Prevention and Treatment for HCV – from modelling to evaluation - an illustration

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Acknowledgements & CoI

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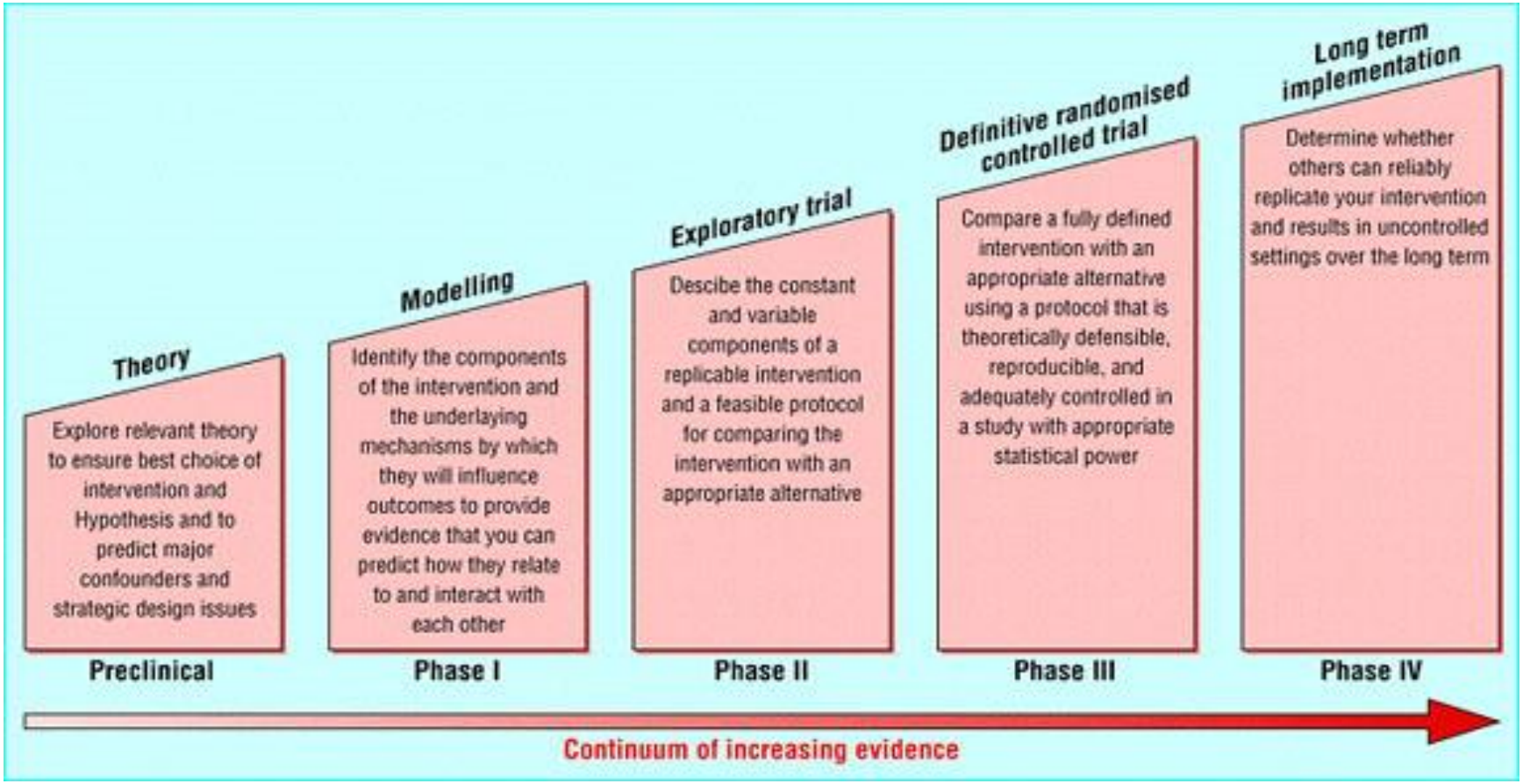
Overview- stages of evaluation

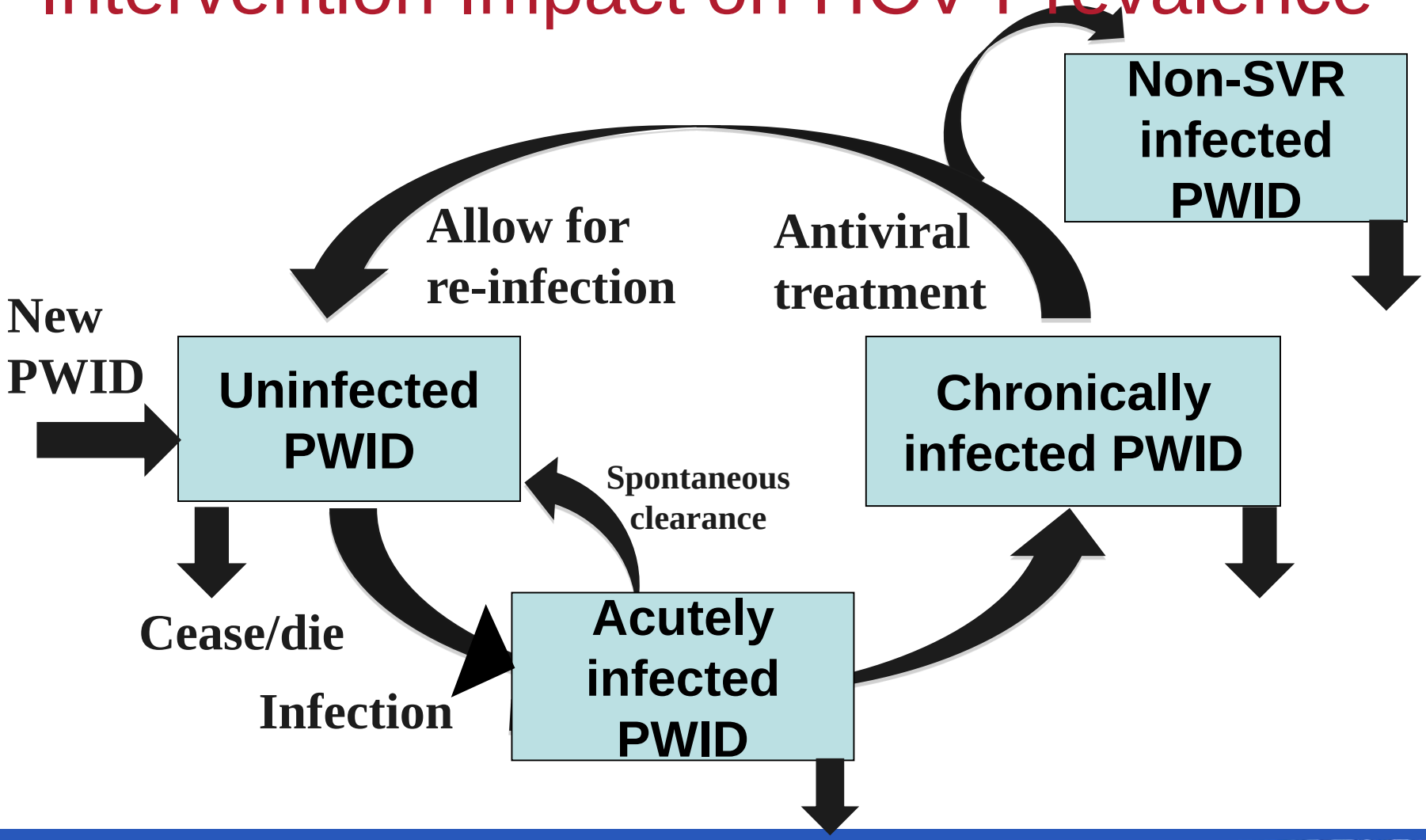
- Theory & Modelling shown that:
  - HCV treatment scale-up critical for HCV prevention in PWID
  - Increasing HCV case-finding in PWID cost-effective
  - Early treatment of PWID cost-effective
  - Current treatment rates unlikely to lead to measurable/observable change in HCV transmission
  - Uncertainty in measuring HCV incidence and prevalence in community surveys & Uncertainty in determining PWID prevalence
  - Phase III trial needs to resolve issues with PWID and HCV measurement

