

# THE LANCET HIV

## Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Justice AC, Goetz MB, Stewart CN, et al. Delayed presentation of HIV among older individuals: a growing problem. *Lancet HIV* 2022; published online Feb 23. [https://doi.org/10.1016/S2352-3018\(22\)00003-0](https://doi.org/10.1016/S2352-3018(22)00003-0).

## Appendix

**Appendix Table 1. Structured Review of Delayed Presentation Publications Last Five Years**

<u>1st Author</u>	<u>Definition of Late Presenter</u>	<u>New Diagnoses (n)</u>	<u>Late Presenters (n, %)</u>		<u>Years</u>	<u>Location</u>	<u>Age Variable (Yrs)</u>	<u>Odds Ratio</u>	<u>95% CI</u>	
Gardner	AIDS	1385	422	31%	2009-14	USA (single site)	65+ vs. 25-44	1.3	0.6	2.6
Nduaguba	AIDS	77844	30359	39%	1996-2001	USA (multisite)	60+ vs.<30	4.0	3.3	4.7
Nduaguba	AIDS	77844	30359	39%	2002-2007	USA (multisite)	60+ vs.<30	4.6	3.9	5.4
Kwobah	CD4<100	10533	2421	23%	2010-11	Kenya (multisite)	>24 vs. <19	1.6	1.0	2.6
Kadam	CD4<200	659	264	40%	2011-15	India (single site)	continuous variable	na		
Honge	CD4<200	3720	1810	48%	2005-13	West Africa (single site)	50+ vs.<30	1.5	1.1	2.0
Senard	CD4<200	186	49	26%	2012-13	France (single site)	continuous variable	1.1	1.0	1.1
Taborelli	CD4<200 or AIDS	16601	7720	47%	1999-13	Italy (multisite) Italians	50+ vs.35-49	1.5	1.4	1.7
Taborelli	CD4<200 or AIDS	4152	2831	68%	1999-14	Italy (multisite) Non- Italians	50+ vs.35-49	0.9	0.7	1.2
Tang	CD4<200 or AIDS	528234	179700	34%	2006-14	China (multisite)	55+ vs.15-24	2.9	2.9	3.0
Mohammadi	CD4<350	4402	2562	58%	1987-2016	Iran (158 sites)	50+ vs.<30	3.6	2.6	4.8
Rava	CD4<350	14876	6635	45%	2004-18	Spain (46 sites)	50+ vs. <30	2.8	2.5	3.1
Ribeiro	CD4<350	356	218	59%	2017	Brazil (single site)	continuous variable	1.0	1.0	1.1
Bath	CD4<350	2469	1342	54%	2008-14	England (multisite)	55+ vs. 16-19	3.5	1.6	7.7
Cuzin	CD4<350	1421	625	44%	2014-15	France (10 sites)	>47 vs. <29	1.9	1.4	2.5
MacCarthy	CD4<350	1970	698	61%	2010	Brazil (3 sites)	45+ vs.18-44	1.7	1.1	2.5
Hu	CD4<350	519	188	38%	2011-14	China (8 cities)	40+ vs.18-24	3.1	1.8	5.5

Gullon	CD4<350	316	158	50%	2007-14	Spain (single site)	>38 vs. <38	2.2	1.3	3.7
Schafer	CD4<350	165	105	64%	2009-11	Germany (single site)	mean age LP 41 vs 32	na		
Miranda	CD4<350 or AIDS	907	459	51%	1984-2017	Portugal (single site)	>56 vs. <30	2.9	1.5	5.9
Jablonowska	CD4<350 or AIDS	1522	682	45%	2016-17	Poland (13 sites)	per decade	1.5	1.4	1.7
Robles	CD4<350 or AIDS	3842	2793	73%	2012-17	Panama (multisite)	>65 vs. 18-24	2.9	1.7	5.0
Palacios-Baena	CD4<350 or AIDS	205	102	50%	2014-18	Spain (single site)	32+ vs. <32	3.4	1.9	6.1
Muelas Fernandez	CD4<350 or AIDS	74	33	45%	2013-18	Spain (single site)	40+ vs. <40	2.6	1.0	6.9
Karaosmanoglu	CD4<350 or AIDS	1673	826	49%	2003-16	Turkey (single site)	>50 vs ≤50	1.8	*	*
Krueger	CD4<350 or AIDS	1644585	Na	na	2013-16	USA (multisite)	45+ vs. 25-44	1.7	*	*
Siwak	CD4<350 or AIDS	3972	2288	58%	2000-15	Poland (14 sites)	60+ vs.<20	5.2	1.9	14.0
Hu	CD4<350 or AIDS	45118	31673	70%	2012-16	China (multisite)	>50 vs. 15-30	1.5	1.4	1.6
Zhonghua	CD4<350 or AIDS	293187	200503	68%	2009-17	China (multisite)	60+ vs. 18-29	2.3	2.3	2.4
Wilton	CD4<350 or AIDS	1819	1476	54%	1999-2013	Canada (multisite)	50+ vs.<30	2.8	1.9	4.1
Lin	CD4<350 or AIDS	436	82	19%	2000-14	Australia (single site)	mean age LP 45 vs 39	na		
Rao	CD4<350 or AIDS	474	356	75%	2012-13	India (single site)	≤50 vs.≤25	4.2	1.3	13.2
Darcis	CD4<350 or AIDS	687	302	44%	2006-17	Belgium (single site)	10 year increments	1.3	1.1	1.5
Wojcik-Cichy	CD4<350 or AIDS	412	259	63%	2009-16	Poland (single site)	10 year increments	1.8	1.4	2.4
Johnson	CD4<350 or AIDS	401	307	77%	2013-16	Sudan (single site)	34+ vs. <34	na		
Jin	CD4<350 or AIDS	7073	2949	42%	2011-15	China (multisite)	60+ vs. 0-19	2.2	1.5	3.1
Gesesew	CD4<350 or AIDS	4900	3268	67%	2003-15	Ethiopia (single site)	50+ vs. 15-24	0.4	0.3	0.6
Fomundam	CD4<350 or AIDS	8138	4817	59%	2014-15	South Africa (35 sites)	50+ vs. <50	1.9	*	*
Levy	CD4<350 or AIDS	356	118	33%	2010-15	Israel (single site)	>50 vs. <50	2.4	1.1	5.0

Raffetti	CD4<350 or AIDS	19391	10471	54%	1985-2013	Italy (multisite)	55+ vs.<25	7.5	6.1	9.2
Brannstrom	CD4<350 or AIDS	575	334	58%	2009-12	Sweden (12 sites)	<u>&gt;50 vs.&lt;30</u>	4.0	2.1	7.6
Kesselring	CD4<500	702	442	63%	2013-15	Canada (multisite)	continuous variable	1.0	1.02	1.05

