# Infectious disease modelling of HIV prevention interventions: A Systematic review and narrative synthesis of compartmental models

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*List of abbreviations*

AIDS, Acquired immune deficiency syndrome; ART, Antiretroviral therapy; bNAbs, Broadly neutralizing HIV-1 antibodies; CE, Cost-effectiveness; EIMC, Early-infant male circumcision; HIC, High income country; HIV, Human immunodeficiency virus; IV, Intravenous; LMIC, Low-and-middle-income countries; MSM, Men who have sex with men ; NA, Not applicable ; PEP, Post-exposure prophylaxis ; PMTCT, Prevention of mother to child transmission; PrEP, Pre-exposure prophylaxis; STI, Sexually transmitted infection ; TRACE, TRAnsparent and Comprehensive Ecological modelling documentation; UNAIDS, The Joint United Nations Programme on HIV and AIDS; VMMC, Voluntary medical male circumcision ;WHO, World health organisation

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## Online Resource 1 –Searches performed in each database

### Medline

1 (HIV or hiv-1 or hiv-2 or AIDS or human immunodeficiency virus or acquired immune deficiency syndrome).ti,ab.
2 exp HIV/
3 exp HIV Infections/
4 1 or 2 or 3
5 (Pre-exposure prophylaxis or pre exposure prophylaxis or PrEP or Broadly Neutralizing HIV-1 Antibod* or BNAB* or Antibody-Mediated or AMP or Circumcis* or vaccin*).ti,ab.
6 exp primary prevention/ or pre-exposure prophylaxis/
7 exp Circumcision, Male/
8 vaccines/ or viral vaccines/ or exp AIDS vaccines/
9 5 or 6 or 7 or 8
10 (model* or cost* or economic evaluation or simulation or math*).ti.
11 models, theoretical/ or models, economic/
12 10 or 11
13 4 and 9 and 12
14 limit 13 to last 5 years

### Embase

1 (HIV or hiv-1 or hiv-2 or AIDS or human immunodeficiency virus or acquired immune deficiency syndrome).ti,ab.
2 exp Human immunodeficiency virus/
3 exp Human immunodeficiency virus infection/
4 1 or 2 or 3
5 (Pre-exposure prophylaxis or pre exposure prophylaxis or PrEP or Broadly Neutralizing HIV-1 Antibod* or BNAB* or Antibody-Mediated or AMP or Circumcis* or vaccin*).ti,ab.
6 exp primary prevention/
7 exp pre-exposure prophylaxis/

8 exp circumcision/
9 vaccine/ or virus vaccine/ or exp Human immunodeficiency virus vaccine/
10 5 or 6 or 7 or 8 or 9
11 (model* or cost* or economic evaluation or simulation or math*).ti.
12 exp mathematical model/ or exp compartment model/
13 11 or 12
14 4 and 10 and 13
15 limit 14 to last 5 years

**Global health**

1 (HIV or hiv-1 or hiv-2 or AIDS or human immunodeficiency virus or acquired immune deficiency syndrome).ti,ab.
2 exp human immunodeficiency viruses/
3 exp hiv infections/
4 1 or 2 or 3
5 (Pre-exposure prophylaxis or pre exposure prophylaxis or PrEP or Broadly Neutralizing HIV-1 Antibod* or BNAB* or Antibody-Mediated or AMP or Circumcis* or vaccin*).ti,ab.
6 circumcision/
7 exp vaccines/
8 5 or 6 or 7
9 (model* or cost* or economic evaluation or simulation or math*).ti.
10 exp mathematical models/
11 9 or 10
12 4 and 8 and 11
13 limit 12 to last 5 years

**Econlit**

1 (HIV or hiv-1 or hiv-2 or AIDS or human immunodeficiency virus or acquired immune deficiency syndrome).ti,ab.
2 (Pre-exposure prophylaxis or pre exposure prophylaxis or PrEP or Broadly Neutralizing HIV-1 Antibod* or BNAB* or Antibody-Mediated or AMP or Circumcis* or vaccin*).ti,ab.
3 (model* or cost* or economic evaluation or simulation or math*).ti.
4 1 and 2 and 3
5 limit 4 to last 5 years

## Online Resource 2 - TRACE appraisal criteria

| TRACE guidelines | Description | Author determined traffic light system | |
|---|---|---|---|
| Problem formulation | ‘The decision-making context in which the model will be used; the types of model clients or stakeholders addressed; a precise specification of the question(s) that should be answered with the model, including a specification of necessary model output’.[1] | Green | Clear justification supplied for why article is being undertaken |
| | | Red | Unclear justification |
| Model description | ‘The model, i.e. a detailed written model description. For individual/agent-based and other simulation models, the ODD protocol is recommended as standard format. For complex submodels, include concise explanations of the underlying rationale. Model users should learn what the model is, how it works, and what guided its design’. [1] | Green | Full detailed differential equations explaining model provided |
| | | Amber | Differential equations provided, however clarity required to enable model to be reproduced |
| | | Red | Differential equations not provided |
| Data evaluation | ‘The quality and sources of numerical and qualitative data used to parameterize the model, both directly and inversely via calibration, and of the observed patterns that were used to design the overall model structure. This critical evaluation will allow model users to assess the scope and the uncertainty of the data and knowledge on which the model is based’. [1] | Green | ▪ Demographics up to date<br>▪ Parameters used in the model are relevant to the population<br>▪ Calibration undertaken clear<br>▪ Expert opinion is not paramount in determining parameter values<br>▪ Any uncertainty in parameters is included in sensitivity analysis |
| | | Amber | Failure for at least one of above |
| | | Red | Failure for three or more of above |
| Conceptual model evaluation | ‘The simplifying assumptions underlying a model’s design, both with regard to empirical knowledge and general, basic principles. This critical evaluation allows model users to understand that model design was not ad hoc but based on carefully scrutinized considerations’. [1] | Green | Adapted from Grimm et al [2]<br>• Conceptual model follows natural history of HIV disease<br>• Compartmental model is appropriate<br>• Complexity of model is appropriate<br>• Assumptions utilised reasonable to form a logistically consistent model* |
| | | Amber | Failure for at least one of above |
| | | Red | Failure for at least two of above |
| Implementation verification | ‘(1) Whether the computer code implementing the model has been thoroughly tested for programming errors, (2) whether the implemented model performs as indicated by the model description, and (3) how the software has been designed and documented to provide necessary usability tools (interfaces, automation of experiments, etc.) and to facilitate future installation, modification, and maintenance.’ [1] | Green | Appropriate testing and documentation of software supplied |
| | | Red | Failure of above |
| Model output verification | ‘(1) How well model output matches observations and (2) how much calibration and effects of environmental drivers were involved in obtaining good fits of model output and data’[1] | Green | Appropriate and clear calibration of parameters performed |
| | | Red | Failure of above |

| | | | |
|---|---|---|---|
| Model analysis | '(1) How sensitive model output is to changes in model parameters (sensitivity analysis), and (2) how well the emergence of model output has been understood.' [1] | Green | Incorporation and analysis of uncertainty and/or sensitivity analyses |
| | | Red | Failure of above |
| Model output corroboration | 'How model predictions compare to independent data and patterns that were not used, and preferably not even known, while the model was developed, parameterized, and verified. By documenting model output corroboration, model users learn about evidence which, in addition to model output verification, indicates that the model is structurally realistic so that its predictions can be trusted to some degree'[1] | Green | Data used to corroborate model results |
| | | Red | Failure of above |

Description provided in the table for each criteria taken directly from Grimm et al.[1]. Traffic light system used to assess the criteria created by the author unless otherwise stated

*Assumptions particularly relevant included: (i) whether interventions affect onward transmission in addition to acquisition risk if a person becomes infected whilst taking the prevention method; (ii) if circumcision is possible for infected individuals in addition to susceptibles; (iii) whether circumcision occurs to individuals prior to them entering the model or whilst they are within the model; (iv) which PrEP/vaccination preparation is under consideration, e.g. oral versus injection or daily versus on demand.

