

EPP 2009

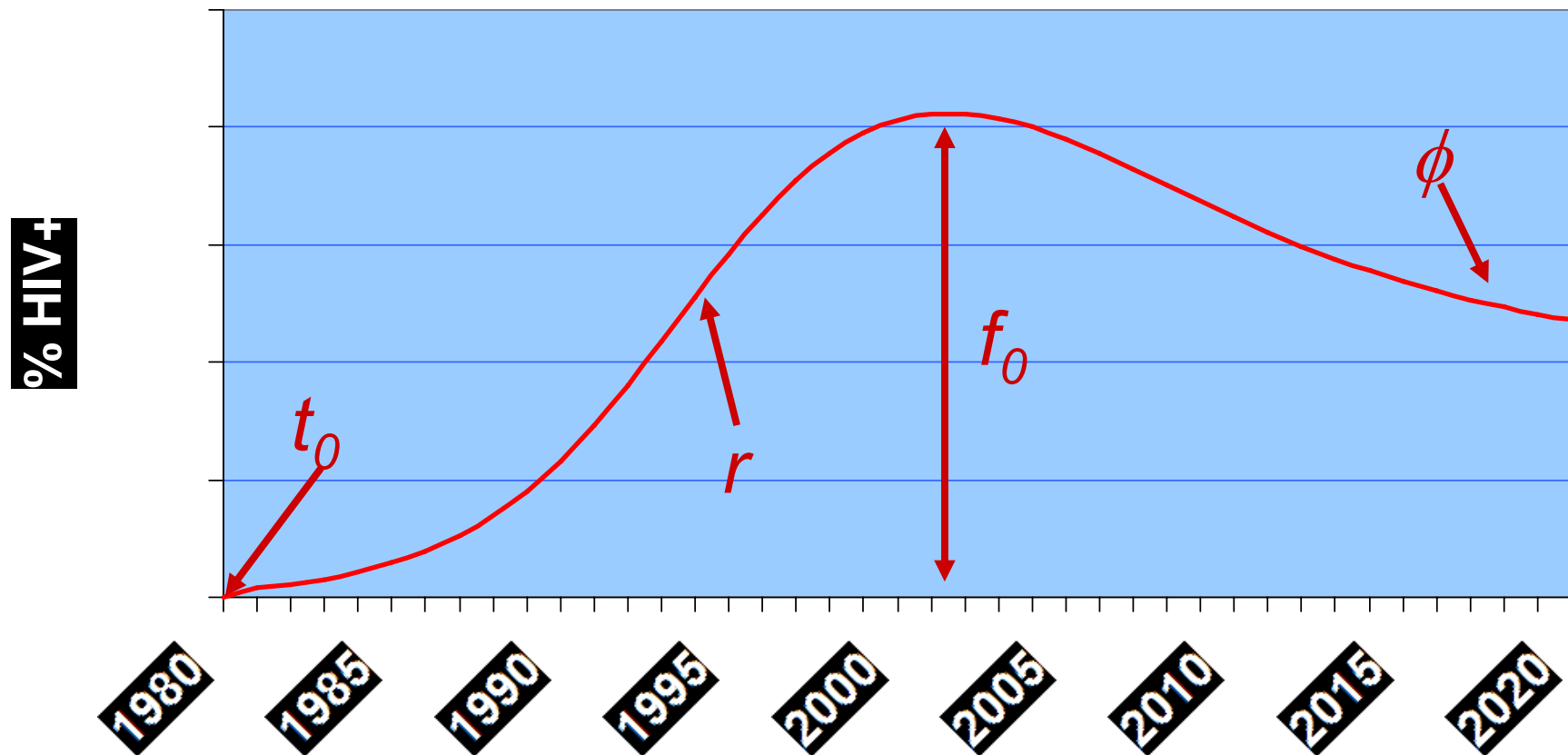
*HIV epidemic trends in the ART era
Low level & concentrated epidemics – part 2*

*UNAIDS/WHO Working Group
on Global HIV/AIDS & STI Surveillance*

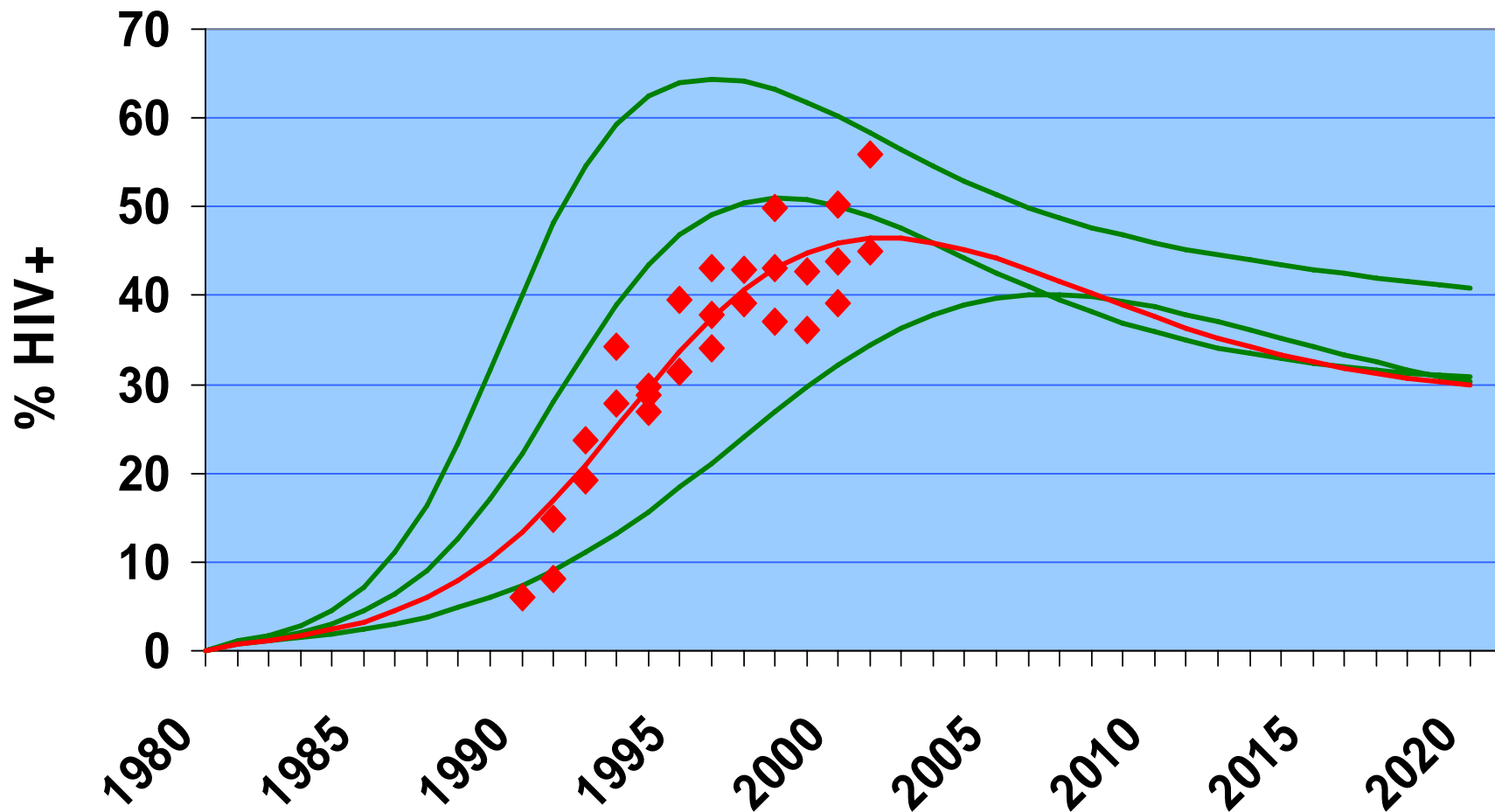
What does EPP fitting do?

- 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
 - ϕ – behavior change parameter

UNAIDS Reference Group model



EPP's job: fit the model to the data

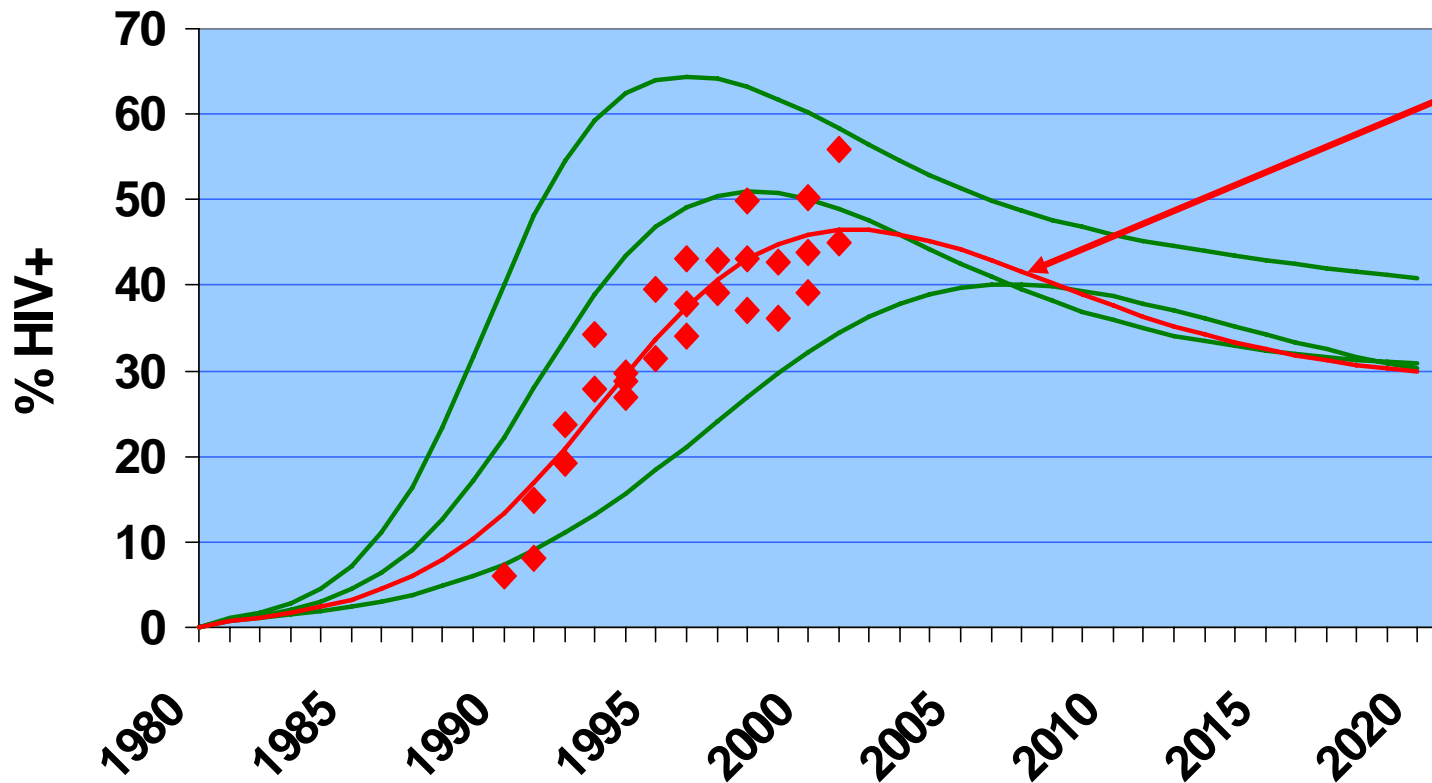


How does EPP 2009 fit data?

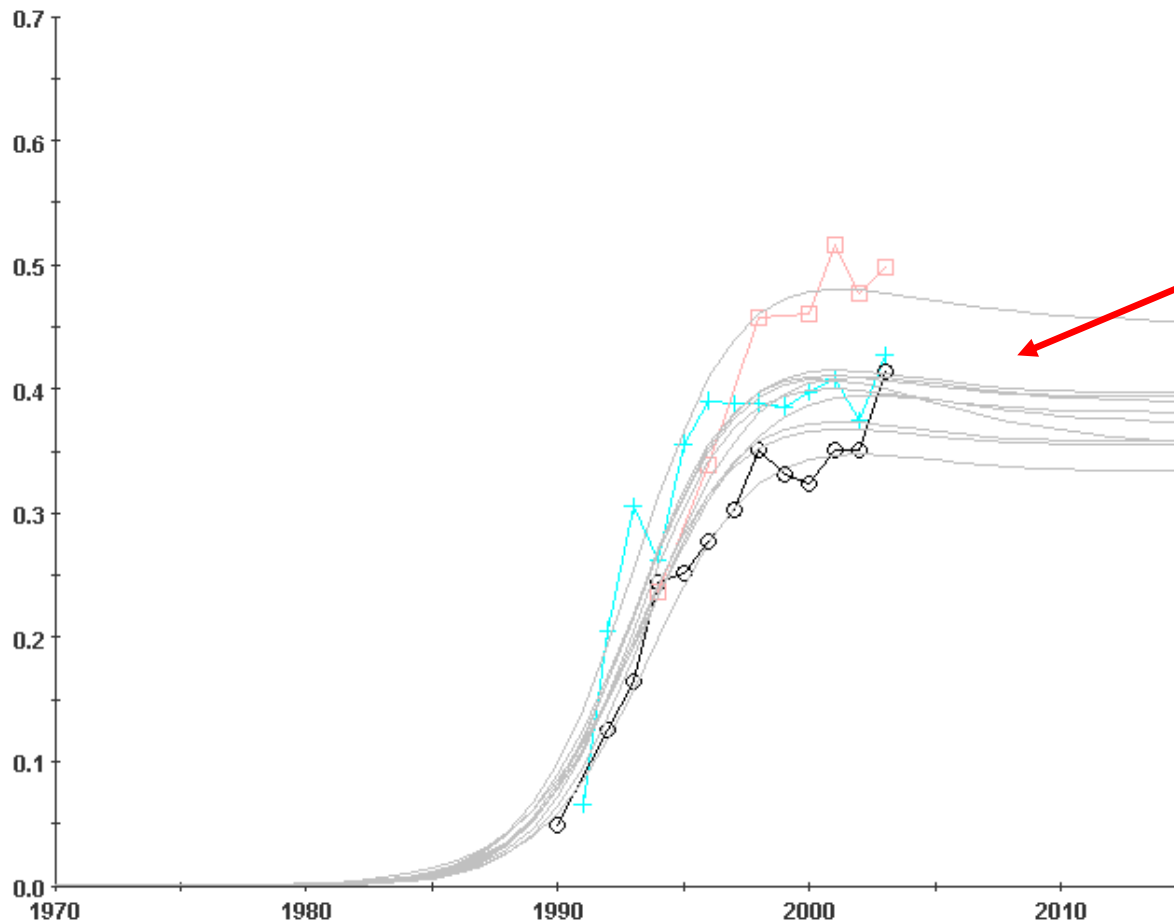
Using a process called IMIS developed by Le Bao & Adrian Raftery