**Appendix Table 2:** Differences in selection, Treat All adoption years, and CD4 measurement clinical practices in the leDEA regional cohorts. *In 2013, the World Health Organization recommended viral load testing (and not CD4 testing) to monitor virologic failure after ART initiation<sup>a</sup> In 2018, the President’s Emergency Plan for AIDS Relief (PEPFAR) reduced their support for CD4 testing to prioritize viral load monitoring.<sup>b</sup> The leDEA region has previously shown a decline in pre-ART CD4 testing after adoption of Treat All policies that is steeper in low-and-middle-income countries than in high-income countries.<sup>c</sup>*

leDEA region	Selection in to the regional cohort	Treat All adoption year (for the majority of countries in the region)	CD4 measurement at presentation for HIV care and ART initiation
North America (NA-ACCORD)	<p>NA-ACCORD contributing clinical cohorts recruit patients at entry into clinical care; this is a dynamic and ongoing process. Contributing cohorts submit data to the NA-ACCORD after the patient successfully links to HIV care, defined as <math>\geq 2</math> HIV clinical visits within 12 months. Data prior to successful linkage to care is not systematically collected on patients, and patients who do not successfully link to care are not included in the NA-ACCORD.</p> <p>The demographics of the NA-ACCORD study population are reflective of all persons with diagnosed HIV in the United States (as reported by the US Centers for Disease Control HIV Surveillance system); demographics are compared annually at <a href="http://www.naaccord.org">www.naaccord.org</a>.</p>	2012	<p>At presentation for HIV care: CD4 measurement has been consistently recommended at presentation for HIV care.</p> <p>At ART initiation: Prior to the adoption of Treat All guidelines, a low CD4 measurement was the predominant stimulus for ART initiation. After the adoption of the Treat All guidelines, ART is initiated regardless of whether a CD4 measurement has occurred. Because guidelines recommend treatment at the time of presentation for care, CD4 is commonly measured at ART initiation and the gap between median CD4 count at presentation for HIV care and at ART initiation has narrowed.<sup>d</sup></p>
Central and South America and the Caribbean (CCASANet)	CCASANet includes routine clinical cohorts from HIV care and treatment clinics in urban centers located in 7 countries: Argentina, Brazil, Chile, Haiti, Honduras, Mexico, and Peru. Participating clinics are principally tertiary, referral care centers except for the clinic in Haiti which provides HIV testing and counselling prior to enrollment. Patients are	2014 (Brazil, Mexico), 2015 (Argentina, Chile, Honduras, Peru), 2016 (Haiti)	The frequency of CD4 cell count testing at clinic entry in CCASANet cohorts has declined from 79% overall in 2015 to 55% in 2019. However, rates of CD4 cell count testing at clinic entry is heterogeneous across clinic sites, ranging from 29% to 94% in 2019.

	observed from HIV clinic entry, regardless of prior ART exposure, and are followed until last clinic contact or death.		
Central Africa	Central Africa leDEA includes all patients ever entering care at HIV care and treatment clinics in Burundi, Democratic Republic of Congo, Republic of Congo and Rwanda, along with patients in Cameroon who consented into the study from 2016 onwards. All patients in the Central Africa cohorts are observed from the time of entering HIV care at a participating clinic and are followed until the time of transfer to another site of care, death or loss-to-follow-up.	2016 (Burundi, Cameroon, Rwanda) 2017 (Democratic Republic of Congo), 2018 (Republic of Congo)	Prior to national adoption of WHO's Treat All guidelines, CD4 testing was recommended at presentation for HIV care and prior to treatment initiation, as CD4 counts were used to assess patient immunological status and treatment eligibility, With national adoption of Treat All guidelines, CD4 testing is no longer required for ascertaining treatment eligibility, and is not routinely conducted for all patients.
East Africa	East Africa contributing clinical cohorts include all patients enrolled in clinical care regardless of the number of visits; this is a dynamic and ongoing process.	2016	At presentation for HIV care: CD4 measurement was recommended at presentation for HIV care until the adoption of Treat All guidelines. Thereafter, CD4 was not regularly tested due to lack of reagents.  At ART initiation: Prior to the adoption of Treat All guidelines, a low CD4 measurement was the predominant guide for ART initiation. After the adoption of the Treat All guidelines, ART is initiated regardless of whether a CD4 measurement has occurred.
West Africa	Participants are enrolled in the leDEA West Africa regional cohort at ART initiation. However, data prior to ART initiation such as first visit into HIV care are also available.	2016	While most countries in West Africa have adopted Treat All guidelines in 2016, it has translated into a heterogeneous situation; some countries experiencing a significant decline in CD4 measures at ART initiation such as Côte d'Ivoire while other have maintain a high proportion of CD4 measures after adoption of Treat All.
Southern Africa	Participants are observed in the leDEA Southern Africa region at ART initiation (as opposed to presentation for HIV care) and then are observed moving forward in time.	2017	As previously shown, the frequency of CD4 testing plateaued or declined in Southern African leDEA-contributing cohorts after 2010; this was reflected in a decline in the percentage of participants who had a CD4 cell count at ART initiation from 78% in 2008 to 40% in 2017.

Asia-Pacific	Participants are enrolled into the IeDEA Asia-Pacific regional cohort (excluding Australia) from two groups: 1) dynamic clinical cohorts that enroll all those seeking clinical care; and 2) closed clinical cohorts that recruit patients to replenish the cohort when participants die, transfer, or are loss to follow-up.	2017-2018	CD4 measurements at presentation for HIV care have been recommended. When ART initiation was distant from entry into HIV care, a repeat CD4 within 6-12 months from the prior test would have been preferred. In the context of the analysis presented in this paper, 34% of those who started ART did not have a CD4 count at ART initiation.
Australia sub-cohort of Asia-Pacific region	Participants were largely enrolled into the Australia sub-cohort from clinical care sites from 1999 to 2002, and between 2009 and 2012. In intervening and subsequent years, recruitment of new participants occurs to replenish the cohort when participants die, transfer, or are loss to follow-up	2015	Under Australian antiretroviral treatment guidelines, CD4 testing is recommended at entry into care and prior to treatment initiation.

a. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach. Geneva: World Health Organization; 2013. Available at: <https://www.who.int/hiv/pub/guidelines/arv2013/en/>

b. Kaiser Family Foundation. The U.S. government engagement in global health: a primer. 2019. Available at: <https://www.kff.org/report-section/the-u-s-government-engagement-in-global-health-a-primer-report/>

c. Brazier E, et al. Effect of national adoption of Treat-All guidelines on pre-ART CD4 testing and viral load monitoring after ART initiation: A regression discontinuity analysis. Clin Infect Dis 2021;ciab222

d. Lee JS, et al. CD4 count at entry into HIV care and at antiretroviral therapy prescription in the US, 2005-2018. Clin Infect Dis 2020;ciaa1904.

