

# Retention in HIV care among Southeast Asian people living with HIV: A systematic review and meta-analysis



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#### **Abstract**

**Background:** Despite the effectiveness of antiretroviral therapy (ART) in reducing HIV-related morbidity and mortality, the retention of HIV care remains suboptimal in Southeast Asia.

**Objective:** This systematic review and meta-analysis aimed to investigate the coverage of retention in care and the likelihood factors for retention in HIV care among Southeast Asian people living with HIV, to inform targeted interventions and policy improvements.

**Methods:** Following the Preferred Reporting Item for Systematic Review and Meta-analysis (PRISMA) guidelines, this study included observational studies reporting factors associated with retention in HIV care among Southeast Asian adults, with searches conducted in PubMed, Scopus, Cochrane Library, and CINAHL up to July 15, 2024. Demographic and clinical factors were analyzed using a random-effects model with the generalized linear mixed-effect model (GLLM) to estimate proportion and the DerSimonian-Laird method to estimate odds ratios (OR) with 95% confidence intervals (CI), assessing heterogeneity using the *I*<sup>2</sup> statistic.

**Results:** Among the eleven studies with 46,480 pooled participants analyzed, the coverage of retention in care revealed a pooled proportion of 75.2% (95% CI: 66.7-82.1). Significant clinical factors associated with a higher likelihood of retention included high CD4 count ( $\geq$ 200 cells/mm³) (OR 2.17 (95%CI: 1.19-3.97, p = 0.01), WHO stage 3-4 (OR 2.06, 95%CI: 1.09-3.87, p = 0.02), not being on ART (OR 6.88, 95%CI: 1.89-25.06, p = 0.001), hemoglobin levels  $\geq$ 10 g/dL (OR 0.50, 95% CI: 0.25-0.99, p = 0.04), and demographic factors of employment (OR 1.18, 95% CI: 1.02-1.38; p = 0.03). Other clinical factors, such as HIV stage, TB co-infection, drug abuse/substance use, and hemoglobin levels, did not significantly affect the likelihood of retention. Similarly, demographic factors such as age, gender, education, marital status, and geographic setting also showed no significant impact on likelihood retention.

**Conclusion:** Retention in care among Southeast Asian people living with HIV was still below 95%. Clinical factors, particularly high CD4 counts, WHO stage, and the absence of ART, were likelihood factors for retention in HIV care, whereas other clinical and demographic factors studied did not show a significant impact. A universal test and treatment strategy is required to improve retention in care.

#### Keywords

Adherence; antiretroviral therapy; CD4 count; HIV care retention; Southeast Asia

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### Background

The widespread use of antiretroviral therapy (ART) has led to a substantial reduction in HIV-related morbidity and mortality (WHO, 2017). ART is also a key strategy for preventing and controlling HIV transmission by significantly lowering the risk of transmission to sexual partners (Broyles et al., 2023). Guidelines recommend initiating ART immediately upon HIV diagnosis, regardless of clinical or immunological status (Rajasuriar et al., 2015; Zhou et al., 2024). Despite significant efforts, ART coverage remains low worldwide.

The Joint United Nations Programme on HIV/AIDS (UNAIDS) has put the '95-95-95' target for national programs to diagnose, ART uptake, and viral suppression, known as the HIV care cascade. UNAIDS designed these HIV goals to close the HIV care coverage and outcomes (Frescura et al., 2022). Globally, progress towards the UNAIDS 95-95-95 target in 2023 showed that 86% of people living with HIV (PLWH) knew their status, 89% of PLWH who knew their status were on ART uptake, and 93% of PLWH accessing ART were virally suppressed (WHO, 2024). Although progress increased, the coverage remained below the target.

Southeast Asia has one of the lowest coverage regions in the HIV care cascade. In Southeast Asia, the percentage of PLWH who know their status is 78%, those on ART is 66%, and those with suppressed viral loads is 64% in 2023 (WHO, 2024). These proportions are lower than the global coverage. The region also lags behind Eastern and Southern Africa, with 92% knowing their status, 90% on ART, and 93% with suppressed viral loads (WHO, 2024). Therefore, a few regions and countries, invariably Southeast Asian regions, face challenges in achieving this goal.

PLWH must be aware of their diagnosis, link to HIV care, and consistently retain HIV care and treatment to gain the full advantages of ART. Retention in HIV care is crucial in the HIV care cascade as it is linked to enhanced survival, fewer HIV-related complications, and lower rates of HIV transmission (Byrd et al., 2019). Retention in care is defined as regular access to HIV medical care for at least one year following the initiation of ART and entry into the HIV clinic (Clouse et al., 2013).

Several studies have shown that PLWH who were retained in HIV care are more likely to achieve viral suppression than those who do not consistently participate in regular care (Crawford, 2014; Mugavero et al., 2012; Yehia et al., 2014). However, retention of care among PLWH in Southeast Asian countries remains low. For instance, only 55% of PLHIV in Indonesia are retained in care (Januraga et al., 2018). Retention in care for PLWH is important to achieve better health outcomes. PLWH who are retained in HIV care are more likely to achieve viral suppression, have better survival rate, and experience lower risk of transmission (Sabin et al., 2017; Yehia et al., 2014). However, there are limited previous review studies about retention proportions and the factors that influence retention in care within the Southeast Asia (Moges et al., 2020; Rooks-Peck et al., 2018). Therefore, this study aimed to systematically identify the coverage of retention in care and the likelihood factors for retention in HIV care among Southeast Asian PLWH, providing an estimate of the proportion of retention in care for targeted interventions and policy improvements.

The findings of this study may have significant implications for ensuring retention care among PLWH in policymaking, health, and nursing practices. Nursing practice and other healthcare professionals identified to enhance ART retention in PLWH include health assessments, education, knowledge delivery, care coordination, and connecting PLWH to the resources (Rouleau et al., 2019). Key practices, such as educating PLWH on managing ART side effects and enhancing self-management skills, were considered standard care to improve retention in care among PLWH (Rouleau et al., 2019). In addition, healthcare providers, governments, and other policymakers or stakeholders could facilitate rapid ART initiation and improve retention in care, as well as retention with viral suppression (Spach, 2024).

