9)	2.2 (1.6-2.9)	0.0 (0.0-0.0)	0.0 (0.0-0.1)	0.2 (0.0-0.4)
Liver	1.8 (0.0-3.7)	1.6 (0.4-2.8)	0.8 (0.4-1.2)	0.0 (0.0-0.0)	0.5 (0.0-1.6)	0.5 (0.1-0.9)
	Females with HIV			Females without HIV		
Infection-unrelated cancer	17.4 (6.1-28.8)	18.4 (11.7-25.2)	18.0 (13.8-22.2)	19.8 (14.1-47.4)	16.1 (5.8-26.3)	19.5 (15.3-23.8)
Infection-related cancer	9.7 (4.9-14.4)	8.9 (5.5-12.3)	7.3 (4.9-9.6)	15.9 (0.0-43.3)	1.7 (0.0-4.1)	2.5 (0.6-4.5)
	Males with HIV			Males without HIV		
Infection-unrelated cancer	14.1 (9.4-18.8)	15.8 (11.8-19.8)	16.3 (11.7-18.6)	26.9 (15.5-38.3)	28.7 (23.1-34.2)	23.6 (20.8-26.3)
Infection-related cancer	21.6 (17.4-25.9)	22.6 (18.1-27.1)	12.6 (9.9-15.3)	4.0 (0.0-9.2)	3.2 (1.3-5.1)	4.0 (2.8-5.3)

¹Restricted to males

Note: ADC= AIDS-defining cancer, NADC= non-AIDS defining cancer.

Supplementary Table S4. Hazard ratios and 95% confidence intervals (CI) from cause-specific models for noncancer death, any cancers, infection-related and infection-unrelated cancers comparing people with and without HIV, by age group and calendar period, Ontario, Canada. 1996-2020

Outcome	Hazard ratios (95% CI)			
	Age 18-39 years	Age 40-59 years	Age 60-79 years	Age 80+ years ¹
<i>Calendar period (1996-2003)</i>				
Death	11.20 (5.42-23.15)*	8.47 (4.95-14.50)*	8.89 (2.88-27.42)*	0.89 (0.36-2.16)
Any cancer	15.54 (6.76-35.69)*	5.31 (3.31-8.50)*	1.58 (0.82-3.04)	0.98 (0.12-7.79)
Infection-unrelated cancer	2.72 (0.98-7.53)	1.70 (0.99-2.93)	1.40 (0.65-2.98)	0.94 (0.12-7.54)
Infection-related cancer ¹	-	-	-	-
<i>Calendar period (2004-2011)</i>				
Death	6.09 (3.66-10.15)*	4.04 (3.16-5.17)*	1.87 (1.27-2.74)*	1.61 (0.97-2.69)
Any cancer	5.13 (3.29-7.99)*	2.57 (2.08-3.19)*	1.31 (0.94-1.81)	1.87 (0.76-4.61)
Infection-unrelated cancer	1.27 (0.70-2.29)	1.06 (0.81-1.39)	0.92 (0.63-1.33)	1.50 (0.58-3.84)
Infection-related cancer	27.52 (10.07-75.15)*	13.52 (8.08-22.63)*	5.24 (2.25-12.23)*	-
<i>Calendar period (2012-2020)</i>				
Death	5.68 (3.55-9.09)*	2.76 (2.29-3.33)*	1.64 (1.30-2.07)*	1.20 (0.85-1.70)
Any cancer	2.69 (1.79-4.05)*	1.70 (1.45-1.99)*	1.03 (0.85-1.25)	1.20 (0.66-2.17)
Infection-unrelated	1.09 (0.64-1.85)	0.96 (0.79-1.17)	0.87 (0.70-1.08)	0.98 (0.52-1.82)
Infection-related cancer	11.14 (4.68-26.49)*	6.84 (4.75-9.84)	2.08 (1.33-3.25)*	-

* Indicates statistical significance with the confidence interval excluding the null value of 1.

