**APPENDIX**

**Table A1**. **Parameters used in the HIV monoinfection, HBV/HIV coinfection, and HCV/HIV coinfection models.** CC: compensated cirrhosis, DC: decompensated cirrhosis, HCC: hepatocellular carcinoma, ART: antiretroviral treatment, PMTCT: preventing mother-to-child transmission initiative, HBIG: hepatitis B immune globulin, HBsAg: HBV surface antigen, HBeAg: HBV e antigen, TDF: tenofovir

| | Base-case parameter value point value (sampling bounds, distribution) | Reference |
|---|---|---|
| **HIV monoinfection** | | |
| Duration infection to CD4=500 off ART | 1.19 years (min 1.12, max 1.26, uniform) | [1, 2] |
| Duration CD4=500 to CD4=350 off ART | 3 years (min 2.97, max 3.02, uniform) | [1, 2] |
| Duration CD4=350 to CD4=200 off ART | 3.7 years (min 3.67, max 3.81, uniform) | [1, 2] |
| Duration CD4=200 to Death off ART | 2.7 years (min 2.5, max 2.9, uniform) | [2, 3] |
| Increased HIV survival on ART | 4-fold | [4-8] |
| Background mortality | Variable, by age | Used 1990 WHO life table values for South Africa for lifespan prior to HIV infection. For baseline analysis, used mixed gender. For vertical transmission sensitivity analysis, use female rates. |
| Proportion with long-term serodiscordant partners | 0.2 (min 0.1, max 0.3, uniform) | [9] |
| HIV serodiscordant couple transmission rate (per year) | | |
| Off ART | 0.1 (min 0.9, max 0.11, uniform) | [10] |
| On ART | Off ART rate reduced by 96% | [11] |
| Fertility rates (per year) | | |
| Age 25 to 30 | 0.1052 | [12]Age-specific fertility rates taken from general population country estimates and weighted by HIV-infection status |
| Age 30 to 35 | 0.0724 | |
| Age 35 to 40 | 0.0423 | |
| Age 40 to 45 | 0.0154 | |
| Age 45 to 50 | 0.0045 | |
| Age 50+ | 0 | |
| Vertical HIV transmission rates (per child) | | |
| PMTCT (maternal ART+ daily nevirapine for infants through end of breastfeeding) | 0.032 | [13]2% perinatally plus 6 mo. breastfeeding at 0.2%pm. Uncertainty ranges not presented. |
| Lifelong ART | 0.013 | [13]0.5% perinatally, 6 mo. breastfeeding at 0.16%pm. Uncertainty ranges not presented. |
| **HCV infection** | | |
| HIV progression rates and HIV response to ART in HCV coinfection | As for HIV monoinfection | [14-20] |
| Mild HCV to moderate HCV in HCV monoinfection (per year) | | |
| Age 25 to 50 | 0.024 (min 0.021, max 0.027, uniform) | [21-23] 7-10% progress to cirrhosis within 20 years from age 25 |
| Age 50 to 60 | 0.048 (min 0.025, max 0.070, uniform) | [21] Weighted equally by gender |
| Age 60 to 70 | 0.084 (min 0.042, max 0.126, uniform) | [21] Weighted equally by gender |
| Age 70+ | 0.114 (min 0.058, max 0.169, uniform) | [21] Weighted equally by gender |
| Moderate HCV to CC in HCV monoinfection | Equal to age-specific mild HCV to moderate HCV rate off ART | [21, 23, 24] Reported fibrosis rates generally linear |
| Factor acceleration in HCV progression to cirrhosis with HIV coinfection without ART | 2.5 (95%CI 1.8-3.4, lognormal) | [25, 26] |
| Impact of ART on coinfection HCV progression to cirrhosis with HIV coinfection with ART | Reduced by 33% | Base-case estimate from meta-analysis[25], but higher impact found in [27], so examine 30-80% in univariate sensitivity analysis. |
| CC to DC (per year) | 0.039 (min 0.03, max 0.048, uniform) | [28-30] One study in HCV/HIV coinfected individuals found an overall outcome (DC+HCC) rate of 6.8% per year[31] (similar to that found in monoinfected individuals[32]) and concluded no significant difference between |