We first randomly generate many curves

Curves come from random combinations of r , f_0 , t_0 and φ

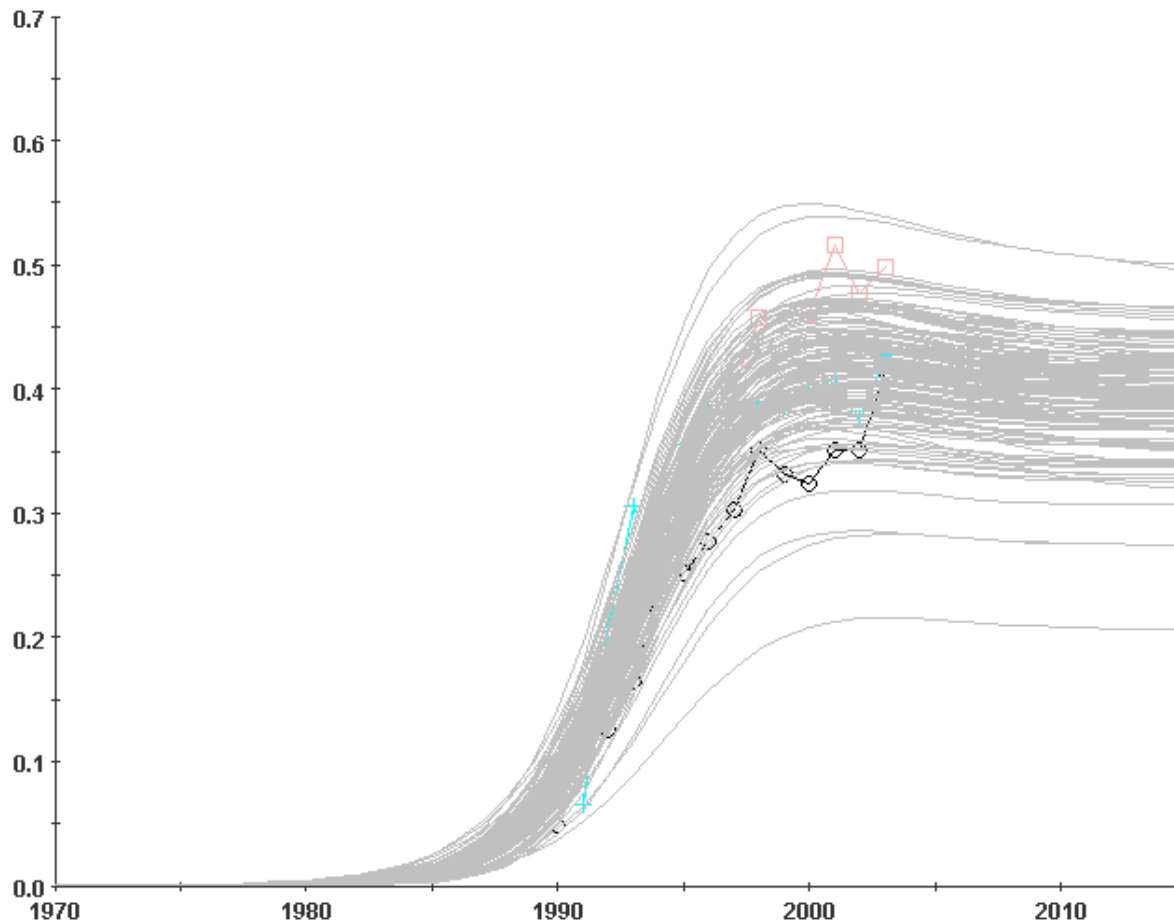


Then sample around highest weight curve



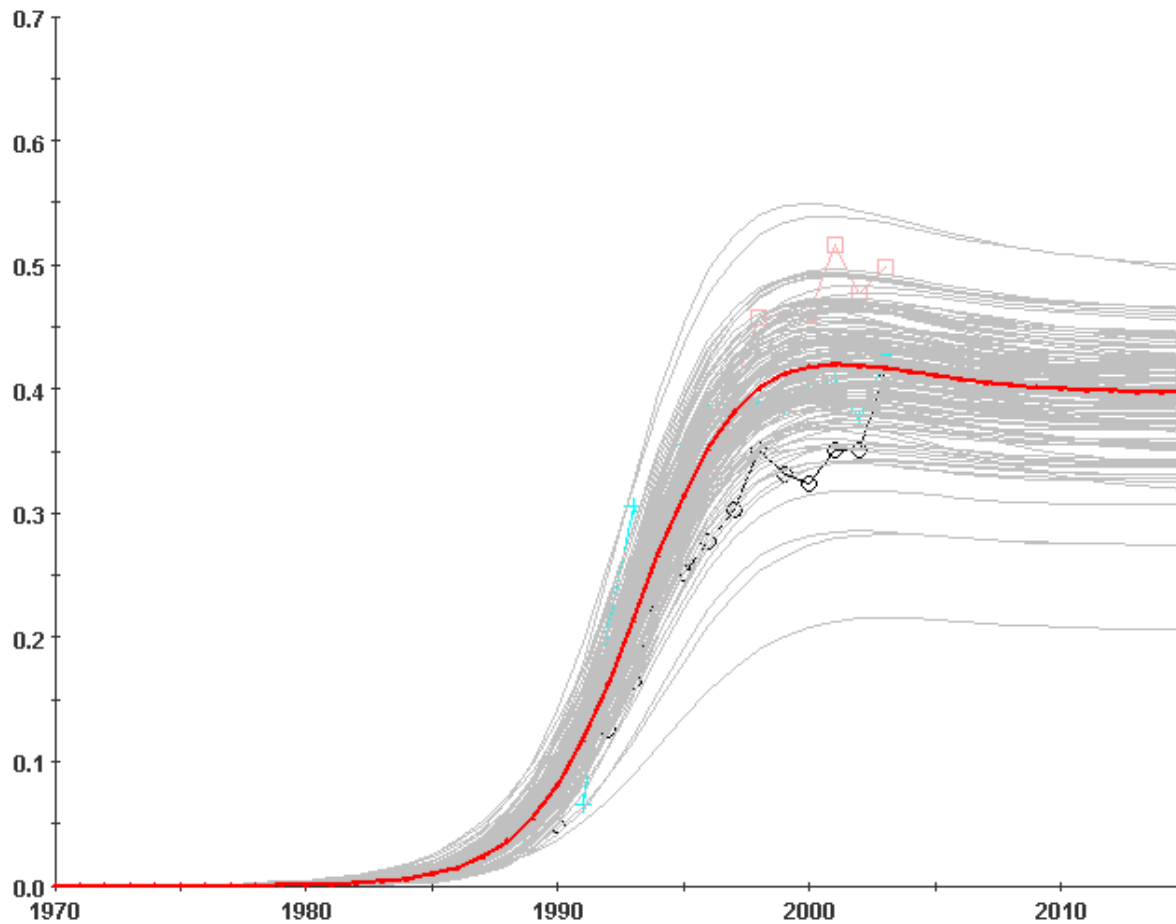
Finds some new curves around the best fitting one, i.e. one with highest weight

EPP 2009 repeats until lots of curves close to data



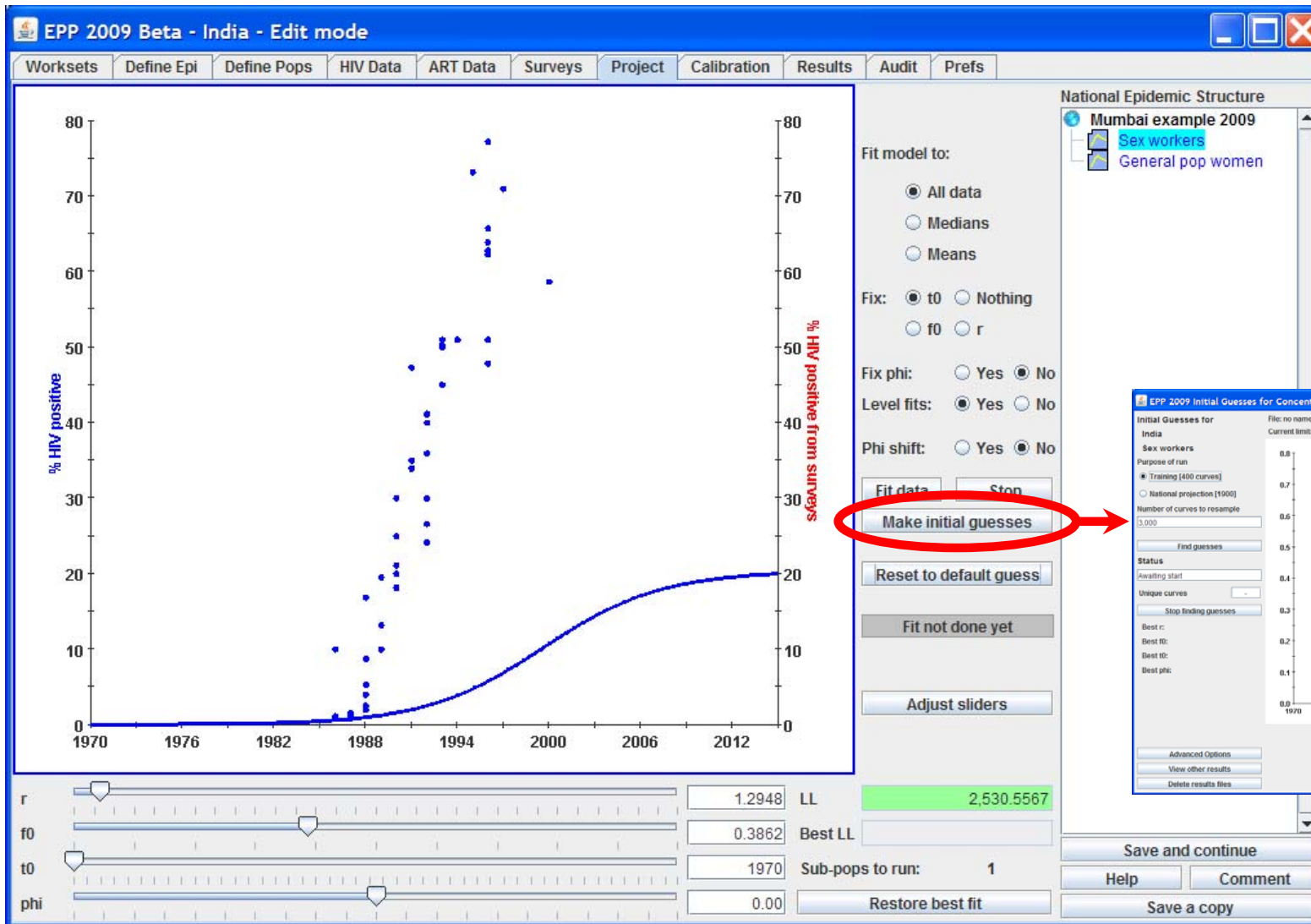
An iterative process that may run up to 200 times and generate many 1000s of curve

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 Initial Guesses page



EPP 2009 Beta - India - Edit mode

Worksets Define Epi Define Pops HIV Data ART Data Surveys Project Calibration Results Audit Prefs

National Epidemic Structure

- Mumbai example 2009
 - Sex workers
 - General pop women

Fit model to:

All data
 Medians
 Means

Fix: t0 Nothing
 f0 r

Fix phi: Yes No

Level fits: Yes No

Phi shift: Yes No

Fit data Stop

Make initial guesses

Reset to default guess

Fit not done yet

Adjust sliders

r: 1.2948 LL: 2,530.5567

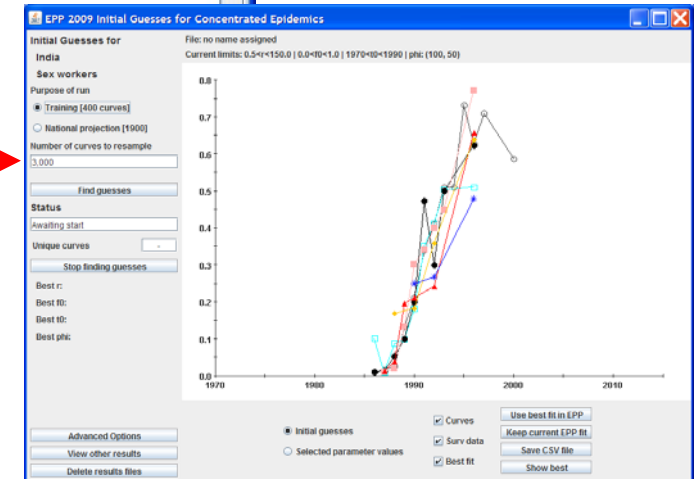
f0: 0.3862 Best LL:

t0: 1970 Sub-pops to run: 1

phi: 0.00 Restore best fit

Save and continue Help Comment Save a copy

You start by clicking “Make initial guesses” on the Project page



EPP 2009 Initial Guesses for Concentrated Epidemics

Initial Guesses for India

Sex workers

Purpose of run

Training (400 curves)
 National projection (1900)

Number of curves to resample: 3,000

Find guesses

Status: Awaiting start

Unique curves: -

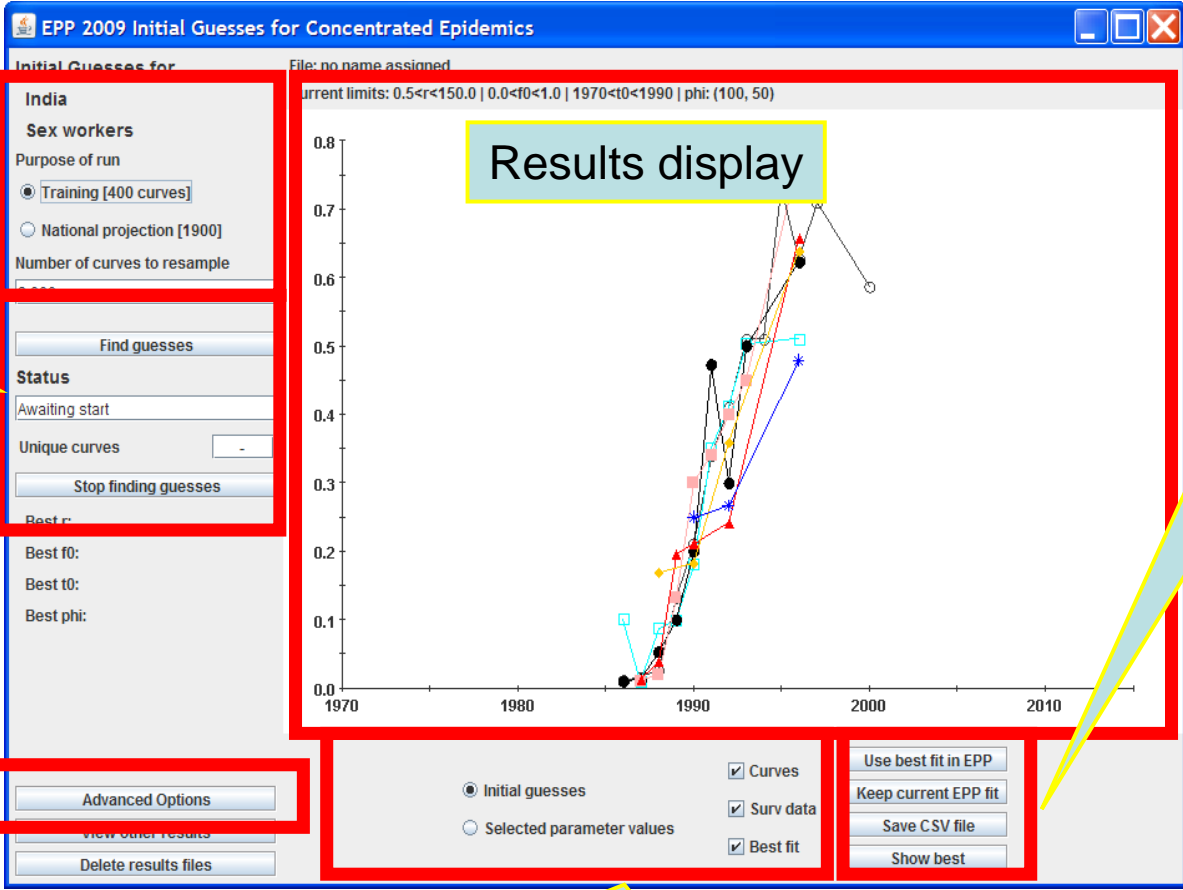
Stop finding guesses

Best r:
 Best f0:
 Best t0:
 Best phi:

Advanced Options View other results Delete results files

Initial guesses Curves Use best fit in EPP
 Selected parameter values Surv data Keep current EPP fit
 Best fit Save CSV file Show best