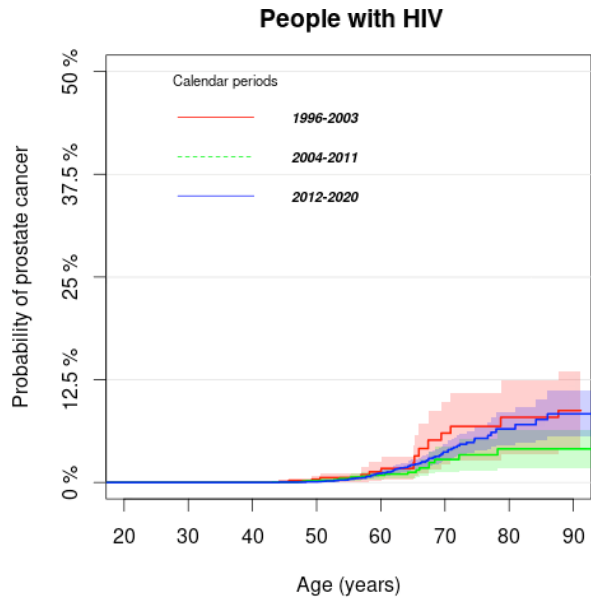
¹Hazard ratios could not be estimated for infection-related cancers in 1996-2003 and for age 80+ across all calendar periods due to small number of events.

Models were stratified by calendar period and adjusted for comorbidity, expected resource utilization and immigration status and included age at follow-up (categorical) and HIV status interaction term.

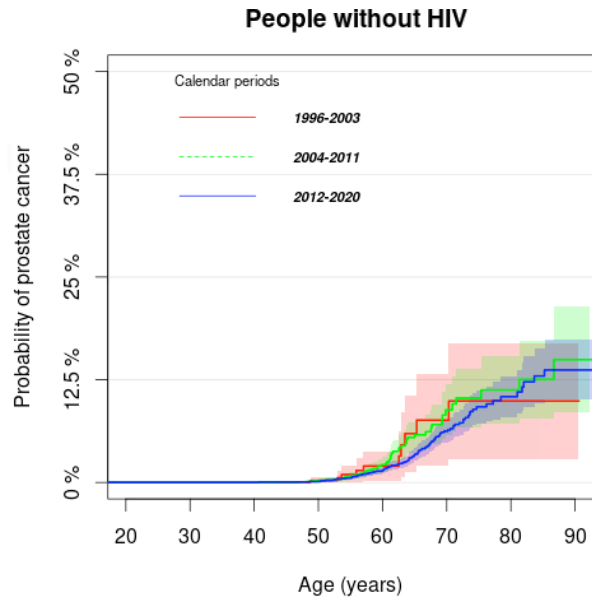
Appendix 1, as supplied by the authors. Appendix to: Nicolau IA, Moineddin R, Antoniou T, et al. Trends in infection-related and infection-unrelated cancer incidence among people with and without HIV infection in Ontario, Canada, 1996–2020: a population-based matched cohort study using health administrative data. *CMAJ Open* 2023.

