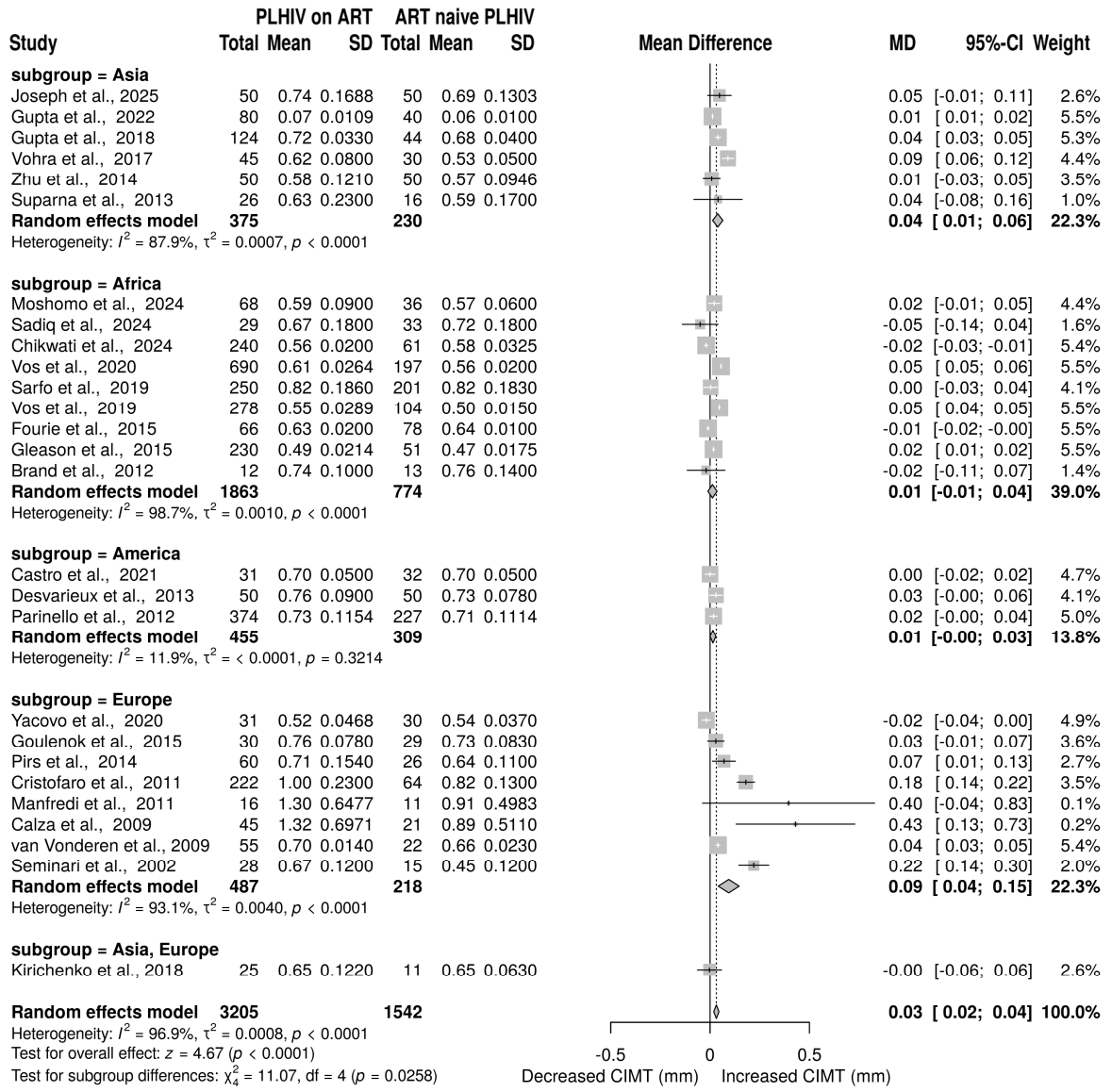
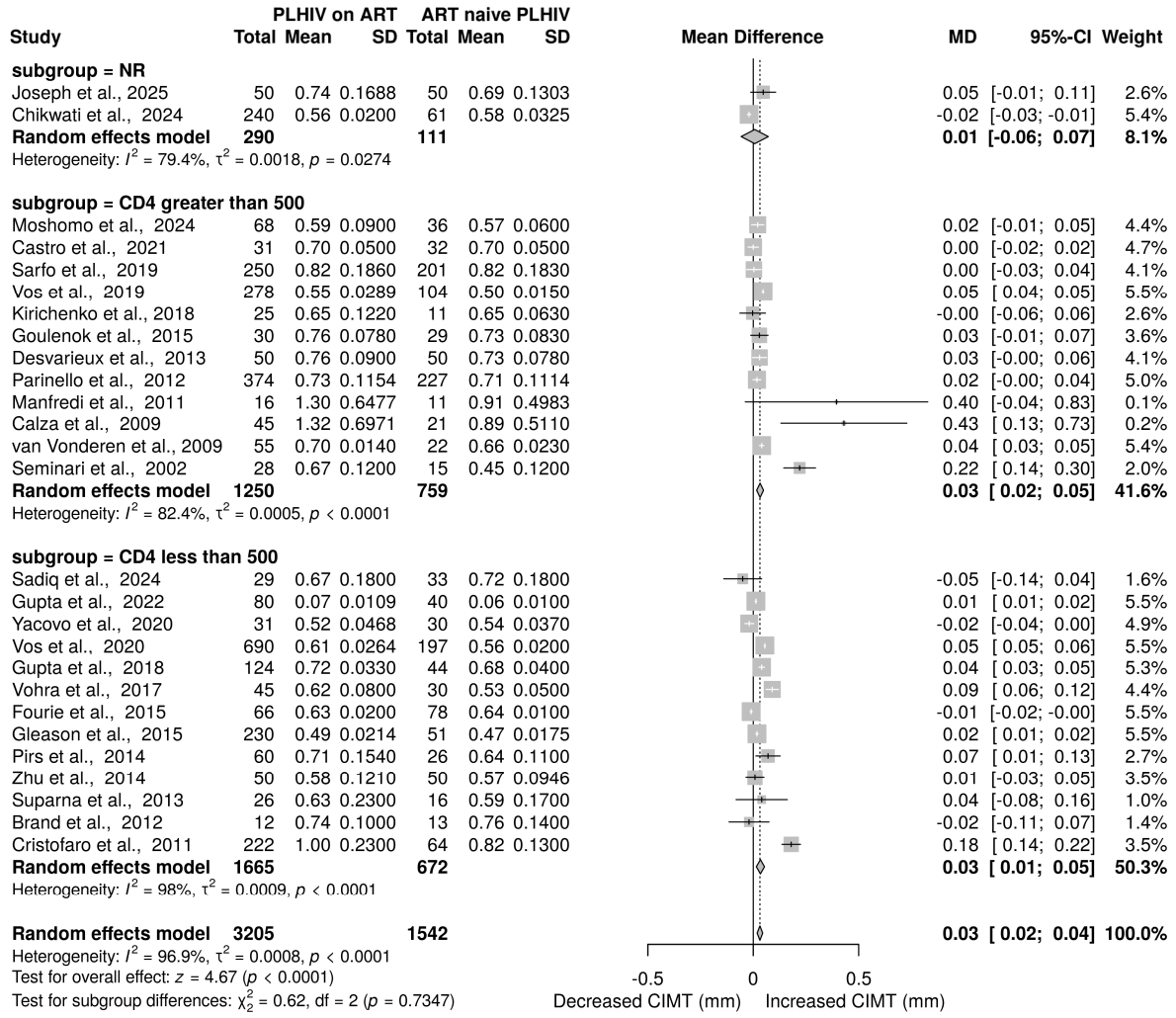
The Association Between HIV Infection and Carotid Intima-Media Thickness in the Era of Antiretroviral Therapy: A Meta-Analysis

Table S1: Search strategy used on databases

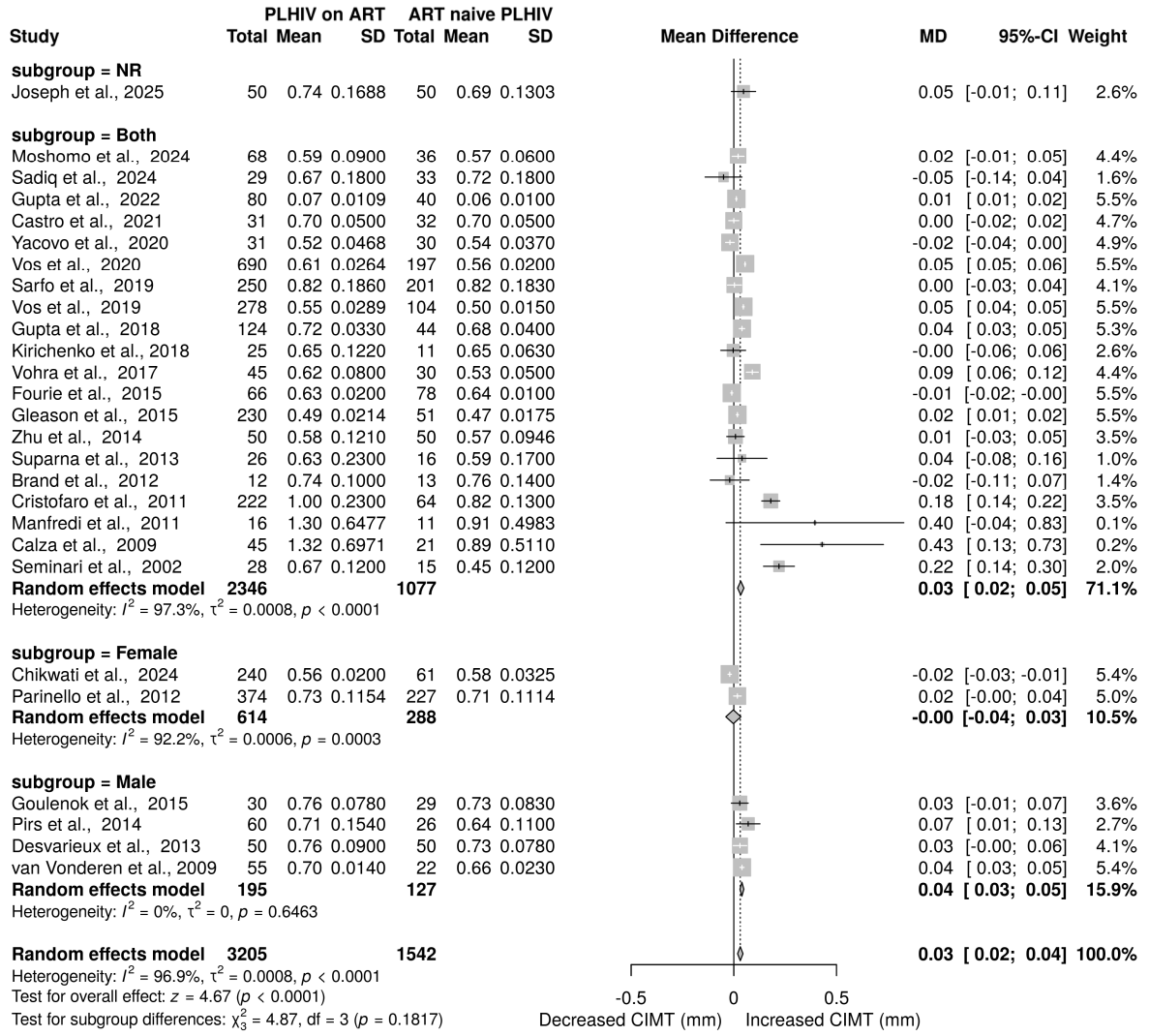
Database	Search	Number
PubMed	(((Antiretroviral therapy) OR (combined antiretroviral therapy)) AND (HIV)) AND (carotid intima media thickness)	271
Scopus	(TITLE-ABS-KEY (carotid AND intima AND media AND thickness) AND TITLE-ABS-KEY (hiv) AND TITLE-ABS-KEY (carotid AND intima AND media AND thickness)) AND (LIMIT-TO (SRCTYPE , "j")) AND (LIMIT-TO (DOCTYPE , "ar")) AND (LIMIT-TO (LANGUAGE , "English"))	390
EBSCOhost	((Title Combined:(Antiretroviral therapy)) OR (TitleCombined:(Highly active antiretroviral therapy))) AND (HIV) AND (Carotid intima media thickness)	59