| | | |
|---|---|---|
| | | HCV/HIV coinfection and monoinfection, and in line with our estimates combining the CC and DC and CC to HCC parameters. |
| CC to HCC (per year) | 0.024 (min 0.014, max 0.034, uniform) | [28-30, 33] |
| DC to HCC (per year) | Equal to CC to HCC death | Assume same as CC to HCC[34] |
| HCC to Death (per year) | 0.55 (min 0.3, max 0.8, uniform) | Survival similar in HCC patients coinfected with HIV[35]. Rates in HCV/HIV coinfection[36] similar to rates in HCV monoinfection[21, 22, 37] |
| DC to Death | | |
| HCV monoinfection (per year) | 0.14 (min 0.11, max 0.17, uniform) | [29, 30] |
| HCV/HIV coinfection | 2.26-fold monoinfection rates (95% CI 1.51-3.38, lognormal) | [38], In line with estimates from coinfected individuals[39, 40]: |
| Proportion with serodiscordant partners | Equal to HIV monoinfection | Assumption |
| HIV transmission rate between serodiscordant couples | Equal to HIV monoinfection | No data, but HIV viral loads do not appear to be elevated in coinfection[41]. |
| Vertical HIV transmission from HCV/HIV coinfected individuals (per child) | Assume equal to HIV monoinfection for all stages | Few data. Weak evidence to indicate HCV infection may increase HIV vertical transmission, but studies are limited by small sample sizes and do not directly compare vertical transmission between monoinfected and coinfected mothers[42]. One US study found an elevated HIV transmission rate from coinfected mothers, but this was only borderline significant when controlling for drug use (AOR 1.64 [95%CI 0.99-2.70]) which could be a potential confounder[43]. It is unclear how well this study translates to developing country settings and settings where drug use is not prevalent. No studies examine the impact of PMTCT or ART on vertical transmission in HCV/HIV coinfection. |
| PMTCT | | |
| Lifelong ART | | |
| Vertical HCV transmission | | |
| HCV monoinfection (per child) | 0.06 (min 0.04, max 0.08, uniform) | [42] |
| HCV/HIV coinfection off ART | 1.9-fold monoinfection (95%CI 1.4-2.7, lognormal) | [44] |
| HCV/HIV coinfection on ART | No impact | Few data. One study found weak evidence for a reduction in transmission[45], but ART known to increase HCV viral loads[46-48]. Conservatively assume no impact. |
| **HBV infection** | | |
| HIV progression and CD4 response to ART | Equal to that of HIV monoinfection | [49-51] |
| HBV to CC off ART for those with high HBV viraemia | | |
| HBV monoinfection (per year) | 0.024 (min 0.01, max 0.0590, triangular) | [52-54] point value, [55, 56] bounds |
| HBV/HIV coinfection with CD4>200 | Equal to HBV monoinfection | [49, 57] |
| HBV/HIV coinfection CD4<200 | 4.6-fold rate of CD4>200 (95% CI 1.5-13.7, lognormal) | [57, 58] |
| HBV to CC on ART for those with high HBV viraemia | | |
| HBV monoinfection (per year) | 0.002 (min 0, max 0.004, uniform) | [59] |
| HBV/HIV coinfection with CD4>200 | Same as monoinfection | [49, 57, 60] |
| HBV/HIV coinfection CD4<200 | 2.3-fold rate for CD4>200 (95% CI 1-5.3, lognormal) | [60]Showed CD4<200 associated with a lack of response and detectable viral load among coinfected individuals on TDF+3TC |
| HBV to CC for those with low HBV viraemia (HBeAg seroconverted) | 0.38-fold that of HBV high viraemia stage, either on or off ART (95%CI 0.24-0.63, lognormal) | [52, 61] |
| Proportion HBsAg+ with high HBV viraemia/active disease | | |
| HBV monoinfection | 0.2 | [62]Expert opinion |
| HBV/HIV coinfection | 0.33 (min 0.21, max 0.45, uniform) | [63] |
| HBV to HCC for those with high HBV | | |

