Supplementary material

Probability of vertical HIV transmission: A systematic review and meta-regression

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Contents

S1. Definitions, current default values, and source of vertical transmission probabilities used in Spectrum-AIM

Table S1.1 describes the definition of vertical transmission categories in the Spectrum-AIM model,[1] the default values used in model versions for UNAIDS global HIV estimates published 2019 through 2024, and source of the default. Most default values are weighted averages of studies identified in the 2018 Mofenson review.[2] Estimates of perinatal transmission probability for women who did not receive PMTCT have not been updated since the 2012 Rollins *et al.* systematic review.[3]

Table S1.1. Default Spectrum-AIM values of perinatal transmission probabilities

Transmission category	Definition	Default value	Source of default value
CD4 < 200	Existing infection, birthing parent did not use PMTCT and had a CD4 < 200.	0.37	Median of studies from Rollins *et al.* 2012 systematic review
CD4 200-350	Existing infection, birthing parent did not use PMTCT and had a CD4 200-350.	0.27	Median of studies from Rollins *et al.* 2012 systematic review
CD4 > 350	Existing infection, birthing parent did not use PMTCT and had a CD4 > 350.	0.15	Median of studies from Rollins *et al.* 2012 systematic review
Maternal seroconversion	Mother seroconverted during pregnancy.	0.181	Weighted average from Mofenson 2018 systematic review update
Maternal single dose nevirapine	Mother received only single dose nevirapine as part of PMTCT.	0.075	Weighted average from Mofenson 2018 systematic review update
WHO 2006 Dual ARV regimen	Mother utilized two ARV regimens for PMTCT.	0.022	Weighted average of studies with women with CD4 > 350 from Mofenson 2018 systematic review update
Option A	Mothers with CD4 > 350 used AZT from week 14 of gestation and single dose nevirapine at the onset of labor. Daily AZT/ 3TC used through 7 days postpartum.	0.041	Weighted average from Mofenson 2015 systematic review update
Option B	Mothers with CD4 > 350 used triple ARVs starting at week 14 of gestation and continued through breastfeeding cessation.	0.019	Weighted average of studies with breastfeeding populations from Mofenson 2018 systematic review update

Mother on ART <4 weeks before delivery	Triple ARVs were initiated <4 weeks before delivery and continued for life.	0.082	Weighted average from Mofenson 2018 systematic review update
Mother on ART >4 weeks before delivery	Triple ARVs were initiated >4 weeks before delivery (but after conception) and continued for life.	0.014	Weighted average from Mofenson 2018 systematic review update
Mother on ART preconception	Mother was on triple ARVs at conception and continued for life.	0.0026	Weighted average from Mofenson 2018 systematic review update

Table S1.2. Default Spectrum-AIM values of monthly breastfeeding transmission probabilities

Transmission category	Definition	Default value	Source of default value
CD4 < 200	Existing infection, birthing parent did not use PMTCT and had a CD4 < 200.	0.0089	Weighted average from Mofenson 2018 systematic review update of studies without a CD4 restriction
CD4 200-350	Existing infection, birthing parent did not use PMTCT and had a CD4 200-350.	0.0081	It is unclear where the default value came from, this was not explicitly estimated in the 2012, 2015, or 2018 reviews.
CD4 > 350	Existing infection, birthing parent did not use PMTCT and had a CD4 > 350.	0.0051	Rollins *et al.* 2012 systematic review
Maternal seroconversion	Mother seroconverted during pregnancy.	0.269	Weighted average from Mofenson 2018 systematic review update
Maternal single dose nevirapine CD4 < 350	Mother received only single dose nevirapine as part of PMTCT.	0.0099	Weighted average from Mofenson 2018 systematic review update
Maternal single dose nevirapine CD4 > 350	Mother received only single dose nevirapine as part of PMTCT.	0.004	Weighted average from Mofenson 2018 systematic review update
WHO 2006 Dual ARV regimen	Mother utilized two ARV regimens for PMTCT.	0.0018	Weighted average of studies that reported extended infant prophylaxis from Mofenson 2018 systematic review update
Option A	Mothers with CD4 > 350 used AZT from week 14 of gestation and single dose nevirapine at the onset of	0.002	Median of studies in the Rollins *et al.* 2012 systematic review.

	labor. Daily AZT/ 3TC used through 7 days postpartum.		
Option B	Mothers with CD4 > 350 used triple ARVs starting at week 14 and continued through breastfeeding cessation.	0.0013	It is unclear where the default value came from, the Mofenson 2018 systematic review had a weighted average of 0.0011.
On ART <4 weeks before delivery	Triple ARVs were initiated <4 weeks before delivery and continued for life.	0.002	Expert opinion from Rollins *et al.* 2012 systematic review
On ART >4 weeks before delivery	Triple ARVs were initiated >4 weeks before delivery (but after conception) and continued for life.	0.0011	Weighted average of studies where birthing parent started ART at any time during pregnancy from Mofenson 2018 systematic review update
On ART preconception	Mother was on triple ARVs at conception and continued for life.	0.0002	Weighted average of studies from Mofenson 2018 systematic review update

S2. 2024 systematic review

S2.2. PRISMA checklist

Table S2.2.1. PRISMA checklist

Topic	No.	Summary	Location
Title	1	Identify the report as a systematic review.	Title
Abstract	2	See the PRISMA 2020 for Abstracts checklist	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Introduction
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Methods
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Methods
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Methods and Supplementary Material S2.3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Methods and Figure 1
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Methods
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Methods and Supplementary Material S2.4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any	Methods and Supplementary Material S2.4

		assumptions made about any missing or unclear information.	
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Not applicable
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Methods and Supplementary Material S2.5 and S2.6
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item 5)).	Methods
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Methods and Supplementary Material S5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Methods and Supplementary Material S4.2
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Methods
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Methods and Supplementary Material S5
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Methods and Supplementary Material S5
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Not applicable
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Methods
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Results and Figure 1

	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Results and Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Supplementary Material S3
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Not applicable
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Supplementary Material S4.2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Not applicable
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Results and Supplementary Material S4
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Results and Supplementary Material S4
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Results and Supplementary Material S4
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not applicable
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Results
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Discussion
	23b	Discuss any limitations of the evidence included in the review.	Discussion
	23c	Discuss any limitations of the review processes used.	Discussion
	23d	Discuss implications of the results for practice, policy, and future research.	Discussion
OTHER INFORMATION			

Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Methods
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Methods
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Abstract
Competing interests	26	Declare any competing interests of review authors.	Abstract
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Methods

Table S2.2.2. PRISMA abstract checklist

Topic	No.	Summary	Reported?
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	No
Synthesis of results	6	Specify the methods used to present and synthesize results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes

Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

S2.3. Search strategy by data source

Table S2.3. Search strategy by data source used in the 2024 updated systematic review

Data source	Search strategy
PubMed (National Center for Biotechnology Information)	(({"HIV Infections"[Mesh] OR "HIV"[Mesh] OR "Acquired Immunodeficiency Syndrome"[Mesh] OR "Antiretroviral Therapy, Highly Active"[Mesh] OR "Anti-HIV Agents"[Mesh] OR "Anti-Retroviral Agents"[Mesh] OR "human immunodeficiency virus"[ti] OR "human immunedeficiency virus"[ti] OR "human immuno deficiency virus"[ti] OR "human immune deficiency virus"[ti] OR HIV[ti] OR HIVl[ti] OR HIV2[ti] OR "acquired immunodeficiency syndrome"[ti] OR "acquired immunedeficiency syndrome"[ti] OR "acquired immunodeficiency syndrome"[ti] OR "acquired immune deficiency syndrome"[ti] OR antiretroviral*[ti] OR "anti retroviral"[ti]) **AND** {"Pregnancy"[Mesh] OR "Pregnancy Complications, Infectious"[Mesh] OR "Pregnant Women"[Mesh] OR "Delivery, Obstetric"[Mesh] OR "Peripartum Period"[Mesh] OR "Postpartum Period"[Mesh] OR "Breast Feeding"[Mesh] OR "Infectious Disease Transmission, Vertical"[Mesh] OR PMTCT[tiab] OR MTCT[tiab] OR "mother to child"[tiab] OR "parent to child"[tiab] OR vertical*[tiab] OR intrauterine[tiab] OR "intra uterine"[tiab] OR intrapartum[tiab] OR "intra partum"[tiab] OR pregnant[tiab] OR pregnancy[tiab] OR prenatal*(tiab] OR "pre natal*"(tiab] OR antenatal*(tiab] OR "ante natal*"(tiab] OR perinatal*(tiab] OR "peri natal*"(tiab] OR puerperium[tiab] OR postnatal*[tiab] OR "post natal*"[tiab] OR postpartum[tiab] OR "post partum"[tiab] OR peripartum[tiab] OR "peri

	partum"[tiab] OR "in utero"[tiab] OR fetomaternal*[tiab] OR "feto maternal*"[tiab] OR "maternal fetal"[tiab] OR fetus*[tiab] OR foetus*[tiab] OR fetal*[tiab] OR foetal*[tiab] OR neonat*[tiab] OR breastfeed*[tiab] OR "breast feeding"[tiab] OR "breast fed"[tiab] OR breastmilk[tiab] OR "breast milk"[tiab] OR delivery[tiab] OR birth[tiab]) **AND** {"Infant"[Mesh] OR "Infant, Newborn"[Mesh] OR "Child"[Mesh] OR infant[tiab] OR infants[tiab] OR infancy[tiab] OR newborn*(tiab] OR "new born"[tiab] OR neonat*(tiab] OR child*(tiab] OR baby[tiab] OR babies[tiab]) **AND** {"Infectious Disease Transmission, Vertical"[Mesh] OR transmit*[tiab] OR transmission*[tiab] OR infection* OR infected)) **OR** (("HIV Infections"[Mesh] OR "HIV infection*"[tiab] OR HIV[ti]) **AND** {"Pregnancy Complications, Infectious"[Mesh] OR "Infectious Disease Transmission, Vertical"[Mesh] OR "vertical transmission"[tiab:~3] OR "vertical infection"[tiab:~3] OR "vertical infections"[tiab:~3] OR "mother to child" OR "parent to child" OR MTCT OR PMTCT OR "perinatal transmission"[tiab:~3] OR "perinatal infection"[tiab:~3] OR "perinatally acquired"[tiab:~3]))) **AND** {"2018"[Date - Publication] : "3000"[Date - Publication]) **AND** "English"[la] **NOT** (("Animals"[Mesh] OR macaque*[tiab]) NOT "Humans"[Mesh]) **NOT** (("Cross-Sectional Studies"[Mesh] OR "editorial"[Publication Type] OR "letter"[Publication Type] OR "comment"[Publication Type] OR "news"[Publication Type] OR "Case Reports" [Publication Type] OR "Case Reports as Topic"[Mesh]) NOT ("Systematic Review" [Publication Type] OR "Meta-Analysis" [Publication Type]))
Embase (Elsevier)	(((('Human immunodeficiency virus infection'/de OR 'acquired immune deficiency syndrome'/de OR 'AIDS related complex'/de OR 'acute HIV infection'/de OR 'Human immunodeficiency virus 1 infection'/de OR 'Human immunodeficiency virus 2 infection'/de OR 'AIDS related complex'/de OR 'human immunodeficiency virus'/exp OR 'highly active antiretroviral therapy'/exp OR 'anti human immunodeficiency virus agent'/de OR 'antiretrovirus agent'/de OR 'human immunodeficiency virus':ti OR 'human immunedeficiency virus':ti OR 'human immunodeficiency virus':ti OR 'human immune deficiency virus':ti OR 'hiv':ti OR 'hivl':ti OR 'hiv2':ti OR 'acquired immunodeficiency syndrome':ti OR 'acquired immunedeficiency syndrome':ti OR 'acquired immuno deficiency syndrome':ti OR 'acquired immune deficiency syndrome':ti OR 'antiretroviral*':ti OR 'anti retroviral':ti) **AND** ('pregnancy'/exp OR 'infectious pregnancy complications'/exp OR 'pregnant woman'/exp OR 'obstetric delivery'/exp OR 'perinatal period'/exp OR 'puerperium'/exp OR 'breast feeding'/exp OR 'vertical transmission'/exp OR 'pmtct':ti,ab,kw OR 'mtct':ti,ab,kw OR

	'mother to child':ti,ab,kw OR 'parent to child':ti,ab,kw OR 'vertical*':ti,ab,kw OR 'intrauterine':ti,ab,kw OR 'intra uterine':ti,ab,kw OR 'intrapartum':ti,ab,kw OR 'intra partum':ti,ab,kw OR 'pregnant':ti,ab,kw OR 'pregnancy':ti,ab,kw OR 'prenatal*':ti,ab,kw OR 'pre natal*':ti,ab,kw OR 'antenatal*':ti,ab,kw OR 'ante natal*':ti,ab,kw OR 'perinatal*':ti,ab,kw OR 'peri natal*':ti,ab,kw OR 'puerperium':ti,ab,kw OR 'postnatal*':ti,ab,kw OR 'post natal*':ti,ab,kw OR 'postpartum':ti,ab,kw OR 'post partum':ti,ab,kw OR 'peripartum':ti,ab,kw OR 'peri partum':ti,ab,kw OR 'in utero':ti,ab,kw OR 'fetomaternal*':ti,ab,kw OR 'feto maternal*':ti,ab,kw OR 'maternal fetal':ti,ab,kw OR 'fetus*':ti,ab,kw OR 'foetus*':ti,ab,kw OR 'fetal*':ti,ab,kw OR 'foetal*':ti,ab,kw OR 'neonat*':ti,ab,kw OR 'breastfeed*':ti,ab,kw OR 'breast feeding':ti,ab,kw OR 'breast fed':ti,ab,kw OR 'breastmilk':ti,ab,kw OR 'breast milk':ti,ab,kw OR 'delivery':ti,ab,kw OR 'birth':ti,ab,kw) **AND** ('infant'/exp OR 'newborn'/exp OR 'child'/exp OR 'infant':ti,ab,kw OR 'infants':ti,ab,kw OR 'infancy':ti,ab,kw OR 'newborn*':ti,ab,kw OR 'new born':ti,ab,kw OR 'neonat*':ti,ab,kw OR 'child*':ti,ab,kw OR 'baby':ti,ab,kw OR 'babies':ti,ab,kw) **AND** ('vertical transmission'/exp OR 'transmit*':ti,ab,kw OR 'transmission*':ti,ab,kw OR 'infection*' OR 'infected')) **OR** (('human immunodeficiency virus infection'/exp OR 'HIV infection*':ti,ab OR hiv:ti) **AND** ('infectious pregnancy complications'/exp OR 'vertical transmission'/exp OR (vertical NEAR/3 (transmission OR infection*)):ti,ab,kw OR 'mother to child':ti,ab,kw OR 'parent to child':ti,ab,kw OR MTCT OR PMTCT OR (perinatal* NEAR/3 (transmission OR infection OR acquired)):ti,ab,kw))) **AND** [english]/lim **AND** (2018-2024]/py **NOT** (('animal'/exp OR 'macaque*':ti,ab,kw) NOT 'human'/exp) **NOT** (('cross-sectional study'/exp OR 'editorial'/exp OR 'letter'/exp OR 'note'/exp OR 'case study'/exp OR 'case study':ti OR 'case report*':ti OR 'cross sectional':ti,ab) NOT ('systematic review'/exp OR 'systematic review (topic)'/exp OR 'meta analysis'/exp OR 'meta analysis (topic)'/exp)) **NOT** 'conference abstract'/exp
CINAHL Complete (EBSCO)	(((MH "HIV Infections" OR MH "HIV Seropositivity" OR MH "Acquired Immunodeficiency Syndrome" OR MH "Human Immunodeficiency Virus+" OR MH "HIV-Positive Persons+" OR MH "Antiretroviral Therapy, Highly Active" OR MH "Anti-HIV Agents+" OR MH "Anti-Retroviral Agents+" OR TI ("human immunodeficiency virus" OR "human immunedeficiency virus" OR "human immunodeficiency virus" OR "human immune deficiency virus" OR HIV OR HIVl OR HIV2 OR "acquired immunodeficiency syndrome" OR "acquired immunedeficiency syndrome" OR "acquired immunodeficiency syndrome" OR "acquired immune deficiency syndrome" OR antiretroviral* OR "anti retroviral")) **AND** (MH "Pregnancy+" OR MH "Childbirth+" OR MH "Pregnancy Complications, Infectious+" OR MH "Expectant Mothers" OR MH "Perinatal Period" OR MH

	"Postnatal Period+" OR MH "Breast Feeding+" OR MH "Disease Transmission, Vertical" OR TI (PMTCT OR MTCT OR "mother to child" OR "parent to child" OR vertical* OR intrauterine OR "intra uterine" OR intrapartum OR "intra partum" OR pregnant OR pregnancy OR prenatal* OR "pre natal*" OR antenatal* OR "ante natal*" OR perinatal* OR "peri natal*" OR puerperium OR postnatal* OR "post natal*" OR postpartum OR "post partum" OR peripartum OR "peri partum" OR "in utero" OR fetomaternal* OR "feto maternal*" OR "maternal fetal" OR fetus* OR foetus* OR fetal* OR foetal* OR neonat* OR breastfeed* OR "breast feeding" OR "breast fed" OR breastmilk OR "breast milk" OR delivery OR birth) OR AB (PMTCT OR MTCT OR "mother to child" OR "parent to child" OR vertical* OR intrauterine OR "intra uterine" OR intrapartum OR "intra partum" OR pregnant OR pregnancy OR prenatal* OR "pre natal*" OR antenatal* OR "ante natal*" OR perinatal* OR "peri natal*" OR puerperium OR postnatal* OR "post natal*" OR postpartum OR "postpartum" OR peripartum OR "peri partum" OR "in utero" OR fetomaternal* OR "feto maternal*" OR "maternal fetal" OR fetus* OR foetus* OR fetal* OR foetal* OR neonat* OR breastfeed* OR "breast feeding" OR "breast fed" OR breastmilk OR "breast milk" OR delivery OR birth)) **AND** (MH "Infant+" OR MH "Infant, Newborn+" OR MH "Child+" OR TI (infant OR infants OR infancy OR newborn* OR "new born" OR neonat* OR child* OR baby OR babies) OR AB (infant OR infants OR infancy OR newborn* OR "new born" OR neonat* OR child* OR baby OR babies)) **AND** (MH "Disease Transmission, Vertical" OR TI (transmit* OR transmission* OR infection* OR infected) OR AB (transmit* OR transmission*))) **OR** ((MH "HIV Infections" OR TI("HIV infection*" OR HIV) OR AB("HIV infection*")) **AND** (MH "Pregnancy Complications, Infectious+" OR MH "Disease Transmission, Vertical" OR (Vertical N3 (transmission OR infection*)) OR "mother to child" OR "parent to child" OR (perinatal N3 (transmission OR infection*)) OR (perinatally N3 acquired) OR MTCT OR PMTCT))) **AND** PY 2018-2024 **AND** LA "English" **NOT** ((MH "Animals") NOT (MH "Human")) **NOT** ((MH "Cross Sectional Studies" OR MH "Case Studies" OR TI ("case report" OR "case reports" OR "case series" OR "cross sectional") OR PT (commentary OR editorial OR letter)) NOT PT ("systematic review" OR "meta analysis")) NOT PT abstract
Global Health (EBSCO)	Limit: Publication Year 2018-2024 ((((DE "HIV infections" OR DE "HIV-1 infections" OR DE "HIV-2 infections" OR DE "human immunodeficiency viruses" OR DE "Human immunodeficiency virus 1" OR DE "Human immunodeficiency virus 2" OR DE "acquired immune deficiency syndrome" OR DE "antiretroviral agents" OR DE "reverse transcriptase inhibitors" OR TI ("human immunodeficiency

	virus" OR "human immunedeficiency virus" OR "human immunodeficiency virus" OR "human immune deficiency virus" OR HIV OR HIVl OR HIV2 OR "acquired immunodeficiency syndrome" OR "acquired immunedeficiency syndrome" OR "acquired immunodeficiency syndrome" OR "acquired immune deficiency syndrome" OR antiretroviral* OR "anti retroviral")) **AND** (DE "pregnancy" OR DE "birth" OR DE "childbirth" OR DE "postpartum period" OR DE "pregnancy complications" OR DE "parturition" OR DE "prenatal period" OR DE "prepartum period" OR DE "puerperium" OR DE "fetus" OR DE "breast feeding" OR DE "human milk" OR DE "vertical transmission" OR DE "maternal transmission" OR TI (PMTCT OR MTCT OR "mother to child" OR "parent to child" OR vertical* OR intrauterine OR "intra uterine" OR intrapartum OR "intra partum" OR pregnant OR pregnancy OR prenatal* OR "pre natal*" OR antenatal* OR "ante natal*" OR perinatal* OR "perinatal*" OR puerperium OR postnatal* OR "post natal*" OR postpartum OR "postpartum" OR peripartum OR "peri partum" OR "in utero" OR fetomaternal* OR "feto maternal*" OR "maternal fetal" OR fetus* OR foetus* OR fetal* OR foetal* OR neonat* OR breastfeed* OR "breast feeding" OR "breast fed" OR breastmilk OR "breast milk" OR delivery OR birth) OR AB (PMTCT OR MTCT OR "mother to child" OR "parent to child" OR vertical* OR intrauterine OR "intra uterine" OR intrapartum OR "intra partum" OR pregnant OR pregnancy OR prenatal* OR "pre natal*" OR antenatal* OR "ante natal*" OR perinatal* OR "peri natal*" OR puerperium OR postnatal* OR "post natal*" OR postpartum OR "postpartum" OR peripartum OR "peri partum" OR "in utero" OR fetomaternal* OR "feto maternal*" OR "maternal fetal" OR fetus* OR foetus* OR fetal* OR foetal* OR neonat* OR breastfeed* OR "breast feeding" OR "breast fed" OR breastmilk OR "breast milk" OR delivery OR birth)) **AND** (DE "children" OR DE "preschool children" OR DE "school children" OR DE "infants" OR DE "neonates" OR DE "neonates" OR TI (infant OR infants OR infancy OR newborn* OR "new born" OR neonat* OR child* OR baby OR babies) OR AB (infant OR infants OR infancy OR newborn* OR "new born" OR neonat* OR child* OR baby OR babies)) **AND** (DE "vertical transmission" OR DE "maternal transmission" OR TI (transmit* OR transmission* OR infection* OR infected) OR AB (transmit* OR transmission*))) **OR** ((DE "HIV infections" OR DE "HIV-1 infections" OR DE "HIV-2 infections" OR TI("HIV infection*" OR HIV) OR AB("HIV infection*")) **AND** (DE "vertical transmission" OR DE "maternal transmission" OR (Vertical N3 (transmission OR infection)) OR "mother to child" OR "parent to child" OR (perinatal N3 (transmission OR infection)) OR (perinatally N3 acquired) OR MTCT OR PMTCT))) **AND** LA "English" **NOT** ((DE "Animals" OR DE "Laboratory