Study
PLHIV on ART
Total Mean SD
ART naive PLHIV
Total Mean SD
Mean Difference
MD 95%-CI Weight
subgroup = Asia
Joseph et al., 2025 50 0.74 0.1688 50 0.69 0.1303 0.05 [-0.01; 0.11] 2.6%
Gupta et al., 2022 80 0.07 0.0109 40 0.06 0.0100 0.01 [0.01; 0.02] 5.5%
Gupta et al., 2018 124 0.72 0.0330 44 0.68 0.0400 0.04 [0.03; 0.05] 5.3%
Vohra et al., 2017 45 0.62 0.0800 30 0.53 0.0500 0.09 [0.06; 0.12] 4.4%
Zhu et al., 2014 50 0.58 0.1210 50 0.57 0.0946 0.01 [-0.03; 0.05] 3.5%
Suparna et al., 2013 26 0.63 0.2300 16 0.59 0.1700 0.04 [-0.08; 0.16] 1.0%
Random effects model 375 230 0.04 [0.01; 0.06] 22.3%
Heterogeneity: I^2 = 87.9%, τ^2 = 0.0007, p < 0.0001
subgroup = Africa
Moshomo et al., 2024 68 0.59 0.0900 36 0.57 0.0600 0.02 [-0.01; 0.05] 4.4%
Sadiq et al., 2024 29 0.67 0.1800 33 0.72 0.1800 -0.05 [-0.14; 0.04] 1.6%
Chikwati et al., 2024 240 0.56 0.0200 61 0.58 0.0325 -0.02 [-0.03; -0.01] 5.4%
Vos et al., 2020 690 0.61 0.0264 197 0.56 0.0200 0.05 [0.05; 0.06] 5.5%
Sarfo et al., 2019 250 0.82 0.1860 201 0.82 0.1830 0.00 [-0.03; 0.04] 4.1%
Vos et al., 2019 278 0.55 0.0289 104 0.50 0.0150 0.05 [0.04; 0.05] 5.5%
Fourie et al., 2015 66 0.63 0.0200 78 0.64 0.0100 -0.01 [-0.02; -0.00] 5.5%
Gleason et al., 2015 230 0.49 0.0214 51 0.47 0.0175 0.02 [0.01; 0.02] 5.5%
Brand et al., 2012 12 0.74 0.1000 13 0.76 0.1400 -0.02 [-0.11; 0.07] 1.4%
Random effects model 1863 774 0.01 [-0.01; 0.04] 39.0%
Heterogeneity: I^2 = 98.7%, τ^2 = 0.0010, p < 0.0001
subgroup = America
Castro et al., 2021 31 0.70 0.0500 32 0.70 0.0500 0.00 [-0.02; 0.02] 4.7%
Desvarieux et al., 2013 50 0.76 0.0900 50 0.73 0.0780 0.03 [-0.00; 0.06] 4.1%
Parinello et al., 2012 374 0.73 0.1154 227 0.71 0.1114 0.02 [-0.00; 0.04] 5.0%
Random effects model 455 309 0.01 [-0.00; 0.03] 13.8%
Heterogeneity: I^2 = 11.9%, τ^2 = < 0.0001, p = 0.3214
subgroup = Europe
Yacovo et al., 2020 31 0.52 0.0468 30 0.54 0.0370 -0.02 [-0.04; 0.00] 4.9%
Goulenok et al., 2015 30 0.76 0.0780 29 0.73 0.0830 0.03 [-0.01; 0.07] 3.6%
Pirs et al., 2014 60 0.71 0.1540 26 0.64 0.1100 0.07 [0.01; 0.13] 2.7%
Cristofaro et al., 2011 222 1.00 0.2300 64 0.82 0.1300 0.18 [0.14; 0.22] 3.5%
Manfredi et al., 2011 16 1.30 0.6477 11 0.91 0.4983 0.40 [-0.04; 0.83] 0.1%
Calza et al., 2009 45 1.32 0.6971 21 0.89 0.5110 0.43 [0.13; 0.73] 0.2%
van Vonderen et al., 2009 55 0.70 0.0140 22 0.66 0.0230 0.04 [0.03; 0.05] 5.4%
Seminari et al., 2002 28 0.67 0.1200 15 0.45 0.1200 0.22 [0.14; 0.30] 2.0%
Random effects model 487 218 0.09 [0.04; 0.15] 22.3%
Heterogeneity: I^2 = 93.1%, τ^2 = 0.0040, p < 0.0001
subgroup = Asia, Europe
Kirichenko et al., 2018 25 0.65 0.1220 11 0.65 0.0630 -0.00 [-0.06; 0.06] 2.6%
Random effects model 3205 1542 0.03 [0.02; 0.04] 100.0%
Heterogeneity: I^2 = 96.9%, τ^2 = 0.0008, p < 0.0001
Test for overall effect: z = 4.67 (p < 0.0001)
Test for subgroup differences: χ^2_4 = 11.07, df = 4 (p = 0.0258)
-0.5
0
0.5
Decreased CIMT (mm)
Increased CIMT (mm)