Evaluating Complex Intervention TasP



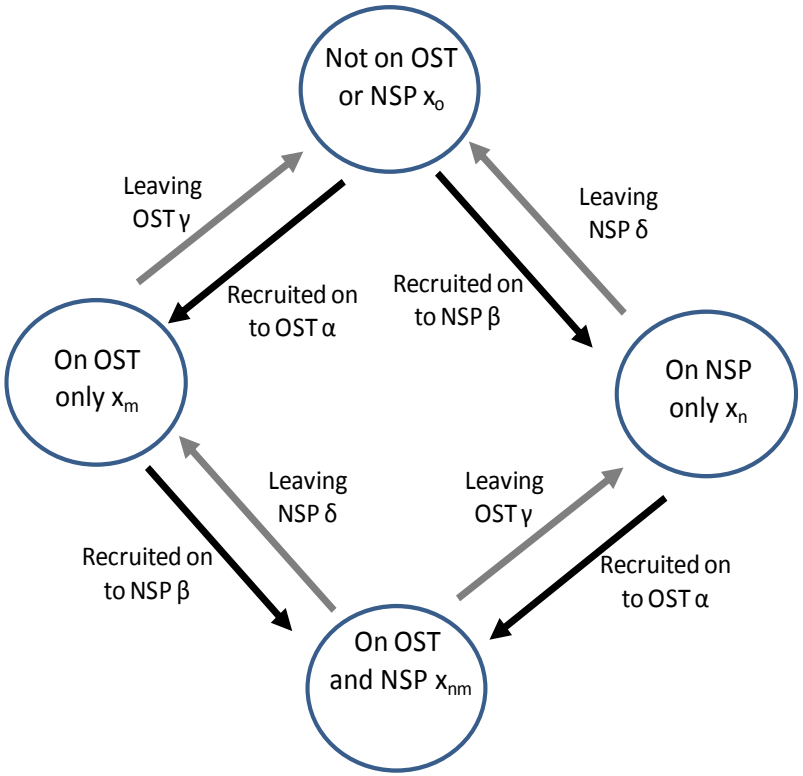
WE HAVE MODELS – WHY HCV TREATMENT IS NEEDED FOR PREVENTION

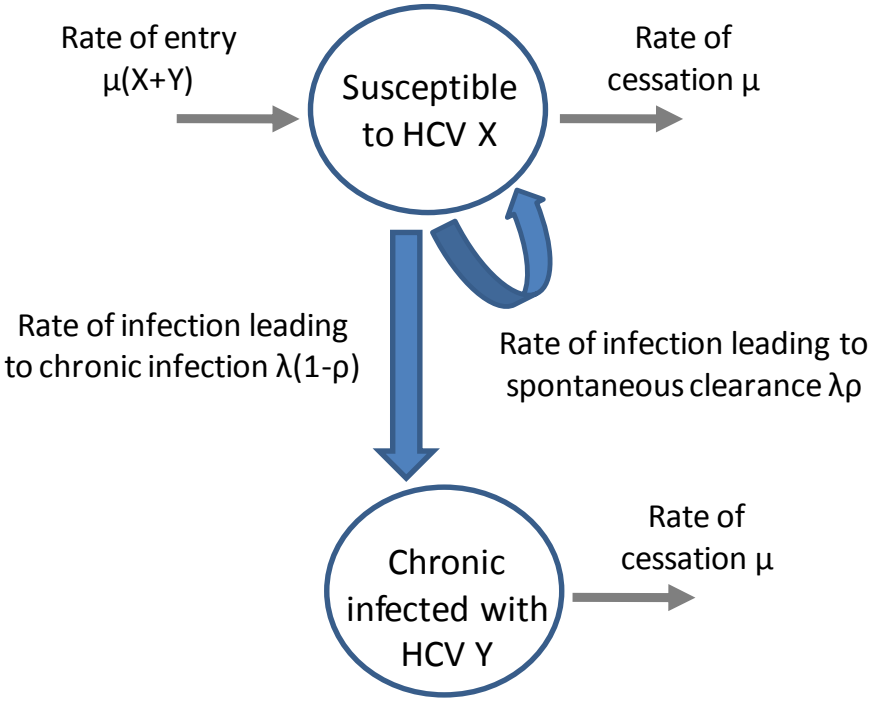
Need Dynamic Model to Assess Intervention Impact on HCV Prevalence



Martin NK, Vickerman P, Foster GR, Hutchinson SJ, Goldberg DJ, and Hickman M. J Hep 2011; 54:1137-44