| | | |
|---|---|---|
| viraemia | | |
| Off ART (per year) | 0.008 (min 0.005, max 0.011, uniform) | [54, 61, 64] |
| On ART | 0.37-fold rate compared to off ART (95% CI 0.15-0.91, lognormal) | [65] Conservatively use entecavir data on impact of progression to HCC. Expert opinion. |
| HBV to HCC for those with low HBV viraemia (HBeAg seroconverted) | | |
| Off ART (per year) | 0.001 (min 0, max 0.004, triangular) | [66, 67] |
| On ART | 0.37-fold rate compared to off ART (95% CI 0.15-0.91, lognormal) | [65] Conservatively use entecavir data on impact of progression to HCC. Expert opinion. |
| CC to DC | | |
| Off ART (per year) | 0.039 (min 0.03, max 0.048, uniform) | [68] |
| On ART | 0.1-fold rate compared to off ART (0-0.2, uniform) | [59] Suggests zero, as only decompensation occurred from those with HCC. Small studies in coinfection suggest zero as well [69] although one reported case of seroconversion hepatitis with rapid decompensation and death[70]. Expert opinion. |
| CC to HCC | | |
| Off ART (per year) | 0.07 (min 0.023, max 0.13, triangular) | [71, 72] point value, [64, 73] range |
| On ART | 0.37-fold rate compared to off ART (95% CI 0.15-0.91, lognormal) | [65] Conservatively use entecavir data |
| DC to HCC | | |
| Off ART | Equal to CC to HCC off ART rate | [74] |
| On ART | Equal to CC to HCC on ART rate | |
| HBV to death for those with high HBV viraemia | 0.0025 (min 0, max 0.005, uniform) | [52, 54, 75] |
| Off ART (per year) | 0.25-fold rate compared to off ART (0-0.5, uniform) | No deaths from HBV in monoinfection [59] or coinfection [76]. Expert opinion. |
| On ART | 0 | |
| HBV to death for those with low HBV viraemia (HBeAg seroconverted) | | |
| CC to Death | | |
| Off ART (per year) | 0.0555 (min 0, max 0.111, uniform) | [68] |
| On ART | 0.25-fold rate compared to off ART (0-0.5, uniform) | No deaths from CC in monoinfection [59], but some reported in a small coinfection study[76]. Expert opinion. |
| DC to Death | | |
| Off ART (per year) | 0.14 (min 0.11, max 0.17, uniform) | [68] |
| On ART | 0.25-fold rate compared to off ART (min 0, max 0.5, uniform) | No deaths from DC in [59] but some reported in a small coinfection study[76]. Expert opinion. |
| HCC to Death (per year) | 0.55 (min 0.3, max 0.8, uniform) | [68] |
| Proportion with serodiscordant partners | Equal to HIV monoinfection | Assumption |
| HIV transmission rate between serodiscordant couples | Equal to HIV monoinfection | No data, but HBV does not appear to increase HIV viral loads in coinfection[77] |
| Vertical HIV transmission from HBV/HIV coinfected individuals | Assume equal to HIV monoinfection for all stages | No data, but HBV does not appear to increase HIV viral loads in coinfection[77] |
| Vertical HBV transmission from HBV/HIV coinfected individuals with high HBV viraemia (per child) | | |
| Vaccination+HBIG (no TDF-PMTCT) | 0.23 (min 0.18, max 0.28, uniform) | [78] PMTCT does not contain TDF in 2010 South African guidelines [79] |
| TDF-PMTCT+vaccination+HBIG | 0.31 relative-risk that of vaccination only (95% CI 0.15-0.63, lognormal) | [80] No data on TDF, so used lamivudine PMTCT among monoinfection. |
| Lifelong ART +vaccination+HBIG | Equal to TDF-PMTCT+vaccination+HBIG | No data, so conservatively assume same as TDF-PMTCT (no additional benefit with lifelong ART) |
| Vertical HBV transmission from HBV/HIV coinfected individuals with HBeAg seroconverted disease | 0 | [81] No data on coinfection, so used monoinfection |