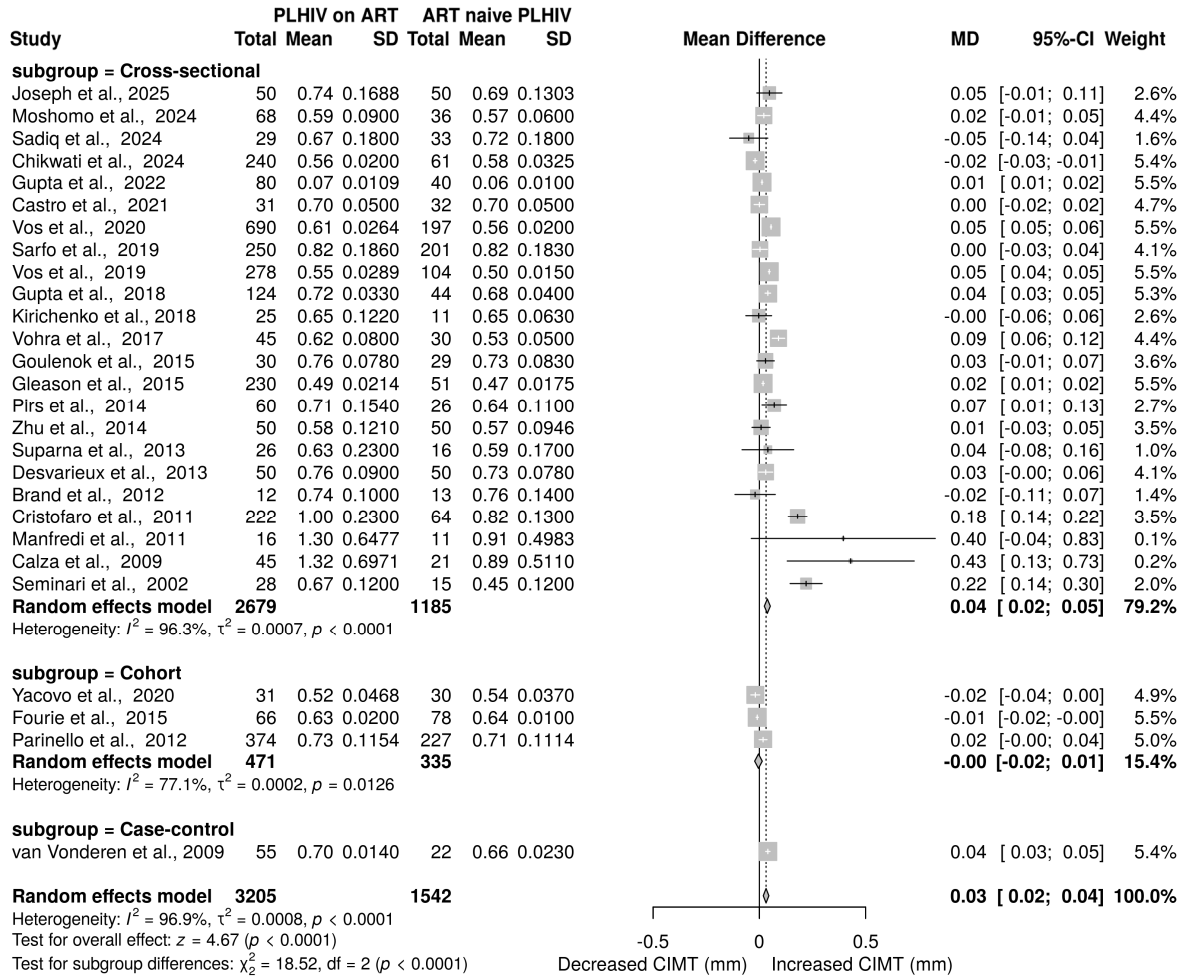
A


PLHIV on ART
ART naive PLHIV
Study
Total Mean SD Total Mean SD
Mean Difference
MD 95%-CI Weight
subgroup = NR
Joseph et al., 2025 50 0.74 0.1688 50 0.69 0.1303 0.05 [-0.01; 0.11] 2.6%
Chikwati et al., 2024 240 0.56 0.0200 61 0.58 0.0325 -0.02 [-0.03; -0.01] 5.4%
Random effects model 290 111 0.01 [-0.06; 0.07] 8.1%
Heterogeneity: I^2 = 79.4%, τ^2 = 0.0018, p = 0.0274
subgroup = CD4 greater than 500
Moshomo et al., 2024 68 0.59 0.0900 36 0.57 0.0600 0.02 [-0.01; 0.05] 4.4%
Castro et al., 2021 31 0.70 0.0500 32 0.70 0.0500 0.00 [-0.02; 0.02] 4.7%
Sarfo et al., 2019 250 0.82 0.1860 201 0.82 0.1830 0.00 [-0.03; 0.04] 4.1%
Vos et al., 2019 278 0.55 0.0289 104 0.50 0.0150 0.05 [0.04; 0.05] 5.5%
Kirichenko et al., 2018 25 0.65 0.1220 11 0.65 0.0630 -0.00 [-0.06; 0.06] 2.6%
Goulenok et al., 2015 30 0.76 0.0780 29 0.73 0.0830 0.03 [-0.01; 0.07] 3.6%
Desvarieux et al., 2013 50 0.76 0.0900 50 0.73 0.0780 0.03 [-0.00; 0.06] 4.1%
Parinello et al., 2012 374 0.73 0.1154 227 0.71 0.1114 0.02 [-0.00; 0.04] 5.0%
Manfredi et al., 2011 16 1.30 0.6477 11 0.91 0.4983 0.40 [-0.04; 0.83] 0.1%
Calza et al., 2009 45 1.32 0.6971 21 0.89 0.5110 0.43 [0.13; 0.73] 0.2%
van Vonderen et al., 2009 55 0.70 0.0140 22 0.66 0.0230 0.04 [0.03; 0.05] 5.4%
Seminari et al., 2002 28 0.67 0.1200 15 0.45 0.1200 0.22 [0.14; 0.30] 2.0%
Random effects model 1250 759 0.03 [0.02; 0.05] 41.6%
Heterogeneity: I^2 = 82.4%, τ^2 = 0.0005, p < 0.0001
subgroup = CD4 less than 500
Sadiq et al., 2024 29 0.67 0.1800 33 0.72 0.1800 -0.05 [-0.14; 0.04] 1.6%
Gupta et al., 2022 80 0.07 0.0109 40 0.06 0.0100 0.01 [0.01; 0.02] 5.5%
Yacovo et al., 2020 31 0.52 0.0468 30 0.54 0.0370 -0.02 [-0.04; 0.00] 4.9%
Vos et al., 2020 690 0.61 0.0264 197 0.56 0.0200 0.05 [0.05; 0.06] 5.5%
Gupta et al., 2018 124 0.72 0.0330 44 0.68 0.0400 0.04 [0.03; 0.05] 5.3%
Vohra et al., 2017 45 0.62 0.0800 30 0.53 0.0500 0.09 [0.06; 0.12] 4.4%
Fourie et al., 2015 66 0.63 0.0200 78 0.64 0.0100 -0.01 [-0.02; -0.00] 5.5%
Gleason et al., 2015 230 0.49 0.0214 51 0.47 0.0175 0.02 [0.01; 0.02] 5.5%
Pirs et al., 2014 60 0.71 0.1540 26 0.64 0.1100 0.07 [0.01; 0.13] 2.7%
Zhu et al., 2014 50 0.58 0.1210 50 0.57 0.0946 0.01 [-0.03; 0.05] 3.5%
Suparna et al., 2013 26 0.63 0.2300 16 0.59 0.1700 0.04 [-0.08; 0.16] 1.0%
Brand et al., 2012 12 0.74 0.1000 13 0.76 0.1400 -0.02 [-0.11; 0.07] 1.4%
Cristofaro et al., 2011 222 1.00 0.2300 64 0.82 0.1300 0.18 [0.14; 0.22] 3.5%
Random effects model 1665 672 0.03 [0.01; 0.05] 50.3%
Heterogeneity: I^2 = 98%, τ^2 = 0.0009, p < 0.0001
Random effects model 3205 1542 0.03 [0.02; 0.04] 100.0%
Heterogeneity: I^2 = 96.9%, τ^2 = 0.0008, p < 0.0001
Test for overall effect: z = 4.67 (p < 0.0001)
Test for subgroup differences: χ^2_2 = 0.62, df = 2 (p = 0.7347)
-0.5
0
0.5
Decreased CIMT (mm)
Increased CIMT (mm)

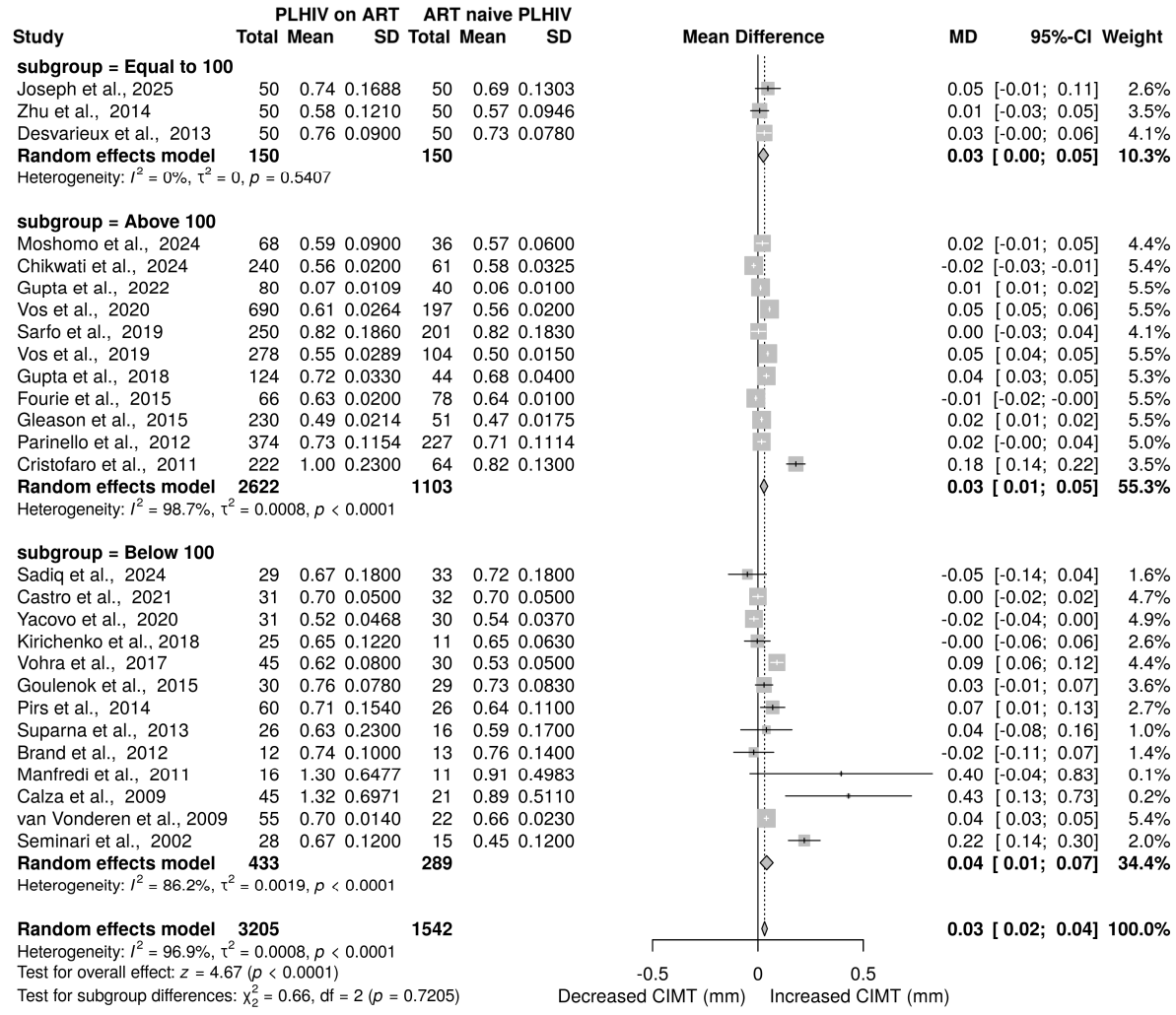
B


Study
PLHIV on ART
Total Mean SD
ART naive PLHIV
Total Mean SD
Mean Difference
MD 95%-CI Weight
subgroup = NR
Joseph et al., 2025 50 0.74 0.1688 50 0.69 0.1303 0.05 [-0.01; 0.11] 2.6%
subgroup = Both
Moshomo et al., 2024 68 0.59 0.0900 36 0.57 0.0600 0.02 [-0.01; 0.05] 4.4%
Sadiq et al., 2024 29 0.67 0.1800 33 0.72 0.1800 -0.05 [-0.14; 0.04] 1.6%
Gupta et al., 2022 80 0.07 0.0109 40 0.06 0.0100 0.01 [0.01; 0.02] 5.5%
Castro et al., 2021 31 0.70 0.0500 32 0.70 0.0500 0.00 [-0.02; 0.02] 4.7%
Yacovo et al., 2020 31 0.52 0.0468 30 0.54 0.0370 -0.02 [-0.04; 0.00] 4.9%
Vos et al., 2020 690 0.61 0.0264 197 0.56 0.0200 0.05 [0.05; 0.06] 5.5%
Sarfo et al., 2019 250 0.82 0.1860 201 0.82 0.1830 0.00 [-0.03; 0.04] 4.1%
Vos et al., 2019 278 0.55 0.0289 104 0.50 0.0150 0.05 [0.04; 0.05] 5.5%
Gupta et al., 2018 124 0.72 0.0330 44 0.68 0.0400 0.04 [0.03; 0.05] 5.3%
Kirichenko et al., 2018 25 0.65 0.1220 11 0.65 0.0630 -0.00 [-0.06; 0.06] 2.6%
Vohra et al., 2017 45 0.62 0.0800 30 0.53 0.0500 0.09 [0.06; 0.12] 4.4%
Fourie et al., 2015 66 0.63 0.0200 78 0.64 0.0100 -0.01 [-0.02; -0.00] 5.5%
Gleason et al., 2015 230 0.49 0.0214 51 0.47 0.0175 0.02 [0.01; 0.02] 5.5%
Zhu et al., 2014 50 0.58 0.1210 50 0.57 0.0946 0.01 [-0.03; 0.05] 3.5%
Suparna et al., 2013 26 0.63 0.2300 16 0.59 0.1700 0.04 [-0.08; 0.16] 1.0%
Brand et al., 2012 12 0.74 0.1000 13 0.76 0.1400 -0.02 [-0.11; 0.07] 1.4%
Cristofaro et al., 2011 222 1.00 0.2300 64 0.82 0.1300 0.18 [0.14; 0.22] 3.5%
Manfredi et al., 2011 16 1.30 0.6477 11 0.91 0.4983 0.40 [-0.04; 0.83] 0.1%
Calza et al., 2009 45 1.32 0.6971 21 0.89 0.5110 0.43 [0.13; 0.73] 0.2%
Seminari et al., 2002 28 0.67 0.1200 15 0.45 0.1200 0.22 [0.14; 0.30] 2.0%
Random effects model 2346 1077 0.03 [0.02; 0.05] 71.1%
Heterogeneity: I^2 = 97.3%, τ^2 = 0.0008, p < 0.0001
subgroup = Female
Chikwati et al., 2024 240 0.56 0.0200 61 0.58 0.0325 -0.02 [-0.03; -0.01] 5.4%
Parinello et al., 2012 374 0.73 0.1154 227 0.71 0.1114 0.02 [-0.00; 0.04] 5.0%
Random effects model 614 288 -0.00 [-0.04; 0.03] 10.5%
Heterogeneity: I^2 = 92.2%, τ^2 = 0.0006, p = 0.0003
subgroup = Male
Goulenok et al., 2015 30 0.76 0.0780 29 0.73 0.0830 0.03 [-0.01; 0.07] 3.6%
Pirs et al., 2014 60 0.71 0.1540 26 0.64 0.1100 0.07 [0.01; 0.13] 2.7%
Desvarieux et al., 2013 50 0.76 0.0900 50 0.73 0.0780 0.03 [-0.00; 0.06] 4.1%
van Vonderen et al., 2009 55 0.70 0.0140 22 0.66 0.0230 0.04 [0.03; 0.05] 5.4%
Random effects model 195 127 0.04 [0.03; 0.05] 15.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.6463
Random effects model 3205 1542 0.03 [0.02; 0.04] 100.0%
Heterogeneity: I^2 = 96.9%, τ^2 = 0.0008, p < 0.0001
Test for overall effect: z = 4.67 (p < 0.0001)
Test for subgroup differences: χ^2_3 = 4.87, df = 3 (p = 0.1817)
-0.5
0
0.5
Decreased CIMT (mm)
Increased CIMT (mm)

