Thembisa versions

This document summarizes the history of the development of the Thembisa model, and explains the key differences between the different versions of the Thembisa model. Users of Thembisa model outputs should rely on the most recent version of the model as far as possible, but may find it useful to refer to this document when trying to understand differences in results between model versions.

Thembisa version 1.0 (February 2014)

This was the first version of the Thembisa model to be published. Although a working paper was published that described the model and presented results [1], the model itself was not published because the demographic assumptions were preliminary and required further work.

Thembisa version 2.4 (May 2016)

Thembisa version 2.4 is an adaptation of Thembisa version 1.0, created for the purpose of an assessment of long-term prospects for HIV control in South Africa (identifying the model variables most critical to future reductions in HIV incidence and assessing South Africa's potential to achieve the 90-90-90 targets) [2]. The following are the most important structural changes relative to version 1.0:

- The modelling of HCT uptake was revised, as described previously [3]. Very briefly, version 2.4 allowed for retesting of individuals who had previously tested positive, assumed a different age pattern of HIV testing, calculated rates of HIV testing from reported numbers of HIV tests, and assumed the same rates of HIV testing in HIV-negative and undiagnosed HIV-positive individuals (after controlling for other factors).
- Version 1.0 did not explicitly model ART interruptions/discontinuations. Version 2.4 makes some allowance for ART interruptions: individuals are still classified according to the time since they *first* started ART, but in each duration category, a proportion of ART patients is assumed to be temporarily interrupting ART. People who temporarily interrupt ART are assumed to have the same infectiousness as untreated individuals, and their CD4 count is assumed to be the same as it was prior to ART initiation.
- A number of parameters have been added into version 2.4 in order to model the uncertainty in the future course of the epidemic. The first of these is the effect of viral suppression on HIV transmission: whereas version 1.0 contained a single assumption about the relative infectiousness of individuals on ART (compared to individuals not receiving ART), version 2.4 includes a number of parameters (the rate of virological suppression in each year, average viral loads prior to ART initiation, and the increase in HIV infectiousness per unit increase in the log viral load).
- New parameters were also introduced into version 2.4 to represent the effect of timing of ART initiation in pregnancy on the probability of mother-to-child transmission. In version 1.0, it was assumed that mothers starting ART in pregnancy all had the same probability of mother-to-child transmission, but the new model allows for changes over time in the mean duration of ART exposure prior to delivery.

- The ratio of female HIV disease progression rates to those in males was changed from 1.0 in version 1.0 of Thembisa to 0.9 in version 2.4.
- Version 2.4 allows for changes over time in the fraction of male births that are circumcised neonatally (version 1.0 assumed this fraction remained constant).

Various parameter values were updated in version 2.4 to reflect updated information on the rollout of HIV prevention and treatment services, and the model was recalibrated to HIV prevalence data and HCT data. However, the demographic parameters have not yet been updated, and the model has therefore not been placed on the Thembisa website.

Thembisa version 2.5 (August 2016)

Thembisa version 2.5 is an adaptation of Thembisa version 2.4. This is the first version of the model to include province-specific parameters (i.e. the model can be run for the country as a whole and for each of the provinces) [4, 5]. The key structural changes to the model are as follows:

- Version 2.5 allows for the rollout of PrEP to commercial sex workers, from mid-2016.
- Version 2.5 includes allowance for PCR testing in HIV-exposed infants at birth (version 2.4 only allowed for PCR testing at 6 weeks of age). However, due to lack of data on the uptake of birth testing and early indications that the uptake of birth testing might compromise the uptake of testing at 6 weeks, the default assumption remains that rates of PCR uptake at birth are zero.
- Version 2.5 allows for the extension of ART eligibility to all children aged 1-4, from mid-2012.

Thembisa version 3.2 (September 2017)

Thembisa version 3.2 is an update to Thembisa version 2.5. Key differences between the two models are as follows:

- Version 3.2 has been extended to include men who have sex with men (MSM).
- Mother-to-child transmission parameters have been revised in version 3.2, with the result that annual numbers of new infections in children have been reduced.
- Changes have been made to the assumed patterns of medical male circumcision uptake, with uptake being highest in adolescent males, independent of sexual risk behaviour.
- Version 3.2 allows for birth testing (in addition to 8-10 week testing) of children born to HIV-positive mothers.
- Version 3.2 allows for changes in rates of CD4 decline over time, potentially as a result of changes in HIV virulence [6].

Thembisa version 4.1 (August 2018)

Thembisa version 4.1 is an update to Thembisa version 3.2. Key differences between the two models are as follows:

- Version 4.1 classifies HIV-positive children according to whether they have been diagnosed HIV-positive, and the model of ART initiation in children has been revised so that children can only start ART if they have been diagnosed.

- The model of PrEP initiation has been revised, to allow for PrEP initiation in MSM as well as to allow for age, sex and risk group differences in PrEP uptake. Assumptions about PrEP efficacy have also been revised upward.
- Assumptions about rates of treatment interruption and resumption of ART after an interruption have been revised substantially, based on recent South African studies.
- The model of viral suppression after ART initiation has been updated to allow for changes in rates of viral suppression over time, and to allow for anticipated increases in viral suppression following the introduction of dolutegravir.
- The output files for version 4.1 are generated using the C++ version of the Thembisa model (previously the output files were generated using the Excel version of the model). This means that the published outputs include 95% confidence intervals.

References

1. Johnson L. THEMBISA version 1.0: A model for evaluating the impact of HIV/AIDS in South Africa. Centre for Infectious Disease Epidemiology and Research, University of Cape Town; 2014. Available: http://www.thembisa.org/content/downloadPage/WPversion1. Accessed 21 April 2016
2. Johnson LF, Chiu C, Myer L, Davies MA, Dorrington RE, Bekker LG, *et al.* Prospects for HIV control in South Africa: a model-based analysis. *Global Health Action* 2016; **9**:30314.
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