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# Interventions to prevent vertical transmission of HIV: an umbrella review of systematic reviews and meta-analyses

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## Abstract

*The aim of this umbrella review of systematic reviews and meta-analyses was to systematically consolidate and evaluate the existing evidence on interventions aimed at preventing vertical transmission of HIV, with a specific focus on assessing their efficacy and clinical applicability. Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, PubMed, Cochrane Library, and Embase were searched for systematic reviews and meta-analyses (up to Feb 2025). Two reviewers independently screened studies and extracted data, including intervention outcomes. Twenty-three systematic reviews and meta-analyses were synthesized, categorizing interventions into seven types: antiretroviral therapy (ART) (n = 7), cesarean delivery (n = 1), vitamins (n = 2), vaginal disinfection (n = 2), partner engagement (n = 3), telemedicine (n = 1), and integrated approaches (n = 7). Based on this, we conclude that ART demonstrated the strongest efficacy to suppress vertical transmission of HIV. Cesarean delivery reduced transmission risk but increased postpartum morbidity. Vitamins and vaginal disinfection had minimal impact. Telemedicine may improve adherence to prevention protocols. Integrated strategies combining ART showed enhanced effectiveness in low-resource settings. In conclusion, the evidence reported in this umbrella review suggests that ART therapy supplemented by other preventive measures is an effective way to reduce the rate of mother to child transmission of HIV. Vitamin supplement and vaginal disinfection had no clear association with the risk of vertical transmission of HIV.*

***Keywords:*** *HIV. AIDS. Vertical transmission. Umbrella review.*

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Received: 20-07-2025
Accepted: 20-09-2025
DOI: 10.24875/AIDSRev.25000017

Available online: 27-11-2025
AIDS Rev. 2025;27(3):104-115
www.aidsreviews.com

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## Introduction

HIV remains a major global health challenge, with an estimated 39. 9 million people living with the virus worldwide as of 2023[1]. As an RNA virus, HIV can be transmitted from a mother to her child during pregnancy and childbirth through exposure to blood, or postnatally through breastfeeding[2,3]. Mother-to-child transmission (MTCT) of HIV, one of the primary routes of HIV transmission, refers to the vertical transmission of the virus from mother living with HIV to her child during pregnancy, labor, delivery, or breastfeeding. In the absence of any preventive interventions, incidence of the transmission infection during pregnancy is estimated to be associated with a 30% probability[4]. Moreover, in the absence of highly active antiretroviral therapy (ART), approximately 50% of children born with HIV die by the age of two, and 80% by the age of five[5]. However, if ART in combination with other interventions is used in time, the risk of vertical transmission can be reduced to < 5%[6].

The prevention of MTCT (PMTCT) program has become global efforts to eliminate the HIV epidemic. In 2023, 62~91% of people living with HIV were aware of their HIV status. Of those who knew their status, 53~78% were receiving treatment, and among those receiving treatment, 58~73% achieved viral suppression[7]. The World Health Organization issued guidelines recommending that all pregnant women living with HIV initiate lifelong ART immediately, irrespective of their CD4 count, providing a range of services to both infants and women living with or at risk of HIV[6]. These include maternal HIV testing, lifelong ART, and a range of other interventions such as vitamin supplement, cesarean delivery, vaginal disinfection, and male partner involvement. It also involves establishing continuous linkages to long-term HIV care and treatment services for women, including the consistent monitoring of viral load throughout pregnancy and breastfeeding[8]. Due to higher rates of HIV transmission among mothers and infants who fall out of care or fail to access services, these inefficiencies significantly reduce PMTCT program impact at both the individual and population levels[9].

Among the wide range of complex interventions available, it is crucial to identify the most simple and useful interventions. These interventions should prioritize accessibility and ease of implementation, ensuring that they can be widely adopted while still achieving optimal outcomes in preventing vertical transmission of HIV. To evaluate the effectiveness and validity of different interventions for vertical transmission of HIV and find what interventions are effective compared with no intervention, we have done an umbrella review of the evidence across existing systematic reviews and meta-analyses. This review will provide decision makers with references, which consider a broader range of HIV prevention measures for mother and child, in particular those measures that have not been previously explored.

## Methods

We conducted an umbrella review of systematic reviews meta-analyses of observational studies and randomized controlled trials (RCTs) that reported on any intervention associated with HIV vertical transmission. This umbrella review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements, and the protocol was registered within the PROSPERO database (registration number: CRD42024623959).