This brings up the EPP 2009 fitting interface



Purpose of run

Start, Stop, and Status

Advanced options

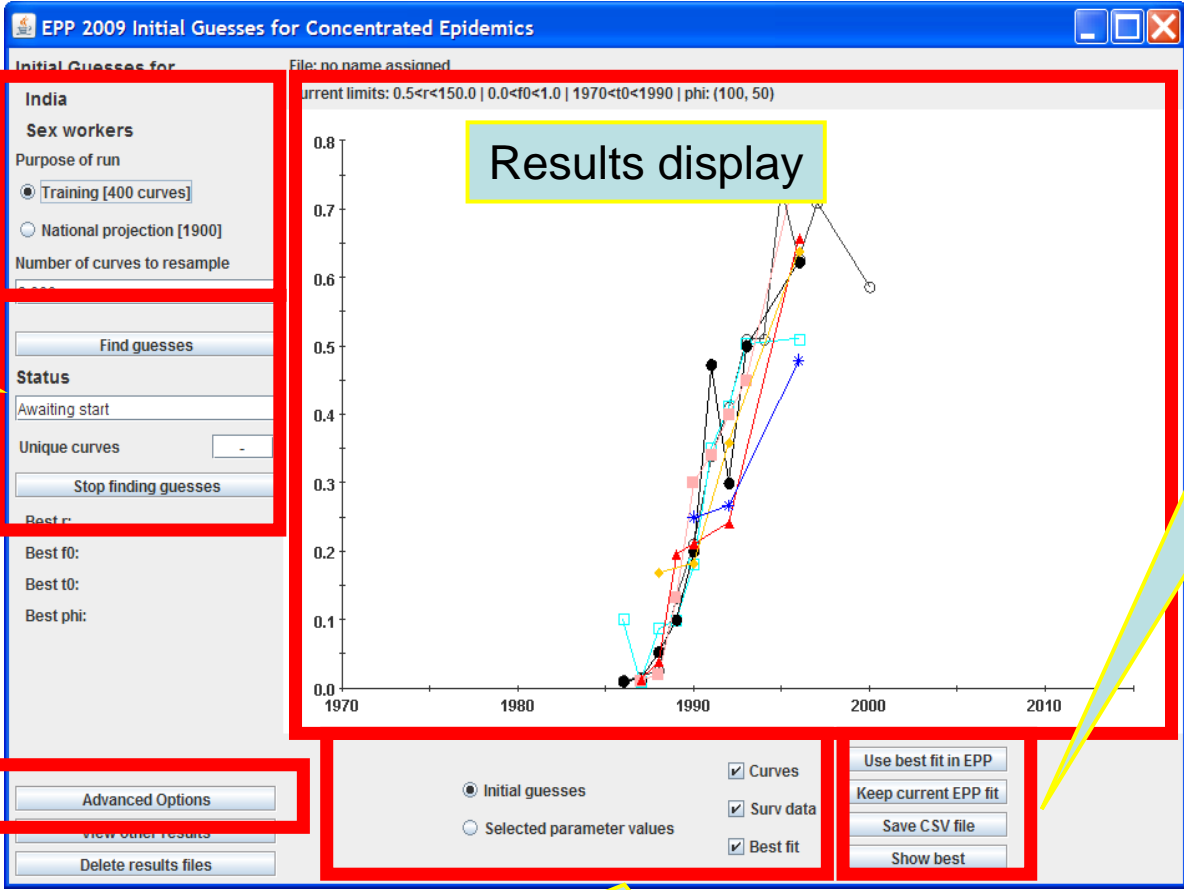
Results display

What to do with results

Display controls

2009 en

11



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

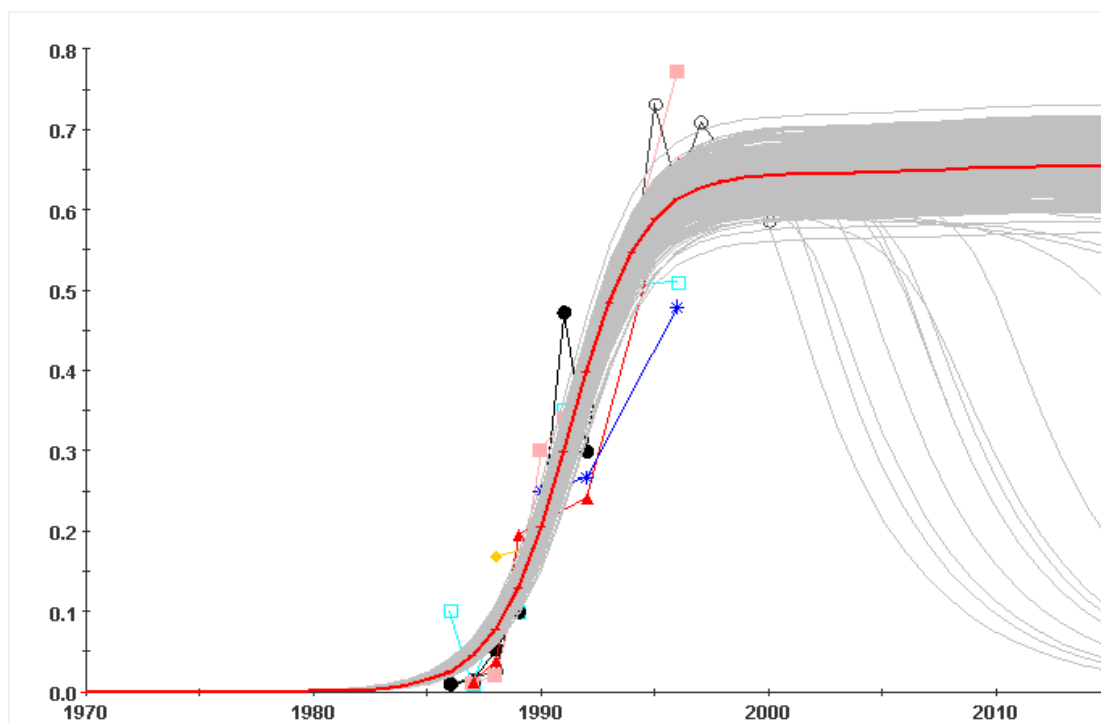
While fitting EPP 2009 also assesses
what range of curves might fit your data

Assessing what fits – 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 , f_0 , ϕ and t_0) 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 show the range of curves that might fit the data

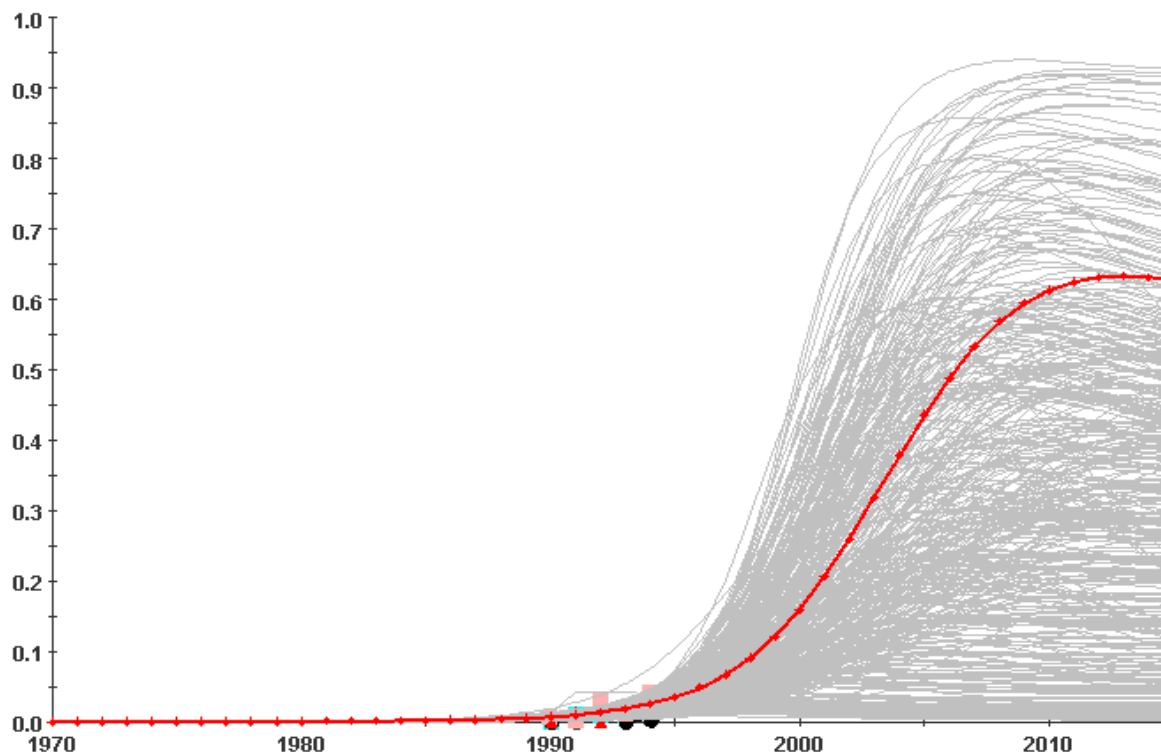
Some data sets have the curves with high weights tightly bundled



Mumbai FSW thru
2003 – future of
epidemic tightly
constrained

Mumbai sex worker data through 2000

Other data sets do not limit the possible curves much at all

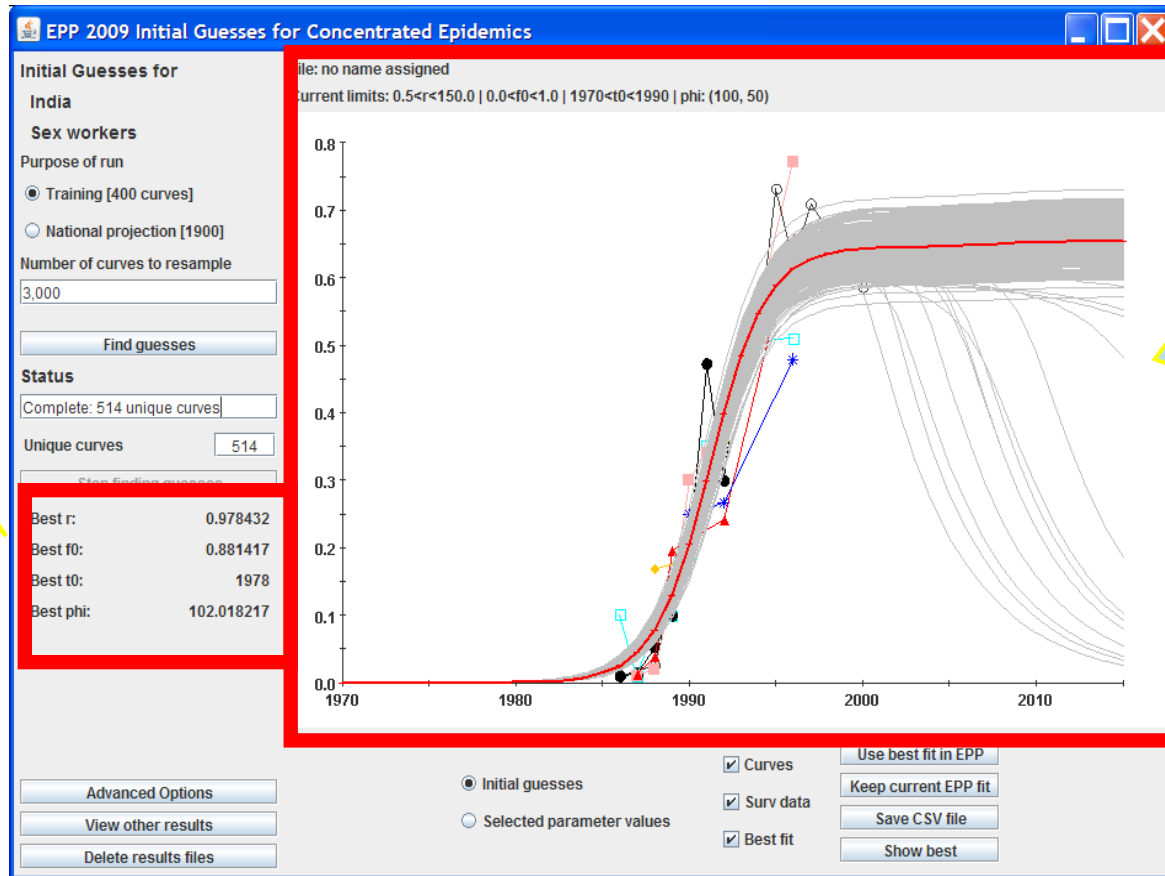


Uncertainty
about the
future is huge

Miscellaneous early Thai ANC data thru 1994

Results of generating initial guesses

Parameters of best fitting curve found in sample

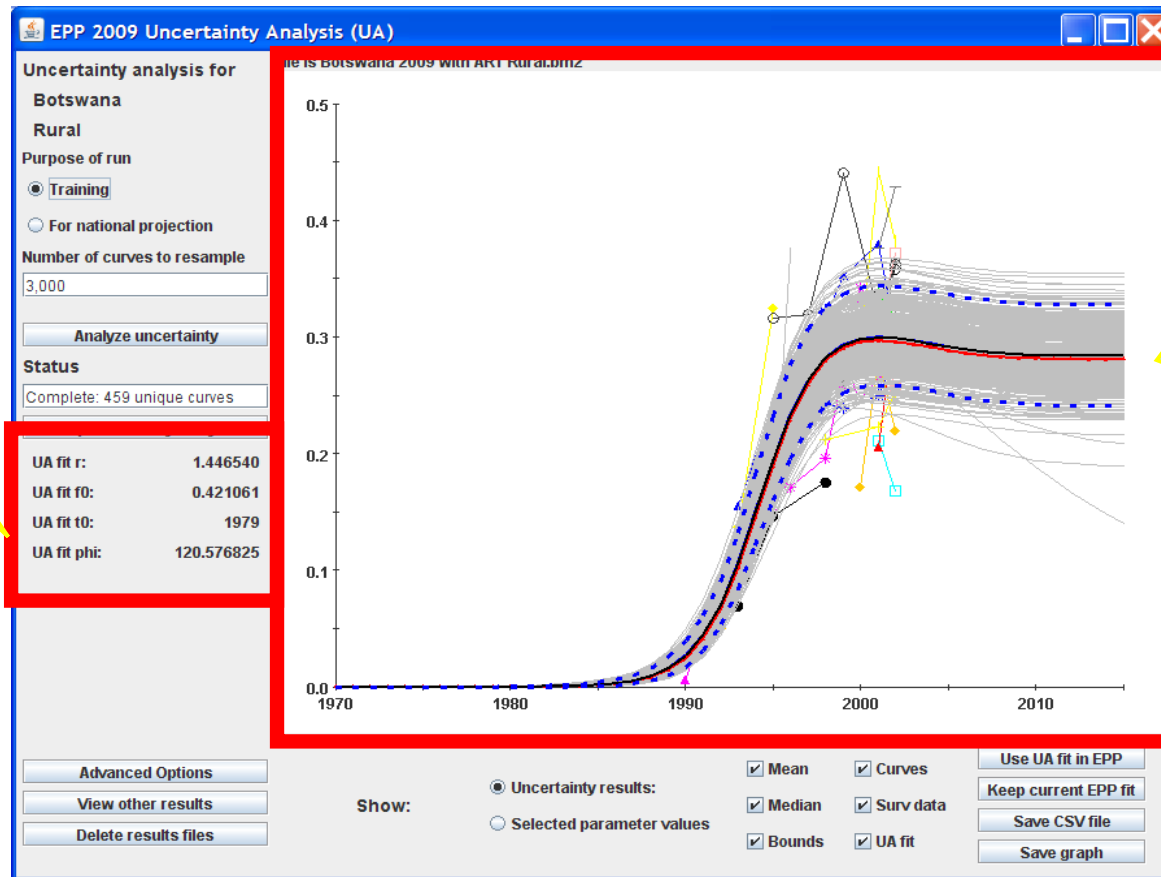


Graph with:
 Surveillance data
 Unique curves (light gray)
 Best curve (UA fit - red)

Limits are shown in a string at the top of the page

Generalized epidemics estimate actual uncertainty

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)

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 (generalized epidemics only)
 - 95% confidence bounds (95% of curves fall between the dashed lines)
- Mean and median (generalized epidemics only)
 - Year by year, the mean & median of all resampled curves

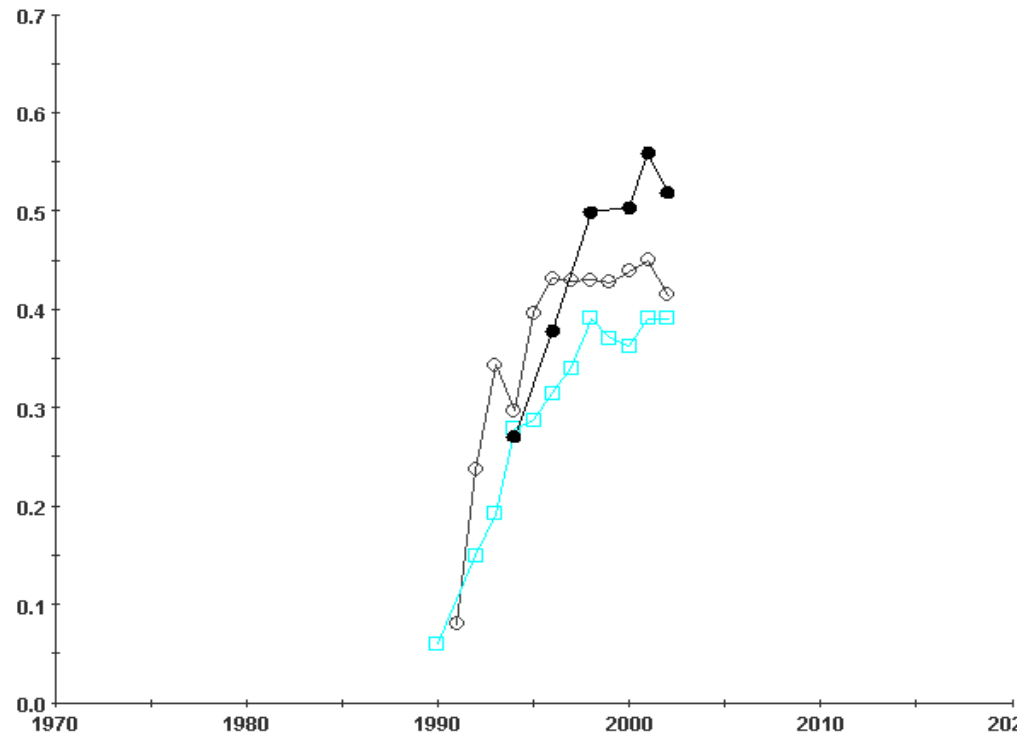
Why no uncertainty for concentrated epidemics?