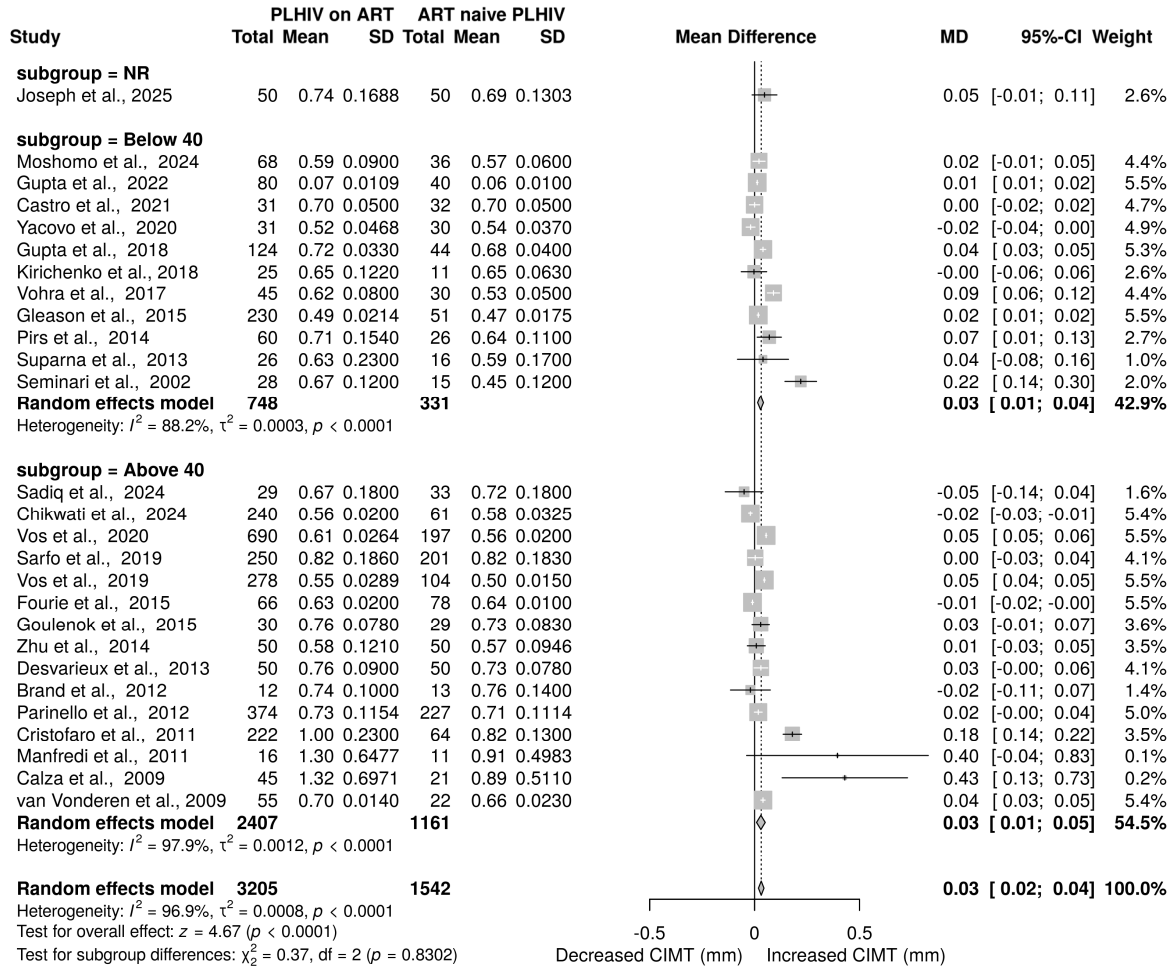
C


PLHIV on ART
ART naive PLHIV
Study
Total Mean SD Total Mean SD
Mean Difference
MD 95%-CI Weight
subgroup = Cross-sectional
Joseph et al., 2025 50 0.74 0.1688 50 0.69 0.1303 0.05 [-0.01; 0.11] 2.6%
Moshomo et al., 2024 68 0.59 0.0900 36 0.57 0.0600 0.02 [-0.01; 0.05] 4.4%
Sadiq et al., 2024 29 0.67 0.1800 33 0.72 0.1800 -0.05 [-0.14; 0.04] 1.6%
Chikwati et al., 2024 240 0.56 0.0200 61 0.58 0.0325 -0.02 [-0.03; -0.01] 5.4%
Gupta et al., 2022 80 0.07 0.0109 40 0.06 0.0100 0.01 [0.01; 0.02] 5.5%
Castro et al., 2021 31 0.70 0.0500 32 0.70 0.0500 0.00 [-0.02; 0.02] 4.7%
Vos et al., 2020 690 0.61 0.0264 197 0.56 0.0200 0.05 [0.05; 0.06] 5.5%
Sarfo et al., 2019 250 0.82 0.1860 201 0.82 0.1830 0.00 [-0.03; 0.04] 4.1%
Vos et al., 2019 278 0.55 0.0289 104 0.50 0.0150 0.05 [0.04; 0.05] 5.5%
Gupta et al., 2018 124 0.72 0.0330 44 0.68 0.0400 0.04 [0.03; 0.05] 5.3%
Kirichenko et al., 2018 25 0.65 0.1220 11 0.65 0.0630 -0.00 [-0.06; 0.06] 2.6%
Vohra et al., 2017 45 0.62 0.0800 30 0.53 0.0500 0.09 [0.06; 0.12] 4.4%
Goulenok et al., 2015 30 0.76 0.0780 29 0.73 0.0830 0.03 [-0.01; 0.07] 3.6%
Gleason et al., 2015 230 0.49 0.0214 51 0.47 0.0175 0.02 [0.01; 0.02] 5.5%
Pirs et al., 2014 60 0.71 0.1540 26 0.64 0.1100 0.07 [0.01; 0.13] 2.7%
Zhu et al., 2014 50 0.58 0.1210 50 0.57 0.0946 0.01 [-0.03; 0.05] 3.5%
Suparna et al., 2013 26 0.63 0.2300 16 0.59 0.1700 0.04 [-0.08; 0.16] 1.0%
Desvarieux et al., 2013 50 0.76 0.0900 50 0.73 0.0780 0.03 [-0.00; 0.06] 4.1%
Brand et al., 2012 12 0.74 0.1000 13 0.76 0.1400 -0.02 [-0.11; 0.07] 1.4%
Cristofaro et al., 2011 222 1.00 0.2300 64 0.82 0.1300 0.18 [0.14; 0.22] 3.5%
Manfredi et al., 2011 16 1.30 0.6477 11 0.91 0.4983 0.40 [-0.04; 0.83] 0.1%
Calza et al., 2009 45 1.32 0.6971 21 0.89 0.5110 0.43 [0.13; 0.73] 0.2%
Seminari et al., 2002 28 0.67 0.1200 15 0.45 0.1200 0.22 [0.14; 0.30] 2.0%
Random effects model 2679 1185 0.04 [0.02; 0.05] 79.2%
Heterogeneity: I^2 = 96.3%, τ^2 = 0.0007, p < 0.0001
subgroup = Cohort
Yacovo et al., 2020 31 0.52 0.0468 30 0.54 0.0370 -0.02 [-0.04; 0.00] 4.9%
Fourie et al., 2015 66 0.63 0.0200 78 0.64 0.0100 -0.01 [-0.02; -0.00] 5.5%
Parinello et al., 2012 374 0.73 0.1154 227 0.71 0.1114 0.02 [-0.00; 0.04] 5.0%
Random effects model 471 335 -0.00 [-0.02; 0.01] 15.4%
Heterogeneity: I^2 = 77.1%, τ^2 = 0.0002, p = 0.0126
subgroup = Case-control
van Vonderen et al., 2009 55 0.70 0.0140 22 0.66 0.0230 0.04 [0.03; 0.05] 5.4%
Random effects model 3205 1542 0.03 [0.02; 0.04] 100.0%
Heterogeneity: I^2 = 96.9%, τ^2 = 0.0008, p < 0.0001
Test for overall effect: z = 4.67 (p < 0.0001)
Test for subgroup differences: χ^2_2 = 18.52, df = 2 (p < 0.0001)
-0.5
0
0.5
Decreased CIMT (mm)
Increased CIMT (mm)

