What Mathematical Models Can Tell Us About Prevention Packages

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Conclusions

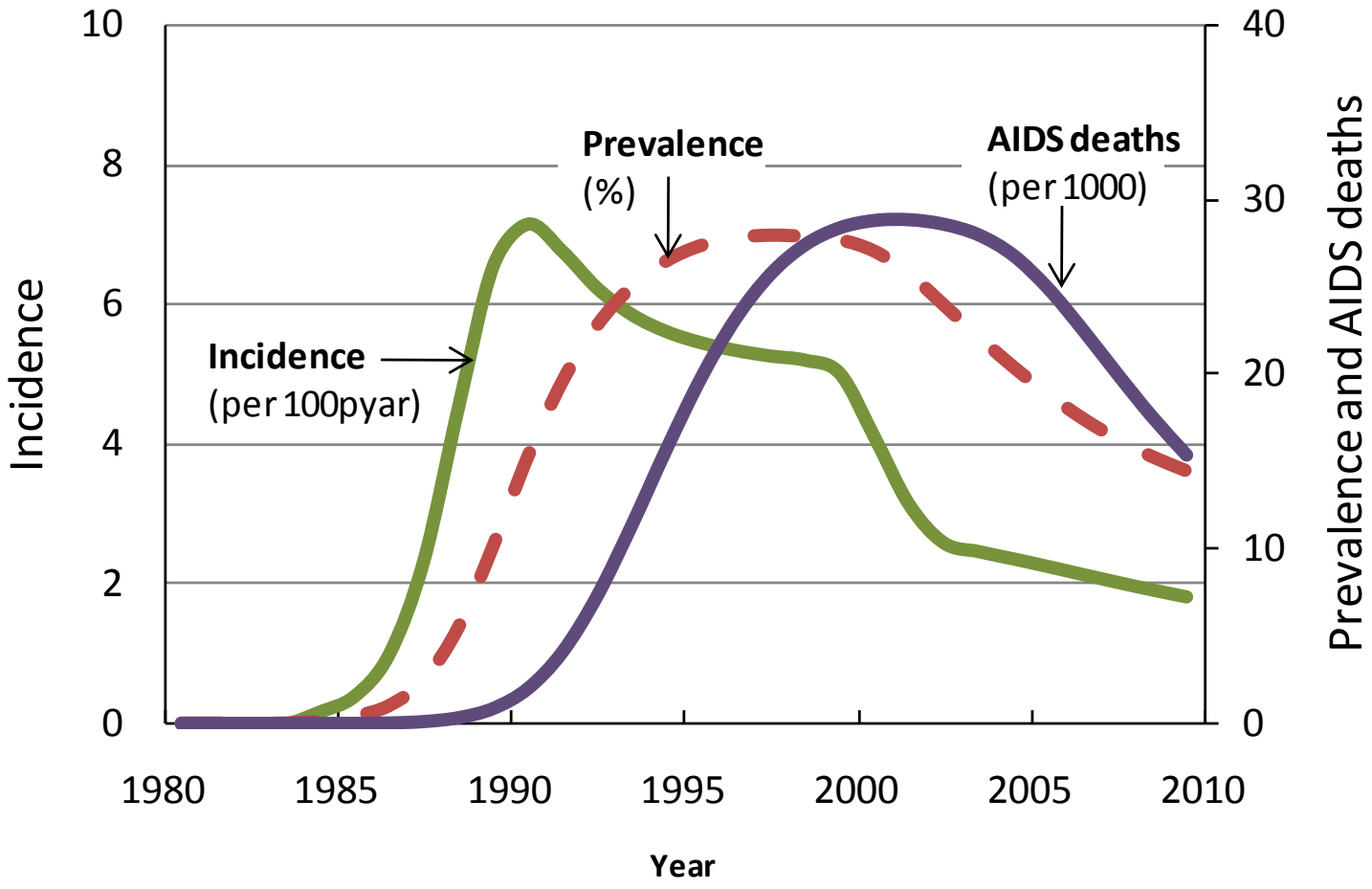
- **Models can really help:**
- **Models do have limitations:**
- **Best use of models in guiding prevention programming is to interpret their results in the light of their assumptions:**

Contents

- Spotting where behaviour change has impacted epidemics:
- Identifying drivers in Generalized Epidemics
- The potential impact of current biomedical interventions.
- Which intervention when?
- Interpreting trials
- General principles of Good' and 'Bad' Combinations Packages.
- Important uncertainties in model output.

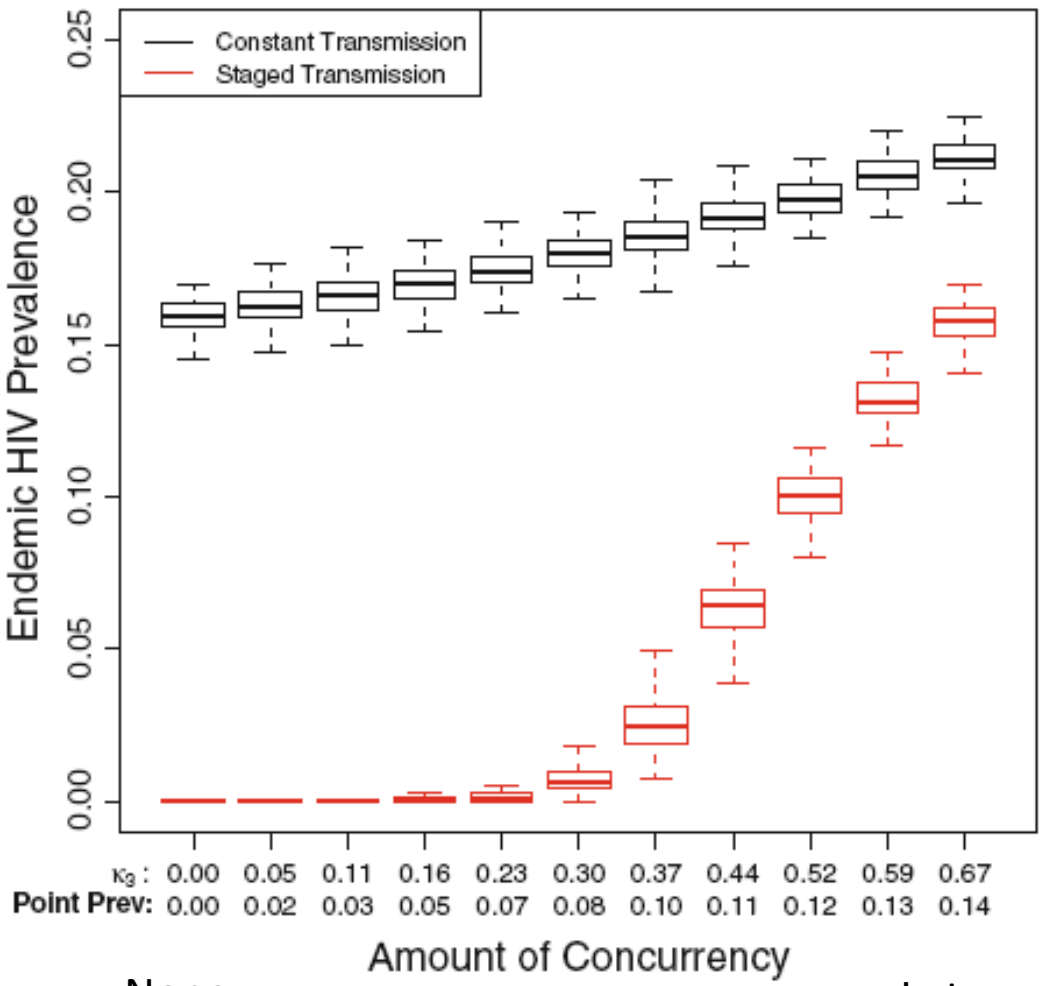
- Different sorts of modelling approach & what models cannot do.