**Table A2. Disability weights**

| | Disability weight (sampling distribution) | Reference/Notes |
|---|---|---|
| **HIV monoinfection** | | |
| CD4 >500 cells/μL | Equal to ART value | [82] No GBD estimate so assumed equal to ART. |
| CD4 350-500 cells/μL | Equal to ART value | [82] No GBD estimate so assumed equal to ART. |
| CD4 200-350 cells/μL | 0.221 (min 0.132, max 0.31, uniform) | [82] symptomatic HIV, pre-AIDS |
| CD4<200 cells/μL | 0.547 (min 0.379, max 0.715, uniform) | [82] AIDS |
| ART | 0.053 (min 0.027, max 0.079, uniform) | [82] |
| **Hepatitis monoinfection** | | |
| Mild chronic HCV | 0.012 (min 0.001, max 0.023, uniform) | No GBD estimate, so used value for mild abdominopelvic problem[82] |
| Moderate HCV | Midpoint between mild chronic HCV and compensated cirrhosis: mean 0.068 | Assumed linear disability increase from mild chronic HCV to compensated cirrhosis, in line with other estimates[22] |
| Chronic HBV | 0.014 (min 0.005, max 0.083, triangular) | No GBD estimate. Calculated the point value by weighting according to proportion active/seroconverted (assume 20% active). We assume no disability for seroconverted state[83], and moderate abdominopelvic problem[82] for active state. Sample from a wide range due to uncertainty. |
| Compensated cirrhosis | 0.123 (min 0.07, max 0.176, uniform) | No GBD estimate, so used value for moderate abdominopelvic problem[82] |
| Decompensated cirrhosis | 0.194 (min 0.115, max 0.273, uniform) | [82] |
| Hepatocellular carcinoma | 0.484 (min 0.325, max 0.643, uniform) | [82] Taken from metastatic cancer |
| **Hepatitis coinfection** | Disability weights were compounded multiplicatively: disability weight=1-((1-HIV disability weight)*(1-hepatitis disability weight)). | |

**Model equations**

In our model, $C_{Hep}^{CD4}$ denotes coinfected individuals, with superscript *CD4=1,2, 3,4* denoting CD4 cell stage CD4>500 cells/μL, CD4 350-500 cells/μL, CD4 200-350 cells/μL, and CD4<200 cells/μL, respectively. The subscript denotes hepatitis disease stage. For the HCV model, *Hep=1,2,3,4,5* denotes mild HCV, moderate HCV, compensated cirrhosis, decompensated cirrhosis, and hepatocellular carcinoma, respectively. For the HBV model there is only one disease stage prior to compensated cirrhosis, so *Hep=1* is empty and *Hep=2* denotes chronic HBV; all other stages are equal between the models.