- Size of at-risk populations is a major source of uncertainty
 - Currently estimates are very poor, very uncertain
 - Reference Group is still exploring how to deal with it realistically
- Samples are much more restricted
 - Geographically
 - Access to populations is more limited (FSW, IDU, MSM, etc.)
 - Data often not representative – convenience samples

But the same approach can let us

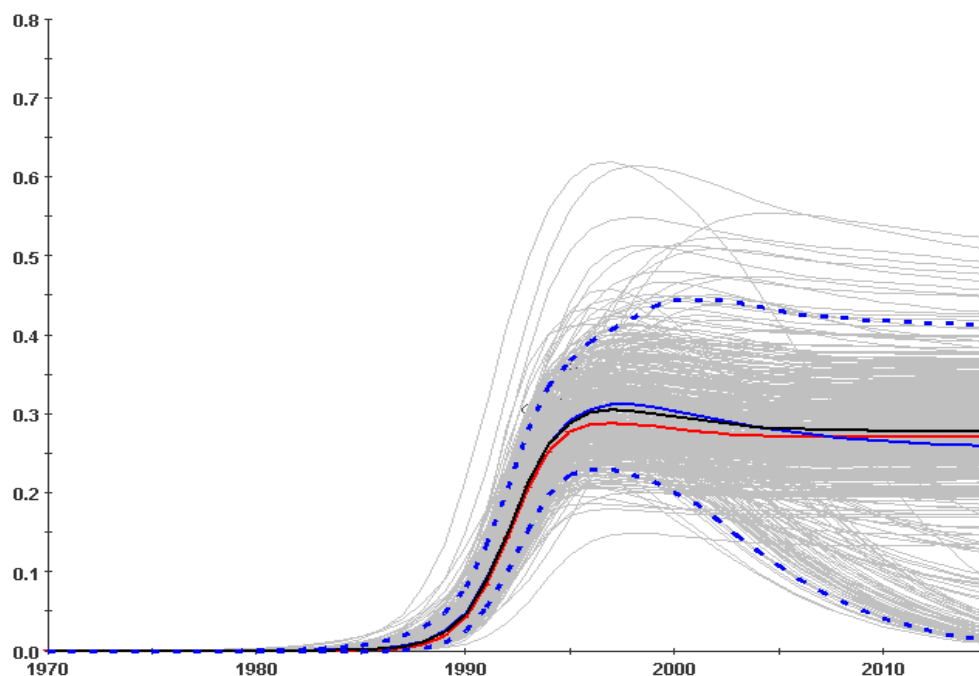
- Find a set of good initial guesses for what the epidemic looks like
- Get an idea of the range of possible curves that might fit the data we have
 - This is not formal “uncertainty” but a more qualitative impression

As more data becomes available projections improve & possible curves narrow



Botswana urban surveillance data through 2003

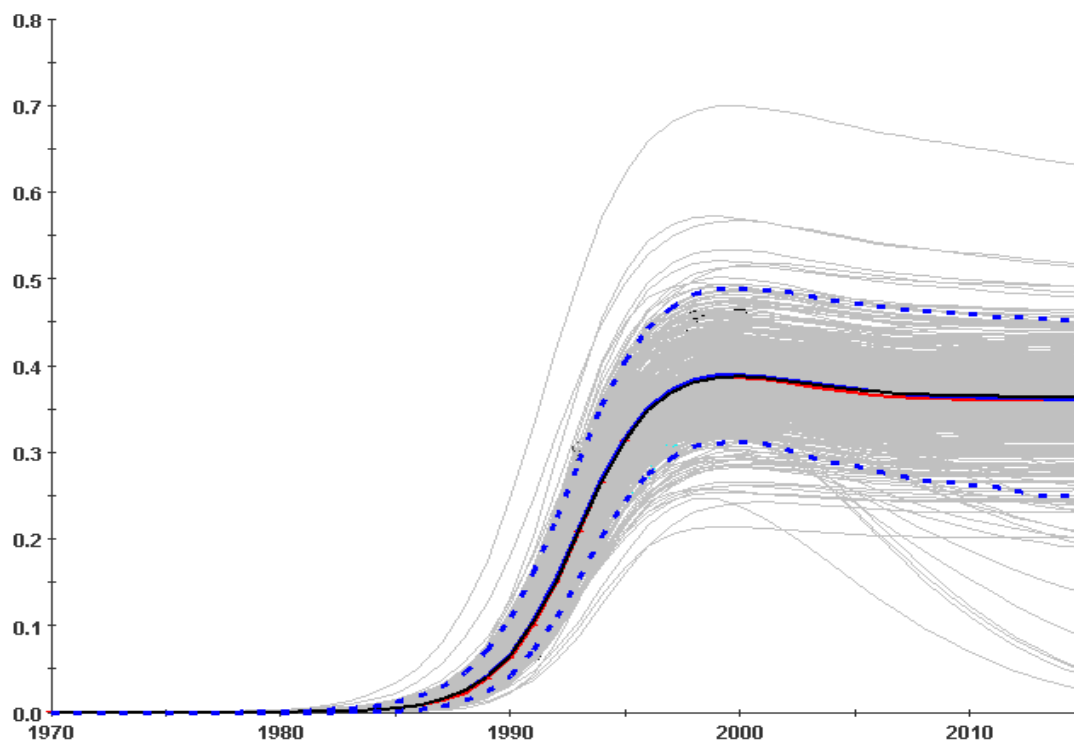
Uncertainty decreases as more data becomes available



Very uncertain

Botswana urban using only data through 1995 – data still rising

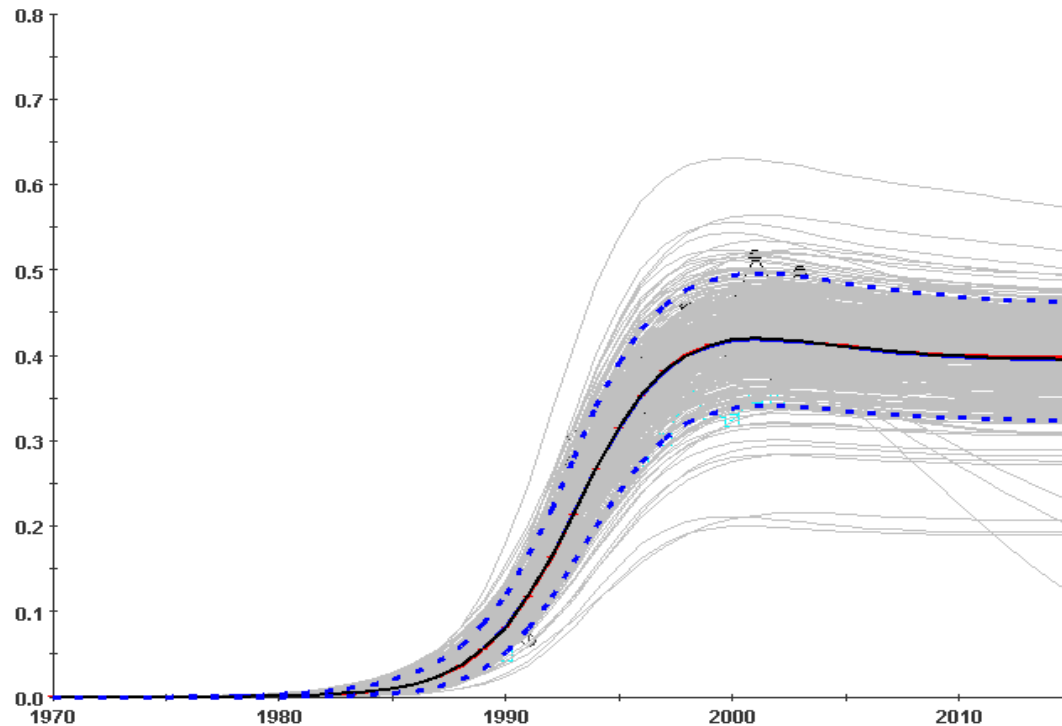
Uncertainty decreases as more data becomes available



Uncertainty
is getting
smaller

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

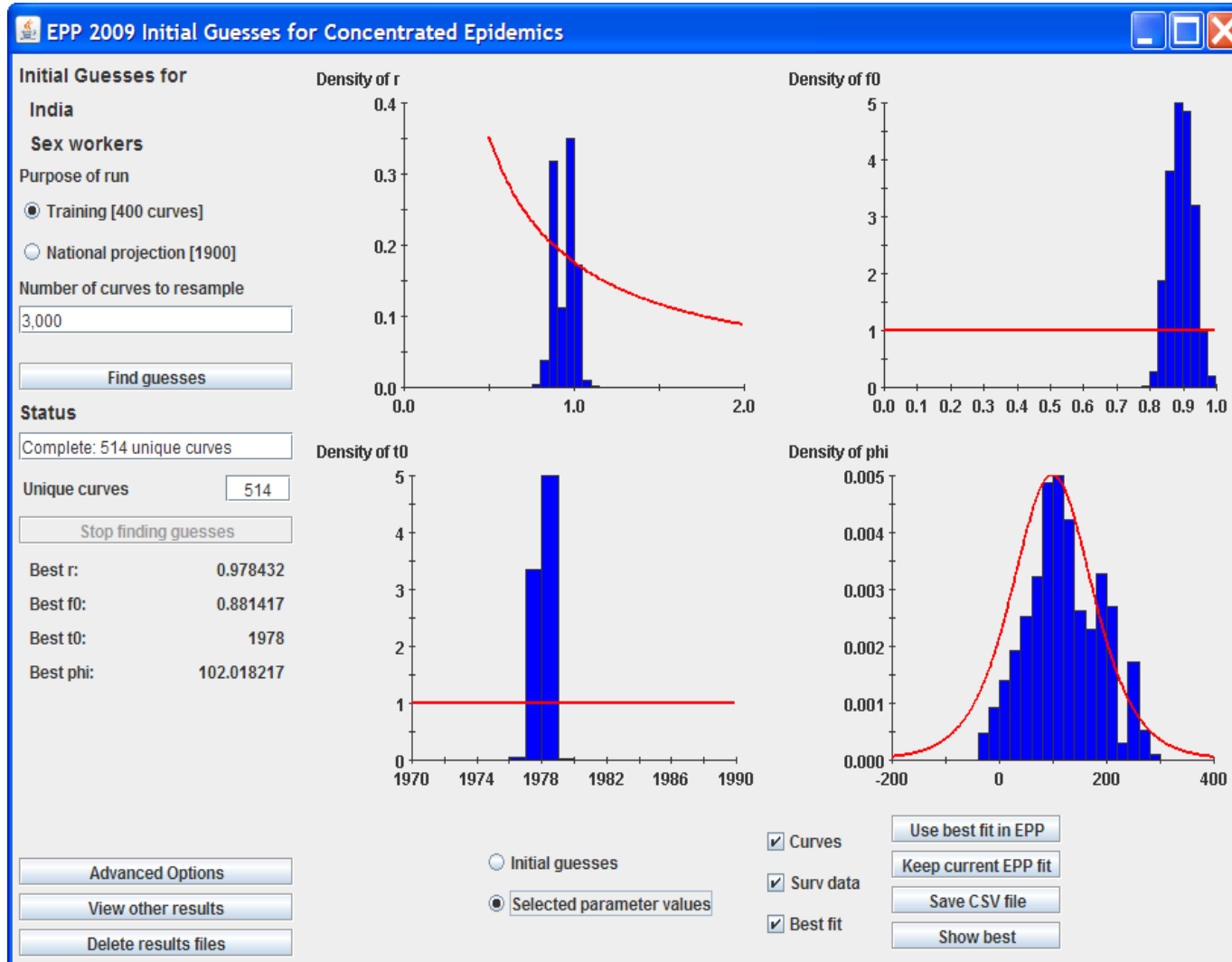
Uncertainty decreases as more data becomes available



Uncertainty
is narrowing
as epidemic
levels off

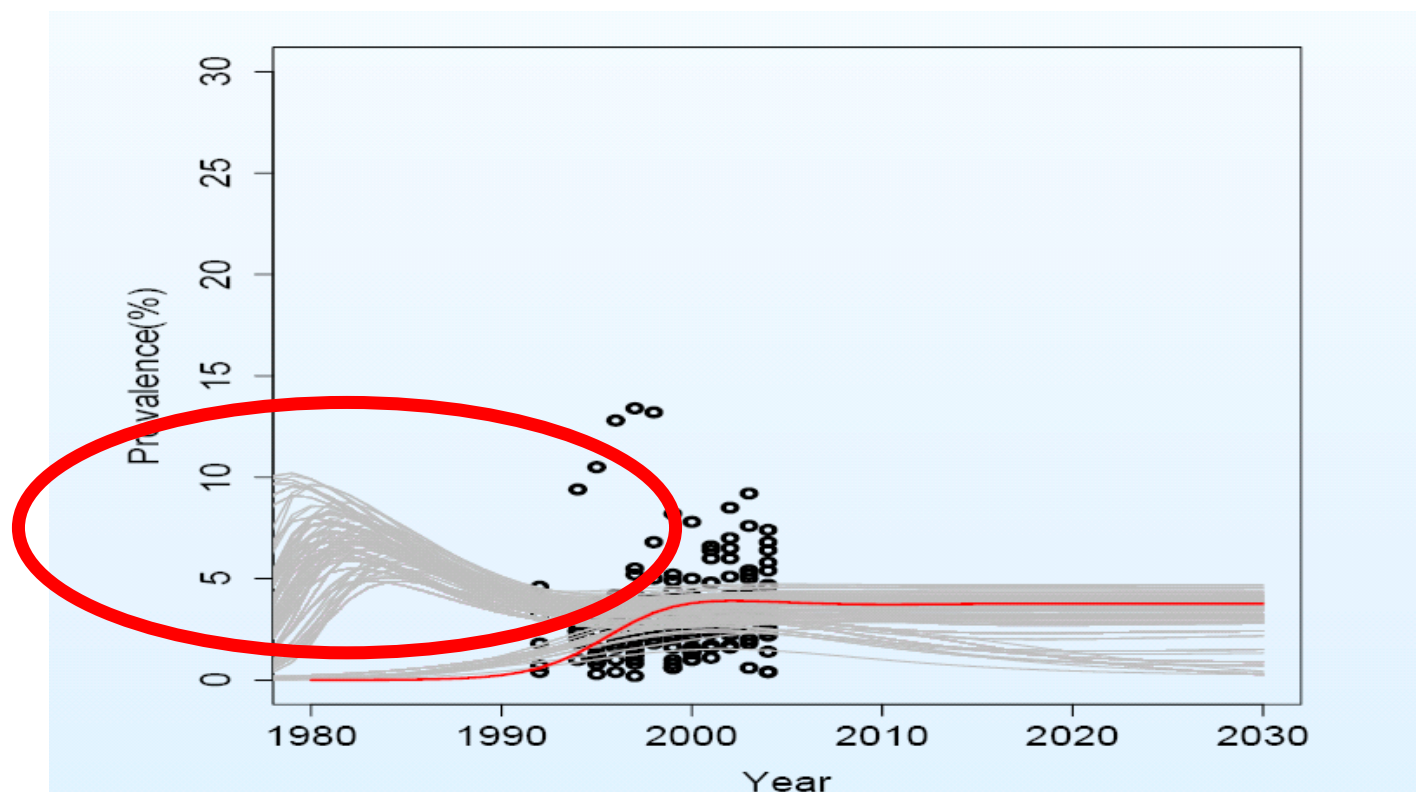
Botswana urban using all data through 2003 – data has leveled off

Display of parameters for the chosen curve



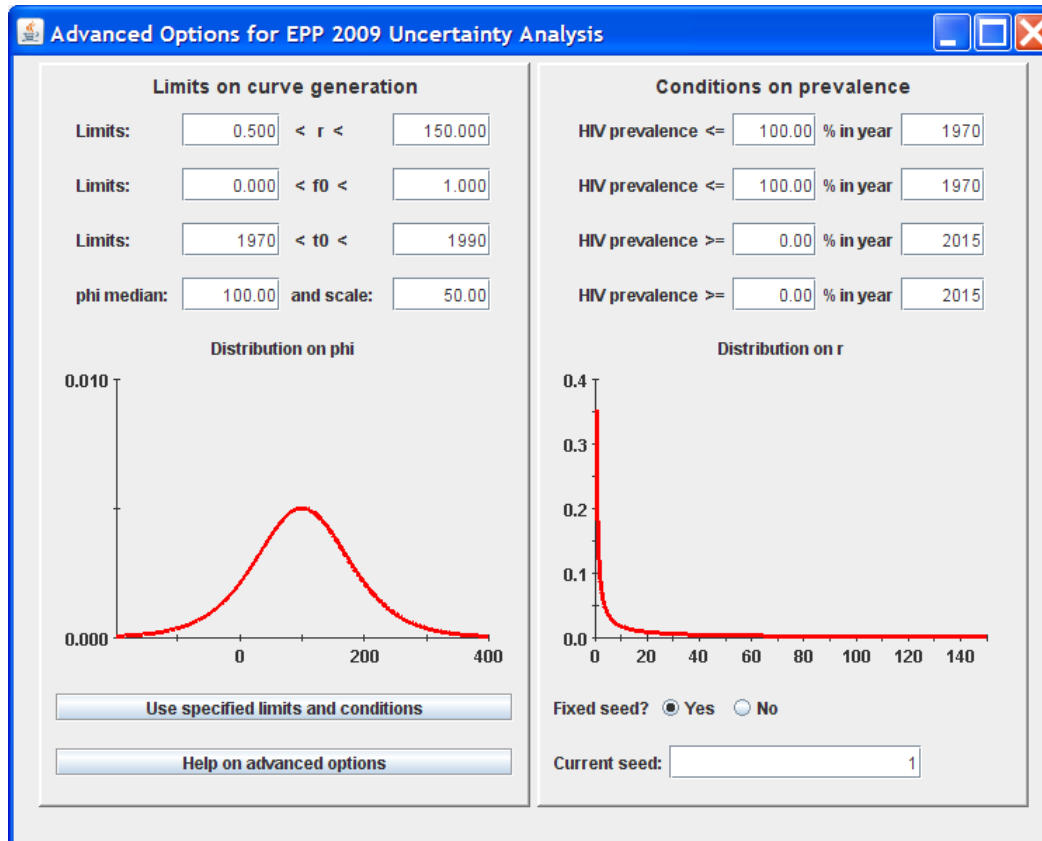
“Selected parameter Values”: Shows histogram of the values of the parameters selected among resampled curves