	Animals") NOT DE "Hominidae") **NOT** ((TI "cross sectional" OR AB "cross sectional" OR ZT "editorial" OR ZT "letter" OR DE "case reports" OR TI "case report" OR TI "case reports" OR TI "case series") NOT (ZU "systematic reviews" OR ZU "meta-analysis"))
Cochrane CENTRAL (Wiley)	Limit - language: English ID Search Hits #1 MeSH descriptor: [HIV Infections] explode all trees 17667 #2 MeSH descriptor: [HIV] explode all trees 4211 #3 MeSH descriptor: [Anti-Retroviral Agents] explode all trees 6112 #4 MeSH descriptor: [Anti-HIV Agents] explode all trees 5128 #5 MeSH descriptor: [Antiretroviral Therapy, Highly Active] explode all trees 1626 #6 (HIV NEXT infection*) OR "human immunodeficiency virus" OR "human immunedeficiency virus" OR "human immune deficiency virus" OR "human immunodeficiency virus" OR HIV OR HIVI OR HIV2 OR "acquired immunodeficiency syndrome" OR "acquired immunedeficiency syndrome" OR "acquired immune deficiency syndrome" OR "acquired immunodeficiency syndrome" OR antiretroviral* OR "anti retroviral" 34501 #7 MeSH descriptor: [Pregnancy] explode all trees 33699 #8 MeSH descriptor: [Pregnancy Complications, Infectious] explode all trees 1616 #9 MeSH descriptor: [Pregnant Women] explode all trees 988 #10 MeSH descriptor: [Delivery, Obstetric) explode all trees 7441 #11 MeSH descriptor: [Peripartum Period] explode all trees 47 #12 MeSH descriptor: [Postpartum Period) explode all trees 2754 #13 MeSH descriptor: [Breast Feeding] explode all trees2878 #14 MeSH descriptor: [Infectious Disease Transmission, Vertical] explode all trees 842 #15 PMTCT OR MTCT OR "mother to child" OR "parent to child" OR vertical* OR intrauterine OR "intra uterine" OR intrapartum OR "intra partum" OR pregnant OR pregnancy OR prenatal* OR (pre NEXT natal*) OR antenatal* OR (ante NEXT natal*) OR perinatal* OR (peri NEXT natal*) OR puerperium OR postnatal* OR (post NEXT natal*) OR postpartum OR "post partum" OR peripartum OR "peri partum" OR "in utero" OR fetomaternal* OR

	(feto NEXT maternal*) OR "maternal fetal" OR fetus* OR foetus* OR fetal* OR foetal* OR neonat* OR breastfeed* OR "breast feeding" OR "breast fed" OR breastmilk OR "breast milk" OR delivery OR birth 186277 #16 MeSH descriptor: [Infant] explode all trees 45750 #17 MeSH descriptor: [Child) explode all trees 81197 #18 infant OR infants OR infancy OR newborn* OR "new born" OR neonat* OR child* OR baby OR babies 265502 #19 transmit* OR transmission* OR infection* OR infected 167225 #20 (#1 OR #2 OR #3 OR #4 OR #5 OR #6) AND (#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15) AND (#16 OR #17 OR #18) AND (#14 OR #19) 2943 #21 (HIV NEXT infection*) OR HIV 33237 #22 (vertical NEAR/3 transmission) OR "mother to child" OR "parent to child" OR MTCT OR PMTCT OR (perinatal NEAR/3 transmission) OR (perinatal NEAR/3 infection*) OR (perinatally NEAR/3 acquired) 1845 #23 (#1 OR #21) AND #22 1327 #24 #20 OR #23 with Publication Year from 2018 to 2024, in Trials 773
Global Index Medicus (World Health Organization)	(tw:(hiv OR "human immunodeficiency virus")) AND (tw:((pregnan* OR childbirth OR breast* OR perinatal* OR prenatal* OR utero OR vertical* OR "mother to child"))) AND (tw:(transmit* OR transmission)) AND La:("en") AND Year_cluster:[2018 to 2024]

S2.4. Variables extracted in systematic review

The following variables were extracted from all included studies:

Study details:

- Author name(s)
- Study title
- Journal
- Publication year
- Geographic region(s) covered (i.e. country or countries)
- Dates of data collection
- Study population(s)
- Total population size

Vertical transmission details:

- Total N of pregnant women or breastfeeding mothers living with HIV
- Total N of infants born to mothers living with HIV, who were tested for HIV
- N of infants who tested HIV-positive
- Events of vertical HIV transmission
- Timing of transmission (perinatal or during breastfeeding)
- Age of child at testing
- Maternal prophylaxis

When available:

- Maternal ART regimens
- Timing of maternal ART initiation
- Infant treatment and prophylaxis
- Maternal viral load or viral suppression information
    a. Timing of viral load test
    b. In viral load suppression, threshold for viral load suppression
- Maternal CD4 count information at baseline
- Infant feeding patterns (breastfed or formula fed, including duration in months)

S2.5. Perinatal transmission probability definition

Perinatal transmission was defined as transmission that occurs before six weeks (1.5 months) after birth. We included studies with both breastfeeding and formula-feeding populations. To model perinatal VT probability, we extracted the number of infections identified before six weeks postpartum and the number of HIV exposed infants.

$$PVT = \frac{HPI_{1.5\ months}}{HEI}$$

Equation S2.2

Perinatal VT (*PVT*) probability was then calculated as the ratio of HIV positive infants ($HPI_{1.5\ months}$) to HIV exposed infants (*HEI*) as shown in Equation S2.2.

S2.6. Monthly breastfeeding transmission probability definition

Breastfeeding transmission was calculated as a monthly transmission probability and considered any vertical transmission that occurred in breastfeeding populations for infants after six weeks of age. The monthly breastfeeding transmission probability (*BFVT*) was then calculated according to Equation S2.3.

$$BFVT = \frac{HPI_{BF_{End}} - HPI_{1.5\ months}}{(HEI - HPI_{1.5\ months}) * (BF_{End} - 1.5)}$$

Equation S2.3

The numerator represents the number of infections that occurred between the end of breastfeeding and the end of the perinatal period as the difference between the number of HIV positive infants at the end of breastfeeding ($HPI_{BF_{End}}$) and at 1.5 months ($HPI_{1.5\ months}$). The denominator represents the number of HIV exposed (*HEI*) but uninfected infants during this period (minus $HPI_{1.5\ months}$) and the number of months between the perinatal period (1.5) and the end of breastfeeding (BF_{End}).

S3. Data used in meta-regression analysis

This section outlines the data used across the four meta-regression analyses and viral load suppression at delivery analysis. First, we present a table with study characteristics, and then for each model we provide full citations of the studies used in each model.

Table S3. Study characteristics of studies included in models one through four

ID	Study	Study years	Location	Maternal PMTCT regimen or infection type	HIV exposed infants	Transmission timing	Model 1: No PMTCT	Model 2: Maternal seroconversion and short course PMTCT	Model 3: Perinatal transmission from women on ART	Model 4: Breastfeeding transmission from women on ART	Viral suppression at delivery model	Added in 2024 systematic review
1	**Aebi-Popp, 2022**	2019-2021	Switzerland	On ART	21	Perinatal			Yes			Yes
					21	Breastfeeding				Yes		
2	**Amone, 2023**	2016-2017	Uganda	Started ART	431	Perinatal			Yes			No
3	**Bailey, 2011**	2000-2009	Europe	Started ART	1,760	Perinatal			Yes			No
4	**Birkhead, 2010**	2002-2006	United States	Infection	41	Perinatal		Yes				No
5	**Black, 2008**	2004-2007	South Africa	Started ART	302	Perinatal			Yes			No
6	**Blonk, 2015**	2010-2014	Europe	On ART	7	Perinatal			Yes		Yes	No
7	**Bornhede, 2018**	2014-2017	Sweden	Started ART	3	Perinatal			Yes		Yes	No
				On ART	10				Yes		Yes	
8	**Carey, 2018**	2008-2014	United Kingdom	Started ART	67	Perinatal			Yes			No
				On ART	65				Yes			
9	**Chasela, 2010**	2006-2008	Malawi	Existing	668	Breastfeeding	Yes					No
				Option A	748			Yes				
10	**Chauhan, 2021**	2016-2018	India	On ART	32	Perinatal			Yes			Yes
11	**Chen, 2019**	2007-2015	China	Started ART	446	Perinatal			Yes			Yes
12	**Chibwesha, 2011**	2007-2010	Zambia	Option B	250	Perinatal		Yes				No
				Started ART	1,813				Yes			
13	**Choi, 2018**	2005-2017	Korea	Started ART	8	Perinatal			Yes		Yes	No
				On ART	8				Yes		Yes	
14	**Coetzee, 2019**	2010	South Africa	Existing	15	Perinatal	Yes					Yes
				Dual ARV	8			Yes				
				Started ART	44				Yes			
				On ART	25				Yes			
15	**Cohan, 2015**	2009-2013	Uganda	Option B	353	Breastfeeding		Yes				No
				Option B	374	Perinatal		Yes				No
				Started ART	353	Breastfeeding				Yes		No
				Started ART	389	Perinatal			Yes			No
16	**Colbers, 2015**	Not reported	Europe	On ART	18	Perinatal			Yes		Yes	No
17	**Colbers, 2015**	Not reported	Europe	On ART	11	Perinatal			Yes			No
18	**Colebunders, 1988**	1986	Democratic Republic of the Congo	Infection	3	Breastfeeding		Yes				No
19	**Connor, 1994**	1991-1993	United States, France	Existing	183	Breastfeeding	Yes					No
20	**Coovadia, 2013**	2008-2011	South Africa, Tanzania, Uganda, Zimbabwe	Existing	434	Breastfeeding	Yes					No
				Dual ARV	819			Yes				
				Option A	418			Yes				
				Single dose Nevirapine, CD4 >350	434			Yes				

ID	Study	Study years	Location	Maternal PMTCT regimen or infection type	HIV exposed infants	Transmission timing	Model 1: No PMTCT	Model 2: Maternal seroconversion and short course PMTCT	Model 3: Perinatal transmission from women on ART	Model 4: Breastfeeding transmission from women on ART	Viral suppression at delivery model	Added in 2024 systematic review
				Single dose Nevirapine, CD4 <350	54			Yes				
21	**Dabis, 1999**	1995-1998	Ivory Coast, Burkina Faso	Existing	113	Breastfeeding	Yes					No
					145	Perinatal	Yes					
22	**De Schacht, 2014**	2008-2011	Mozambique	Infection	29	Breastfeeding		Yes				No
23	**Delicio, 2011**	2000-2009	Brazil	Started ART	12	Perinatal			Yes			No
24	**Dinh, 2015**	2011-2012	South Africa	Infection	212	Perinatal		Yes				No
25	**Dinh, 2018**	2013	Zimbabwe	Option B	338	Perinatal		Yes				No
				On ART	415				Yes			
26	**Dryden-Peterson, 2011**	2009-2010	Botswana	Option A	170	Perinatal		Yes				No
				Started ART	114				Yes			
				On ART	144				Yes			
27	**Ejikunle, 2019**	2015-2016	Nigeria	Infection	5	Perinatal		Yes				Yes
28	**Ekpini, 1997**	1990-1994	Ivory Coast	Infection	12	Breastfeeding		Yes				No
29	**Embree, 2000**	1986-1997	Kenya	Infection	12	Breastfeeding		Yes				No
30	**Ewenighi-Amankwah, 2020**	Not reported	Nigeria	On ART	122	Perinatal			Yes			Yes
31	**Finocchario-Kessler, 2015**	2010-2012	Kenya	Dual ARV	904	Perinatal		Yes				No
				Option A	904			Yes				
				Option B	219			Yes				
32	**Flynn, 2018**	2011-2014	Malawi, South Africa, Zimbabwe, Uganda, Zambia, Tanzania, India	Dual ARV	503	Breastfeeding		Yes				No
				Option A	503			Yes				
				Option B	648			Yes				
33	**Frange, 2020**	2010-2018	France	On ART	247	Perinatal			Yes		Yes	Yes
34	**Ganter, 2019**	2008-2014	France	Started ART	16	Perinatal			Yes			Yes
				On ART	78				Yes			
35	**Gibb, 2012**	2003-2009	Uganda, Zimbabwe	On ART	172	Perinatal			Yes			No
					172	Breastfeeding				Yes		
36	**Gill, 2017**	2013-2014	Rwanda	Option B	381	Breastfeeding		Yes				No
				Started ART	205					Yes		
				On ART	381					Yes		
				Option B	205	Perinatal		Yes				
				Started ART	205				Yes			
				On ART	381				Yes			
37	**Giuliano, 2014**	2008-2009	Malawi	Option B	276	Breastfeeding		Yes				No
				Started ART	276					Yes		
				Option B	278	Perinatal		Yes				
				Started ART	278				Yes			
38	**Goga, 2015**	2010	South Africa	Dual ARV	1532	Perinatal		Yes				No
				Option A	1532			Yes				

ID	Study	Study years	Location	Maternal PMTCT regimen or infection type	HIV exposed infants	Transmission timing	Model 1: No PMTCT	Model 2: Maternal seroconversion and short course PMTCT	Model 3: Perinatal transmission from women on ART	Model 4: Breastfeeding transmission from women on ART	Viral suppression at delivery model	Added in 2024 systematic review
39	**Goga, 2016**	2011-2013	South Africa	Dual ARV	2113	Perinatal		Yes				No
				Existing	63		Yes					
				Option A	2113			Yes				
				Option B	890			Yes				
				Started ART	890				Yes			
40	**Goga, 2020**	2012-2014	South Africa	On ART	635	Perinatal			Yes			Yes
41	**Guay, 1999**	1997-1999	Uganda	Single dose Nevirapine	310	Perinatal		Yes				No
42	**Habib, 2021**	2015-2017	Iran	Existing	20	Perinatal	Yes					Yes
43	**Harrington, 2019**	2015-2016	Malawi	Started ART	264	Perinatal			Yes			Yes
44	**Hira, 1990**	1985-1986	Zambia	Infection	19	Breastfeeding		Yes				No
45	**Hoffman, 2010**	2004-2008	South Africa	Existing	23	Perinatal	Yes					No
				Single dose Nevirapine	1534			Yes				
				Started ART	730				Yes			
				On ART	143				Yes			
46	**Humphrey, 2010**	1997-2000	Zimbabwe	Infection	334	Breastfeeding		Yes				No
47	**Huntington, 2011**	1996-2009	United Kingdom	On ART	340	Perinatal			Yes			No
48	**Iliff, 2005**	1997-2000	Zimbabwe	Existing	4367	Perinatal	Yes					No
49	**João, 2012**	2013-2018	Argentina, Brazil, South Africa, Tanzania, Thailand, United States	Started ART	307	Perinatal			Yes			Yes
50	**Kesho Bora, 2010**	2005-2008	Burkina Faso, Kenya, South Africa	Option B	154	Breastfeeding		Yes				No
				Single dose Nevirapine, CD4 >350	283			Yes				
				Single dose Nevirapine, CD4 <350	184			Yes				
51	**Kesho Bora, 2011**	2005-2008	Burkina Faso, Kenya, South Africa	Option A	284	Perinatal		Yes				No
				Option B	333	Breastfeeding		Yes				
					166	Perinatal		Yes				
52	**Kilweo, 2009**	2004-2006	Tanzania	Option B	441	Breastfeeding		Yes				No
				Started ART	423				Yes			
				Option B	364	Perinatal		Yes				
53	**Kim, 2013**	2009-2011	Malawi	On ART	262	Perinatal			Yes			No
					262	Breastfeeding				Yes		No
54	**Kuhn, 2010**	Not reported	Zambia	Existing	993	Breastfeeding	Yes					No
55	**Lallemant, 2004**	2001-2003	Thailand	Dual ARV	636	Perinatal		Yes				No
				Option A	508			Yes				

ID	Study	Study years	Location	Maternal PMTCT regimen or infection type	HIV exposed infants	Transmission timing	Model 1: No PMTCT	Model 2: Maternal seroconversion and short course PMTCT	Model 3: Perinatal transmission from women on ART	Model 4: Breastfeeding transmission from women on ART	Viral suppression at delivery model	Added in 2024 systematic review
56	**Le Roux, 2019**	Not reported	South Africa	Infection	7	Breastfeeding		Yes				Yes
57	**Liang, 2009**	2007	China	Infection	106	Perinatal		Yes				No
58	**Lima, 2016**	2008-2013	Brazil	Infection	9	Breastfeeding		Yes				No
59	**Loh, 2021**	2008-2015	Singapore	Started ART	42	Perinatal			Yes			Yes
				On ART	46				Yes			
60	**Malaba, 2022**	2018	South Africa, Uganda	Started ART	268	Perinatal			Yes			Yes
					268	Breastfeeding				Yes		
61	**Mandelbrot, 2015**	2000-2011	France	Started ART	4267	Perinatal			Yes		Yes	No
				On ART	3505				Yes		Yes	
62	**Marazzi, 2010**	2005-2009	Malawi, Mozambique	Option B	2528	Breastfeeding		Yes				No
				Started ART	2926					Yes		
				Option B	3081	Perinatal		Yes				
				Started ART	3081				Yes			
63	**Marinda, 2011**	1997-2000	Zimbabwe	Existing	3285	Perinatal	Yes					No
				Infection	422			Yes				
64	**Martinson, 2007**	2003-2005	South Africa	Single dose Nevirapine	108	Perinatal		Yes				No
65	**Mayaux, 1995**	1986-1994	France	Existing	236	Perinatal	Yes					No
66	**Meggi, 2018**	2014-2016	Mozambique	Option A	6	Perinatal		Yes				Yes
67	**Meyers, 2015**	2010-2013	China	Started ART	1994	Perinatal			Yes			No
68	**Moodley, 2003**	1999-2000	South Africa	Single dose Nevirapine	663	Perinatal		Yes				No
69	**Myer, 2017**	2013-2014	South Africa	Option B	555	Perinatal		Yes			Yes	No
				Started ART	555				Yes		Yes	
70	**Namukwaya, 2011**	2007-2009	Uganda	Dual ARV	1161	Perinatal		Yes				No
				Option A	1161			Yes				
				Single dose Nevirapine	367			Yes				
71	**Ndarukwa, 2019**	2014-2016	Zimbabwe	Started ART	841	Perinatal			Yes			Yes
				On ART	289				Yes			
72	**Nduati, 2000**	1992-1997	Kenya	Existing	165	Breastfeeding	Yes					No
73	**Nesheim, 2007**	2001-2005	United States	Infection	4	Perinatal		Yes				No
74	**Ngoma, 2015**	2008-2009	Zambia	Option B	219	Perinatal		Yes				No
				Started ART	219				Yes			
75	**Nlend, 2013**	2008-2012	Cameroon	Option A	110	Perinatal		Yes				No
				Started ART	285				Yes			
76	**Nyandiko, 2010**	2002-2007	Kenya	Single dose Nevirapine	69	Perinatal		Yes				No
77	**Olana, 2016**	2006-2014	Ethiopia	Existing	102	Perinatal	Yes					No
				Dual ARV	50			Yes				
				Option A	50			Yes				
78	**Ørbæk, 2017**	2002-2014	Denmark	On ART	247	Perinatal			Yes			No
79	**Palasanthiran, 1993**	1980-1989	Australia	Infection	11	Breastfeeding		Yes				No

