SETTINGS AND STRATEGIES FOR HCV ELIMINATION: HOW MODELING CAN INFORM OUR EFFORTS

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DISCLOSURES

I have received unrestricted research grants from Gilead and honoraria from Merck, AbbVie, and Gilead

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ACHIEVING ELIMINATION

- WHO “Elimination as a public health threat” targets for 2030
  - 90% reduction in HCV incidence
  - 65% reduction in HCV-related mortality
- Modeling has generated hypothesis that elimination achievable with traditional prevention interventions and HCV treatment as prevention (TasP)
- **Policymakers need empirical evidence of HCV TasP** (clinical trial, natural experiment or observational study)
- **Countries need advice on how to achieve these targets with limited resources (& impact evaluation afterwards)**
- Modeling crucial to providing this information

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PHASES AND USES OF MODELING

Pre-intervention/trial	During	Post-intervention/trial

• **Understanding the epidemic:**
  • Who are key drivers/risk groups?
  • What is future burden in country and risk groups?
• **Intervention planning:**
  • What scale-up/targeting is needed to achieve desired effect?
  • What key data need to be collected to measure an effect?
  • Where do key uncertainties lie?
  • What are the financial implications?
  • What is the optimal strategy with limited resources?
	• **Interim evaluation:**
	  • Are we on track?
	  • What do we need to change?
		• **Interpretation:**
		  • Disentangling likely impact of intervention
		• **Extrapolation:**
		  • Long-term population impact
		  • Economic evaluation

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TALK OUTLINE

- Modeling to inform **HCV treatment as prevention trials**
- Modeling to inform **national and regional planning** to achieve WHO elimination targets
  - General populations
  - High risk populations
  - Economic considerations

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MODELING TO INFORM TREATMENT AS PREVENTION TRIALS

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SToP-C goals

- To evaluate the impact of rapid scale-up of DAA treatment on incidence and prevalence of HCV infection in the prison setting
- To develop a translational framework for subsequent establishment of treatment-as-prevention programs in the prison sector

S T O P C

MODELING AS PART OF STOP-C

- **Pre-trial:**
  - Predict enrollment and treatment rates required to reach study endpoints
  - Identify key factors which may affect study outcome
- **During trial:**
  - Revise required sample size and treatment rate estimates based on surveillance phase and enrollment data
- **Post-trial:**
  - Interpret trial findings
  - Impact if scaled up
  - Evaluate cost-effectiveness

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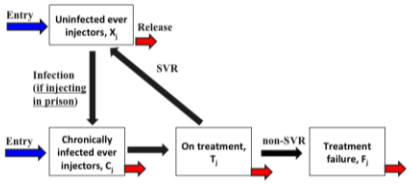
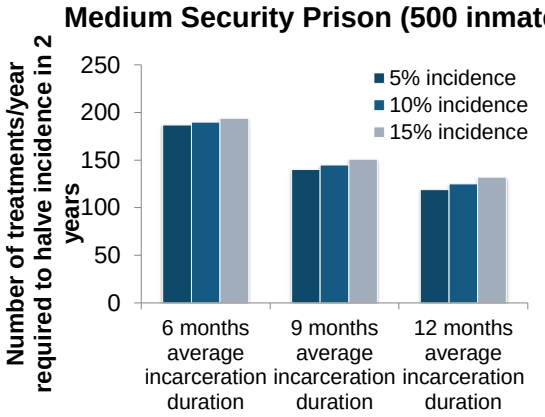
Pre-trial analysis:



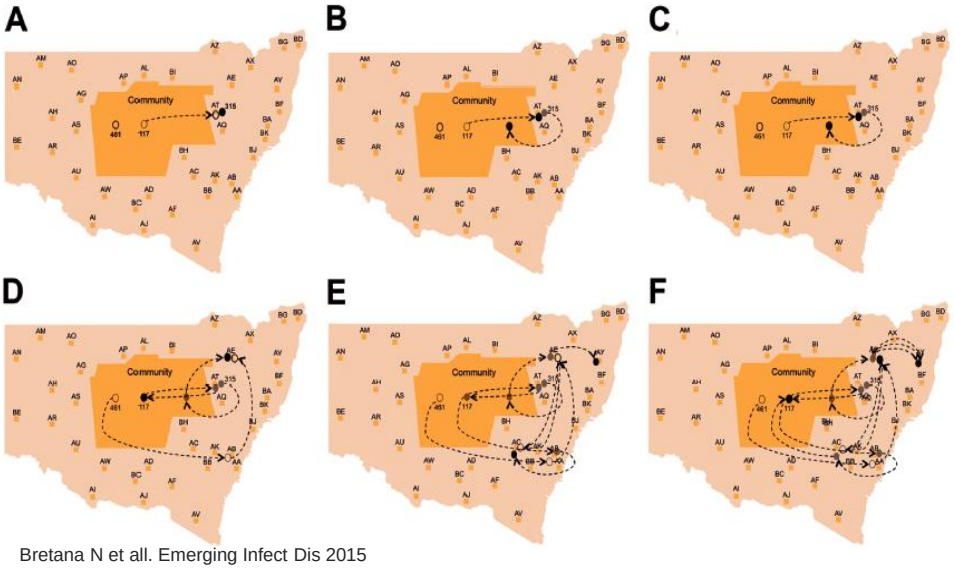


Key findings:

- Higher incidence requires slightly more treatments
- Required sample size more sensitive to **prison turnover**
- **Higher turnover, more treatments required**

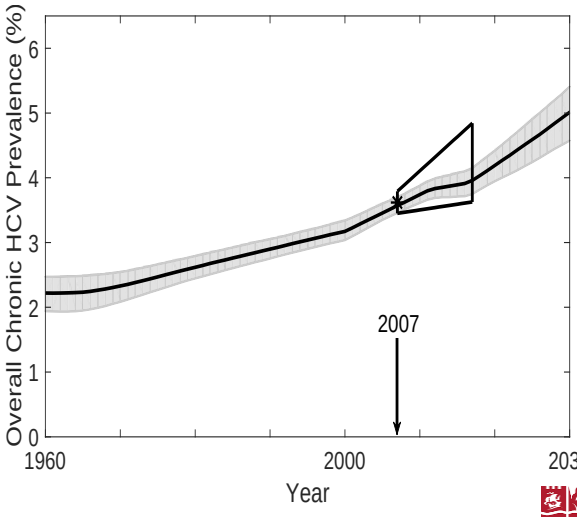
Martin NK and Vickerman P (unpublished)

MOVEMENT AMONG PWID PRISONERS IN NSW



Bretana N et all. Emerging Infect Dis 2015

PAKISTAN: MODELING TO UNDERSTAND EPIDEMIC



- Number of infections and burden will increase massively
  - By 2030, estimated
    - 12.6m chronic infections
    - 1.1m incident infections
- Transmission highly disseminated

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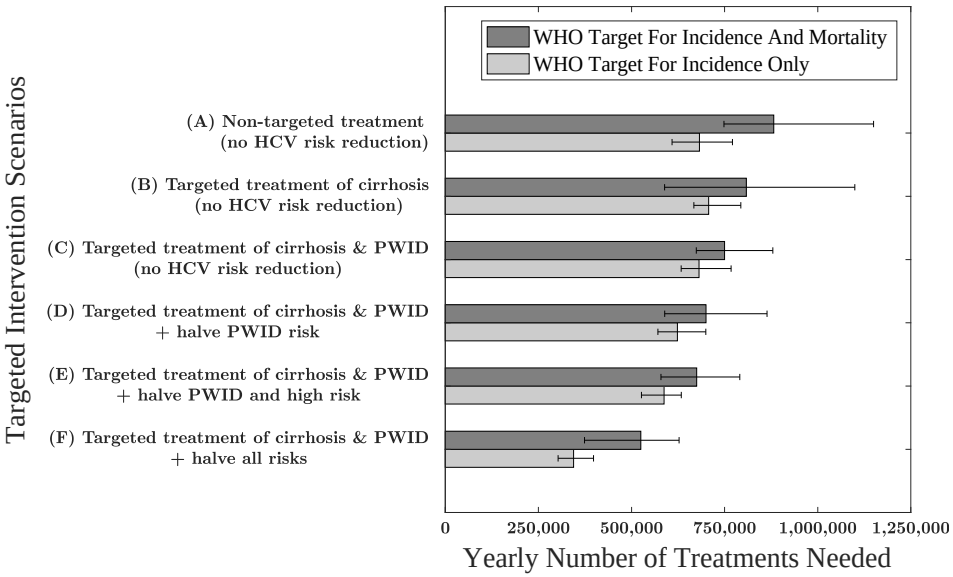
Aaron Lim, Peter Vickerman, et al (under review)

PAKISTAN: MODELING SCALE-UP AND TARGETING TO ACHIEVE ELIMINATION



Aaron Lim, Peter Vickerman, et al (under review)