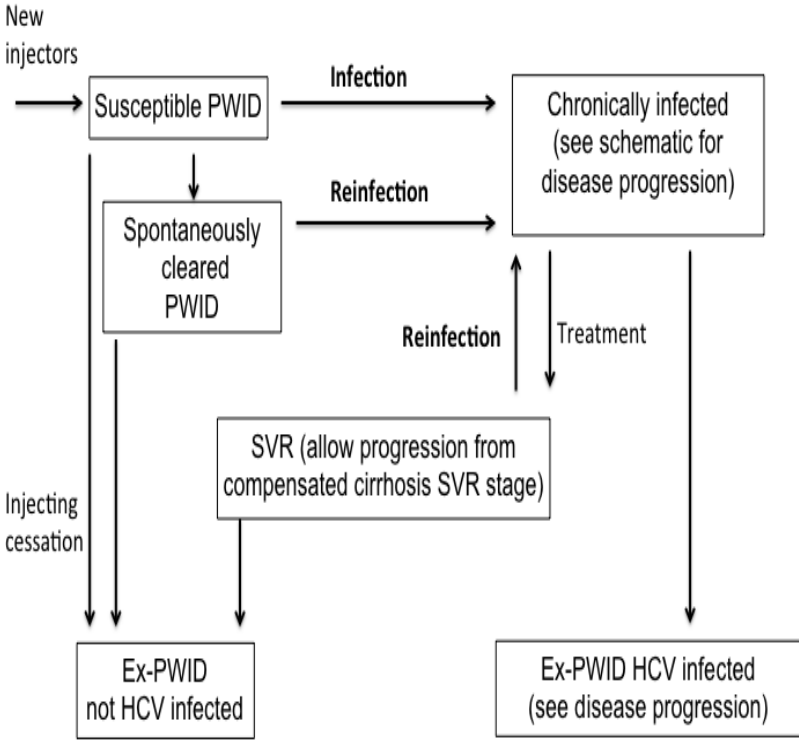
Modeling transitions between OST and NSP & transmission of HCV