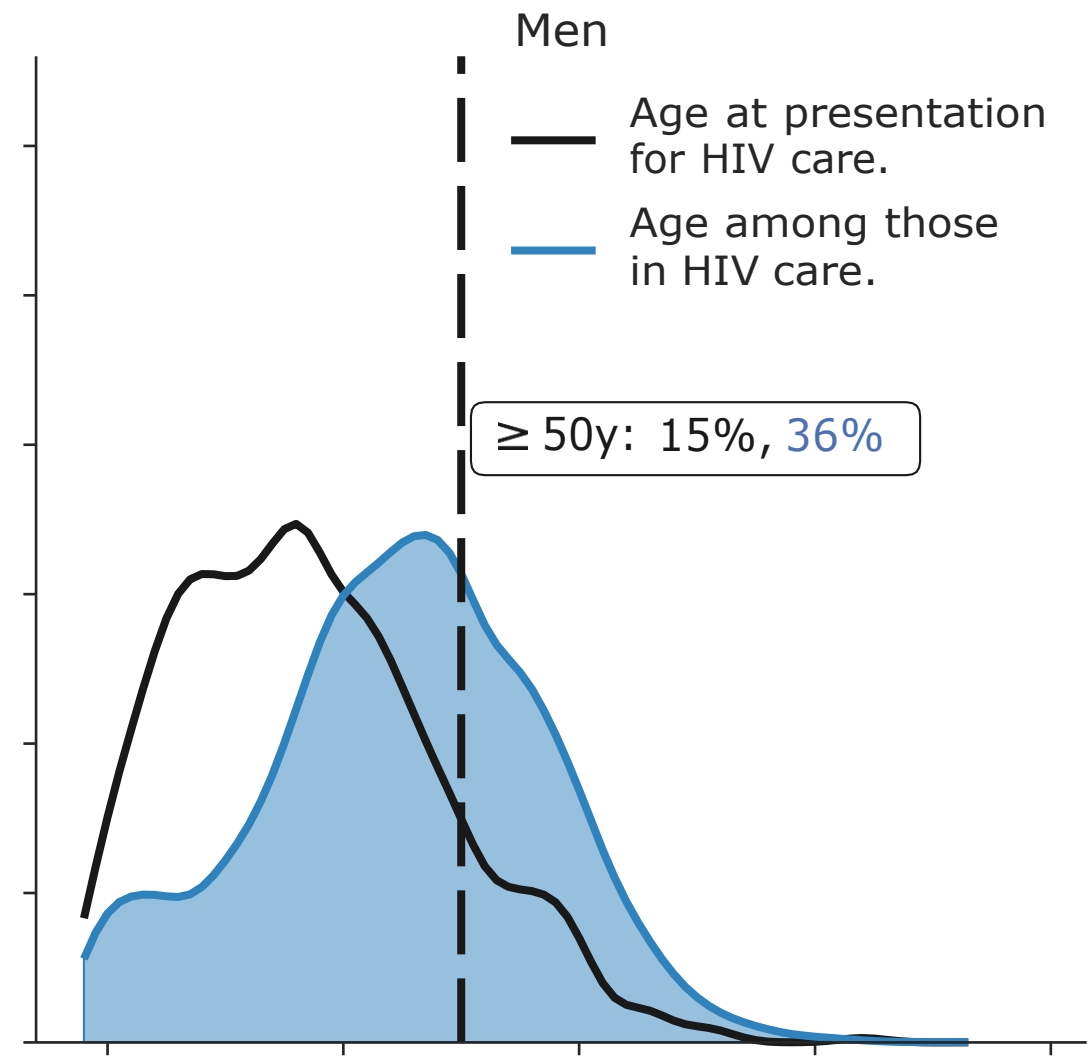
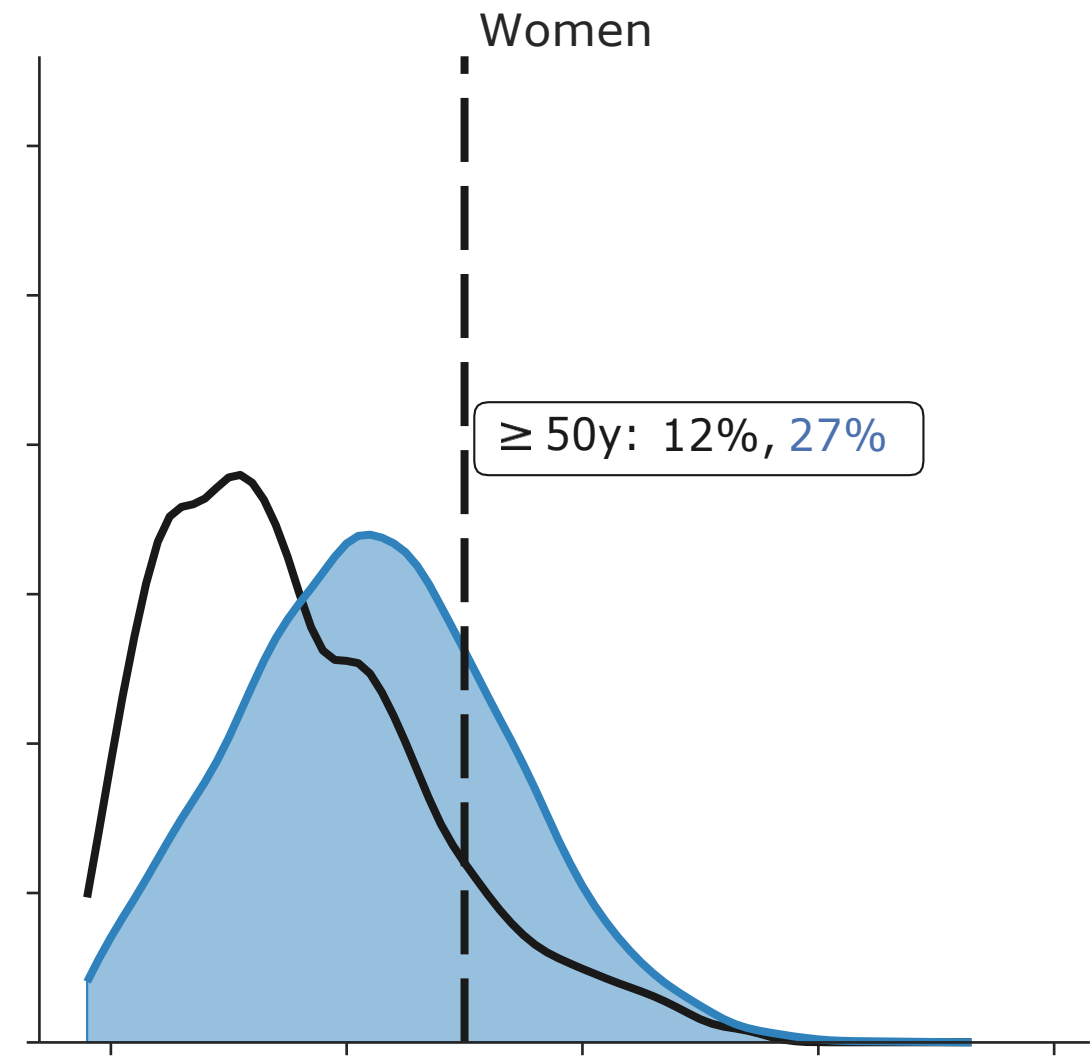
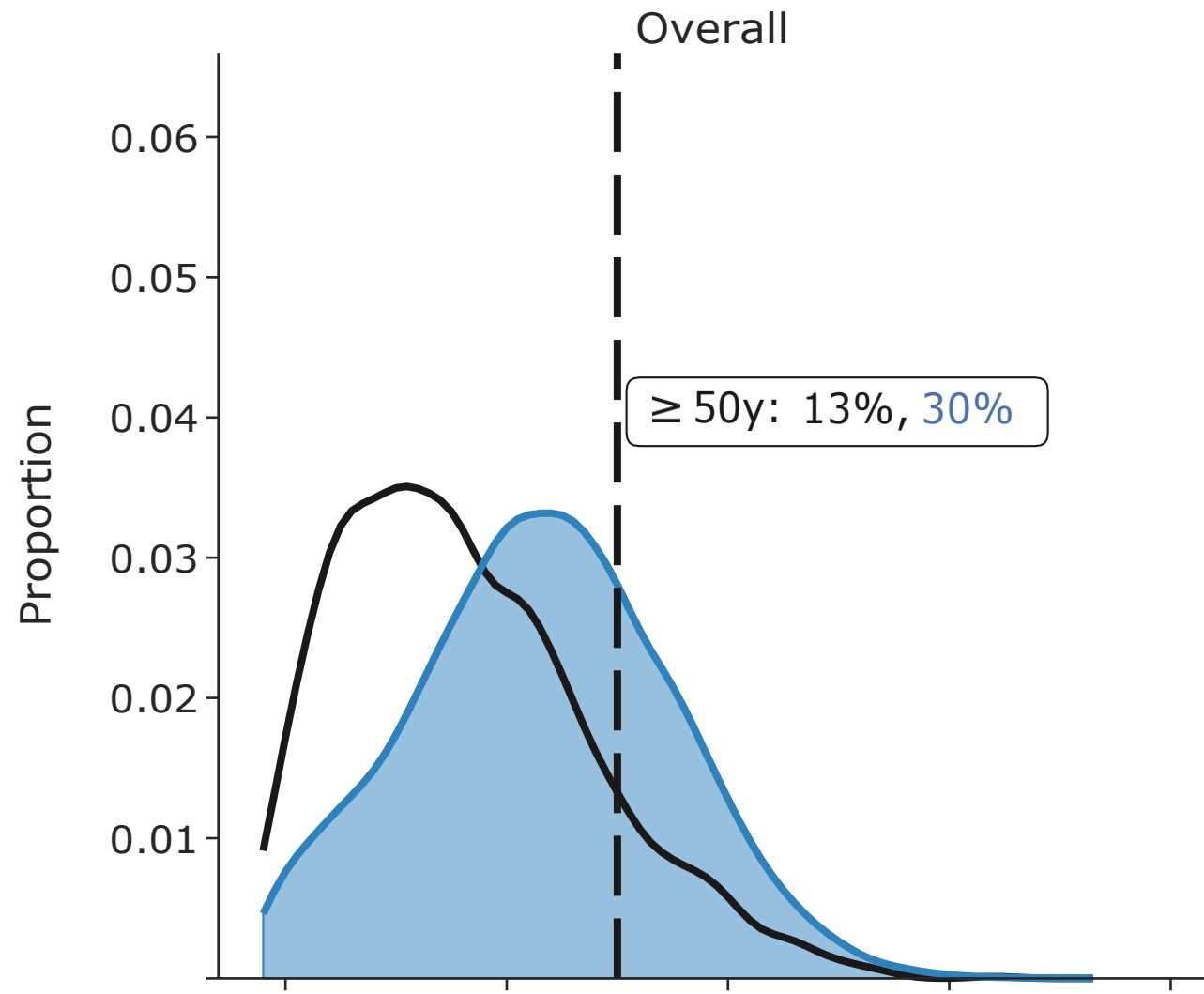
e. Zaniewski E, et al. Trends in CD4 and viral load testing 2005-2018: multi-cohort study of people living with HIV in Southern Africa. J Int AIDS Soc 2020;23(7):e25546