### *Search strategy*

Two reviewers conducted literature searches in duplicate through three databases (PubMed, Cochrane Library, and Embase), using the search strategy provided in supplementary table 1, up until 22 January 2024. Before completing the formal work, we updated the process to include all newly retrieved qualified literature up to February 28, 2025. This ensured that the study incorporated the most recent and relevant findings. The key words were as follows: “infant,” “child,” “pregnancy,” “pregnant women,” “postpartum period,” “parturition,” “mother-child relations,” “breast feeding,” “lactation,” “non-invasive prenatal testing,” “HIV,” “acquired immunodeficiency syndrome,” “systematic review,” and “meta-analysis.” The use of English language was applied as a limiting criterion, as the majority of reviews are predominantly published in English. We attempted to hand search the proceedings of relevant conferences for articles overlooked by the electronic search and unpublished data. Any discrepancies between the reviewers in the search of studies were resolved through discussion, ensuring consensus and the integrity of the review process.

### *Selection criteria and study selection*

Predefined eligibility criteria were as follows: systematic reviews, meta-analyses, or both, of individual

observational studies and RCTs which assessed interventions aimed at preventing vertical transmission of HIV. Studies were required: (1) women with a confirmed history of HIV infection or exposure; (2) identification of one or more specific intervention strategies; and (3) report on the outcomes related to vertical transmission of HIV, as for example, HIV infection status of the child.

Exclusion criteria were as follows: (1) narrative reviews; and (2) systematic reviews/meta-analyses that focused on other diseases related to vertical transmission rather than HIV.

For the selection of articles, we initially evaluated the titles and abstracts of the identified articles to determine the approximate range. A full-text reading was conducted for those the articles which were eligible. In addition, an active search was continued in each of the electronic platforms, utilizing our provided literature criteria until the date of submission. Finally, the authors tried to contact if the full text or supplementary materials of any selected article were unavailable.

## Data extraction and quality assessment

Data extraction and quality assessment were independently performed by two investigators and any disagreement was resolved by consensus. From each eligible systematic review of observational studies, we abstracted the following information: (1) first author's last name; (2) year of publication; (3) summary of findings; and (4) article comments. We primarily recorded a statement summarizing the authors' main interpretations of their research findings. From each meta-analysis of observational studies or RCTs, we extracted data on the studies included in the analysis: specific relative risk estimates (risk ratio, odds ratio [OR], hazard ratio, or incident risk ratio, as reported by the authors of the meta-analysis), along with 95% confidence interval (CI), the percentages of heterogeneity ($I^2$ coefficient), the result of Egger test, and the number of events and studies in each meta-analysis.

To evaluate the methodological quality of the included systematic reviews and meta-analyses, the A measurement tool to assess systematic reviews (AMSTAR) 2 and PRISMA tool was used. The instrument AMSTAR 2 retains ten entries of the previous AMSTAR version and includes a total of 16 entries. AMSTAR is a widely recognized and extensively utilized tool, allowing authors, health professionals and policy makers to perform rapid, consistent, and reproducible evaluations of the quality of systematic reviews of RCTs evaluating healthcare interventions. Based on the original version, AMSTAR2 gains advantages in simplification, precision and justification. Seven of 16 domains are considered as critical, as they can particularly affect the validity of the review. The quality assessment rating according to the AMSTAR 2 tool is as follows: (1) high: no or one non-critical weakness, (2) moderate: more than one non-critical weakness, (3) low: one critical flaw with or without non-critical weaknesses, and (4) critically low: more than one critical flaw with or without non-critical weaknesses[10]. The guideline PRISMA is made up of a 27-item checklist and a four-phase flow diagram, replacing the original name quality of reporting of meta-analyses and encompassing both systematic reviews and meta-analyses statement[11]. PRISMA emphasizes ways in which authors can use to ensure transparent and comprehensive reporting of systematic reviews and meta-analyses; however, it does not directly address the methodology or conduct of systematic reviews and is not intended to be a quality assessment tool[12]. We use it to judge whether the review meets the criteria.

## Overlapping reviews

The inclusion of the results from systematic reviews with overlapping associations could lead to multiple inclusions in the original study, introducing bias into the results and estimates. When two or more reviews evaluated the same intervention measures and outcomes, we assessed their research methods, contents, and findings, compared them and ultimately retained one. Reviews with substantial overlap were excluded. However, if a review included recent clinical trials or other updates that could impact the results, it was included. When more than one meta-analysis addressed the same association between interventions and outcomes, we tended to include the one with the largest number of main studies to avoid duplication.

## Data analysis

We conducted descriptive analysis for systematic reviews and assessed the association between each intervention and vertical transmission of HIV. For cases where more than one systematic review yielded the same outcome, we evaluated whether their main reported conclusions align. We also conducted a thorough analysis of the results from the meta-analysis. When the outcomes of more than one meta-analysis of observational studies for the same mentioned intervention exhibit consistency, we verified the validity of

conclusions regarding the research content, magnitude, and level of statistical significance. Summary tables describing review characteristics and findings were presented.

### *Patient and public involvement*

No patients were involved in setting the research question, conducting the study and writing the results. We plan to disseminate the research findings through knowledge translation activities, including personal and institutional social media, and medical education for healthcare professionals. We also aim to collaborate with local policymakers to promote the application of the findings.