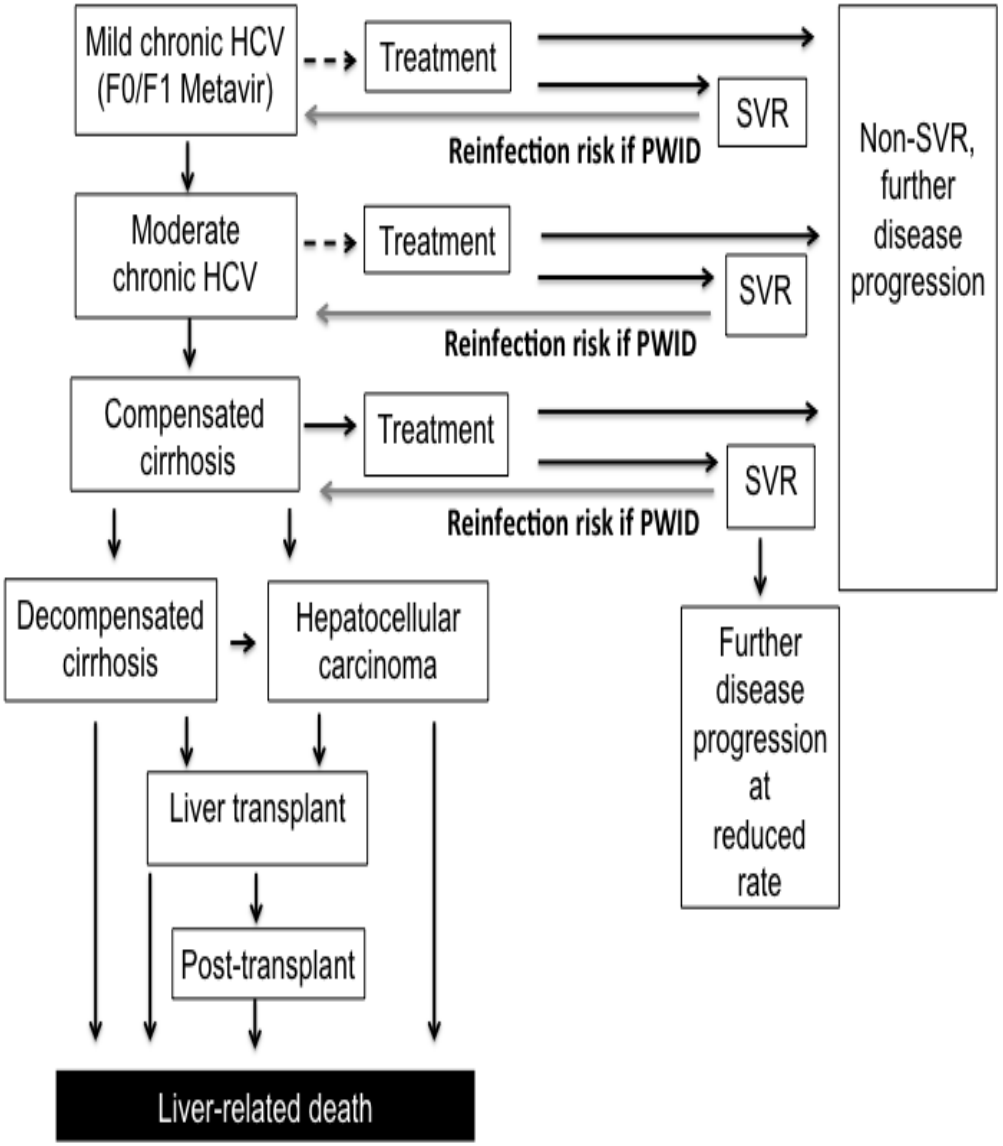




Vickerman et al Addiction 2012
doi:10.1111/j.1360-0443.2012.03932.x

Modelling PWID and ex-PWID populations and HCV disease progression

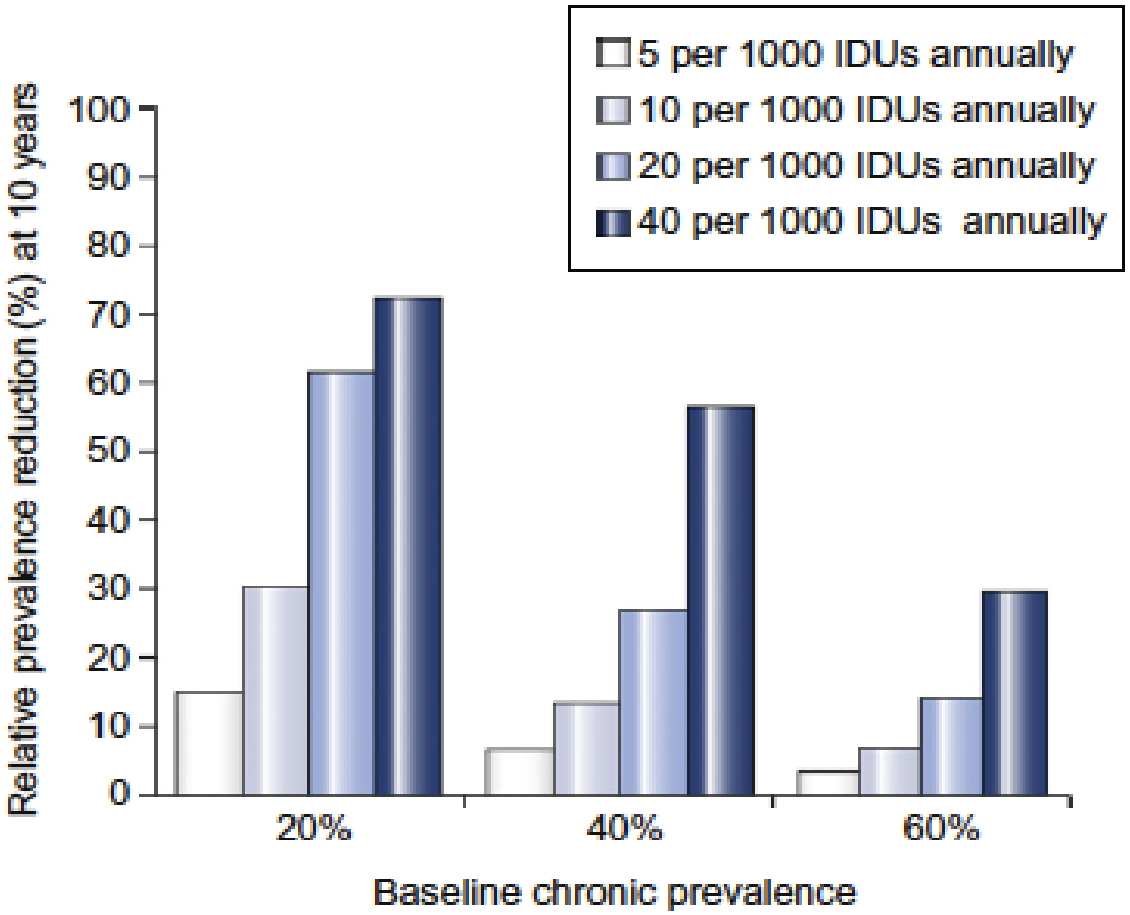




Martin N et al The cost-effectiveness of HCV antiviral treatment for infection drug user populations. *Hepatology* 2012; 55(1):49-57.

MODELLING HCV TREATMENT AS PREVENTION

HCV RELATIVE PREVALENCE REDUCTIONS AT 10 YEARS WITH PEGIFN+RBV



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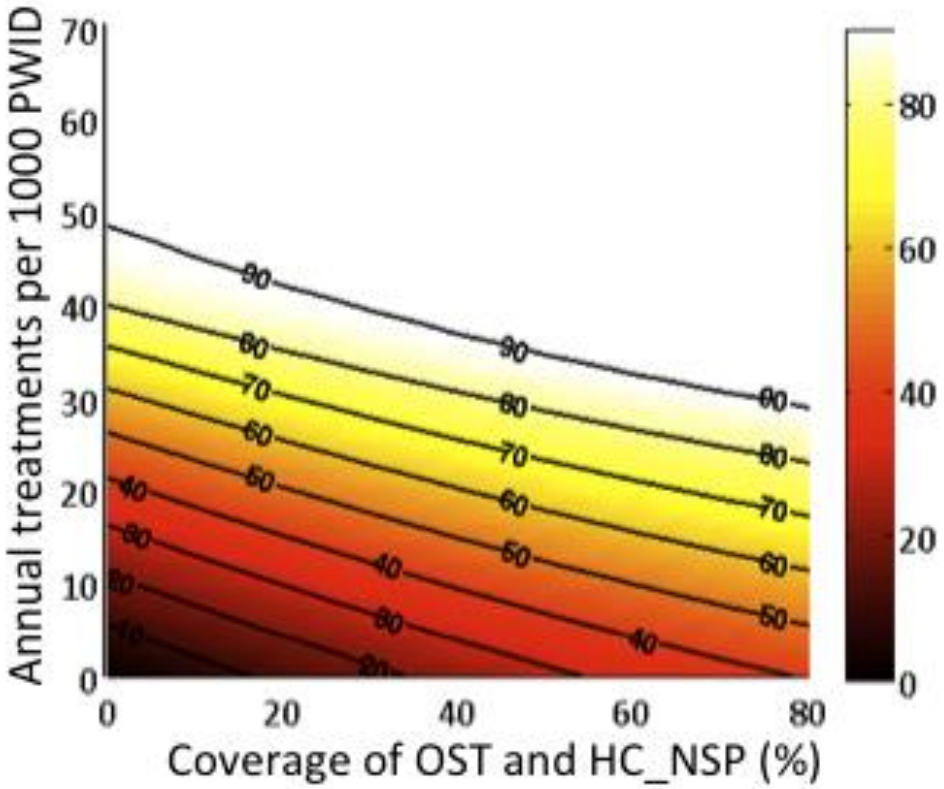
Martin NK, Vickerman P, Foster GR, Hutchinson SJ, Goldberg DJ, and Hickman M. J Hep 2011; 54:1137-44

COMBINATION PREVENTION SCALE-UP (OST/NSP/DAAS): 10 YEAR RELATIVE PREVALENCE REDUCTIONS WITH NO BASELINE COVERAGE OF OST/NSP AND USING DAAs

40% chronic prevalence



- Dark red: modest (<20%) impact, high HCV
- Orange: ~50% impact
- White: >80% impact

- >40% reduction requires HCV treatment
- OST&NSP increases benefit of HCV treatment

