TRENDS IN CANCER INCIDENCE IN DIFFERENT MODERN ART-ERAS AMONG PEOPLE LIVING WITH HIV (PLWH)

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BACKGROUND

- Cancer is one of the leading causes of death amongst PLWH [1-2].
- Whilst the incidences of AIDS defining cancers (ADCs) have significantly decreased since the mid-1990s with combination antiretroviral therapy (ART), studies have shown mixed results on changes in the incidence of non-ADCs (NADCs) [3-5].
- There are limited international data assessing cancer trends across different contemporary ART eras.

METHODS

- Participants from the D:A:D and RESPOND cohort collaborations were followed from baseline (defined in D:A:D as the latest of study entry or 1 Jan 2006 and in RESPOND as the latest of local cohort enrolment or 1 Jan 2012) until earliest of first cancer (excluding pre-cancers, non-melanoma skin cancers, and relapse), final follow-up, or 1 Feb 2016 in D:A:D or 31 Dec 2019 in RESPOND.
- For individuals with cancer prior to baseline, cancer during follow-up was only counted if the cancer type was different from the one which occurred prior to baseline.
- Age-standardized (according to the age distribution of the combined D:A:D and RESPOND cohorts in 2015) cancer incidence rates (IRs) were calculated from 2006-2019.
- Poisson regression was used to assess temporal trends.

Table 1: Baseline characteristics

		Overall	
		n	(%)
		66636	(100)
Gender	Male	49425	(74.2)
Ethnicity	White	37193	(55.8)
	Black	6505	(9.8)
BMI (kg/m²)	<18.5	2762	(4.1)
	≥25	15232	(22.9)
Smoking status	Current	22487	(33.7)
	Previous	8506	(12.8)
HIV risk	MSM	29892	(44.9)
ART history	ART Naive	22983	(34.5)
	ART Experienced, VL<200 cps/mL	30425	(45.7)
	ART Experienced, VL≥200 cps/mL	11995	(18.0)
Prior AIDS or non-AIDS cancer		3160	(4.7)
Prior AIDS (non-cancer) event		13536	(20.3)
		Median	**IQR**
Baseline date, month/year		12/05	(01/04, 01/12)
Age, years		40.9	(34, 48)
CD4 cell count at baseline, cells/mm³		455	(295, 647)
Total duration of previous ART, years		5.6	(2.1-8.5)

Abbreviations: BMI-body mass index; MSM-men who have sex with men; ART-antiretroviral; VL-viral load. Percentage of unknown variable: Ethnicity 30.9, body mass index 23.8, HIV risk 5.3, smoking status 29.2, prior AIDS 2.6, prior cancer 0.2

Age-standardized incidences of all cancer, AIDS-defining cancers, and infection-related cancers decreased over time from 2006-2019 in the RESPOND and D:A:D cohort collaborations.

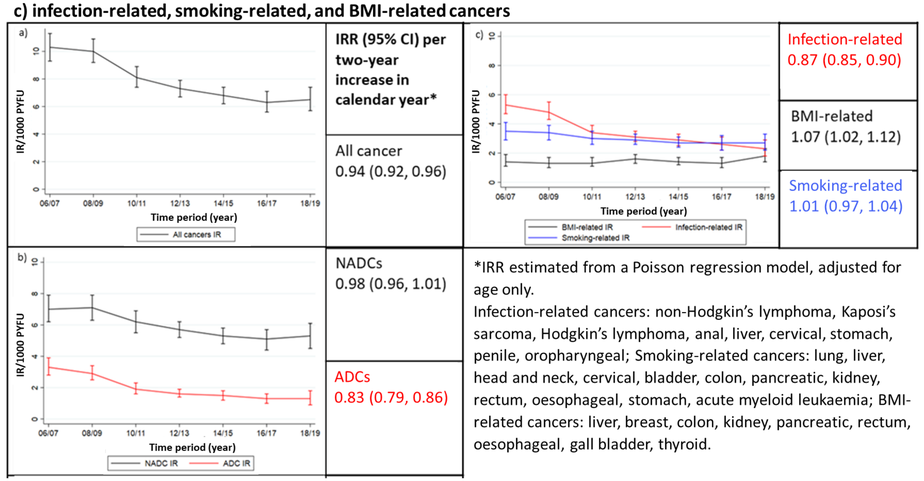
The incidence of non-AIDS defining cancers and smoking-related cancers remained constant over time, whilst BMI-related cancers increased.

- Cancers were split into ADCs and NADCs, and into infection-related (IRCs), smoking-related (SRCs), and BMI-related cancers (BRCs; defined in Figure 1 footnote, groups were not mutually exclusive).