## Results

The detailed literature selection is shown in figure 1. Our research yielded 1797 articles in total (i.e., 1114 from Embase, 585 PubMed, and 98 Cochrane). Records screened 1325 articles, and while retrieval scanning, and eligibility assessing gave us 63 results. A compilation of articles that were excluded after a thorough review of the full text, along with the reasons is presented in supplementary table 2. We identified 23 relevant systematic reviews and meta-analyses on preventing vertical transmission of HIV (eight of systematic review, two of meta-analysis, and 13 of systematic review and meta-analysis).

### *Overall evaluation*

According to the prevention measures and outcome, we assigned systematic reviews and meta-analyses to seven groups: ART therapy (n = 7), cesarean delivery (n = 1), vitamin supplement (n = 2), vaginal disinfection (n = 2), male partner involvement (n = 3), telemedicine (n = 1), and integration (n = 7). Sixteen (69.6%) systematic reviews and meta-analyses included studies from multiple countries and regions, and 2 (8.7%) specifically selected the studies of low-income and middle-income countries, with 1 (4.3%) including studies performed only in Europe and 4 (17.4%) performed in Africa. Tables 1 and 2 list the summary of findings and outcomes that each of the meta-analytic (Table 1) and systematic (Table 2) mention in their outcome and result. In table 1, the outcomes for male partner participation, psychological interventions, Phone-based reminders on uptake of early infant diagnosis (EID), and antiretroviral intervention are defaulted to HIV infection status of the child, with more detailed measures listed below. Therefore, we provided a note in parentheses following the header. For Vitamin A supplementation and cesarean delivery, in addition to extracting the result of HIV infection status of the child, there are also other extracted results.

### *Quality assessment of studies*

At the end of this paper, the evaluation of the methodological quality of each systematic review and meta-analysis according to AMSTAR-2 and PRISMA criteria is, respectively, provided in supplementary tables 3 and 4. Scoring through AMSTAR-2 items, 20 systematic reviews and meta-analyses were rated as critically low quality, two as low, and only one, White et al., 2014[13], as middle quality. Similar results can be found in the PRISMA table, with eight articles totally scoring over 30.

### *ART therapy*

For antiretrovirals, six out of seven systematic reviews and meta-analyses found a reduction in vertical transmission of HIV[13-23], while one showed no clear benefit[18]. Nucleoside analog reverse transcriptase inhibitors (NRTIs) such as zidovudine (ZDV) and lamivudine (3TC), together with non-nucleoside NRTI, namely, nevirapine (NVP), either alone or in combinations, however, still worked as the most effective antiretroviral regimen. This was confirmed by Suksomboon et al., 2007[15], finding ZDV in reducing the risk of vertical transmission of HIV by 43% (95% CI: 29-55%). In the same line, Chigwedere, et al., 2008[17], discovered a significant reduction of 10.6% (95% CI: 8.6-13.1) at 4-6 weeks comparing with 21.0% (95% CI: 15.5-27.7) transmission for placebo. In comparisons of ART regimens, ZDV (0.50, 95% CI: 0.33-0.74) and ZDV/3TC (0.13, 95% CI: 0.05-0.31) demonstrated high to moderate certainty of evidence for efficacy when compared to other drug treatment regimens[14].

### *Cesarean delivery*

Investigated in one systematic review[24], elective cesarean section substantially reduced the risk of MTCT. Postpartum morbidity (PPM) of cesarean delivery was below 22% in most (n = 4) trials, and it was generally higher than those who had vaginal deliveries. Modes of delivery had a significant impact on the rate of MTCT, both on those based on allocations (cesarean