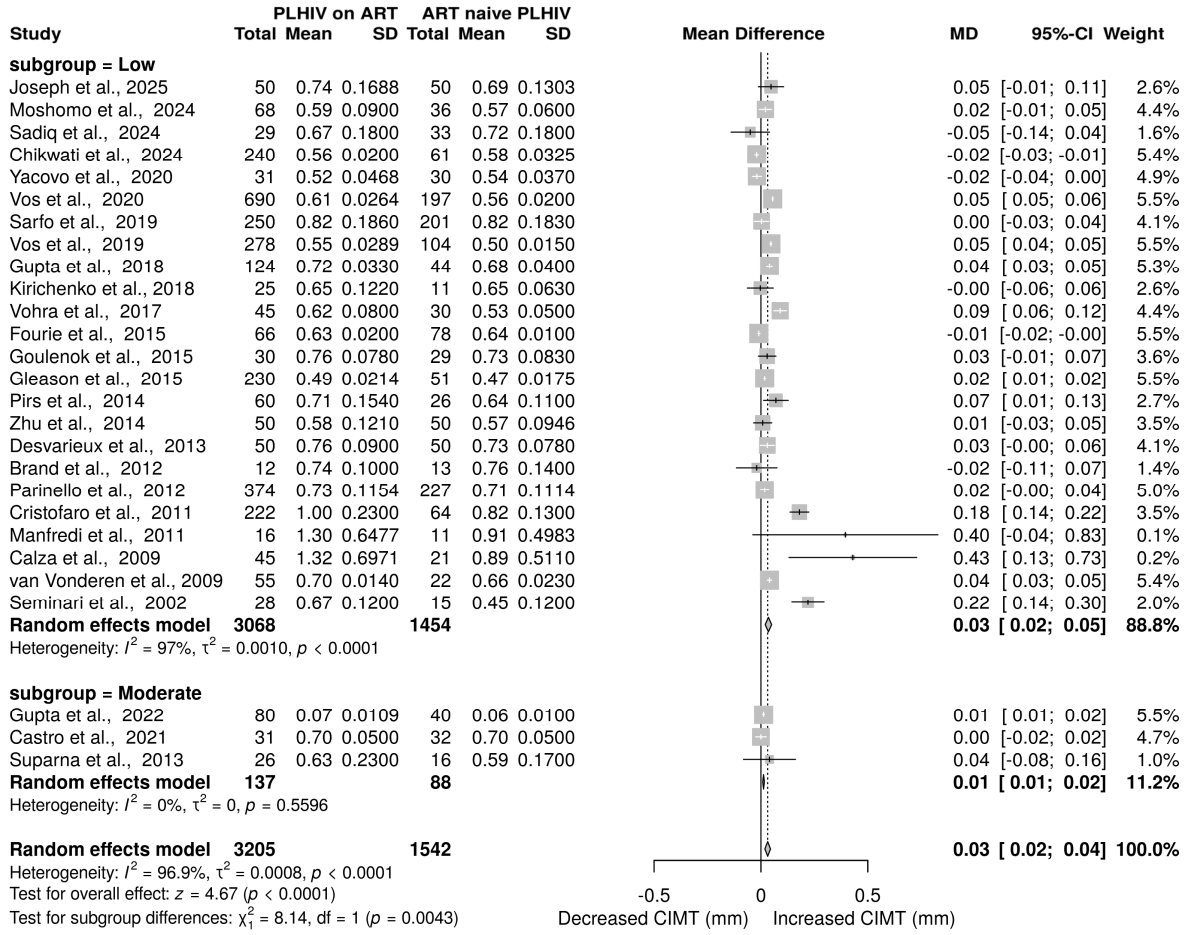
D


Study
PLHIV on ART Total Mean SD
ART naive PLHIV Total Mean SD
Mean Difference
MD 95%-CI Weight
subgroup = Equal to 100
Joseph et al., 2025 50 0.74 0.1688 50 0.69 0.1303 0.05 [-0.01; 0.11] 2.6%
Zhu et al., 2014 50 0.58 0.1210 50 0.57 0.0946 0.01 [-0.03; 0.05] 3.5%
Desvarieux et al., 2013 50 0.76 0.0900 50 0.73 0.0780 0.03 [-0.00; 0.06] 4.1%
Random effects model 150 150 0.03 [0.00; 0.05] 10.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.5407
subgroup = Above 100
Moshomo et al., 2024 68 0.59 0.0900 36 0.57 0.0600 0.02 [-0.01; 0.05] 4.4%
Chikwati et al., 2024 240 0.56 0.0200 61 0.58 0.0325 -0.02 [-0.03; -0.01] 5.4%
Gupta et al., 2022 80 0.07 0.0109 40 0.06 0.0100 0.01 [0.01; 0.02] 5.5%
Vos et al., 2020 690 0.61 0.0264 197 0.56 0.0200 0.05 [0.05; 0.06] 5.5%
Sarfo et al., 2019 250 0.82 0.1860 201 0.82 0.1830 0.00 [-0.03; 0.04] 4.1%
Vos et al., 2019 278 0.55 0.0289 104 0.50 0.0150 0.05 [0.04; 0.05] 5.5%
Gupta et al., 2018 124 0.72 0.0330 44 0.68 0.0400 0.04 [0.03; 0.05] 5.3%
Fourie et al., 2015 66 0.63 0.0200 78 0.64 0.0100 -0.01 [-0.02; -0.00] 5.5%
Gleason et al., 2015 230 0.49 0.0214 51 0.47 0.0175 0.02 [0.01; 0.02] 5.5%
Parinello et al., 2012 374 0.73 0.1154 227 0.71 0.1114 0.02 [-0.00; 0.04] 5.0%
Cristofaro et al., 2011 222 1.00 0.2300 64 0.82 0.1300 0.18 [0.14; 0.22] 3.5%
Random effects model 2622 1103 0.03 [0.01; 0.05] 55.3%
Heterogeneity: I^2 = 98.7%, τ^2 = 0.0008, p < 0.0001
subgroup = Below 100
Sadiq et al., 2024 29 0.67 0.1800 33 0.72 0.1800 -0.05 [-0.14; 0.04] 1.6%
Castro et al., 2021 31 0.70 0.0500 32 0.70 0.0500 0.00 [-0.02; 0.02] 4.7%
Yacovo et al., 2020 31 0.52 0.0468 30 0.54 0.0370 -0.02 [-0.04; 0.00] 4.9%
Kirichenko et al., 2018 25 0.65 0.1220 11 0.65 0.0630 -0.00 [-0.06; 0.06] 2.6%
Vohra et al., 2017 45 0.62 0.0800 30 0.53 0.0500 0.09 [0.06; 0.12] 4.4%
Goulenok et al., 2015 30 0.76 0.0780 29 0.73 0.0830 0.03 [-0.01; 0.07] 3.6%
Pirs et al., 2014 60 0.71 0.1540 26 0.64 0.1100 0.07 [0.01; 0.13] 2.7%
Suparna et al., 2013 26 0.63 0.2300 16 0.59 0.1700 0.04 [-0.08; 0.16] 1.0%
Brand et al., 2012 12 0.74 0.1000 13 0.76 0.1400 -0.02 [-0.11; 0.07] 1.4%
Manfredi et al., 2011 16 1.30 0.6477 11 0.91 0.4983 0.40 [-0.04; 0.83] 0.1%
Calza et al., 2009 45 1.32 0.6971 21 0.89 0.5110 0.43 [0.13; 0.73] 0.2%
van Vonderen et al., 2009 55 0.70 0.0140 22 0.66 0.0230 0.04 [0.03; 0.05] 5.4%
Seminari et al., 2002 28 0.67 0.1200 15 0.45 0.1200 0.22 [0.14; 0.30] 2.0%
Random effects model 433 289 0.04 [0.01; 0.07] 34.4%
Heterogeneity: I^2 = 86.2%, τ^2 = 0.0019, p < 0.0001
Random effects model 3205 1542 0.03 [0.02; 0.04] 100.0%
Heterogeneity: I^2 = 96.9%, τ^2 = 0.0008, p < 0.0001
Test for overall effect: z = 4.67 (p < 0.0001)
Test for subgroup differences: χ^2_2 = 0.66, df = 2 (p = 0.7205)
-0.5
0
0.5
Decreased CIMT (mm)
Increased CIMT (mm)