#### **Methods**

#### Study Design

This study used a systematic review design following the Preferred Reporting Items for Systematic Reviews and Metaanalysis (PRISMA) guidelines (Page et al., 2021). This study was registered in the Open Science Framework (OSF) (Maulana et al., 2024).

#### **Eligibility Criteria**

Inclusion criteria were defined according to the Population, Concept, Context (PCC) framework. This study included PLWH from an adult population. This concept involves factors affecting retention in care. Retention in care was defined as the number of PLWH adhering to HIV medical care for at least one year following the initiation of ART and entry into the HIV clinic (Clouse et al., 2013; Valenzuela et al., 2015). The context was HIV clinical settings across Southeast Asia. The exclusion criteria were: (1) non-observational studies, case reports, reviews, non-peer-reviewed articles, abstract-only articles; (2) articles not in English.

#### **Search Strategy and Study Selection**

A systematic literature search was conducted using multiple databases, including PubMed, Scopus, Cochrane, and CINAHL, covering articles published from inception to July 15, 2024. The following search terms were used: "associated factors" OR "effecting factors" OR "barrier factors" OR "facilitator factors" OR factors) AND "hiv care cascade" OR "continuum of care" OR "hiv care continuum" OR "linkage to care" OR screening OR testing OR diagnosis OR "retention in care" OR "retained in care") AND (hiv OR "human immunodeficiency virus" OR aids OR immunodeficiency syndrome" OR hiv/aids). The search strategy is detailed in Supplementary File 1. Duplicate records were removed using reference management software (Mendeley). Two independent reviewers (SM and SA) screened the titles and abstracts and assessed the full texts. Discrepancies were resolved through discussions.

#### **Data Extraction**

Data extraction was independently performed by two authors (SM and SA). Disagreements were resolved by discussion and consensus. Data extraction using a predefined standardized form included details such as author(s), year of publication, study design, geographic location, sample size, and the number of PLWH who were retained in HIV care. Moreover, this study found several likelihood factors for retention in HIV care and classified them as either demographic or clinical. *Demographic Factors:* 

- Age: divided into two groups: <40 and ≥40 years. Age
  was categorized into two groups (<40 years and ≥40
  years) because individuals aged ≥40 years are more
  likely to have comorbid conditions, which can
  complicate their health status and potentially affect
  their retention of HIV care (Wu et al., 2014).</li>
- Gender: categorized as male and female.
- Educational Level: categorized as low (no formal or primary education) or high (secondary education or above).
- Employment Status: divided into employed and unemployed.
- · Marital Status: classified as single and married.
- Geographic Setting: distinguished between rural and urban areas.

#### Clinical Factors:

- CD4 Count: categorized into <200 cells/mm³ and ≥200 cells/mm³.</li>
- The HIV Stage (WHO Stages): divided into early (I and II) and advanced stages (III and IV).
- A history of ART: classified into yes (previously on ART) and no (not previously on ART).
- Co-infection with TB: divided into yes and no.
- Drug/Substance Abuse: categorized into yes and no.
- Hemoglobin (Hb) levels: divided into two groups: <10 and ≥10 g/dL.

#### **Statistical Analysis**

Statistical analyses were conducted using the 'metafor" and "meta" packages in R software (version 4.4.1, The R Foundation for Statistical Computing, Vienna, Austria) for the meta-analysis of the proportion and likelihood factors. The pooled proportion was estimated using the generalized linear mixed-effect model (GLLM) and odds ratios (OR) using the DerSimonian-Laird (DL) random effects method with their 95% confidence intervals (CI). The "meta" package was used to estimate the DL, while "metafor" was used to estimate the GLMM. Heterogeneity among studies was assessed using the  $I^2$  statistic, with values >50% indicating substantial heterogeneity (Higgins et al., 2003). A random-effects model was applied irrespective of the degree of heterogeneity.

Additionally, subgroup analyses were performed to explore potential sources of heterogeneity and assess the effects of specific study characteristics on outcomes. To evaluate the robustness of the findings, we conducted sensitivity analyses by systematically excluding individual studies to determine their impact on the pooled estimates. Publication bias was assessed visually using funnel plots and quantitatively using Egger's test. Furthermore, the trim-and-fill method was applied to adjust for potential publication bias by estimating and imputing missing studies, thereby providing corrected effect size estimates.

#### **Quality Assessment and Publication Bias**

The Newcastle-Ottawa Scale (NOS) was employed to assess the quality of each study included, utilizing eight items for quality appraisal, which are grouped into 'selection,' 'comparability,' and 'outcome' categories. Two authors (SM and SA) independently evaluated the studies based on cohort selection, comparability, and outcome assessments (Supplementary File 2). Discrepancies in the quality assessments were resolved through discussion.

#### Results

#### **Study Selection**

The selection process of the studies included in this metaanalysis is shown in **Figure 1**. The initial search yielded 6,686 records from multiple databases. After removing 3,220 duplicates, 3,466 relevant articles were screened. Of the 3,466 articles, 23 were assessed for eligibility. Of these, 12 reports were excluded for reasons including focus on linkage to care (1), intervention to improve retention in care (1), reengagement strategies (2), service availability (1), qualitative study design (1), and evidence specific to the United States (3) and Africa (2). Ultimately, 11 studies were included in the analysis (Abdulrahman et al., 2017; Eamsakulrat & Kiertiburanakul, 2022; Eustaquio et al., 2021; Hoang et al., 2022; Januraga et al., 2018; Lay et al., 2017; Muth et al., 2017; Nugroho et al., 2018; Rahmalia et al., 2019; Thai et al., 2009; Thida et al., 2014).