Spotting where behaviour change has impacted epidemics



Hallett et al Epidemics 2009; Halperin et al., Plos Med. In Press

Concurrency as a driver of the epidemic?



None

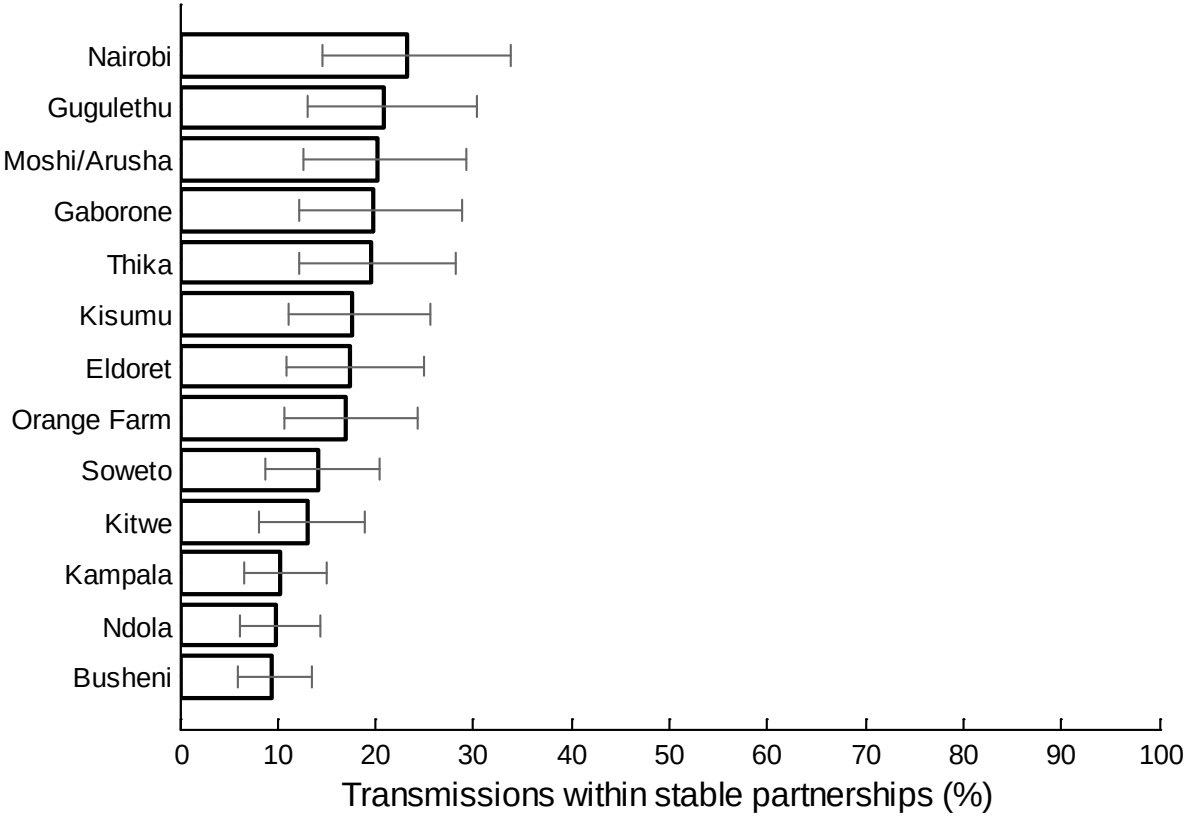
Lots

What models don't tell us is whether or how we can intervene to reduce that metric.