We model a closed cohort of coinfected individuals who begin the model at age 25. The model is initialized with all individuals in the highest CD4 cell stage and mildest hepatitis stage, so for the HCV model $C_1^1 = 1000$, and for the HBV model $C_2^1 = 1000$. Transition rates between CD4 cell counts are denoted by $\sigma_{ART}^{CD4}$, which are dependent on CD4 stage and ART status (with *ART=0,1* representing the values off and on ART, respectively). Background mortality, $\mu(t)$, is time-dependent, to represent the age-dependent mortality of the cohort. The transition rates from mild to moderate HCV ($\alpha_{\mathrm{ART}}(\mathrm{t})$) and moderate HCV to compensated cirrhosis ($\beta_{\mathrm{ART}}(\mathrm{t})$) are dependent on time (to represent age-dependent parameters) and ART status. The transition rate from chronic HBV to compensated cirrhosis ($\beta_{\mathrm{ART}}^{CD4}$) is dependent on ART status and CD4 cell count. Other liver-related transition rates are from compensated cirrhosis to decompensated cirrhosis ($\gamma_{\mathrm{ART}}$), compensated cirrhosis to hepatocellular carcinoma ($\delta_{\mathrm{ART}}$), and decompensated cirrhosis to hepatocecllular carcinoma ($\zeta_{\mathrm{ART}}$).

The HBV model includes excess liver-related mortality from chronic HBV ($\vartheta_{ART}$), compensated cirrhosis ($\nu_{ART}$), decompensated cirrhosis ($\kappa_{ART}$) and hepatocellular carcinoma($\upsilon$). It also includes a transition from chronic HBV to hepatocellular carcinoma ($\eta_{ART}$). By contrast, the HCV model only includes excess mortality from decompensated cirrhosis ($\kappa$) and hepatocellular carcinoma($\upsilon$), and no transition from moderate HCV to HCC, such that $\vartheta = 0$ and $\nu = 0$, and $\eta = 0$.

Overall, the impact of ART is assumed to affect transition rates between CD4 cell counts ($\sigma_{ART}^{CD4}$). For HCV/HIV coinfection model, ART is also assumed to affect the transition from mild HCV to moderate HCV ($\alpha_{\mathrm{ART}}$) and moderate HCV to compensated cirrhosis ($\beta_{\mathrm{ART}}(\mathrm{t})$). For the HBV/HIV coinfection model, ART is assumed to affect all liver-related transition rates except from hepatocellular carcinoma to death ($\upsilon$).

The different ART eligibility scenarios are modeled as follows:

- For ART at CD4<350, *ART=0* for *CD4=1,2* and *ART=1* for *CD4=3,4*.
- For ART at CD4<500, *ART=0* for *CD4=1* and *ART=1* for *CD4=2,3,4*.
- For immediate ART, *ART=1* for *CD4=1,2,3,4*.

For individuals with CD4>500 cells/μL:

$$\frac{dC_1^1}{dt} = -(\alpha_{ART}(t) + \sigma_{ART}^1 + \mu(t))C_1^1$$

$$\frac{dC_2^1}{dt} = \alpha_{ART}(t)C_1^1 - (\beta_{ART}^{CD4}(t) + \eta_{ART} + \sigma_{ART}^1 + \vartheta_{ART} + \mu(t))\, C_2^1$$

$$\frac{dC_3^1}{dt} = \beta_{ART}^{CD4}(t)C_2^1 - (\gamma_{ART} + \delta_{ART} + \sigma_{ART}^1 + \nu_{ART} + \mu(t))C_3^1$$

$$\frac{dC_4^1}{dt} = \gamma_{ART}C_3^1 - (\zeta_{ART} + \sigma_{ART}^1 + \kappa_{ART} + \mu(t))\, C_4^1$$

$$\frac{dC_5^1}{dt} = \eta_{ART}C_2^1 + \delta_{ART}C_3^1 + \zeta_{ART}C_4^1 - (\sigma_{ART}^1 + \upsilon + \mu(t))C_5^1$$

