Cancer-related mortality in people with HIV (PWH) compared to the general population (2006-2023)

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CROI Conference on Retroviruses and Opportunistic Infections
February 22 to 25, 2026 | Denver, Colorado

BACKGROUND

In the ART era, cancer remains a leading cause of morbidity and higher mortality in people with HIV (PWH) compared to general population. This burden reflects immune dysfunction, chronic inflammation, oncogenic viral co-infections, aging, and behavioural risk factors. Large longitudinal cohorts, as ICONA, are essential to quantify long-term trends in cancer-related excess mortality in PWH.

OBJECTIVES

- Quantify excess cancer-related mortality among PWH using standardized mortality ratios.
- Assess temporal trends in cancer mortality across ART-era calendar periods.
- Compare mortality between virus-related and non–virus-related malignancies.

METHODS

We analysed antiretroviral-naïve people with HIV (PWH) enrolled in the ICONA national prospective cohort between 2006 and 2023. Deaths were identified through active follow-up and classified using ICD-10 codes. Cancer-related deaths were grouped as virus-related or non–virus-related malignancies. Person-years accrued from cohort entry to death or last follow-up. Standardized mortality ratios (SMRs) were calculated by comparing observed deaths with expected deaths based on age-, sex-, geographic area–, and calendar period–specific mortality rates from the Italian general population. SMRs and 95% confidence intervals were estimated assuming a Poisson distribution. Analyses were stratified by cancer type and calendar period to assess temporal trends in excess mortality.

Table 1. Baseline Characteristics of 15,061 PWH

	Total N. (%)	Death N. (%)[a]	Death with/for cancer N. (%)[a]
All	**15,061 (100.0)**	**721 (4.8)**	**269 (1.8)**
Sex at birth			
Male	12,167 (80.8)	560 (4.6)	224 (1.8)
Female	2,894 (19.2)	161 (5.6)	45 (1.6)
Italian	11,286 (74.9)	585 (5.2)	231 (2.1)
Age at enrolment (years):			
Median (IQR)	39 (31-48)	49 (40-58)	50 (43-59)
Mode of HIV acquisition:			
Men who have sex with men	7,188 (47.7)	212 (2.9)	98 (1.4)
Heterosexual intercourse	5,964 (39.6)	332 (5.6)	124 (2.1)
Use of intravenous drugs	981 (6.5)	111 (11.3)	23 (2.3)
Other/unknown	*928 (6.2)*	*67 (7.2)*	*24 (2.6)*
Smoker at enrolment			
No	7,688 (51.1)	341 (4.4)	142 (1.9)
Yes	5,940 (39.4)	315 (5.3)	100 (1.7)
Not available	*1,433 (9.5)*	*65 (4.5)*	*27 (1.9)*

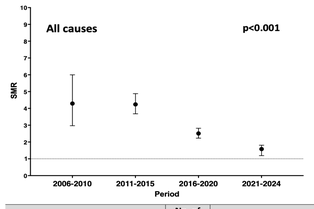
RESULTS

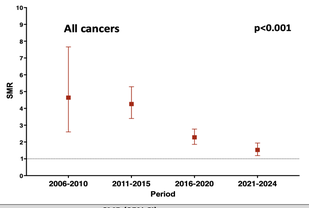
Between 2006 and 2023, a total of 15,061 antiretroviral-naïve people with HIV (PWH) were enrolled in the ICONA cohort, contributing 102258.2 person-years of follow-up (PYFU), with a median follow-up of 6.4 years (IQR 2.6–10.4). Baseline demographic and clinical characteristics are summarized in **Table 1**.
Crude mortality rate for any cancer : 2.63 death /1000 PYFU

Cancer-related mortality in people with HIV remained higher than in the general population despite ART. AIDS-defining cancer mortality declined, but non–AIDS-defining cancers were the main drivers of excess mortality. Despite improving trends, significant disparities persisted.

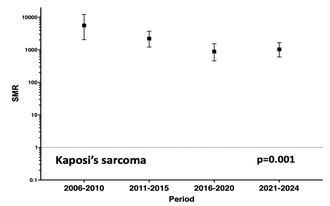
Figure 2. Trend over time of standardized mortality ratios (SMR) for all causes mortality, cancer-related mortality, in selected AIDS-defining cancers, and in non AIDS-defining cancers (NADMs) according to virus-related oncogenesis

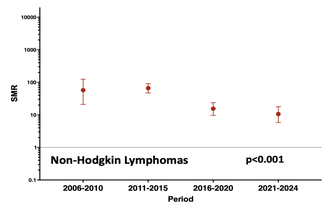
Type/Site	No. of deaths	SMR (95% CI) 2006-2010	2011-2015	2016-2020	2021-2024
All causes of death	721	4.29 (2.97-6.00)	4.24 (3.68-4.88)	2.51 (2.23-2.82)	1.58 (1.37-1.81)
All malignancies	269	4.64 (2.60-7.66)	4.26 (3.40-5.29)	2.28 (1.86-2.77)	1.53 (1.19-1.94)