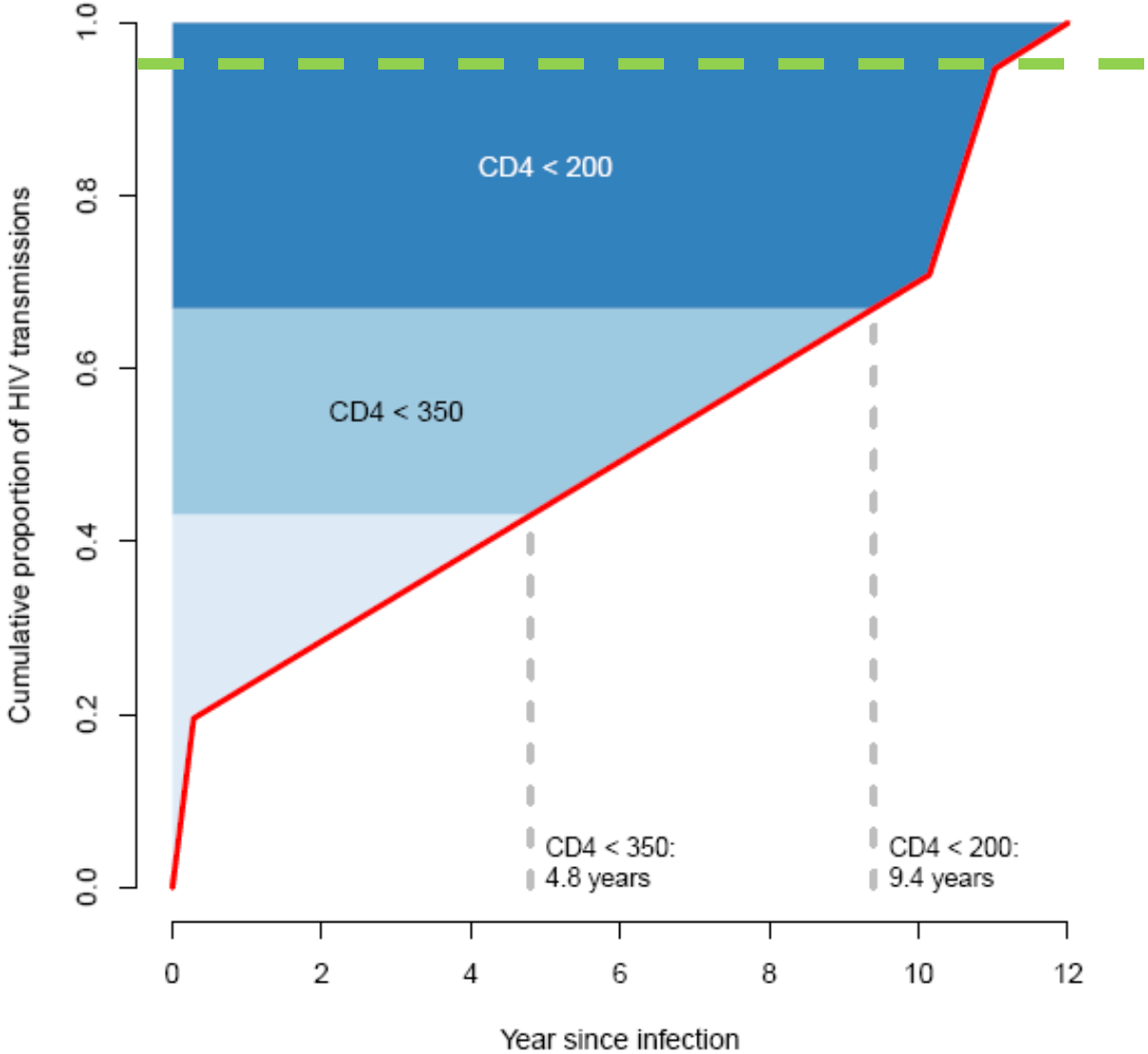
Eaton, Hallett & Garnett, 2010

Identifying drivers in Generalized Epidemics

Stable sero-discordant Partnerships as a driver of the epidemic?



The impact of current biomedical interventions.



Eaton, Hallett et al.

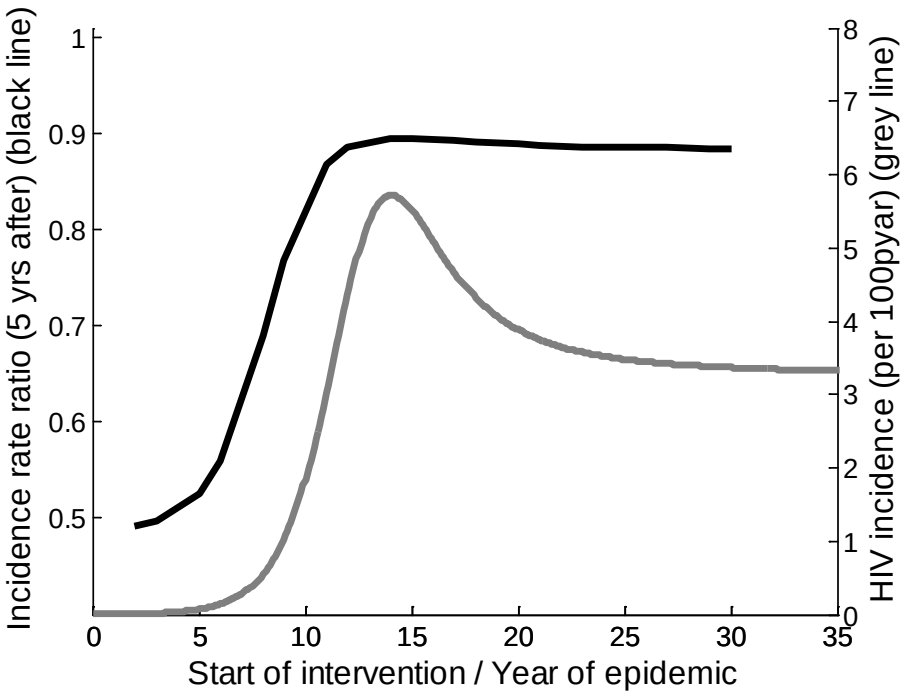
Which intervention when?

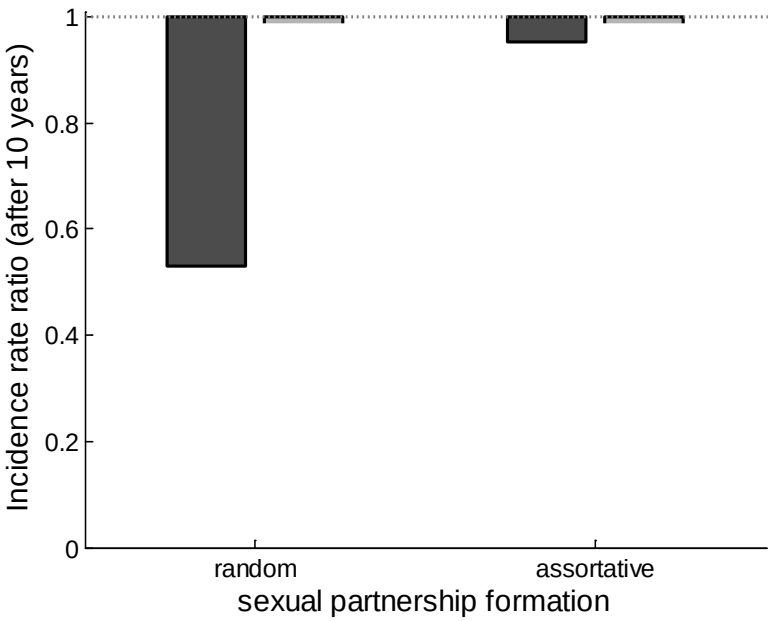
Hallett, Heffron, Baeten, Celum et al., Forthcoming

Which intervention when?