Many curves can fit the same data – some we know are not realistic



Source: Adrian Raftery

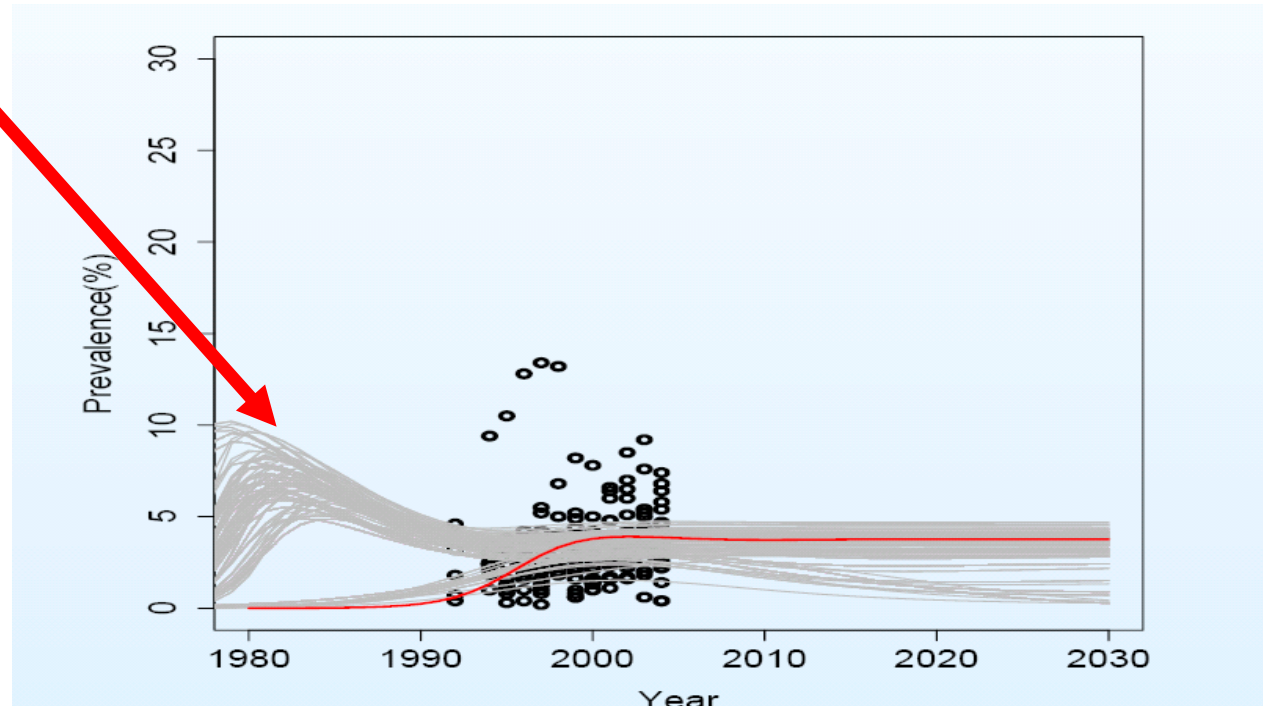
For this we have “Advanced Options”



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
 - $Prev < 1\%$ 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 ϕ
- 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 ϕ
- Can change distributions (following review of selected parameter values):
 - Change median of ϕ distribution to 0 or -50 or -100 if prevalence declines after peak (from default 100)
 - Change distribution of t_0 to 1980 – 1990 if epidemic known to have started after 1980 (from default 1970-1990)

Limit and distributions in “Advanced Options”

Advanced Options for EPP 2009 Uncertainty Analysis

Limits on curve generation

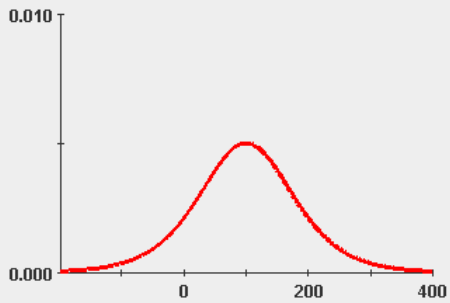
Limits: < r <

Limits: < f0 <

Limits: < t0 <

phi median: and scale:

Distribution on phi



Use specified limits and conditions

Help on advanced options

Conditions on prevalence

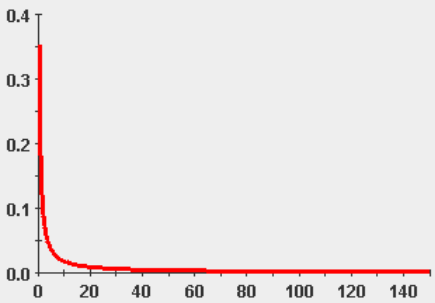
HIV prevalence <= % in year

HIV prevalence <= % in year

HIV prevalence >= % in year

HIV prevalence >= % in year

Distribution on r

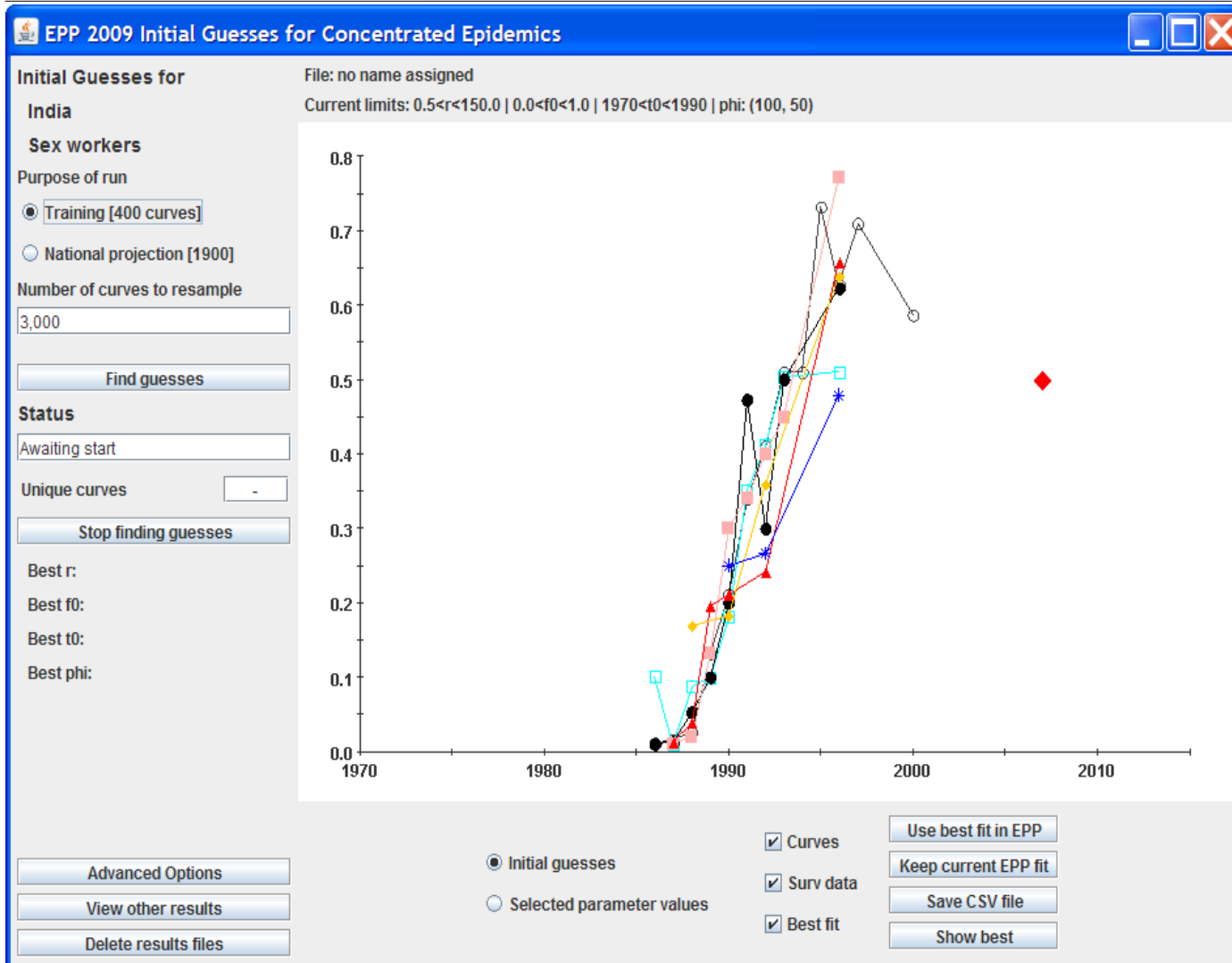


Fixed seed? Yes No

Current seed:

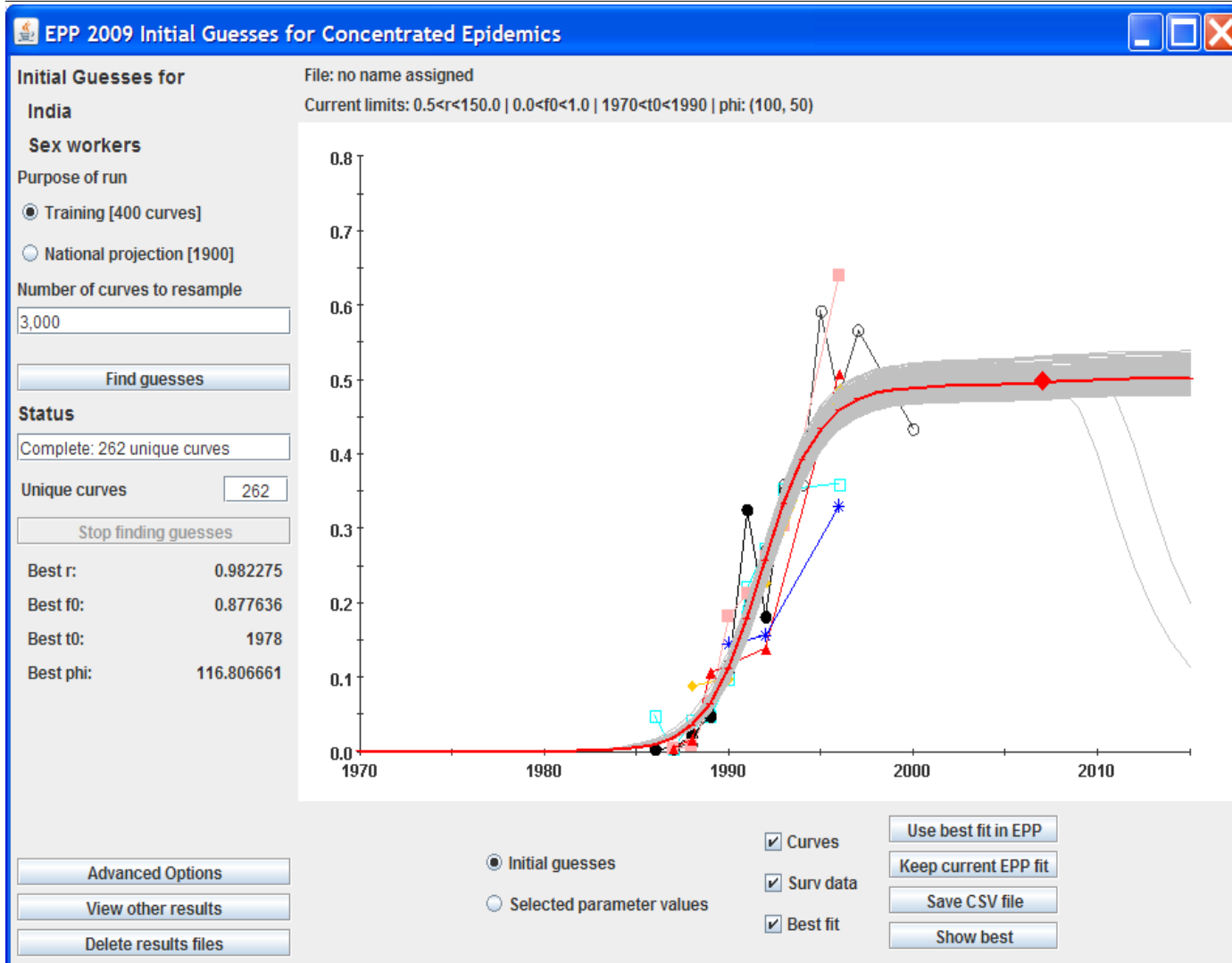
Parameter
 limits and
 distributions

What happens if we include surveys?



Surveys show up in red on the graph before fitting

What happens if we include surveys?



After fitting
 chosen curves
 more restricted

- Surveys
 assumed to
 be better
 estimates

Data is scaled
 downward to
 calibrate thru
 the survey
 value

Two key things to note here

- If only one survey, calibrated UA fit curve may not go exactly through survey point
 - But this is adjusted for on the Calibration page
- Range of curves selected is usually narrower than those without survey
 - Assumption is that survey accurately reflects true population prevalence, subject to measured error
 - Error of survey affects the curves resampled

To select another curve – click “Show best”

#	r	f0	t0	phi	Count
0	10.0504	0.0495	1977	117.9016	15
1	8.2845	0.0555	1976	42.7654	4
2	7.5154	0.0585	1975	47.7581	2
3	10.5115	0.0494	1978	205.9372	28
4	11.3515	0.0461	1978	143.0453	9
5	7.6573	0.0570	1975	69.5751	8
6	7.4688	0.0584	1975	58.7342	7
7	10.8260	0.0491	1978	130.4350	10
8	10.1533	0.0483	1977	108.5822	11
9	9.2658	0.0523	1977	97.5206	13
10	8.1073	0.0568	1976	100.3339	17
11	9.3037	0.0512	1976	89.7123	7
12	9.8620	0.0509	1977	108.6300	18
13	11.8889	0.0474	1979	156.7652	14
14	7.2373	0.0598	1975	3.7496	15
15	9.3153	0.0519	1977	85.6581	13
16	7.8828	0.0566	1975	167.3915	31
17	7.4867	0.0501	1975	68.7153	7

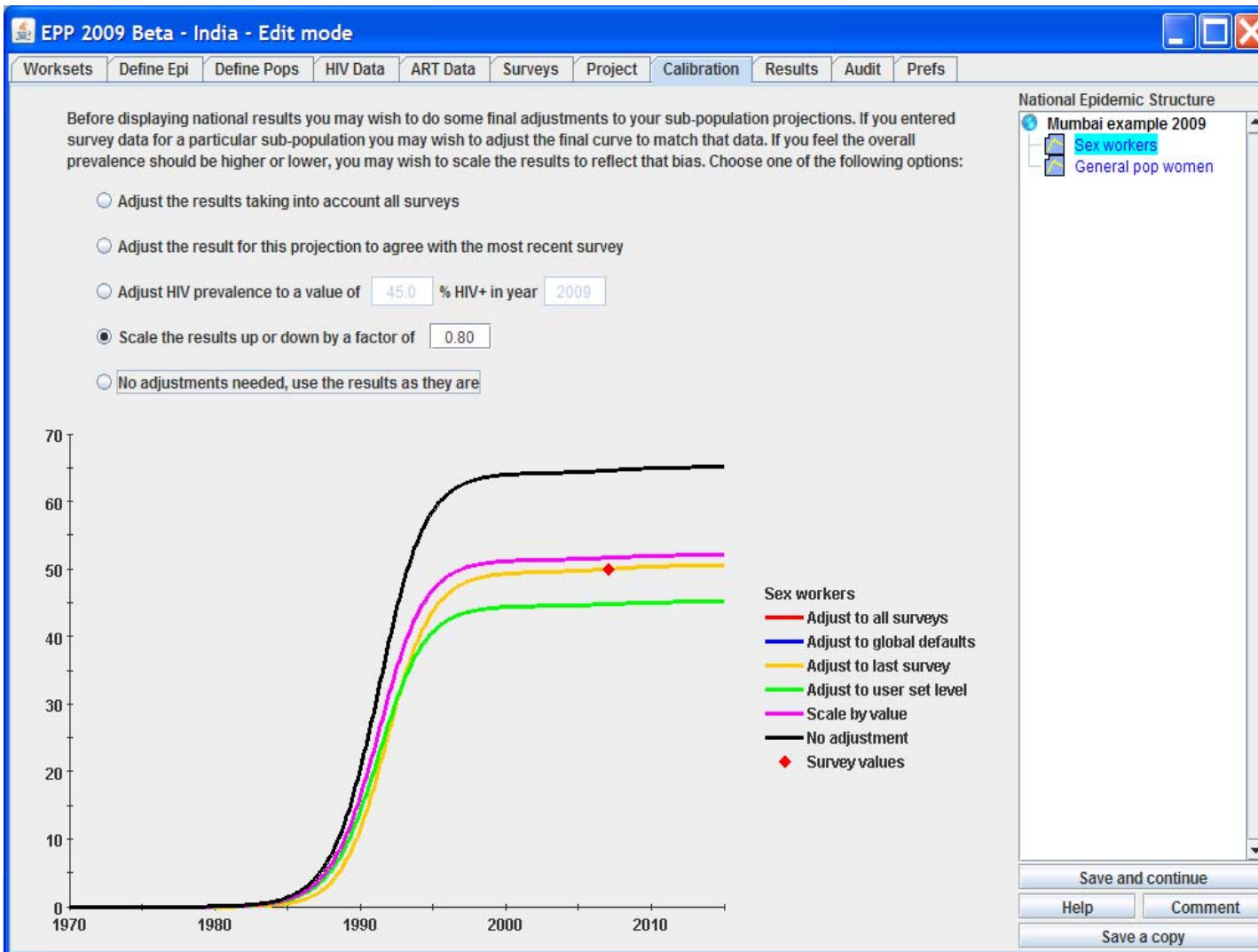
Sorted by how well they fit the data. Higher in the list means a closer fit

You can keep this window open and experiment with typing the r, f0, t0 and phi values into the Projection Page

Summary of fitting an epidemic in EPP 2009

- On the Project page, click on “Make initial guesses”
- Set any limits or prevalence conditions under “Advanced Options”
- Click on “Find guesses”
- If happy with best guess, click on “Use best fit in EPP”
- On the Project page, hit “Save and continue”
 - If you don’t, will lose it and need to re-run

The EPP 2009 Calibration page



5 calibration options provided

Display shows the result of each option

One you choose will be used to change the outcomes on the Results page

How might you use the calibration options?