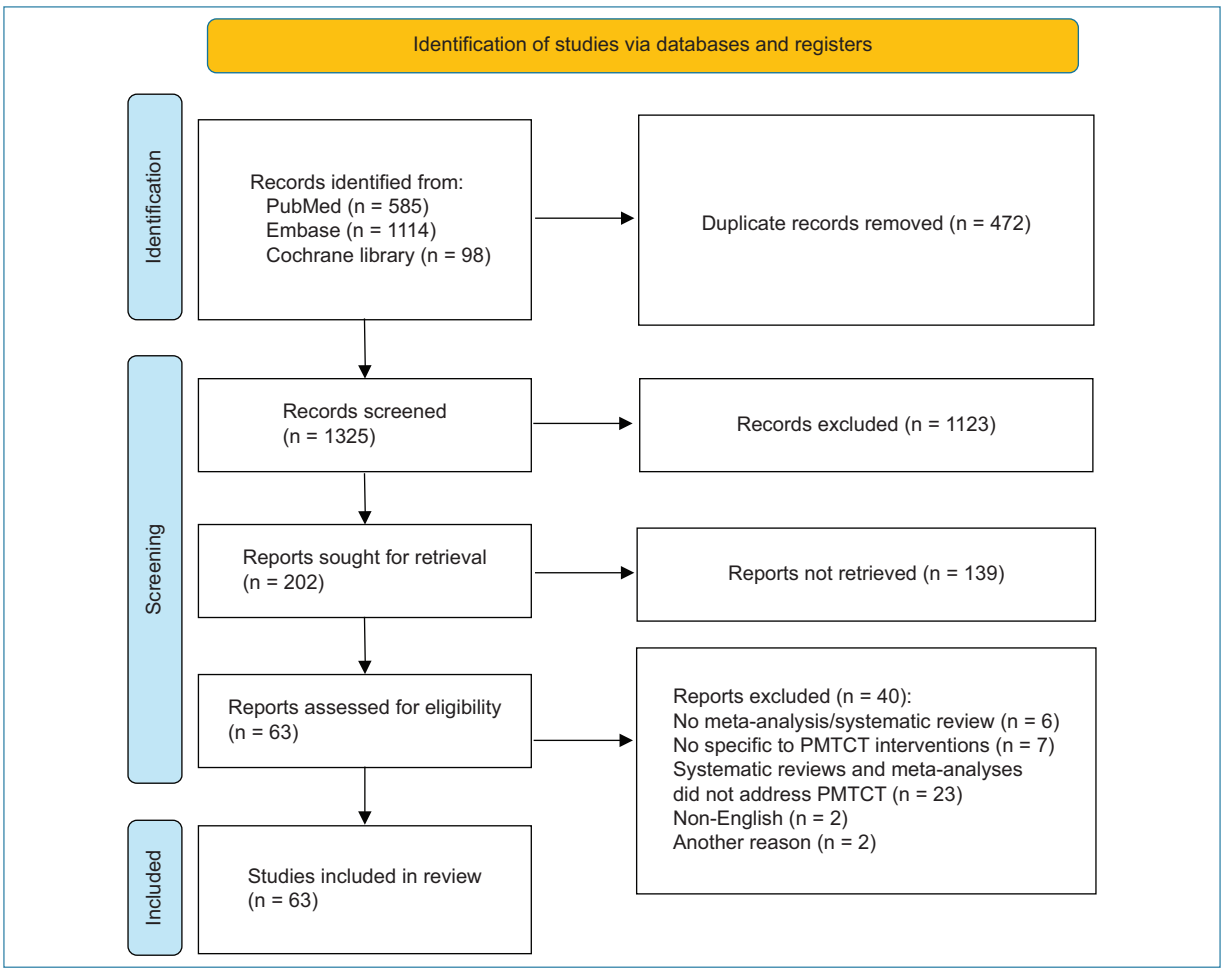


**Figure 1.** Flow chart of eligible studies.

section: 1.8%; vaginal delivery: 10.5%) and those based on the actual modes of delivery (cesarean section 3.5%; vaginal: 10.2%).

## Vitamin supplement

Vitamin supplement was investigated in two reviews, and both of them had meta-analysis. The higher relative risk (RR) of HIV infection status of the child was 1.07 (95% CI: 0.91-1.26) in a meta-analysis on giving Vitamin A supplements[25], whereas the lower was 1.05 (95% CI: 0.78-1.41)[26]; both studies gathered data from South Africa. It was shown in both reviews that Vitamin A supplementation had little or no effect on the transmission of HIV from mother to child.

## Vaginal disinfection

Regarding vaginal disinfection, two included reviews performed meta-analysis. Due to the lack of sufficient and conclusive evidence, it is difficult to obtain a strong viewpoint on the effect of vaginal disinfection on vertical transmission of HIV. Wiysonge et al., 2005[27], found 6% reduction in the risk of MTCT of HIV (OR 0.93, 95% CI 0.65-1.33), with no significant heterogeneity between the trials. Moreover, the pooled data of another review have RR of 0.94 (95% CI: 0.71-1.25)[28].

## Male partner involvement

Three systematic reviews[29-31], two of which conducted a meta-analysis of this intervention, stated that more research of male partner involvement was needed to study the role of relationship dynamics. The higher overall pooled unadjusted OR was 3.08 (95% CI: 2.58-3.68) in a meta-analysis on promoting male partner involvement, and the pooled adjusted OR was 1.78 (95%CI: 1.35-2.34)[30]; the lower OR found in sub-Saharan Africa (SSA) was 1.02 (95% CI: 0.59-1.44)[31].