HIGH RISK POPULATIONS

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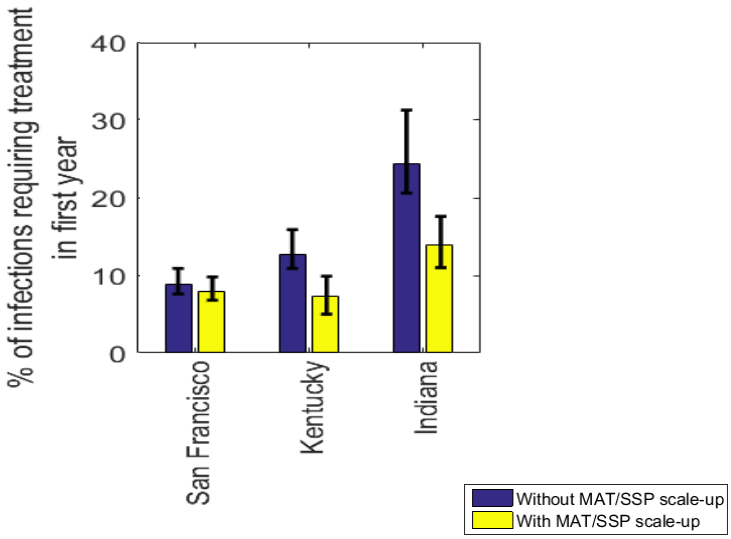
AMONG PWID IN US:
REQUIRED ELIMINATION SCALE-UP SETTING-SPECIFIC



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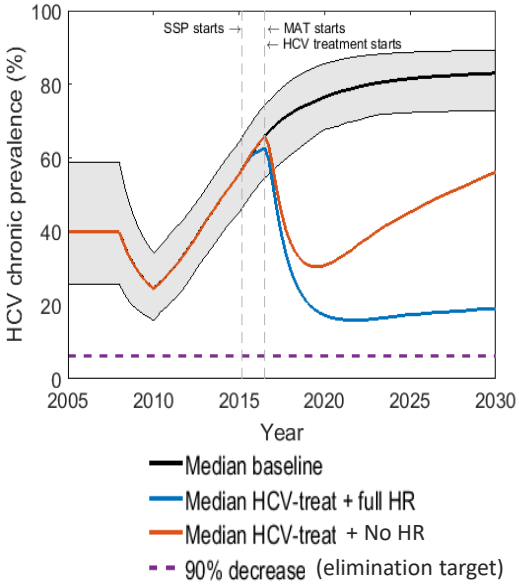
Fraser H et al, Addiction 2017 and Fraser in preparation

EXAMINING ISSUES SURROUNDING RETREATMENT IN SCOTT COUNTY, INDIANA

IF NO RETREATMENT

- HCV epidemic can rebound due to reinfection
- Harm reduction can maintain impact
- BUT cannot reach WHO target



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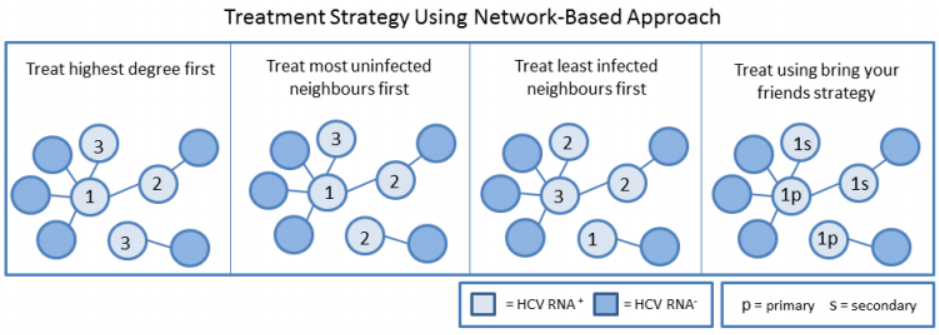
Fraser H et al, Addiction 2017

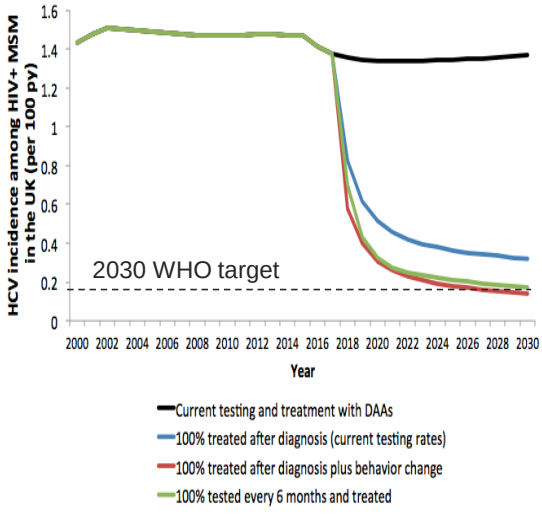
MODELING NETWORK-BASED STRATEGIES AMONG PWID: TREAT YOUR FRIENDS



Hellard et al. Hepatology 2014

Burnet Institute

AMONG HIV+ MSM IN THE UK



- **Difficult to reduce low incidence by 90% (to <0.14%) by 2030**
- Treatment alone **can** dramatically reduce incidence
- Elimination requires treatment plus:
  - Enhanced testing or
  - Behavior reduction

