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Risk factors associated with pulmonary arterial hypertension among HIV-infected adults: A meta-analysis and systematic review

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Table 1. Characteristics of the studies reported risk factors associated with PAH among PLWH

	Country	Study design	Sample size	Diagnostic criteria	Inclusion/exclusion criteria	Age (mean/median)	Male %	ART %	Duration of HIV infection (mean, months)	CD4 count, cells/μL	HIV RNA Load copies	PAH %	Risk of bias
Reinsch, 2008	France	Cross sectional	802	PSAP > 35 mmHg	Inclusion: HIV-infected people; Exclusion: age < 18 years, an unstable cardiovascular status in the 4 weeks before the screening visit, current hospitalization and pregnancy	44.3	83.4	85.3	93	508	34973 ± 73113	4.7	Low
Sitbon, 2008	France	Cross sectional	277	V_{TR} > 2.5 m/s (PSAP > 30 mmHg) in combination with symptoms of dyspnea and was confirmed by RHC	Inclusion: HIV-infected people with symptoms of dyspnea; Exclusion: dyspnea explained by known severe pulmonary function impairment or by known severe heart disease, severe anemia, other cardiac complications due to HIV Infection, chronic thro mboembolic disease, connective tissue disease, patients who were hospitalized	42.3	55	85.6	120	< 200 (%): 20%	< 400, 66%	0.46	Low
Quezada, 2012	Spain	Cross sectional	392	PSAP > 35 mmHg	Inclusion: HIV-infected people	46.9	83.4	84	156	577	Viral load detectable, n (%): 81 (23.8)	9.9	Low
Sliwa, 2012	South Africa	Cross sectional	520	PSAP > 35 mmHg	Inclusion: HIV-infected people with ***de novo*** presentations of heart disease and other cardiovascular disease	40	38	54	NA.	N.A.	N.A.	9.8	Moderate
Isasti, 2013	Spain	Cross sectional	194	PSAP > 40 mmHg	Inclusion: asymptomatic HIV-infected patients, older than 18 years of age; Exclusion: patients with structural heart disease of any etiology, be pregnant or lactating	47	85.2	94	131.5	495	Viral load detectable, n (%): 15 (11.9)	2.6	Moderate
Ten Freyhaus, 2014	Germany	Prospective cohort	220	PSAP > 35 mmHg	Inclusion: HIV-infected people	44	84.1	100	N.A.	400	< 50 (< 50-1738821)	7.7	Low
Sangal, 2014	USA	Retrospective cohort	43	PSAP > 40 mmHg	Inclusion: HIV-HCV coinfected patients	52	67	88	228	450	Viral load detectable, n (%): 29 (43)	25.6	Low
Schwarze-Zander, 2015	Germany	Cross sectional	374	PSAP > 30 mmHg	Inclusion: HIV-infacted patients	46	80	87	100.8	476	Viral load detectable, n (%): 94 (25)	6.1	Moderate
Brittan, 2018	USA	Prospective cohort	2831	PSAP > 40 mmHg	Inclusion: HIV-infected patients	57	98	72	N.A.	CD4 < 200 cells/ml, n (%): 599 (21.2)	Viral load detectable, n (%): 948	27.6	Low
Huluka, 2020	Ethiopia	Cross sectional	315	PSAP > 35 mmHg	Inclusion: HIV participants ≥ 18 years old. Exclusion: Patients with evidence of Group 2 PAH on echo cardiography and those with already known Group 3 PAH from ILD, COPD, or post-tuberculosis structural parenchymal pathologies	44.5	72.7	N.A.	123.9	480	Viral load detectable, n (%): 20 (6.3)	14	Moderate

PAH: pulmonary arterial hypertension; PLWH: people living with HIV; N.A.: not available; PSAP: pulmonary systolic artery pressure; V_{TR}: peak velocity of tricuspid regurgitation; RHC: right heart catheterization; HCV: hepatitis C virus; ILD: Interstitial lung disease; COPD: Chronic obstructive pulmonary disease.