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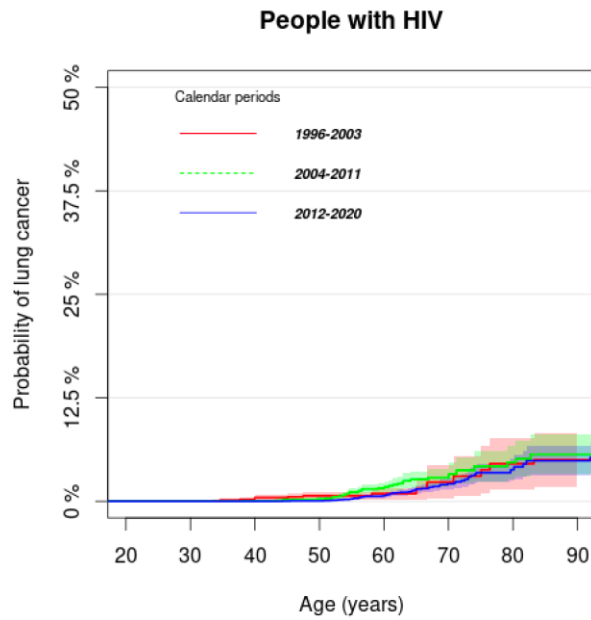
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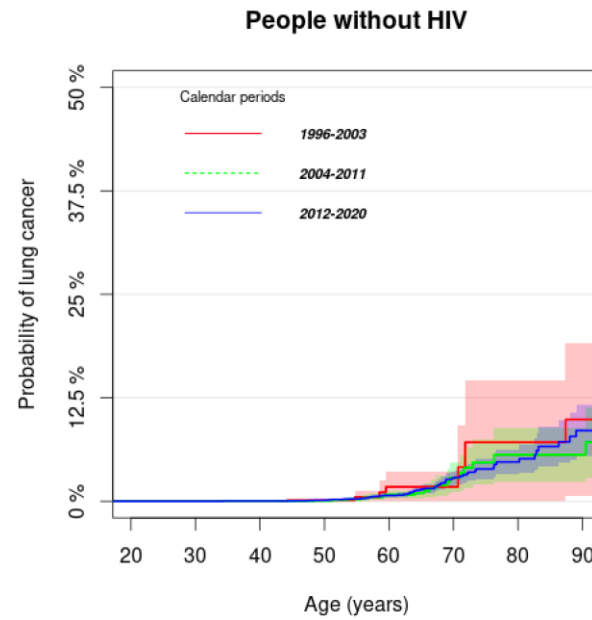
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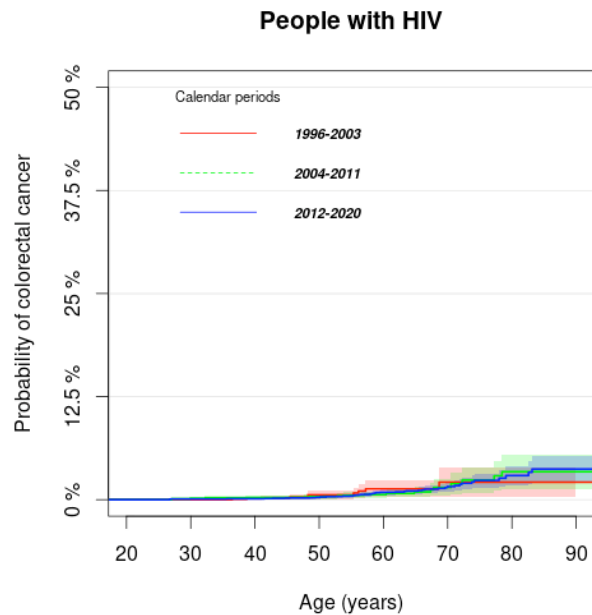
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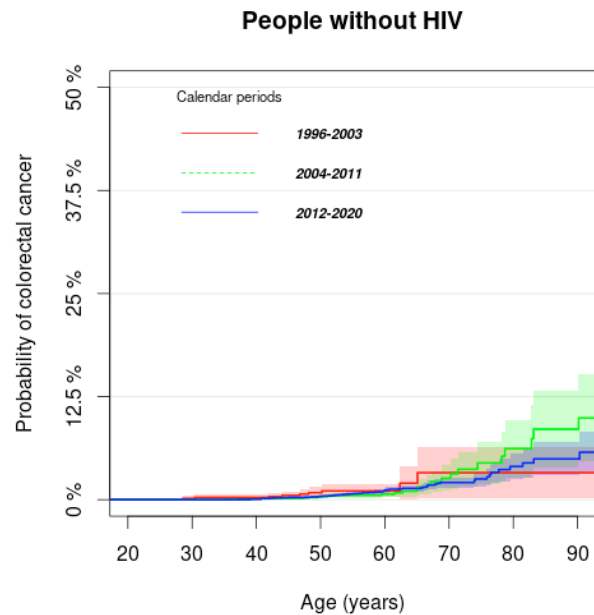
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E)