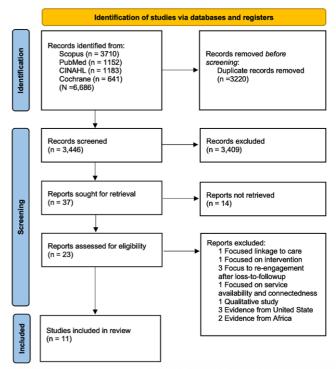


Figure 1 PRISMA flow diagram

#### **Characteristic of Included Studies**

A total of 46,480 participants from eleven studies were included. Studies have involved participants from various countries in the Southeast Asian region, including Indonesia, Thailand, the Philippines, Malaysia, Vietnam, and Cambodia (Abdulrahman et al., 2017; Eamsakulrat & Kiertiburanakul, 2022; Eustaquio et al., 2021; Hoang et al., 2022; Januraga et al., 2018; Lay et al., 2017; Muth et al., 2017; Nugroho et al., 2018; Rahmalia et al., 2019; Thai et al., 2009). The total number of participants across all studies was mainly from Indonesia and Cambodia. The study designs varied; four included studies were cross-sectional, five retrospective, and two prospective cohort studies.

Most studies focused on the general population of PLWH (n = 8), with specific studies targeting men who have sex with men MSM (n = 2) and FESW (n = 1). The gender distribution in the studies showed a higher representation of males than females. Most participants were under 40, possessed a higher level of education, held employment, and resided in urban areas. Clinical characteristics showed that most participants had a CD4 count of less than 200 cells/mm3, and most had not yet initiated ART. One-third of the participants had a history of tuberculosis, and only a few reported substances were used. WHO staging varied, with a higher proportion in stages 2-4, and a few participants had hemoglobin levels indicating anemia (<10 g/dL). The characteristics of the included studies are shown in Table 1 and Supplementary File 3.

Table 1 Characteristic of included studies

			Table 1 Characteristic of included studies		
	No. of studies (N = 11)	No. of retentions in care* (n (%))	References		
Country Indonesia Cambodia Malaysia Thailand Philippine Vietnam Myanmar	3 2 1 1 1 1 1	2597 (7.04) 5367 (14.55) 182 (0.49) 227 (0.62) 2368 (6.42) 17529 (47.52) 8615 (23.36)	(Januraga et al., 2018; Nugroho et al., 2018; Rahmalia et al., 2019) (Lay et al., 2017; Muth et al., 2017; Thai et al., 2009) (Abdulrahman et al., 2017) (Eamsakulrat & Kiertiburanakul, 2022) (Eustaquio et al., 2021) (Hoang et al., 2022) (Thida et al., 2014)		
Design Cross-sectional Prospective cohort Retrospective cohort	4 2 5	21057 (57.09) 533 (1.45) 15295 (41.47)	(Abdulrahman et al., 2017; Hoang et al., 2022; Lay et al., 2017; Nugroho et al., 2018) (Januraga et al., 2018; Muth et al., 2017) (Eamsakulrat & Kiertiburanakul, 2022; Eustaquio et al., 2021; Rahmalia et al., 2019; Thai et al., 2009; Thida et al., 2014)		
Population group General PLWH	8	31171 (84.51) 2566 (6.96)	(Abdulrahman et al., 2017; Eamsakulrat & Kiertiburanakul, 2022; Hoang et al., 2022; Januraga et al., 2018; Muth et al., 2017; Rahmalia et al., 2019; Thai et al., 2009; Thida et al., 2014) (Eustaquio et al., 2021; Nugroho et al., 2018)		
FESW Gender Male	4	3148 (8.53) 3527 (60.95)	(Lay et al., 2017)  (Abdulrahman et al., 2017; Lay et al., 2017; Rahmalia et al., 2019; Thai et al., 2009)		
Female Age <40 ≥40	4 4	2260 (39.05) 18451 (84.17) 3470 (15.83)	(Abdulrahman et al., 2017; Eustaquio et al., 2021; Hoang et al., 2022; Rahmalia et al., 2019)		
Education Lower High	4 4	610 (22.55) 2095 (98.50)	(Abdulrahman et al., 2017; Januraga et al., 2018; Nugroho et al., 2018; Rahmalia et al., 2019)		
Occupation Employed Unemployed Marital status	4 4	3513 (75.56) 1136 (24.44)	(Abdulrahman et al., 2017; Eustaquio et al., 2021; Januraga et al., 2018; Rahmalia et al., 2019)		
Single Married Geographic	3	1154 (46.80) 1312 (53.20)	(Januraga et al., 2018; Nugroho et al., 2018; Rahmalia et al., 2019)		
setting Rural Urban	3	4996 (27.90) 12913 (72.10)	(Abdulrahman et al., 2017; Hoang et al., 2022; Nugroho et al., 2018)		
CD4 <200 ≥200 Has been ART	4 4	2989 (57.65) 2196 (42.35)	(Eustaquio et al., 2021; Januraga et al., 2018; Rahmalia et al., 2019; Thai et al., 2009; Thida et al., 2014)		
Yes No Has been with TB	3	1399 (48.29) 1498 (51.71)	(Nugroho et al., 2018; Rahmalia et al., 2019; Thai et al., 2009)		
Yes No Substance use	3	1052 (33.86) 2055 (66.14)	(Rahmalia et al., 2019) (Nugroho et al., 2018; Thai et al., 2009)		
Yes No WHO staging	2 2	455 (17.73) 2111 (82.27)	(Eustaquio et al., 2021; Nugroho et al., 2018)		
1-2 2-4 Haemoglobin	3	3080 (29.35) 7414 (70.65)	(Januraga et al., 2018; Thai et al., 2009; Thida et al., 2014)		
<10 (anemia) ≥10 (normal) NOS score	3	7117 (65.97) 3671 (34.03)	(Rahmalia et al., 2019; Thai et al., 2009; Thida et al., 2014)		
7 8	1 10	198 (0.54) 36687 (09.46)	(Nugroho et al., 2018) (Abdulrahman et al., 2017; Eamsakulrat & Kiertiburanakul, 2022; Eustaquio et al., 2021; Hoang et al., 2022; Januraga et al., 2018; Lay et al., 2017; Muth et al., 2017; Rahmalia et al., 2019; Thai et al., 2009)		

Note. PLWH, people living with HIV; MSM, men who have sex with men; SD, standard deviation; IR, interval range; NA, not available; NOS, Newcastle-Ottawa Scale | \*Pooled people living with retained care = 28270

#### **Coverage of Retention in Care**

The coverage of retention in care among Southeast Asian people living with HIV revealed a pooled proportion of 75.2% (95% CI: 66.7; 82.1). Approximately two-thirds of PLWH in Southeast Asia remain engaged in care programs, although

the exact retention rate can vary between 66.7% and 82.1% in the population. However, this coverage was still below the target achievement for the HIV care cascade (95%). Additionally, heterogeneity was significant ( $I^2 = 99.5\%$ ). The coverage of retention in care is shown in **Figure 2**.