ID	Study	Study years	Location	Maternal PMTCT regimen or infection type	HIV exposed infants	Transmission timing	Model 1: No PMTCT	Model 2: Maternal seroconversion and short course PMTCT	Model 3: Perinatal transmission from women on ART	Model 4: Breastfeeding transmission from women on ART	Viral suppression at delivery model	Added in 2024 systematic review
80	**Pellowski, 2019**	2012-2015	South African	Option A	239	Perinatal		Yes				Yes
81	**Peltier, 2009**	2005-2007	Rwanda	Option B	532	Perinatal		Yes				No
				Started ART	227	Breastfeeding				Yes		
82	**Perry, 2016**	2007-2012	United Kingdom	On ART	178	Perinatal			Yes			No
				Started ART	493				Yes			
83	**Peters, 2017**	2012-2014	United Kingdom	On ART	1749	Perinatal			Yes			No
84	**PETRA Study Team, 2002**	1996-2000	Tanzania, South Africa, Uganda	Existing	303	Perinatal	Yes					No
					303	Breastfeeding	Yes					
85	**Prieto, 2012**	2000-2007	Spain	Existing	68	Perinatal	Yes					No
				Started ART	244				Yes			
86	**Rollins, 2007**	2004-2005	South Africa	Infection	172	Perinatal		Yes				No
87	**Roongpisuthipong, 2001**	1992-1994	Thailand	Infection	15	Perinatal		Yes				No
88	**Sagna, 2015**	2009-2013	Burkina Faso	Option A	136	Perinatal			Yes			No
89	**Salazar-Austin, 2018**	2011-2014	South Africa	Dual ARV	48	Perinatal			Yes			No
				Option A	48				Yes			
				Option B	150				Yes			
				Option B	171	Breastfeeding			Yes			
90	**Samuel, 2014**	2004-2010	United Kingdom	On ART	68	Perinatal				Yes	Yes	No
91	**Schalkwijk, 2017**	Not reported	Europe	On ART	15	Perinatal				Yes	Yes	No
92	**Scott, 2017**	2002-2009	United States	Started ART	44	Perinatal				Yes		No
93	**Shaffer, 1999**	1996-1997	Thailand	Existing	195	Perinatal	Yes					No
94	**Shapiro, 2006**	2005-2006	Botswana	Dual ARV	345	Perinatal		Yes				No
				Option A	345			Yes				
95	**Shapiro, 2010**	2006-2008	Botswana	Option B	553	Perinatal		Yes				No
				Option B	703	Breastfeeding		Yes				
				Started ART	480					Yes		
96	**Sibiude, 2023**	2000-2017	France	Started ART	7448	Perinatal			Yes		Yes	No
				On ART	6606				Yes		Yes	
97	**SWEN Study Team, 2008**	2001-2007	Ethiopia, Uganda, India	Single dose Nevirapine	986	Perinatal		Yes				No
98	**Thomas, 2011**	2003-2009	Kenya	Option B	487	Perinatal		Yes				No
				Started ART	487				Yes			
				Option B	522	Breastfeeding		Yes				
				Started ART	457					Yes		
	Tiam, 2019	2014-2016	Lesotho	Started ART	370	Perinatal			Yes			Yes

ID	Study	Study years	Location	Maternal PMTCT regimen or infection type	HIV exposed infants	Transmission timing	Model 1: No PMTCT	Model 2: Maternal seroconversion and short course PMTCT	Model 3: Perinatal transmission from women on ART	Model 4: Breastfeeding transmission from women on ART	Viral suppression at delivery model	Added in 2024 systematic review
99				On ART	249				Yes			
100	Tonwe-Gold, 2007	2003-2005	Ivory Coast	Option A	122	Perinatal		Yes				No
				Option B	52	Breastfeeding		Yes				
				Single dose Nevirapine, CD4 >350	86			Yes				
101	Tookey, 2016	2003-2013	United Kingdom	Started ART	2905	Perinatal			Yes		Yes	No
				On ART	968				Yes		Yes	
102	Torpey, 2012	2007-2010	Zambia	Option A	2366	Perinatal		Yes				No
				Single dose Nevirapine	1143			Yes				
103	Tovo, 1991	1980-1989	Italy	Infection	10	Perinatal		Yes				No
104	Townsend, 2014	2000-2011	United Kingdon, Ireland	Existing	54	Perinatal	Yes					No
				Started ART	3422				Yes			
				On ART	2105				Yes			
105	Tubiana, 2013	2007-2010	France	Started ART	36	Perinatal			Yes		Yes	No
106	Van de Perre, 1991	1988	Rwanda	Infection	15	Breastfeeding		Yes				No
107	Van Schalkwyk, 2013	2008-2010	South Africa	Started ART	127	Perinatal			Yes			No
108	Wiktor, 1999	1996-1998	Ivory Coast	Existing	119	Perinatal	Yes					No
					115	Breastfeeding	Yes					
109	Yusuf, 2022	Not reported	United States	On ART	10	Perinatal			Yes		Yes	Yes
					9	Breastfeeding				Yes		
110	Zijenah, 2022	2017-2018	Zimbabwe	Started ART	179	Perinatal			Yes		Yes	Yes
				On ART	272				Yes		Yes	
				Started ART	61	Breastfeeding				Yes		

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S4. Meta-regression model estimates

S4.1 Regression tables for all models

Table S4.1.1. Regression table for models one, two, three, and four used to estimate VT probabilities compatible with Spectrum-AIM

Model one: VT probability from women not receiving PMTCT					
Covariate		**Estimate (logit)**	**95% confidence interval**	**Estimate (odds ratio)**	**95% confidence interval**
Intercept		-1.61	(-1.81, -1.41)	0.20	(0.16, 0.24)
CD4 midpoint (per 100 cells increase, centered on CD4 = 500 mm^3)		-0.23	(-0.28, -0.17)	0.80	(0.75, 0.84)
Perinatal transmission (Reference)		0.0	(Reference)	1.00	(Reference)
Breastfeeding transmission		-3.22	(-3.84, -2.60)	0.04	(0.02, 0.07)
Interaction between CD4 midpoint and breastfeeding transmission		0.17	(-0.21, 0.54)	1.18	(0.81, 1.72)
Model two: VT probability from maternal seroconversion or short course PMTCT					
Covariate		**Estimate (logit)**	**95% confidence interval**	**Estimate (odds)**	**95% confidence interval**
Transmission timing	**Category**				
Perinatal	**Infection**	-1.51	(-1.92, -1.09)	0.222	(0.147, 0.335)
	SDNVP	-2.4	(-2.75, -2.05)	0.091	(0.064, 0.129)
	Dual ARV	-3.43	(-3.85, -3.02)	0.032	(0.021, 0.049)
	Option A	-3.43	(-3.73, -3.14)	0.032	(0.024, 0.043)
	Option B	-4.02	(-4.28, -3.77)	0.018	(0.014, 0.023)
Breastfeeding (monthly)	**Infection**	-0.93	(-1.34, -0.53)	0.222	(0.147, 0.335)
	SDNVP, <350	-4.73	(-6.45, -3.01)	0.394	(0.263, 0.591)
	SDNVP, >350	-5.64	(-7.43, -3.84)	0.009	(0.002, 0.049)
	Dual ARV	-6.19	(-7.49, -4.88)	0.004	(0.001, 0.021)
	Option A	-6.21	(-7.35, -5.06)	0.002	(0.001, 0.008)
	Option B	-6.57	(-7.31, -5.84)	0.002	(0.001, 0.006)
Model three: Perinatal transmission probability from women receiving ART by timing of initiation					
Covariate		**Estimate (logit)**	**95% confidence interval**	**Estimate (odds ratio)**	**95% confidence interval**
Intercept		-4.55	(-4.77, -4.33)	0.011	(0.009, 0.013)
Weeks on ART before delivery (centered on 20 weeks)		-0.06	(-0.07, -0.04)	0.944	(0.932, 0.957)
Late ART initiation (<4 weeks before delivery)		0.65	(-0.06, 1.35)	1.914	(0.946, 3.873)
Model four: Monthly breastfeeding transmission from women receiving lifelong ART					
Covariate		**Estimate (logit)**	**95% confidence interval**	**Estimate (odds ratio)**	**95% confidence interval**
Intercept (on ART preconception)		-8.72	(-10.07, -7.36)	0.000	(0.000, 0.001)
ART started during pregnancy		2.07	(0.64, 3.51)	7.939	(1.892, 33.322)

Table S4.1.2. Regression table for model three with fixed effects on ART regimen class

Covariate	Estimate (logit)	95% confidence interval	Estimate (odds ratio)	95% confidence interval
Intercept	-4.45	(-4.70, -4.19)	0.012	(0.009, 0.015)
Weeks on ART before delivery (centered on 20 weeks)	-0.06	(-0.07, -0.04)	0.946	(0.933, 0.959)
Late ART initiation (<4 weeks before delivery)	0.67	(-0.03, 1.38)	1.96	(0.971, 3.956)
ART class				
NNRTI (reference)	0.00	(Reference)	1.00	(Reference)
INSTI	-1.04	(-1.97, -0.11)	0.355	(0.140, 0.898)
PI	-0.10	(-0.51, 0.32)	0.907	(0.599, 1.371)
Miscellaneous regimens	-0.07	(-0.64, 0.51)	0.933	(0.525, 1.660)

Table S4.1.3. Regression table for viral load suppression model by ART regimen class and timing of ART initiation

Covariate	Estimate (logit)	95% confidence interval	Estimate (odds ratio)	95% confidence interval
Intercept	2.28	(1.42, 2.95)	9.76	(4.15, 19.04)
ART class				
NNRTI (reference)	0.00	(Reference)	1.00	(Reference)
INSTI	0.67	(-0.71, 2.18)	1.96	(0.49, 8.87)
PI	-0.74	(-1.45, 0.01)	0.48	(0.23, 1.01)
Miscellaneous regimens	0.00	(-0.82, 0.77)	1.00	(0.44, 2.16)
Later ART initiation (After 1st trimester)	-0.7	(-1.29, -0.12)	0.49	(0.28, 0.88)
Interaction with INSTI	-2.71	(-5.55, -0.09)	0.07	(0.00, 0.91)
Interaction with PI	-0.19	(-0.99, 0.57)	0.82	(0.37, 1.76)
Interaction with miscellaneous regimens	-0.70	(-2.90, 1.42)	0.50	(0.06, 4.16)

S4.2 Study-level and pooled estimates of vertical transmission probability

This analysis incorporates data from previous systematic reviews of VT probability and fits four meta-regression models to produce estimates of VT probability compatible with Spectrum-AIM. Here we present pooled estimates from the four meta-regression models presented in the main text (model one, model two, model three, and model 4) in forest plots ('Modelled: 2024'). We also present the weighted average of the studies used to produce the default VT used in Spectrum-AIM ('Weighted average: default') and estimates from models two and four fit to the default studies ('Modelled: default'). When using the default data, there was insufficient data to fit model one and model three. For each category, we give reasons for excluding studies that had been used in the default estimates but are not used in this analysis.

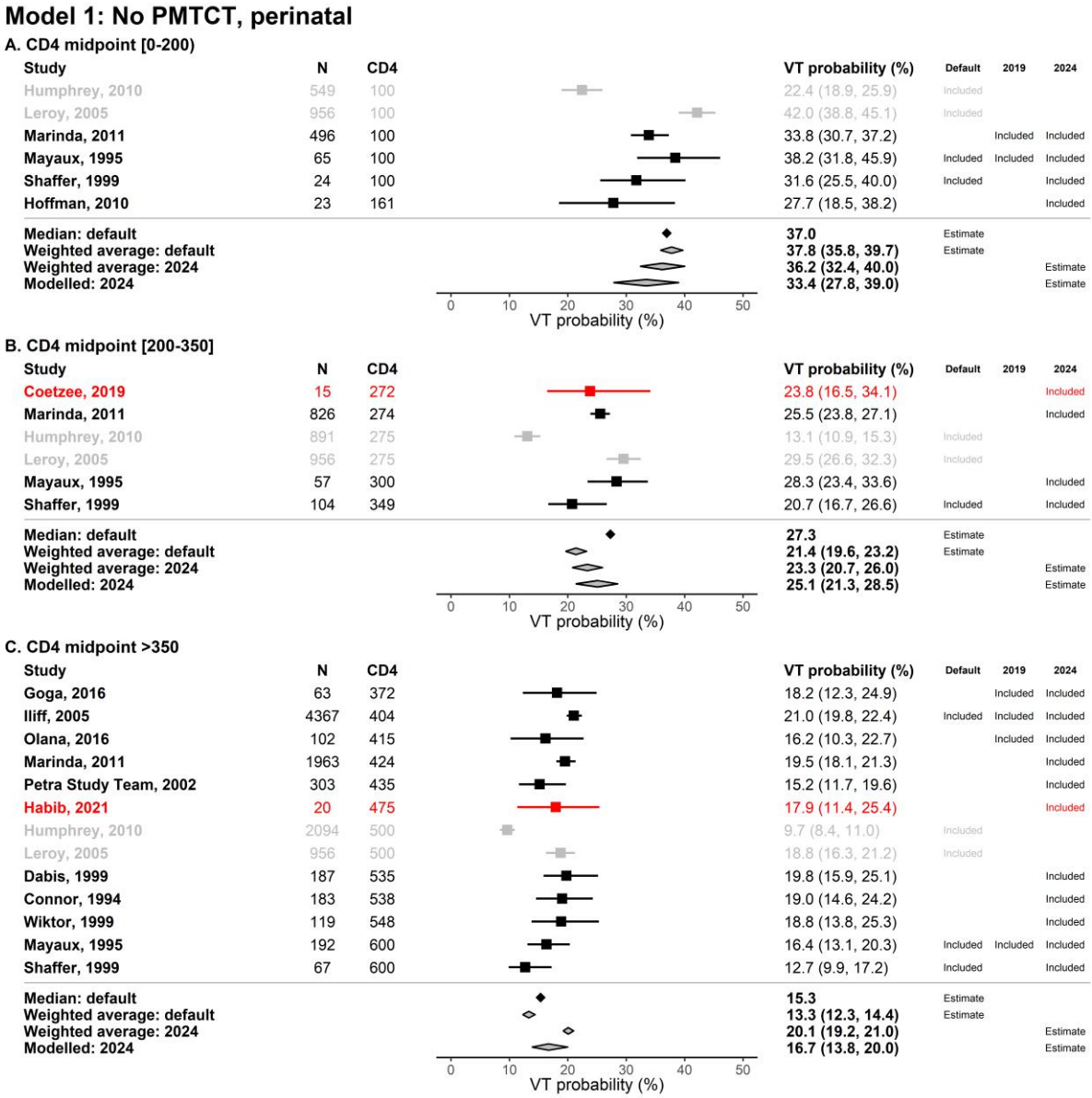


Figure S4.2.1 Pooled estimates of perinatal VT among women not receiving PMTCT.

Results are stratified by the Spectrum-AIM defined CD4 ranges. The following pooled estimates are presented: median of studies included in the default VT probabilities ('Median: default'), the weighted average of studies included in the default VT probabilities ('Weighted average: default'), the weighted average of studies included in this analysis ('Weighted average: 2024'), and the results of the model one ('Modelled: 2024'). Humphrey 2010 was excluded as it was not a peer-reviewed study and Leroy 2005 was excluded as it was a pooled analysis using data from other included studies.

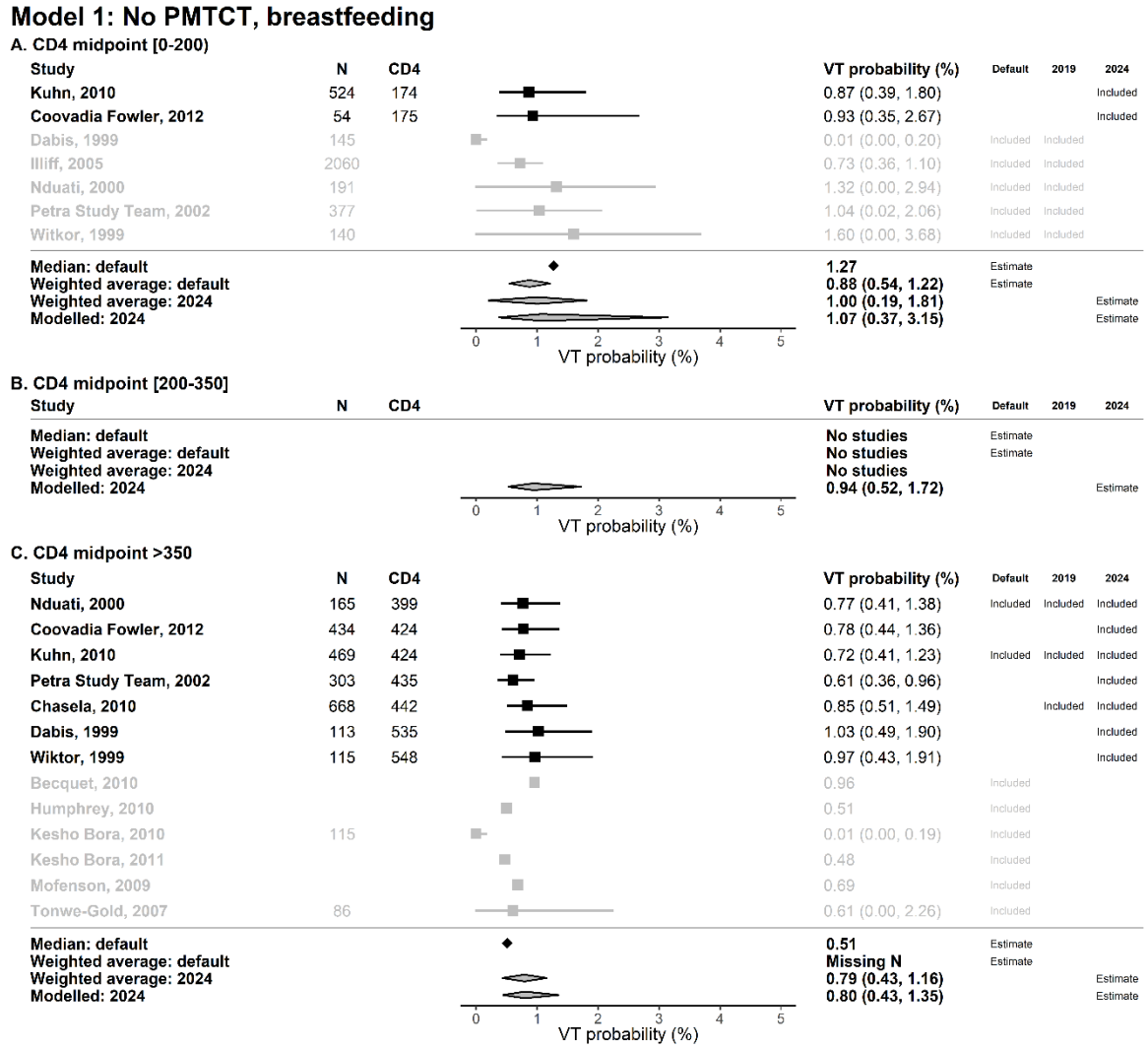


Figure S4.2.2 Pooled estimates of breastfeeding VT among women not receiving PMTCT. Results are stratified by the Spectrum-AIM defined CD4 ranges. The following pooled estimates are presented: median of studies included in the default VT probabilities ('Median: default'), the weighted average of studies included in the default VT probabilities ('Weighted average: default'), the weighted average of studies included in this analysis ('Weighted average: 2024'), and the results of the model one ('Modelled: 2024'). Kesho Bora 2010, Kesho Bora 2011, and Tonwe-Gold 2007 were excluded as mothers received AZT. Becquet 2010, Humphrey 2010, and Mofenson 2009 were excluded as they were not peer-reviewed studies. Iliff 2005 was excluded as it was a pooled analysis using data from other included studies.

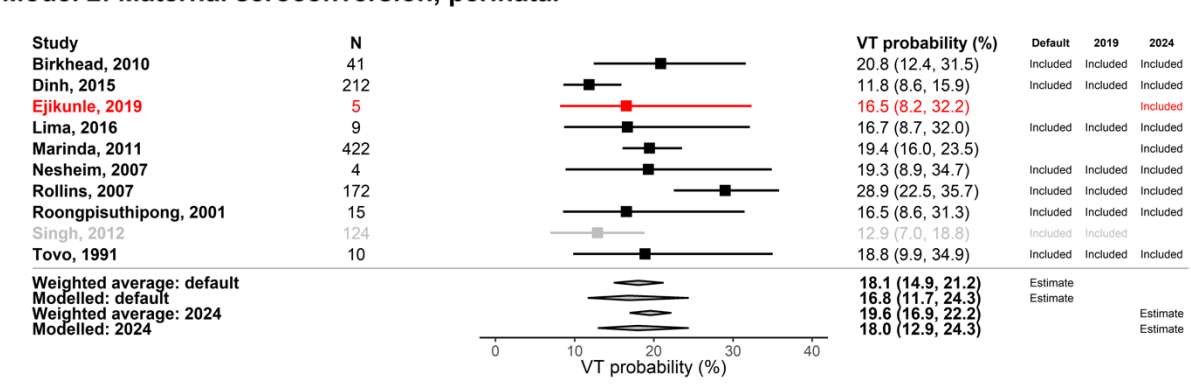


Figure S4.2.3 Pooled estimates of VT among women who seroconverted during pregnancy. The following pooled estimates are presented: the weighted average of studies included in the default VT

probabilities ('Weighted average: default'), estimates from model two fit to the default studies ('Modelled: default'), the weighted average of studies included in this analysis ('Weighted average: 2024'), and the results of the model two ('Modelled: 2024'). Singh 2012 was excluded as it was not a peer-reviewed study.

