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## Introduction

- Cancer is relatively rare in childhood in general population (incidence 0.14 per 1,000 person-years) [1]
- Immunosuppression and increased susceptibility to oncogenic viruses means people living with HIV are at higher risk of some cancers
- In adults, AIDS-defining malignancies (ADM) have decreased, however, non-AIDS defining malignancies (NADM) have remained constant or increased over the last decade
- Data in children are limited

## Objective

Investigate trends over time and predictors of malignancies among children and young people with HIV

## Methods

- Children diagnosed with HIV and in paediatric care, from 17 cohorts in 15 countries, were included. Data were from routine HIV care.
- Time at risk began at birth for those with vertically-acquired HIV, and first date in HIV care for others
- Individuals were followed to death, loss-to-follow-up, last visit in paediatric care, or last visit in adult care if data available post-transfer
- Malignancies were classified as ADM or NADM using CDC 2014 surveillance criteria
- Risk factors for any malignancy were explored using Poisson regression, and for mortality following a malignancy diagnosis using Cox regression

## Results

### Patient characteristics

- 9,632 patients were included, of whom 8,311 (87%) had vertically acquired HIV and 8,720 (91%) ever initiated ART
- 2,069 (21%) from UK/Ireland, 877 (9%) from Thailand, 2,280 (24%) from Russia or Ukraine, and 4,406 (46%) from the rest of Europe
- Median year of entry to HIV care 1999 (IQR 1993, 2005)
- Median follow-up 12.9 years (IQR 7.1, 17.5), including 2.8 (1.2, 5.0) in adult care (in 553 patients who had data available after transfer, out of 2,021 who had transferred)

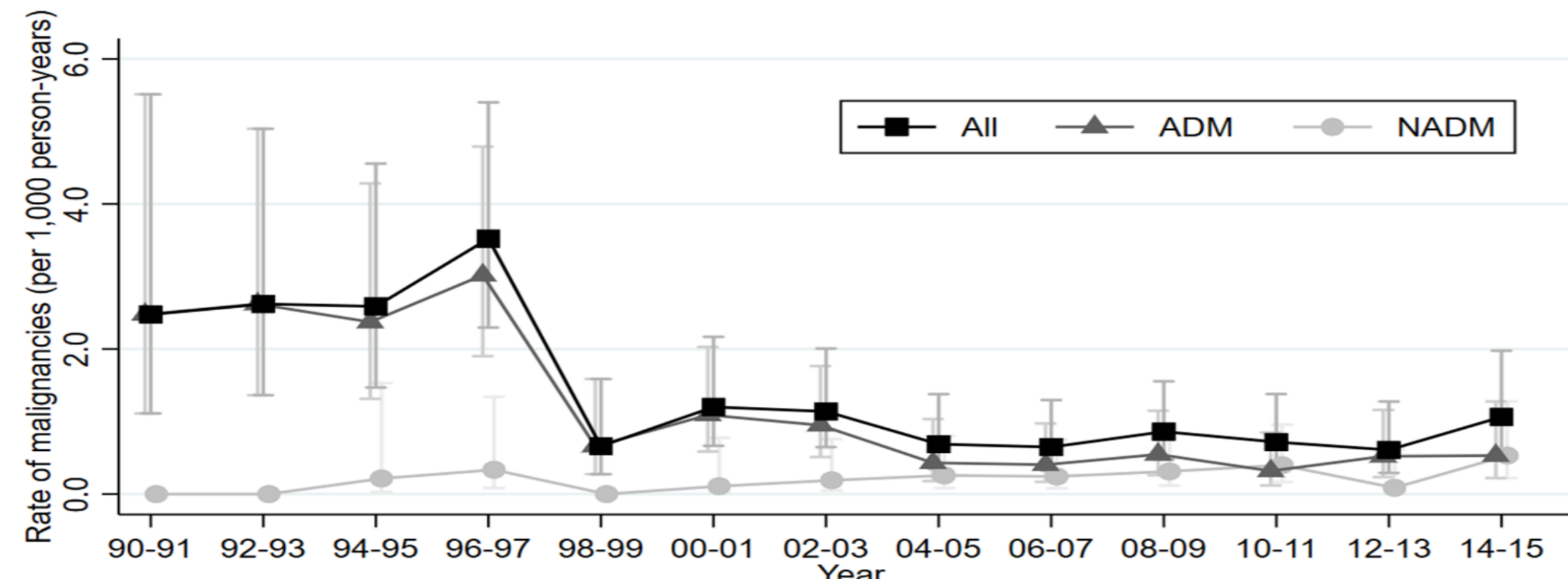
### Malignancy events

- 140 (1.5%) of patients had a malignancy
  - 112 (80%) were ADM - most common: Non-Hodgkin Lymphoma (n=83), Kaposi Sarcoma (n=25)
  - 27 (19%) were NADM - most common: Hodgkin Lymphoma (n=15), hepatocellular carcinoma (n=2)
  - 1 unspecified
- Characteristics at malignancy diagnosis:
  - Diagnosed within 6 months of entry to HIV care: 23% for ADM vs. 7% NADM
  - Age at diagnosis (years): 9.9 (IQR 4.6, 14.6) for ADM vs. 10.1 (8.0, 16.4) for NADM
  - CD4%: 15 (6, 23) for ADM vs. 19 (9, 25) for NADM

