EPP 2009
HIV epidemic trends in the ART era
Generalized epidemics

UNAIDS/WHO Working Group
on Global HIV/AIDS & STI Surveillance
UNAIDS Estimation & Projection Package 2009

• Objectives
  – Build models of national epidemics
    • Geographically appropriate
    • Containing the key sub-populations
  – Provide short-term projections of HIV prevalence (<5 years)
  – Serve as input to Spectrum for assessing incidence, impacts, ART and PMTCT needs, etc.
EPP’s job: fit the model to the data

% HIV+


2009 en
What’s new in EPP 2009?

• Includes influence of ART on prevalence and incidence in fitting the epidemic
• Uses an improved algorithm to generate better fits and more accurate uncertainties
• Allows user to calibrate projections after fitting
• Permits changing urban/rural populations
• Calculates and displays contributions to incidence from urban and rural populations
What are the steps in modeling a national HIV epidemic?
Steps in making an EPP projection

• Create a workset, i.e., a new national projection

• Define your epidemic
  – What sub-epidemics and sub-populations are important in your country

• Define population characteristics (size & demographics) of each sub-population

• Enter HIV data for each sub-population

• Enter ART data – national & sub-population
Steps in making an EPP projection

• Provide any **surveys** you wish to use in fitting
• Fit the epidemic and estimate uncertainty
• Calibrate to make any final adjustments
• Adjust for urban/rural population changes
• Generate results for the national epidemic
  – Prevalence and incidence trends
  – Produce files for Spectrum (*.spt and *.spu)
• Document decisions in “Comments” boxes
EPP 2009 leads you through each important step

Each “tab” represents a step in the process

Note new larger interface – more data shown, bigger graphs
The EPP Worksets page

• What is a workset?
  – A national epidemic composed of smaller epidemics in different sub-populations and/or geographic areas

• What can I do on this page?
  – Load an existing workset
  – Create a new workset, choose the country, enter notes
  – Create a workset from a template
  – Create a new template
The EPP Define Epi page

Create your own epidemic tree in panel on the right
Need to know - defining an epidemic

• What are sub-populations and sub-epidemics?
  – Sub-population is an epidemic in a specific group
    • Has a population size and HIV & ART data associated with it
  – A sub-epidemic is an epidemic made up from multiple epidemics in sub-populations and/or other sub-epidemics

• Sub-populations can have special characteristics
  – Urban, rural or both
  – Client, FSW, IDU, MSM, low-risk
The Define Pops page

• What can I do on this page?
  – Set the overall national population & population base year
  – Define population sizes for your sub-populations
  – Define demographic parameters (Generalized)
  – Display populations without an HIV epidemic
The Define Pops page
A bigger HIV data page

Data is entered by sites for each sub-pop

For each site give HIV prevalence & sample size
ANC surveillance data

• Enter HIV prevalence and sample size
• Classify ANC sites as urban and rural. Some countries have in the past also used “semi-urban” but surveys that we will use for calibration typically have estimates for urban and rural areas only
• Use same definition of urban/rural as is used for census and Demographic and Health Survey
EPP 2009’s first big change – ART Data

Enters number on 1st and 2nd line ART nationally

Divides that ART among the sub-populations
Why an ART data page?

- ART is expanding rapidly across the globe
- People live much longer on ART
- This means HIV prevalence increases
ART increases HIV prevalence

Without ART

With ART
EPP 2009 has expanded model with ART

- **Entrants by “birth” at age 15**
- **Not at-risk population**
- **Death**
- **Uninfected at-risk population**
- **Infected at-risk population**

Number gated by access slots. All untreated + newly eligible have equal chance.

- **$U$** Untreated
- **$E$** Newly eligible for ART
- **$L_1$** First-line ART
- **$L_2$** Second-line ART

- Death
The ART data page – what’s on it?

• First year survival on ART
  – Default 0.86 (based on review of survival in cohorts [Lewden et al] and lost to FU [Brinkhof et al: 40% mortality overall; 47% mortality at public ART centers in sub-Saharan Africa])
  – As countries increase early access, first year survival can increase (up to about .90?)