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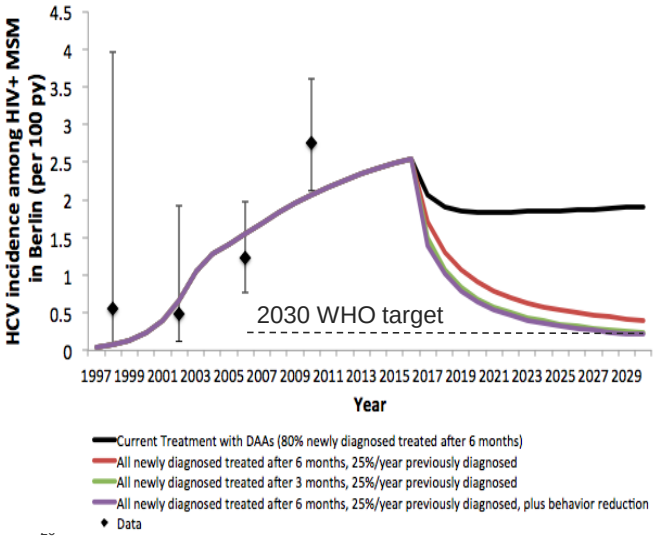
Preliminary work based on Martin NK et al. CID 2016

AMONG HIV+ MSM IN BERLIN: A SETTING WITH INCREASING INCIDENCE AND HIGH TREATMENT RATES



- **Even more difficult to eliminate in a setting with increasing incidence with existing high testing/treatment.**
- Elimination likely requires both treatment and behavior change

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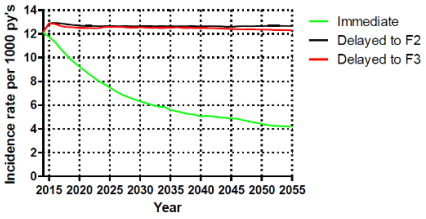
Martin NK and Ingiliz P et al, preliminary work

MOVING TOWARDS EVALUATION PHASE: HIV+ MSM IN THE NETHERLANDS

Pre-scale up model: at most ~20% reduction in 2 years…BUT:



Observed: halving in acute HCV incidence 2014-2016 with widespread scale-up

2014		**2016**
A-HCV **n=93**		A-HCV **n=49**
PYFUn=8290		PYFUn=8961
11.2/1000PYFU (95% CI 9-14)	➡	**5.5**/1000PYFU (95% CI 4-7)
1.1% per year		**0.55**% per year

Need modeling disentangling the likely impact of treatment scale-up on observed incidence declines

Boerekamp A et al. CROI 2017 abstract 137LB

Hullegie SJ et al. CROI 2015 abstract 536

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ECONOMIC CONSIDERATIONS

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MODELING WITHIN ECONOMIC EVALUATIONS

- **Cost-effectiveness of existing or proposed interventions:** Is it good value for money?
- **Budgetary impact:** How much will it cost?
- **Resource allocation:** How should we divide/target/prioritize our budget?
- **Value of future research:** How much should we spend for further research to reduce uncertainty, and on what?

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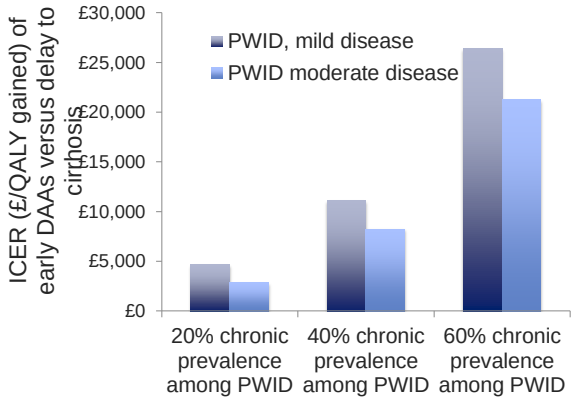
COST-EFFECTIVENESS: HCV TREATMENT AMONG PWID