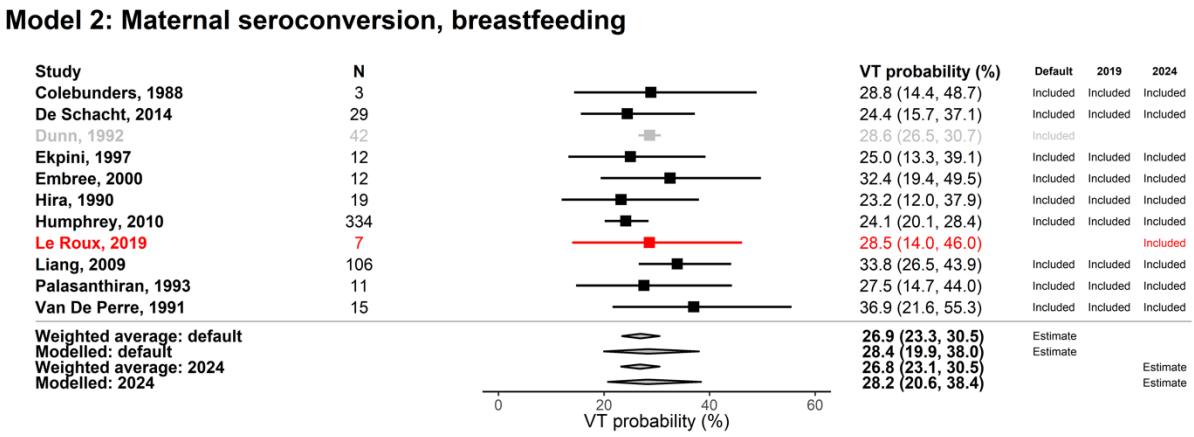


Figure S4.2.4 Pooled estimates of VT among women who seroconverted during breastfeeding. The following pooled estimates are presented: the weighted average of studies included in the default VT probabilities ('Weighted average: default'), estimates from model two fit to the default studies ('Modelled: default'), the weighted average of studies included in this analysis ('Weighted average: 2024'), and the results of the model two ('Modelled: 2024'). Singh 2012 was excluded as it was not a peer-reviewed study. Dunn 1992 was excluded as it was a pooled analysis using data from other included studies.

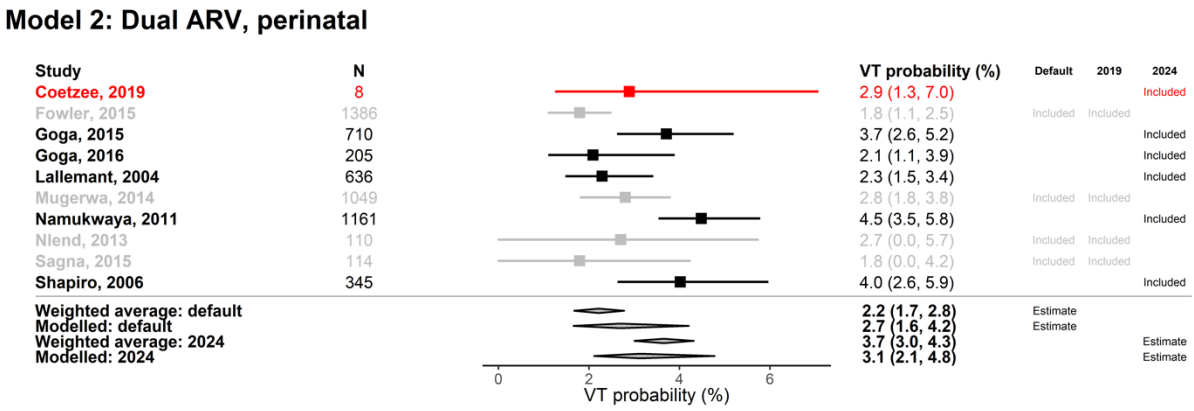


Figure S4.2.5 Pooled estimates of perinatal VT among women receiving dual ARV. The following pooled estimates are presented: the weighted average of studies included in the default VT probabilities ('Weighted average: default'), estimates from model two fit to the default studies ('Modelled: default'), the weighted average of studies included in this analysis ('Weighted average: 2024'), and the results of the model two ('Modelled: 2024'). Fowler 2015 and Mugerwa 2014 were excluded as they were not peer-reviewed studies and Nlend 2013 and Sagna 2015 were excluded as they excluded WLHIV with CD4 <350.

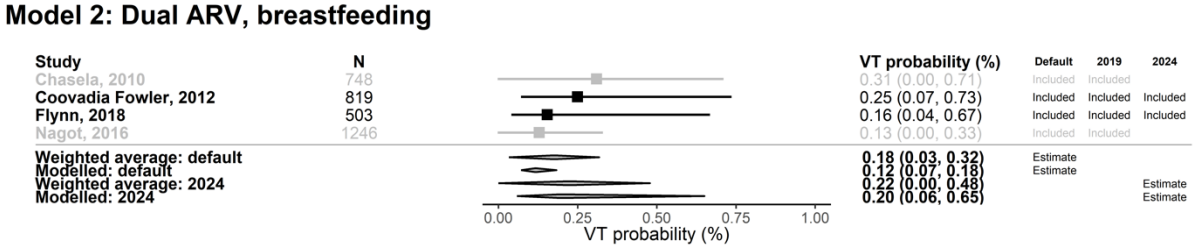


Figure S4.2.6 Pooled estimates of breastfeeding VT among women receiving dual ARV. The following pooled estimates are presented: the weighted average of studies included in the default VT probabilities ('Weighted average: default'), estimates from model two fit to the default studies ('Modelled: default'), the weighted average of

studies included in this analysis (‘Weighted average: 2024’), and the results of the model two (‘Modelled: 2024‘). Chasela 2010 and Nagot 2016 was excluded as they excluded WLHIV with CD4 < 350.

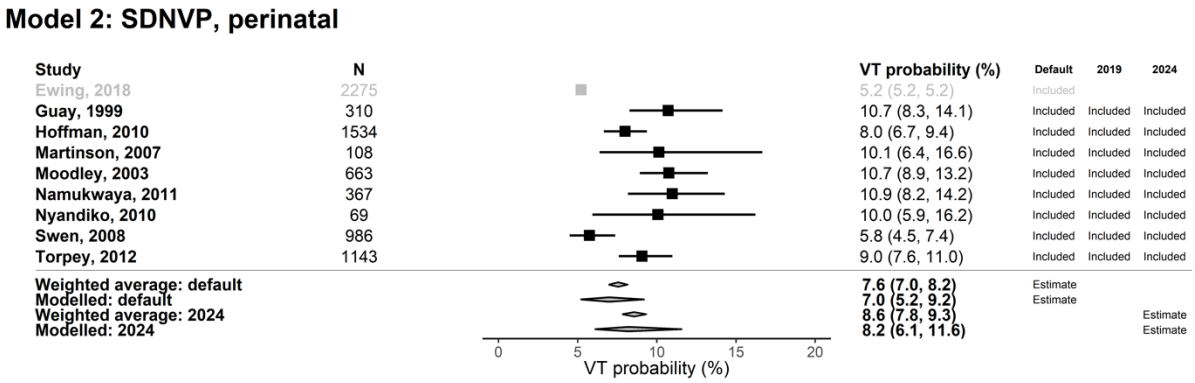


Figure S4.2.7 Pooled estimates of perinatal VT among women receiving single dose nevirapine. The following pooled estimates are presented: the weighted average of studies included in the default VT probabilities (‘Weighted average: default’), estimates from model two fit to the default studies (‘Modelled: default’), the weighted average of studies included in this analysis (‘Weighted average: 2024’), and the results of the model two (‘Modelled: 2024‘). Ewing 2018 was excluded as it was not a peer-reviewed study.

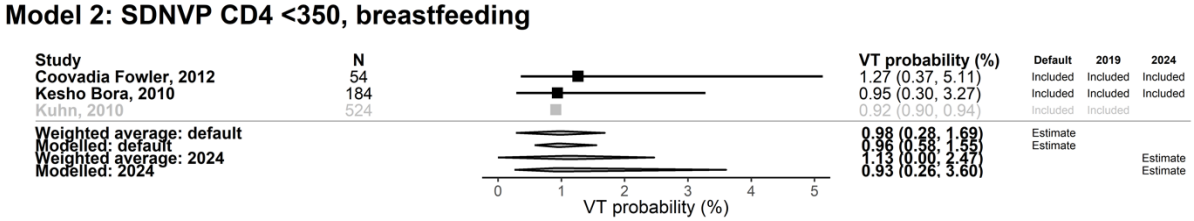


Figure S4.2.8 Pooled estimates of breastfeeding VT among women with CD4 < 350 receiving single dose nevirapine. The following pooled estimates are presented: the weighted average of studies included in the default VT probabilities (‘Weighted average: default’), estimates from model two fit to the default studies (‘Modelled: default’), the weighted average of studies included in this analysis (‘Weighted average: 2024’), and the results of the model two (‘Modelled: 2024‘). Kuhn 2010 was excluded as WLHIV were receiving ART.

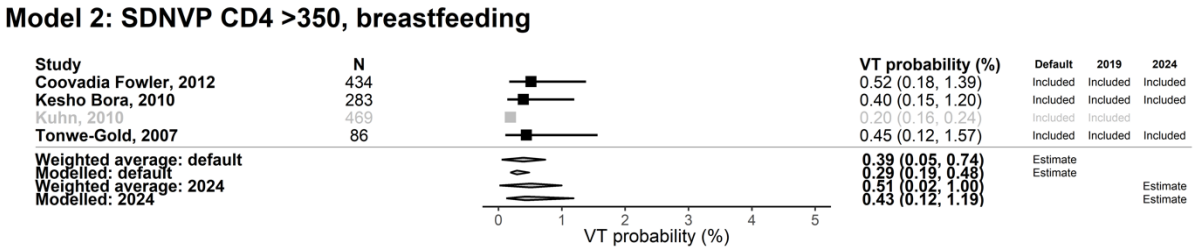


Figure S4.2.9 Pooled estimates of breastfeeding VT among women with CD4 >350 receiving single dose nevirapine. The following pooled estimates are presented: the weighted average of studies included in the default VT probabilities (‘Weighted average: default’), estimates from model two fit to the default studies (‘Modelled: default’), the weighted average of studies included in this analysis (‘Weighted average: 2024’), and the results of the model two (‘Modelled: 2024‘). Kuhn 2010 was excluded as WLHIV were receiving ART.

Model 2: Option A, perinatal

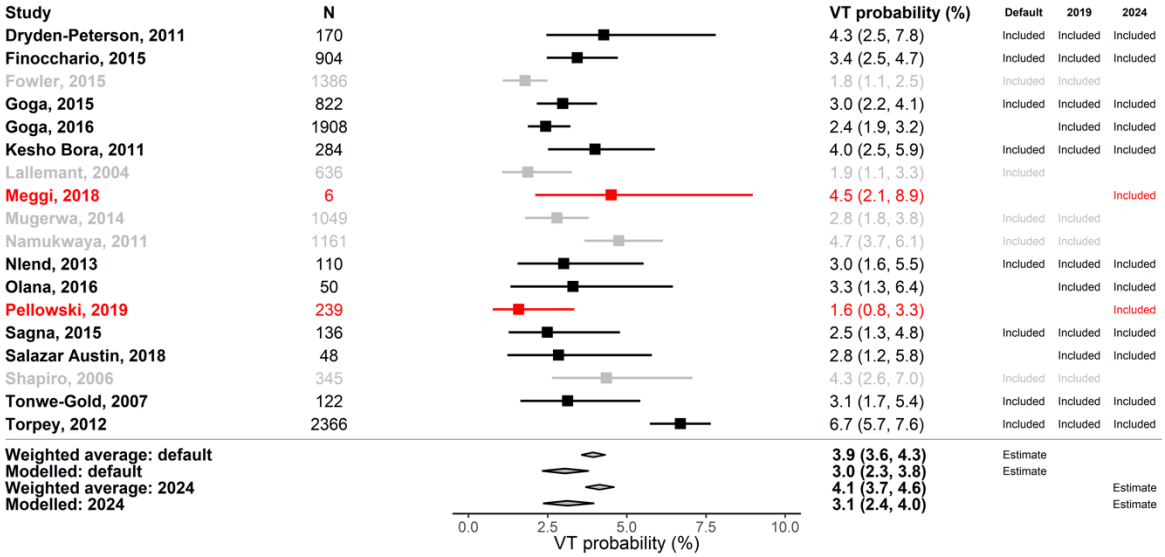


Figure S4.2.10 Pooled estimates of perinatal VT among women receiving Option A. The following pooled estimates are presented: the weighted average of studies included in the default VT probabilities ('Weighted average: default'), estimates from model two fit to the default studies ('Modelled: default'), the weighted average of studies included in this analysis ('Weighted average: 2024'), and the results of the model two ('Modelled: 2024'). Fowler 2015 and Mugerwa 2014 were excluded as they were not peer-reviewed studies, all other studies that were excluded had women who initiated AZT at 28 weeks rather than 14 weeks.

Model 2: Option A, breastfeeding

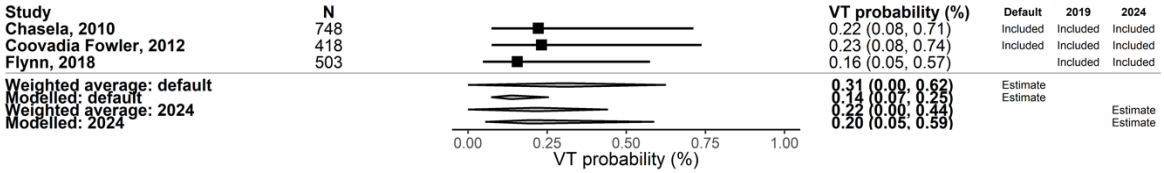


Figure S4.2.11 Pooled estimates of breastfeeding VT among women receiving Option A. The following pooled estimates are presented: the weighted average of studies included in the default VT probabilities ('Weighted average: default'), estimates from model two fit to the default studies ('Modelled: default'), the weighted average of studies included in this analysis ('Weighted average: 2024'), and the results of the model two ('Modelled: 2024').

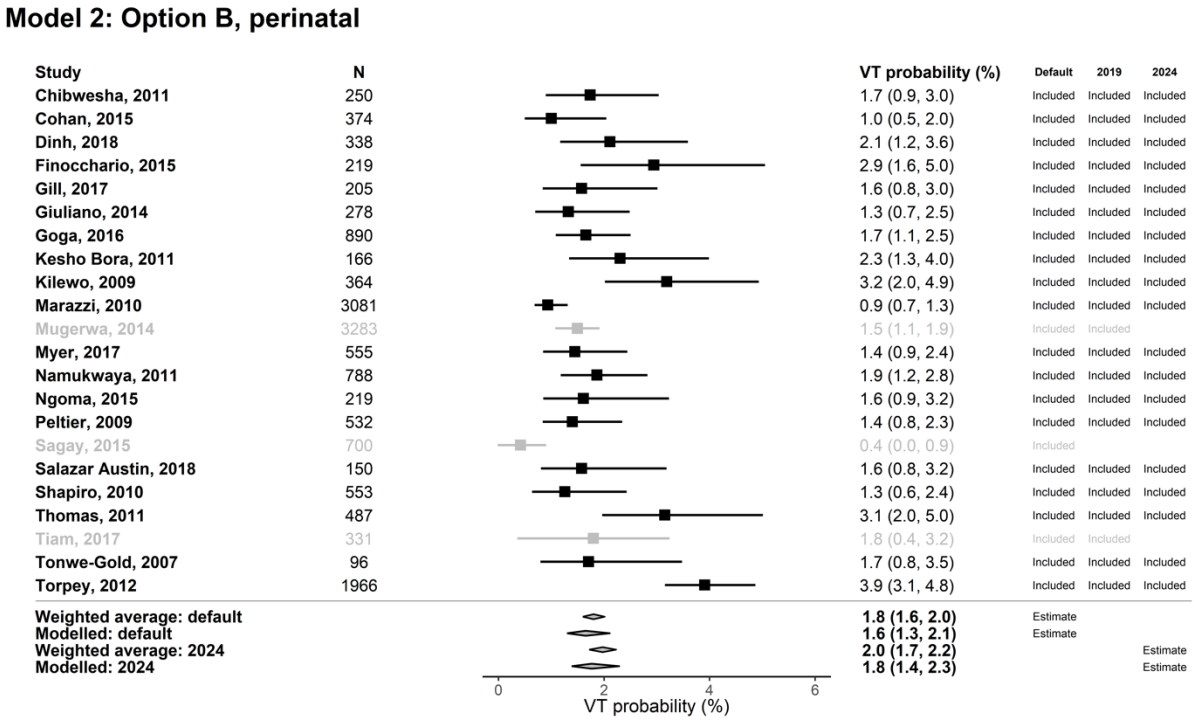


Figure S4.2.12 Pooled estimates of perinatal VT among women receiving Option B. The following pooled estimates are presented: the weighted average of studies included in the default VT probabilities ('Weighted average: default'), estimates from model two fit to the default studies ('Modelled: default'), the weighted average of studies included in this analysis ('Weighted average: 2024'), and the results of the model two ('Modelled: 2024'). Mugerwa 2014 and Tiam 2017 were excluded as they were not peer-reviewed studies. Sagay 2015 was excluded as we could not determine the timing of the HIV test.

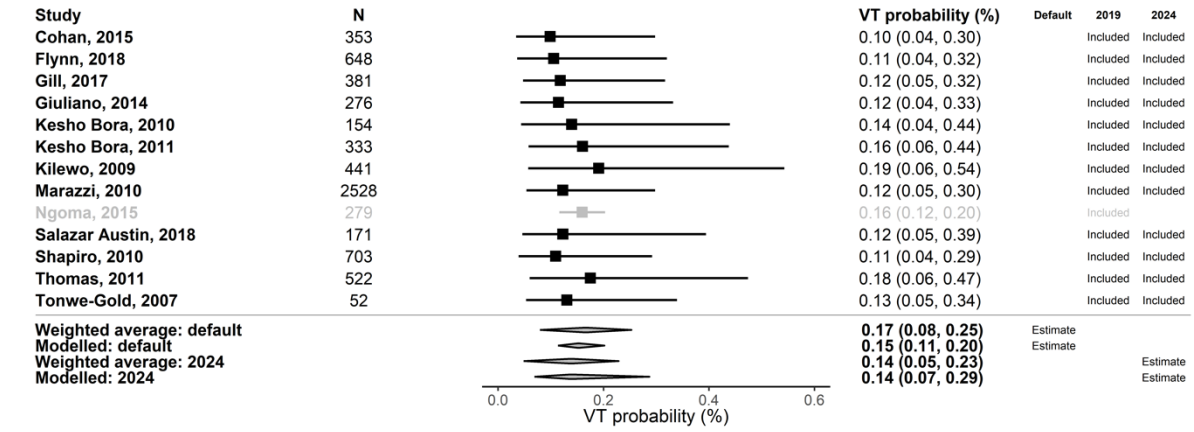
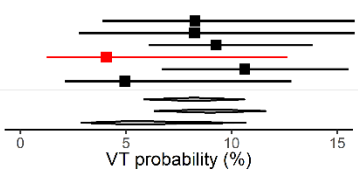


Figure S4.2.13 Pooled estimates of breastfeeding VT among women receiving Option B. The following pooled estimates are presented: the weighted average of studies included in the default VT probabilities ('Weighted average: default'), estimates from model two fit to the default studies ('Modelled: default'), the weighted average of studies included in this analysis ('Weighted average: 2024'), and the results of the model two ('Modelled: 2024'). Ngoma 2015 was excluded as it did not restrict to women with CD4 >350.