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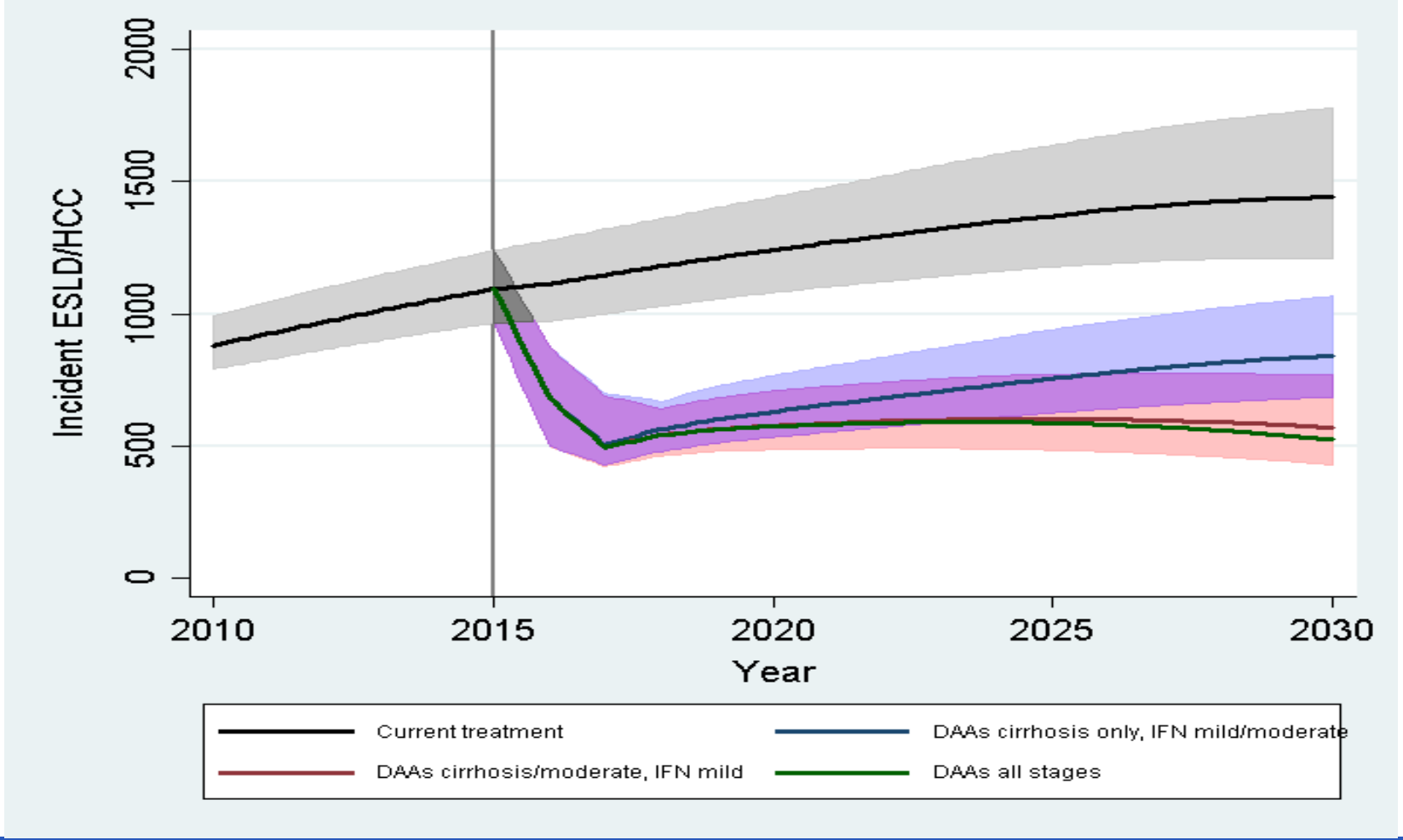
Martin NK, Hickman M, Hutchinson SJ, Goldberg DJ, and Vickerman P. Combination interventions to prevent HCV transmission among people who inject drugs: modelling the impact of antiviral treatment, needle and syringe programmes, and opiate substitution therapy. Clinical Infectious Diseases 2013

TREATMENT PRIORITISATION – WHO SHOULD GET NEW DAA

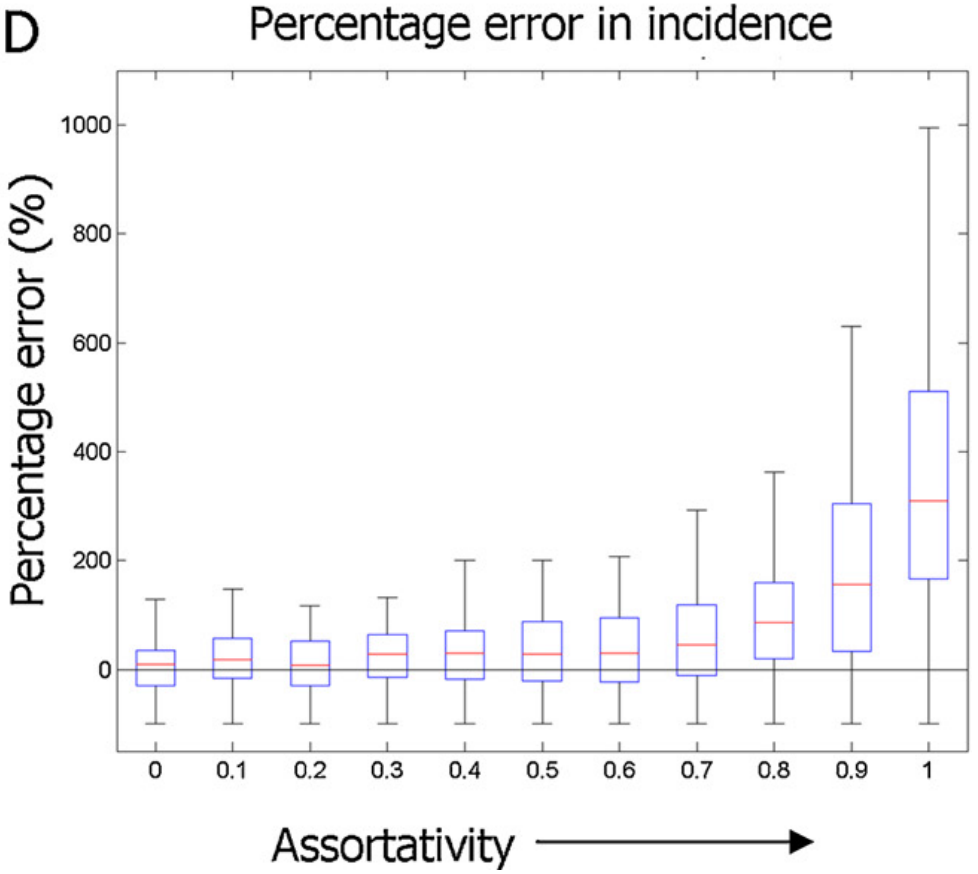
Projected incidence of ESLD or HCC under current treatment rates or targeted scale up