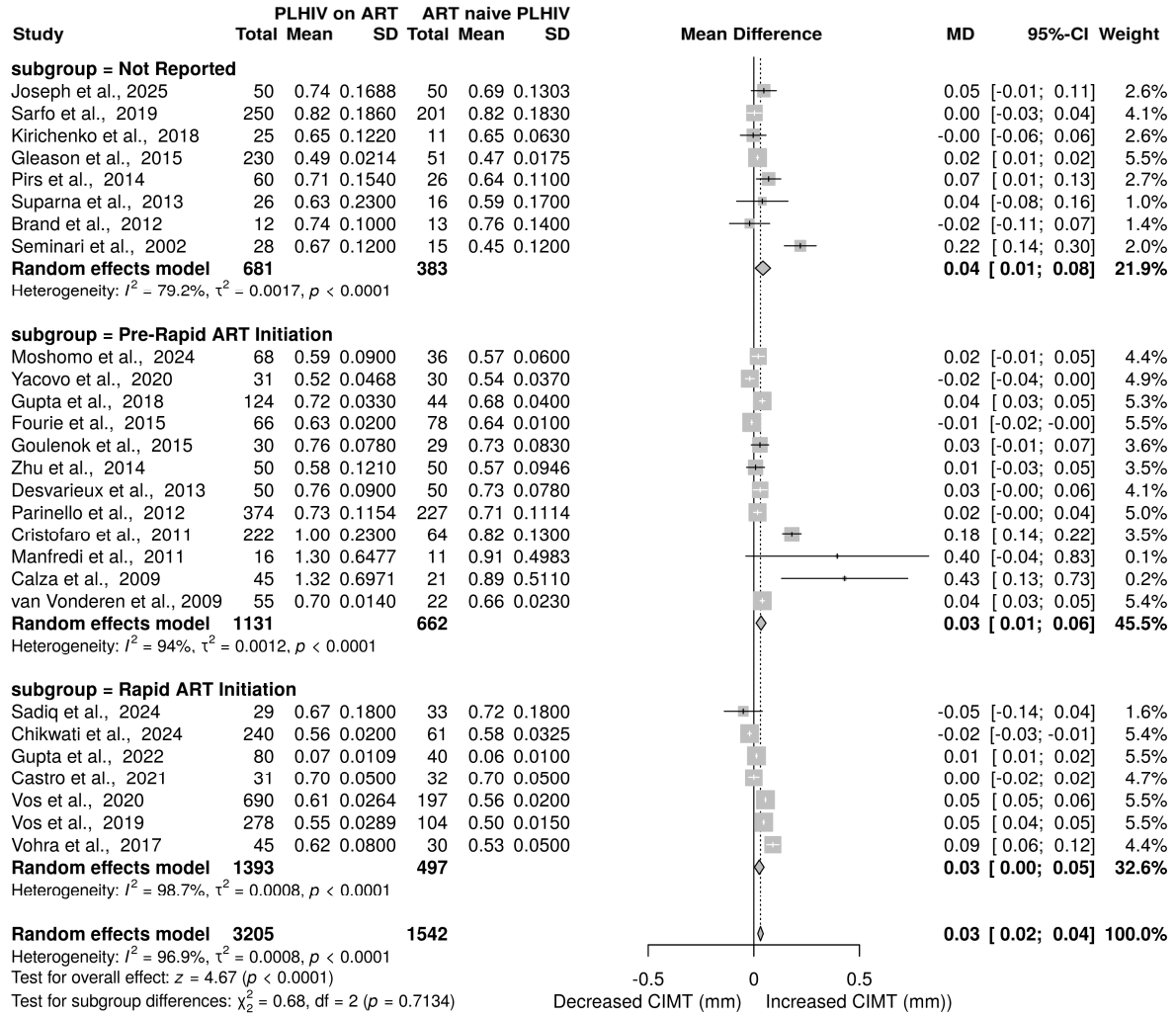
E


Study
PLHIV on ART
Total Mean SD
ART naive PLHIV
Total Mean SD
Mean Difference
MD 95%-CI Weight
subgroup = NR
Joseph et al., 2025 50 0.74 0.1688 50 0.69 0.1303 0.05 [-0.01; 0.11] 2.6%
subgroup = Below 40
Moshomo et al., 2024 68 0.59 0.0900 36 0.57 0.0600 0.02 [-0.01; 0.05] 4.4%
Gupta et al., 2022 80 0.07 0.0109 40 0.06 0.0100 0.01 [0.01; 0.02] 5.5%
Castro et al., 2021 31 0.70 0.0500 32 0.70 0.0500 0.00 [-0.02; 0.02] 4.7%
Yacovo et al., 2020 31 0.52 0.0468 30 0.54 0.0370 -0.02 [-0.04; 0.00] 4.9%
Gupta et al., 2018 124 0.72 0.0330 44 0.68 0.0400 0.04 [0.03; 0.05] 5.3%
Kirichenko et al., 2018 25 0.65 0.1220 11 0.65 0.0630 -0.00 [-0.06; 0.06] 2.6%
Vohra et al., 2017 45 0.62 0.0800 30 0.53 0.0500 0.09 [0.06; 0.12] 4.4%
Gleason et al., 2015 230 0.49 0.0214 51 0.47 0.0175 0.02 [0.01; 0.02] 5.5%
Pirs et al., 2014 60 0.71 0.1540 26 0.64 0.1100 0.07 [0.01; 0.13] 2.7%
Suparna et al., 2013 26 0.63 0.2300 16 0.59 0.1700 0.04 [-0.08; 0.16] 1.0%
Seminari et al., 2002 28 0.67 0.1200 15 0.45 0.1200 0.22 [0.14; 0.30] 2.0%
Random effects model 748 331 0.03 [0.01; 0.04] 42.9%
Heterogeneity: I^2 = 88.2%, τ^2 = 0.0003, p < 0.0001
subgroup = Above 40
Sadiq et al., 2024 29 0.67 0.1800 33 0.72 0.1800 -0.05 [-0.14; 0.04] 1.6%
Chikwati et al., 2024 240 0.56 0.0200 61 0.58 0.0325 -0.02 [-0.03; -0.01] 5.4%
Vos et al., 2020 690 0.61 0.0264 197 0.56 0.0200 0.05 [0.05; 0.06] 5.5%
Sarfo et al., 2019 250 0.82 0.1860 201 0.82 0.1830 0.00 [-0.03; 0.04] 4.1%
Vos et al., 2019 278 0.55 0.0289 104 0.50 0.0150 0.05 [0.04; 0.05] 5.5%
Fourie et al., 2015 66 0.63 0.0200 78 0.64 0.0100 -0.01 [-0.02; -0.00] 5.5%
Goulenok et al., 2015 30 0.76 0.0780 29 0.73 0.0830 0.03 [-0.01; 0.07] 3.6%
Zhu et al., 2014 50 0.58 0.1210 50 0.57 0.0946 0.01 [-0.03; 0.05] 3.5%
Desvarieux et al., 2013 50 0.76 0.0900 50 0.73 0.0780 0.03 [-0.00; 0.06] 4.1%
Brand et al., 2012 12 0.74 0.1000 13 0.76 0.1400 -0.02 [-0.11; 0.07] 1.4%
Parinello et al., 2012 374 0.73 0.1154 227 0.71 0.1114 0.02 [-0.00; 0.04] 5.0%
Cristofaro et al., 2011 222 1.00 0.2300 64 0.82 0.1300 0.18 [0.14; 0.22] 3.5%
Manfredi et al., 2011 16 1.30 0.6477 11 0.91 0.4983 0.40 [-0.04; 0.83] 0.1%
Calza et al., 2009 45 1.32 0.6971 21 0.89 0.5110 0.43 [0.13; 0.73] 0.2%
van Vonderen et al., 2009 55 0.70 0.0140 22 0.66 0.0230 0.04 [0.03; 0.05] 5.4%
Random effects model 2407 1161 0.03 [0.01; 0.05] 54.5%
Heterogeneity: I^2 = 97.9%, τ^2 = 0.0012, p < 0.0001
Random effects model 3205 1542 0.03 [0.02; 0.04] 100.0%
Heterogeneity: I^2 = 96.9%, τ^2 = 0.0008, p < 0.0001
Test for overall effect: z = 4.67 (p < 0.0001)
Test for subgroup differences: χ^2_2 = 0.37, df = 2 (p = 0.8302)
-0.5
0
0.5
Decreased CIMT (mm)
Increased CIMT (mm)

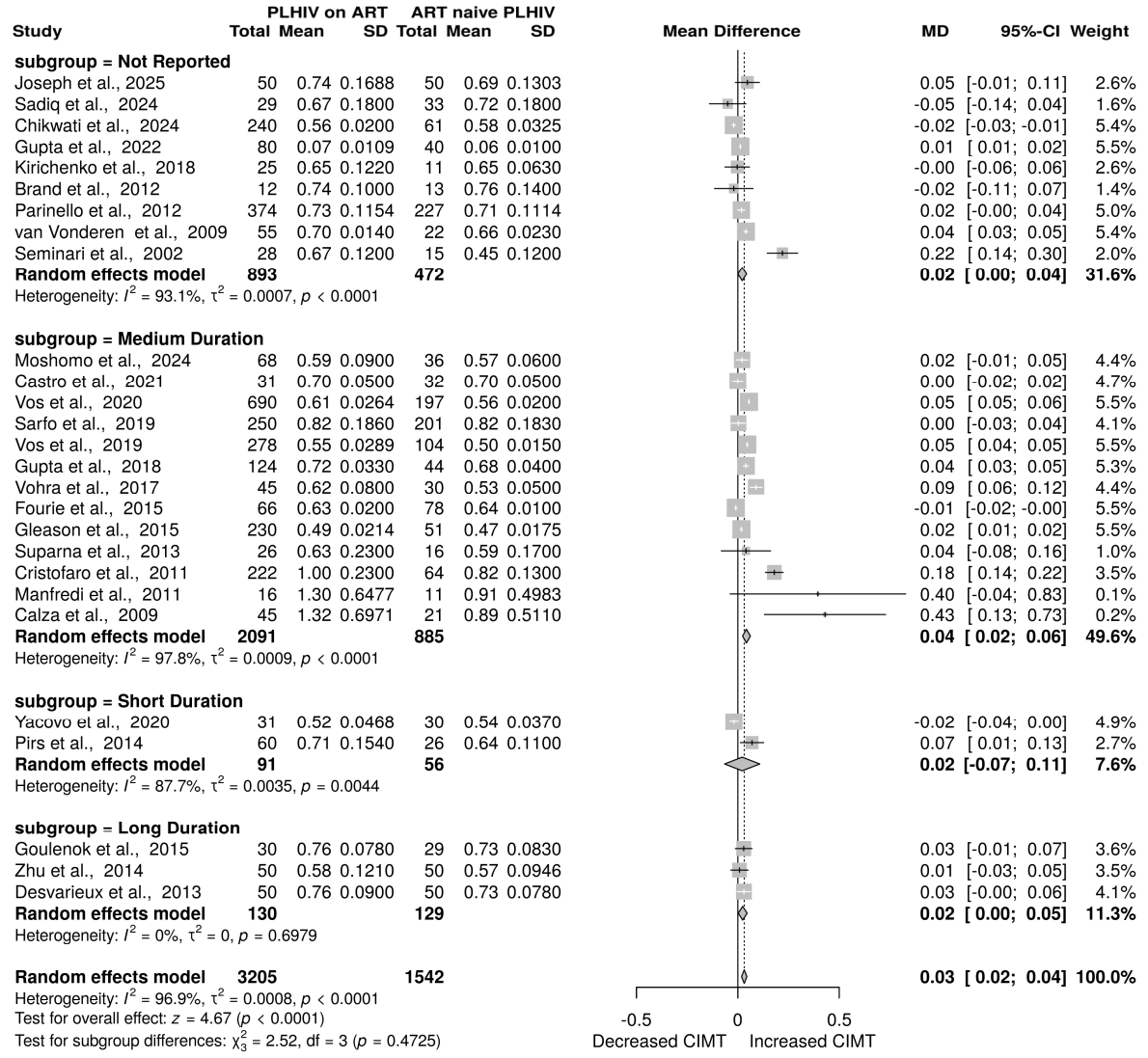
F


Study
PLHIV on ART
Total Mean SD
ART naive PLHIV
Total Mean SD
Mean Difference
MD 95%-CI Weight
subgroup = Low
Joseph et al., 2025 50 0.74 0.1688 50 0.69 0.1303 0.05 [-0.01; 0.11] 2.6%
Moshomo et al., 2024 68 0.59 0.0900 36 0.57 0.0600 0.02 [-0.01; 0.05] 4.4%
Sadiq et al., 2024 29 0.67 0.1800 33 0.72 0.1800 -0.05 [-0.14; 0.04] 1.6%
Chikwati et al., 2024 240 0.56 0.0200 61 0.58 0.0325 -0.02 [-0.03; -0.01] 5.4%
Yacovo et al., 2020 31 0.52 0.0468 30 0.54 0.0370 -0.02 [-0.04; 0.00] 4.9%
Vos et al., 2020 690 0.61 0.0264 197 0.56 0.0200 0.05 [0.05; 0.06] 5.5%
Sarfo et al., 2019 250 0.82 0.1860 201 0.82 0.1830 0.00 [-0.03; 0.04] 4.1%
Vos et al., 2019 278 0.55 0.0289 104 0.50 0.0150 0.05 [0.04; 0.05] 5.5%
Gupta et al., 2018 124 0.72 0.0330 44 0.68 0.0400 0.04 [0.03; 0.05] 5.3%
Kirichenko et al., 2018 25 0.65 0.1220 11 0.65 0.0630 -0.00 [-0.06; 0.06] 2.6%
Vohra et al., 2017 45 0.62 0.0800 30 0.53 0.0500 0.09 [0.06; 0.12] 4.4%
Fourie et al., 2015 66 0.63 0.0200 78 0.64 0.0100 -0.01 [-0.02; -0.00] 5.5%
Goulenok et al., 2015 30 0.76 0.0780 29 0.73 0.0830 0.03 [-0.01; 0.07] 3.6%
Gleason et al., 2015 230 0.49 0.0214 51 0.47 0.0175 0.02 [0.01; 0.02] 5.5%
Pirs et al., 2014 60 0.71 0.1540 26 0.64 0.1100 0.07 [0.01; 0.13] 2.7%
Zhu et al., 2014 50 0.58 0.1210 50 0.57 0.0946 0.01 [-0.03; 0.05] 3.5%
Desvarieux et al., 2013 50 0.76 0.0900 50 0.73 0.0780 0.03 [-0.00; 0.06] 4.1%
Brand et al., 2012 12 0.74 0.1000 13 0.76 0.1400 -0.02 [-0.11; 0.07] 1.4%
Parinello et al., 2012 374 0.73 0.1154 227 0.71 0.1114 0.02 [-0.00; 0.04] 5.0%
Cristofaro et al., 2011 222 1.00 0.2300 64 0.82 0.1300 0.18 [0.14; 0.22] 3.5%
Manfredi et al., 2011 16 1.30 0.6477 11 0.91 0.4983 0.40 [-0.04; 0.83] 0.1%
Calza et al., 2009 45 1.32 0.6971 21 0.89 0.5110 0.43 [0.13; 0.73] 0.2%
van Vonderen et al., 2009 55 0.70 0.0140 22 0.66 0.0230 0.04 [0.03; 0.05] 5.4%
Seminari et al., 2002 28 0.67 0.1200 15 0.45 0.1200 0.22 [0.14; 0.30] 2.0%
Random effects model 3068 1454 0.03 [0.02; 0.05] 88.8%
Heterogeneity: I^2 = 97%, τ^2 = 0.0010, p < 0.0001
subgroup = Moderate
Gupta et al., 2022 80 0.07 0.0109 40 0.06 0.0100 0.01 [0.01; 0.02] 5.5%
Castro et al., 2021 31 0.70 0.0500 32 0.70 0.0500 0.00 [-0.02; 0.02] 4.7%
Suparna et al., 2013 26 0.63 0.2300 16 0.59 0.1700 0.04 [-0.08; 0.16] 1.0%
Random effects model 137 88 0.01 [0.01; 0.02] 11.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.5596
Random effects model 3205 1542 0.03 [0.02; 0.04] 100.0%
Heterogeneity: I^2 = 96.9%, τ^2 = 0.0008, p < 0.0001
Test for overall effect: z = 4.67 (p < 0.0001)
Test for subgroup differences: χ^2_1 = 8.14, df = 1 (p = 0.0043)
-0.5
0
0.5
Decreased CIMT (mm)
Increased CIMT (mm)