Model 3: Perinatal transmission among women on ART

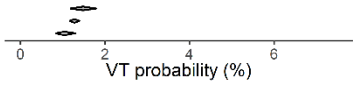
A. ART initiated in last month

Study	N	Weeks	VT probability (%)	Default	2019	2024
Bailey, 2011	41	1	8.24 (3.90, 16.31)			Included
Delicio, 2011	12	1	8.23 (2.77, 19.67)			Included
Chibwesha, 2011	187	2	9.23 (6.09, 13.76)	Included	Included	Included
Coetzee, 2019	11	2	4.08 (1.28, 12.58)			Included
Hoffman, 2010	151	2	10.58 (6.68, 15.44)	Included	Included	Included
Scott, 2017	44	2	4.95 (2.13, 12.77)	Included	Included	Included
Weighted average: default			**8.22 (5.84, 10.60)**	Estimate		
Weighted average: 2024			**8.97 (6.32, 11.62)**			Estimate
Modelled: 2024			**5.23 (2.87, 10.66)**			Estimate



B. ART initiated before last month

Study	N	Weeks	VT probability (%)	Default	2019	2024
Thomas, 2011	487	5	3.81 (2.52, 5.49)			Included
Chibwesha, 2011	242	6	3.60 (2.24, 6.29)	Included	Included	Included
Choi, 2018	3	6	2.22 (0.74, 7.21)			Included
Gantner, 2019	16	6	1.99 (0.66, 5.29)			Included
Goga, 2016	163	6	2.11 (1.02, 4.32)			Included
Malaba, 2022	135	6	1.92 (0.88, 4.04)			Included
Malaba, 2022	133	6	1.39 (0.58, 3.25)			Included
Mandelbrot, 2015	990	6	2.08 (1.41, 3.07)			Included
Meyers, 2015	248	6	3.63 (2.11, 6.17)			Included
Siubiude, 2022	1408	6	1.58 (1.05, 2.24)			Included
Siubiude, 2022	418	6	2.17 (1.29, 3.69)			Included
Siubiude, 2022	214	6	1.53 (0.81, 2.85)			Included
Tookey, 2016	640	6	2.00 (1.24, 3.09)			Included
Joao, 2021	82	8	2.11 (0.89, 4.33)			Included
Gill, 2017	205	9	1.71 (0.78, 3.08)			Included
Joao, 2021	78	9	3.49 (1.59, 7.76)			Included
Van Schalkwyk, 2013	65	9	2.07 (0.96, 4.60)			Included
Zijenah, 2022	73	9	2.43 (0.99, 5.12)			Included
Chibwesha, 2011	196	10	3.37 (1.86, 6.24)	Included	Included	Included
Van Schalkwyk, 2013	57	10	1.74 (0.69, 4.34)			Included
Nlend, 2013	285	12	1.71 (0.89, 3.36)			Included
Tubiana, 2013	36	12	1.64 (0.72, 5.22)			Included
Black, 2008	302	13	0.88 (0.37, 2.02)			Included
Chen, 2019	446	13	3.70 (2.40, 5.60)			Included
Dryden-Peterson, 2011	114	13	1.33 (0.58, 2.82)			Included
Prieto, 2012	244	13	1.82 (0.73, 3.91)			Included
Bornhede, 2018	3	14	1.49 (0.44, 4.55)			Included
Giuliano, 2014	278	14	1.11 (0.45, 2.52)			Included
Van Schalkwyk, 2013	90	14	1.13 (0.42, 2.78)			Included
Hoffman, 2010	157	16	3.21 (1.63, 6.41)	Included	Included	Included
Joao, 2021	71	16	1.35 (0.56, 3.13)			Included
Joao, 2021	76	16	1.32 (0.51, 3.18)			Included
Peltier, 2009	227	16	1.33 (0.56, 2.84)			Included
Perry, 2016	306	17	0.66 (0.29, 1.57)			Included
Townsend, 2014	3422	17	0.64 (0.46, 0.94)			Included
Carey, 2018	67	18	0.95 (0.35, 2.42)			Included
Cohan, 2015	195	18	0.70 (0.28, 1.63)			Included
Cohan, 2015	194	18	0.76 (0.33, 1.80)			Included
Harrington, 2019	264	18	2.06 (0.92, 3.97)			Included
Ngoma, 2015	219	18	1.29 (0.62, 2.67)			Included
Perry, 2016	187	19	0.69 (0.26, 1.61)			Included
Zijenah, 2022	97	19	1.40 (0.59, 3.75)			Included
Amone, 2023	431	20	1.42 (0.76, 2.84)			Included
Choi, 2018	3	20	1.03 (0.33, 3.24)			Included
Goga, 2016	727	20	1.62 (0.98, 2.70)			Included
Goga, 2020	803	20	1.69 (1.10, 2.62)			Included
Loh, 2021	42	20	0.92 (0.33, 2.30)			Included
Mandelbrot, 2015	2619	20	0.84 (0.58, 1.24)			Included
Marazzi, 2010	3081	20	0.83 (0.57, 1.19)			Included
Myer, 2017	555	20	1.17 (0.55, 2.25)			Included
Ndarukwa, 2019	841	20	1.52 (0.97, 2.50)			Included
Siubiude, 2022	1574	20	0.93 (0.66, 1.46)			Included
Siubiude, 2022	1463	20	0.72 (0.46, 1.20)			Included
Siubiude, 2022	897	20	0.65 (0.35, 1.24)			Included
Tiam, 2019	370	20	1.27 (0.73, 2.79)			Included
Tookey, 2016	2155	20	0.69 (0.45, 1.08)			Included
Bailey, 2011	1719	21	1.11 (0.70, 1.64)			Included
Coetzee, 2019	33	22	0.77 (0.22, 2.43)			Included
Chibwesha, 2011	1188	26	2.02 (1.47, 2.90)	Included	Included	Included
Meyers, 2015	946	26	0.69 (0.37, 1.25)			Included
Hoffman, 2010	422	30	3.90 (2.43, 5.78)	Included	Included	Included
Zijenah, 2022	16	32	0.63 (0.22, 1.74)			Included
Choi, 2018	2	34	0.45 (0.16, 1.45)			Included
Mandelbrot, 2015	658	34	0.42 (0.20, 0.85)			Included
Siubiude, 2022	290	34	0.37 (0.16, 0.79)			Included
Siubiude, 2022	362	34	0.45 (0.19, 0.96)			Included
Siubiude, 2022	437	34	0.37 (0.20, 0.77)			Included
Tookey, 2016	110	34	0.38 (0.16, 0.86)			Included
Scott, 2017	1801		0.50 (0.17, 0.83)	Included		
Weighted average: default			**1.48 (1.17, 1.79)**	Estimate		
Weighted average: 2024			**1.28 (1.16, 1.39)**			Estimate
Modelled: 2024			**1.04 (0.83, 1.31)**			Estimate



C. ART initiated preconception

Study	N	Weeks	VT probability (%)	Default	2019	2024
Aebi-Popp, 2022	21	40	0.35 (0.09, 0.95)			Included
Blonk, 2015	7	40	0.35 (0.12, 1.09)	Included	Included	Included
Bornhede, 2018	10	40	0.31 (0.11, 1.02)	Included	Included	Included
Carey, 2018	65	40	0.28 (0.11, 0.93)	Included	Included	Included
Chauhan, 2021	32	40	0.34 (0.11, 1.10)			Included
Choi, 2018	8	40	0.31 (0.11, 1.16)			Included
Coetzee, 2019	25	40	0.28 (0.08, 0.86)			Included
Colbers, 2015a	18	40	0.35 (0.10, 1.16)	Included	Included	Included
Colbers, 2015b	11	40	0.33 (0.10, 0.87)	Included	Included	Included
Dinh, 2018	415	40	0.71 (0.30, 1.61)	Included	Included	Included
Dryden-Peterson, 2011	144	40	0.28 (0.10, 0.74)	Included	Included	Included
Ewenighi-Amankwah, 2020	122	40	0.30 (0.10, 0.95)			Included
Frange, 2020	247	40	0.26 (0.09, 0.80)			Included
Gantner, 2019	78	40	0.29 (0.09, 0.85)			Included
Gibb, 2012	172	40	0.27 (0.09, 0.79)	Included	Included	Included
Gill, 2017	382	40	0.31 (0.12, 0.84)	Included	Included	Included
Goga, 2020	635	40	0.84 (0.43, 1.57)			Included
Hoffman, 2010	143	40	0.80 (0.34, 1.94)	Included	Included	Included
Huntington, 2011	340	40	0.33 (0.12, 0.95)	Included	Included	Included
Kim, 2013	262	40	0.28 (0.10, 0.79)	Included	Included	Included
Loh, 2021	46	40	0.30 (0.10, 0.84)			Included
Mandelbrot, 2015	3505	40	0.22 (0.12, 0.42)	Included	Included	Included
Ndarukwa, 2019	289	40	0.68 (0.30, 1.37)			Included
Orbaek, 2017	247	40	0.26 (0.09, 0.77)	Included	Included	Included
Perry, 2016	178	40	0.22 (0.07, 0.57)	Included	Included	Included
Peters, 2017	1749	40	0.24 (0.10, 0.47)	Included	Included	Included
Samuel, 2014	68	40	0.45 (0.13, 1.30)	Included	Included	Included
Schalkwijk, 2017	15	40	0.35 (0.11, 1.06)	Included	Included	Included
Siubiude, 2022	6606	40	0.18 (0.11, 0.29)			Included
Tiam, 2019	249	40	0.40 (0.17, 0.97)			Included
Tookey, 2016	968	40	0.32 (0.15, 0.74)	Included	Included	Included
Townsend, 2014	2105	40	0.22 (0.11, 0.37)	Included	Included	Included
Yusuf, 2022	10	40	0.33 (0.10, 1.18)			Included
Zijenah, 2022	272	40	0.39 (0.15, 1.04)			Included
Sagay, 2015	700		0.43 (0.00, 0.91)	Included		
Weighted average: default			**0.26 (0.17, 0.36)**	Estimate		
Weighted average: 2024			**0.25 (0.18, 0.32)**			Estimate
Modelled: 2024			**0.33 (0.23, 0.48)**			Estimate

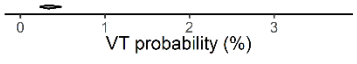


Figure S4.2.14 Pooled estimates of perinatal VT among women receiving ART. The following pooled estimates are presented: the weighted average of studies included in the default VT probabilities ('Weighted average: default'), the weighted average of studies included in this analysis ('Weighted average: 2024'), and the results of the model three ('Modelled: 2024'). Scott 2017 was excluded as we could not determine whether ART initiation occurred before or during pregnancy and Sagay 2015 was excluded as we could not determine paediatric test timing.

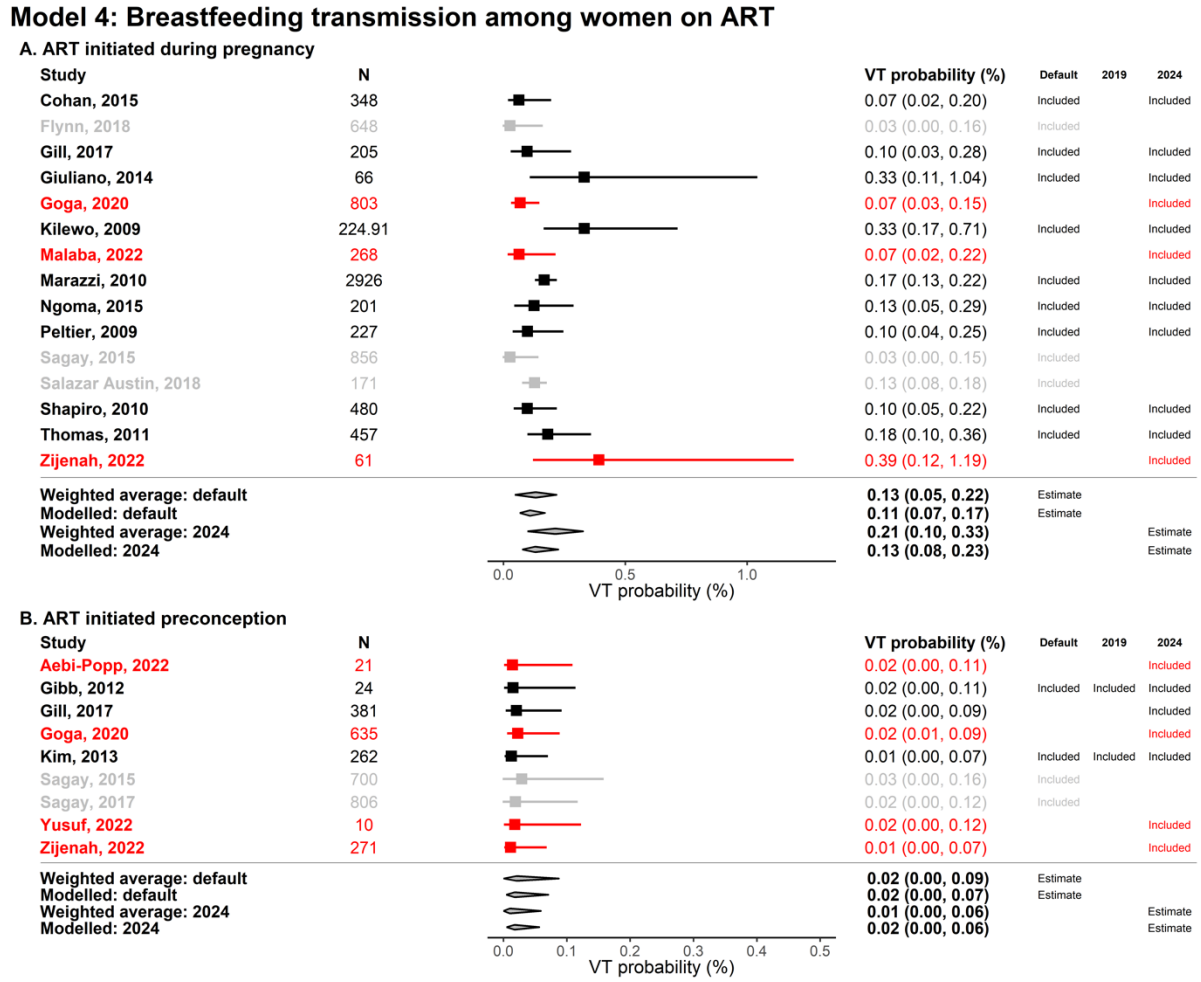


Figure S4.2.15 Pooled estimates of breastfeeding VT among women receiving ART. The following pooled estimates are presented: the weighted average of studies included in the default VT probabilities ('Weighted average: default'), estimates from model four fit to the default studies ('Modelled: default'), the weighted average of studies included in this analysis ('Weighted average: 2024'), and the results of the model four ('Modelled: 2024'). Flynn 2018, Sagay 2017, and Salazar Austin 2018 were excluded as we could not determine whether ART initiation occurred before or during pregnancy and Sagay 2015 was excluded as we could not determine paediatric test timing.

S5. Sensitivity analyses on meta-regression model assumptions

S5.1. Model one: VT probability from women not receiving PMTCT

Model one included data from 16 studies that reported data about transmissions among women who did not receive PMTCT stratified by CD4 count. This including two new studies published since the 2018 review (Supplementary material S3.1). For the continuous CD4 covariate in model 1, we summarized the CD4 distribution among the study population by the approximate midpoint CD4. Here we assess (1) the sensitivity of model estimates to how the CD4 midpoint was defined from each study and (2) the sensitivity of estimates at different CD4 midpoints.

S5.1.1. Sensitivity to CD4 midpoint calculation

Data included in model one reported CD4 among the study population in one of two formats: (1) women with CD4 in a given range (e.g. 200 – 350 mm^3) or (2) median CD4 of women who did not receive PMTCT care at baseline. If a study reported CD4 as a range, we took the median of the upper and lower bound (e.g. a range of 200-350 was extracted as 275). If a study reported CD4 using the second method (median CD4), the median was extracted.

Studies that stratified participates by CD4 range categories often reported vertical transmission probability data stratified by CD4 range, meaning that one study often reported multiple observations. Among studies that reported perinatal transmission among women not receiving PMTCT, four studies reported transmission by CD4 range. Three of the four studies reported transmission among three CD4 ranges. Nine studies reported perinatal transmission among women not on PMTCT that were not stratified by CD4 range, but did report a median CD4 among the study population. Among studies that reported breastfeeding transmission among women not receiving PMTCT, two studies reported transmission by CD4 range. One of the two studies reported transmission among multiple CD4 ranges. Four studies reported breastfeeding transmission among women not on PMTCT that were not stratified by CD4 range, but did report a median CD4 among the study population. Studies used in model one and method of CD4 reporting are listed in Table S5.1.1.1.

Table S5.1.1.1. Studies used in model one and method of CD4 reporting

Study	Location	Study years	Transmission type	CD4	VT	N	Method of CD4 reporting
Hoffman, 2010	South Africa	2004 - 2008	Perinatal	161	0.17	23	Median
Coetzee, 2019	South Africa	2010 - 2010	Perinatal	272	0.13	15	Median
Goga, 2016	South Africa	2011 - 2013	Perinatal	372	0.13	63	Median
Olana, 2016	Ethiopia	2006 - 2014	Perinatal	415	0.13	102	Median
Petra Study Team, 2002	Tanzania, South Africa, Uganda	2000 - 2000	Perinatal	435	0.13	303	Median

Habib, 2021	Iran	2015 - 2017	Perinatal	475	0.20	20	Median
Dabis, 1999	Ivory Coast, Burkina Faso	1995 - 1998	Perinatal	535	0.29	145	Median
Connor, 1994	USA and France	1991 - 1993	Perinatal	538	0.22	183	Median
Wiktor, 1999	Ivory Coast	1996 - 1998	Perinatal	548	0.22	119	Median
Marinda, 2011	Zimbabwe	1997 - 2000	Perinatal	99.5	0.36	496	CD4 range
Mayaux, 1995	France	1986 - 1994	Perinatal	99.5	0.43	65	CD4 range
Shaffer, 1999	Thailand	1996 - 1997	Perinatal	99.5	0.38	24	CD4 range
Marinda, 2011	Zimbabwe	1997 - 2000	Perinatal	274.5	0.24	826	CD4 range
Mayaux, 1995	France	1986 - 1994	Perinatal	300	0.26	57	CD4 range
Shaffer, 1999	Thailand	1996 - 1997	Perinatal	349.5	0.18	104	CD4 range
Iliff, 2005	Zimbabwe	1997 - 2000	Perinatal	404	0.21	4367	CD4 range
Marinda, 2011	Zimbabwe	1997 - 2000	Perinatal	424.5	0.20	1963	CD4 range
Mayaux, 1995	France	1986 - 1994	Perinatal	600	0.17	192	CD4 range
Shaffer, 1999	Thailand	1996 - 1997	Perinatal	600	0.13	67	CD4 range
Petra Study Team, 2002	Tanzania, South Africa, Uganda	1996 - 2000	BF (monthly)	435	0.01	303	Median
Chasela, 2010	Malawi	2004 - 2010	BF (monthly)	442	0.01	668	Median
Dabis, 1999	Ivory Coast, Burkina Faso	1995 - 1998	BF (monthly)	535	0.01	113	Median
Wiktor, 1999	Ivory Coast	1996 - 1998	BF (monthly)	548	0.02	115	Median
Kuhn, 2010	Zambia		BF (monthly)	174.5	0.01	524	CD4 range
Coovadia Fowler, 2012	South Africa, Tanzania, Uganda, Zimbabwe	2008 - 2011	BF (monthly)	424.5	0.01	434	CD4 range
Kuhn, 2010	Zambia		BF (monthly)	424.5	0.00	469	CD4 range

As these two formats (CD4 range and median CD4) are not directly comparable, we conducted a subgroup analysis to assess the sensitivity of model one results to the difference in method of CD4 reporting. The subgroups we analysed were (1) studies that reported a CD4 range ("CD4 range" model) and (2) studies that reported a CD4 median ("median CD4" model). We re-fit model one to these different subgroups using Equation

S5.1. Model one's fit to all data as presented in the main text is also copied below ("all data" model).

$$\text{logit}(VT) = \beta_0 * [BF = 0] + \beta_1 * [BF = 1] + \beta_2 * CD4_{Midpoint} + \beta_3 * BF * CD4_{Midpoint} + \mu_0 + \mu_1$$

Equation S5.1

The following description of Equation S5.1 is copied from the main text: "*Model one included fixed effects for perinatal (β_0) and monthly breastfeeding transmission (β_1), a fixed effect for CD4 midpoint (β_1, per 100 mm^3 centred at 500 mm^3), and a fixed effect for the interaction between CD4 midpoint and breastfeeding transmission (β_2). More information on how the CD4 midpoint was extracted from each study is detailed in Supplementary Material S5.1. Random effects were included for study and observation (μ_0 and μ_1, respectively).*"

Table S5.1.1.2. Sensitivity analysis is of model 1 results to CD4 midpoint assumption for data used in model one

Covariate	Estimates of the "all data" model (logit) (n = 12,021)		Estimates of the "CD4 range" model (logit) (n = 9642)		Estimates of the "median CD4" model (logit) (n = 2379)	
Intercept	-1.61	(-1.81, -1.41)	-1.57	(-1.65, -1.48)	-1.47	(-1.63, -1.30)
CD4 midpoint (per 100 cells increase, centered on CD4 = 500 mm^3)	-0.23	(-0.28, -0.17)	-0.24	(-0.29, -0.18)	0.33	(0.10, 0.56)
Perinatal transmission (Reference)	0.0	(Reference)	0.0	(Reference)	0.0	(Reference)
Breastfeeding transmission	-3.22	(-3.84, -2.60)	-4.05	(-5.33, -2.77)	-2.88	(-3.58, -2.19)
Interaction between CD4 midpoint and breastfeeding transmission	0.17	(-0.21, 0.54)	-0.08	(-0.59, 0.43)	0.2	(-0.92, 1.32)

The covariates of the "all data" model one and "CD4 range" model one fit had overlapping confidence intervals (Table S5.1.1.2). The "all data" model one and "median CD4" model one fit were significantly different from each other. While the "all data" model one had a negative estimate for the effect of CD4 midpoint on VT probability (-0.2 (-0.3 - -0.2)), the "median CD4" model had a positive estimate for the effect of CD4 midpoint on VT probability (0.4 (0.1-0.7)).