Hallett, Heffron, Baeten & Celum. Forthcoming

Interpreting trials

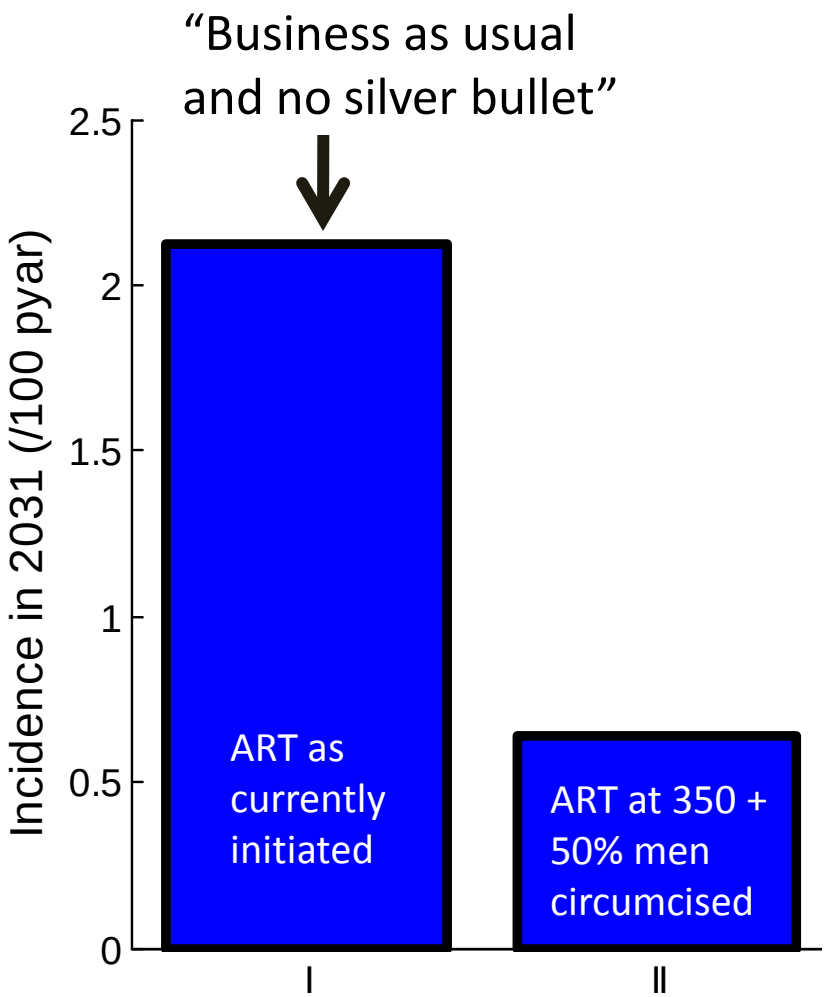




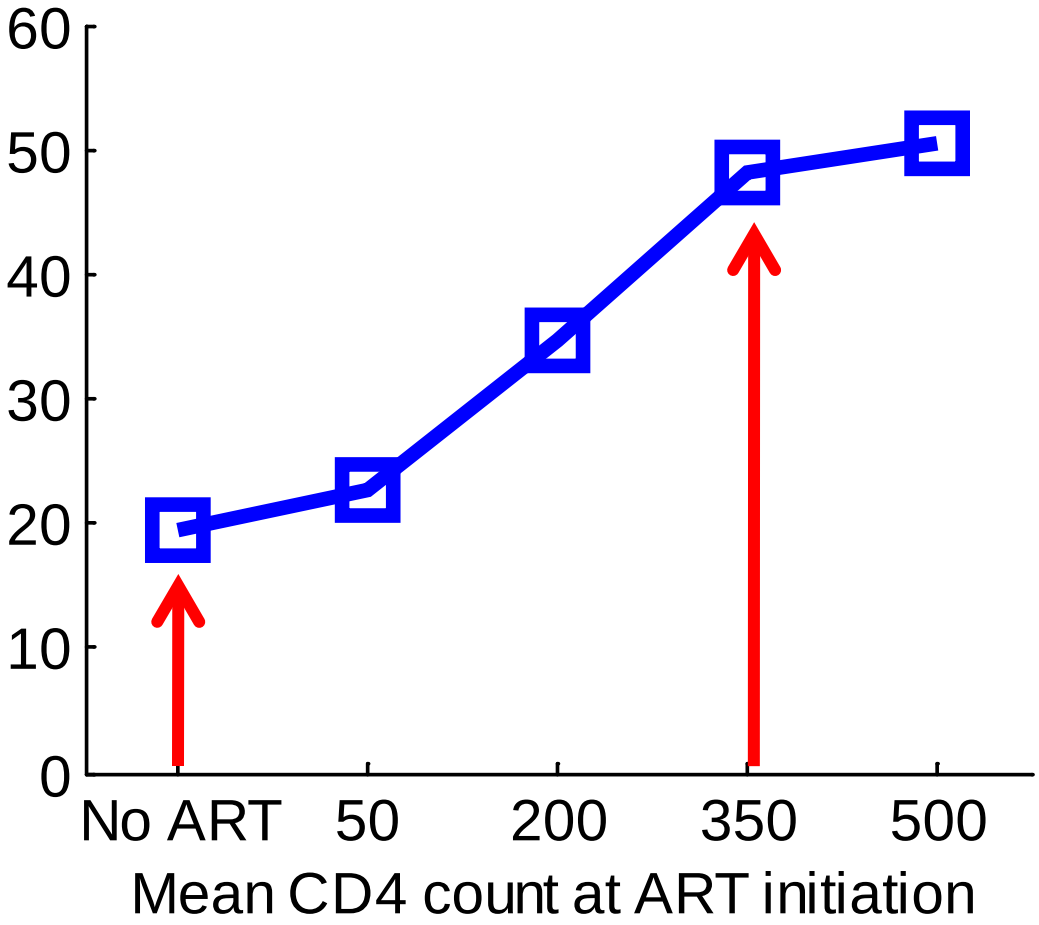
Interventions don't exist in a vacuum.