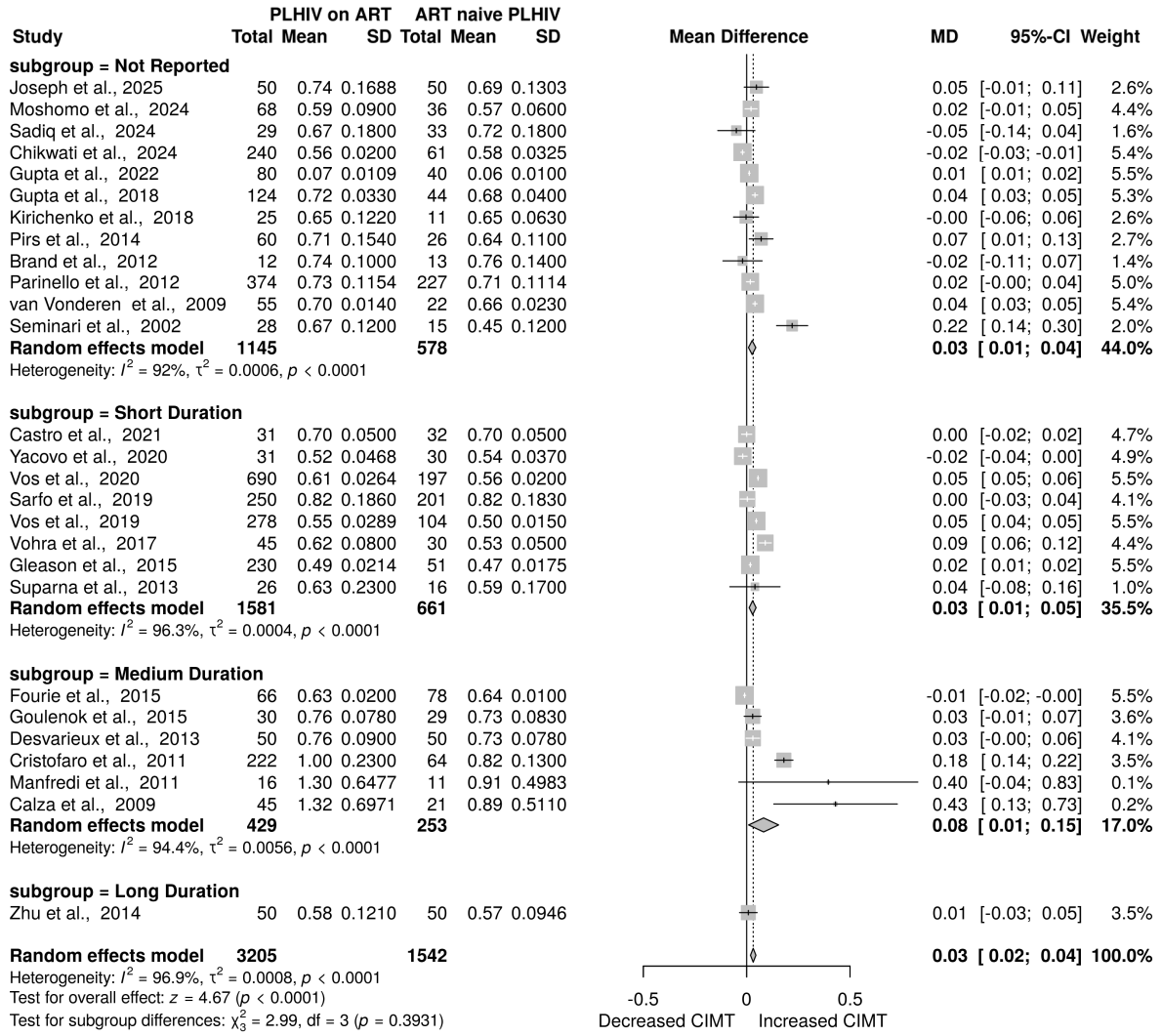
G


Study
PLHIV on ART Total Mean SD
ART naive PLHIV Total Mean SD
Mean Difference
MD 95%-CI Weight
subgroup = Not Reported
Joseph et al., 2025 50 0.74 0.1688 50 0.69 0.1303 0.05 [-0.01; 0.11] 2.6%
Sarfo et al., 2019 250 0.82 0.1860 201 0.82 0.1830 0.00 [-0.03; 0.04] 4.1%
Kirichenko et al., 2018 25 0.65 0.1220 11 0.65 0.0630 -0.00 [-0.06; 0.06] 2.6%
Gleason et al., 2015 230 0.49 0.0214 51 0.47 0.0175 0.02 [0.01; 0.02] 5.5%
Pirs et al., 2014 60 0.71 0.1540 26 0.64 0.1100 0.07 [0.01; 0.13] 2.7%
Suparna et al., 2013 26 0.63 0.2300 16 0.59 0.1700 0.04 [-0.08; 0.16] 1.0%
Brand et al., 2012 12 0.74 0.1000 13 0.76 0.1400 -0.02 [-0.11; 0.07] 1.4%
Seminari et al., 2002 28 0.67 0.1200 15 0.45 0.1200 0.22 [0.14; 0.30] 2.0%
Random effects model 681 383 0.04 [0.01; 0.08] 21.9%
Heterogeneity: I^2 = 79.2%, τ^2 = 0.0017, p < 0.0001
subgroup = Pre-Rapid ART Initiation
Moshomo et al., 2024 68 0.59 0.0900 36 0.57 0.0600 0.02 [-0.01; 0.05] 4.4%
Yacovo et al., 2020 31 0.52 0.0468 30 0.54 0.0370 -0.02 [-0.04; 0.00] 4.9%
Gupta et al., 2018 124 0.72 0.0330 44 0.68 0.0400 0.04 [0.03; 0.05] 5.3%
Fourie et al., 2015 66 0.63 0.0200 78 0.64 0.0100 -0.01 [-0.02; -0.00] 5.5%
Goulenok et al., 2015 30 0.76 0.0780 29 0.73 0.0830 0.03 [-0.01; 0.07] 3.6%
Zhu et al., 2014 50 0.58 0.1210 50 0.57 0.0946 0.01 [-0.03; 0.05] 3.5%
Desvarieux et al., 2013 50 0.76 0.0900 50 0.73 0.0780 0.03 [-0.00; 0.06] 4.1%
Parinello et al., 2012 374 0.73 0.1154 227 0.71 0.1114 0.02 [-0.00; 0.04] 5.0%
Cristofaro et al., 2011 222 1.00 0.2300 64 0.82 0.1300 0.18 [0.14; 0.22] 3.5%
Manfredi et al., 2011 16 1.30 0.6477 11 0.91 0.4983 0.40 [-0.04; 0.83] 0.1%
Calza et al., 2009 45 1.32 0.6971 21 0.89 0.5110 0.43 [0.13; 0.73] 0.2%
van Vonderen et al., 2009 55 0.70 0.0140 22 0.66 0.0230 0.04 [0.03; 0.05] 5.4%
Random effects model 1131 662 0.03 [0.01; 0.06] 45.5%
Heterogeneity: I^2 = 94%, τ^2 = 0.0012, p < 0.0001
subgroup = Rapid ART Initiation
Sadiq et al., 2024 29 0.67 0.1800 33 0.72 0.1800 -0.05 [-0.14; 0.04] 1.6%
Chikwati et al., 2024 240 0.56 0.0200 61 0.58 0.0325 -0.02 [-0.03; -0.01] 5.4%
Gupta et al., 2022 80 0.07 0.0109 40 0.06 0.0100 0.01 [0.01; 0.02] 5.5%
Castro et al., 2021 31 0.70 0.0500 32 0.70 0.0500 0.00 [-0.02; 0.02] 4.7%
Vos et al., 2020 690 0.61 0.0264 197 0.56 0.0200 0.05 [0.05; 0.06] 5.5%
Vos et al., 2019 278 0.55 0.0289 104 0.50 0.0150 0.05 [0.04; 0.05] 5.5%
Vohra et al., 2017 45 0.62 0.0800 30 0.53 0.0500 0.09 [0.06; 0.12] 4.4%
Random effects model 1393 497 0.03 [0.00; 0.05] 32.6%
Heterogeneity: I^2 = 98.7%, τ^2 = 0.0008, p < 0.0001
Random effects model 3205 1542 0.03 [0.02; 0.04] 100.0%
Heterogeneity: I^2 = 96.9%, τ^2 = 0.0008, p < 0.0001
Test for overall effect: z = 4.67 (p < 0.0001)
Test for subgroup differences: χ^2_2 = 0.68, df = 2 (p = 0.7134)
-0.5
0
0.5
Decreased CIMT (mm)
Increased CIMT (mm))