- In concentrated epidemics, data is often biased
 - If have IBBS or ad hoc surveys, might calibrate data to agree with it
 - If surveillance preferentially from high prevalence areas, might adjust downward
 - If have multiple sex worker pops but surveillance in only one, may need to calibrate for prevalence differences
- ANC data overestimates female prevalence & needs adjustment, you might:
 - Calibrate to general population female prevalence from national survey
 - Adjust downward to correct for age structure of ANC population
 - Adjust downward for geographic representativeness (e.g. urban/rural differences)

EPP 2009 Pop change page (generalized only)

EPP 2009 Alpha - Botswana - Review Mode

Worksets Define Epi Define Pops HIV Data ART Data Surveys Project Calibration Pop change Results Prefs

The percentage of the national population living in urban areas may change. Because urban and rural HIV prevalence is often very different, such population shifts can affect your national prevalence results. The top of the table below shows the United Nations Population Division trends for the percentage of urban population and the current overall percentage of urban population from your projections. Most people will not need to change these values. However, should you wish to adjust the percentage of urban and rural population, you can do so by changing the values in the lower part of the table. In all cases, you should reduce the unassigned population percentage in each year to zero. If you wish to match the UN urban percentages, click "Adjust to UN values" at the bottom of the page. When done, click on "Save and continue" to review your final national prevalence results.

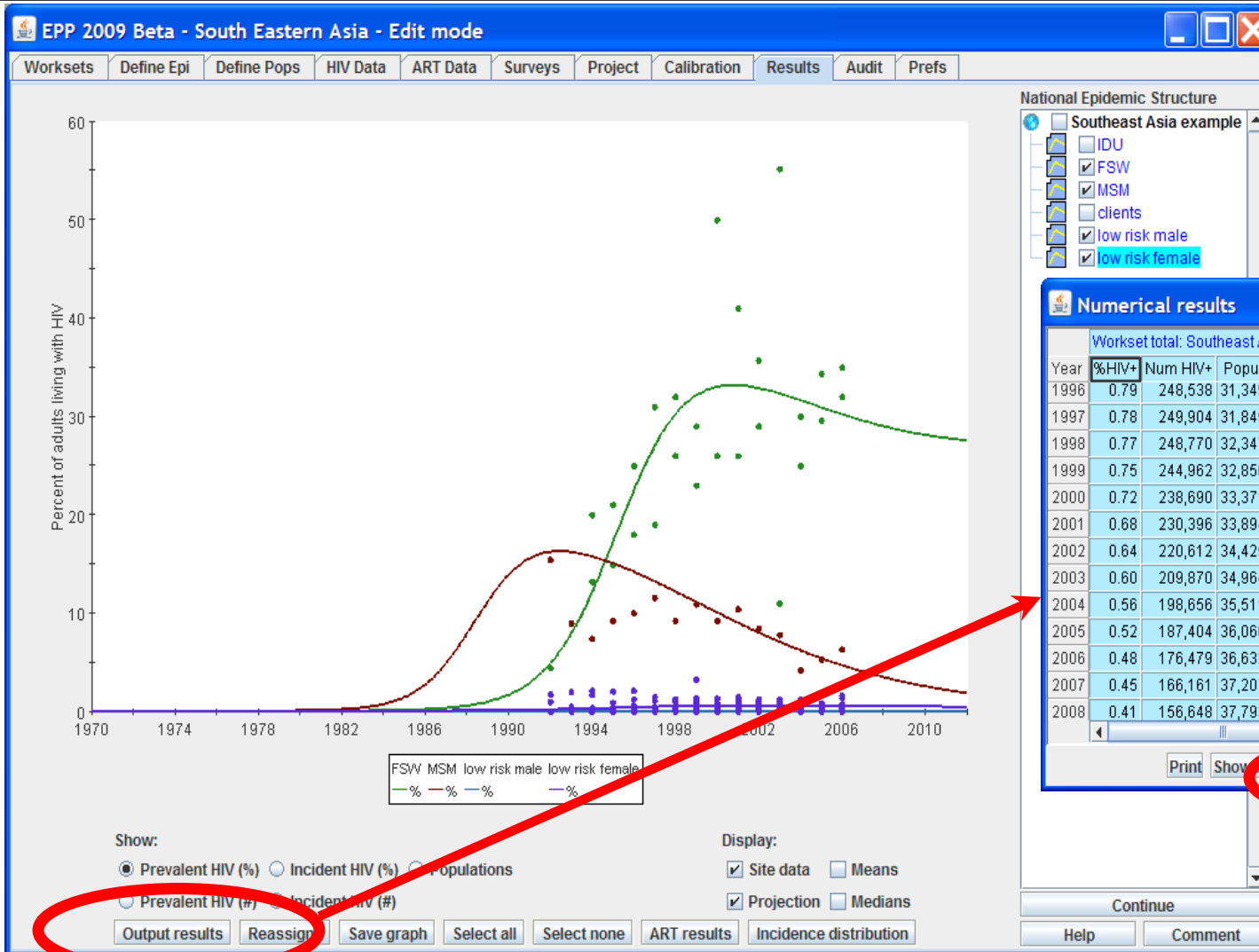
Year	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979
National urban population										
UN Pop Division % urban	15.0	15.8	16.7	17.5	18.3	19.2	20.0	20.8	21.7	22.5
Current workset % urban	16.0	16.9	17.8	18.7	19.6	20.5	21.4	22.3	23.2	24.0
Percentage of national population in each sub-population										
Still to be assigned among sub-populations (%)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Urban	16.0	16.9	17.8	18.7	19.6	20.5	21.4	22.3	23.2	24.0
Rural	84.0	83.1	82.2	81.3	80.4	79.5	78.6	77.7	76.8	75.9

Adjust to UN values Help Comment Save a copy Save and continue

Top row – UN Pop % urban
 2nd row – your workset's % urban

Bottom – distribution of population among your sub-pops

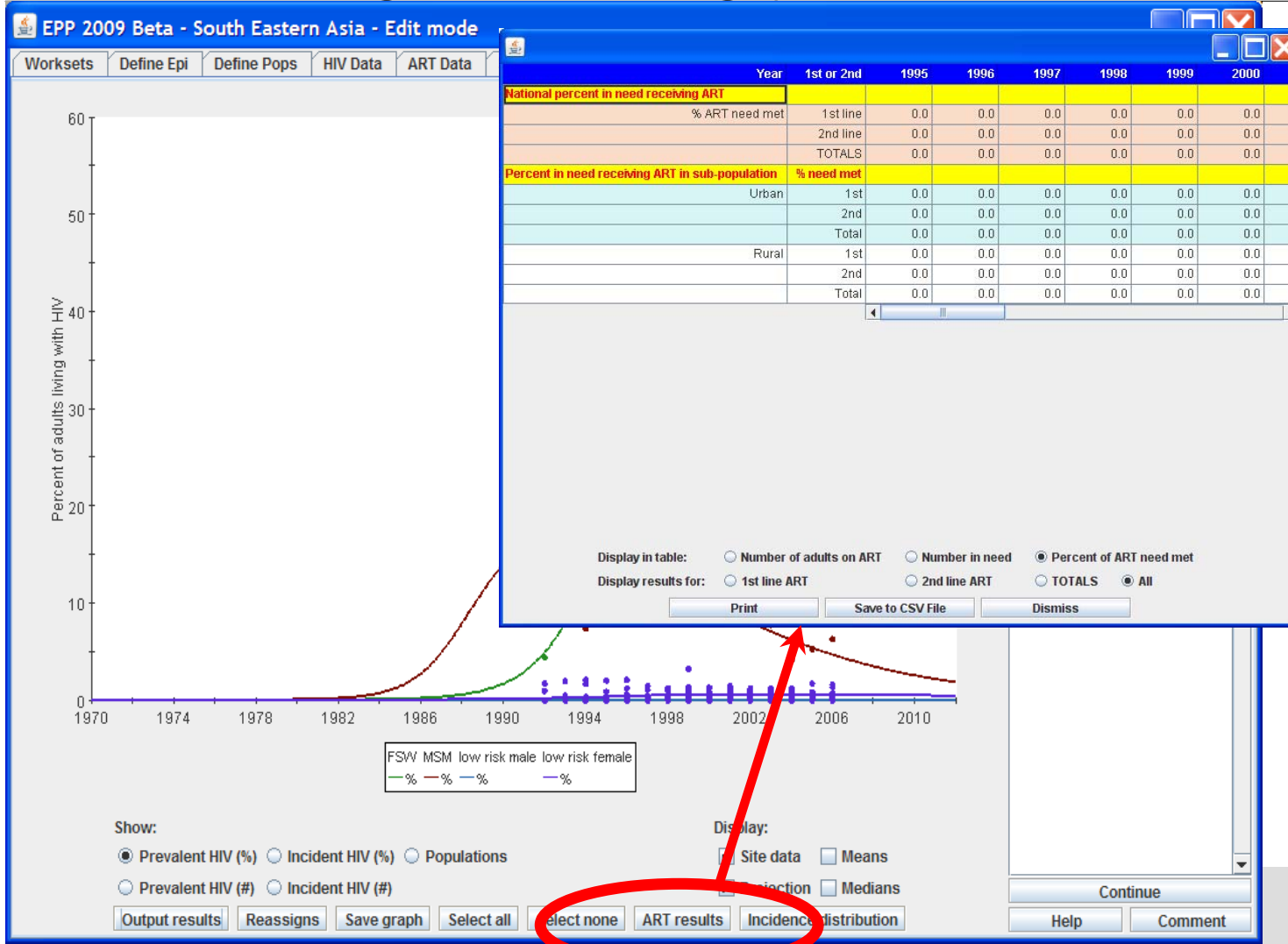
Results page – putting your projections together



“Output results”

- show outcomes
- create Spectrum file “*.spt”

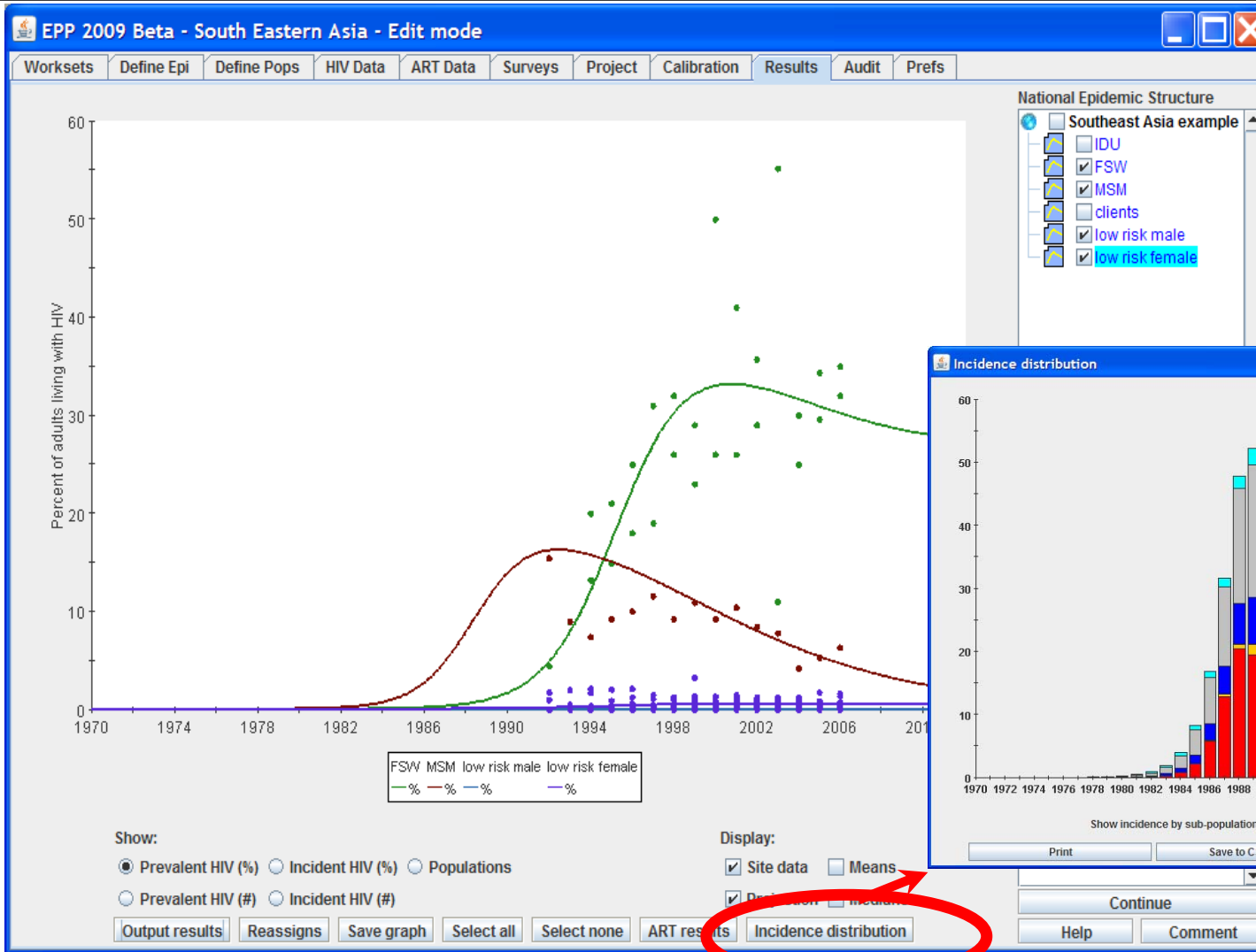
Results page – putting your projections together



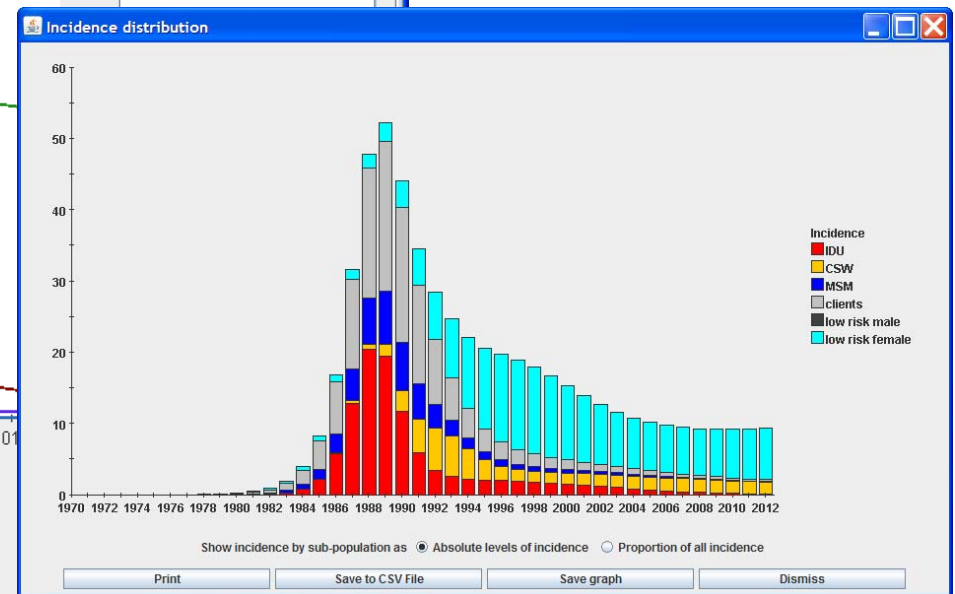
“ART results”

- 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.

