Temporal Trends of Cardiovascular Disease Incidence in People with HIV from 2001–2021

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BACKGROUND

- Cardiovascular disease (CVD) is one of the leading causes of mortality in people with HIV[1]
- Most previous studies of temporal CVD trends were conducted nationally, with follow-up ending several years ago[2,3]

METHODS

- Participants from the D:A:D[4] and RESPOND[5] cohorts were followed from baseline (D:A:D: latest of study entry or 2001; RESPOND: local cohort enrolment or 2012) until the earliest of first CVD, final follow-up, or 2016 in D:A:D/ 2021 in RESPOND (censoring date)
- CVD outcome: Composite endpoint consisting of rigorously defined type I myocardial infarctions (MIs), strokes, invasive cardiovascular procedures (ICPs)
- Age-standardised CVD incidence rates (IRs) were estimated from 2001–2021 with Poisson regression used to assess temporal CVD trends, adjusted for age and cohort
  - Additionally adjusted for each CVD risk predictor separately: *Demographics* (sex/gender, ethnicity/race, HIV transmission risk), *CVD risk factors* (smoking, BMI, diabetes, hypertension, dyslipidemia, chronic kidney disease), and *HIV-related factors* (prior AIDS, CD4 nadir, ART-experience/viral suppression status, time from HIV diagnosis to ART initiation); all time-updated where applicable
- Interaction terms were included in the regression models to assess whether temporal trends differ in subgroups of interest

Table 1. Baseline characteristics, stratified by CVD event occurrence

		Overall		CVD event		No CVD event	
		n	%	n	%	n	%
All		66,680	100	2,811	4.2	63,869	95.8
Sex/Gender	Male	49,286	73.9	2.467	87.8	46,819	73.3
	Female	17,334	26.0	344	12.2	16,990	26.6
Ethnicity/race	White	37,279	55.9	1,679	59.7	35,600	55.7
	Black	6,517	9.8	109	3.9	6,408	10.0
HIV acquisition group	MSM	28,661	43.0	1,443	51.3	27,218	42.6
	IDU	10,702	16,0	416	14.8	10,286	16,1
BMI (kg/m²)	>30	12,106	18.2	597	21.2	11,509	18.0
Smoking status	Current smokers	25,331	38.0	1,315	46.8	24,016	37.6
Hypertension		5,131	7.7	533	19.0	4.598	7.2
Diabetes		2,143	3.2	282	10.0	1,861	2.9
Dyslipidemia		29,880	44.8	1,951	69.4	27,929	43.7
Chronic kidney disease		244	0.4	29	1.0	215	0.3
		Median (IQR)		Median (IQR)		Median (IQR)	
Age		40 (33–47)		48 (41–56)		39 (33–47)	
CD4 count		437 (270–630)		420 (258–617)		438 (271–630)	

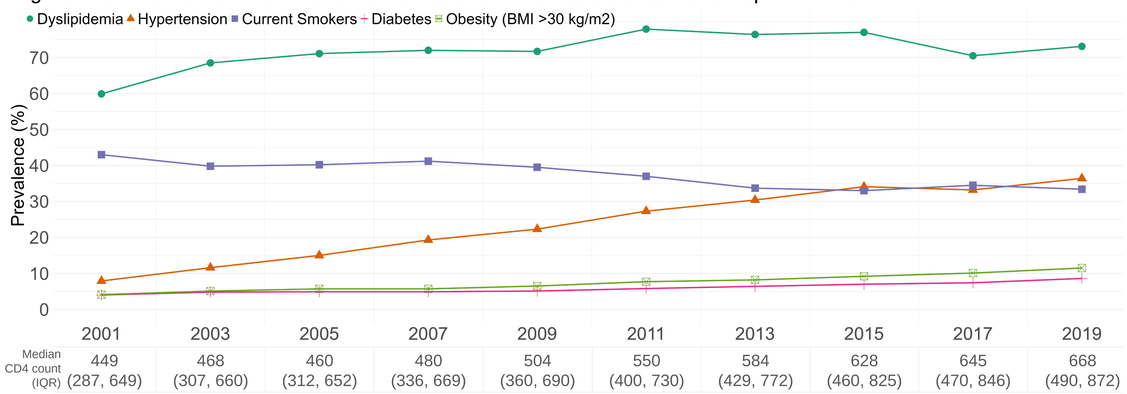
Abbr.: CVD- cardiovascular disease; MSM-men who have sex with men; IDU-intravenous drug use; BMI-body mass index; IQR-interquartile range

References: [1] Tusch et al. CROI 2023 [2] Klein et al. CID, 2015 [3] Rasmussen et al. Lancet HIV, 2015 [4] Friis-Møller et al. AIDS, 2003 [5] Neesgaard et al. Microorganisms, 2020

In the RESPOND and D:A:D cohort collaborations, the **cardiovascular disease** incidence rate **decreased** from 2001 to 2021. Increasing prevalence of **hypertension** may have **contributed** to a **slower decline** over time.