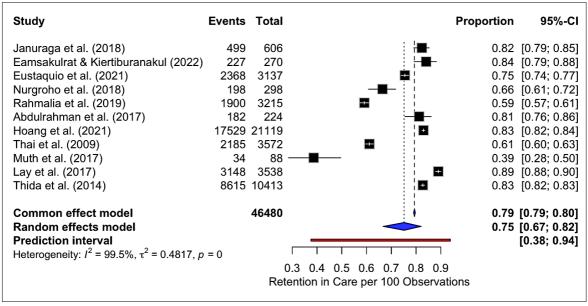


Figure 2 Forest plot for proportion of retention in care

Subgroup analysis by period showed that the pooled estimate for the current 10-year period was higher at 84.6% (95% CI: 77.0%-90.0%), while linkage to care over more than 10 years showed a slightly lower estimate of 73.2% (95% CI: 61.0%-82.6%). Subgroup analysis by year showed no significant difference (p = 0.06) and still showed substantial heterogeneity in each group. Subgroup analysis by population groups showed that men who had sex with men (MSM) had a pooled estimate of 71.8% (95% CI: 65.3%-77.6%) with substantial heterogeneity ( $I^2 = 91.4\%$ ). Female entertainment workers (FEWS) had a notably higher estimate of 89.0% (95% CI: 65.3%-77.6%), although heterogeneity could not be assessed due to the inclusion of only one study. Subgroup analysis by group showed a significant group difference (p < 0.0001).

In the subgroup analysis by country, the pooled estimates of the linkage to HIV care among Southeast Asian PLWH showed considerable variation. Countries with pooled estimates above the overall average included Thailand, which had the highest estimate at 84.1% (95% CI: 79.2%-88.2%), followed closely by Vietnam at 83.0% (95% CI: 82.5%-83.5%), Myanmar (82.7%, 95% CI: 66.7-82.1), and Malaysia 81.2% (95% CI: 75.5%-86.1%). In contrast, countries with pooled estimates below the overall average included the Philippines at 75.5% (95% CI: 73.9%-77.0%), Indonesia at 70.3% (95% CI: 57.3%-80.6%), and Cambodia at 67.0% (95% CI: 38.1%-87.0%). Indonesia and Cambodia showed substantial heterogeneity, with I2 values of 98.2% and 99.7%, respectively. Although there were a limited number of studies on grouping, subgroup analysis by country showed a significant difference (p < 0.0001).

A subgroup analysis was also performed using the study design. The pooled estimates of the linkage to HIV care varied

across different studies. The estimates of retention in care across studies were 84.7% (95% CI: 76.5%-90.4%,  $I^2$  = 98.5%), 63.6% (95% CI: 30.2%-87.5%,  $I^2$  = 98.5%), and 73.6% (95% CI: 63.5%-81.8%,  $I^2$  = 99.6%) for the cross-sectional, prospective cohort, and retrospective cohort, respectively. Substantial heterogeneity was observed. However, subgroup analysis according to study design showed no significant group differences (p = 0.10). The detailed subgroup analysis of the pooled estimate of linkage to HIV care across variables that are potential sources of heterogeneity can be seen in **Table 2** and **Supplementary File 4**.

#### **Demographic Factor**

This meta-analysis evaluated the likelihood of six demographic factors (age, gender, education, employment, marital status, and geographic setting) associated with retention in care (Abdulrahman et al., 2017; Eustaquio et al., 2021; Hoang et al., 2022; Januraga et al., 2018; Lay et al., 2017; Nugroho et al., 2018; Rahmalia et al., 2019; Thai et al., 2009). The findings of this meta-analysis showed that PLWH with unemployed individuals had better retention in care than did PLWH with employees (OR 1.18, 95% CI: 1.02-1.38; p =0.03). However, there was no significant difference in retention for age groups under 40 and 40 years and above (OR 1.69, 95% CI: 0.45-6.30, p = 0.43), gender (OR 1.02, 95% CI: 0.82-1.27, p = 0.85), education level (OR 0.69, 95% CI: 0.34-1.39, p = 0.30), marital status (OR 0.88, 95% CI: 0.75-1.02, p =0.09), and geographic setting (rural vs. urban) (OR: 0.71; 95% CI: 0.42-1.20, p = 0.20). These findings show that most demographic factors were not significantly associated with retention in care. Details of the meta-analysis of the likelihood of demographic factors associated with retention in care are shown in Figure 3.

Table 2 Pooled estimate of the proportion of linkage to HIV care among Southeast Asian PLWH and subgroup analysis by potential variable

Variable	Number of studies	Pooled sample	Pooled estimate, % (95%CI)	l²
Year	12ª		p = 0.06*	
Ever	11	46,480	75.2 (66.7; 82.1)	99.5
Current 10 years	4	8905	84.6 (77.0; 90.0)	99.2
More than 10 years	8	36575	73.2 (61.0; 82.6)	99.7
Population group	11		p <0.0001**	
PLWH	8	39507	73.7 (62.9; 82.3)	99.2
MSM	2	3435	71.8 (65.3; 77.6)	91.4
FEWS	1	3538	89.0 (65.3; 77.6)	NA
Country	11		p <0.0001**	
Indonesia	3	4119	70.3 (57.3; 80.6)	98.2
Cambodia	3	7198	67.0 (38.1; 87.0)	99.7
Malaysia	1	224	81.2 (75.5; 86.1)	NA
Thailand	1	270	84.1 (79.2; 88.2)	NA
Vietnam	1	21119	83.0 (82.5; 83.5)	NA
Philippine	1	3137	75.5 (73.9; 77.0)	NA
Myanmar	1	10413	82.7 (66.7; 82.1)	NA
Study design	11		p = 0.10*	
Cross-sectional	4	24179	84.7 (76.5; 90.4)	98.5
Prospective cohort	2	694	63.6 (30.2; 87.5)	98.5
Retrospective cohort	5	20607	73.6 (63.5; 81.8)	99.6

Note. FEWS= Female entertainment workers; PLWH= people living with HIV; MSM= men who have sex with men; NA= not available; <sup>a</sup>The total number of included studies was 11. However, one study (Hoang et al., 2022) is included in both 'Current 10 years' and 'More than 10 years' categories, as it spans both time periods; \*not significant differences; \*\*significant differences.