The difference in effect of CD4 midpoint on VT probability among women not receiving PMTCT was driven by three studies that reported both high CD4 medians and transmission rates (Dabis 1999, Connor 1994, and Wiktor 1999, Table S5.1.1.1). Excluding these three studies resulted in a negative CD4 midpoint fixed effect. These studies collected data in the early stage of the HIV epidemic (1991 to 1998 across the three studies), reported high transmission rates and CD4 medians. This may may reflect high incidence among women of childbearing age. In acute HIV infection, both CD4 and viral load are high, and so women with high CD4 can have higher risk of vertical transmission than women no longer in the acute infection stage.[4] Dabis 1999 describes data from the placebo group of the DITRAME trial which had high average CD4 and viral load; among women who transmitted the mean CD4 was 358 and the mean viral load was approximately 55,000.[5] Similar data was not available Connor 1994 and Wiktor 1999.

The observations from these three studies (Dabis, Connor, and Wiktor) represent 31% of the available data in the "median CD4" model and are the only observations with CD4 midpoints above 500. The results of the "median CD4" model are confounded by studies that reflect an earlier HIV epidemic, where transmission probability may be high among high CD4 values due to high incidence rates. When all data is used, the effect of these studies is diluted as there is more data about transmission among women with high CD4 values. The meta-regression framework then imposes larger study and observation level random effects on observations from Dabis 1999, Connor 1994, and Wiktor 1999. Although subgroup analysis shows that model one results are sensitive to the format of CD4 midpoint reporting, the difference in transmission may be confounded by other study characteristics (specifically study year and epidemic stage) rather than due to reporting a CD4 median itself.

S5.1.2 Sensitivity to CD4 midpoint used to produce estimates for Spectrum

For women not receiving PMTCT, Spectrum-AIM stratifies transmission probabilities by CD4 range. These are CD4 <200, 200-350, and >350. To produce model based estimates of VT probabilities compatible with Spectrum-AIM's stratification, we used CD4 midpoints of 100, 275, and 500 ("Main text value" in Table S5.1.2). We assessed the sensitivity of our estimates to this choice by considering alternate uses of model one that could be used to approximate the Spectrum-AIM CD4 categories. Alternate approaches included: the mean of all transmission probabilities for CD4 midpoints within the Spectrum-AIM ranges ("Mean across range" in Table S5.1.2), the lowest CD4 of the Spectrum-AIM ranges ("Lowest CD4" in Table S5.1.2), and the highest CD4 of the Spectrum-AIM range ("Highest CD4" in Table S5.1.2). For the >350 category, the highest CD4 we considered was 650 mm^3.

Table S5.1.2 Sensitivity of model one VT estimates to CD4 midpoint chosen to produce Spectrum-AIM compatible estimates

	CD4 range	Main text value		Mean across range		Lowest CD4		Highest CD4	
Perinatal	<200	33.4	(27.8, 39.0)	33.1	(26.0, 41.8)	38.8	(32.0, 45.7)	28.6	(24.0, 32.7)
	200-350	25.1	(21.3, 28.5)	25.1	(20.0, 30.8)	28.6	(24.0, 32.6)	22.1	(18.8, 25.4)
	>350	16.7	(13.8, 20.0)	16.8	(11.4, 23.2)	22.1	(18.8, 25.2)	12.5	(9.9, 15.7)
BF (monthly)	<200	1.1	(0.4, 3.2)	1.1	(0.4 3.5)	1.2	(0.3, 4.8)	1.0	(0.5, 2.2)
	200-350	0.9	(0.5, 1.7)	0.9	(0.5, 1.8)	1.0	(0.5, 2.2)	0.9	(0.5, 1.5)
	>350	0.80	(0.4, 1.4)	0.8	(0.4, 1.5)	0.9	(0.5, 1.5)	0.7	(0.3, 1.9)

Perinatal transmission rates were within a -4.7% to 5.6% absolute difference range of the main text values estimated using the CD4 midpoints of 100, 275, and 500. Breastfeeding transmission rates were within a -0.1% to 0.1% absolute difference range of the main text values. The largest difference was among perinatal transmission with CD4 >350 (Table S5.1.2). The midpoint of 500 produced a transmission probability of 16.7% (13.8–20.0%). The highest CD4 in that range (CD4 = 650) had a transmission rate of 12.5% (9.9%–15.7%) while the lowest CD4 in that range (CD4 = 351) had a transmission rate of 22.1% (18.8–25.2%). If CD4 testing data shows that most women have high CD4 values (> 500), the VT probability used in Spectrum may be overestimating VT. However, given high PMTCT coverage, most women who are exposed to the VT probabilities for women not receiving PMTCT will have been those who were not retained on care. Treatment interruption is associated with rapid decline in CD4 count and increase in viral load after interruption, indicating that VT probability in this group is unlikely to be underestimated.[6]

S5.2. Model three: perinatal transmission probability from women receiving ART by timing of initiation

Model three included data from 57 studies (Supplementary material S3.3). Here we assess the sensitivity of model three's fit to the calculation used to extract a time on ART midpoint from each study.

S5.2.1 Sensitivity to time on ART data extraction

Publications reported time on ART before delivery in one of four ways: (1) median or mean number of weeks on ART before delivery, (2) median or mean gestational week of ART initiation, (3) a range of gestational weeks when women initiated ART (either reported as a trimester or through exclusion criteria), and (4) women who were on ART pre-conception.

To maximize the number of studies used, we used all reporting types and attributed a number of "weeks on ART midpoint" for studies where women used lifelong ART during pregnancy. The minimum value accepted was 0.5, indicating that the women initiated ART one week before delivery and the maximum value accepted was 40, indicating that the women initiated ART preconception. We preferentially extracted median (or mean) weeks on ART before delivery or median (mean) gestational week of ART initiation. As described in Supplementary Material S2, for countries that reported time on ART using the third method (a range of weeks), we contacted authors to request a median number of weeks on ART before delivery for the cohort. For the remaining studies where median time on ART was not available and the only information was a range of weeks when women initiated ART, we used the median of this range to determine the weeks on ART midpoint. The method used to derive the weeks on ART is shown for each study used in model three in Table S5.2.1.1.

Table S5.2.1.1. Data used to estimate effect of time on ART on VT estimates

Study	Location	Study years	Weeks on ART midpoint	VT events	N	Method to derive number of weeks on ART[A]
Bailey, 2011	Europe	2000 - 2009	1	5	41	3
Delicio, 2011	Brazil	2000 - 2009	1	2	12	3
Chibwesha, 2011	Zambia	2007 - 2010	2	17	187	3
Coetzee, 2019	South Africa	2010 - 2010	2	0	11	3
Hoffman, 2010	South Africa	2004 - 2008	2	14	151	3
Scott, 2017	USA	2002 - 2009	2	2	44	3
Tubiana, 2013	France	2007 - 2010	3.2	1	36	1
Thomas, 2011	Kenya	2003 - 2009	5	20	487	3
Choi, 2018	Korea	2005 - 2017	6	0	3	3
Gantner, 2019	France	2008 - 2014	6	0	16	3
Goga, 2016	South Africa	2011 - 2013	6	2	163	3
Malaba, 2018	South Africa And Uganda	2022 - 2018	6	3	135	3
Malaba, 2018	South Africa And Uganda	2022 - 2018	6	0	133	3
Mandelbrot, 2015	France	2000 - 2011	6	21	990	3
Meyers, 2015	China	2010 - 2012	6	11	248	3
Siubiude, 2017	France	2000 - 2023	6	36	2152	3
Tookey, 2016	UK	2003 - 2013	6	13	640	3
Zijenah, 2022	Zimbabwe	2017 - 2018	6	2	56	3

Gill, 2017	Rwanda	2013 - 2014	9.6	3	205	1
Joao, 2021	Argentina, Brazil, South Africa, Tanzania, Thailand, USA	2013 - 2018	11.5	7	393	3
Nlend, 2013	Cameroon	2012 - 2008	12	5	285	1
Black, 2008	South Africa	2004 - 2007	13	1	302	2
Chen, 2019	China	2007 - 2015	13	19	446	3
Prieto, 2012	Spain	2000 - 2007	13	5	244	3
Dryden-Peterson, 2011	Botswana	2009 - 2010	13.1	1	114	2
Bornhede, 2018	Sweden	2014 - 2017	14	0	3	3
Giuliano, 2014	Malawi	2008 - 2009	14	2	278	2
Townsend, 2014	UK and Ireland	2007 - 2011	17.3	21	3422	2
Perry, 2016	UK	2007 - 2012	17.9	1	306	2
Carey, 2018	UK	2008 - 2014	18	0	67	2
Harrington, 2019	Malawi	2015 - 2016	18	7	264	2
Ngoma, 2015	Zambia	2008 - 2009	18	3	219	3
Cohan, 2015	Uganda	2009 - 2013	18.8	1	374	2
Perry, 2016	UK	2007 - 2012	19.6	1	187	2
Amone, 2016	Uganda	2017 - 2023	20	7	431	3
Choi, 2018	Korea	2005 - 2017	20	0	3	3
Goga, 2016	South Africa	2011 - 2013	20	14	727	3
Loh, 2021	Singapore	2008 - 2015	20	0	42	3
Mandelbrot, 2015	France	2000 - 2011	20	22	2619	3
Myer, 2017	South Africa	2013 - 2014	20	7	555	2
Ndarukwa, 2019	Zimbabwe	2014 - 2016	20	13	841	3
Siubiude, 2017	France	2000 - 2023	20	31	4147	3
Tiam, 2019	Lesotho	2014 - 2016	20	5	370	3
Tookey, 2016	UK	2003 - 2013	20	13	2155	3
Zijenah, 2022	Zimbabwe	2017 - 2018	20	2	106	3
Marazzi, 2010	Malawi and Mozambique	2005 - 2009	20.1	25	3081	2
Bailey, 2011	Europe	2000 - 2009	21	19	1719	3
Chibwesha, 2011	Zambia	2007 - 2010	22	42	1626	3
Coetzee, 2019	South Africa	2010 - 2010	22	0	33	3
Hoffman, 2010	South Africa	2004 - 2008	22	28	579	3
Van Schalkwyk, 2013	South Africa	2008 - 2010	24	1	127	3
Meyers, 2015	China	2010 - 2012	26	5	946	3
Choi, 2018	Korea	2005 - 2017	34	0	2	3
Mandelbrot, 2015	France	2000 - 2011	34	3	658	3
Siubiude, 2017	France	2000 - 2023	34	6	1149	3
Tookey, 2016	UK	2003 - 2013	34	0	110	3
Zijenah, 2022	Zimbabwe	2017 - 2018	34	0	17	3
Aebi-Popp, 2022	Switzerland	2019 - 2021	40	0	17	4
Blonk, 2015	Europe	2010 - 2014	40	0	7	4
Bornhede, 2018	Sweden	2014 - 2017	40	0	10	4
Carey, 2018	UK	2008 - 2014	40	0	65	4
Chauhan, 2021	India	2016 - 2018	40	0	32	4
Choi, 2018	Korea	2005 - 2017	40	0	8	4
Coetzee, 2019	South Africa	2010 - 2010	40	0	25	4
Colbers, 2015a	Europe		40	0	18	4
Colbers, 2015	Europe	2009 - 2014	40	0	11	4
Dinh, 2018	Zimbabwe	2013 - 2013	40	5	415	4

Dryden-Peterson, 2011	Botswana	2009 - 2010	40	0	144	4
Ewenighi-Amankwah, 2020	Nigeria		40	0	122	4
Frange, 2020	France	2010 - 2018	40	0	247	4
Gantner, 2019	France	2008 - 2014	40	0	78	4
Gibb, 2012	Uganda, Zimbabwe	2003 - 2009	40	0	172	4
Gill, 2017	Rwanda	2014 - 2016	40	1	382	4
Goga, 2020	South Africa	2012 - 2014	40	7	635	4
Hoffman, 2010	South Africa	2004 - 2008	40	1	143	4
Huntington, 2011	UK	1996 - 2009	40	1	340	4
Kim, 2013	Malawi	2009 - 2011	40	0	262	4
Loh, 2021	Singapore	2008 - 2015	40	0	46	4
Mandelbrot, 2015	France	2000 - 2011	40	6	3505	4
Ndarukwa, 2019	Zimbabwe	2014 - 2016	40	4	289	4
Orbaek, 2017	Denmark	2002 - 2014	40	0	247	4
Perry, 2016	UK	2007 - 2012	40	0	178	4
Peters, 2017	UK	2012 - 2014	40	3	1749	4
Sagay, 2015	Nigeria	2010 - 2012	40	3	700	4
Samuel, 2014	UK	2004 - 2010	40	1	68	4
Schalkwijk, 2017	Europe	-	40	0	15	4
Siubiude, 2017	France	2000 - 2023	40	9	6606	4
Tiam, 2019	Lesotho	2014 - 2016	40	1	249	4
Tookey, 2016	UK	2003 - 2013	40	4	968	4
Townsend, 2014	UK and Ireland	2007 - 2011	40	4	2105	4
Yusuf, 2022	USA	-	40	0	1	4
Zijenah, 2022	Zimbabwe	2017 - 2018	40	1	272	4

[A] (1) Reported median or mean weeks on ART before delivery
(2) Reported median or mean gestational week of ART initiation
(3) Reported a range of gestational weeks during which women initiated ART
(4) Reported women who were on ART pre-conception

As these two formats are not directly comparable, we conducted a subgroup analysis to assess the sensitivity of model three results to the difference in method for extracting the "weeks on ART midpoint". The subgroups we analysed were (1) studies that reported a median number of weeks on ART before delivery, studies that reported ART was initiated in the last four weeks of pregnancy, and transmission among women on ART preconception (methods one, two, and four above, "Median weeks reported" below) and (2) studies that reported a range of gestational weeks when women initiated ART or transmission among women on ART preconception (methods three and four above, "Range of weeks reported" below). We re-fit model three to these different subgroups using Equation S5.2. Model one's fit to all data as presented in the main text is also copied below ("All data" model).

$$\text{logit}(PVT) = \beta_0 + \beta_1 * T_{weeks} + \beta_2 * late\ initation + \mu_0 + \mu_1$$

Equation S5.2

The following description of Equation S5.2 is copied from the main text: "*Model three included a fixed intercept term (β_0), a fixed effect (β_1) for weeks on ART during pregnancy before delivery (T_{Weeks}, centred on ART initiated 20 weeks before delivery), and a fixed effect for late ART initiation (β_2, ART initiated less than four weeks before delivery). Where available, we extracted the median number of weeks on ART before delivery. Assumptions*

surrounding weeks on ART before delivery are outlined in Supplementary Material S5.2. Random effects were included for study and observation (μ_0 and μ_1, respectively)."

Table S5.2.1.2. Sensitivity analysis is of model three results to time on ART midpoint assumption

Covariate	Estimates of the "All data" model (logit) (n = 55,240)		Estimates of the "Median weeks reported" model (logit) (n = 30,479)		Estimates of the "Range of weeks reported" model (logit) (n = 45,351)	
Intercept	-4.55	(-4.77, -4.33)	-4.82	(-5.14, -4.51)	-4.42	(-4.67, -4.17)
Weeks on ART before delivery (centered on 20 weeks)	-0.06	(-0.07, -0.04)	-0.05	(-0.07, -0.03)	-0.06	(-0.07, -0.05)
Late ART initiation (<4 weeks before delivery)	0.65	(-0.06, 1.35)	1.49	(0.67, 2.31)	0.57	(-0.14, 1.29)

The "all data" model three and "range of weeks reported" model three fit were not significantly different from each other (Table S5.2.1.2). The "all data" model three and "median weeks reported" model three fit were significantly different from each other. The late ART initiation covariate was significantly positive in the "median weeks reported" model, whereas in the "all data" model it was positive, but not significant.

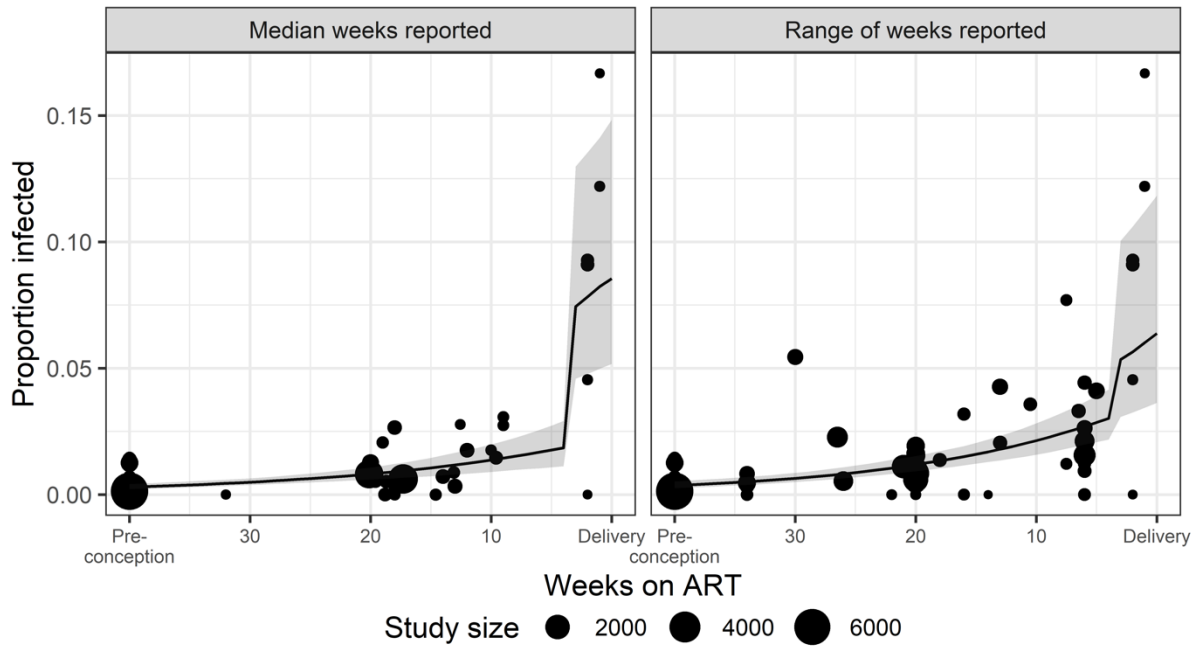


Figure S5.2.1. Effect of definition of weeks on ART midpoint on model three estimates of perinatal VT probability

The "all data" and "range of weeks reported" models included more studies where women initiated ART in the final ten weeks of pregnancy. These studies had VT probabilities ranging

from 0% to approximately 7.5%, making it so that the studies with late ART initiation weren't significantly higher than what was captured in the "weeks on ART" covariate.

S5.3 Geographic region as a confounder of ART class's effect on VT probability

Because 9/12 studies that reported perinatal transmission among women receiving an INSTI-based regimen occurred in high-income countries, we assessed geographic region as a confounder of ART class's effect on VT probability. To do so, we fit a modified version of model three, with fixed effects on ART class and geographic region. Geographic region was coded as: Sub-Saharan Africa (SSA, reference), non SSA, or multiple regions.

Table S5.3. Geographic region as a potential confounder for ART class's effect on VT probability

	No geographic region fixed effect		**Geographic region fixed effect**	
Covariate	Estimate (logit)	95% confidence interval	Estimate (logit)	95% confidence interval
Intercept	-4.45	(-4.70, -4.19)	-4.27	(-4.52, -4.01)
Weeks on ART before delivery (centered on 20 weeks)	-0.06	(-0.07, -0.04)	-0.05	(-0.07, -0.04)
Late ART initiation (<4 weeks before delivery)	0.67	(-0.03, 1.38)	0.89	(-0.02, 1.81)
ART class				
NNRTI (reference)	0.00	(Reference)	0.00	(Reference)
INSTI	-1.04	(-1.97, -0.11)	-0.84	(-1.84, 0.17)
PI	-0.10	(-0.51, 0.32)	0.02	(-0.43, 0.47)
Miscellaneous regimens	-0.07	(-0.64, 0.51)	0.16	(-0.45, 0.77)
Geographic region	Not included			
SSA			0.00	(Reference)
Non-SSA			-0.51	(-1.07, 0.04)
Multiple regions			-0.26	(-1.17, 0.66)

In the model that included geographic region, the non-SSA region had the lowest VT probability when a NNRTI-based regimen was initiated 20 weeks before delivery, although the regions didn't differ significantly (Table S5.3). While in the model without geographic region specified INSTI-based regimens had significantly lower VT when ART was started 20 weeks before delivery, including geographic region in the mode made this effect not significant. This suggests that the effects of ART regimen class on perinatal VT are confounded by the study geographic region.