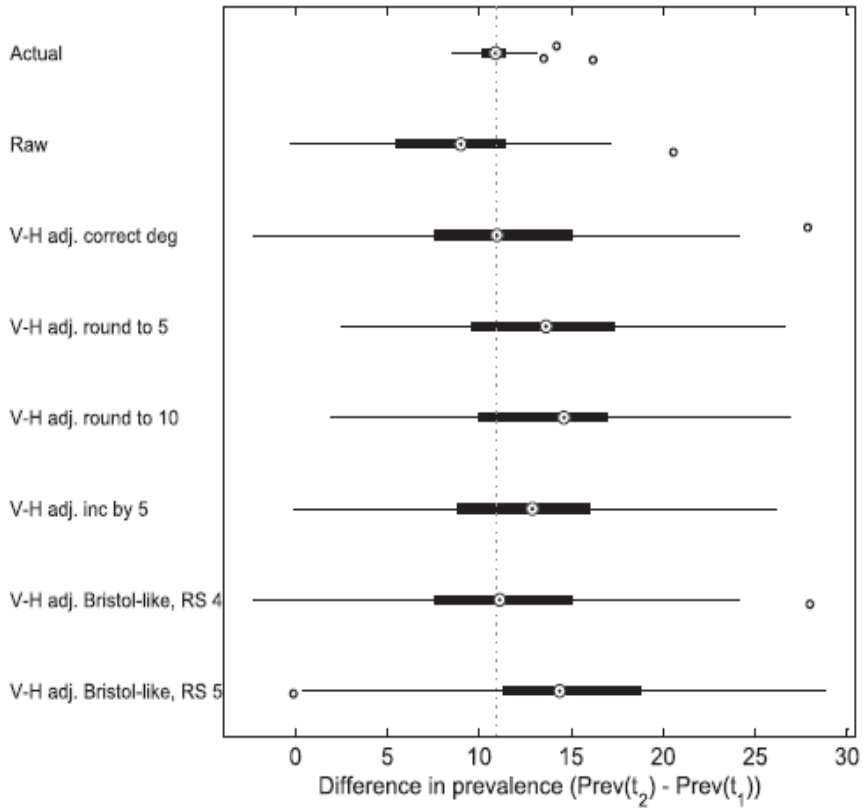


ARE CURRENT HCV TREATMENT RATES SUFFICIENT TO ACHIEVE A MEASURABLE CHANGE IN HCV TRANSMISSION?

PHASE III – TREATMENT AS PREVENTION MEASURING OUTCOME PROBLEMS

Repeated surveys of HCV incidence and prevalence in PWID can be biased (a lot)





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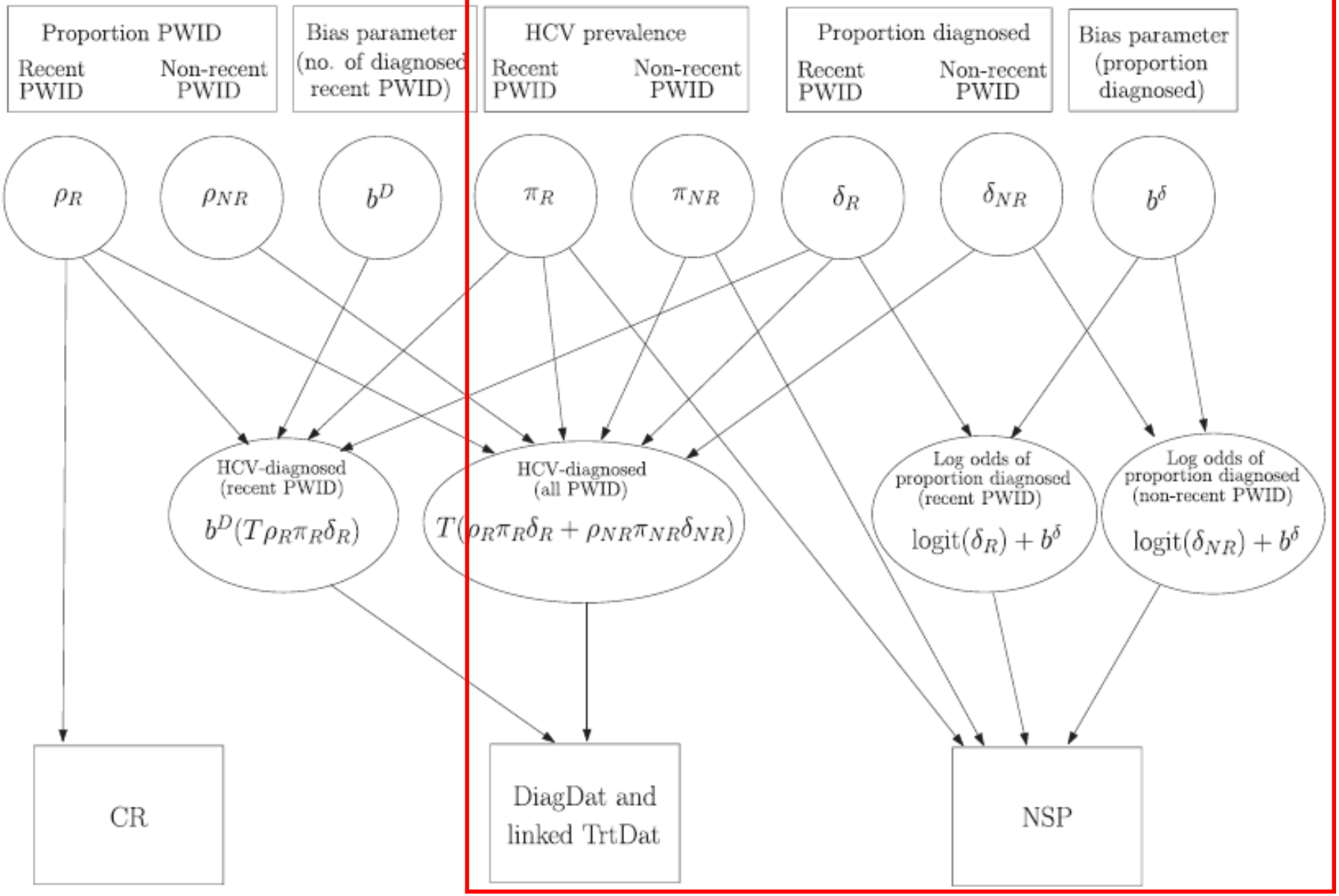
Mills et al Drug and Alcohol Dependence 2012;126 :324-32 & 2014; 142: 120-6