- DAAs cost-effective for PWID in UK, Australia, Netherlands[1-3]
- More cost-effective in low prevalence settings, as greater prevention benefit



Martin NK et al. J Hepatol 2016
Scott N et al. J Gastro Hep 2016
[24]Van santen DK PLoS ONE 2016

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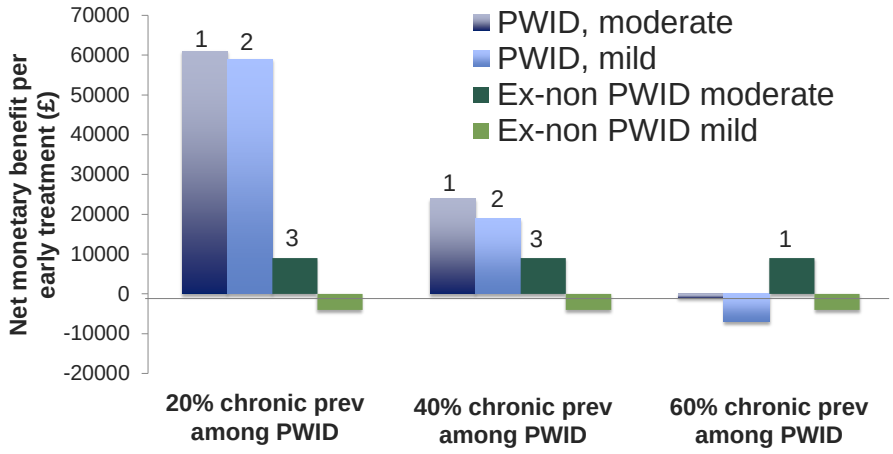
RESOURCE ALLOCATION: DAA PRIORITIZATION IN THE UK



*£20,000 willingness to pay.
Martin NK et al. J Hepatol 2016: 65(1):17-25.

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VALUE OF FURTHER RESEARCH: HCV SCREENING IN UK MIGRANTS

- Expected value of perfect information analysis (EVPI)
- Tells us:
  - **Maximum governments should spend** on further research to reduce uncertainty in cost-effectiveness
  - **What further research would be of most value** in identifying whether intervention is cost-effective

Miners A, Martin NK, Hickman M, Vickerman P. J Viral Hep 2015

EVPI associated with HCV screening in migrant populations in the UK

Parameter	Population EVP(P)I (million)
Overall decision level	£3.80
WTP £20 000 per additional QALY	£4.07
1% HCV Ab+ seroprevalence	£1.13
1% HCV Ab+ seroprevalence and WTP £20 000	£0.10
Intervention effect (absolute probability of testing)	Negligible
Probability of treatment uptake	£0.21
Background probability of testing	Negligible
Utilities	£1.07
SVR health states	£0.87
Intervention cost	£0.43
Disease costs	Negligible
Transition probabilities	£0.02
Initial distribution across HCV disease states	Negligible

DISCUSSION: MODELING USES AND LIMITATIONS

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MODELING LIMITATIONS AND DIRECTIONS

- Modeling alone insufficient evidence for HCV treatment as prevention
  - **Need real-world empirical data** with key outcome measures of population incidence/prevalence (not just SVR or reinfection)
  - Yet, modeling should be embedded within these trials to aid design, implementation, and evaluation.
- **Highly reliant on good data**
  - Large population based surveys gold standard but no good for concentrated epidemics
  - Other routine surveillance should be used – repeat testing of high risk groups, acute HCV testing – track HCV prevalence and incidence in population at risk
  - Estimate size of population at risk
  - Better estimates of full economic (including societal) costs and benefits of HCV action/inaction

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ACKNOWLEDGEMENTS

Health Protection Scotland: Sharon Hutchinson, David Goldberg, Esther Aspinall
Queen Mary's London: Graham Foster
University College London: Alicia Thornton, Caroline Sabin, Huw Price
Public Health England: Valerie Delpech
Imperial College London: Mark Nelson, Graham Cooke, Emma Thomson
Burnet Institute: Margaret Hellard
University of New South Wales: Greg Dore, Jason Grebely, Andrew Lloyd
CDC: Jon Zibbell, John Ward
Center for Infectology Berlin: Patrick Ingiliz

FUNDERS: US Center for Disease Control, Gilead Sciences, National Institute for Drug Abuse R01 DA037773-01A1, UCSD Center for AIDS Research (P30 AI036214), UK EPSRC, UK National Institute for Health Research Health Protection Research Unit (NIHR HPRU) in Evaluation of Interventions at University of Bristol. The views expressed are those of the authors and not necessarily those of the UK NHS, UK NIHR, UK Department of Health.

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