• National adult ART coverage
  – Number nationally on 1st line, 2nd line ART + totals

• Distribution of ART among the sub-populations
  – Prevalence impact depends on treatment numbers
  – We recognize it may be challenging to gather
Summary of features of ART data page

- User fills in blue cells only, others automatic
- Can specify sub-population distribution as
  - Absolute numbers on ART in sub-population or
  - Percent of national ART in that sub-population
- “Still to be assigned” must be zero before leaving page
  - NOTE: needs to be true for both 1st and 2nd line ART
- Remember to check inputs against calculated coverage (on “Results” page: ART results)
Providing more input to fitting – Surveys Page

Can enter up to 3 surveys for each sub-pop
Surveys in EPP 2009

- If you enter surveys, they will be used in fitting the epidemic
- Consider effect of non-response on HIV prevalence: use adjusted HIV prevalence correcting for the effect of non-response (per Mishra et al and Marston et al: see hand-out)
- If you do not enter surveys in generalized epidemics, EPP will automatically calibrate
  - Fits to ANC data are adjusted downward
  - Adjustment based on an average of national survey prevalence to ANC prevalence in countries with national surveys
  - Urban and rural adjustments are slightly different, on average approximately 0.8 (see Gouws et al, Brown et al, Alkema et al)
What does EPP fitting do?

• Fits plausible epidemiological model to existing data

• Modified Reference Group model – 4 fitting parameters
  – $r$ – controlling the rate of growth
  – $f_0$ – the proportion of new risk pop entrants
  – $t_0$ – the start year of the epidemic
  – $\phi$ – behavior change parameter
EPP’s job: fit the model to the data
How does EPP 2009 fit data?
Using a process called IMIS
developed by Le Bao & Adrian Raftery
We first randomly generate many curves.

Curves come from random combinations of $r$, $f_0$, $t_0$ and $\varphi$.

High weight – fits the data closely. Take its values for $r$, $f_0$, $t_0$ and $\varphi$. 
Then sample around highest weight curve

Finds some new curves around the best fitting one, i.e. one with highest weight.
EPP 2009 repeats until lots of curves close to data

An iterative process that may run up to 200 times and generate many 1000s of curves
EPP 2009 picks the best one as the UA fit

The one that fits the data best is chosen as the UA fit
This is done on the Uncertainty Analysis Page

You get to this when clicking “Assess uncertainty” on the Project page
The EPP 2009 fitting interface

Purpose of run
Start, Stop, and Status
Advanced options

Results display
Display controls

What to do with results
Important features of fitting interface

• Two modes
  – Training
    • Generates about 400 curves (if not fitting to surveys)
    • Takes about 2-5 minutes
  – For national projection
    • Generates about 1900 curves (if not fitting to surveys)
    • Takes 30 minutes or more for most data sets
While fitting EPP 2009 also assesses the uncertainty in the fit.
Assessing uncertainty – Bayesian melding

Developed by Adrian Raftery, Leontine Alkema and Le Bao for EPP

• Randomly generate lots of curves using IMIS procedure
  – Select a lot of (r, f0, phi and t0) values

• Compare the curves with the data
  – Calculate “goodness” of fit and assign a weight
  – Likelihood function is used as a weight on the curve
  – High likelihood means a curve is a good fit and gets a high weight

• Resample a smaller number of curves from the curves originally calculated
  – But, resample according to the weight assigned
  – The curves that fit better get picked more often

• Keep the resampled curves, throw away the others
• These curves provide an estimate of the uncertainty
Some countries have the curves with high weights tightly bundled.

Botswana urban through 2002

Botswana urban through 2003 – future of epidemic tightly constrained
In other countries the data does not constrain possible curves much at all.

Uncertainty about the future is huge.

Senegal urban through 2003
As more data becomes available, projections should improve & uncertainty fall.

Botswana urban surveillance data through 2003.
Uncertainty decreases as more data becomes available

Botswana urban using only data through 1995 – data still rising

Very uncertain
Uncertainty decreases as more data becomes available

Botswana urban using only data through 2000 – points starting to level off

Uncertainty is getting smaller
Uncertainty decreases as more data becomes available

Uncertainty is narrowing as epidemic levels off

Botswana urban using all data through 2003 – data has leveled off
Uncertainty can be seen in fitting results display

Parameters of best fitting curve found in sample

Graph with:
- Surveillance data
- Unique curves (light gray)
- Bounds (dashed lines)
- Best curve (UA fit - red)
- Mean (blue)
- Median (black)

UA fit – the curve with best fit to the available data of those sampled
What do the checkboxes at the bottom refer to?