**Appendix Figure 1 a-z.** Distribution of People Presenting for Care and In Care by Age, Sex, and IEDEA Region



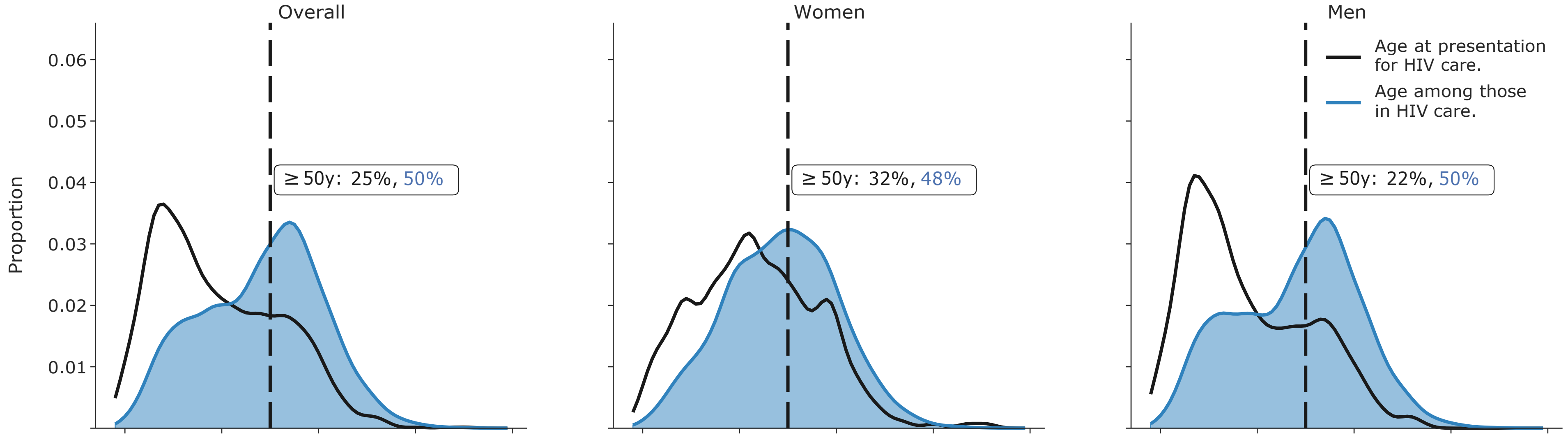


# IeDEA Central Africa Region (2019)

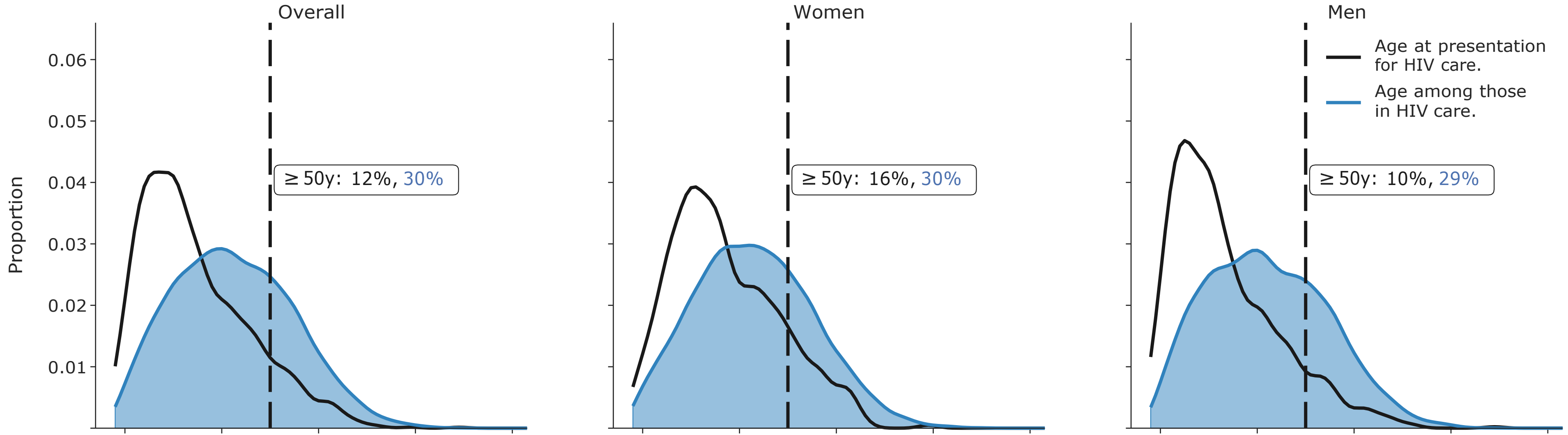


— Age at presentation for HIV care.  
— Age among those in HIV care.