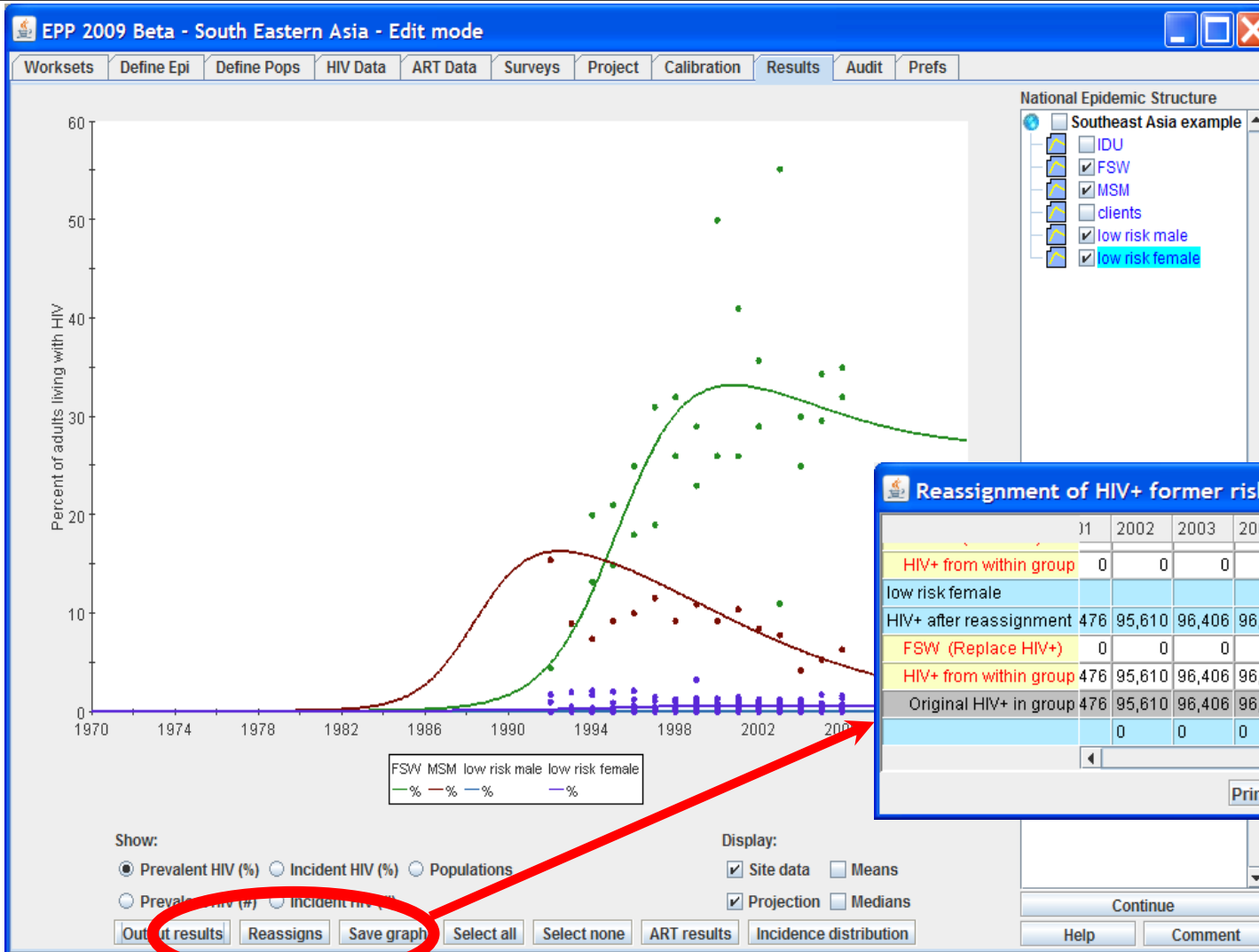
Results page – putting your projections together



“Incidence distribution”
 - Shows how sub-pops contribute to national incidence



Results page – putting your projections together



“Reassigns”
 - Shows the source of prevalence in pops reassigned prevalence

Finally, you can run an Audit check

EPP 2009 Alpha - India

Worksets Define Epi Define Pops HIV Data ART Data Surveys Project Calibration Results **Audit** Prefs

Population size checks (% of male/female pop)

	LOW	HIGH	CURRENT
FSW	0.20	0.80	
Client	1.00	20.00	
MSM	2.00	5.00	
Male IDU	0.00	0.70	

Maximum HIV prevalence checks

	MAX	CURRENT
FSW	40.00	
Client	20.00	
MSM	40.00	
Male IDU	70.00	

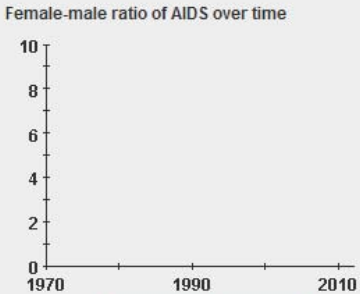
Low risk to high risk ratio check

Your ratio is:

Maximum ratio was in year

Above values for region: South and Southeast Asia

Female-male ratio of AIDS over time



Year	Female AIDS	Male AIDS
1985	-	-
1986	-	-
1987	-	-
1988	-	-
1989	-	-
1990	-	-
1991	-	-
1992	-	-

The Audit check page

Checks your population sizes against observed values elsewhere

Looks at M/F ratios in AIDS cases

So to review, to fit a concentrated epidemic

- Fill in data until you get to Projection Page as in the past (and documented in the EPP manual)
- Press “Make initial guesses” button on Projection page
- Press “Find guesses” button & wait for it to finish
- Either
 - Press the “Use best fit in EPP”
 - Click on “Show best” and enter the values for r , f_0 , t_0 and ϕ you like on the Projection Page
- 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

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

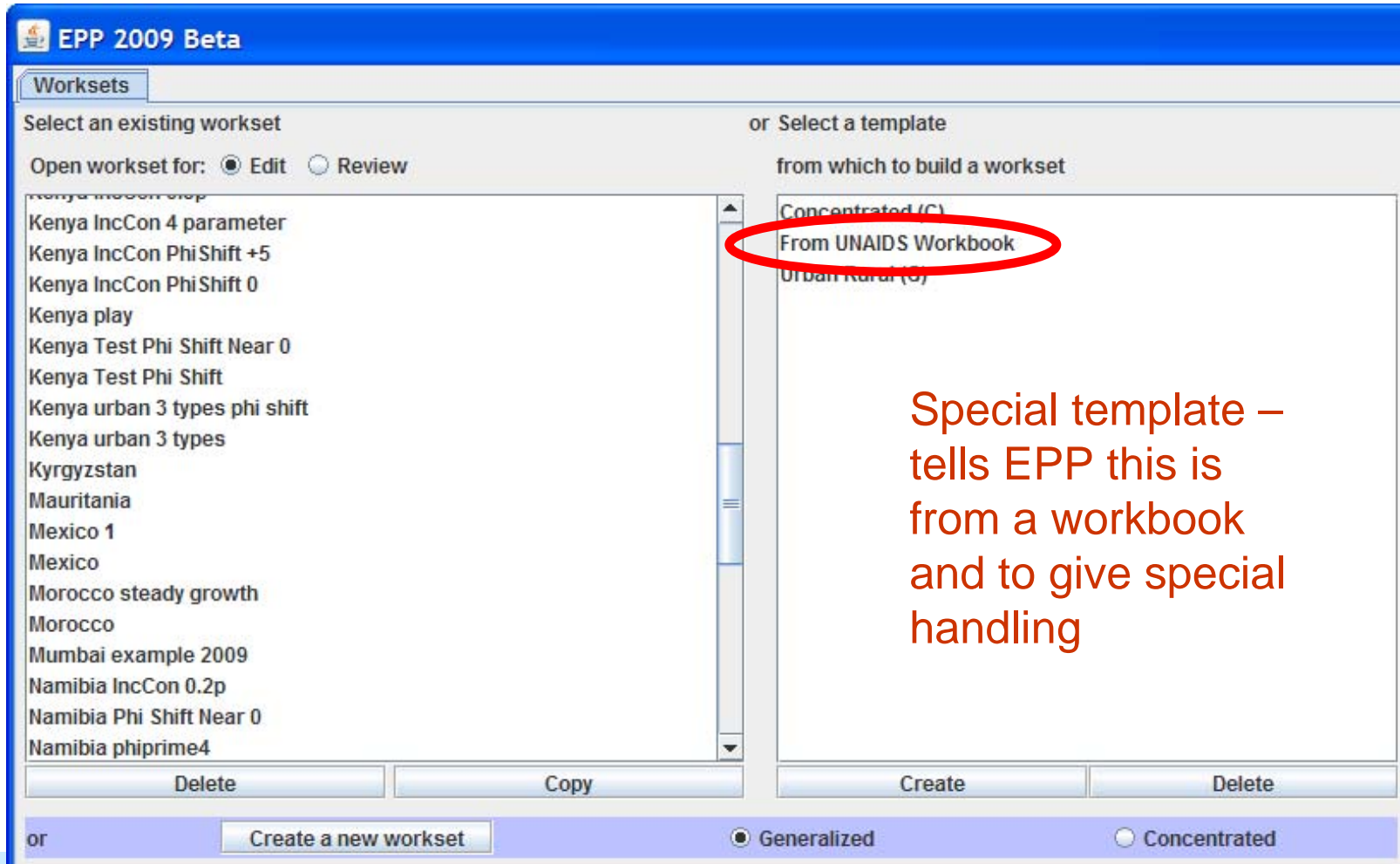
Special features in EPP 2009

Workbook trend fits

Workbook trends require special handling

- Often done in extremely low prevalence settings
- They only have a single “site”
 - If use small sample sizes, uncertainty is large
 - Result is poor fits
 - So we adjust sample sizes to 100,000 automatically
- To tell EPP to do this, use “From UNAIDS workbook” template

On Worksets page, use “From UNAIDS Workbook”



EPP 2009 Beta

Worksets

Select an existing workset

Open workset for: Edit Review

Kenya IncCon 4 parameter
Kenya IncCon Phi Shift +5
Kenya IncCon Phi Shift 0
Kenya play
Kenya Test Phi Shift Near 0
Kenya Test Phi Shift
Kenya urban 3 types phi shift
Kenya urban 3 types
Kyrgyzstan
Mauritania
Mexico 1
Mexico
Morocco steady growth
Morocco
Mumbai example 2009
Namibia IncCon 0.2p
Namibia Phi Shift Near 0
Namibia phiprime4

or Select a template

from which to build a workset

Concentrated (C)
From UNAIDS Workbook
Urban Rural (R)

Delete Copy Create Delete

or Generalized Concentrated

Special template – tells EPP this is from a workbook and to give special handling

Gives a projection with only a “Workbook trend”

EPP 2009 Beta - Guatemala - Edit mode

Worksets Define Epi Define Pops HIV Data ART Data Surveys Project Calibration Pop change Results Prefs

Data in % (0.0 to 100) for: Workbook trend

Year	In 997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
MEDIAN PREV		0.60		0.85					0.86		0.95		
MEAN PREV		0.60		0.85					0.86		0.95		
Site 1 (%)	<input checked="" type="checkbox"/>	-	0.60	-	0.85	-	-	-	0.86	-	0.95	-	-
(N)		-	300	-	300	-	-	-	300	-	300	-	-