Online Resource 3 - Characteristics of included studies

| Lead author | Year | Country | Population | Model | HIV prevention interventions modelled | Other interventions modelled | Modes of transmission | Costs or CE | Drug resistance | Risk compensation | Interventions targeted at subgroups | Outcomes modelled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Adamson [3] | 2019 | United States | MSM | Deterministic compartmental | PrEP, vaccine | HIV testing, ART | Sexual | CE | No | Yes | Yes | New infections averted, total costs, ICER of vaccines compared with no vaccine availability |
| Afassinou [4] | 2017 | Botswana | General population | Deterministic compartmental | PrEP; | ART | Sexual | NA | Yes | No | No | Number of new HIV infections where PrEP and ART are used in combination and how this varies dependent on level of PrEP drug resistance |
| Akudibillah [5] | 2017 | South Africa | General population | Deterministic compartmental | PrEP; circumcision | ART | Sexual | Costs | No | No | Yes | HIV incidence, infection-years, deaths and costs dependent on intervention combinations and targeting |
| Alsallaq [6] | 2017 | Kenya | Heterosexual | Deterministic compartmental | PrEP, circumcision | HIV testing, ART, condoms, risk reduction counselling | Sexual | CE | No | No | Yes | Infections averted, DALYS, costs for individual and combination prevention methods dependent on age group |
| Anderson [7] | 2018 | Kenya | MSM, heterosexual, FSW | Deterministic compartmental | PrEP, circumcision | ART, condoms | Sexual | NA | No | No | Yes | Strength of each indicator in predicting long-term changes in incidence dependent on type of epidemic |
| Awad [8] | 2015 (a) | Zambia | Heterosexual | Deterministic compartmental | circumcision | NA | Sexual | CE | No | Yes | Yes | VMMCs per infection averted, cost per infection averted dependent on age, |

| Lead author | Year | Country | Population | Model | HIV prevention interventions modelled | Other interventions modelled | Modes of transmission | Costs or CE | Drug resistance | Risk compensation | Interventions targeted at subgroups | Outcomes modelled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | geographic and risk prioritisation |
| Awad [9] | 2015 (b) | Zimbabwe | Heterosexual | Deterministic compartmental | circumcision | NA | Sexual | CE | No | Yes | Yes | VMMCs per infection averted and cost per infection averted dependent on which subgroups are prioritised in the VMMC program |
| Awad [10] | 2017 | Zambia | Heterosexual | Deterministic compartmental | circumcision | NA | Sexual | NA | No | Yes | Yes | VMMCs per infection averted dependent on who is included in the VMMC program and subsequent uptake |
| Bernard [11] | 2017 | United States | MSM, heterosexual | Deterministic compartmental | PrEP (oral) | HIV testing, ART | Sexual, intravenous drug use | CE | No | No | Yes | HIV infections averted, cost/QALY gained for single and combination interventions. Also what interventions should be used in combination for optimum impact |
| Bernard [12] | 2016 | United States | MSM, heterosexual | Deterministic compartmental | PrEP | HIV testing, ART | Sexual, intravenous drug use | CE | No | No | Yes | Infections averted, change in prevalence, costs, ICER for implementing PrEP in differing delivery conditions |
| Blaizot [13] | 2017 | South Africa | Heterosexual | Deterministic compartmental | PrEP, circumcision | ART | Sexual | NA | No | No | Yes | Impact of individual and combination interventions on HIV prevalence, incidence and population |

| Lead author | Year | Country | Population | Model | HIV prevention interventions modelled | Other interventions modelled | Modes of transmission | Costs or CE | Drug resistance | Risk compensation | Interventions targeted at subgroups | Outcomes modelled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | viral load. How prioritisation affects results |
| Blaizot [14] | 2016 | Kenya | Heterosexual | Deterministic compartmental | PrEP, circumcision | ART | Sexual | NA | No | No | Yes | Impact of individual and combination interventions on HIV prevalence, incidence and population viral load. How prioritisation affects results |
| Blaizot [15] | 2015 | Kenya | Heterosexual | Deterministic compartmental | PrEP, circumcision | ART | Sexual | NA | No | No | Yes | HIV incidence dependent on intervention implemented using the parametrised model |
| Borquez [16] | 2020 | Peru | MSM, transgender female sex works, female sex workers, transgender women | Deterministic compartmental | PrEP | ART, risk reduction counselling | Sexual | NA | No | No | Yes | HIV infections prevented over ten years if PrEP is prioritised to stimulant users versus random allocation. Also reduction in cardiovascular disease and suicide if PrEP is combined with a stimulant deterrent |
| Borquez [17] | 2019 | Peru | Transgender women sex workers, and their partners, and clients | Deterministic compartmental | PrEP | ART, condoms | Sexual | CE | No | No | Yes | Reduction in HIV incidence, total cost and ICER when all interventions applied in standard scale up and enhanced scale up scenarios |
| Cremin [18] | 2017 | Kenya | MSM, heterosexual, | Deterministic compartmental | PrEP, circumcision | ART, condoms | Sexual | CE | No | No | Yes | For a given level of spending, what is the optimal combination |

| Lead author | Year | Country | Population | Model | HIV prevention interventions modelled | Other interventions modelled | Modes of transmission | Costs or CE | Drug resistance | Risk compensation | Interventions targeted at subgroups | Outcomes modelled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | female sex workers | | | | | | | | | prevention strategy (including who to tarhet) that will optimise infections averted by calculating impact and total spending compared with status quo Price of PrEP varied to identify at which point it becomes included in the optimal solution |
| Cremin [19] | 2015 (a) | Kenya | Heterosexual | Deterministic compartmental | PrEP, circumcision | ART, condoms | Sexual | CE (PrEP only) | No | No | Yes | Cost per infection averted as adherence, cost and risk group targeting are varied |
| Cremin [20] | 2015 (b) | Mozambique | Heterosexual | Deterministic compartmental | PrEP, circumcision | ART | Sexual | CE (PrEP only) | No | No | Yes | Cost per infection averted when providing partners of miners PrEP during the miners return versus all year |
| de Montigny [21] | 2018 | South Africa | General population | Deterministic compartmental | Vaccine | ART | Sexual | CE | No | No | No | Infections averted depended on vaccine efficacy and choice of vaccine delivery |
| Dimitrov [22] | 2015 | Multi-country | MSM (United States), General population (South Africa) | Deterministic compartmental | Vaccine, circumcision | ART | Sexual | NA | No | Yes | No | Considering three approaches to the time when the new clade specific vaccines are introduced, how will this affect new HIV infection |

| Lead author | Year | Country | Population | Model | HIV prevention interventions modelled | Other interventions modelled | Modes of transmission | Costs or CE | Drug resistance | Risk compensation | Interventions targeted at subgroups | Outcomes modelled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | numbers versus nonmatched vaccine |
| Drabo [23] | 2016 | United States | MSM | Deterministic compartmental | PrEP | ART | Sexual | CE | Yes | No | No | How does HIV incidence and cost-effectiveness vary dependent on which interventions are in place |
| Glaubius [24] | 2019 | South Africa | Heterosexual | Deterministic compartmental | PrEP (vaginal ring), circumcision | ART, condoms | Sexual | CE | Yes | No | Yes | Upon prioritising vaginal ring PrEP by HIV incidence, age or FSW status how does this affect ICER, cumulative HIV infections, life years lived and costs |
| Glaubius [25] | 2016 (a) | South Africa | Heterosexual | Deterministic compartmental | PrEP (injectable), circumcision | ART | Sexual | CE | Yes | No | Yes | Dependent on how injectable PrEP is prioritised and coverage achieved, measured HIV infections, life years and costs/ICERs |
| Glaubius [26] | 2016 (b) | South Africa | Heterosexual | Deterministic compartmental | PrEP (injectable), circumcision | ART | Sexual | NA | Yes | No | Yes | Compared to no PrEP how does the number of drug-resistance infections change when injectable PrEP is introduced. How is this impacted by PrEP factors (e.g. adherence) and the level of cross-resistance between ART and PrEP |
| Gromov [27] | 2018 | United States | MSM | Deterministic compartmental | PrEP | ART | Sexual | NA | No | No | Yes | Number of infection cases over the course of 50 years |