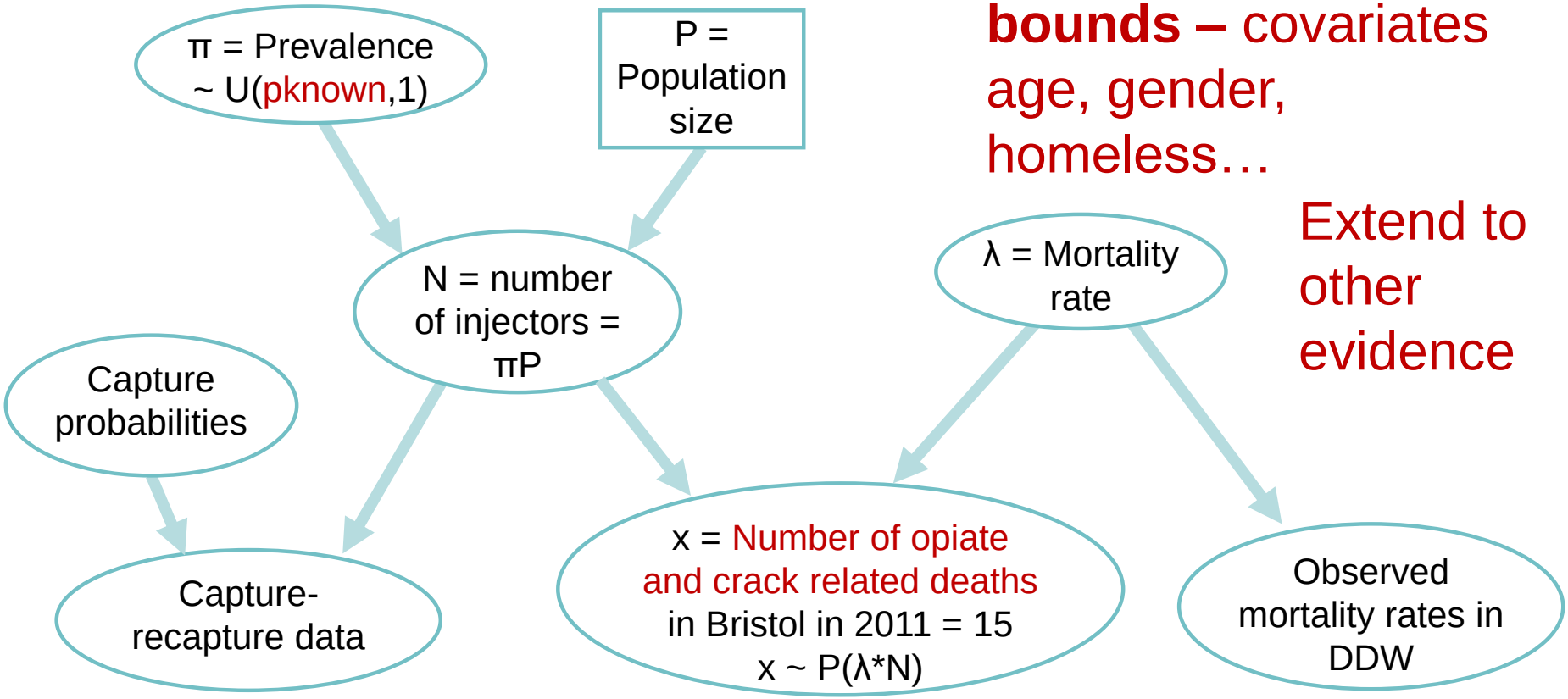


Prevost et al Addiction 2015. Relationship between the parameters and the data sources. Circles denote the unknown parameters (or functions of parameters) which are to be estimated. Squares denote the data sources.

Prevalence Estimation – data conflicts & uncertainty

- Small problem: Bristol PWID prevalence (CRC)
  - Bayesian CRC 0.9% (2770, 95%Cr-I 2570-3110) conflicts with published standard CRC estimates 0.5% (1500, 95%CI 1230-1760)
- Big problem: England PWID/opioid prevalence
  - Standard CRC analysis suggest prevalence of 1.6 million (1.2 – 2.3 million)
  - Revised analysis/non CRC method: 276,000 (249,000 – 313,000) 0.80% (0.72 - 0.91%)