S6. Implications of estimated VT probabilities for Spectrum-AIM's estimates of paediatric HIV infections

We used our estimates of VT probability in Spectrum-AIM model to assess the change in the number of perinatal and breastfeeding infections compared to those calculated using the default VT probabilities. For women not receiving any treatment, we used model one to estimated VT probability at the following CD4 midpoints: 100, 275, and 500. These were used to align with the Spectrum-AIM CD4 categories of <200, 200-350, and >350. For women receiving lifelong ART, used model three to estimate perinatal VT for weeks on ART of 2, 20, and 40 weeks to represent the Spectrum-AIM's perinatal transmission categories of on ART of <4 weeks, for 4-39 weeks before delivery, and preconception. For breastfeeding transmission probabilities, we used model four to estimate a monthly breastfeeding VT probability for women who initiated ART preconception and women who initiated ART during pregnancy. Probabilities of VT for women who seroconverted during pregnancy or breastfeeding and women who received short-course PMTCT were estimated using model two. The values used in this analysis are listed in Table 1 and Table 2 of the main text.

Using the 2024 published publicly available Spectrum-AIM files for Malawi, Rwanda, Democratic Republic of the Congo, and Burkina Faso, we calculated the percent change in the number of perinatal infections (Equation S6.1), breastfeeding infections (Equation S6.2), and total paediatric infections (Equation S6.3) in the years 2000, 2010, 2015, and 2023. These countries were chosen as they represent a country in Southern, Eastern, Central, and Western Africa respectively, and these years represent a variety of PMTCT strategies and coverages.

$$Percent\ change_{Perinatal} = \frac{(Infections_{\ Perinatal,MR} - Infections_{\ Perinatal,Default})}{Infections_{\ Perinatal,Default}} * 100$$

Equation S6.1

In Equation S6.1, $Infections_{\ Perinatal,MR}$ represented the number of perinatal infections that resulted from using the VT probabilities estimated in the meta-regression analysis, $Infections_{\ Perinatal,Default}$ represented the number of perinatal infections that resulted from using the default Spectrum-AIM VT probabilities, and $Percent\ change_{Perinatal}$ represented the percent change in perinatal infections.

$$Percent\ change_{BF} = \frac{(Infections_{\ BF,MR} - Infections_{\ BF,Default})}{Infections_{\ BF,Default}} * 100$$

Equation S6.2

In Equation S6.2, $Infections_{\ BF,MR}$ represented the number of breastfeeding infections that resulted from using the VT probabilities estimated in the meta-regression analysis, $Infections_{\ BF,Default}$ represented the number of breastfeeding infections that resulted from using the default Spectrum-AIM VT probabilities, and $Percent\ change_{BF}$ represented the percent change in breastfeeding infections.

$$Percent\ change_{Total} = \frac{(Infections_{\ Total,MR} - Infections_{\ Total,Default})}{Infections_{\ Total,Default}} * 100$$

Equation S6.3

In Equation S6.3, $Infections_{Total,MR}$ represented the number of vertical infections that resulted from using the VT probabilities estimated in the meta-regression analysis, $Infections_{Total,Default}$ represented the number of vertical infections that resulted from using the default Spectrum-AIM VT probabilities, and $Percent\ change_{Total}$ represented the percent change in vertical infections.