Hallett et al.m, IJE 2007

The impact of current biomedical interventions.



Marginal Impact Of Circumcision Intervention (% reduction incidence)



Two Principles of Intervention Impact

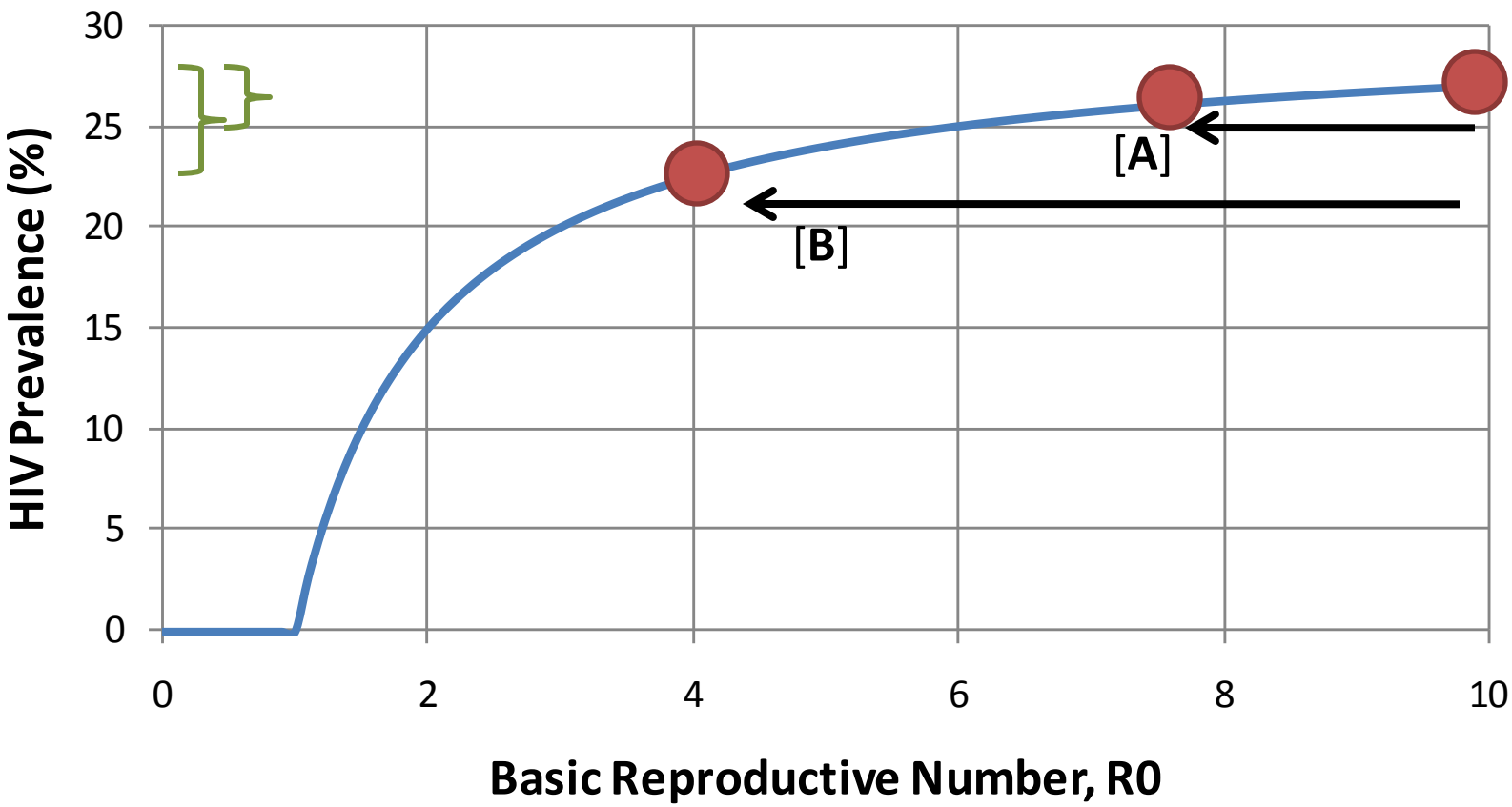
- "Synergies"

Whereby two interventions have a joint impact greater than the sum of their parts; One "*Potentiates*" the other.

- "Redundancies"