| Lead author | Year | Country | Population | Model | HIV prevention interventions modelled | Other interventions modelled | Modes of transmission | Costs or CE | Drug resistance | Risk compensation | Interventions targeted at subgroups | Outcomes modelled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | by epidemic phase (epidemic or endemic), PrEP treatment regime, and allocation strategy |
| Hansson [28] | 2020 | Sweden | MSM | Deterministic compartmental | PrEP (oral) | ART | Sexual | NA | No | No | Yes | HIV prevalence dependent on how PrEP is targeted and the preference of the population to casual versus steady partners How varying the effectiveness and testing rate whilst receiving PrEP affects HIV prevalence |
| Kelly [29] | 2018 | Multi-country | MSM, heterosexual, FSW | Deterministic compartmental | PrEP, circumcision | HIV testing, ART, PMTCT, condoms | Sexual, vertical, intravenous drug use | CE | No | No | Yes | New infections averted if countries optimally allocated their resources (1) if additional funding (2) if there is redistribution of international funds Increase in current annual funds needed to reduce HIV incidence by 90% |
| Li [30] | 2018 | China | MSM | Deterministic compartmental | PrEP (oral) | HIV testing, ART, condoms | Sexual | CE | No | Yes | Yes | New infections and cost/QALY over the next 20 years dependent on how PrEP is implemented and inclusion of testing or test and treat strategies |

| Lead author | Year | Country | Population | Model | HIV prevention interventions modelled | Other interventions modelled | Modes of transmission | Costs or CE | Drug resistance | Risk compensation | Interventions targeted at subgroups | Outcomes modelled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MacFadden [31] | 2016 | Canada | MSM | Dynamic, stochastic compartmental | PrEP (oral) | HIV testing, ART, condoms | Sexual | CE | No | No | Yes | Cost/QALY dependent on how PrEP is implemented |
| Marukutira [32] | 2020 | Botswana | Citizens and migrants | Deterministic compartmental | PrEP, circumcision | ART, condoms, PEP | Sexual, vertical, intraveous drug use | NA | No | No | Yes | New HIV infections and deaths if status quo continues, if an increased budget is provided to reach 909090 targets for citizens only and finally including migrants |
| McGillen [33] | 2018 | Zimbabwe | MSM, heterosexual, FSW | Deterministic compartmental (Anderson) | PrEP, circumcision | ART | Sexual | CE | No | No | Yes | compared to no VMMC, how many infections has VMMC averted among men and women by the end of 2016 If there are no further interventions, how will the circumcisions up to 2016 impact incidence into the future versus if UNAIDS targets are also met |
| Medlock [34] | 2017 | Multi-country | General population | Deterministic compartmental | Vaccine | HIV testing, ART | Sexual | NA | No | No | No | Infections averted under differing scenarios |
| Mitchell [35] | 2016 | India | MSM, heterosexual, FSW | Deterministic compartmental | PrEP (oral) | ART | Sexual | NA | No | No | Yes | Proportion of new infections averted amongst FSW/MSM and the general population dependent on how PrEP is prioritised |

| Lead author | Year | Country | Population | Model | HIV prevention interventions modelled | Other interventions modelled | Modes of transmission | Costs or CE | Drug resistance | Risk compensation | Interventions targeted at subgroups | Outcomes modelled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mitchell [36] | 2015 | Nigeria | Serodiscordant couples | Deterministic compartmental | PrEP, circumcision | ART, condoms | Sexual | CE (PrEP only) | No | No | Yes | Cost of intervention per DALY and also number of infections prevented when interventions implemented individually or in combination |
| Nichols [37] | 2016 | Netherlands | MSM | Deterministic compartmental | PrEP (oral) | ART | Sexual | CE | No | No | Yes | Cost of PrEP per QALY gained when used daily versus on demand |
| Palk [38] | 2018 | Denmark | MSM | Deterministic compartmental | PrEP | HIV testing, ART | Sexual | NA | No | No | No | New infections by 2030 with and without PrEP introduction relative to the elimination threshold incidence |
| Pharaon [39] | 2020 | Canada, US | MSM | Deterministic compartmental | PrEP | HIV testing, ART, condoms, STI testing, gonnorhoea treatment | Sexual | NA | No | Yes | No | Gonorrhoea prevalence following PrEP introduction and variation dependent on STI testing frequency, condom use and sexual risks |
| Punyacharoensin [40] | 2016 | United Kingdom | MSM | Deterministic compartmental | PrEP | HIV testing, ART, risk reduction counselling | Sexual | NA | No | Yes | Yes | Infections averted dependent on intervenion(s) chosen and risk group of MSM |
| Rozhnova[41] | 2018 | Netherlans | MSM | Deterministic compartmental | PrEP (oral) | ART | Sexual | NA | No | No | Yes | HIV prevalence and incidence, levels of uptake, efficacy and duration necessary for HIV elimination. |

| Lead author | Year | Country | Population | Model | HIV prevention interventions modelled | Other interventions modelled | Modes of transmission | Costs or CE | Drug resistance | Risk compensation | Interventions targeted at subgroups | Outcomes modelled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Shen [42] | 2018 | United States | MSM | Deterministic compartmental | PrEP | ART | Sexual | CE | Yes | No | No | Infections prevented, number of new drug-resistant infections, gain in QALYs and cost per QALY gained dependent on risk level targeted for PrEP |
| Smith [43] | 2020 | South Africa | Heterosexual | Deterministic compartmental | PrEP (oral, injectable), circumcision | ART, condoms | Sexual | NA | No | No | Yes | Infections averted dependent on risk groups receiving long actign PrEP. Intervention use required to avert an infection |
| Smith [44] | 2016 | South Africa | Heterosexual | Deterministic compartmental | PrEP (oral, injectable, vaginal ring), vaccine (P5-like vaccine, idealised vaccine and bNAbs), circumcision | ART, condoms | Sexual | Costs | No | No | Yes | Optimum mix of interventions to avert greatest number of infections for the budget available Also which interventions have greatest impact for the budget available |
| Stuart [45] | 2018 | South Africa | MSM, heterosexual, FSW | Deterministic compartmental | PrEP, circumcision | HIV testing, ART, condoms | Sexual, vertical, intravenous drug use | Costs | No | No | Yes | Infections averted, deaths averted and treatment investments upon meeting the fasttrack targets and additionally upon scaling up other prevention interventions (e.g. circumcision) |

| Lead author | Year | Country | Population | Model | HIV prevention interventions modelled | Other interventions modelled | Modes of transmission | Costs or CE | Drug resistance | Risk compensation | Interventions targeted at subgroups | Outcomes modelled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| van de Vijver [46] | 2019 | Germany | MSM | Deterministic compartmental | PrEP (oral) | ART | Sexual | CE | No | No | Yes | Infections averted after two years scale up and ten years full implementation of PrEP<br><br>Costs of PrEP over implementation period<br><br>Savings resulting from PrEP due to reduction in HIV-related costs |
| van Vliet [47] | 2019 | South Africa | Heterosexual | Deterministic compartmental | PrEP (injectable) | ART, contraceptives | Sexual | CE | No | No | Yes | Number and percentage of infections averted with long acting PrEP use versus not, dependent on ART coverage<br><br>Price of PrEP and ART coverage at which PrEP would be cost effective |
| Ying [48](55) | 2015 | Uganda | Serodiscordant couples | Deterministic compartmental | PrEP, circumcision | ART, condoms | Sexual, vertical | CE (PrEP only) | No | Yes | Yes | HIV infections and DALYs averted. Also ICER per HIV infection averted |
| Zhang [49] | 2020 | China | MSM | Deterministic compartmental | circumcision | NA | Sexual | NA | No | No | No | New HIV cases dependent on coverage level |
| Zhang [50] | 2019 | China | MSM | Deterministic compartmental | circumcision | NA | Sexual | CE | No | No | Yes | New HIV cases and number VMMC needed to avert a HIV case under varying VMMC rates |