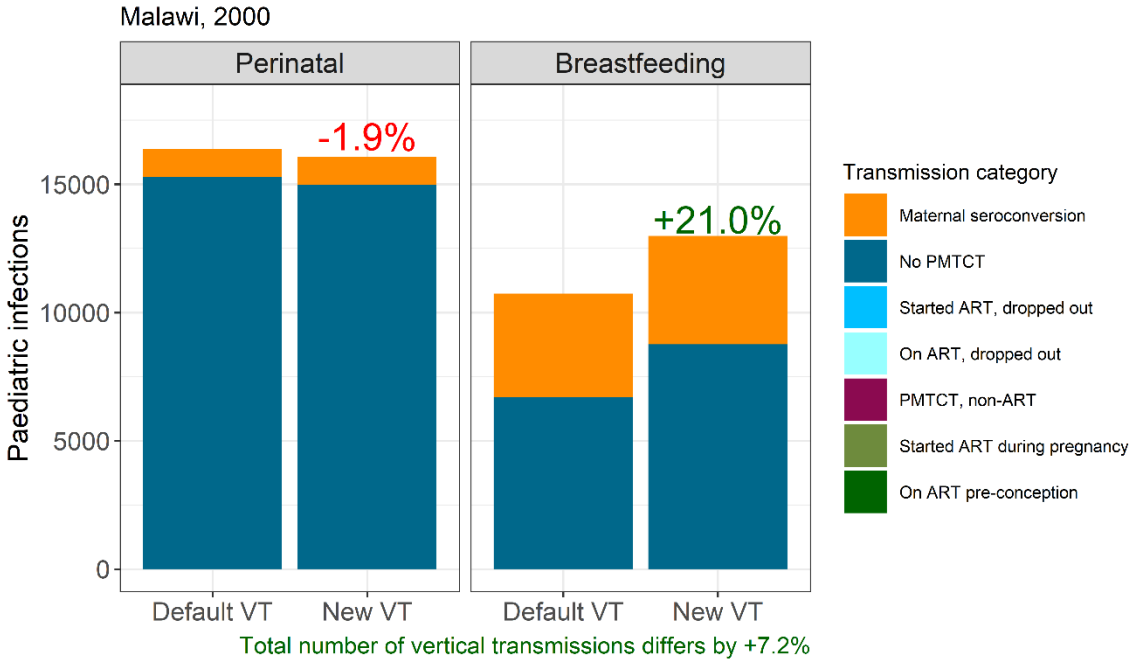


Figure S6.1. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Malawi 2000

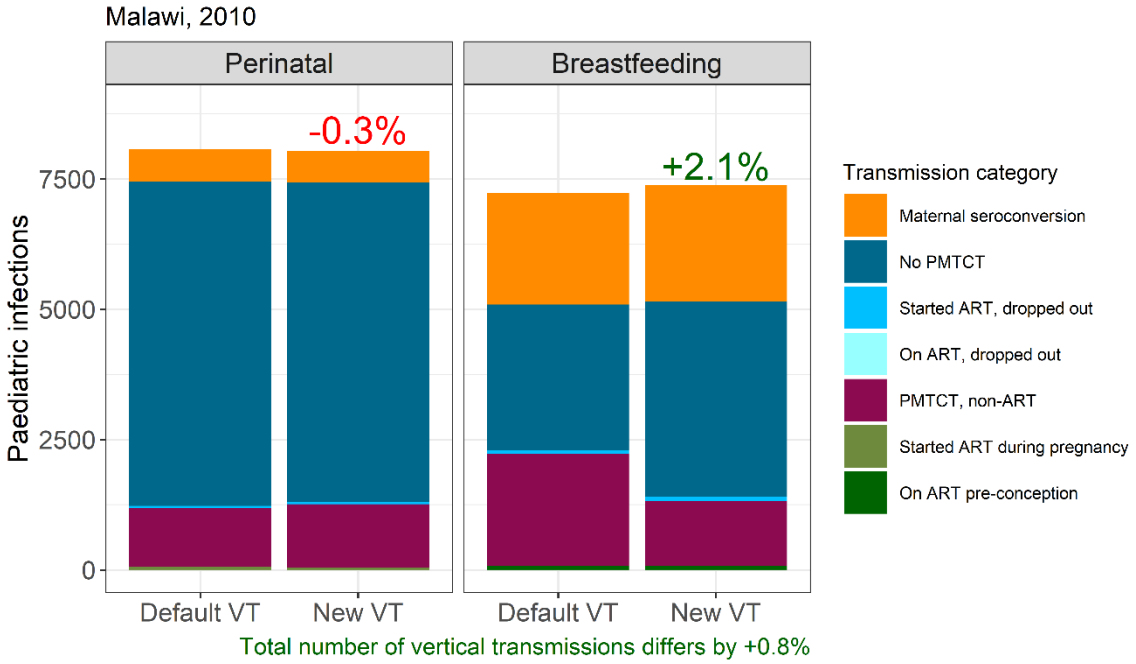


Figure S6.2. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Malawi 2010

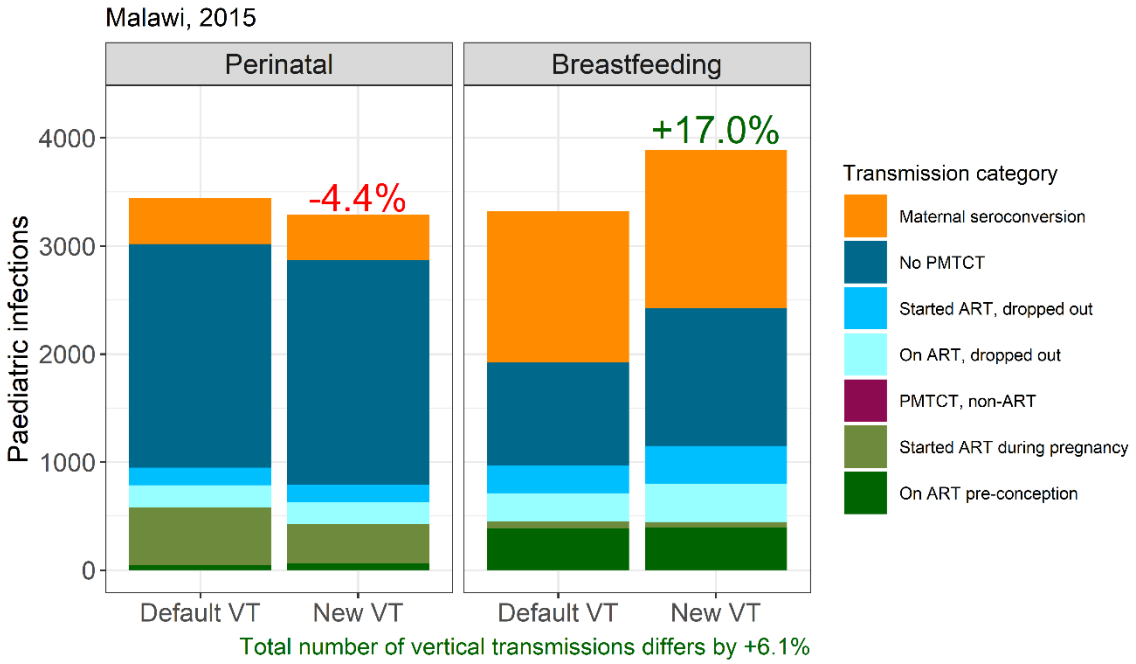


Figure S6.3. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Malawi 2015

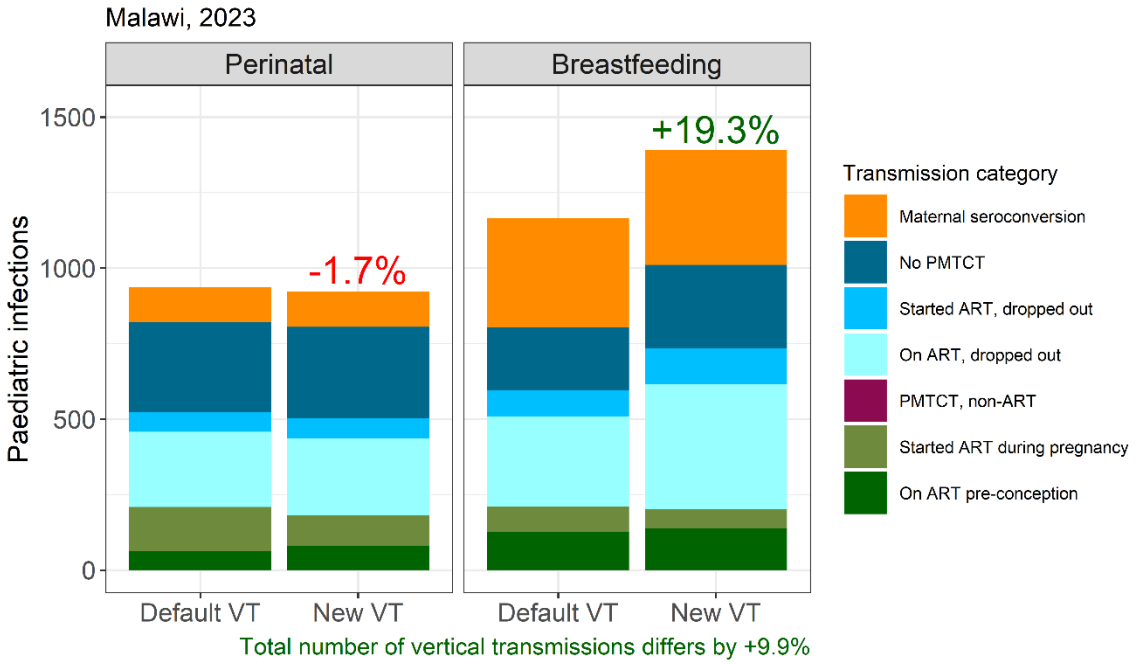


Figure S6.4. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Malawi 2023

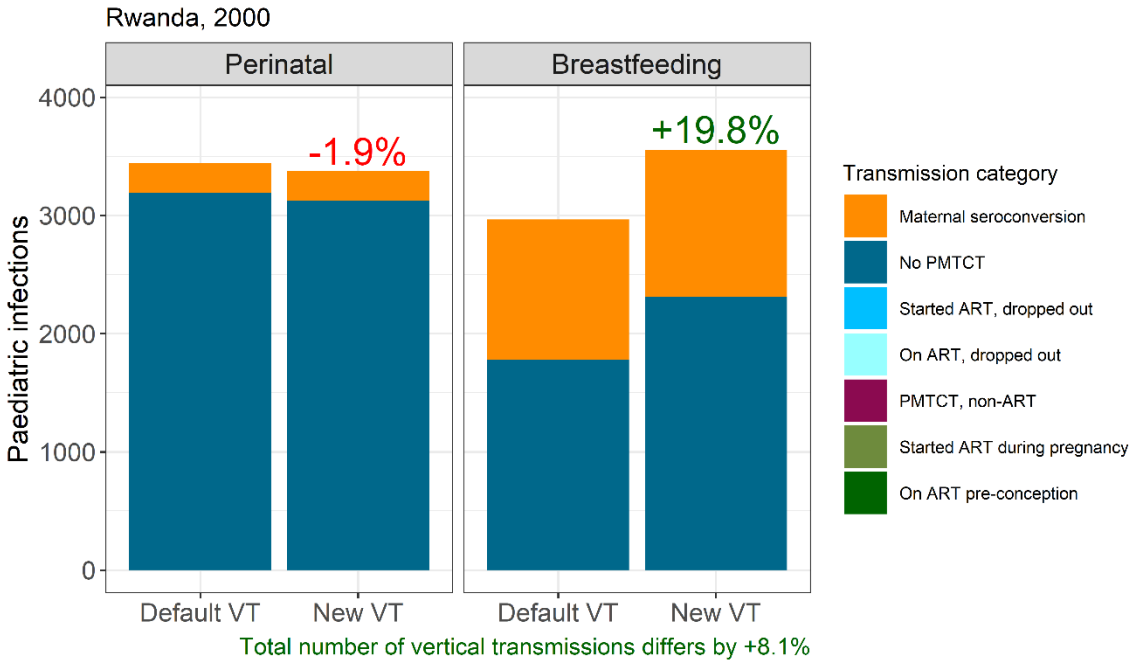


Figure S6.5. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Rwanda 2000

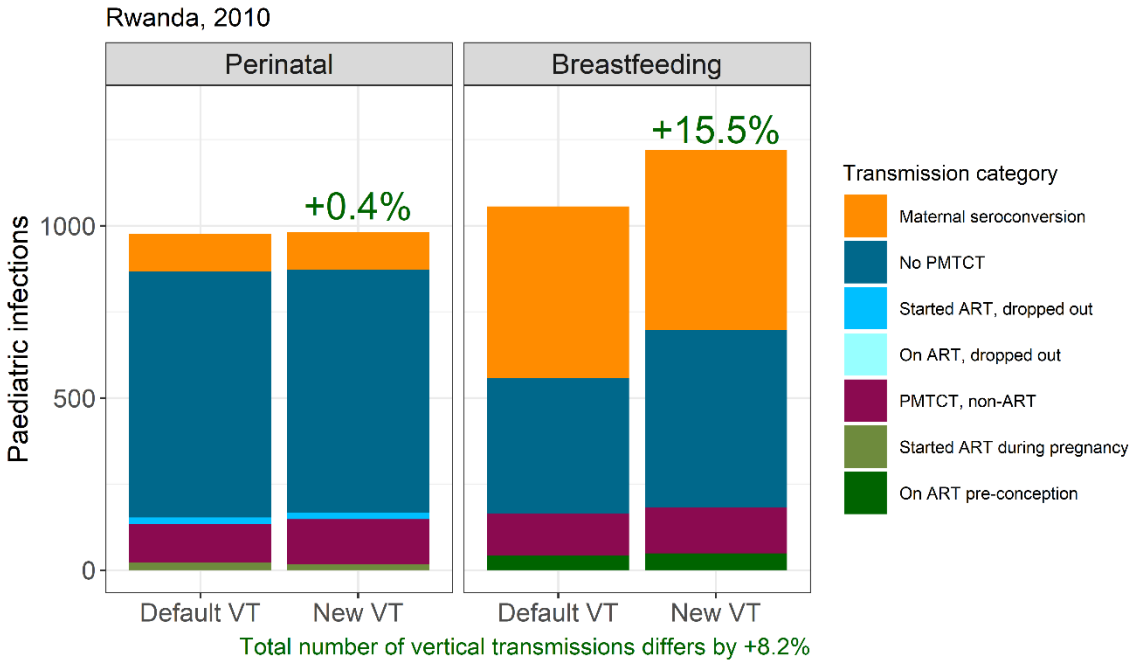


Figure S6.6. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Rwanda 2010

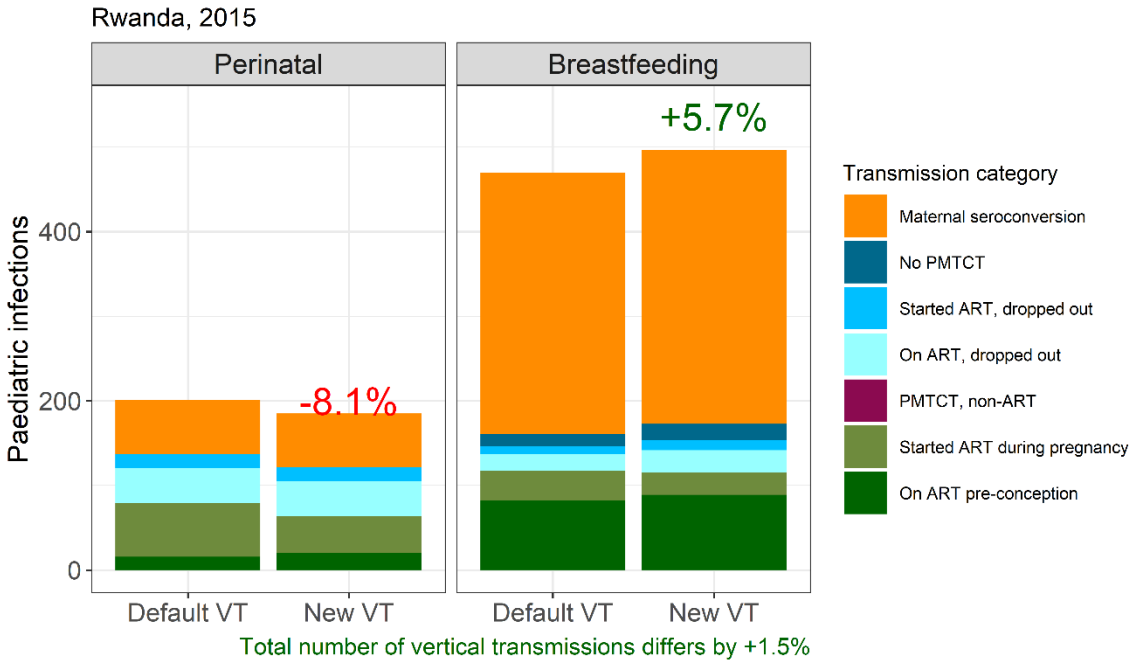


Figure S6.7. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Rwanda 2015

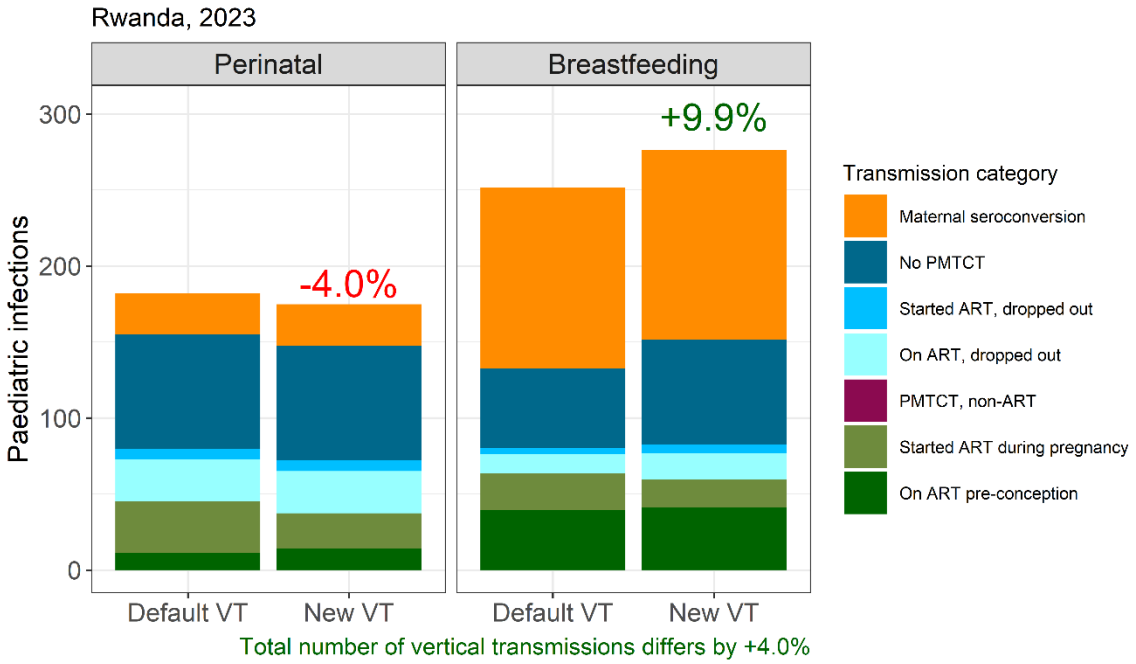


Figure S6.8. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Rwanda 2023

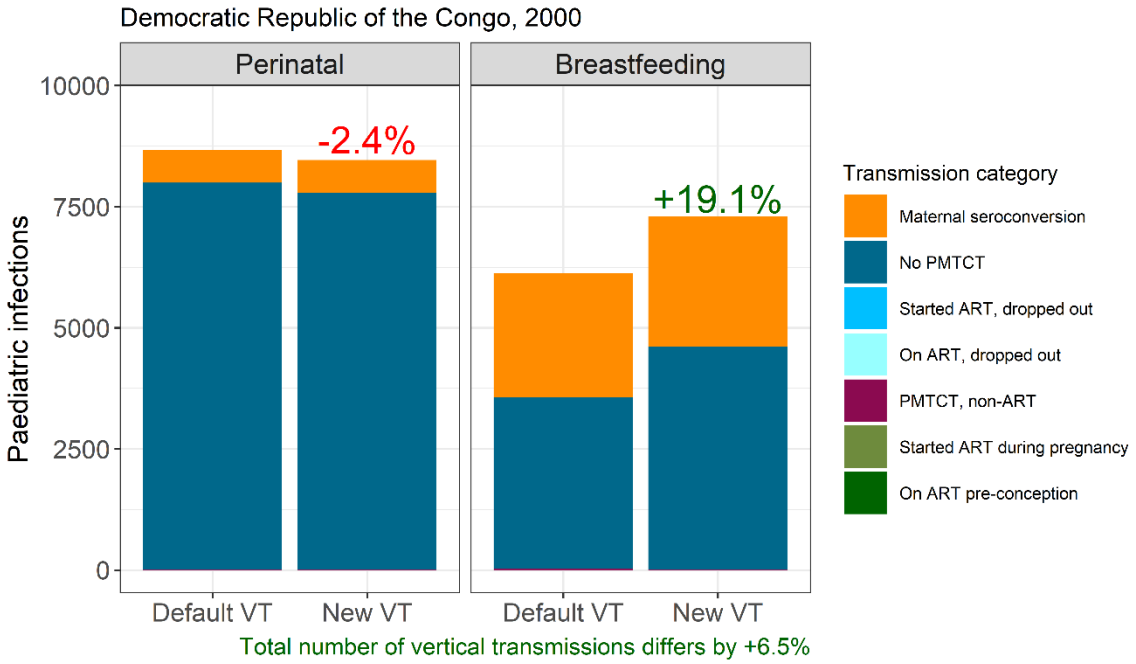


Figure S6.9. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Democratic Republic of the Congo 2000

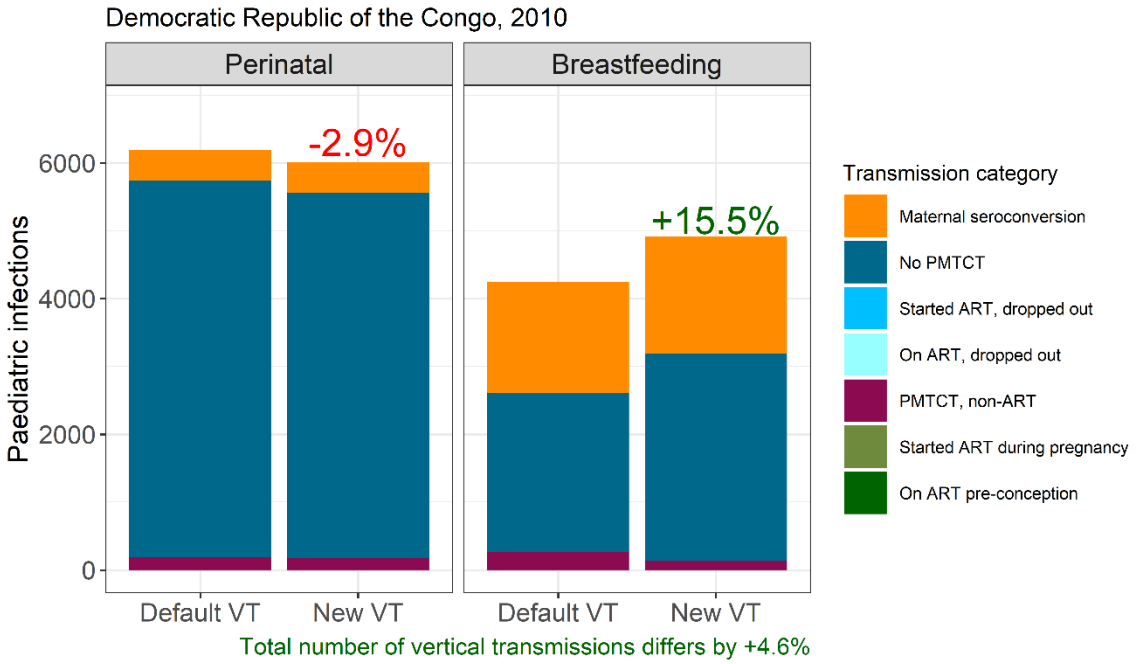


Figure S6.10. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Democratic Republic of the Congo 2010

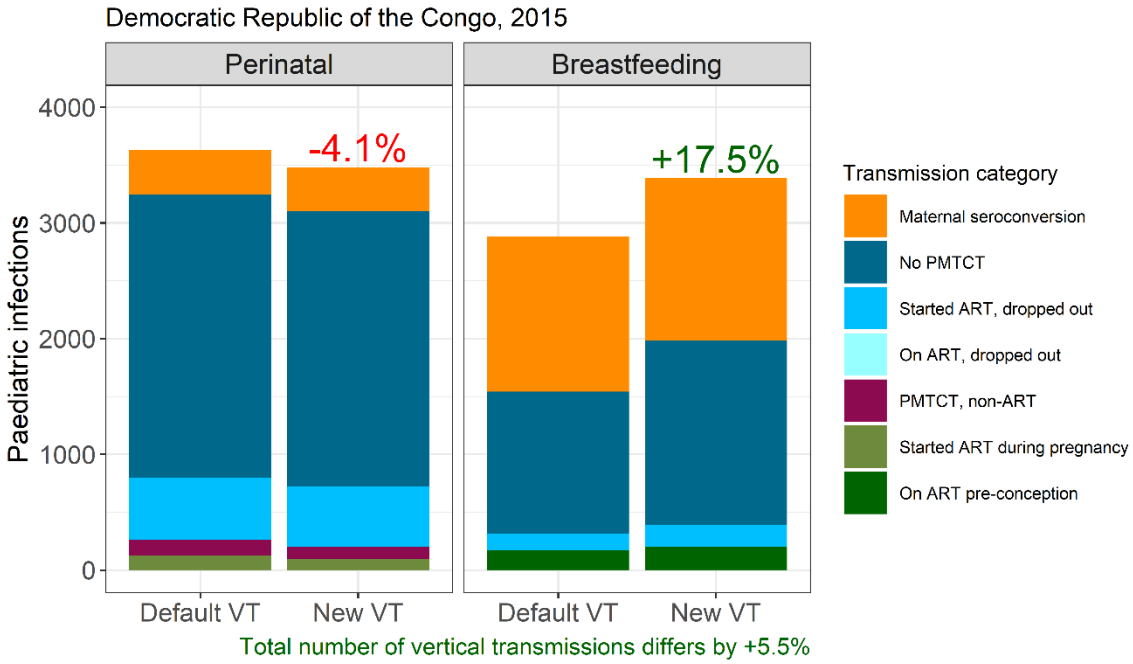


Figure S6.11. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Democratic Republic of the Congo 2015

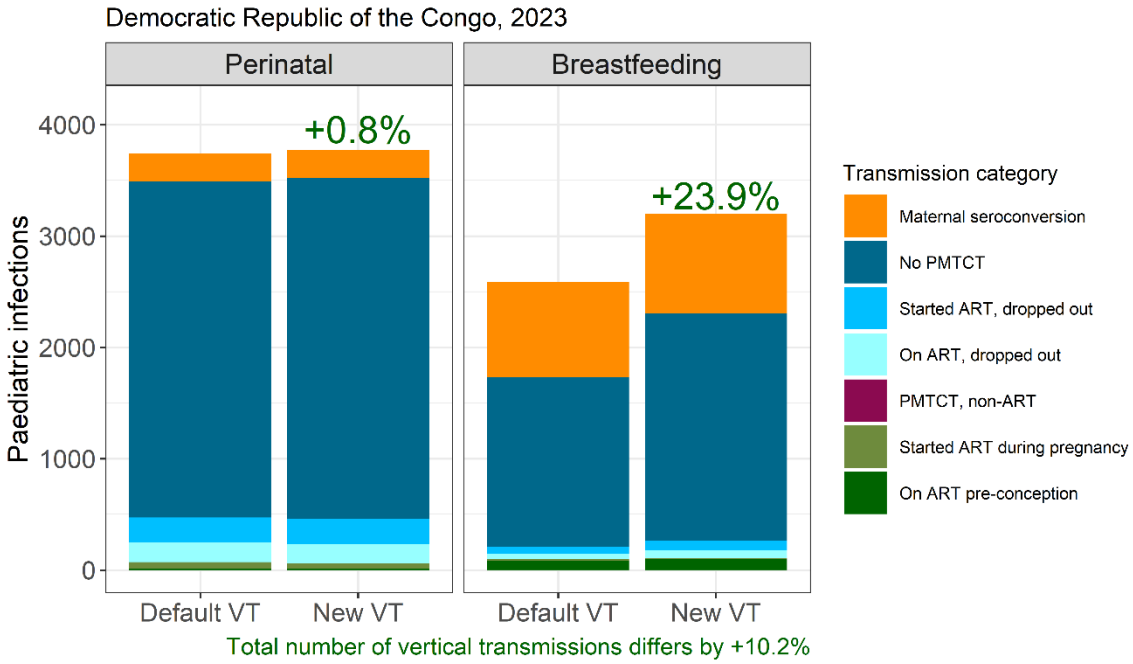


Figure S6.12. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Democratic Republic of the Congo 2023

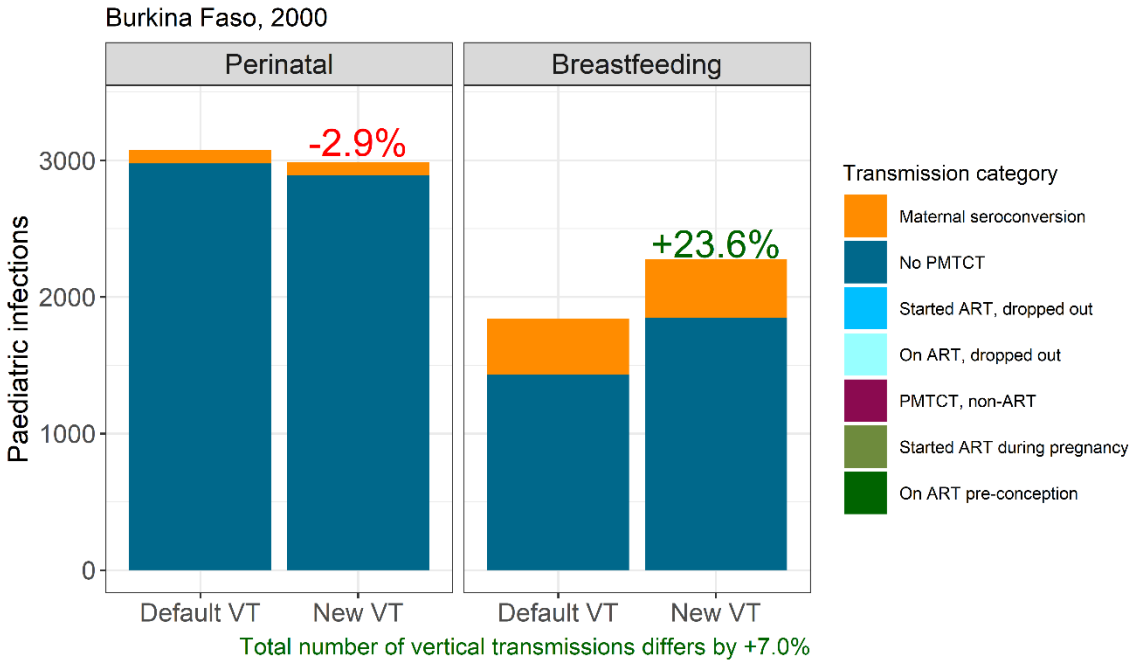


Figure S6.13. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Burkina Faso 2000

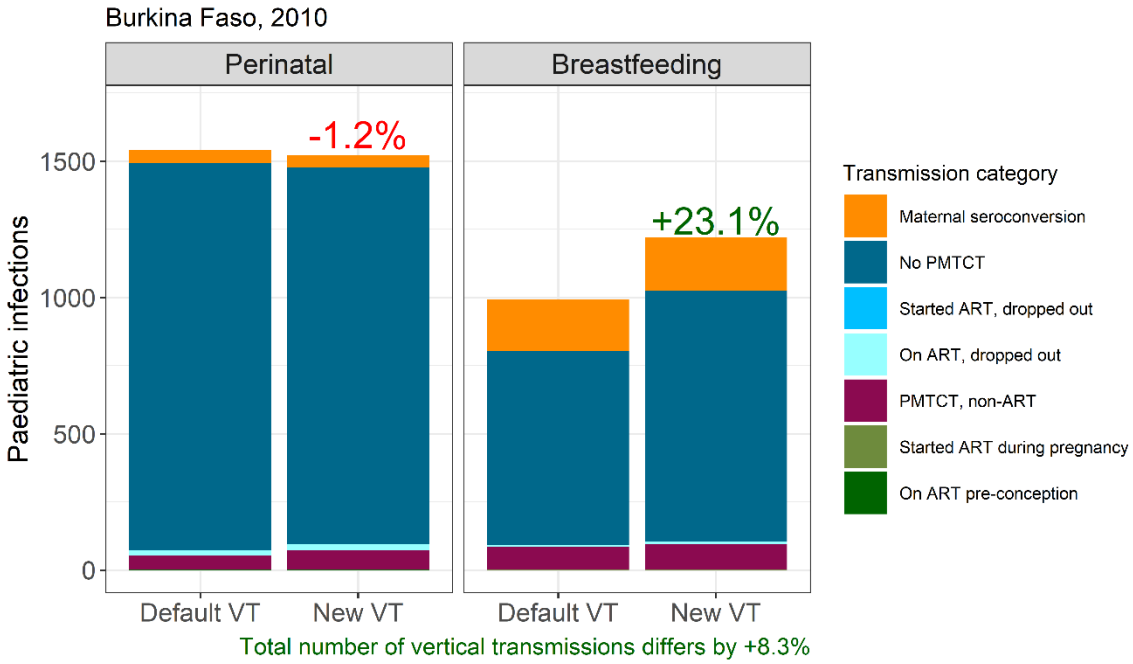


Figure S6.14. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Burkina Faso 2010

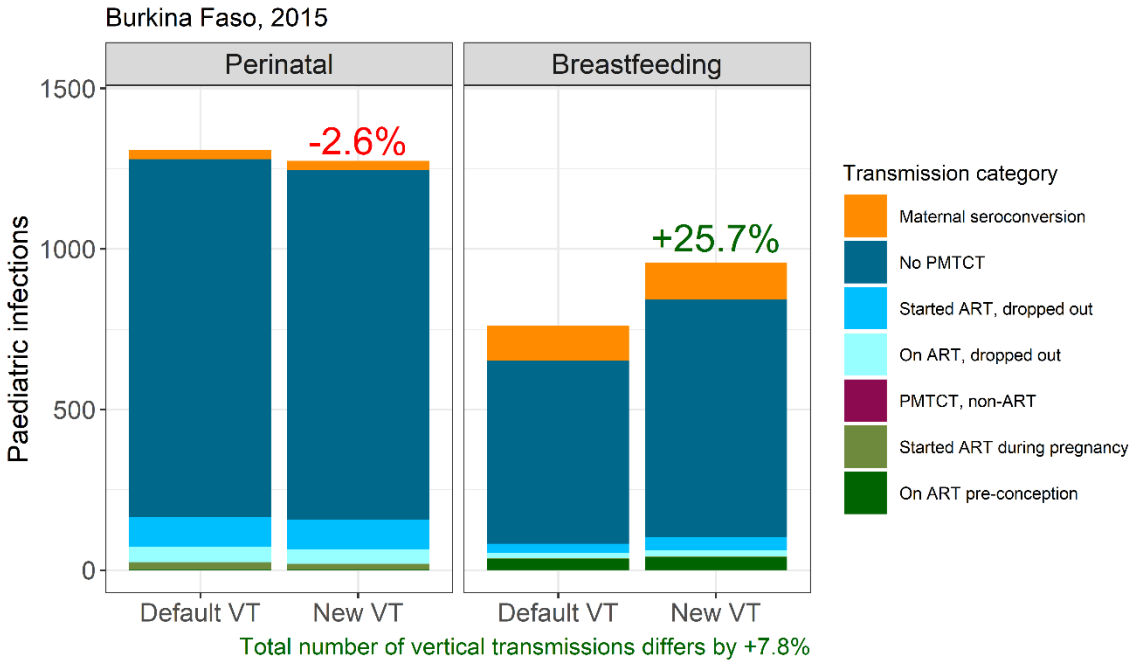


Figure S6.15. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Burkina Faso 2015

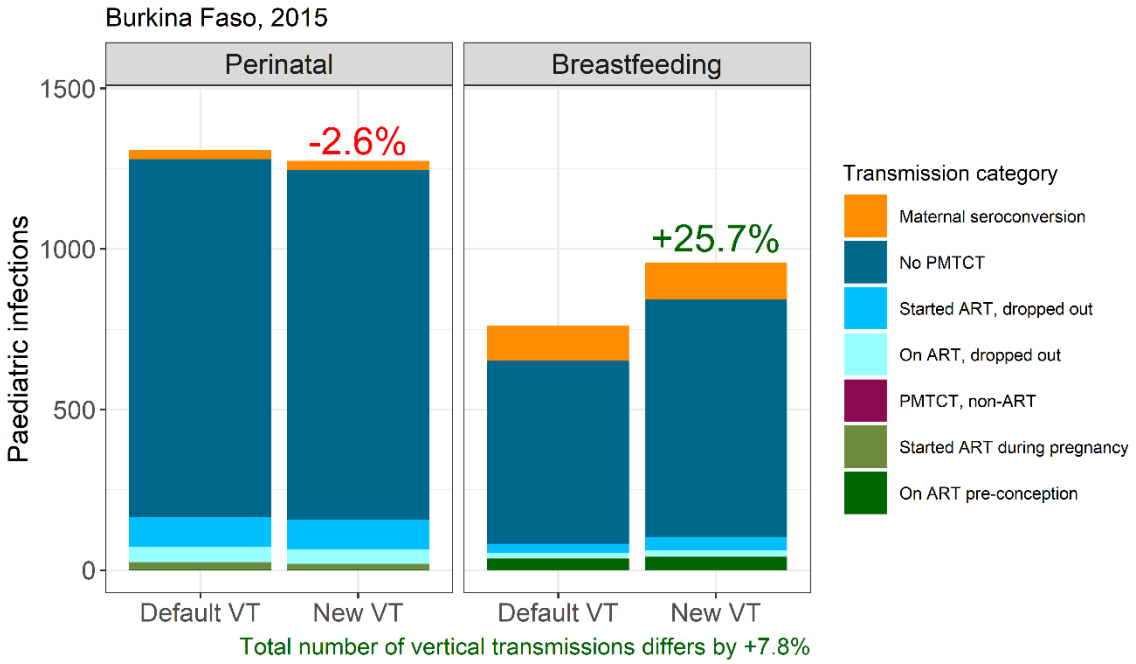


Figure S6.16. Change in vertical infections due to estimated vertical transmission probabilities by infection timing, Burkina Faso 2023

S7. References

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