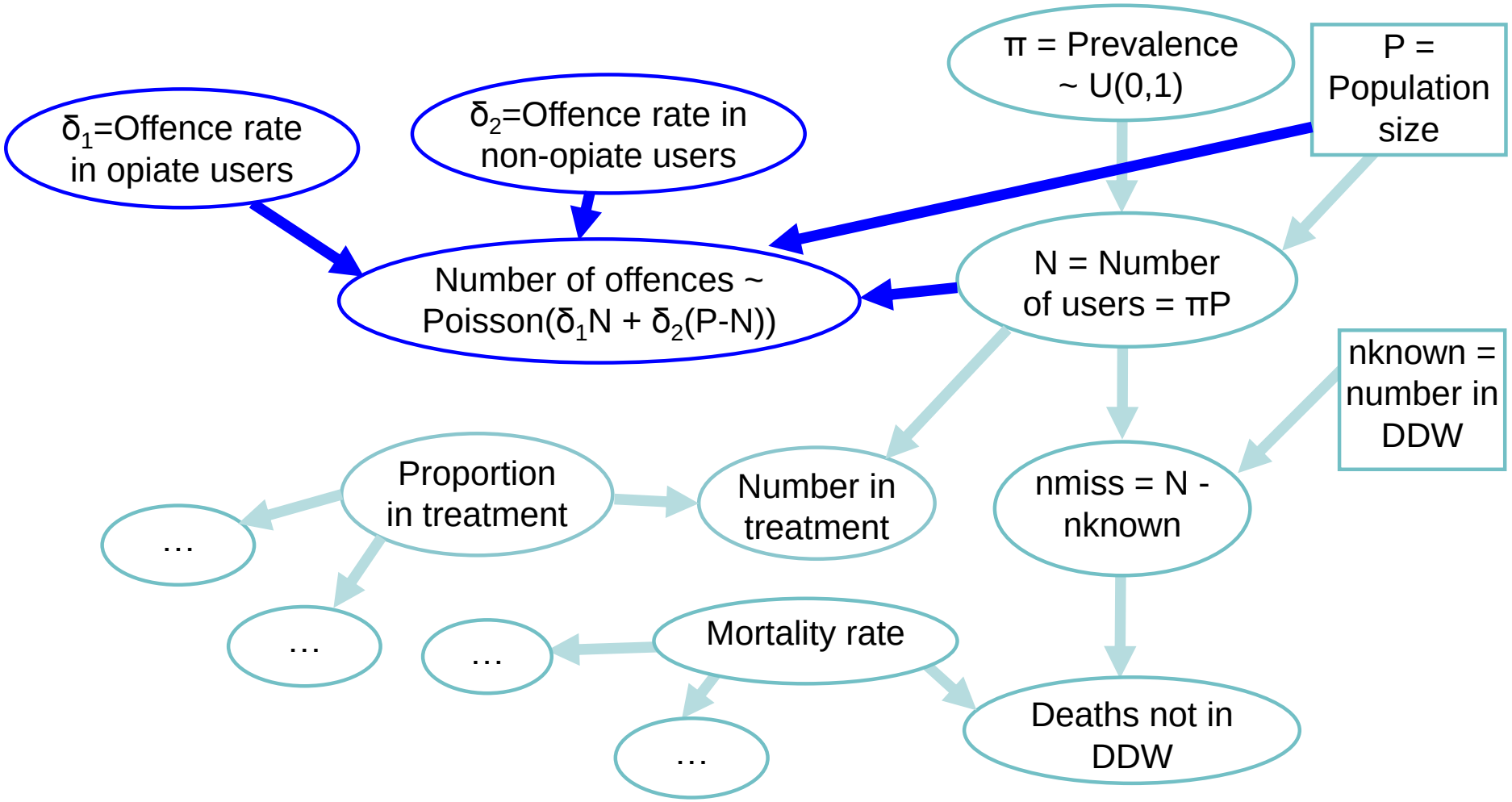
CRC viewed in a Bayesian framework



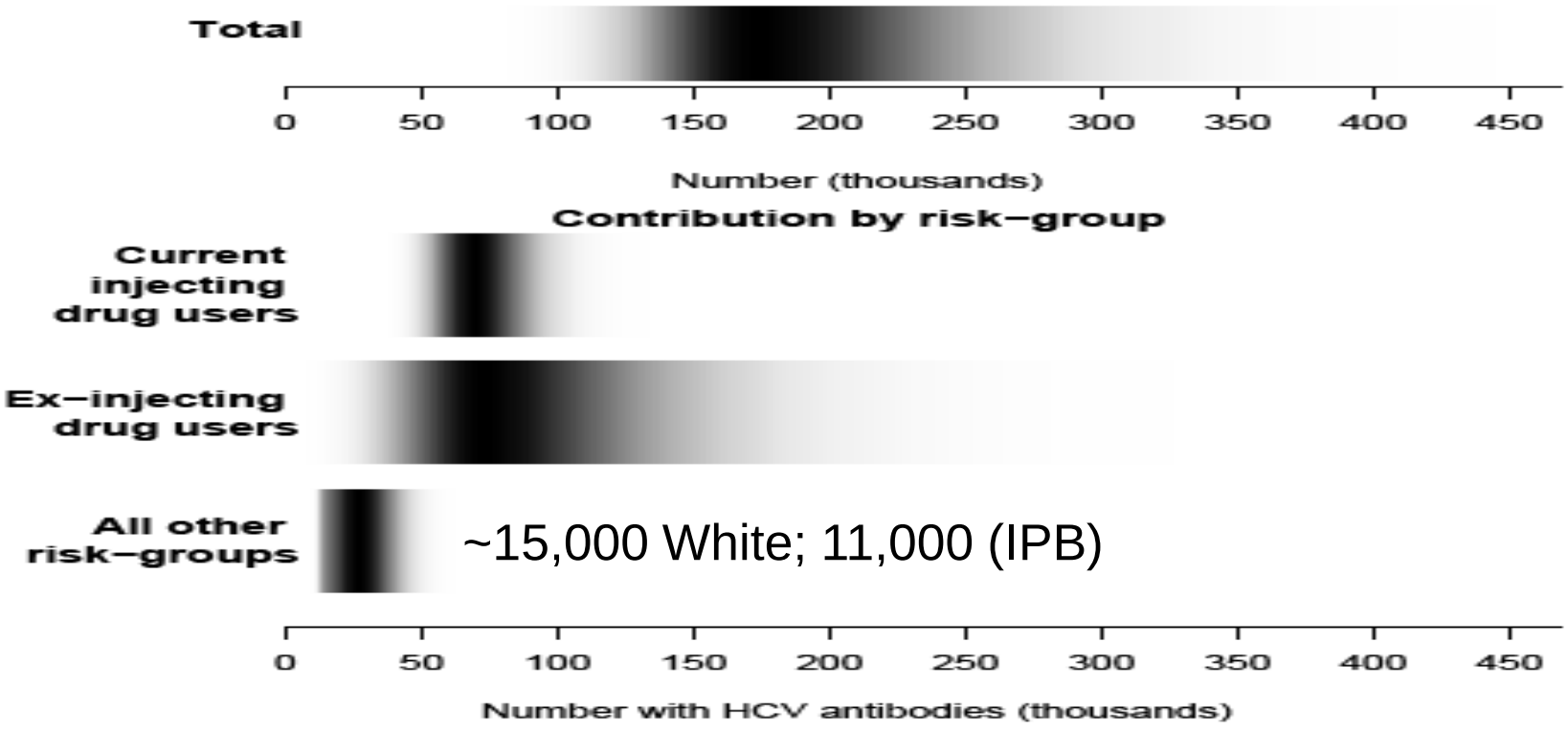
Number known PWID enforce lower bounds – covariates age, gender, homeless…

Extend to other evidence

Prevalence Estimation – Mortality data, treatment data, crime rates



Measuring HCV among PWID



Sweeting et al. Biostatistics 2008; De Angelis et al, Statistics in Med Research 2009; Ross et al EJPH 2011

HCV TAsP Evaluation issues

- Outcome = HCV incidence & chronic prevalence in PWID in the community
  - Phase II will assess SVR and re-infection rates (but not surrogate markers of TAsP effectiveness)
  - Multiple samples and sources of evidence to account for uncertainty
  - Large HCV treatment scale-up in discrete low prevalence setting
- PWID prevalence
  - Combine evidence and data sources
  - Needed for treatment scale-up targets & phase IV evaluation