The heterogeneity was substantial for age ( $I^2 = 99.2\%$ ), gender ( $I^2 = 82.4\%$ ), education ( $I^2 = 91.4\%$ ), and geographic setting ( $I^2 = 69.4\%$ ), indicating significant variability in the included studies for these factors. By contrast, heterogeneity was not significant for employment ( $I^2 = 15.5\%$ ) or marital status ( $I^2 = 0\%$ ). This heterogeneity contributes to overestimation and variation of effects across studies. A sensitivity analysis to account for outliers is shown in **Supplementary File 5**.

Although the heterogeneity was still substantial, the heterogeneity of age outcome was reduced to  $I^2$  = 63.6% after excluding the study by Rahmalia et al. (2019). Heterogeneity for gender and education also significantly reduced to  $I^2$  = 0% after excluding the studies by Thai et al. (2009) and Nugroho et al. (2018), respectively. A sensitivity analysis for the geographical setting was not performed because of the limited number of studies included.

One demographic factor from one study showed that race is a likelihood factor for retention in care. Indian races were less likely to retain care than Malays (OR 0.234, 95% CI: 0.063-0.869, p = 0.030) (Abdulrahman et al., 2017).

#### **Clinical Factor**

The meta-analysis evaluated the likelihood of six clinical factors (CD4 count, HIV stage [WHO stages], ART status, TB co-infection, drug abuse/substance use, and hemoglobin levels) on retention in care (**Figure 4**) (Eustaquio et al., 2021; Januraga et al., 2018; Nugroho et al., 2018; Rahmalia et al., 2019; Thai et al., 2009; Thida et al., 2014). The findings of the meta-analysis showed that people with CD4 count  $\geq$ 200 cells/mm³ (OR 2.17, 95% CI: 1.19-3.97, p = 0.01), HIV stage 3-4 (OR 2.06, 95% CI: 1.09-3.87, p = 0.02), not receiving ART (OR 6.88, 95% CI: 1.89-25.06, p = 0.001) were more likely to

be retained in care. Although the OR was not large, PLWH with hemoglobin levels  $\geq$ 10 g/dL (OR 0.50, 95% CI: 0.25-0.99, p = 0.04) were also more likely to be retained in care. Non-significant associations were observed for TB co-infection (OR 1.55, 95% CI: 0.91-2.63, p = 0.10) and drug abuse/substance use (OR 1.20, 95% CI: 0.92-1.58, p = 0.18).

These findings showed that ART status, HIV stage, CD4 count, and Hb were significantly associated with retention in care, whereas the other factors were not. Additionally, heterogeneity was substantial for HIV stage (I<sup>2</sup> = 85.6%), CD4 count ( $I^2 = 97.2\%$ ), ART status ( $I^2 = 94.4\%$ ), TB co-infection ( $I^2$ = 94.7%), and hemoglobin levels ( $I^2$  = 97.1%), indicating significant variability in the included studies for these factors. In contrast, heterogeneity was not significant for drug abuse or substance use  $(I^2 = 0\%)$ . Heterogeneity contributed to overestimation across studies. A sensitivity analysis to account for outliers is shown in Supplementary File 5. Although the heterogeneity was still substantial, the heterogeneity of the CD4 outcome was reduced to  $I^2 = 93.0\%$ after excluding the study by Eustaquio et al. (2021). Sensitivity analysis for WHO staging, ART, and TB infection outcomes was not performed because of the limited number of included studies.

Several factors were identified without a meta-analysis of the likelihood factors for retention in care. PLWH in the heterosexual group were more likely to be retained in HIV care, particularly on ART, than the bisexual group among the Malaysian PLWH population, with an OR of 4.199 (95% CI: 1.040-16.957, p=0.04) (Abdulrahman et al., 2017). Moreover, PLWH with a BMI <18 (OR 2.87, 95% CI: 2.13-3.83; p <0.001), sexual transmission infection (ISTI) co-infection (OR 0.69, 95%CI: 0.48; 0.10, p=0.048), and late ART initiation (p=0.028) had lower retention (Abdulrahman et al., 2017).

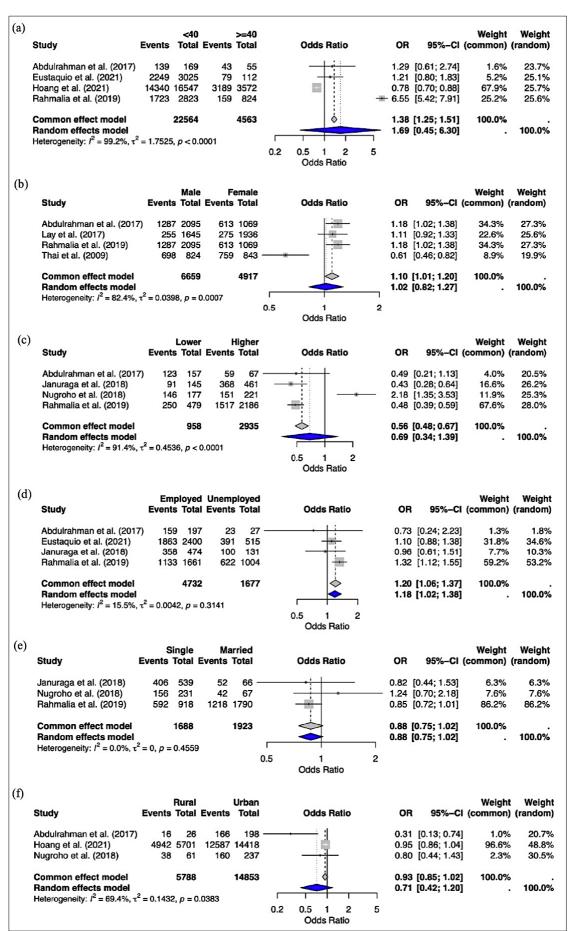


Figure 3 Forest plot for demographic factors

Note. (a) age (b) gender (c) education (d) employment (e) marital status (f) geographic setting