**Table 1.** Findings and outcomes of meta-analyses

| Outcome | Meta-analysis metric | No. of studies in each MA | No. of events | Total | Relative risk (95% CI) | p | $I^2$ (95% CI) | Egger test p |
|---|---|---|---|---|---|---|---|---|
| Vitamin A supplementation | | | | | | | | |
| HIV infection status of the child[25] | RR | 5 | 652 | 4428 | 1.07 (0.91-1.26) | 0.41 | 52.81 | NA |
| Antepartum supplementation[25] | RR | 2 | 81 | 650 | 0.85 (0.67-1.09) | 0.21 | 0 | NA |
| Postpartum supplementation[25] | RR | 1 | 346 | 2248 | 1.11 (0.98-1.27) | 0.11 | NA | NA |
| Antepartum and postpartum supplementation[25] | RR | 2 | 225 | 1530 | 1.17 (0.86-1.59) | 0.32 | 67.17 | NA |
| Prevention of MTCT[26] | RR | 3 | 770* | 2503 | 1.05 (0.78-1.41) | 0.2 | 75 | NA |
| Vaginal disinfection | | | | | | | | |
| HIV infection status of the child[27] | OR | 2 | 74 | 708 | 0.93 (0.65-1.33) | 0.68 | 0 | NA |
| Cesarean delivery | | | | | | | | |
| HIV infection status in the child[32] | RR | 1 | 3 | 370 | 0.17 (0.05-0.55) | 0 | NA | NA |
| Mother-to-child transmission[21] | OR | 8 | 80 | 4459 | 0.33 (0.25-0.44) | < 0.001 | NA | NA |
| Male partner participation | | | | | | | | |
| ARV/ART uptake improvement[33] | RR | 4 | 221 | 811 | 1.12 (0.98-1.28) | 0.10 | 67 | NA |
| The impact on safe infant feeding practices[30] | OR | 6 | NA | 3598 | 3.08 (2.58-3.69) | 0.000 | 85.6 | NA |
| Impact of individual male involvement approaches[29] | OR | 17 | NA | 12330 | 1.02 (0.59-1.44) | 0.000 | 92.9 | NA |
| Psychological interventions | | | | | | | | |
| ARV/ART uptake improvement on initiation[33] | RR | 4 | 549 | 1292 | 1.01 (0.93-1.09) | 0.85 | 69 | NA |
| ARV/ART uptake improvement on uptake of EID[33] | RR | 4 | 425 | 1122 | 1.00 (0.94-1.07) | 1.00 | 45 | NA |
| Phone-based reminders on uptake of EID | | | | | | | | |
| ARV/ART uptake improvement[33] | RR | 5 | 1049 | 2170 | 1.18 (1.05-1.32) | 0.005 | 83 | NA |
| Telemedicine | | | | | | | | |
| HIV transmission[23] | RR | 3 | NA | 851 | 0.52 (0.08, 3.36) | 0.062 | 64 | 0.31 |
| Antiretroviral intervention | | | | | | | | |
| Antenatal ART (1 drug)[21] | OR | 8 | 52 | 4622 | 0.31 (0.23-0.42) | < 0.0001 | NA | NA |
| Antenatal ART (2 drug)[21] | OR | 8 | 34 | 4622 | 0.56 (0.38-0.83) | 0.004 | NA | NA |
| Antenatal ART (3 drug or more)[21] | OR | 8 | 668 | 4622 | 1.38 (1.19-1.61) | < 0.0001 | NA | NA |
| Administered ART[20] | OR | 4 | 1558 | 3244 | 0.01 (0.00-0.02) | 0.19 | 0.08 | 0.589 |

(*Continues*)

**Table 1.** Findings and outcomes of meta-analyses *(continued)*

| Outcome | Meta-analysis metric | No. of studies in each MA | No. of events | Total | Relative risk (95% CI) | p | I2 (95% CI) | Egger test p |
|---|---|---|---|---|---|---|---|---|
| **Antiretroviral drugs efficacy (HIV infection status in the child)** | | | | | | | | |
| A. Single agent regimens | | | | | | | | |
| Zidovudine[15] | RR | 5 | 96 | 1538 | 0.63 (0.45-0.90) | < 0.0001 | NA | NA |
| Any zidovudine[32] | RR | 4 | 79 | 1250 | 0.54 (0.42-0.69) | < 0.0001 | 23 | NA |
| Short course zidovudine[32] | RR | 3 | 70 | 1002 | 0.60 (0.46-0.79) | 0 | 0 | NA |
| Short course zidovudine (breast feeding)[32] | RR | 2 | 52 | 619 | 0.64 (0.47-0.88) | 0.01 | 0 | NA |
| Nevirapine[32] | RR | 1 | 37 | 496 | 0.58 (0.40-0.83) | 0 | NA | NA |
| Intrapartum ZDV[21] | OR | 8 | 763 | 4622 | 1.20 (1.03-1.39) | 0.019 | NA | NA |
| Intrapartum sdNVP[21] | OR | 8 | 138 | 4622 | 0.93 (0.76-1.14) | 0.491 | NA | NA |
| ZDV[14] | OR | 14 | NA | 8961 | 0.13 (0.05-0.31) | 0.998 | 0.000 | NA |
| B. Combination antiretroviral therapy | | | | | | | | |
| Zidovudine plus lamivudine[15] | RR | 1 | 80 | 1093 | 0.57 (0.45-0.72) | 0.0105 | NA | NA |
| HIVIG plus zidovudine[32] | RR | 1 | 9 | 454 | 0.67 (0.29-1.55) | 0.35 | NA | NA |
| ZDV/Lamivudine (3TC)[14] | OR | 14 | NA | 8961 | 0.50 (0.33-0.74) | NA | NA | NA |
| Combination therapy | | | | | | | | |
| Integration of HIV and antenatal care[34] | OR | 2 | NA | 1887 | 2.69 (1.25-5.78) | 0.0113 | 59.26 | NA |