Online Resource 4 – Assessment of included studies using the TRACE criteria

| Lead author | Year | Problem formulation | Model description | Data evaluation | Conceptual model | Implementation verification | Model output verification | Model analysis | Model output corroboration |
|---|---|---|---|---|---|---|---|---|---|
| Adamson [3] | 2019 | | | | | | | | |
| Afassinou [4] | 2017 | | | | | | | | |
| Akudibillah [5] | 2017 | | | | | | | | |
| Alsallaq [6] | 2017 | | | | | | | | |
| Anderson [7] | 2018 | | | | | | | | |
| Awad (a) [8] | 2015 | | | | | | | | |
| Awad (b) [9] | 2015 | | | | | | | | |
| Awad [10] | 2017 | | | | | | | | |
| Bernard [11] | 2017 | | | | | | | | |
| Bernard [12] | 2016 | | | | | | | | |
| Blaizot [13] | 2017 | | | | | | | | |
| Blaizot [14] | 2016 | | | | | | | | |
| Blaizot [15] | 2015 | | | | | | | | |
| Borquez [16] | 2020 | | | | | | | | |
| Borquez [17] | 2019 | | | | | | | | |
| Cremin [18] | 2017 | | | | | | | | |
| Cremin (a) [19] | 2015 | | | | | | | | |
| Cremin (b) [20] | 2015 | | | | | | | | |
| de Montigny [21] | 2018 | | | | | | | | |
| Dimitrov [22] | 2015 | | | | | | | | |
| Drabo [23] | 2016 | | | | | | | | |
| Glaubius [24] | 2019 | | | | | | | | |
| Glaubius (a) [25] | 2016 | | | | | | | | |
| Glaubius (b) [26] | 2016 | | | | | | | | |
| Gromov [27] | 2018 | | | | | | | | |
| Hansson [28] | 2020 | | | | | | | | |
| Kelly [29] | 2018 | | | | | | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Li [30] | 2018 | | | | | | | | |
| MacFadden [31] | 2016 | | | | | | | | |
| Marukutira [32] | 2020 | | | | | | | | |
| McGillen [33] | 2018 | | | | | | | | |
| Medlock [34] | 2017 | | | | | | | | |
| Mitchell [35] | 2016 | | | | | | | | |
| Mitchell [36] | 2015 | | | | | | | | |
| Nichols [37] | 2016 | | | | | | | | |
| Palk [38] | 2018 | | | | | | | | |
| Pharaon [39] | 2020 | | | | | | | | |
| Punyacharoensin [40] | 2016 | | | | | | | | |
| Rozhnova [41] | 2018 | | | | | | | | |
| Shen [42] | 2018 | | | | | | | | |
| Smith [43] | 2020 | | | | | | | | |
| Smith [44] | 2016 | | | | | | | | |
| Stuart [45] | 2018 | | | | | | | | |
| van de Vijver [46] | 2019 | | | | | | | | |
| van Vliet [47] | 2019 | | | | | | | | |
| Ying [48] | 2015 | | | | | | | | |
| Zhang [49] | 2020 | | | | | | | | |
| Zhang [50] | 2019 | | | | | | | | |

TRACE, TRAnsparent and Comprehensive Ecological modelling documentation

Online resource 5 - Model characteristics considered in the analysis


Compartments: Susceptible, HIV infection, AIDS infection

Strata: i = Risk group (low sexual risk or high sexual risk)

Parameters: α = rate HIV infected individuals progress to AIDs infection

Rate of infection = The rate at which susceptible individuals become infected

An illustration of a simple compartmental model example, to outline the model characteristics considered in the analysis. Individuals in this example can progress from a status of being susceptible to HIV, to being infected with HIV at the rate of infection. Individuals can then progress to developing AIDS at rate α

## Online Resource 6 - Data extracted from included studies regarding how interventions were included in the models

### a. PrEP

| Lead Author | Year | Does PrEP affect onward transmission? | Is the PrEP preparation studied in the model clear? | PrEP adherence considered? | PrEP costs included | PrEP compartment/strata details and parameters | Force of infection |
|---|---|---|---|---|---|---|---|
| Adamson [3] | 2019 | No | Yes | | PrEP 30 day supply cost and also cost of clinic visit (e.g. lab test, HIV test, STI test costs) | Stratification: On PrEP, on PrEP and vaccine, infected on PREP<br><br>(1) Fraction of people starting PrEP by risk status (2) fraction discontinuing prep (3) Fraction vaccinated and prep who stop taking prep and move to vaccinated only (4) annual rate of screening for PrEP users | (1) PrEP efficacy in reducing susceptibility per act (2) rate of condom use by uninfected individuals on prep |
| Afassinou [4] | 2017 | Yes | Yes | Yes | | 3 compartments<br>Susceptible on PrEP, infected despite prep, infected prior to starting prep<br><br>(1)Proportion taking PrEP who were infected prior to starting prep (2)proportion of susceptibles enrolled in a PrEP regimen (= awareness level) (3) Rate people infected whilst on prep start treatment (quicker than those who weren't on prep as their prep education alters their decisions regarding ongoing treatment)<br><br>Not modelled adherence separately, but said PrEP adherence level may be regarded as a measure of the PrEP awareness level | (1)efficacy* (2) acquisition and infectiousness (in force of infection)<br>*Not in force of infection but multiplier of it |
| Akudibillah [5] | 2017 | No | No | | Costs consists of cost of infections, cost of deaths, and cost of treatment (PrEP and ART) | Compartments: 2 for females: PrEP for susceptible medium risk or high risk. 1 for males: PrEP for susceptible medium risk (no high risk for males)<br>(1) Rate drop out of treatment(2) PrEP uptake rate (3) rate change from medium to high risk (and vice versa) whilst on prep | (1) transmissibility reduced if the uninfected partner is on PrEP |
| Alsallaq [6] | 2017 | No | Yes | | including service and drug costs | 2 strata<br>not on prep, on prep<br>(1) Proportion of female population initially eligible for prep (2) Parameter for moving girls from no prep to prep | (1) reduction in the risk of HIV acquisition because of PrEP |