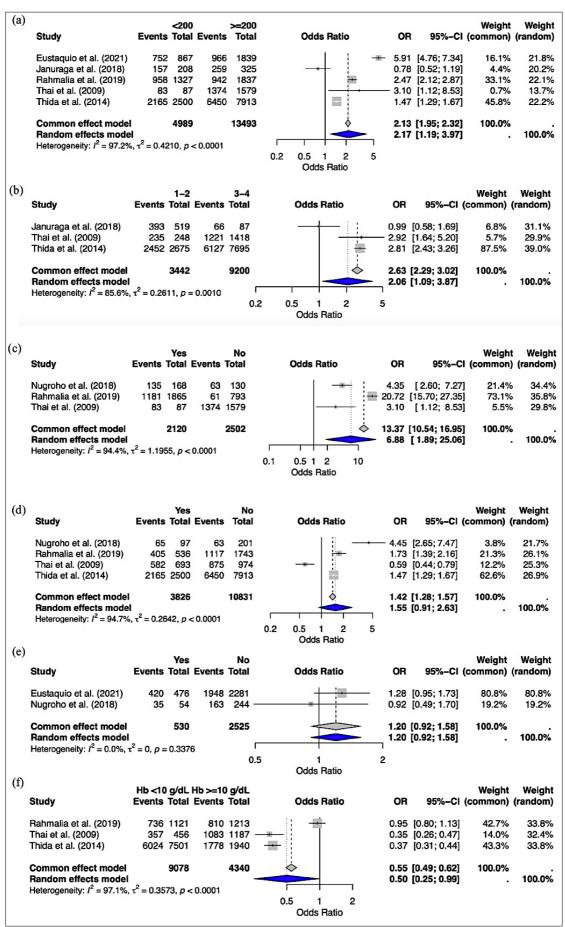


Figure 4 Forest plot for clinical factors

Note. (a) CD4 (b) WHO staging (c) Has been on ART (d) Has been with TB coinfection (e) Drug/substance abuse (f) Hemoglobin/Hb

#### **Healthcare System and Community Factor**

Several factors related to healthcare systems are associated with the retention of HIV care. One-stop services and having more than five health professionals had a statistically significant impact on retention (Hoang et al., 2022). Additionally, accessibility of medical insurance was significantly associated with retention (OR 2.84, 95% CI: 1.27-6.34, p <0.05) and availability of Internet access to obtain information (OR 2.15, 95% CI: 1.00-4.59, p <0.05) (Nugroho et al., 2018).

Several factors related to the community factors are also associated with the retention of HIV care. Being associated with an HIV-related organization has been shown to have good retention (OR 4.16, 95% CI: 1.38-12.56; OR 0.4, 95% CI: 0.247-0.95, respectively) (Muth et al., 2017; Nugroho et al., 2018). Additionally, PLWH with peer education are more likely to have greater retention in care (p <0.001) (Hoang et al., 2022).

#### **Publication Bias**

The removal of each study resulted in any changes in statistical robustness (e.g., gender, educational outcomes) and study heterogeneity (e.g., age, sex, and educational outcomes), as shown by sensitivity analysis. Assessment of publication bias revealed an asymmetrical funnel plot in relation to the estimated retention of care (Figure 5). The regression-based Egger's test results showed the existence of small-study effects in the estimated retention of care outcomes (p = 0.319). The trim-and-fill analysis demonstrated that the pooled effect estimate remained significant after imputation of five additional studies, with an adjusted estimate of 85.9% (95% CI: 79.49%-91.29%, p < 0.001).

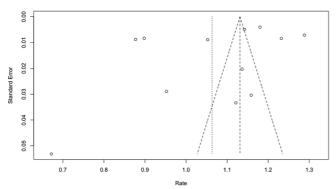


Figure 5 Funnel plot for included studies

#### Discussion

Maintaining retention in HIV care is essential for better health outcomes, reducing mortality in public healthcare settings, and minimizing the likelihood of viral rebound (Crawford, 2014). Suboptimal retention rates in HIV care present a significant barrier to effective treatment, and are associated with poorer health outcomes and an increased rate of HIV transmission (Li, 2019).

This present study estimated the pooled proportion of retention in HIV care among Southeast Asian individuals living with HIV. The study found a pooled proportion of 84.6% over the current 10 years period. Thailand, Vietnam, Myanmar, and Malaysia had a higher proportion of retention in care, exceeding the overall average. Thailand and Vietnam are

recognized as a pioneer in reducing stigma and discrimination in healthcare settings across Asia. Both countries have implemented strong national policies and programs to foster an inclusive healthcare environment, which is crucial for effective HIV care. For instance, Thailand has provided access to friendly, high-quality HIV services. Thailand also committed to financing a national HIV response through co-financing and government support (Sustainale HIV Financing in Transition, 2024). Civil society has successfully advocated Thai governments for equal access, an issue commonly linked to patient retention in HIV services (Siraprapasiri et al., 2016). These initiatives have created safety, particularly from stigma and discrimination, and mobilized community support for PLWH, encouraging them to be retained in care. Literature suggests that stigma and discrimination are barriers to retaining individuals in HIV care (Gesesew et al., 2017). Although stigma remains a classic and common reason PLWH do not retain care, the included studies in the present metaanalysis provided limited data on this issue.

This present meta-analysis also assessed factors associated with the likelihood of HIV care. Among the demographic variables, only employment status notably affected retention, with unemployed individuals more likely to be retained in care than those who were employed. Significant clinical factors associated with improved retention in care included higher CD4 counts, WHO staging 3-4, individuals not on ART, and Hb >10 g/dL, enhanced care retention. Additionally, healthcare system factors such as the presence of one-stop services, a sufficient number of health professionals, and access to medical insurance and internetbased health information are essential for improving retention (Hoang et al., 2022; Nugroho et al., 2018). Community factors also significantly affect retention, with involvement in HIVrelated organizations and participation in peer education programs being beneficial (Muth et al., 2017; Nugroho et al., 2018).