*Due to the lack of data on HIV infected infants in one of the literatures, only the data provided in the other two literature are used here.
OR: odds ratio; CI: confidence interval; MTCT: mother-to-child transmission; ART: antiretroviral therapy; ZDV: zidovudine; EID: early infant diagnosis; sdNVP: single-dose nevirapine.

### *Telemedicine*

One systematic review and meta-analysis investigated the effectiveness of this intervention, which stated that it is beneficial to PMTCT of HIV[23]. The study reported a pooled relative risk (RR) of 0.52 (95% CI: 0.08-3.36), suggesting that telemedicine, as an innovative public health intervention, has the potential to significantly enhance the quality and efficiency of PMTCT services.

### *Intervention combination*

Five systematic reviews and one meta-analysis identified the useful intervention to decrease the risk of vertical transmission of HIV infection, either one or combination[8,21,22,32-34]. A combined approach to HIV treatment advocates using ART as the main therapeutic measure, while adding other therapeutic measures to complement it. Antenatal or intrapartum antiretroviral prophylaxis had important roles in PMTCT program, with varied implementation and utility in different countries and regions.

## Discussion

This detailed umbrella review integrates existing systematic reviews and meta-analyses into one accessible document. This evaluation updates the previous systematic review on the relationship between PMTCT interventions and HIV vertical transmission rates and provides recommendations for research and practice.

### *Principal findings*

Evidence from the umbrella review suggests that the current use of PMTCT interventions: ART therapy, cesarean delivery, male partner involvement, and combination treatment is associated with reducing the rate of mother to child transmission of HIV. The reviews on ART and the recently published studies suggest that ZDV, lamivudine (3TC), and NVP – whether used as monotherapy, dual regimen, or triple regimen – are effective in reducing the risk of vertical transmission of HIV, both in short-term and long-term use, especially ZDV and ZDV/3TC. ART prophylaxis, given to mothers or infants during pregnancy or breastfeeding, may also reduce the risk of acquiring HIV infant death. At the same time, if breastfeeding is sustained, ART prophylaxis in infants (and potentially pregnant

**Table 2.** Findings and outcomes of systematic reviews

| Author | Year | Interventions | Summary of findings | Comments |
|---|---|---|---|---|
| Read and Newell[24] | 2005 | Cesarean delivery | One clinical trial and five observational studies evaluated the safety of cesarean section among HIV-1-infected women, which indicate ECS can substantially reduce the risk of MTCT in North America and Europe. In developing countries, the risks and benefits associated with ECS remain unknown. | The number studies including in this study is moderate. |
| Wiysonge et al.[27] | 2005 | Vaginal disinfection | Two trials did not find effective evidence of vaginal disinfection on the risk of MTCT of HIV infection and infant mortality. | The lack of quantity in the experiments result in limited results. |
| Horvath et al.[22] | 2009 | Exclusive breastfeeding, extended antiretroviral prophylaxis | Six randomized clinical trials and one intervention cohort study indicated breastfed children had lower rates of MTCT of HIV as well as higher 3-month mortality rates than who also received solids. Regarding antiretroviral prophylaxis, administration of nevirapine alone or nevirapine with ZDV until the age of 14 weeks prevents more transmission. | Another meta-analysis supports this review. |
| Wedderburn et al.[18] | 2023 | Co-trimoxazole prophylaxis | The including 4 studies identified co-trimoxazole prophylaxis continued beyond the end of breastfeeding in Uganda did not impact all-cause mortality or other infectious morbidity. | The number of studies including in this study is small. |
| Hampanda et al.[31] | 2022 | Male partner participation | The vast majority of studies in this review (four out of five) did not report a relationship between their specific couple-based intervention approach and any specific PMTCT-related health outcome. The theoretical basis for couples-focused HIV approaches for PMTCT is currently lacking. | Other studies have shown that the effect of male involvement is unclear. |
| Takah et al.[30] | 2018 | Male partner participation | Most of the 6 cohort studies showed male partner involvement has a positive impact on the uptake of safe infant feeding practices. | The meta-analysis included in this study confirmed this conclusion. |
| Vrazo et al.[8] | 2018 | Accessibility to ANC, ART services | 11 articles evaluated interventions in PMTCT program that significantly improve service uptake and retention of HIV-infected pregnant and breastfeeding women and their infants along the cascade. | Other PMTCT included studies came to the same conclusion. |
| Puchalski Ritchie et al.[34] | 2019 | Accessibility to ANC, ART services, integrations | Three of eighteen studies found small positive effects of integration of HIV and ANC, alone or as part of a complex intervention, on ART use during pregnancy. Effects of integration on PMTCT outcomes during labor and delivery and post-delivery were less clear. | The outcome is consistent with the findings of corresponding meta-analysis. |
| Takah et al.[29] | 2017 | Male partner participation | 17 studies showed complex community interventions had a higher effect in the combined model, whereas in the adjusted model, enhanced psychosocial interventions have a higher effect. | The findings from this systematic review are similar to other studies. |
| Mills et al.[26] | 2005 | Vitamin supplementation | 4 trials showed supplementation with multivitamins did not decrease MTCT. The results were conflicting. | The number of studies included is small and affect the estimates of effect. |
| Wiysonge et al.[12] | 2017 | Vitamin A supplementation | Five trials showed vitamin A supplements have uncertain effect on preterm delivery, stillbirth, or maternal death. | Included meta-analysis supports this review. |