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|---|---|---|---|---|---|---|---|
| Anderson [7] | 2018 | No | No | | | Strata: on or off prep<br>(1) proportion entering population already on PrEP<br>(2) uptake dependent on number already on PrEP per group and the maximum PrEP coverage for that group | (1) Efficacy at reducing acquisition |
| Bernard [11] | 2017 | No | Yes | | | 10 compartments:<br>5 For PWID (one for on prep, four for infected on prep)<br>5 for opioid agonist therapy (one for on prep, four for infected on prep)<br>Variables: (1) Rate at which PWID enter PrEP program | (1) Reduction in chance of sexual HIV acquisition (2) Reduction in chance of HIV acquisition via injection |
| Bernard [12] | 2016 | No | Yes | | | 10 compartments:<br>5 For PWID (one for on prep, four for infected on prep)<br>5 for opioid agonist therapy (one for on prep, four for infected on prep)<br>Variables: (1) Rate at which PWID enter PrEP program | (1) Reduction in chance of sexual HIV acquisition (2) Reduction in chance of HIV acquisition via injection |
| Blaizot [13] | 2017 | No | No | | | | (1) Proportion undertaking intervention (2) reduction in susceptibility |
| Blaizot [14] | 2016 | No | No | | | | (1) Proportion undertaking intervention (2) reduction in susceptibility |
| Blaizot [15] | 2015 | No | No | | | | (1) Proportion undertaking intervention (2) reduction in susceptibility |
| Borquez [16] | 2020 | No | No | Yes | | 7 Compartments<br>One susceptible compartment, four infected despite PrEP dependent on CD4 count and two for those on treatment following PrEP<br>3 strata: good, average, poor prep adherence<br>Variables: (1) distribution to adherence group (2) coverage of prep | (1) proportion of sex acts protected by PrEP dependent on adherence<br>(2) efficacy of prep |
| Borquez [17] | 2019 | No | No | Yes | PrEP drug and associated costs (including HIV rapid test, renal function test, physician/nurse/psychologist/social worker charge) | | (1) Coverage<br>(2) Adherence<br>(3) Efficacy at reducing acquisition<br>(4) rate people on PrEP test for HIV<br><br>Adherence incorporated in efficacy |

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| Cremin [18] | 2017 | No | Yes | Yes | direct costs (eg, antiretrovirals, laboratory tests), related costs (eg, outreach and demand creation), and indirect costs (eg, management, utilities, and transportation) | Four strata based on eligibility and adherence (well or poor).<br><br>(1) proportion of uninfected given PrEP specified for gender and risk group<br>(2) rate of uptake in given risk group and gender<br>(3) time at which the PrEP intervention begins<br>(4) Adherence<br>(5) drop out<br>(6) Fraction of individuals eligible for PrEP | (1) proportion of sex acts protected by PrEP adherence<br>(2) Efficacy at reducing acquisition |
| Cremin [19] | 2015 (a) | No | No | Yes | Costs of PrEP per person-year PrEP budget | Four strata based on eligibility and adherence (well or poor).<br><br>(1) Fraction of population eligible for PrEP (defined separately by sex and risk group) in the year the epidemic starts (2) proportion of PrEP users that are good adherers (3) rate at which individuals initiate PrEP (includes time intervention begins and coverage for a given risk group) | (1) Proportion of sex acts protected by PrEP in good adherers (2) Proportion of sex acts protected by PrEP in poor adherers<br>Includes residual protection of PrEP |
| Cremin [20] | 2015 (b) | No | No | Yes | PrEP cost per person per year | 4 strata: not eligible for PrEP, eligible for PrEP, receiving PrEP adhering well, receiving PrEP adhering poorly.<br><br>(1) Have fraction of population for each strata and risk group (2) proportion good adherers (3) scale up rate of PrEP (4) time PrEP implemented | (1) Efficacy of acquisition risk for males and females (Efficacy refers to the protection afforded by perfect use of a product)<br>(2) adherence |
| Drabo [23] | 2016 | Yes | Yes | Yes | Cost PrEP for 30 days, also includes associated costs including testing and counselling | Compartment: On or off PrEP, infected whilst on PrEP (in primary or asymptomatic stages)<br><br>Strata: For infected on PrEP, whether drug-sensitive or drug-resistant<br><br>Variables: (1) PrEP initiation rate dependent on uninfected or infected (2) rate of PrEP discontinuation dependent on uninfected or infected (3) rate testing for those infected whilst on PrEP | (1) Reduction in sexual infectivity owing to PrEP (2) acquisition efficacy (3) adherence |
| Glaubius [24] | 2019 | Yes | Yes | Yes | Cost PrEP per person per year | Stratification<br>Not on PrEP; on PrEP<br><br>Variables: (1) PrEP initiation rate (2) Spectrum of adherence(3) rate stop | (1) efficacy acquisition-based on whether resistant strain (2) efficacy transmission |

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| | | | | | | prep (4) PrEP persistance (assume women generally replace ring monthly for 3 years) | |
| Glaubius [25] | 2016 (a) | No | Yes | | PrEP costs per person per year (includes diagnostics and overheads) | Stratification<br>Not on PrEP; on PrEP following a successful injection; on PrEP following an unsuccessful injection<br><br>Variables: (1) PrEP initiation rate (2) proportion of PrEP injections successful (3) Individuals leave PrEP due to dropout or completion of their course of PrEP injections (4) Rate individuals on PrEP with PrEP-sensitive HIV infection develop virus with acquired PrEP resistance (5) individuals attending for PrEP are tested prior to injection | (1) Efficacy following successful injection dependent on HIV strain |
| Glaubius [26] | 2016 (b) | No | Yes | | | Stratification<br>Not on PrEP; on PrEP following a successful injection; on PrEP following an unsuccessful injection<br><br>Variables: (1) PrEP initiation rate (2) proportion of PrEP injections successful (3) Individuals leave PrEP due to dropout or completion of their course of PrEP injections (4) Rate individuals on PrEP with PrEP-sensitive HIV infection develop virus with acquired PrEP resistance (variant Q2) (5) individuals attending for PrEP are tested prior to injection | (1) Efficacy following successful injection dependent on HIV strain |
| Gromov [27] | 2018 | No | No | | Monthly cost of PrEP, enrolment costs | One compartment: on prep<br><br>Variables (1) Rate at which PrEP fails or is cancelled (2) relative rate at which individuals are sampled and then put on PrEP | People in prep compartment cannot become infected (100% efficacy), therefore no force of infection applies |
| Hansson [28] | 2020 | No | Yes | | | Compartments (33)<br>Single individuals 3 (susceptible on prep, infected on prep, chronic infection on prep). Dependent on whether susceptible, acute or chronic infection and also whether individual is single/in a relationship<br><br>(1) Rate high/low-active individuals start PrEP (2) ART initiation rate for high-actives on PrEP (3) Rate of testing for high-active on PrEP<br><br>Being on prep leads to increased testing | (1) Efficacy |

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| Kelly [29] | 2018 | No | No | | unit costs | | (1) fractional reduction in transmission probability per act due to prep (2) probability that an individual is on prep |
| Li [30] | 2018 | No | Yes | Yes | Annual cost of PrEP (including PrEP drug cost and clinics cost) | One compartment - On PrEP<br><br>(1) Uptake (2) drop out | (1) Efficacy at reducing acquisition (depends on adherence) (2) Change in condom use for those on prep |
| MacFadden [31] | 2016 | No | Yes | Yes | Annual PrEP drug cost per patient includes such costs as physician-visit and nursing costs, diagnostic testing | 2 compartments (on PrEP, whether high risk or low risk)<br><br>variables (1) PrEP initiation rate per year (2) PrEP cessation rate per year | (1) Efficacy (as a surrogate for adherence) * not included in force of infection but multiplier of |
| Maruku tira [32] | 2020 | No | No | | | | (1) fractional reduction in transmission probability per<br>act due to prep (2) probability that an individual is on prep |
| McGillen [33] | 2018 | No | No | | | Strata: on and off prep<br><br>(1) proportion entering population already on PrEP<br>(2) uptake dependent on number already on PrEP per group and the maximum PrEP coverage for that group | (1) Efficacy at reducing acquisition |
| Mitchell [35] | 2016 | No | Yes | Yes | | One compartment - On PrEP<br><br>(1) Uptake<br>(2) dropout | (1) Efficacy at reducing acquisition<br>(2) Adherence |
| Mitchell [36] | 2015 | No | No | Yes | PrEP drug costs and also accounted for start-up costs (training and mass media campaigns), | PrEP compartment<br><br>(1) drop out (2) become infected (3) No longer take prep as partner initiates ART (4) % HIV negative partners who accept and start using PREP | (1) Effectiveness (efficacy x adherence) |