- **Surv data** – the actual surveillance values
  - Presented by site so you can see site trends
- **Curves** – the unique resampled curves
- **UA fit curve** – the most likely among the sampled curves
  - “best fit” for us
- **Bounds**
  - 95% confidence bounds (95% of curves fall between the dashed lines)
- **Mean and median**
  - Year by year, the mean & median of all resampled curves
Display of parameters for the chosen curve

“Selected parameter Values”: Shows histogram of the values of the parameters selected among resampled curves
Many curves can fit the same data – some we know are not realistic

Source: Adrian Raftery
For this we have “Advanced Options”

Conditions on prevalence: right hand side
Conditions on prevalence (right hand side)

- Sometimes we get a cluster of curves we know are not feasible
- Condition
  - $\text{Prev} < 1\%$ in 1985 will eliminate these
- Apply with caution or you can eliminate valid curves
Limits on curve generation (left hand side)

- We need to generate a lot of curves
  - Done by giving random values for $r$, $f_0$, $t_0$ and $\phi$
- It’s better if we generate ones that are more likely to fit
  - We throw fewer of the curves away
- So we can restrict the range on $r$, $f_0$, $t_0$ and $\phi$
- Can change distributions (following review of selected parameter values):
  - Change median of $\phi$ distribution to 0 or -50 or -100 if prevalence declines after peak (from default 100)
  - Change distribution of $t_0$ to 1970 – 1980 if epidemic known to have started before 1980 (from default 1970-1990)
Prior parameter distributions in “Advanced Options”

Prior distributions: left hand side
What happens if we include surveys?

Surveys show up in red on the graph before fitting.
What happens if we include surveys?

After fitting uncertainty bounds are narrower

- Surveys assumed to be better estimates

ANC data is downward scaled
The EPP 2009 Calibration page

6 calibration options provided

Display shows the result of each option

One you choose will be used to change the outcomes on the Results page
The EPP 2009 Pop change page

Top row – UN Pop % urban
2nd row – your workset’s % urban
Bottom – distribution of population among your sub-pops
Results page – putting your projections together

"Output results" - show outcomes - create Spectrum file ‘*.spt’
Results page – putting your projections together

“Show uncertainty”
- Gives national uncertainty from combining projections
Saving an uncertainty file for Spectrum

- Click “Save Spectrum uncertainty file”
- A file with the extension *.spu will be saved, which can be read by Spectrum
“ART results”
- Summarizes ART findings for National projection
- Check whether ART coverage for future projection is reasonable. If not, go back to ART data and change inputs.
Results page – putting your projections together

“Incidence distribution” - Shows how sub-pops contribute to national incidence
So to review, to fit a generalized epidemic

• Fill in everything until you get to Projection Page as in the past (and documented in the EPP 2007 manual)
• Press “Assess uncertainty” button on Projection page
• Press “Analyze uncertainty” button & wait for it to finish
• Press the “Use UA fit in EPP”
• On the Projection Page, hit “Save and Continue”
  – This is important – DON’T FORGET IT!!!(you’ll lose results)
• Move on to fitting the next sub-population
So to review, fitting an epidemic (continued)

• On the Results page, generate a Spectrum file by:
  – Pushing “Output results”
  – On that display, pushing “Write Spectrum File”
  – This generates a *.spt file in the eppout directory

• Press “Show Uncertainty” button on Results page to see national uncertainty results

• Generate a Spectrum uncertainty file by:
  – Pushing “Save Spectrum uncertainty file” on the National Uncertainty Results page
  – This generates a *.spu file in the eppout directory

• Take a well deserved rest
Warning

• Do not use older EPP files from EPP 2007
  – Many things have changed in EPP 2009
  – Files will run, but may give wrong results
$\phi$ – shift

- Advanced users – under development
- Deals with following situations:
  - ANC prevalence declines so steep that the prevalence trend implies implausibly low incidence
  - Prevalence decline followed by stabilisation or increase of prevalence
- Use advanced options to set prior distributions of additional parameters
Modified Reference Group model
Incidence in final year
ϕ shift – example parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>UA fit r</td>
<td>1.926920</td>
</tr>
<tr>
<td>UA fit f0</td>
<td>0.230830</td>
</tr>
<tr>
<td>UA fit t0</td>
<td>1971</td>
</tr>
<tr>
<td>UA fit phi</td>
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</tr>
<tr>
<td>UA fit phi'</td>
<td>-0.031191</td>
</tr>
<tr>
<td>UA phi' start</td>
<td>2002</td>
</tr>
<tr>
<td>UA phi' end</td>
<td>2015</td>
</tr>
</tbody>
</table>
EPP 2009 – review mode

- Can open a projection w/o changing it
- Disables saves
- Indicated two ways:
  - Title bar says “Review mode”
  - “Save & continue” becomes “Continue” and is yellow
- Two ways to exit
  - On Workset Page, click “Edit” mode
  - On any page, hit “Save a copy”
Review mode – the interface
Example of complete run-through of the process for a country with calibration

Demonstration and The End