*(Continues)*

**Table 2.** Findings and outcomes of systematic reviews *(continuation)*

| Author | Year | Interventions | Summary of findings | Comments |
|---|---|---|---|---|
| Suksomboon et al.[15] | 2007 | ART (ZDV, lamivudine, nevirapine) | Fifteen trials found antiretroviral drugs either alone or in combinations of two or three drugs, had been shown to be effective in reducing maternal-infant transmission of HIV. | Another meta-analysis of ART included in the study came to the same conclusion. |
| Siegfried et al.[16] | 2011 | ART | Twenty-five trials found the combination of antiretroviral drugs can decrease mother-to-child transmission of HIV. | This finding was also confirmed by the inclusion of three studies on ART. |
| Brocklehurst[32] | 2002 | ART (ZDV, nevirapine), cesarean section, immunoglobulin | Five trials found ZDV and nevirapine made a reduction in the risk of PMTCT transmission. Cesarean section also was very effective in decreasing the risk of mother-to-child transmission of HIV infection. However, the effect of HIV hyperimmune immunoglobulin to ZDV appears to be similar with ZDV and non-specific immunoglobulin. | Other studies of different PMTCT interventions support this conclusion. |
| White et al.[13] | 2014 | Antiretroviral prophylaxis | Seven studies showed antiretroviral prophylaxis is efficacious in preventing mother-to-child transmission of HIV through breastfeeding. | The meta-analysis incorporated within this review provides support for the findings. |
| Ambia and Mandala[33] | 2016 | Male partner involvement, mobile phone-based reminder, home visiting, peer mentoring, integration of PMTCT into routine pregnancy and infant, community health workers support | 12 of 34 studies found mobile phone-based reminders could increase the uptake of early infant HIV testing and male partner involvement in PMTCT reduced infant HIV transmission. However, increasing ARV/ART uptake showed no benefit of psychological interventions. | The trials included in this systematic review were mainly from sub-Saharan Africa, which led to limitations. |
| Wiysonge et al.[28] | 2007 | Vaginal disinfection | Two trials showed vaginal microbicide had no effect on the risk of MTCT of HIV infection and infant mortality. | Another meta-analysis of vaginal disinfection included in the study came to the same conclusion. |
| Beste et al.[19] | 2018 | Antiretroviral prophylaxis | Four included studies suggested using prolonged prophylaxis in breastfed infants can reduce breastfeeding transmission rates. | The number of included studies was small and the evidence was limited. |
| Li et al.[23] | 2024 | Telemedicine | 3 of 17 studies suggested that telemedicine cannot improve HIV transmission directly. However, in terms of early infant diagnosis, breastfeeding, and retention, it made sense. | The meta-analysis incorporated within this review provides support for the findings. |
| Mehrabi et al.[14] | 2024 | ART regimen | 14 trials provided high-to moderate-certainty evidence that both ZDV/3TC and ZDV are more effective in lowering the likelihood of mother-to-child transmission. Additionally, ZDV/3TC was associated with reduced odds of stillbirth. | Included meta-analysis supports this review. |
| Xu et al.[20] | 2024 | ART vitamin A supplementation | Seven articles indicated that prescribing ART effectively reduce the risk of mother-to-child transmission of HIV during breastfeeding. However, the effectiveness of high-dose vitamin A remains unclear. | The findings of this study are consistent with the results of other studies on ART drugs and the results of two studies on vitamin A supplement. |

ECS: elective cesarean section; MTCT: mother-to-child transmission; PMTCT: prevention of mother-to-child transmission; ANC: antenatal care; ART: antiretroviral therapy; ZDV: zidovudine.