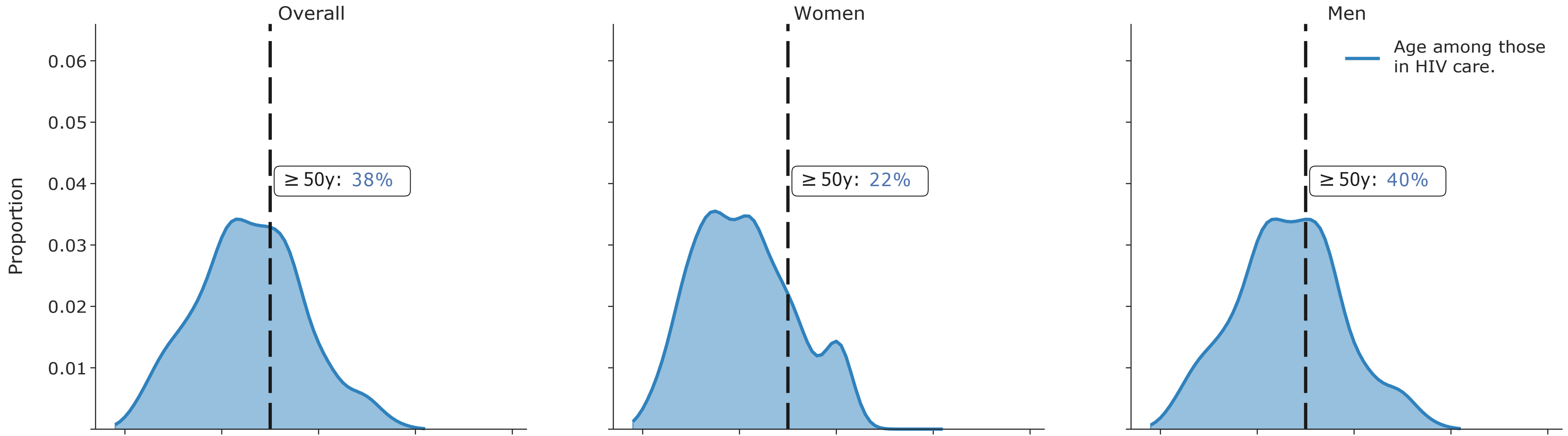
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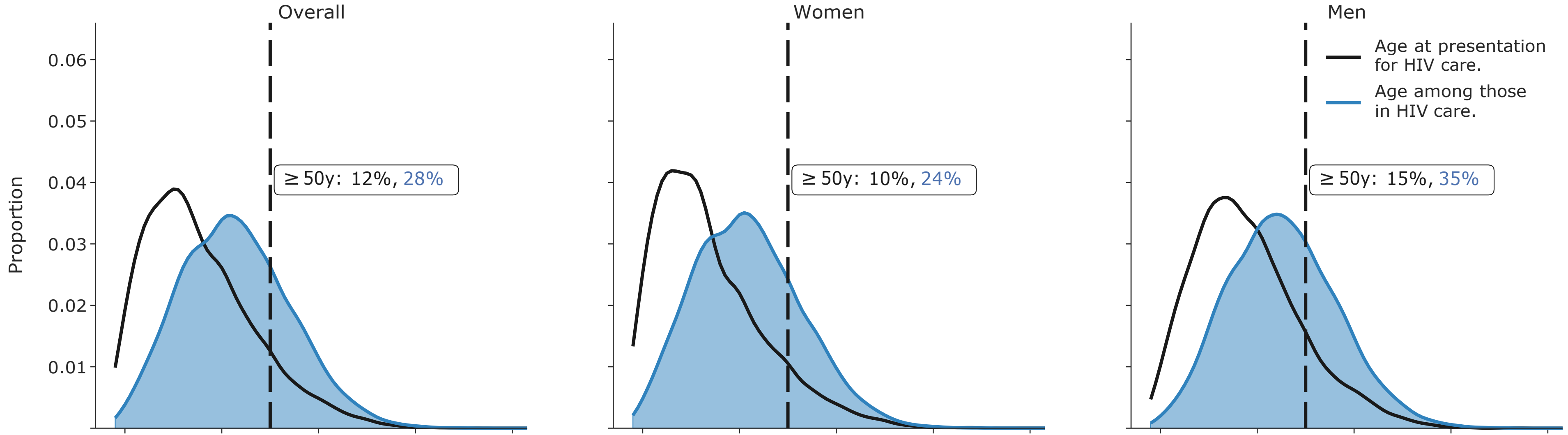
# IeDEA Central and South America and the Caribbean Region (2019)



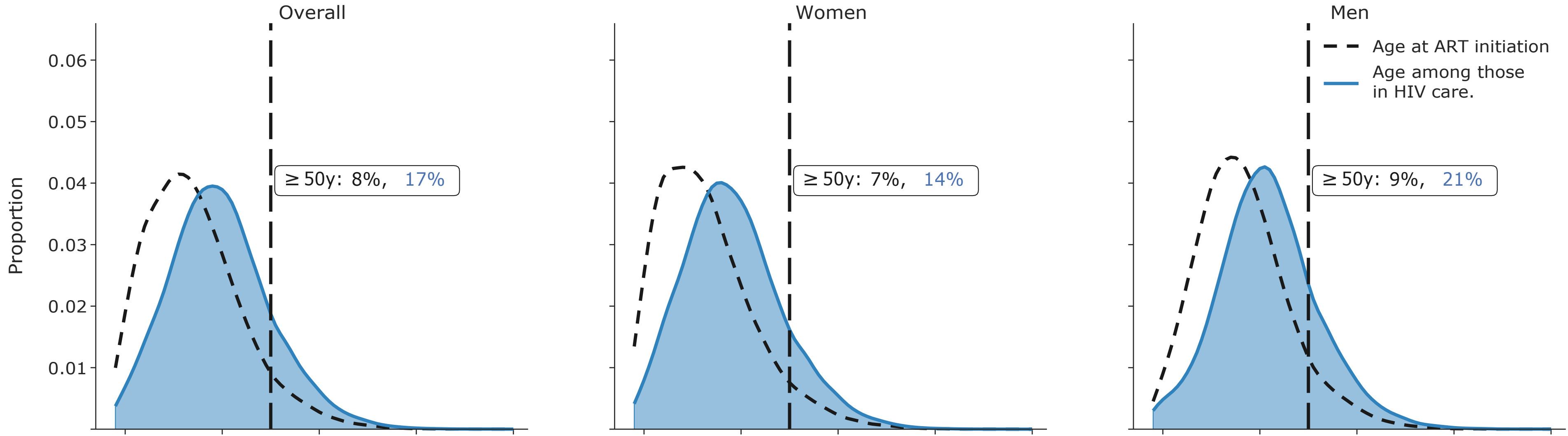
# IeDEA Asia-Pacific Region - Australia Sub-Cohort (2016)