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Supplementary Table 2. Prevalence and level of risk factor by PAH status among included studies

	Age		Duration of HIV infection, months		ART duration, months		CD4 count, cells/mL		HIV RNA load copies		ART (%)		MSM (%)		IVDUs (%)	
	PAH (+)	PAH (–)	PAH (+)	PAH (–)	PAH (+)	PAH (–)	PAH (+)	PAH (–)	PAH (+)	PAH (–)	PAH (+)	PAH (–)	PAH (+)	PAH (–)	PAH (+)	PAH (–)
Reinsch, 2008	48.3 ± 8.4***	43.5 ± 10.1	115.1 ± 71.6	99.5 ± 71.1	N.A.	N.A.	431 ± 271	498 ± 301	24620 ± 30724	41165 ± 92371	92%	85.%	61%	57%	8%	11%
Sitbon, 2008	41.51 ± 8.04	42.40 ± 9.03	10.17 ± 6.42	9.87 ± 5.74	N.A.	N.A.	N.A.	N.A.	Viral load<400 copies/ml: 66%	Viral load<400 copies/ml: 66%	86%	86%	11.4%	25%	51%***	21.9%
Quezada, 2012	46.04 ± 8.49	45.12 ± 10.04	149.87 ± 55.2	186.9 ± 49.25	96.2 ± 47.9	115.12 ± 33.19	613.12 ± 290.48	584.84 ± 478.46	Detectable viral load: 38.4%***	Detectable viral load: 18.6%	85%	84%	34.5%	54.9%	44%**	25%
Sliwa, 2012	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Isasti, 2013	56.3 ± 7.6	46.1 ± 9.4	159.6 ± 92.4	122.5 ± 88.4	149.3 ± 79.2	83.3 ± 67.2	363.3 ± 126.7	545.5 ± 259.5	Detectable viral load: 0%	Detectable viral load: 87.8%	100%	94%	N.A.	N.A.	N.A.	N.A.
ten Freyhaus, 2014	47 (21-75)	46 ± 22	N.A.	N.A.	N.A.	N.A.	340 (10-700)	420 (10-1500)	<50 (<50-292,414)	<50 (<50-1,738,821)	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Sangal, 2014	53 (45-57)	52 (46-57)	216.35 ± 53.36	215.36 ± 96.93	N.A.	N.A.	337.21 ± 138.27	460.87 ± 236.72	Detectable viral load: 36%	Detectable viral load: 41%	N.A.	N.A.	N.A.	N.A.	64%	59%
Schwarze -Zander, 2015	51 ± 12	45 ± 10	102 ± 56.4	118.8 ± 93.6	N.A.	N.A.	428 ± 278	517 ± 270	N.A.	N.A.	96%	87%	13%***	45%	21.7%	7%
Brittan, 2018	57.9 ± 10.0	56.7 ± 9.8	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	Viral load<500 copies/ml: 68.6%	Viral load<500 copies/ml: 61%	61%	66%	N.A.	N.A.	N.A.	N.A.
Huluka, 2020	N.A.	N.A.	118.68 ± 46.44	124.8 ± 48.48	117 ± 46.56	114.84 ± 47.28	430.5 ± 160.35	488.07 ± 228.00	Detectable viral load: 0%	Detectable viral load: 7.4%.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.

	Males (%)		African descent (%)		Smoking history (%)		Dyslipidemia (%)		Diabetes (%)		Hypertension (%)		Detectable viral load (%)		HCV (%)	
	PAH (+)	PAH (–)	PAH (+)	PAH (–)	PAH (+)	PAH (–)	PAH (+)	PAH (–)	PAH (+)	PAH (–)	PAH (+)	PAH (–)	PAH (+)	PAH (–)	PAH (+)	PAH (–)
Reinsch, 2008	90%	80%	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Sitbon, 2008	71%*	53%	17%	26%	N.A.	26%	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	34%	N.A.	N.A.	N.A.
Quezada, 2012	67%*	85%	N.A.	N.A.	41.0%	N.A.	20.5%	36%	7.7%	9%	17.9%	15%	39%**	19%	39%	26%
Sliwa, 2012	45%	38%	97%***	86%	N.A.	86%	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Isasti, 2013	100%	85%	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	20%	8.5%	40%	17%	0%	7%	0%	28%
ten Freyhaus, 2014	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	35%	15%	N.A.	N.A.	N.A.	N.A.
Sangal, 2014	73%	63%	36%	38%	82%	38%	N.A.	N.A.	36%	16%	36%	38%	N.A.	N.A.	N.A.	N.A.
Schwarze-Zander, 2015	65%	82%	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Brittan, 2018	98%	97%	61%	48%	77%	48%	67%	69%	44.2%	33%	95%	89%	39%	31%	43%	41%
Huluka, 2020	36%	26%	N.A.	N.A.	9%	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	0%	7%	N.A.	N.A.

PAH: pulmonary arterial hypertension; N.A.: not available; ART: antiretroviral therapy; MSM: men who have sex with men; IVDUs: intravenous drug users; HCV: hepatitis c virus; *p<0.05, **p<0.01, ***p<0.001.