For individuals with CD4 350-500 cells/μL:

$$\frac{dC_1^2}{dt} = \sigma_{ART}^1 C_1^2 - (\alpha_{ART}(t) + \sigma_{ART}^2 + \mu(t))C_1^2$$

$$\frac{dC_2^2}{dt} = \sigma_{ART}^1 C_2^2 + \alpha_{ART}(t)C_1^2 - (\beta_{ART}^{CD4}(t) + \eta_{ART} + \sigma_{ART}^2 + \vartheta_{ART} + \mu(t))\, C_2^2$$

$$\frac{dC_3^2}{dt} = \sigma_{ART}^1 C_3^2 + \beta_{ART}^{CD4}(t)C_2^2 - (\gamma_{ART} + \delta_{ART} + \sigma_{ART}^2 + \nu_{ART} + \mu(t))C_3^2$$

$$\frac{dC_4^2}{dt} = \sigma_{ART}^1 C_4^2 + \gamma_{ART}C_3^2 - (\zeta_{ART} + \sigma_{ART}^2 + \kappa_{ART} + \mu(t))\, C_4^2$$

$$\frac{dC_5^2}{dt} = \sigma_{ART}^1 C_5^2 + \eta_{ART}C_2^2 + \delta_{ART}C_3^2 + \zeta_{ART}C_4^2 - (\sigma_{ART}^2 + \upsilon + \mu(t))C_5^2$$

For individuals with CD4 200-350 cells/μL:

$$\frac{dC_1^3}{dt} = \sigma_{ART}^2 C_1^3 - (\alpha_{ART}(t) + \sigma_{ART}^3 + \mu(t))C_1^3$$

$$\frac{dC_2^3}{dt} = \sigma_{ART}^2 C_2^3 + \alpha_{ART}(t)C_1^3 - (\beta_{ART}^{CD4}(t) + \eta_{ART} + \sigma_{ART}^3 + \vartheta_{ART} + \mu(t))\, C_2^3$$

$$\frac{dC_3^3}{dt} = \sigma_{ART}^2 C_3^3 + \beta_{ART}^{CD4}(t)C_2^3 - (\gamma_{ART} + \delta_{ART} + \sigma_{ART}^3 + \nu_{ART} + \mu(t))C_3^3$$

$$\frac{dC_4^3}{dt} = \sigma_{ART}^2 C_4^3 + \gamma_{ART}C_3^3 - (\zeta_{ART} + \sigma_{ART}^3 + \kappa_{ART} + \mu(t))\, C_4^3$$

$$\frac{dC_5^3}{dt} = \sigma_{ART}^2 C_5^3 + \eta_{ART}C_2^3 + \delta_{ART}C_3^3 + \zeta_{ART}C_4^3 - (\sigma_{ART}^3 + \upsilon + \mu(t))C_5^3$$

For individuals with CD4<200 cells/μL:

$$\frac{dC_1^4}{dt} = \sigma_{ART}^3 C_1^4 - (\alpha_{ART}(t) + \sigma_{ART}^4 + \mu(t))C_1^4$$

$$\frac{dC_2^4}{dt} = \sigma_{ART}^3 C_2^4 + \alpha_{ART}(t)C_1^4 - (\beta_{ART}^{CD4}(t) + \eta_{ART} + \sigma_{ART}^4 + \vartheta_{ART} + \mu(t))\, C_2^4$$

$$\frac{dC_3^4}{dt} = \sigma_{ART}^3 C_3^4 + \beta_{ART}^{CD4}(t)C_2^4 - (\gamma_{ART} + \sigma_{ART}^4 + \delta_{ART} + \nu_{ART} + \mu(t))C_3^4$$

$$\frac{dC_4^4}{dt} = \sigma_{ART}^3 C_4^4 + \gamma_{ART} C_3^4 - (\zeta_{ART} + \sigma_{ART}^4 + \kappa_{ART} + \mu(t))\, C_4^4$$
$$\frac{dC_5^4}{dt} = \sigma_{ART}^3 C_5^4 + \eta_{ART} C_2^4 + \delta_{ART} C_3^4 + \zeta_{ART} C_4^4 - (\sigma_{ART}^4 + \upsilon + \mu(t)) C_5^4$$

**Monoinfection**

For HIV monoinfection, all liver-related transition rates are set to zero. For HCV monoinfection or HBV monoinfection analyses, all HIV-progression rates are set to zero.