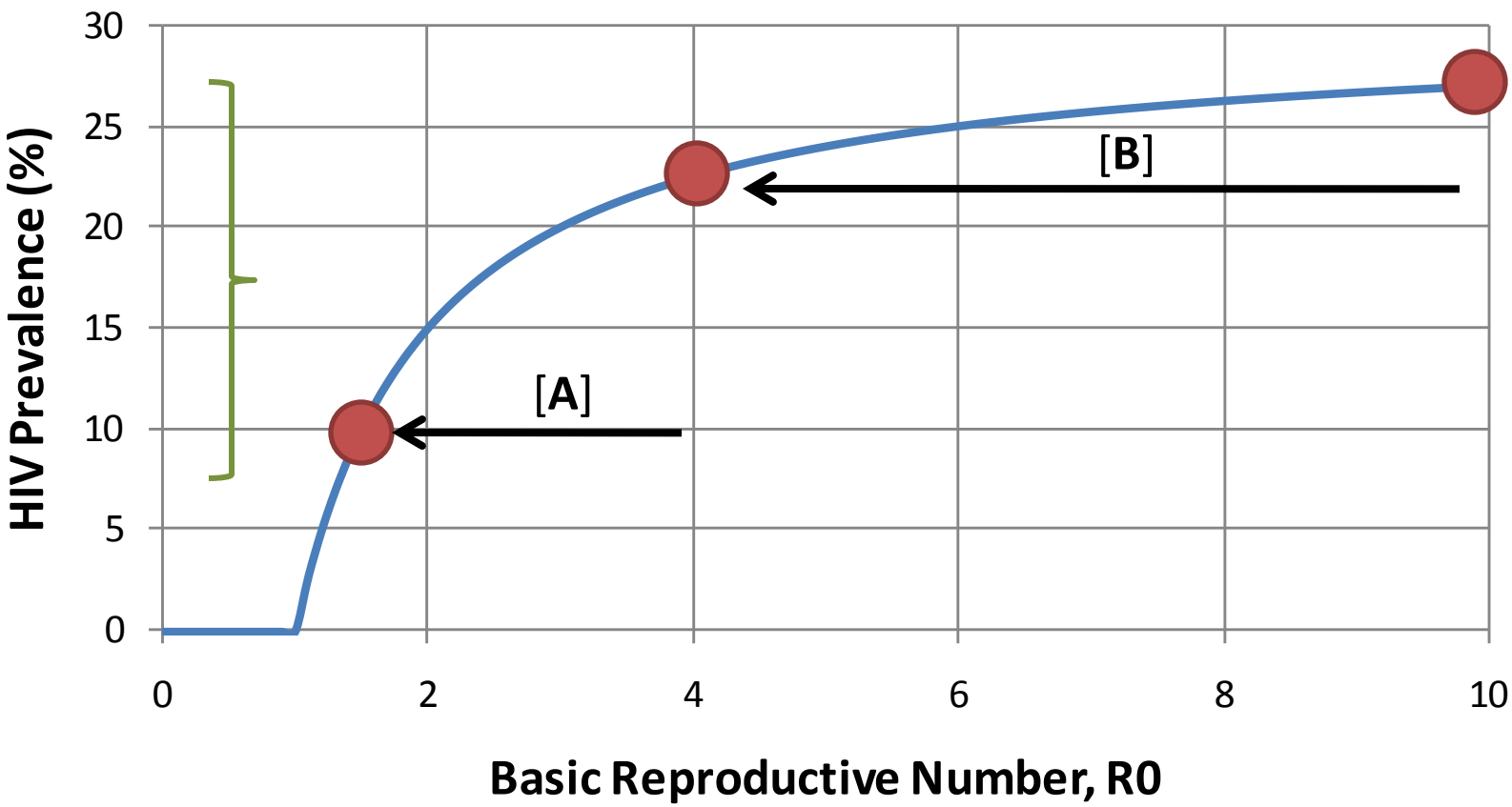
Whereby applying two interventions have a joint impact *less* than the sum of their parts.

Apply Interventions [A] and [B] in isolation.



Robustness of infectious spread

Apply Interventions [A] and [B] together.



Was it [A]? Was it [B]? Was it mostly B or mostly A?
Do (A) and (B) “work” in isolation?

Maximize synergy of low-medium efficacy

Combine low-medium efficacy interventions

Aim for overlap in same population

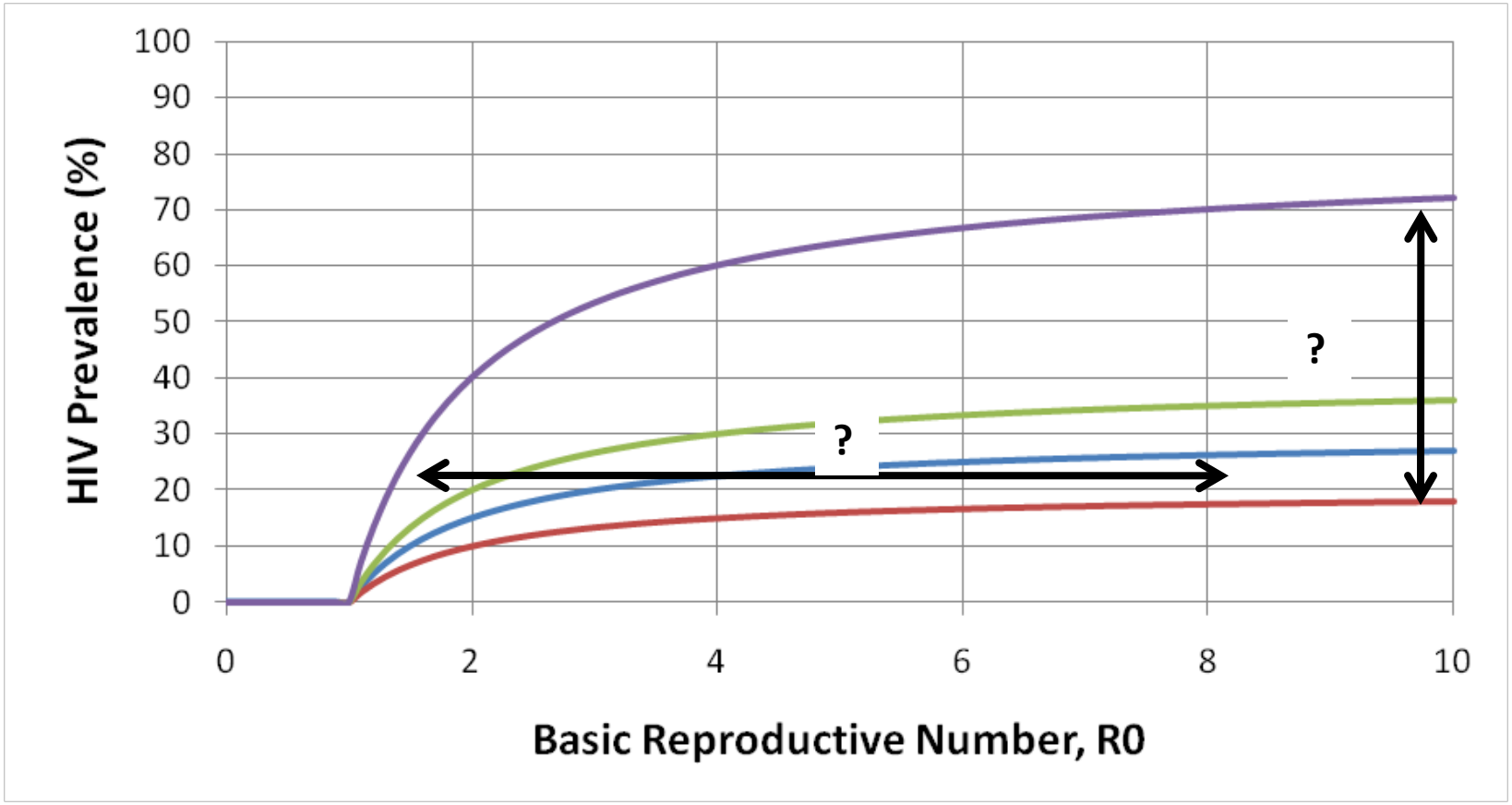
Targeting to those at highest risk

High efficacy interventions:

Sometimes aim for coverage rather than pairing it with something else.