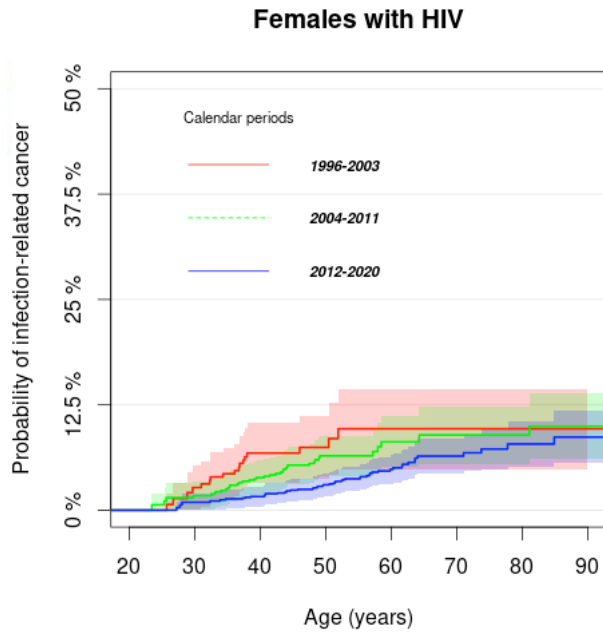


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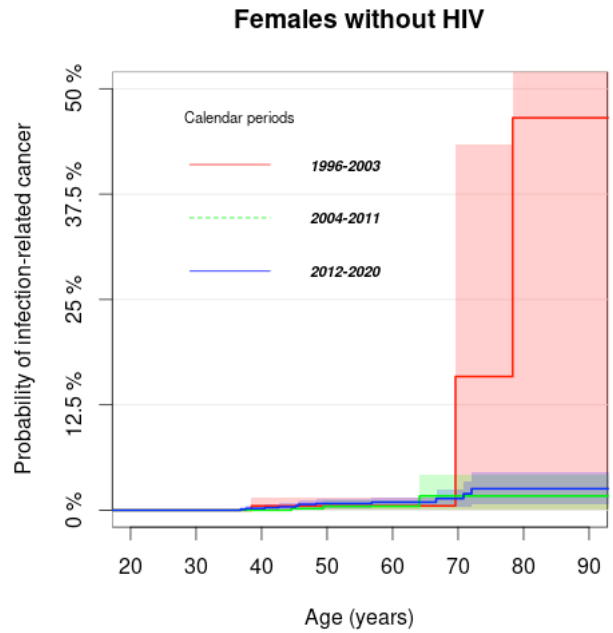


Supplementary Figure S1. Cumulative incidence of prostate (Panels A and B; restricted to males), lung (Panels C and D) and colorectal cancer (Panels E and F) for people with and without HIV by calendar period with age as the time scale, Ontario, Canada