women) must be continued. This is critical because discontinuation of preventive treatment may lead to a cumulative rise in the rate of HIV transmission to infants. However, the potential adverse effects of ART in pregnant women and their infants, as well as maternal resistance and response to subsequent ART following prevention need further study[13,16]. Evidence from observational studies and RCTs show that male partner involvement such as verbal encouragement, complex community intervention, and enhanced psychosocial interventions is beneficial to promote the PMTCT program to some extent and we still need to actively promote it. This measure is predominantly applied to cohabiting or married couples, with the observational timeframe extending from pregnancy through the postpartum period. However, the outcomes often exhibit considerable variability due to the influence of both the "micro social context" (e.g., interpersonal dynamics and communication patterns) and broader macro-social factors (e.g., cultural norms and socioeconomic conditions)[31,35]. These elements can significantly impact the efficacy of couple-based HIV interventions. Cesarean section can be used as an effective supplementary strategy to prevent vertical transmission of HIV-1 in women living with HIV, particularly in cases where ART is not feasible or only ZDV is taken[24]. Although the incidence of PPM is generally higher in acquiring HIV-1 women undergoing cesarean section, both major and minor PPM can be avoided by addressing and managing known risk factors specific to this population. Telemedicine is a valuable tool for supporting the prevention of vertical transmission of HIV. It is particularly effective in improving EID, promoting breastfeeding practices, and enhancing retention in care[23]. The evidence was inconclusive on the association between vitamin supplementation and HIV vertical transmission; meanwhile, the possibility of harm cannot be excluded[25,26]. No association was found between vaginal microbicides and the risk of MTCT of HIV[27,28]. Both vitamin supplementation and vaginal disinfection require high-quality RCTs to investigate the impact on the rate of vertical transmission of HIV.

## *Strengths and weaknesses*

Our results should be interpreted with caution. Firstly, as with all literature reviews, the quality is directly related to the quality of the included studies. We evaluated the quality of all included studies and selected those with low-level evidence. The lack of high-quality research as well as the loss of metadata in most selected reviews could contribute to their inconsistency. At the same time, a considerable part of the systematic review and meta-analysis included insufficient number of studies, which may undermine the credibility of the resulting evidence. Although we conducted an extensive search across multiple databases, the systematic reviews and meta-analyses included in this umbrella review primarily originated from SSA, leading to a regional bias in the evidence. Heterogeneity lowered the reliability of the identified associations. Future observational studies should aim to better identify high-risk groups by employing advanced methods to assess interventions associated with the prevention of vertical transmission of HIV. Moreover, the field of perinatal maternal and infant health research faces a number of obstacles traditionally related to the socioeconomic, cultural, and psychosocial challenges of conducting research in these vulnerable populations, which requires more extensive and compliant measures.

Despite the above limitations, the main strengths of this work are the comprehensive search and the use of quantitative and qualitative methods to assess evidence credibility. This umbrella review synthesizes evidence from various published sources of evidence, considering the convergence of findings across diverse research designs. A comprehensive search strategy was employed across three major scientific literature databases, with independent study selection and data extraction conducted by two investigators to identify relevant reviews. Systematic reviews and meta-analyses that met the inclusion criteria were incorporated following the screening process. Furthermore, to the best of our knowledge, this is the first umbrella review that systematically synthesizes data on the association between vertical transmission of HIV and various PMTCT interventions, while assessing the certainty and strength of the evidence using well-recognized criteria. The methodological quality of the studies included in the review was assessed with the AMSTAR 2 tool, which is a widely recognized instrument with strong evidence of validity and reliability. Where applicable, the reviews will be examined to ensure the validity of the evidence. Both automated tools and manual screening were employed to eliminate duplicate counts. The methodological rigor of this review was further reinforced by adherence to the PRISMA guidelines, which provide a standardized framework for conducting and reporting systematic reviews.

## Conclusion

The evidence reported in this umbrella review suggests that ART therapy supplemented by other preventive measures is the most effective way to reduce the rate of vertical transmission of HIV. More prospective studies are needed to confirm the most effective dosage and duration of ART drugs. Similarly, prospective studies with a longer duration of follow-up are needed to characterize maternal resistance and maternal response to subsequent ART after maternal prophylaxis. Meanwhile, further researches to clarify the impact of vitamin supplement and vaginal disinfection are required. Using HIV prevention measures during pregnancy at early stage can significantly enhance the prognosis for both the mother and the unborn child in cases of HIV exposure. Legal and public health policy makers, with researchers, should consider this evidence synthesis when developing policies for preventing vertical transmission of HIV and designing future epidemiological or experimental research agendas. In addition, updated guidelines are essential to translate these findings into clinical practice.

## Supplementary data

Supplementary data are available at DOI: 10.24875/AIDSRev.25000017. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

## Funding

None.

## Conflicts of interest

None.

## Ethical considerations

**Protection of humans and animals.** The authors declare that no experiments involving humans or animals were conducted for this research.

**Confidentiality, informed consent, and ethical approval.** The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

**Declaration on the use of artificial intelligence.** The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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