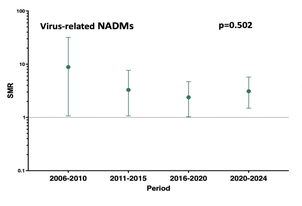


Type/Site	No. of deaths	SMR (95% CI) 2006-2010	2011-2015	2016-2020	2021-2024
Virus-related	159	41.22 (22.53-69.16)	27.27 (20.76-35.18)	8.91 (6.45-12.00)	9.23 (6.68-12.43)
Kaposi's sarcoma	49	5578.82 (2047.33-12142.75)	2209.80 (1208.12-3707.68)	878.83 (454.10-1535.13)	1030.03 (600.03-1649.18)
Non-Hodgkin Lymphomas (All types)	80	57.37 (21.05-124.87)	66.39 (47.21-90.76)	15.54 (9.62-23.75)	10.62 (5.81-17.83)





Type/Site	No. of deaths	SMR (95% CI) 2006-2010	2011-2015	2016-2020	2021-2024
Virus-related NADMs	25	8.83 (1.07-31.91)	3.29 (1.07-7.68)	2.39 (1.03-4.71)	3.11 (1.49-5.73)
Non virus-related NADMs	107	0.35 (0.01-1.93)	1.33 (0.84-2.00)	1.43 (1.08-1.85)	0.64 (0.42-0.94)



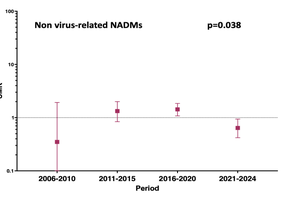
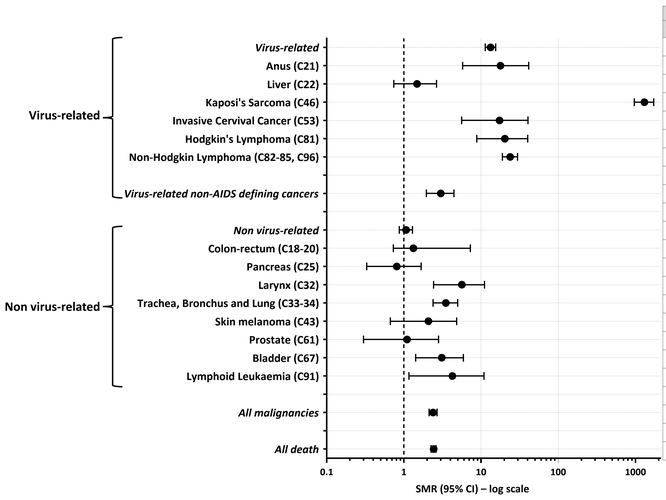


Figure 1. Standardized mortality ratios (SMR) and 95% Confidence Intervals (CI) for selected cancers



	N . Deaths Observed	Expected	SMR (95% CI)
Virus-related	***159***	***11.99***	***13.26 (11.28-15.49)***
Anus (C21)	5	0.28	**17.82 (5.79-41.58)**
Liver (C22)	11	7.42	1.48 (0.74-2.65)
Kaposi's Sarcoma (C46)	49	0.04	**1304.24 (964.88-1724.27)**
Invasive Cervival Cancer (C53)	5	0.29	**17.35 (5.63-40.49)**
Hodgkin's Lymphoma (C81)	8	0.39	**20.34 (8.78-40.08)**
Non-Hodgkin Lymphoma (C82-85, C96)	80	3.36	**23.80 (18.87-29.62)**
Virus-related non-AIDS defining cancers	***25***	***8.30***	***3.01 (1.95-4.45)***
Non virus-related	***107***	***100.38***	*1.07 (0.87-1.29)*
Colon-rectum (C18-20)	14	10.51	1.33 (0.73-7.28)
Pancreas (C25)	7	8.60	0.81 (0.33-1.68)
Larynx (C32)	8	1.42	**5.64 (2.43-11.11)**
Trachea, Bronchus and Lung (C33-34)	31	8.86	**3.50 (2.38-4.97)**
Skin melanoma (C43)	5	2.41	2.08 (0.67-4.85)
Prostate (C61)	4	3.64	1.10 (0.30-2.81)
Bladder (C67)	9	2.90	**3.10 (1.42-5.88)**
Lymphoid Leukaemia (C91)	4	0.94	**4.25 (1.16-10.89)**
All malignancies	**269**	**112.37**	**2.39 (2.12-2.70)**
All death	**721**	**296.45**	**2.43 (2.26-2.62)**

CONCLUSIONS

- ✓Cancer-related mortality remains significantly higher in people with HIV (PWH) compared with the general population in the modern ART era.
- ✓Marked reduction in mortality due to AIDS-defining cancers have been observed, but substantial excess risk persists.
- ✓Non–AIDS-defining cancers represent the main drivers of cancer mortality in PWH, including both virus-related and non–virus-related malignancies.
- ✓Temporal trends suggest partial improvement, yet disparities in cancer outcomes between PWH and the general population remain.
- ✓Persistent immune dysregulation, viral co-infections, aging, and modifiable risk factors likely contribute to ongoing excess mortality.
- ✓Strengthening cancer prevention, targeted screening, and integrated HIV–oncology care is essential to reduce long-term cancer burden in PWH.

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