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| | | | | | drug, laboratory tests and logistics, and facility delivery costs. | | |
| Nichols [37] | 2016 | No | Yes | | Yearly cost of daily PrEP, yearly cost on-demand prep, also includes costs of OP clinic visit, OP visit to HIV specialist, testing, monitoring | 10 compartments: One susceptible and on PrEP, one infected despite being on PrEP. Then 8 compartments for CD4 progression after infection wilst on PrEP<br><br>(1) rate people on PrEP test for HIV<br>(2) Uptake<br>(3) drop out | (1) Efficacy at reducing acquisition<br><br>On-demand PrEP and daily PrEP are assumed to have equal efficacy |
| Palk [38] | 2018 | No | No | | | | Not in force of infection, but multiplier of it:<br>(1) proportion of susceptibles on PrEP<br>(2) factor risk of infection is reduced by for those on PREP |
| Pharaon [39] | 2020 | No | Yes | | | Two compartments<br>On PrEP or on prep and infected with gonorrhoea<br><br>(1) PREP uptake rate (2) Rate people on prep get infected with gonorrhoea (accounts for increased risk due to being on prep) (3) testing frequency for HIV/Gonorrhoea whilst on PrEP | People in prep compartment cannot become infected (100% efficacy), therefore no force of infection applies |
| Punyac haroensin [40] | 2016 | Yes | Yes | | None | 3 compartments (uninfected, HIV undiagnosed, HIV diagnosed whilst on PrEP).<br><br>(1) Rate people with HIV infection whilst on PrEP move fromacute infection to next infection stage<br>(2) rate people on PrEP test for HIV<br>(3) uptake<br>(4) drop out | (1) Efficacy at reducing acquisition (not in force of infection, but multiplier of it) (2) reduced infectiousness of people infected whilst on PrEP to pass on to others (3) increased sexual partners following intervention |

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|---|---|---|---|---|---|---|---|
| Rozhnova [41] | 2018 | Yes | Yes | | No | 2 compartments: susceptible on PrEP, infected despite PrEP use<br><br>(1) Average duration of taking PrEP (2) Annual PrEP uptake rate per risk group (3)annual uptake rate for ART for people on PrEP per risk group | (1) Reduction in infectivity owing to PrEP (2) Efficacy |
| Shen [42] | 2018 | No | Yes | | Annual cost of PrEP | Compartments:<br>Susceptible no PrEP, susceptible PrEP<br><br>(1) PrEP coverage<br>(2) rate discontinuing PrEP<br>(3) PrEP receiving rate (per year) | N.B. Not in force of infection, but multiplier of<br>(1) Efficacy against drug sensitive strains (2) Efficacy against drug resistant strains |
| Smith [43] | 2020 | No | Yes | Yes | | Stratified as on PrEP or not<br>Coverage is defined as the coverage of "good users" benefiting from the efficacy values - takes into account adherence<br><br>(1) Have fraction of population for each strata and risk group to be on PrEP (2) scale up rate of PrEP (3) time PrEP implemented | (1) Efficacy of reducing acquisition risk for males and females |
| Smith [44] | 2016 | No | Yes | Yes | All interventions consider fixed and variable costs | Stratified as on PrEP or not<br>Coverage is defined as the coverage of "good users" benefiting from the efficacy values - takes into account adherence<br><br>(1) Have fraction of population for each strata and risk group (2) scale up rate of PrEP (3) time PrEP implemented | (1) Efficacy of acquisition risk for males and females (Efficacy refers to the protection afforded by perfect use of a product) The proportion of sex acts protected by PrEP represents adherence |
| Stuart [45] | 2018 | No | No | | unit cost PrEP | | (1) fractional reduction in transmission probability per act due to prep (2) probability that an individual is on prep |
| van de Vijver [46] | 2019 | Yes | Yes | | daily PrEP costs and additional costs including for clinic visits, tests and indirect costs (including pay of sick leave) | 6 compartments<br>Susceptible on PrEP, Infected on PrEP (5 compartments based on CD4 count)<br><br>Variables: (1) rate start PrEP (2) rate discontinue prep (3) rate diagnosed when infected whilst on Prep | (1) Force of inflection for those receiving prep to become infected, incorporates effectiveness<br>(2) those infected whilst on prep have differing infectiousness |

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| van Vliet [47] | 2019 | Yes | Yes | | long-acting PrEP costs based on an average use of five years and included drug, lab, testing, overheads | 12 Compartments -<br>Dependent on susceptible or progressing through stages of PrEP and type of contraception the individual uses<br><br>Variables: (1) Proportion women who start other contraceptives and long-acting PrEP (2) Proportion women who discontinue other contraceptives and long-acting PrEP (3) Proportion depot medroxyprogesterone acetate (DMPA) users who start using long- acting PrEP (4) Proportion DMPA and long-acting PrEP users who discontinue long-acting PrEP (5) Discontinuation rate for contraceptive whilst on PrEP (6) rate of switching contraceptive type whilst on PrEP | (1) Effectiveness of PrEP at reducing acquisition risk<br>(2) the infectiousness of women who become HIV infected despite the use of long-acting PrEP is lowered with the effectiveness of long-acting PrEP |
| Ying [48] | 2015 | Not stated | No | | PrEP costs included that of the drug and also start up, personnel, lab test costs | Stratified by on PrEP and circumcised or not<br><br>(1) dropout rate from PrEP (2) coverage of PrEP | (1) Efficacy (2) condom use among PrEP users |

## b. Circumcision

| Lead Author | Year | When can circumcision occur? | Does Circumcision affect onward transmission? | Circumcision costs included | Circumcision compartment/strata details and parameters | force of infection |
|---|---|---|---|---|---|---|
| Akudibillah [5] | 2017 | Not stated | No | | | (1) male circumcision, education and condom use are aggregated in the HIV risk per sex act and are assumed constant for the span of the model |
| Alsallaq [6] | 2017 | Circumcision occurs both at birth and whilst in the model | No | Circumcision cost per male circumcised | 2 Strata: circumcised versus not<br><br>(1) Proportion of population initially circumcised at childhood or adolescence (2) circumcision rate<br>(3) target circumcision coverage value | (1) Reduction in risk of HIV acquisition because of circumcision |