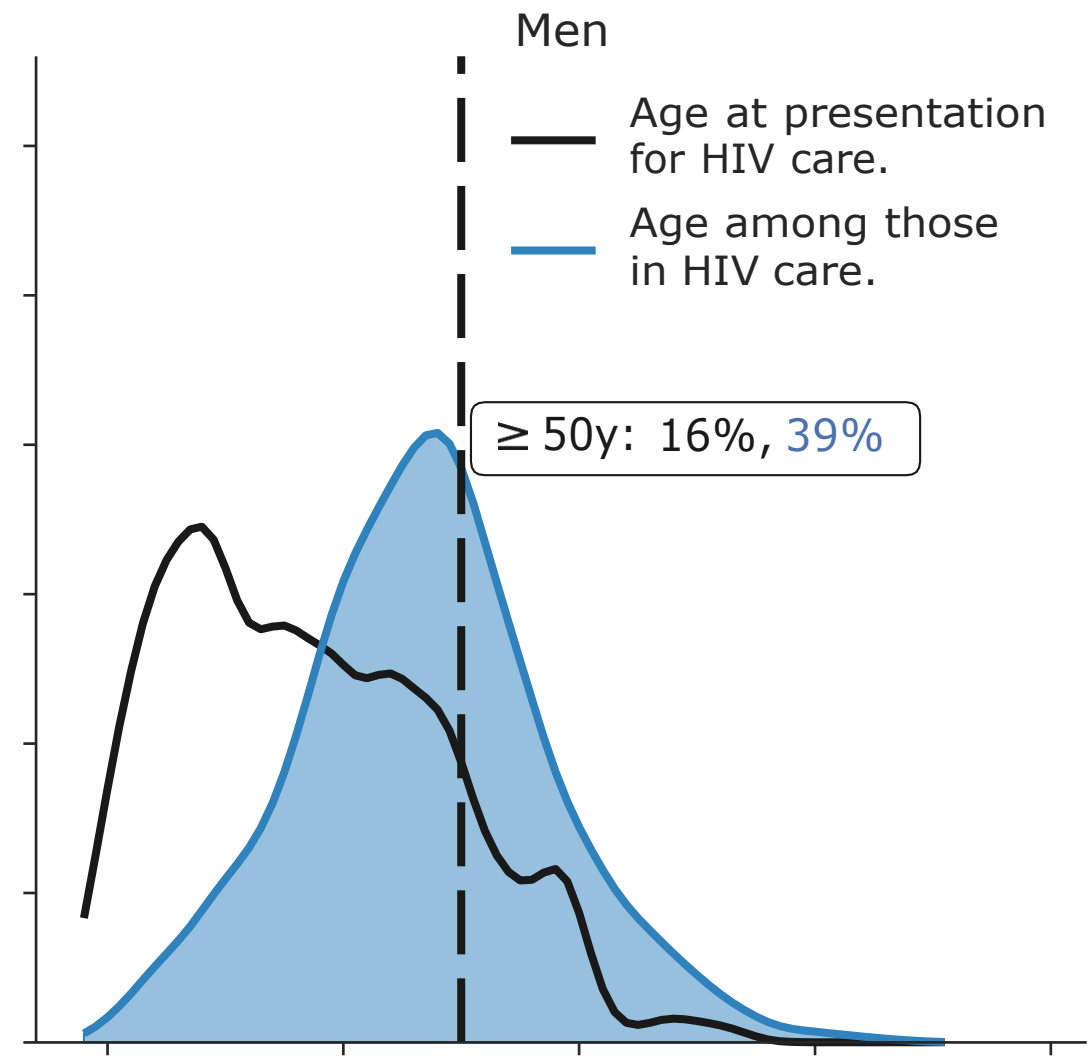
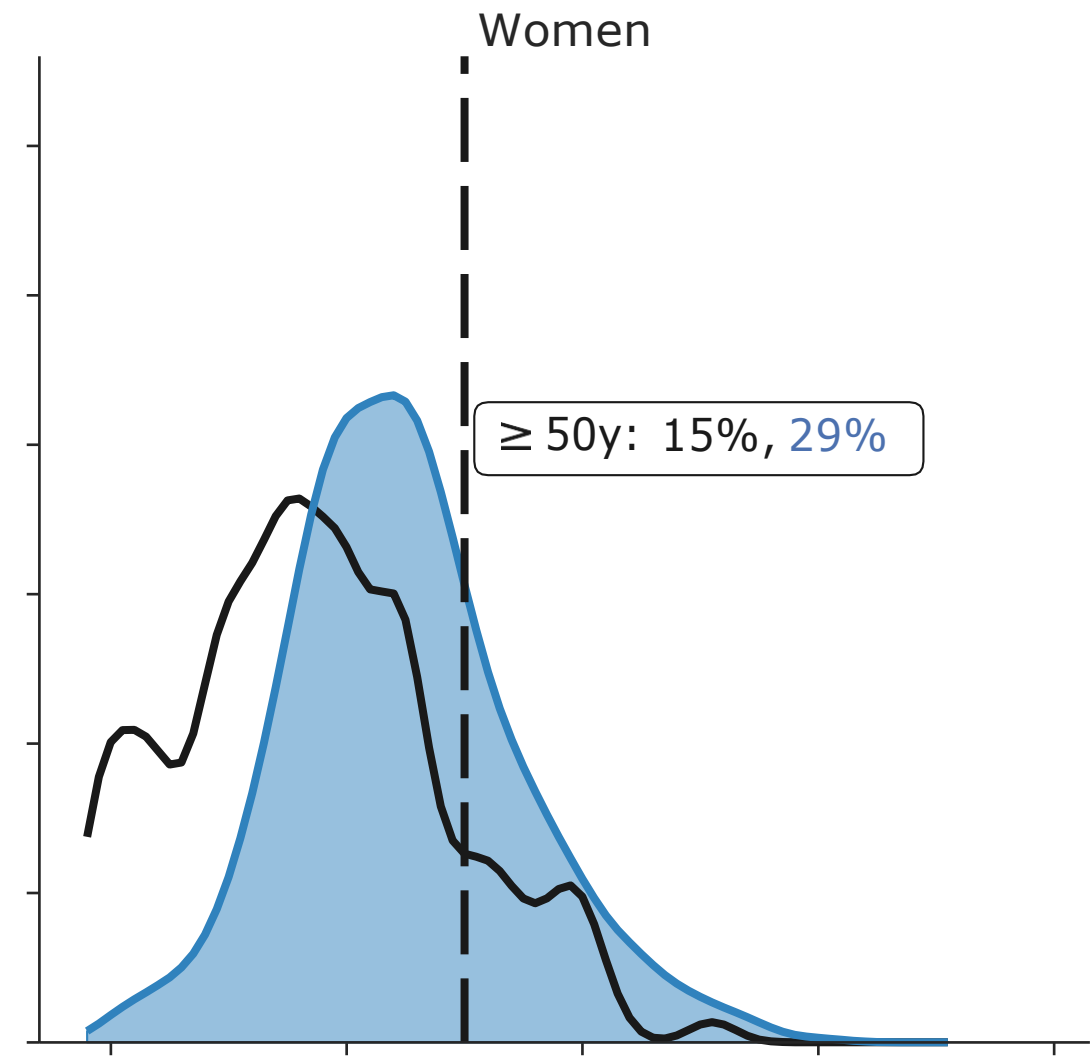
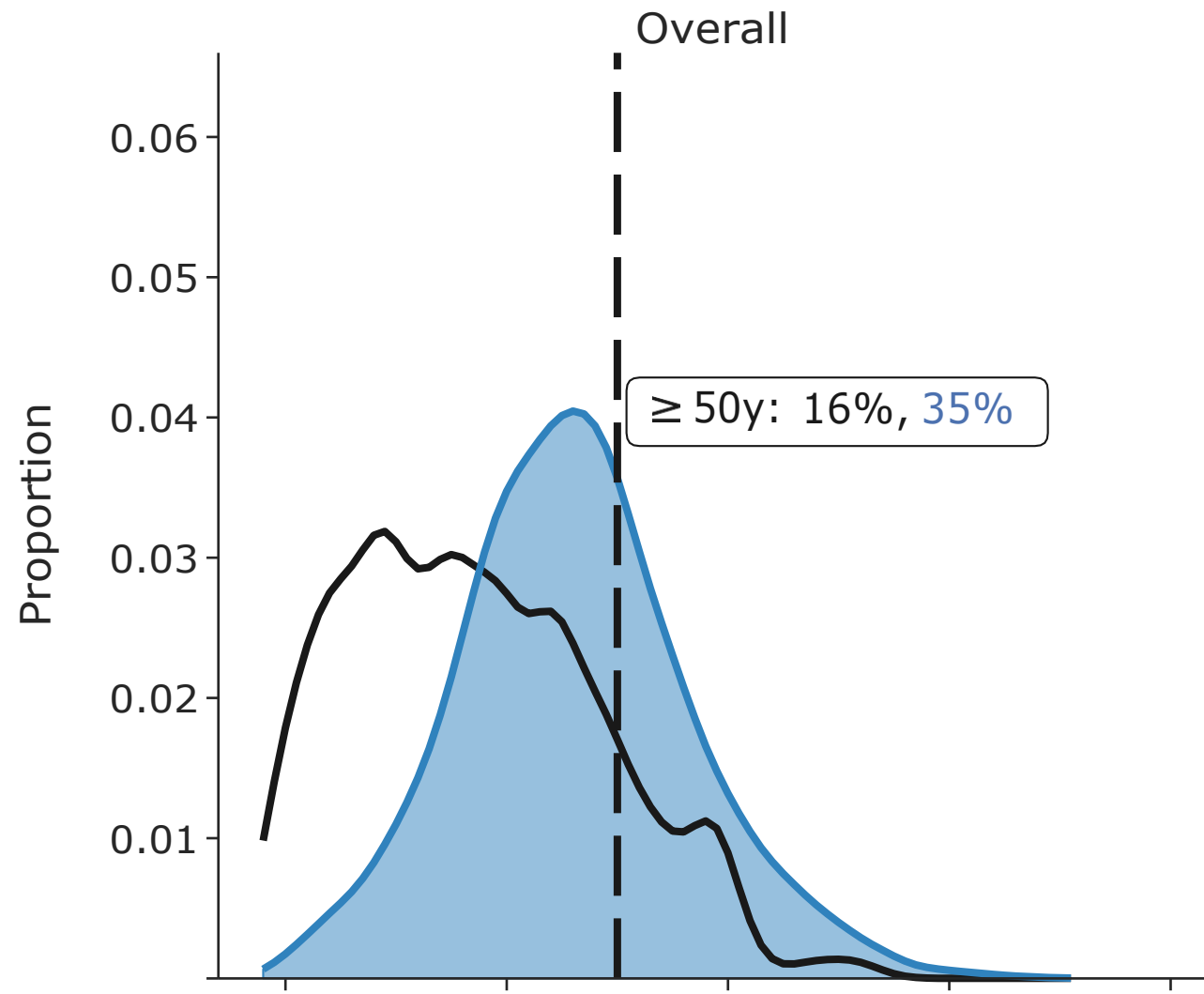
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