H


Study
PLHIV on ART
ART naive PLHIV
Total Mean SD Total Mean SD
Mean Difference
MD 95%-CI Weight
subgroup = Not Reported
Joseph et al., 2025 50 0.74 0.1688 50 0.69 0.1303 0.05 [-0.01; 0.11] 2.6%
Sadiq et al., 2024 29 0.67 0.1800 33 0.72 0.1800 -0.05 [-0.14; 0.04] 1.6%
Chikwati et al., 2024 240 0.56 0.0200 61 0.58 0.0325 -0.02 [-0.03; -0.01] 5.4%
Gupta et al., 2022 80 0.07 0.0109 40 0.06 0.0100 0.01 [0.01; 0.02] 5.5%
Kirichenko et al., 2018 25 0.65 0.1220 11 0.65 0.0630 -0.00 [-0.06; 0.06] 2.6%
Brand et al., 2012 12 0.74 0.1000 13 0.76 0.1400 -0.02 [-0.11; 0.07] 1.4%
Parinello et al., 2012 374 0.73 0.1154 227 0.71 0.1114 0.02 [-0.00; 0.04] 5.0%
van Vonderen et al., 2009 55 0.70 0.0140 22 0.66 0.0230 0.04 [0.03; 0.05] 5.4%
Seminari et al., 2002 28 0.67 0.1200 15 0.45 0.1200 0.22 [0.14; 0.30] 2.0%
Random effects model 893 472 0.02 [0.00; 0.04] 31.6%
Heterogeneity: I^2 = 93.1%, τ^2 = 0.0007, p < 0.0001
subgroup = Medium Duration
Moshomo et al., 2024 68 0.59 0.0900 36 0.57 0.0600 0.02 [-0.01; 0.05] 4.4%
Castro et al., 2021 31 0.70 0.0500 32 0.70 0.0500 0.00 [-0.02; 0.02] 4.7%
Vos et al., 2020 690 0.61 0.0264 197 0.56 0.0200 0.05 [0.05; 0.06] 5.5%
Sarfo et al., 2019 250 0.82 0.1860 201 0.82 0.1830 0.00 [-0.03; 0.04] 4.1%
Vos et al., 2019 278 0.55 0.0289 104 0.50 0.0150 0.05 [0.04; 0.05] 5.5%
Gupta et al., 2018 124 0.72 0.0330 44 0.68 0.0400 0.04 [0.03; 0.05] 5.3%
Vohra et al., 2017 45 0.62 0.0800 30 0.53 0.0500 0.09 [0.06; 0.12] 4.4%
Fourie et al., 2015 66 0.63 0.0200 78 0.64 0.0100 -0.01 [-0.02; -0.00] 5.5%
Gleason et al., 2015 230 0.49 0.0214 51 0.47 0.0175 0.02 [0.01; 0.02] 5.5%
Suparna et al., 2013 26 0.63 0.2300 16 0.59 0.1700 0.04 [-0.08; 0.16] 1.0%
Cristofaro et al., 2011 222 1.00 0.2300 64 0.82 0.1300 0.18 [0.14; 0.22] 3.5%
Manfredi et al., 2011 16 1.30 0.6477 11 0.91 0.4983 0.40 [-0.04; 0.83] 0.1%
Calza et al., 2009 45 1.32 0.6971 21 0.89 0.5110 0.43 [0.13; 0.73] 0.2%
Random effects model 2091 885 0.04 [0.02; 0.06] 49.6%
Heterogeneity: I^2 = 97.8%, τ^2 = 0.0009, p < 0.0001
subgroup = Short Duration
Yacovo et al., 2020 31 0.52 0.0468 30 0.54 0.0370 -0.02 [-0.04; 0.00] 4.9%
Pirs et al., 2014 60 0.71 0.1540 26 0.64 0.1100 0.07 [0.01; 0.13] 2.7%
Random effects model 91 56 0.02 [-0.07; 0.11] 7.6%
Heterogeneity: I^2 = 87.7%, τ^2 = 0.0035, p = 0.0044
subgroup = Long Duration
Goulenok et al., 2015 30 0.76 0.0780 29 0.73 0.0830 0.03 [-0.01; 0.07] 3.6%
Zhu et al., 2014 50 0.58 0.1210 50 0.57 0.0946 0.01 [-0.03; 0.05] 3.5%
Desvarieux et al., 2013 50 0.76 0.0900 50 0.73 0.0780 0.03 [-0.00; 0.06] 4.1%
Random effects model 130 129 0.02 [0.00; 0.05] 11.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.6979
Random effects model 3205 1542 0.03 [0.02; 0.04] 100.0%
Heterogeneity: I^2 = 96.9%, τ^2 = 0.0008, p < 0.0001
Test for overall effect: z = 4.67 (p < 0.0001)
Test for subgroup differences: χ^2_3 = 2.52, df = 3 (p = 0.4725)
-0.5
0
0.5
Decreased CIMT
Increased CIMT

I



J

Figure S1: Subgroup analysis for CIMT in ART compared to ART-naïve. A. Subgroup analysis for CIMT in ART compared to ART-naïve based on continent of publication. B. Subgroup analysis for CIMT in ART compared to ART-naïve based on CD4 count for patients on ART. C. Subgroup analysis for CIMT in ART compared to ART naive patients based on gender. D. Subgroup analysis for CIMT in ART compared to ART naive patients based on study design. E. Subgroup analysis for CIMT in ART compared to ART naive patients based on sample size. F. Subgroup analysis for CIMT in ART compared to ART naive patients based on age. G. Subgroup analysis for CIMT in ART compared to ART naive patients based on the risk of bias. H. Subgroup analysis for CIMT in ART compared to ART naive patients based on WHO adoption of rapid ART initiation. I. Subgroup analysis based on the duration of HIV infection since diagnosis in PLHIV on ART. J. Subgroup analysis based on the duration of HIV infection since diagnosis in PLHIV on ART naive patients.

Table S2: Sensitivity analysis, showing the effect of the exclusion of one study on CIMT in PLHIV on ART compared to ART-naïve

		95% Confidence Intervals			
Excluded study	**Effect size**	**Lower**	**Upper**	**p**	**I^2**
Joseph et al.,	0.03	0.02	0.04	< 0.0001	97
Moshomo et al.,	0.03	0.02	0.05	< 0.0001	97
Sadiq et al.,	0.03	0.02	0.05	< 0.0001	97
Chikwati et al.,	0.03	0.02	0.05	<0.0001	96.5
Gupta et al.,	0.03	0.02	0.05	<0.0001	96.7
Castro et al.,	0.03	0.02	0.05	< 0.0001	97
Yacovo et al.,	0.03	0.02	0.05	< 0.0001	97
Vos et al.,	0.03	0.02	0.04	<0.0001	95.2
Sarfo et al.,	0.03	0.02	0.05	< 0.0001	97
Vos et al.,	0.03	0.02	0.05	<0.0001	96.7
Gupta et al.,	0.03	0.02	0.04	<0.0001	97
Kirichenko et al.,	0.03	0.02	0.05	< 0.0001	97
Vohra et al.,	0.03	0.02	0.04	<0.0001	97
Fourie et al.,	0.03	0.02	0.05	< 0.0001	96
Goulenok et al.,	0.03	0.02	0.05	<0.0001	97
Pirs et al.,	0.03	0.02	0.05	<0.0001	97
Zhu et al.,	0.03	0.02	0.04	< 0.0001	97
Gleason et al.,	0.03	0.02	0.05	< 0.0001	97
Suparna et al.,	0.03	0.02	0.04	< 0.0001	97
Desvarieux et al.,	0.03	0.02	0.05	<0.0001	97
Brand et al.,	0.03	0.02	0.05	< 0.0001	97
Parinello et al.,	0.03	0.02	0.05	< 0.0001	97

Cristofaro et al.,	0.03	0.01	0.04	<0.0001	96.9
Manfredi et al.,	0.03	0.012	0.04	< 0.0001	97
Calza et al.,	0.03	0.02	0.04	< 0.0001	97
van Vonderen et al.,	0.03	0.02	0.05	<0.0001	97
Seminari et al.,	0.03	0.01	0.04	< 0.0001	96.9

Table S3: Quality assessment of cohort studies using the Newcastle–Ottawa scale.

	Selection				**Comparability**	**Exposure**				
Study	Representativeness of Cohort	Selection of Non-Exposed Cohort	Ascertainment of Exposure	Outcome Not Present at Start	Comparability of Cohorts	Assessment of Outcome	Assessment of Outcome	Adequacy of Follow-Up	Total Score	Quality
Parrinello et al., 2012	★	★	★	★	★	★	★	★	8	High
Fourie et al., 2015	☆	★	★	★	★	★	★	★	7	High
Yacovo et al., 2020	★	★	★	★	★	★	★	★	8	High

Table S4: Quality assessment of case-control studies using the Newcastle–Ottawa scale.

	Selection				**Comparability**	**Exposure**				
Study	Case definition Adequate ?	Representativeness of the cases	Selection of controls	Definition of controls	Based on design and analysis	Ascertainment of exposure	Same method for cases and controls	Non-response rate	Total Score	Quality
Vohra & Bharti, 2017	★	★	★	★	★	★	★	☆	7	High
Van Vonderen et al., 2009	★	☆	★	★	★★	★	★	★	8	High

Table S5: Quality assessment of cross-sectional studies using the Newcastle–Ottawa scale.

	Selection				**Comparability**	**Exposure**			
Study	Representativeness of sample	Sample size	Nonrespondents	Ascertainment of exposure	Based on Design and Analysis	Assessment of outcome	Statistical test	Total Score	Quality
Joseph et al., 2025	★	★	★	★★	☆	★	★	7	High
Chikwati et al., 2024	★	★	☆	★★	★	★★	★	8	High
Sarfo et al., 2019	★	★	☆	★★	★	★★	★	8	High
Vos et al., 2019	★	★	☆	★★	★	★★	★	8	High
Gupta et al., 2018	★	☆	☆	★★	★	★★	★	7	High
Kirichenko et al., 2018	★	☆	☆	★★	★	★★	★	7	High
Sadiq et al., 2024	★	☆	★	★★	★	★★	★	8	High
Moshomo et al., 2024	★	☆	★	★★	★	★★	★	8	High
Gupta et al., 2022	★	☆	★	★★	☆	★	★	6	Moderate
Castro et al., 2021	★	☆	★	★	★	★	★	6	Moderate
Vos et al., 2020	★	★	☆	★	★	★★	★	7	High
Gleason et al., 2015	★	☆	☆	★★	★	★★	★	7	High
Goulenok et al., 2015	★	☆	☆	★★	★	★★	★	7	High
Pirs et al., 2014	★	☆	☆	★★	★	★★	★	7	High

Zhu et al., 2014	★	☆	☆	★★	★	★★	★	7	High
Desvarieux et al., 2013	★	★	★	★★	★	★★	★	9	High
Suparna et al., 2013	★	☆	★	★	★	★★	☆	6	Moderate
Manfredi et al., 2011	★	☆	★	★★	★	★★	★	8	High
Brand et al., 2011	★	☆	★	★★	★	★★	★	8	High
Cristofaro et al., 2011	★	☆	★	★★	★	★★	★	8	High
Calza et al., 2009	★	☆	★	★	★	★★	★	7	High
Seminari et al., 2002	★	☆	★	★	★	★★	★	7	High