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| Anderson [7] | 2018 | Circumcision occurs both at birth and whilst in the model | No | | Four strata for males: circumcised with and without PrEP and uncircumcised with and without PrEP<br><br>(1) Rate of circumcision due to scale-up campaign - scaled up at fixed rate and Baseline circumcision rate<br>(2) date the intervention scale-up is commenced<br>(3) maximum coverage for intervention<br>(4) proportion entering model already circumcised | (1) Reduction in HIV acquisition due to circumcision |
| Awad [8] | 2015 (a) | Circumcision occurs both at birth and whilst in the model | Yes | Considered a fixed VMMC unit cost and a cost dependent on age | Stratified by circumcision status<br><br>Parameters: (1) Fraction of the male population that is circumcised before starting sexual activity (baseline circumcision) (2) Average rate at which non-circumcised males are being circumcised as part of a voluntary medical male circumcision intervention | (1) increase in effective rate of partner change due to risk compensation following circumcision (2) efficacy against acquisition (3) reduction in risk of transmission |
| Awad [9] | 2015 (b) | Circumcision occurs both at birth and whilst in the model | Yes | VMMC unit cost | Stratified by circumcision status<br><br>Parameters: (1) Fraction of the male population that is circumcised before starting sexual activity (baseline circumcision) (2) Average rate at which non-circumcised males are being circumcised as part of a voluntary medical male circumcision intervention | (1) increase in effective rate of partner change due to risk compensation following circumcision (2) efficacy against acquisition (3) reduction in risk of transmission |
| Awad [10] | 2017 | Circumcision occurs both at birth and whilst in the model | YEs | | Stratified by circumcision status<br><br>Parameters: (1) Fraction of the male population that is circumcised before starting sexual activity (baseline circumcision) (2) Average rate at which non-circumcised males are being circumcised as part of a voluntary medical male circumcision intervention | (1) increase in effective rate of partner change due to risk compensation following circumcision (2) efficacy against acquisition (3) reduction in risk of transmission (4) relative risk of HIV male-to-female transmission during wound healing compared with males who are not circumcised [know time span of wound healing] |
| Blaizot [13] | 2017 | Not stated | No | | | (1) Proportion undertaking intervention (2) reduction in susceptibility |
| Blaizot [14] | 2016 | Not stated | No | | | (1) Proportion undertaking intervention (2) reduction in susceptibility |
| Blaizot [15] | 2015 | Not stated | No | | | (1) Proportion undertaking intervention (2) reduction in |

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|---|---|---|---|---|---|---|
| | | | | | | susceptibility |
| Cremin [18] | 2017 | Circumcision occurs both at birth and whilst in the model | No | $60 per man circumcised | 2 strata: one signifies uncircumcised, one signifies circumcised<br>(1) date the intervention scale-up is commenced<br>(2) Rate of circumcision due to campaign - scaled up at fixed rate<br>(3) maximum coverage for intervention<br>(4) fraction of population entering the model circumcised (represents those circumcised atbirth or during adolescence) | (1) Reduction in HIV acquisition due to circumcision<br><br>assumed to have no effect on HIV transmission between men |
| Cremin [19] | 2015 (a) | Circumcision occurs both at birth and whilst in the model | No | | 3 strata: uncircumcised males, circumcised males, newly circumcised males in the healing period<br><br>(1) date the intervention scale-up is commenced<br>(2) Rate of circumcision due to campaign - scaled up at fixed rate<br>(3) fraction of population entering the model circumcised (represents those circumcised at birth or during adolescence)<br>(4) rate of wound healing (assumed 6 weeks) | (1) Reduction in HIV acquisition due to circumcision<br><br>assumed to have no effect on HIV transmission between men |
| Cremin [20] | 2015 (b) | Circumcision occurs both at birth and whilst in the model | No | | 3 strata; uncircumcised males, circumcised males, newly circumcised males in the healing period<br><br>(1) date the intervention scale-up is commenced<br>(2) Rate of circumcision due to campaign - scaled up at fixed rate<br>(3) fraction of population entering the model circumcised (represents those circumcised at birth or during adolescence)<br>(4) rate of wound healing (assumed 6 weeks) | (1) Reduction in HIV acquisition due to circumcision<br><br>assumed to have no effect on HIV transmission between men |
| Dimitrov [22] | 2015 | Not stated | No | | | (1) reduction in HIV acquisition risk<br>(2) proportion of circumcised men |
| Glaubius [24] | 2019 | Prior to entering model | No | $ per circumcision | Strata: Circumcised or not for males<br><br>Variable (1) the proportion who debut (at age 15) with circumcision (2) rate of extra circumcision due to VMMC program (no restriction on capping this) | (1) efficacy |

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|---|---|---|---|---|---|---|
| Glaubius [25] | 2016 (a) | Circumcision occurs both at birth and whilst in the model | No | $ per circumcision | Strata: Circumcised or not for males<br><br>Variable (1) the proportion who debut (at age 15) with circumcision (2) rate of extra circumcision due to VMMC program for those entering the model (3) rate of extra circumcision for people in the model | (1) efficacy |
| Glaubius [26] | 2016 (b) | Circumcision occurs both at birth and whilst in the model | No | | Strata: Circumcised or not for males<br><br>Variable (1) the proportion who debut (at age 15) with circumcision (2) rate of extra circumcision due to VMMC program for those entering the model (3) rate of extra circumcision for people in the model | (1) efficacy |
| Kelly [29] | 2018 | Not stated | No | unit costs | Stratification - susceptible circumcised | (1) fractional reduction in transmission probability per act due to circumcision (2) the probability that an individual is circumcised.<br><br>Applies only to males, applies to heterosexual and MSM for insertive penile anal intercourse where the insertive man is circumcised |
| Marukutira [32] | 2020 | Not stated | No | | Stratification - susceptible circumcised | (1) fractional reduction in transmission probability per act due to circumcision (2) the probability that an individual is circumcised.<br><br>Applies only to males, applies to heterosexual and MSM for insertive penile anal intercourse where the insertive man is circumcised |
| McGillen [33] | 2018 | Circumcision occurs both at birth and whilst in the model | No | Unit cost of VMMC per procedure; weighted average of surgical method and setting | Four strata for males: circumcised with and without PrEP and uncircumcised with and without PrEP<br><br>(1) Rate of circumcision due to scale-up campaign - scaled up at fixed rate and Baseline circumcision rate<br>(2) date the intervention scale-up is commenced<br>(3) maximum coverage for intervention<br>(4) proportion entering model already circumcised<br>If scale up exceeds target then scale up ceases | (1) Reduction in HIV acquisition due to circumcision |

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|---|---|---|---|---|---|---|
| Mitchell [36] | 2015 | Not stated | No | | | (1) Proportion of men circumcised (2) efficacy of circumcision |
| Smith [43] | 2020 | Circumcision occurs both at birth and whilst in the model | No | | 2 strata: one signifies uncircumcised, one signifies circumcised<br><br>(1) date the intervention scale-up is commenced<br>(2) Rate of circumcision due to campaign - scaled up at fixed rate<br>(3) fraction of population entering the model circumcised (represents those circumcised atbirth or during adolescence) | (1) Reduction in HIV acquisition due to circumcision<br><br>assumed to have no effect on HIV transmission between men |
| Smith [44] | 2016 | Circumcision occurs both at birth and whilst in the model | No | Fixed costs - $5 million launch (high coverage only) plus $27·5–36·3 million per population group per year<br><br>Variable costs - $42 per person | 2 strata: one signifies uncircumcised, one signifies circumcised<br><br>(1) date the intervention scale-up is commenced<br>(2) Rate of circumcision due to campaign - scaled up at fixed rate<br>(3) fraction of population entering the model circumcised (represents those circumcised atbirth or during adolescence) | (1) Reduction in HIV acquisition due to circumcision<br><br>assumed to have no effect on HIV transmission between men |
| Stuart [45] | 2018 | Not stated | No | Cost per MMC | Stratification - susceptible circumcised | (1) fractional reduction in transmission probability per act due to circumcision (2) the probability that an individual is circumcised.<br><br>Applies only to males, applies to heterosexual and MSM for insertive penile anal intercourse where the insertive man is circumcised |
| Ying [48] | 2015 | Prior to entering model | No | | 4 Strata: circumcision or not and PrEP or not<br><br>(1) number of births circumcised (2) coverage of circumcision (3) Proportion of births that are circumcised | (1) reduction in acquisition risk due to circumcision*<br><br>*Not in force of infection, but multiplier of |