### Rates

- Rates per 1,000 person-years (95% confidence interval (CI)):
  - Any malignancy: 1.18 (1.00, 1.40)
    - Among those on ART ≥6 months, virally suppressed and with no immunosuppression: 0.35 (0.18, 0.68)
  - ADM: 0.94 (0.79, 1.14) / NADM: 0.23 (0.16, 0.33)
- Rates of ADM decreased over time, and of NADM increased (Fig 1)

**Figure 1: Rates of malignancies over calendar time, overall and for ADM and NADM**



### Mortality after a malignancy diagnosis

- Overall, 58 (41%) patients with a malignancy died, at a median 2.4 (IQR 0.6, 8.8) months after diagnosis.
- Those diagnosed before 1996 were more likely to die by 3 years (68.0% (95% CI 51.9%, 83.1%)), with no change over time from 1996 onwards (30.6% (19.7%, 45.6%), 25.2% (12.1%, 47.8%), 33.7% (17.5%, 58.6%) for 1996-2003, 2004-2009 and after 2010 resp.)
- Multivariable analysis: only earlier calendar year of malignancy diagnosis and vertically-acquired HIV were associated with higher risk.

### Risk factors for a malignancy diagnosis

- In multivariable analysis, risk factors for any malignancy were (Table 1):
  - male sex
  - being from a European cohort
  - vertically acquired HIV
  - current severe immunosuppression
  - current viral load greater than 400 copies/ml
  - earlier calendar year, for those not on ART only
  - older current age (especially for those not on treatment)

**Table 1: Risk factors for any malignancy**

		aRR	95% CI	p
Sex	Female	0.63	0.45, 0.89	0.009
	Male	1.00	-	
Region	UK/Ireland	1.00	-	0.017
	Thailand	0.16	0.04, 0.69	
	Russia/Ukraine	0.66	0.29, 1.54	
	Rest of Europe	1.28	0.81, 2.02	
Mode of HIV acquisition	Vertical	1.00	-	0.049
	Other	0.58	0.31, 0.98	
Current WHO immune stage	Not severe	1.00	-	<0.001
	Severe	3.95	2.48, 6.29	
Current BMI-for-age z-score	>2	1.00	-	0.114
	-2 to 2	2.01	0.32, 12.53	
	<-2	5.25	0.49, 56.12	
Current viral load >400 copies/ml	Suppressed	1.00	-	0.027
	Unsuppressed	1.80	1.01, 3.71	
Current calendar year	Among those not on ART			0.414
	<1996	1.00	-	
	1996 - 2003	1.41	0.52, 3.84	
	2004 - 2009	0.63	0.17, 2.42	
Among those on ART <6 months	<1996	1.00	-	0.999
	1996 - 2003	1.11	0.21, 5.77	
	2004 - 2009	0.00	0.00, >1000.00	
	≥2010	1.10	0.16, 7.51	
Among those on ART ≥6 months	<1996	1.00	-	0.001
	1996 - 2003	0.41	0.23, 0.74	
	2004 - 2009	0.25	0.12, 0.51	
	≥2010	0.22	0.10, 0.51	
Current age (years)	Among those not on ART			0.003
	<5	1.00	-	
	5 - <10	2.52	0.98, 6.46	
Among those on ART <6 months	<5	1.00	-	0.036
	5 - <10	3.63	0.60, 21.80	
	10 - <15	7.95	1.38, 45.88	
Among those on ART ≥6 months	<5	1.00	-	0.019
	5 - <10	17.65	2.261, 137.72	
	10 - <15	1.09	0.56, 2.12	
	≥15	1.18	1.18, 4.83	

aRR: adjusted rate ratio; CI: confidence interval

- Risk factors for ADM were similar to those overall.
- For NADM, only current severe immunosuppression and non-vertically acquired HIV were risk factors.

## Conclusions

- The rate of AIDS-defining malignancies declined markedly following introduction of combination ART, with the rate for those on ART, virally suppressed and immunologically well similar to that in the general population.
- There was an increasing risk with age among those not on treatment, but a smaller increase seen for those on ART long term.
- Even in recent years one-third of individuals with a malignancy died within 3 years of diagnosis, which is higher than the estimated 20% mortality following childhood cancer in the general population [2]. Possible causes should be explored and steps taken to address this.

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## References

- [1] Steliarova-Foucher et al, Lancet Oncology, 2018
- [2] Gatta et al, Lancet Oncology, 2014