Minimize overlap with different interventions, unless different modalities.

Dodd, White, Garnett, 2010; Alsallaq et al., Forthcoming

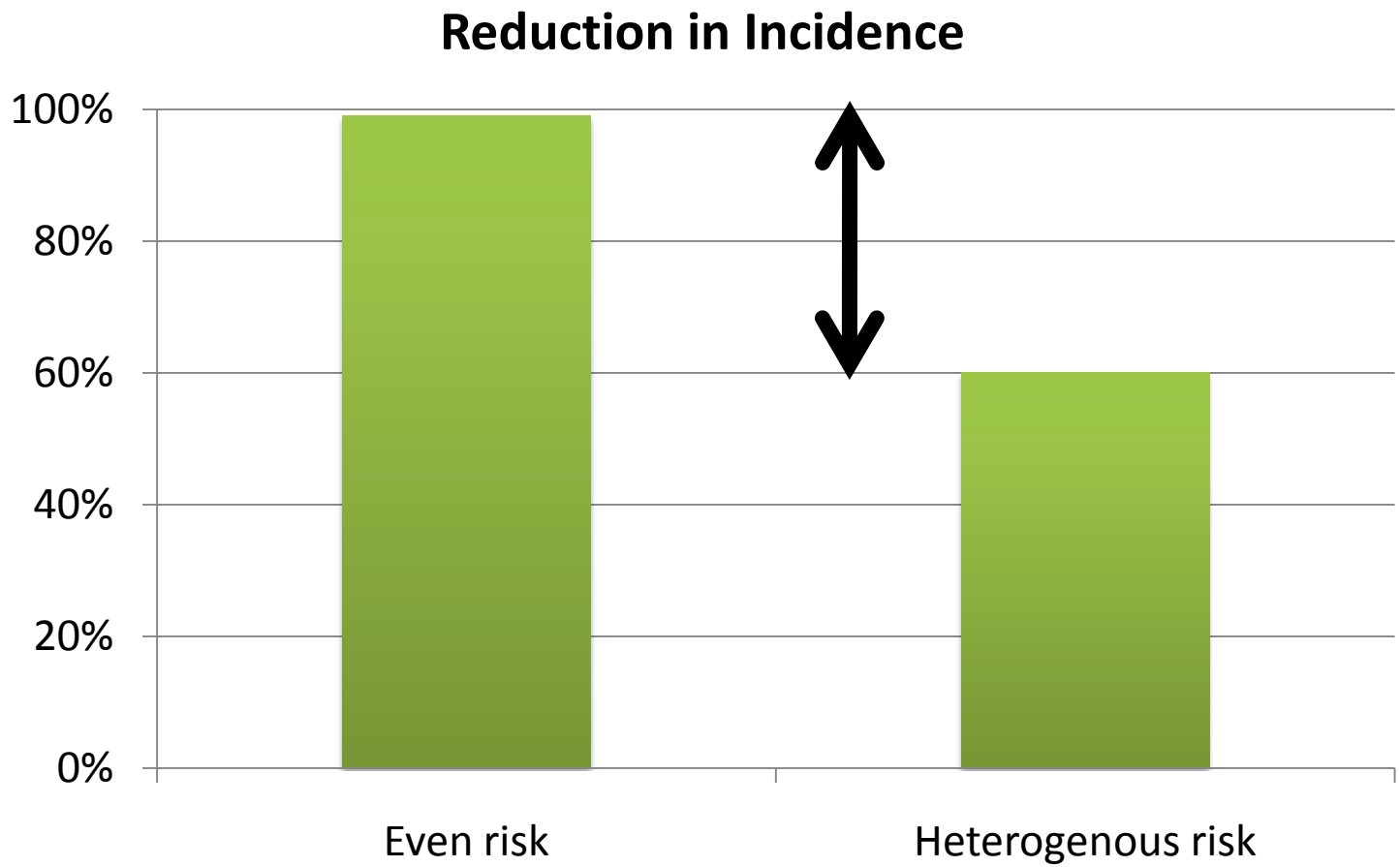


Impact of combination prevention sensitive to the pattern of transmission assumed in the population.

-Make the right assumption.
- *Or*, draw conclusion that are not sensitive to that assumption.

Important uncertainties in model output.

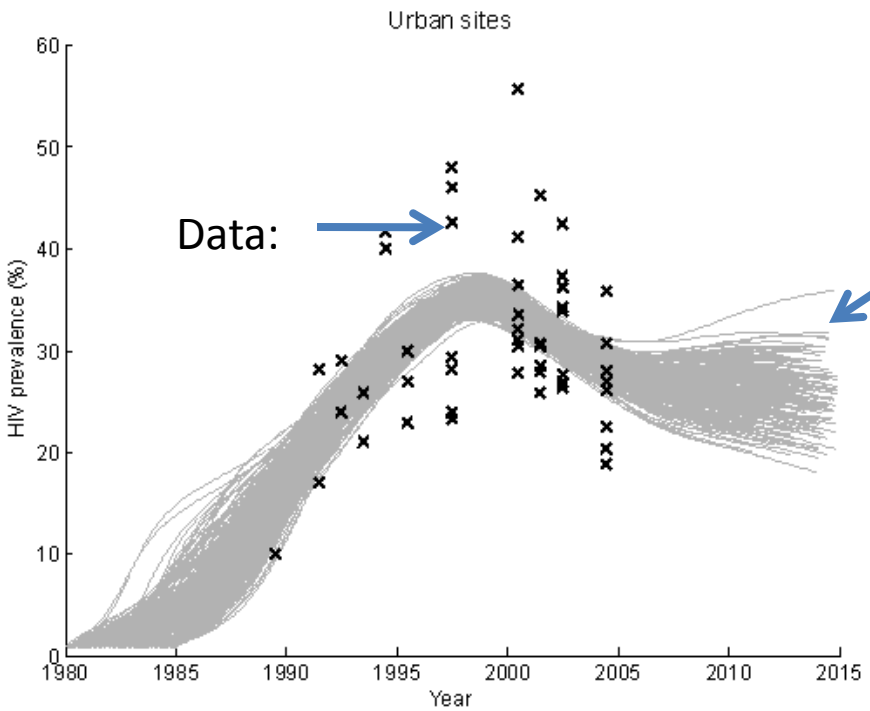
"Test and treat" intervention for 80% of the population + 40% reduction in risk.