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|---|---|---|---|---|---|---|
| Zhang [49] | 2020 | Circumcision occurs both at birth and whilst in the model | Not stated | | Stratification: Circumcised or not<br><br>(1) VMMC coverage rate (rate change from uncircumcised to circumcised) (2) Rate people enter model already circumcised | (1) transmission rate for circumcised (different to uncircumcised) |
| Zhang [50] | 2019 | Circumcision occurs both at birth and whilst in the model | Not stated | Cost of voluntary medical male circumcision | Stratification: Circumcised or not<br><br>(1) VMMC coverage rate (rate change from uncircumcised to circumcised) (2) Rate people enter model already circumcised | (1) transmission rate for circumcised (different to uncircumcised) |

c. Vaccination

| Lead Author | Year | Does vaccination affect onward transmission? | Vaccination costs included | Vaccination compartment/strata and parameters | force of infection |
|---|---|---|---|---|---|
| Adamson [3] | 2019 | No | Vaccine cost (per series) includes associated costs including lab tests, STI tests | 2 strata: Vaccinated or on PrEP and vaccinated<br><br>(1) Fraction of people vaccinated during 5-year campaigns starting 2025 by PrEP status (2) Fraction vaccinated and prep who stop taking prep and move to vaccinated only | (1) Vaccine efficacy in reducing susceptibility per act (2) rate of condom use by uninfected individuals vaccinated and on prep<br><br>Separate force of infection for vaccinated and vaccinated with PrEP |
| de Montigny [21] | 2018 | Yes | Price per dose of vaccine and also includes costs supply chain, service delivery, and rapid HIV testing at each dose | 13 compartments:<br>Divided by immune response to the vaccine (high or low responders) and<br>whether susceptoble or infected<br><br>Parameters<br>(1) Fraction of population who will be high responders (versus) low (2) Rate of diagnosis for those vaccinated (3) Vaccination rate in susceptible individuals who will have high vaccine efficacy(4) Vaccination rate in susceptible individuals who will have low vaccine efficacy(5) Time in first vaccine compartment (6 months) (6) Time in second vaccine compartment (one year) (7) Time in third vaccine compartment (6 months) | Efficacy<br>High responders: 3 efficacies dependent on time since vaccination<br>Low responders: similarly 3 efficacies (all set to zero) |

| | | | | | | |
|---|---|---|---|---|---|---|
| Dimitrov [22] | 2015 | No | | ART cost avoided due to infections prevented over 20 years are shown in | Four compartments; two susceptible (one for vaccinated with non-matched vaccine, one for vaccinated with new clade-specific vaccine) and two infected (one for infected when unvaccinated and one whilst vaccinated)<br><br>1) Fraction entering population already vaccinated<br>2) loss of protection for vaccines due to waning immunity and missed revaccination<br>3) Revaccination rate - rate people vaccinated with non-matched vaccine are revaccinated with clade- specific vaccine<br>4) Rate of developing AIDs for people infected when vaccinated | 1) Efficacy of non-matched vaccine 2)Efficacy of clade-specific vaccine 3)Reduction in condom use of those vaccinated |
| Medlock [34] | 2017 | No | | | One compartment: Vaccinated against HIV<br><br>(1) Vaccination rate | (1) vaccine efficacy*<br><br>*Not in force of infection, but multiplier of |
| Smith [44] | 2016 | No | | Fixed and variable costs (cost vaccine per person per year) | Stratified by whether on an intervention or not<br><br>(1) Effective coverage (represents usage and adherence) (2) Intervention scale-up is linear over a fixed period of time and the target coverage is maintained thereafter | (1) Efficacy of reducing acquisition risk |

Online Resource 7 - List of model parameters and percentage of articles reviewed including each parameter

| | Lower quality studies* | | | Higher quality studies* | | |
|---|---|---|---|---|---|---|
| | PrEP | Circumcision | Vaccination | PrEP | Circumcision | Vaccination |
| **Intervention uptake** | | | | | | |
| - Is intervention uptake to be included in the model? | 100% | 100% | 100% | 100% | 100% | 100% |
| Does uptake of the intervention occur at birth | - | 53% | - | - | 89% | - |
| Does uptake of the intervention occur throughout life | - | 53% | - | - | 67% | - |
| In addition to susceptibles, can infected individuals take up the intervention? | - | 41% | - | - | 56% | - |
| Does uptake vary dependent on whether the intervention is made available continuously or via campaigns | - | - | 0% | - | - | 33% |
| Is uptake dependent on the number already taking the intervention | 10% | 0% | 100% | 0% | 0% | 33% |
| Is uptake dependent on the budget available | 5% | - | - | 0% | - | - |
| Is uptake dependent on age | 19% | 18% | 50% | 26% | 44% | 0% |
| Is uptake dependent on risk group | 43% | 12% | 50% | 68% | 22% | 33% |
| Is uptake dependent on key populations (MSM, FSW, sex workers, PWID) | 14% | 0% | 50% | 37% | 11% | 0% |
| Is uptake dependent on gender | 29% | 6% | 50% | 26% | 0% | 0% |
| Is uptake dependent on partners' ART use | 10% | - | - | 5% | - | - |
| Is uptake dependent on whether an individual is a citizen or migrant | 5% | 6% | - | 0% | 0% | - |
| Is uptake dependent on geographical location | - | 0% | - | - | 22% | - |
| **Drop out** | | | | | | |
| Can individuals drop out from the intervention? | 33% | - | 50% | 63% | - | 33% |
| For those enrolled on an intervention, does drop out differ per subgroup | 5% | - | 0% | 21% | - | 0% |
| **Adherence** | | | | | | |
| Does intervention adherence affect efficacy? | 19% | - | - | 26% | - | - |
| **Intervention eligibility** | | | | | | |
| Is there intervention eligibility criteria? | 14% | - | - | 11% | - | - |

| | | | | | | |
|---|---|---|---|---|---|---|
| Does intervention eligibility differ per subgroup | 14% | - | - | 11% | - | - |
| **Risk group** | | | | | | |
| Can individuals move between risk groups? | 5% | - | - | 0% | - | - |
| **Intervention efficacy** | | | | | | |
| Does the intervention reduce HIV acquisition risk? | 100% | 100% | 100% | 100% | 100% | 100% |
| Does intervention efficacy depend on the sensitivity/resistance of the HIV strain | 0% | - | - | 11% | - | - |
| Does efficacy vary immediately following the intervention due to wound healing | - | 12% | - | - | 0% | - |
| Does efficacy vary dependent on sexual preference (e.g. MSM) | - | 41% | - | - | 11% | - |
| Does intervention effectiveness vary dependent on time since administering intervention | - | - | 0% | - | - | 33% |
| Is the use of intervention efficacy or effectiveness impactful? | | | Efficacy | | | Efficacy |
| Does the intervention reduce transmission risk? | 14% | 6% | - | 21% | 22% | - |
| Is there increased HIV testing (and diagnosis) for those infected whilst taking the intervention | 19% | - | - | 26% | - | - |
| Does the rate of HIV disease progression differ for those infected whilst taking the intervention | 19% | - | - | 32% | - | - |
| Does efficacy vary immediately following the intervention due to wound healing | - | 18% | - | - | 0% | - |
| **Drug resistance** | | | | | | |
| Are there concerns that the roll out of the intervention could impact or be impacted by drug resistance? | 5% | - | - | 21% | - | - |
| **Risk compensation** | | | | | | |
| Are there concerns regarding risk compensation when the intervention is rolled out? | 5% | 6% | 50% | 37% | 22% | 33% |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Residual protection** | | | | | | |
| Does the intervention offer residual protection? | 5% | - | - | 11% | - | - |
| **Reliability** | | | | | | |
| Can the intervention itself be unsuccessful even when correctly administered? | 0% | - | 0% | 11% | - | 33% |

*A high-quality study was defined as having two or fewer red status' and no more than one amber across the eight TRACE criteria

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