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Multiple interventions to control the spread of HIV: Synergistic, additive or redundant?

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Models of infectious disease transmission

- We are interested in the population-level effect of processes occurring at the individual level.
- An uninfected individual's risk of becoming infected per unit time depends upon the prevalence of infectious individuals (a population-level characteristic)
  - (and rate of contact between individuals, infectiousness of infected individuals, etc).
- So transmission of infection in a population is a dynamic process - requires dynamic models for prediction & analysis of putative programmes.

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Background

- HIV prevention essential if treatment is to be afforded.
- No single intervention is sufficient to control transmission.
- Limited resources → maximise efficiency.
- How to combine interventions to do this?
  - i.e. how to avoid redundancy?
  - (Potential antagonism not addressed here.)

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Basic reproductive number, R_0

- Measures how effectively infection spreads:
  - higher R_0 – harder to control (and higher endemic prevalence).
- R_0 is the average number of secondary infections occurring from a single infected individual in a totally susceptible population.
- An epidemic requires that transmission from an infected individual causes on average more than one new infection (i.e. $R_0 > 1$) so amplification occurs.
- Interventions aim to reduce $R_0<1$.

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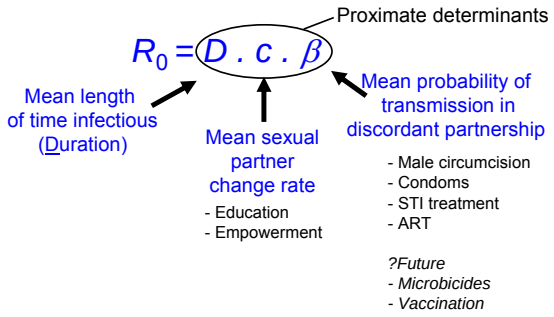
HIV's basic reproductive number



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Redundancy in effect on R_0

- Combined interventions will have a less-than-additive effect on R_0
- … even if they act independently on different proximate determinants.
- Example:
  - Intervention 1 alone reduces R_0 by 20%
  - Intervention 2 alone reduces R_0 by 30%
  - Combined they reduce R_0 by **44%**, not 50%
  - i.e. $R_0(1\text{-}0.2)(1\text{-}0.3) = R_0(0.8)(0.7) = 0.56R_0$

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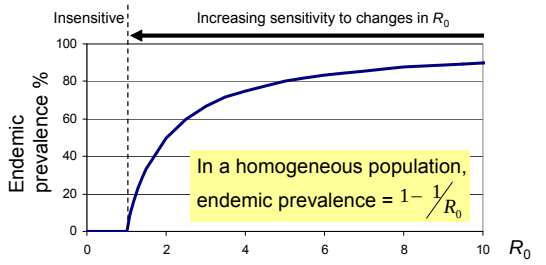
R_0 & endemic prevalence

- But, R_0 and endemic prevalence are non-linearly related
- i.e. proportionate endemic prevalence ↓ ≠ proportionate R_0 ↓



Heterogeneity in HIV risk

- Models and interventions need to take account of heterogeneous risks of HIV acquisition and transmission.

Conclusions

- Combined interventions have a less-than-additive effect in ↓ R_0.
- But R_0 → endemic prevalence non-linear: combined interventions are almost never additive, but synergistic or redundant.
- Generally, interventions should be combined, not selected between – 'and' not 'or'.
- Interventions which are insufficiently effective singly may be worth implementing together, due to synergy.
- To maximise efficiency, target each intervention effectively – i.e. at the appropriate risk group.