RESULTS

- Overall, 66,636 individuals were included (Table 1): 35,436 from D:A:D, 21,281 from RESPOND, 9,919 included in both collaborations.
- During 489,856 person-years of follow-up (PYFU; median FU 7.5 years [IQR 3.8-11.6]), there were 3634 incident cancers (IR 7.4/1000 PYFU [95% CI 7.2-7.7]):
  1078 ADCs and 2556 NADCs; 1775 were IRCs, 1273 SRCs, and 608 BRCs.
- The most common incident cancers were non-Hodgkin lymphoma (n=517), Kaposi's sarcoma (473), lung cancer (391), and anal cancer (269).
- Age-standardized IRs for overall cancers, ADCs, and IRCs slightly decreased over time, whilst NADCs and SRCs remained fairly constant, and BRCs increased (Figure 1).
- After adjusting for a wide range of potential confounders, the IR of all cancers, ADCs, and IRCs decreased over time, whilst NADCs and SRCs slightly increased and BRCs substantially increased (Table 2).

Figure 1 - Age-standardized incidence rates over time of: a) all cancers, b) AIDS and non-AIDS cancers, c) infection-related, smoking-related, and BMI-related cancers



*IRR estimated from a Poisson regression model, adjusted for age only.
Infection-related cancers: non-Hodgkin's lymphoma, Kaposi's sarcoma, Hodgkin's lymphoma, anal, liver, cervical, stomach, penile, oropharyngeal; Smoking-related cancers: lung, liver, head and neck, cervical, bladder, colon, pancreatic, kidney, rectum, oesophageal, stomach, acute myeloid leukaemia; BMI-related cancers: liver, breast, colon, kidney, pancreatic, rectum, oesophageal, gall bladder, thyroid.

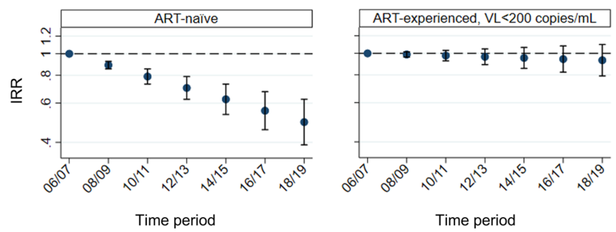
Table 2: Change in incidence of cancer per 2-year increase in calendar year, adjusted for potential confounders

All cancer			ADCs			NADCs		
IRR	**(95% CI)**	**P**	**IRR**	**(95% CI)**	**P**	**IRR**	**(95% CI)**	**P**
0.96	(0.94, 0.98)	0.001	0.83	(0.79, 0.86)	<0.0001	1.03	(1.00, 1.06)	0.038
IRCs			**SRCs**			**BRCs**		
IRR	**(95% CI)**	**P**	**IRR**	**(95% CI)**	**P**	**IRR**	**(95% CI)**	**P**
0.87	(0.85, 0.90)	<0.0001	1.05	(1.01, 1.09)	0.008	1.10	(1.04, 1.16)	0.001

IRR calculated from a Poisson regression model adjusted for age, gender, ethnicity, CD4 count, CD4 nadir, prior cancer, ART-experience and viral suppression status (all fixed at baseline) and smoking status, BMI, hepatitis C, hepatitis B, hypertension, diabetes, AIDS event, cardiovascular disease, end stage and renal liver disease (all time-updated)

- There was a significant interaction between time period and baseline ART-experience for all cancers (interaction p<0.0001; Figure 2). For ART-naïve participants, cancer incidence decreased over time and for those ART-experienced, cancer incidence remained constant.

Figure 2: Change in the age-adjusted incidence of cancer, by time period compared to 2006-2007, stratified by ART-experience at baseline



n cancers	128	181	120	158	142	87	60	236	241	227	307	326	177	131
n NADCs	39	68	57	83	81	47	38	196	203	205	272	291	163	122
n ADCs	89	113	63	75	61	40	22	40	38	22	35	35	14	9

IRR calculated from a Poisson regression model, adjusted for age and including an interaction term between time period and ART-experience at baseline

LIMITATIONS

- Median age of 41 years may be too young to fully assess cancer incidence.
- Median follow-up of 7.5 years may be too short for some individuals to develop cancer.
- Other factors could explain the trends, e.g. alcohol use, family history of cancer, or use of cancer screening, which are not collected in the cohorts.

CONCLUSIONS

- In this large cohort collaboration with extensive follow-up, the age-standardized incidence of all cancers, ADCs, and IRCs significantly decreased from 2006-2019, whilst NADCs and SRCs remained constant and BRCs significantly increased.
- Adjusting for demographics, HIV-related factors, co-infections and comorbidities did not fully explain the trends seen; further research is needed to better understand the causes of these cancer trends.

References: [1] Weber R, et al. HIV Med. 2013 [2] Bedimo R, et al. CID. 2004 [3] Park LS, et al. AIDS. 2016 [4] Worm SW, et al. BMC Infect Dis. 2013 [5] INSIGHT START Study Group. NEJM. 2015

The RESPOND Study Group: https://www.chip.dk/Studies/RESPOND/Study-Group

The D:A:D Study Group: https://www.chip.dk/Studies/DAD/Study-Group