Figure 1. Age-standardised IRs over time for all CVD events and MIs, strokes and ICPs

Figure 2. Distribution of traditional CVD risk factors in individuals under follow-up over time



Median CD4 count (IQR)	2001	2003	2005	2007	2009	2011	2013	2015	2017	2019
	449 (287, 649)	468 (307, 660)	460 (312, 652)	480 (336, 669)	504 (360, 690)	550 (400, 730)	584 (429, 772)	628 (460, 825)	645 (470, 846)	668 (490, 872)

RESULTS

- Overall, 66,680 participants were included (Table 1)
- Over a median follow-up of 8.8 years (IQR 4.6–13.1; 586,510 total person-years of follow-up, PYFU), there were 2,811 CVD events: 1,363 MIs, 768 strokes and 680 ICPs
- Crude incidence rate 4.8/1000 PYFU (95% CI 4.6–5.0)
- Age-standardised IRs decreased from 9.2 in 2001–2002 to 3.8/1000 PYFU in 2019–2021 (Figure 1)
- The decline was most noticeable between 2001–2009 and larger for MIs than for strokes and ICPs
- While the smoking prevalence decreased, the proportion of individuals with dyslipidemia, hypertension, obesity and diabetes increased from 2001–2019 (Figure 2)
- Among the PYFU with the respective comorbidity, the proportion exposed to CVD preventive measures also increased over time (antihypertensives 42.3% in 2001–2010 vs 49.4% in 2011–2021; antidiabetics 48.0% vs 56.9%; lipid-lowering drugs 12.4% vs 19.1%)

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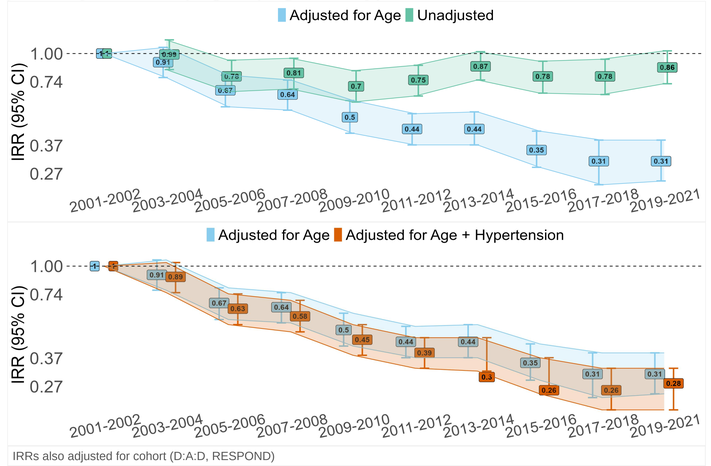
Figure 3. Change in CVD incidence per two-year increase in calendar year, adjusted for a) age, b) age and hypertension



IRRs also adjusted for cohort (D:A:D, RESPOND)

- After adjusting for age, the CVD IR declined over time; additional adjustment for hypertension strengthened the declining estimates (Figure 3). Adjustment for changes in other CVD risk factors did not affect the temporal trends
- The declining CVD incidence per two years time was independent of sex/gender, recent virological failure (viral load of >200 copies/mL), smoking status, diabetes, and multimorbidity burden (all interaction P>0.1)

LIMITATIONS

- Residual confounding from factors not collected (e.g., diet, physical activity) cannot be ruled out
- Potential underestimation of risk factors in early years due to a change towards better ascertainment (e.g., blood pressure) over time

CONCLUSIONS

- Combining two large, multinational cohort collaborations showed that despite an increasing prevalence of several CVD risk factors, age-standardised CVD IRs have significantly decreased from 2001 to 2021
- An increasing hypertension prevalence may have contributed to a slower decline in CVD incidence over time
- A declining CVD incidence is concurrent with a higher proportion being treated for comorbidities, having fewer smokers and more individuals being stable on effective ART regimens

RESPOND Study Group: https://chip.dk/Research/Studies/RESPOND/Study-group
D:A:D Study Group: https://chip.dk/Research/Studies/DAD/Study-Group