The present meta-analysis revealed a pooled proportion of retention in HIV care at 75.2% among Southeast Asian people living with HIV, which is slightly higher than the 70.65% (95% CI: 68.19 to 80.6) in Ethiopia, which was lower than that in Southeastern United States (91.7%) and Sub-Saharan Africa (>85%) (Du Toit et al., 2014; Kay et al., 2021; Moges et al., 2020; Wilkinson et al., 2015). Despite the geographical and contextual differences, a few studies have highlighted a substantial gap in achieving a 95% target for HIV care retention.

In the present study, key factors associated with retention in care included having CD4 > 200 and never having received ART, while other clinical and demographic factors showed no significant association. In the United States, certain populations remain engaged in care but not on ART (Christopoulos et al., 2015). For those not on ART, regular engagement in care allows healthcare providers to monitor their condition, offer prophylactic treatment, and initiate ART once clinically indicated. However, the Centers for Disease Control and Prevention (CDC) recommend that PLWH initiate ART, regardless of the CD4 count (CDC, n.d.). Furthermore, patients are concerned about the side effects (e.g., anemia) and toxicities of ART, as well as the lack of acceptance or disclosure of their HIV status, and worries about social stigma as a reason for not being on ART (Christopoulos et al., 2015).

The findings of the present meta-analysis align with previous meta-analyses that showed that Hb≥10 or normal hemoglobin status are associated with greater retention in care, suggesting that PLWH who experience fewer side effects (e.g., anemia) are more likely to be retained for care (Moges et al., 2020).

In contrast, Moges et al. (2020) identified the substantial barrier to retention in care, such as being unmarried, nondisclosed HIV status, poor drug adherence, poor functional status, underweight, and advanced clinical stage. Additionally, facilitators of retention in care in their study included the absence from opportunistic infections, normal hemoglobin levels, and non-substance use (Moges et al., 2020). Furthermore, a meta-analysis by Rooks-Peck et al. (2018) concluded that mental health diagnoses or symptoms are significantly associated with lower odds of retention in HIV care (OR = 0.94; 95% CI: 0.90-0.99). While (Moges et al., 2020) focused on a broader range of clinical and sociodemographic factors, our study highlighted the critical role of CD4 counts, WHO stages, and ART status in retention in care. Additionally, unlike the finding of Rooks-Peck et al. (2018), the present meta-analysis did not identify mental health as a significant factor associated with in care in Southeast Asia.

The present study revealed that unemployed individuals had better retention in HIV care than their employed counterparts. This finding contrast with previous reviews that reported a positive association between employment and care retention and other HIV care cascades, including testing, linkage to care, and adherence (Maulsby et al., 2020). Moreover, the Centers for Disease Control and Prevention (CDC) has emphasized the importance of employment for the majority of working age PLWH (CDC, 2018). CDC suggests that being unemployed and job loss can critically affect social well-being and overall health (CDC, 2018). This discrepancy in findings could be attributed to regional differences and variations in healthcare and social support systems, indicating a complex and multifaceted relationship between employment status and HIV care retention. In Southeast Asia, stigma and discrimination are barriers to achieving the HIV care cascade, such as retention in care (Ikeda et al., 2019). PLWH are three times more likely to experience unemployment than the national unemployment average, largely due to factors such as HIV stigma index, discrimination, restrictive policies, and practices.

The present study revealed that clinical conditions, such as low initial CD4 count (<200 cells/mm3), WHO staging 3-4, and history of ART in PLWH, were associated with higher likelihood of retention in care. This finding aligns with previous study showing that advanced HIV stages are associated with a higher symptom burden (Ewetola et al., 2021). Adeola et al. (2020) reported that higher symptoms were associated with increased retention in care at 12 months. The finding of present meta-analysis also aligns with a previous review from Sub-Saharan Africa, which observed that ART initiation at substantially low CD4 counts among most PLWH was more likely associated with retention in care (Lahuerta et al., 2013). PLWH who initiate ART at a later stage are more likely to have lower retention in care (Abdulrahman et al., 2017). During these periods, PLWH may also be reluctant to accept their HIV-positive status, leading to the need for repeated testing

and further delays in their engagement with care services (Nash et al., 2016). Therefore, early linkage to care is critical to prevent a decline in CD4 count, which can help PLWH retain their care. However, PLWH are likely to face challenges in maintaining care due to the different sites between the test and treatment services. It also affects the retention of care among PLWH. Support is also essential to help patients understand their condition, manage their treatment, and retain care.

At the community level, the present study found that PLWH engaged with HIV-related organizations and peer education were more likely to retain care (Vannakit et al., 2020). This finding aligns with previous research showing that peer interventions might significantly enhance retention in care (Genberg et al., 2016).

#### Implications to Improve Early Retention

As HIV testing and treatment have been successfully expanded, the remaining challenges to ensuring that no one is left behind call for a shift in the HIV response. This shift should focus on enhancing adherence and retention, moving beyond awareness of HIV status. This study identified the likelihood factors of retention in HIV care, with significant implications for care practices and policymaking in Southeast Asia.

Nurses and other healthcare professionals should identify the risk factors for loss to follow-up or decreased retention in HIV care following care initiation. They could continue monitoring through retention measures (e.g., visit adherence, patient visits within time intervals, etc.) and alignment with the desired visit frequency. The integration of data sources (e.g., administrative databases, medical records, and community surveillance) can improve retention in care monitoring (Spach, 2024). Nurses also need to provide a holistic and patientcentered approach to improve retention. The need to adopt this model of care is an integral part of nursing philosophy (Spach, 2024). Furthermore, nurse-led interventions through home visiting programs in primary health care can potentially improve retention in care (Perriat et al., 2018). However, HIV stigma can be overcome through home visits. To minimize stigma, nurses and other clinicians could consider a remotebased intervention (e.g., Internet-based intervention, textbased reminder) as an alternative to improve retention in care and adherence (Nugroho et al., 2018; Wang et al., 2019). Such a remote-based program could be a continuum of HIV care in community settings.