Some models assume this.... ***... But others assume this.***

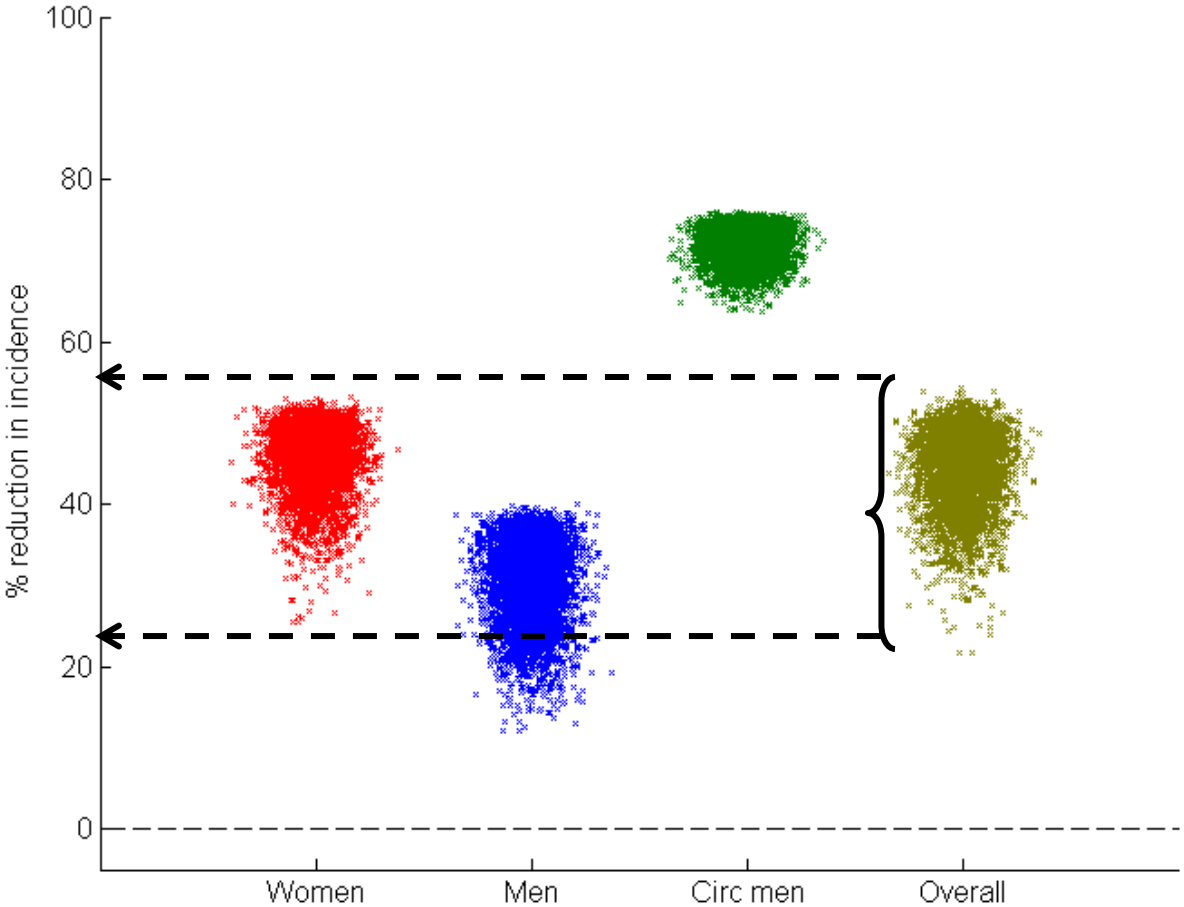
Important uncertainties in model output.

Example: large circumcision scale-up in Zimbabwe



Different model fits to the same data

Now, apply <u>same</u> circumcision intervention to alternative model fits



Uncertainties in impact of combination prevention likely to be greater.

Each dot shows the projected impact of a circumcision intervention using one model fit to data. The different model fits provide different (*equally valid)* ways of representing the epidemiological context in this setting.

Different sorts of modelling approach

Models of couples only

Modes of Transmission model

GOALS

"Network models"

Expressions of

✓"Clean" results.
✓Fundamental insights.
✓ Simple parameters
✓Flexible (multiple settings and quickly)

— Strong simplifying assumptions.
—Key features of system omitted?
— Mismatches between parameter meanings and real data.

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Complicated Deterministic Models (incl. Pair models)

"Proof of concept" Microsimulation models

✓More 'real world' features incorporated
✓Allows more detailed
✓Theoretically attractive
✓Very specific

—Complex details represented without data to inform.
—Model behaviour poorly understood.
—Long-time to fully analyze.

Data-based microsimulation model

Different sorts of modelling approach

- Choosing what to leave out.
- Balancing complexity with tractability.
- Marrying model parameters to available data.
- Quantifying and representing uncertainties in models.

But most of all...

- ** Understanding the implications of simplifying assumptions on the results of interest.**

Verifying that the model is suitable for tackling the question of interest.

Understanding the implications of simplifying assumptions

- Some of the ‘big picture’ things can be represented using neat and simple approaches, and the insight this provides compared to no modelling information is substantial.
- Simplifications can be ‘benign’ for the interpretation of particular results.

- Not always obvious/ possible to understand implications of assumptions from inside one model.

- But in many models, key simplifying assumptions do impose an important influence on the results obtained.

  – *Sometimes, that’s the best that can be done: model results often still useful but have to understand the context.*

→ *Modelling Consortium*: More model comparison / modelling bake-offs / more peer-review for models.

- More model validation:
  - Against HIV incidence end-points
  - With coverage etc indicators in a format usable in models.

Conclusions

- **Models can really help:**
  - Identifying drivers in generalized epidemics; guides about impact of interventions; strategic choices in combination approaches, etc etc.
- **Models do have limitations:**
  - Often substantial uncertainties in model output.
  - Simplifying assumptions sometimes influence results. (so can complicating assumptions)
- **Best use of models in guiding prevention programming is to interpret their results in the light of their assumptions:**
  - Understand how assumptions can influence results
  - Quantify uncertainty in results
  - Compare models with different structures to increase robustness of conclusions.