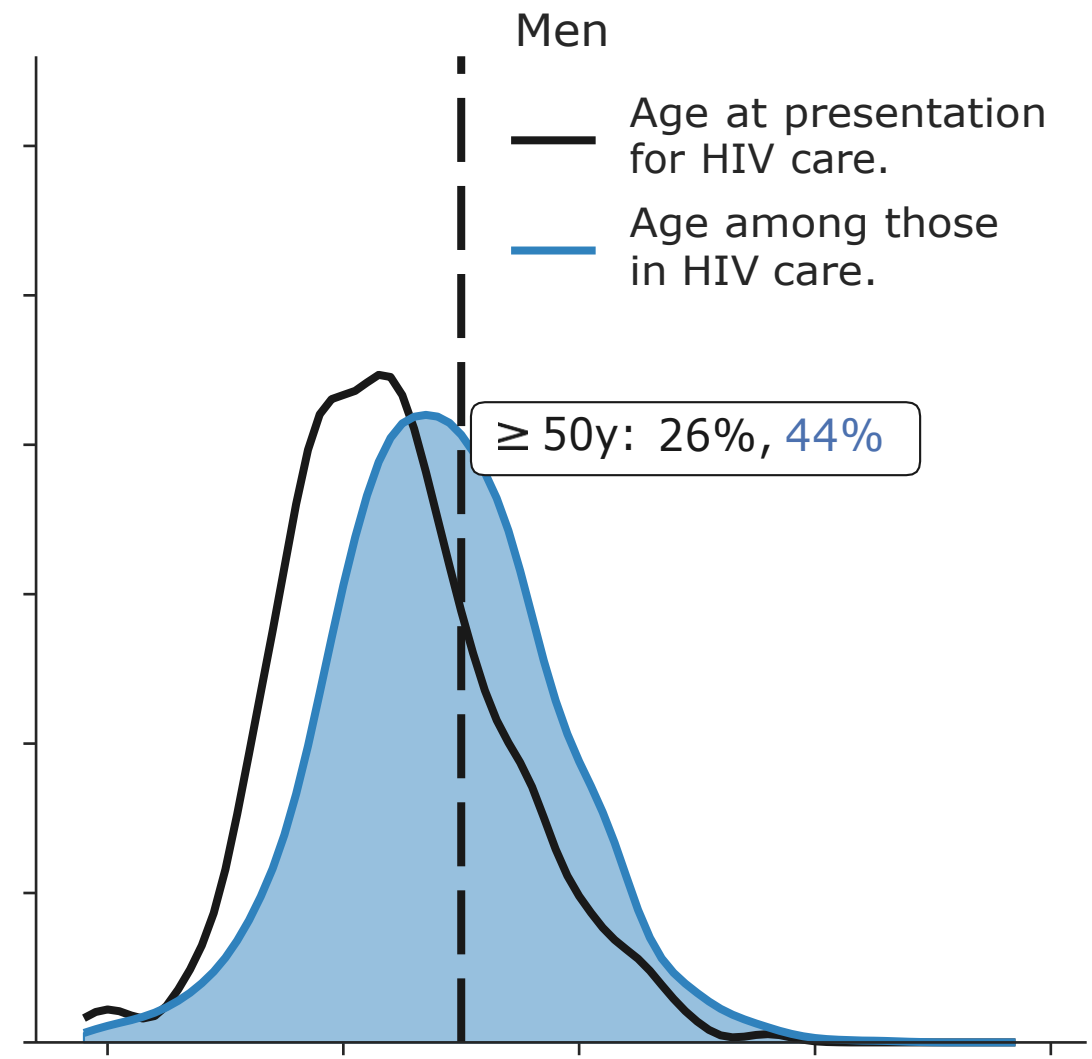
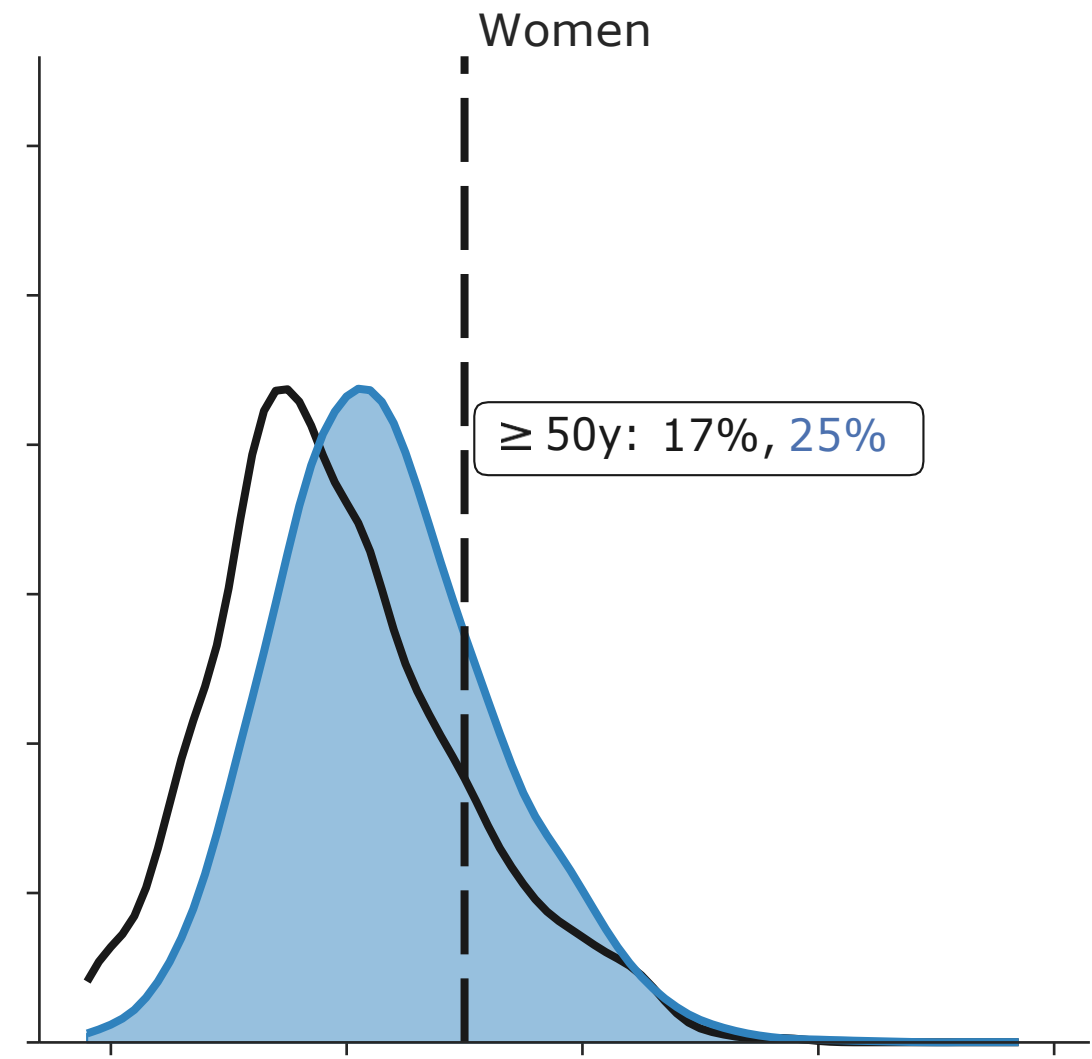
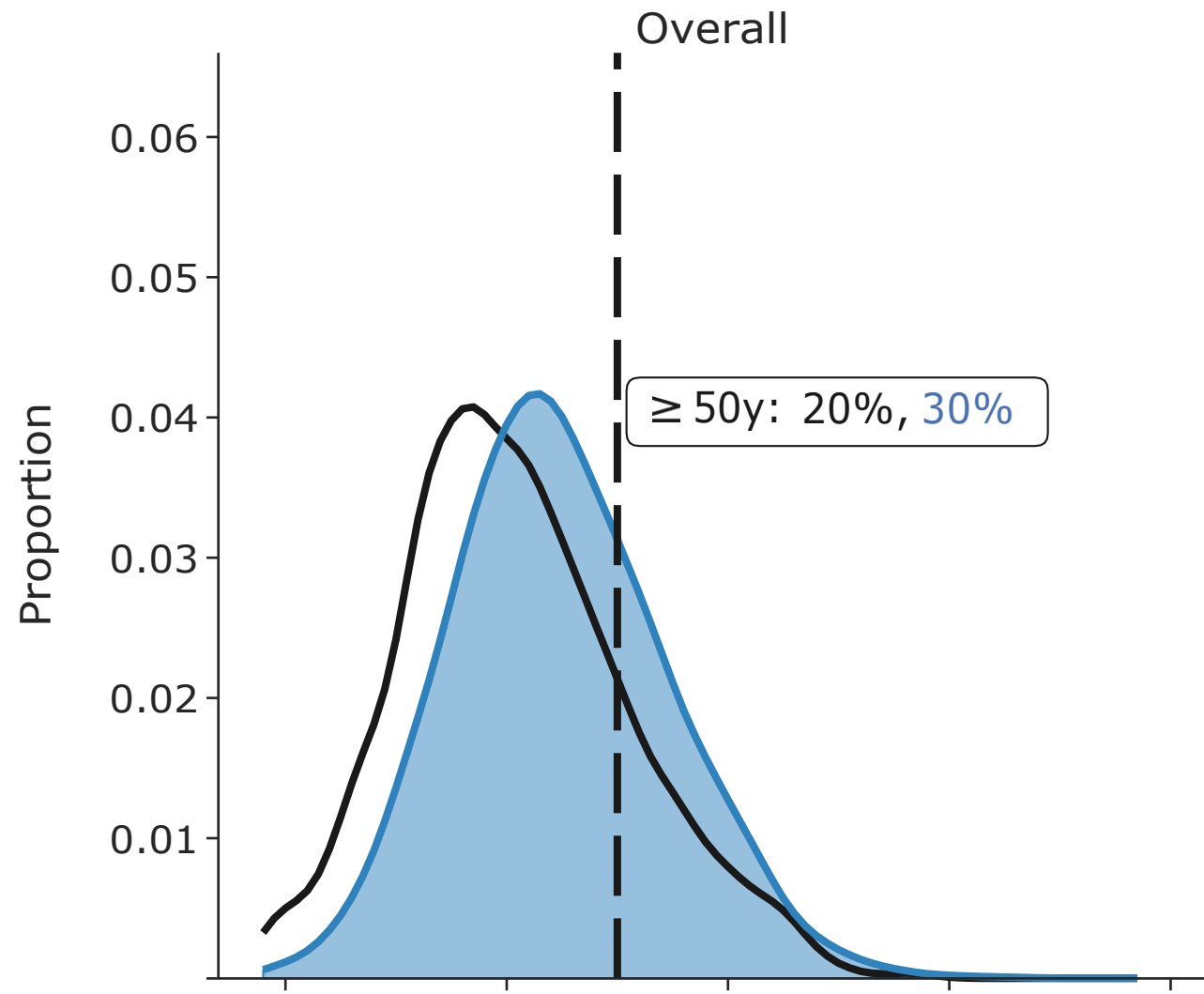
# IeDEA Southern Africa Region (2017)



# IeDEA Asia-Pacific Region (2019)



# IeDEA West Africa Region (2017)



— Age at presentation for HIV care.  
— Age among those in HIV care.