**Discontinuation sensitivity analysis**

For the discontinuation sensitivity analysis, we duplicate the model compartments and allow for movement out of ART stages to their respective disease stage with no ART coverage. Those who discontinue are not eligible for reinitiation on ART.

**Sexual partners sensitivity analysis**

For this analysis, we include a separate population of long-term serodiscordant heterosexual partners, denoted by $S^n$ , with superscript *n=0* denoting susceptible partners, *n=1,2,3,4* denoting HIV-monoinfected partners with CD4 cell counts CD4>500 cells/μL, CD4 350-500 cells/μL, CD4 200-350 cells/μL, and CD4<200 cells/μL, respectively. Additionally, *n=5* denotes uninfected partners who are no longer at risk due to death of their coinfected partner. We assume only a fraction of the coinfected population has long-term serodiscordant heterosexual partners ($\psi$), and therefore the initial conditions for the partners analysis are $S^0 = \psi 1000$, where $S^{n=1\ldots5} = 0$. Partners can become infected at an average rate weighted by the proportion of the coinfection population who are on or off ART. In this term, *N* represents the total size of the coinfected population. The annual risk of HIV transmission within a serodiscordant partnership if the partner is not on ART is ($\pi$), which we assume is reduced by a factor $\Gamma$ when on ART.

All partners are subject to background mortality rates ($\mu(t)$) equal to that of coinfection. Partners stop being at risk of infection at an annual rate ($\theta(C_{HBV}^{CD4})$), which is determined by calculating the proportion of coinfected individuals dying each year. Partners who are HIV-infected transition through the CD4 stages at a rate $\sigma_{ART}^{CD4}$, which is dependent on their CD4 stage (*CD4=1,2,3,4*) and also their ART status (*ART=0, 1* for off or on ART, respectively). ART eligibility for monoinfected partners is defined as the eligibility for the 'baseline' analysis- e.g. CD4<350 cells/μL for partners in the analysis which compares initiation for coinfected individuals at CD4<500 cells/μL versus CD4<350 cells/μL, and CD4<500 cells/μL for partners when the analysis compares immediate ART eligibility compared to CD4<500 cells/μL. The equations for sexual partners are:

$$\frac{dS^0}{dt} = -\frac{\pi \sum_{CD4=1\ldots4} C_0^{CD4} + \Gamma\pi \sum_{CD4=1\ldots4} C_1^{CD4}}{N} S^0 - (\theta(C_{ART}^{CD4}) + \mu(t)) S^0$$

$$\frac{dS^1}{dt} = \frac{\pi \sum_{CD4=1\ldots4} C_0^{CD4} + \Gamma\pi \sum_{CD4=1\ldots4} C_1^{CD4}}{N} S^0 - (\sigma_{ART}^1 + \mu(t))S^1$$
$$\frac{dS^2}{dt} = \sigma_{ART}^1 S^1 - (\sigma_{ART}^2 + \mu(t))S^2$$
$$\frac{dS^3}{dt} = \sigma_{ART}^2 S^2 - (\sigma_{ART}^3 + \mu(t))S^3$$
$$\frac{dS^4}{dt} = \sigma_{ART}^3 S^3 - (\sigma_{ART}^4 + \mu(t))S^4$$
$$\frac{dS^5}{dt} = \theta\left(C_{ART}^{CD4}\right)S^0 - (\mu(t))S^5$$