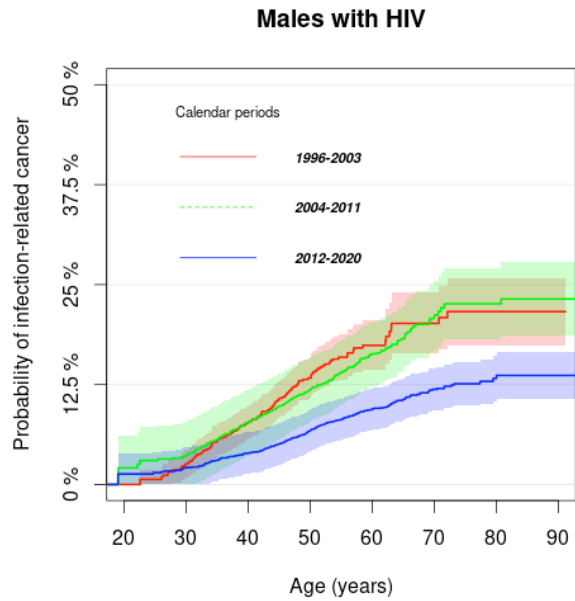
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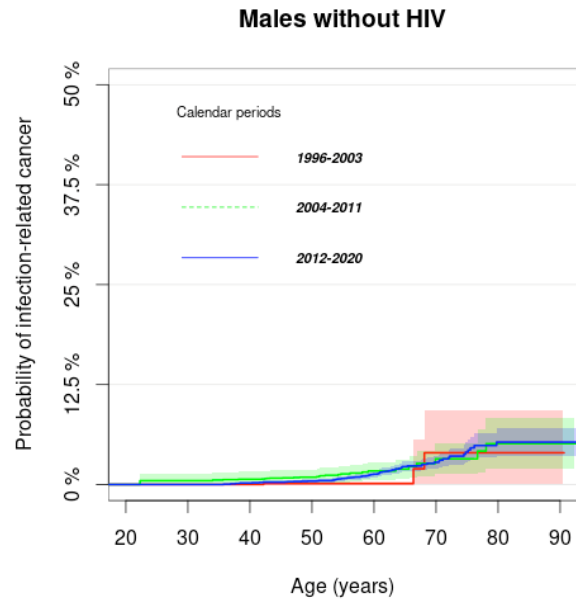
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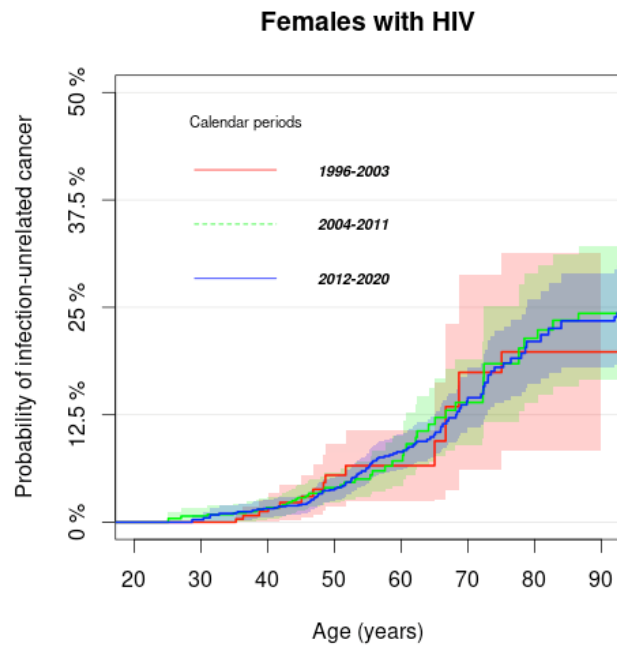
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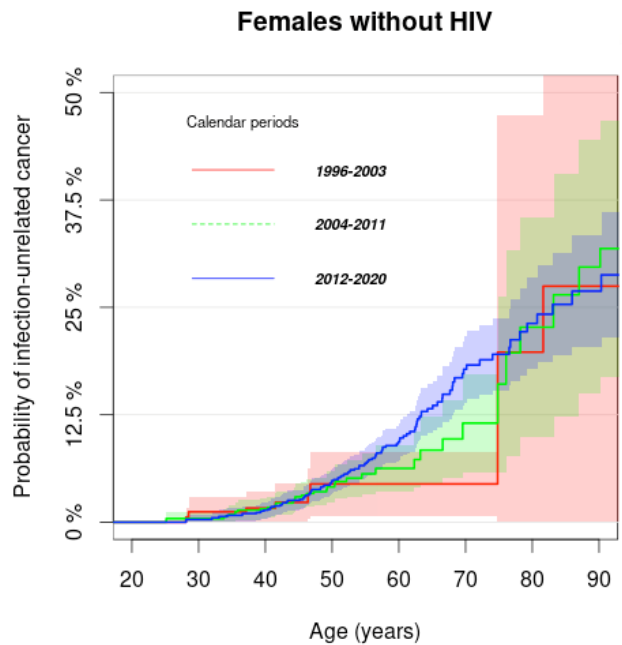
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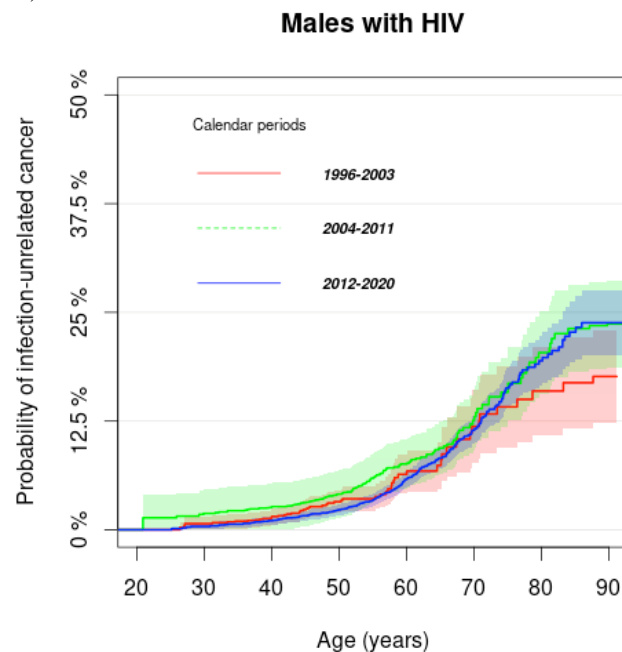
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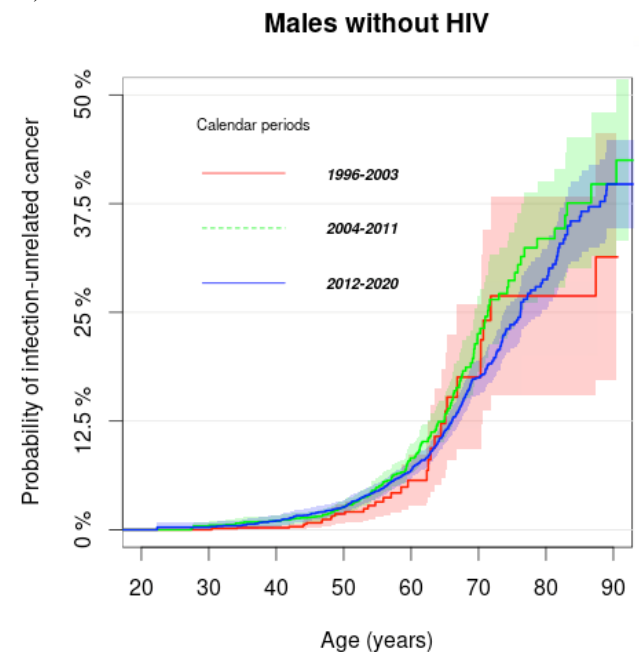
F)



G)



H)



Supplementary Figure S2. Sex-specific cumulative cancer incidence for infection-related cancers (Panels A-D) and infection-unrelated cancers (Panels E-H) for people with and without HIV by calendar period with age as the time scale, Ontario, Canada