National Geographic Structure

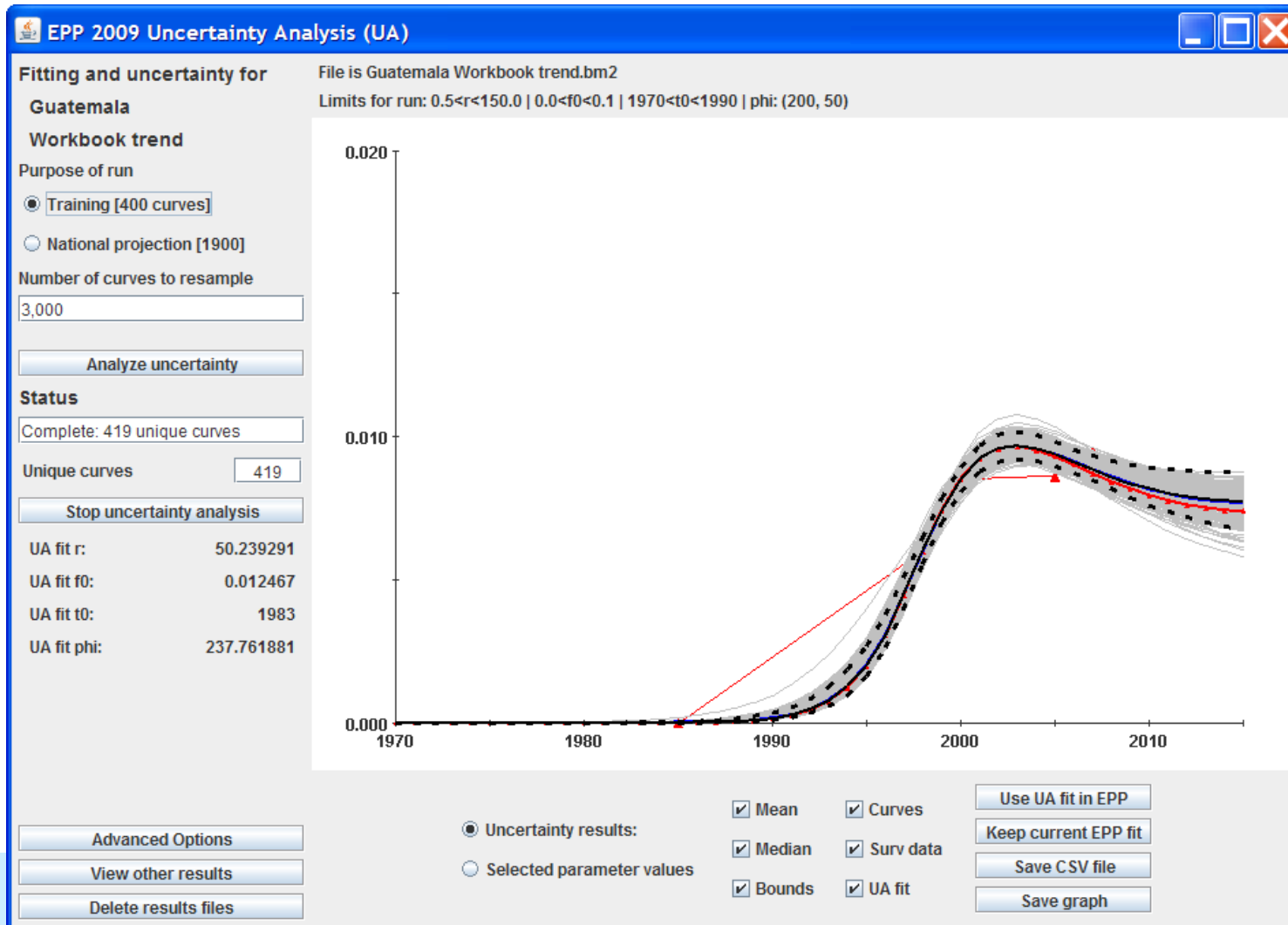
- Guatemala
 - Workbook trend

Save and continue Help Comment Save a copy

Add sites Delete sites Undelete sites Print

Sub-populations with no data: 0 Display: % HIV N Both

This single curve is fit with the usual procedure



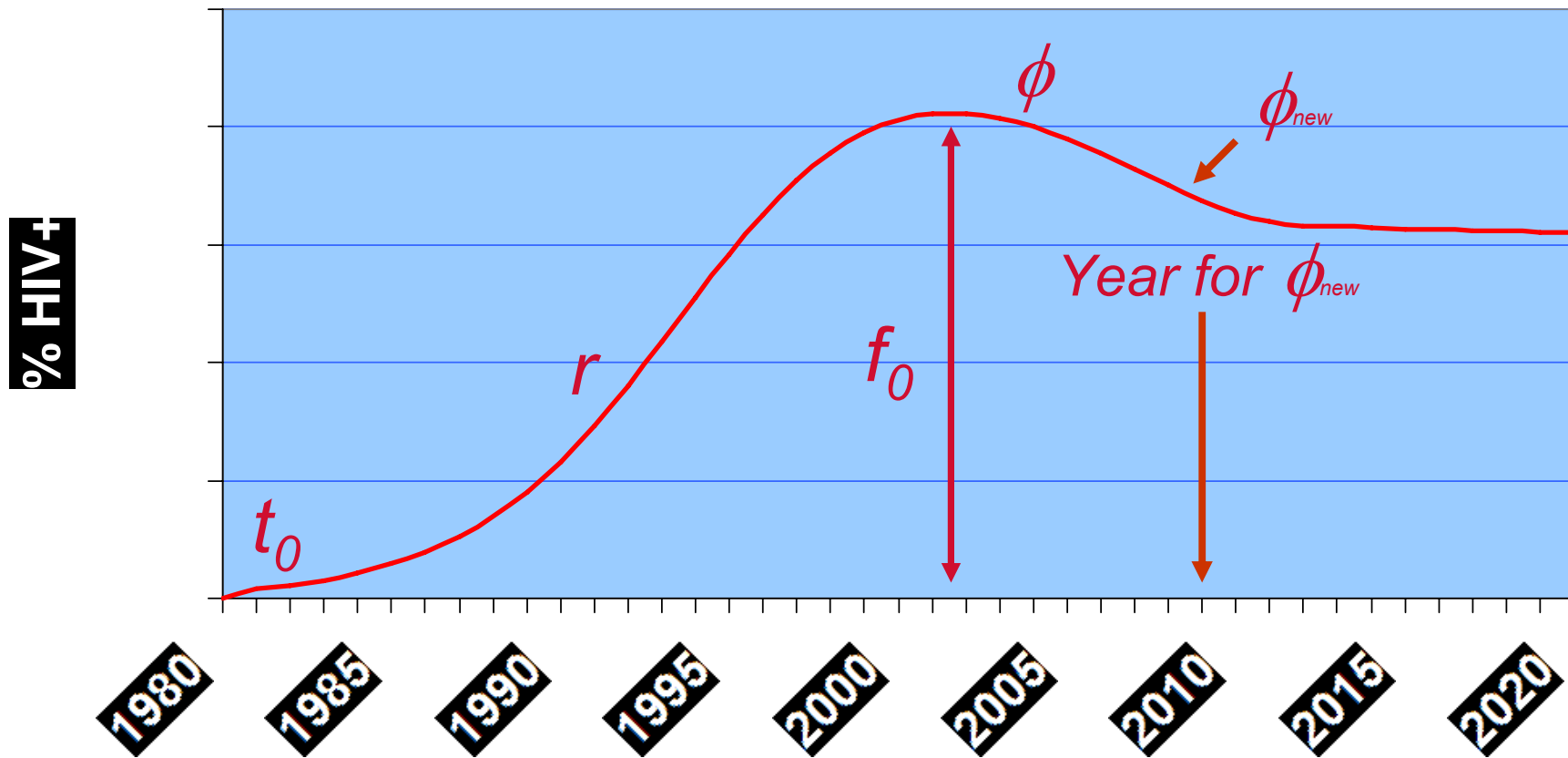
Special features in EPP 2009

Phi shifts

Addressing steep declines - ϕ – shift

- Advanced users – under development
- Deals with following situations:
 - Fitted prevalence declines so steeply that the trend implies implausibly low incidence
 - Prevalence decline followed by stabilization or increase of prevalence
- Use Advanced Options to set prior distributions of 2 additional parameters
 - A new value of ϕ
 - The year in which it changes

Modified Reference Group model



Phi shift allows additional limits & conditions

Advanced Options for EPP 2009 Uncertainty Analysis

Limits on curve generation

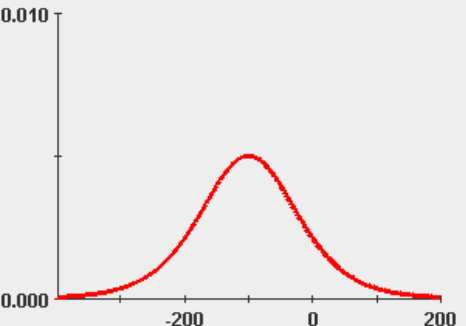
Limits: < r <

Limits: < f0 <

Limits: < t0 <

phi median: and scale:

Distribution on phi



Use specified limits and conditions

Help on advanced options

Conditions on prevalence

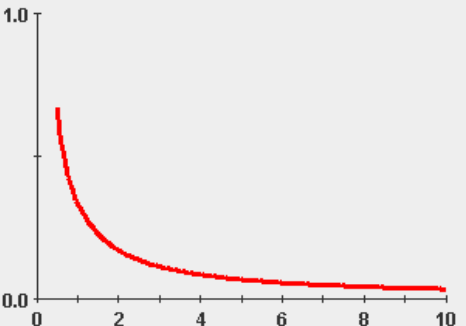
HIV prevalence <= % in year

HIV prevalence <= % in year

HIV prevalence >= % in year

HIV prevalence >= % in year

Distribution on r



Fixed seed? Yes No

Current seed:

Limits and conditions for phi shift

phi' median: and scale:

Earliest possible year for phi change:

Incidence in final year (%) >

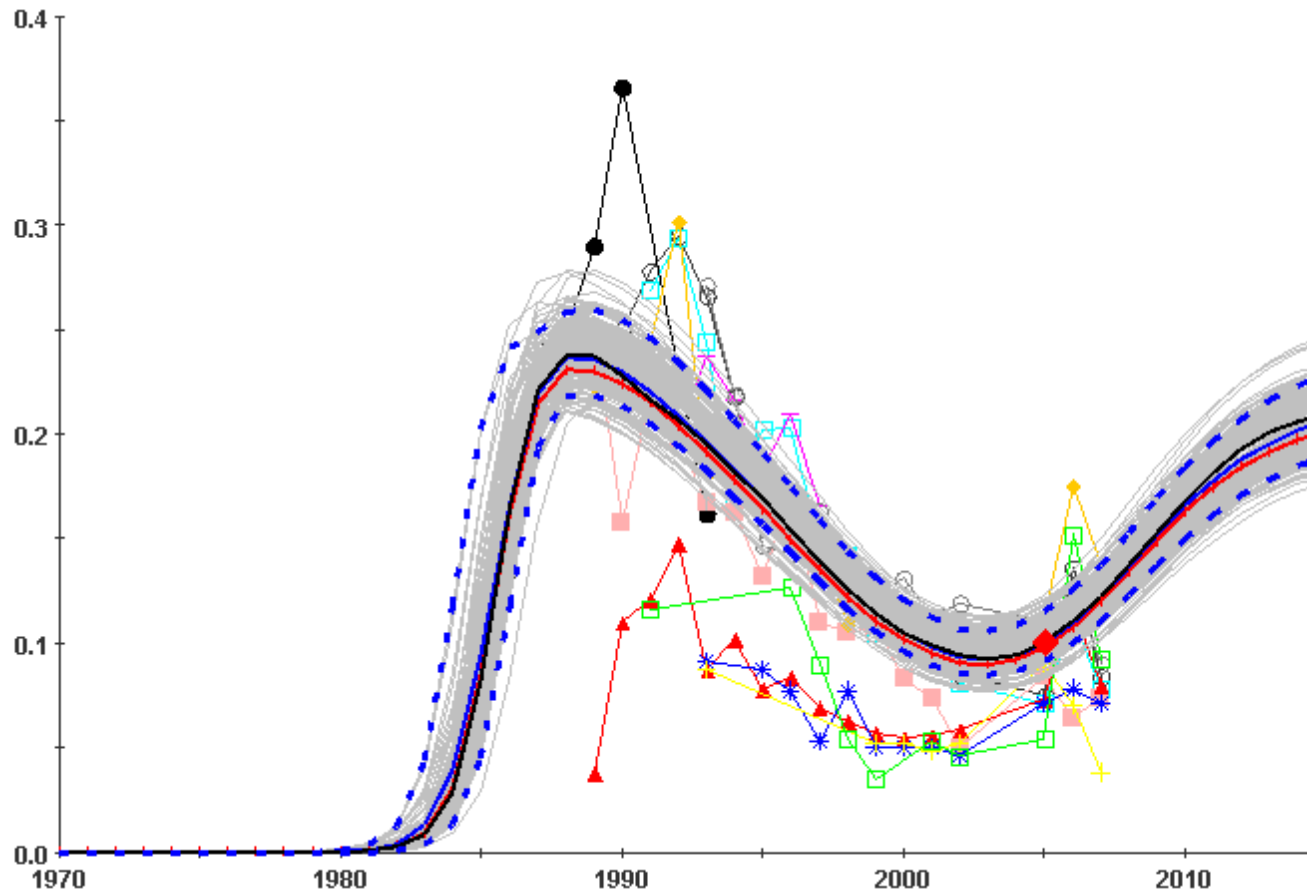
Conditions: < phi' <

Under “Advanced Options”

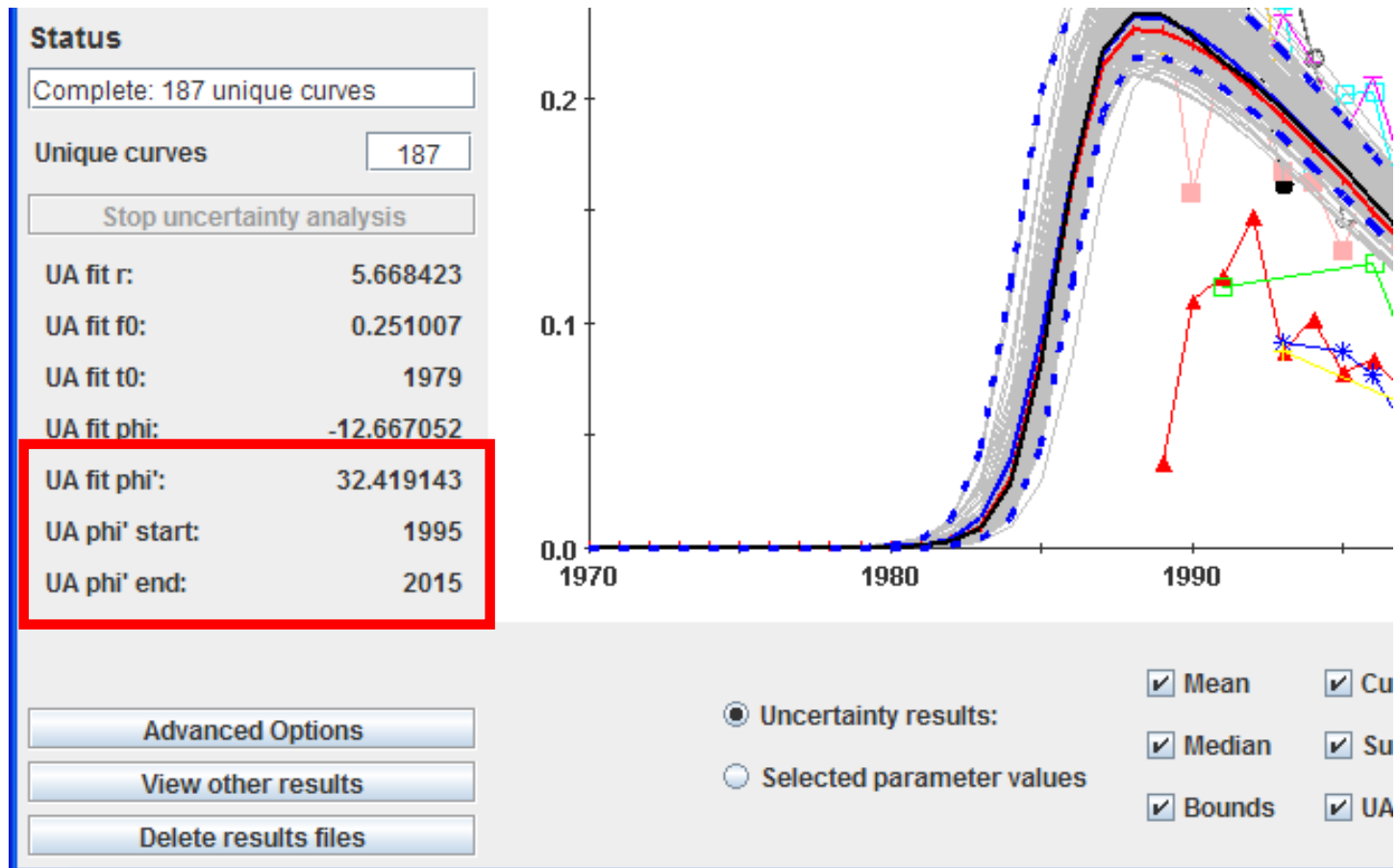
Most important
- incidence constraint in final year

Limits on phi'
- zero or slightly negative
- represents risk recovery

ϕ – shift - example

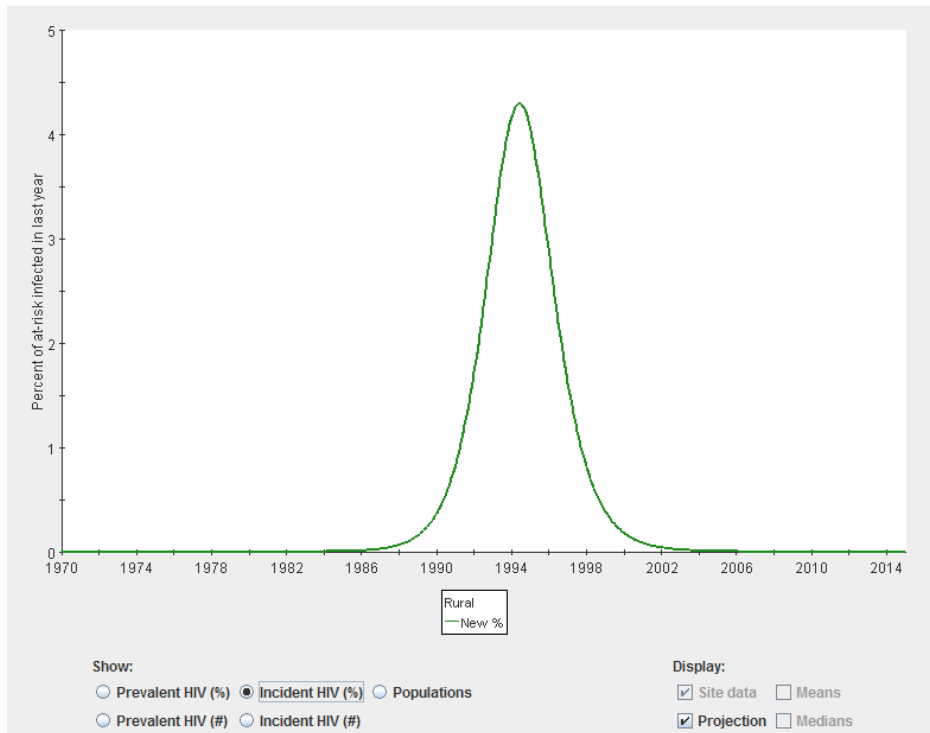


ϕ – shift – additional parameters

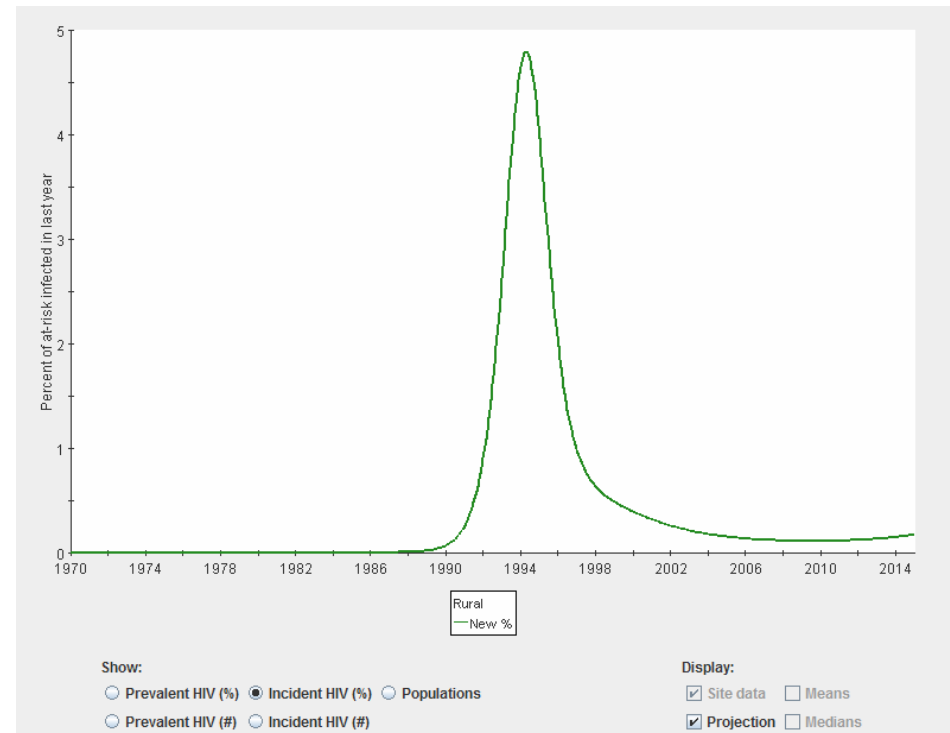


Phi shift to solve zero incidence problem

Without phi shift – zero incidence



With phi shift – low, stable incidence



Example of complete run-through of the process for a country with calibration

Demonstration and The End