**Fertility sensitivity analysis**

In this sensitivity analysis, we explore the impact of early ART on vertical transmission of HIV and HBV or HCV. We only evaluate the relative change in vertical transmissions of HIV and HCV or HBV, and do not calculate an estimate of efficiency (incremental person-years of ART per DALY averted) as the model projects different numbers of babies born in the intervention and baseline scenarios due to changes in life-expectancy on ART. For this analysis, we model a separate cohort of female coinfected individuals, who are subject to female-specific mortality rates. The number of births is determined by the age-specific fertility rates (taken from general population country-estimates and weighted by HIV+ status[12]). We assume all mothers receive prevention of mother-to-child transmission (PMTCT) initiatives, including ART through the end of breastfeeding (for those not on lifelong ART), and daily nevirapine throughout breastfeeding for the infant[79]. We assume a risk of vertical transmission of HIV of 1.3% if the mother is on lifelong ART (0.5% perinatally, plus 0.16% per month postnatally while breastfeeding[13]), 3.2% if the mother is on PMTCT (2% perinatally, plus 0.2% per month postnatally[13]), assuming a 6 month duration of breastfeeding. We assume the children are subject to a risk of infection which is dependent on the proportion of coinfected women on lifelong ART at the time of birth.

*HBV/HIV coinfection*

For HBV vertical transmission, we assumed that infants of all women (regardless of ART status) received passive-active immunization and hepatitis B immune globulin (HBIG) at birth. We assume no vertical transmission of HBV from HBeAg seroconverted mothers. HBV vertical transmission rates are approximately 23% in chronic HBV monoinfected mothers with active disease whose infants receive passive-active immunization and HBIG at birth[78]. A meta-analysis found that the relative risk of vertical transmission from mothers on ART to infants (with passive-active immunization) as compared to immunization only is 0.31 (0.15-0.63)[80]. We found no evidence to indicate that transmission rates or impact of ART were different in HBV/HIV coinfection compared to HBV monoinfection.

*HCV/HIV coinfection*

HCV vertical transmission rates are low, at about 4-8% in HCV monoinfected mothers, and the progression of pediatric HCV infection is very slow with few clinical symptoms in the first 15 years[42, 84]. There is good evidence that coinfection with HIV increases HCV vertical transmission, with a meta-analysis finding an increase by about 1.9-fold [95%CI 1.4-2.7][44]. However, the impact of ART on HCV transmission is unclear as data are limited. One 2005 European study among 184 women found weak evidence that HAART was associated with a reduction in transmission in coinfected mothers (AOR 0.26 [95%CI 0.07-1.01], p=0.05)[45] but no other studies have explored this, and the mechanism by which ART could reduce vertical HCV transmission is unclear as some studies indicate ART increases HCV viral load[20, 46-48]. We therefore assume a 1.9-fold increase in HCV vertical transmission as compared to HCV monoinfection, and we assume ART does not impact HCV vertical transmission.

It is unclear whether HCV infection increases HIV vertical transmission. HIV viral loads do not appear to be elevated during pregnancy[41]. There is weak evidence to indicate HCV infection may increase HIV vertical transmission, but studies are limited by small sample sizes and do not directly compare vertical transmission between monoinfected and coinfected mothers[42]. One study in the US directly compares HIV transmission between monoinfected individuals to coinfected individuals found an elevated HIV transmission rate from coinfected mothers, but this was only borderline significant when controlling for drug use (AOR 1.64 [95%CI 0.99-2.70]) which could be a potential confounder[43]. It is unclear how well this study translates to developing country settings and settings where drug use is not prevalent. As a conservative assumption, we assume HCV does not increase HIV vertical transmission. Finally, there are no studies exploring the impact of ART on HIV vertical transmission in coinfected individuals, so we assume impact is equal to HIV monoinfected individuals.

Finally, vertical transmission of HCV/HIV coinfection does occur, albeit at a lower rate than transmission of the monoinfections from coinfected mothers, at a rate of around 4%[42]. No studies have examined the impact of ART on coinfection transmission. Due to the low vertical transmission rate of coinfection, the uncertainty surrounding the impact of ART, and the fact that pediatric coinfection disease progression is likely to be dominated by HIV, will neglect vertical transmission of HCV/HIV coinfection.

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