Continuum of care monitoring in clinical settings through identification of high CD4 counts and ongoing ART as critical determinants of retention underscores the need for the aggressive implementation of "universal test and treat" strategies. These strategies ensure that individuals are not only tested promptly but also started on ART immediately following diagnosis, regardless of CD4 count, which could mitigate the challenges of late ART initiation identified in our findings (Girum et al., 2020; Nicol et al., 2023). Policies supporting same-day ART initiation could substantially decrease barriers to treatment entry, thereby enhancing retention by simplifying the care continuum and making it more accessible.

Leadership initiatives and financial stability enhance ART coverage. Countries should establish stakeholder committees to govern and coordinate the universal health coverage. National legislation must be in place to create a system of

universal health coverage financed by domestic sources, international sources, or a combination of sources (Gostin et al., 2020; UNAIDS, 2019). Additionally, strengthening primary and community healthcare workers is essential for widespread service delivery and universal health coverage (UNAIDS, 2019).

Although the present study did not find any Southeast Asian literature linking stigma with retention in care, previous study has suggested that stigma and discrimination are barriers to retaining individuals in HIV care (Gesesew et al., 2017). Ensuring quality services and a public health strategy that is free from stigma are critical to achieving equitable healthcare for all and global HIV response goals. However, there is no single intervention that can create and sustain change; a variety of approaches are needed to address HIVrelated stigma in the long term (Ferguson et al., 2023). The most effective programs are achieved by establishing partnerships, engaging leaders, and placing communities at the core. These include components targeted at a variety of socio-ecological levels and actors (Pulerwitz et al., 2015; Stangl et al., 2019). The Health Stigma and Discrimination Framework can inform the development of interventions and programs. Mass communication initiatives may be implemented to help the general public understand a health condition and to dispel misconceptions regarding the transmission of HIV and risk populations. Nations are legally obligated to create and enforce rules and policies that ensure equal access to high-quality healthcare and address the underlying factors that contribute to health inequalities, such as social stigma and discrimination (WHO, 2015).

#### Limitation

This study comprehensively identified the factors influencing retention in HIV care in Southeast Asia, and the findings have implications for practice and policymaking. However, this study has several limitations. This study was registered in the OSF but not in PROSPERO, which may have impacted the indexing of the review protocol. Additionally, the meta-analysis showed high heterogeneity among the included studies, which could be attributed to the diverse methodologies, population characteristics, and healthcare settings across the studies. This heterogeneity may affect the generalizability of the findings across Southeast Asian contexts. Although the robustness of the conclusion is unclear, a subgroup analysis was performed to identify the source of heterogeneity. However, meta-regression was not considered in the present meta-analysis because the included studies had fewer than ten studies across covariates. While the generalized linear mixed-effects model (GLMM) was used to estimate pooled proportions, it may be sensitive to model assumptions and require careful specification of random effects. Similarly, the DerSimonian-Laird (DL) random-effects method, although widely used, has limitations in handling substantial heterogeneity, as it relies on an estimated between-study variance that may be unstable in cases with a small number of studies or extreme variability. This present meta-analysis did not consider performing a Bayesian meta-analysis to estimate the proportion and OR. It offers advantages in combining prior information and provides a more robust uncertainty estimate, which could be beneficial in addressing heterogeneity across studies.

This analysis of the present study utilized dichotomous data to determine likelihood factors and odds ratios (OR). Consequently, the analysis focused on identifying factors associated with the likelihood of retention in HIV care. However, further meta-regression analysis is recommended to provide a more comprehensive understanding of the influencing factors. Moreover, the exclusion of non-English-language studies could have omitted the relevant regional research, potentially skewing the results. Despite these limitations, this study provides valuable insights into the dynamics of HIV care retention and highlights critical areas for targeted intervention and policy improvement.

#### Conclusion

The present study concluded a pooled proportion of retention in HIV care among Southeast Asian people living with HIV of 75.2%, underscoring a significant gap in achieving a 95% target for HIV care retention. This study identified significant clinical factors more likely associated with retention enhancement, including a high CD4 count, WHO stage 3-4, not being on ART during enrollment, and employment. Moreover, healthcare system factors such as the presence of one-stop services and a sufficient number of health professionals, along with access to medical insurance and Internet-based health information, are important for improving retention. Community factors, such as access to peer groups and peer education, play significant role in retention in care.

The present study highlights the importance of universal testing and treatment strategies and shows that employment status may influence adherence to care. Nursing practices have evolved to support these insights. Healthcare professionals, especially nurses and social care providers, should advocate for and facilitate rapid HIV testing and immediate initiation of ART through same-day ART programs to enhance early intervention through effective counseling. Community outreach and engagement are crucial for maintaining patient engagement in care programs. By implementing these targeted nursing practices in communityintegrated primary healthcare within a supportive and adaptive healthcare system, retention rates can be significantly improved, ultimately leading to better health outcomes and a reduced HIV transmission rate across Southeast Asia. These interventions not only align with clinical needs but also embrace the socioeconomic dynamics that influence healthcare engagement, marking a critical step forward in the region's HIV response.

#### **Declaration of Conflicting Interest**

No conflict of interest to declare.

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None to declare.

#### **Authors' Contributions**

**SM** contributed to the study's conception and design, data acquisition, and data analysis, wrote the first draft of the manuscript, revised the final draft, and gave final approval of the version to be published. **KI** contributed to writing the manuscript's first draft, revised the final draft, and approved the

version to be published. **IP** contributed to writing the manuscript's first draft, revising the final draft, and giving final approval for the version to be published. **SA** contributed to the data acquisition and data analysis, wrote the first draft of the manuscript, revised the final draft, and gave final approval of the version to be published. **YH** contributed to revising the final draft and approved the version to be published.

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#### **Ethical Consideration**

Not applicable.

#### **Data Availability**

The dataset generated during and analyzed during the current study is available from the corresponding author upon reasonable request.

#### Declaration of Use of AI in Scientific Writing

The authors used ChatGPT/DeepL in the writing process to improve readability and remove grammatical errors. However, the authors took full responsibility for the content.

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