Treatment and Prevention to Eliminate Hepatitis C.

The TAP Study

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Centre for Research Excellence into Injecting Drug Use

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Declarations

- NHMRC fellowship
- Burnet receives infrastructure support from the Victorian Government
- Gilead Sciences
- Abbvie

Acknowledgements

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- Scott Bowden and team - VIDRL

Hepatitis C - epidemiology

- Over 130 - 150 million people worldwide ~ 3% of the worlds population have been exposed to HCV
- An estimated 310,000 Australians, have been exposed to HCV, with 220,000 ongoing infection
- Estimated that 6,000 - 10,000 new HCV infections annually
- People who inject drugs (PWID) - key drivers of HCV transmission in many developed countries including Australia

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Hepatitis C in people who inject drugs

- PWID are at greatest risk of HCV infection
  - HCV RNA^{+} rates 40 – 60% in most countries.
  - HCV incidence - 5-40% per annum.
- Current levels of HCV treatment uptake among PWID are low and will not reduce HCV prevalence among PWID.
  - Estimate - 3 / 1000 PWID treated per year in Melbourne
- Future treatment regimens for HCV will have
  - Fewer side effects
  - High effectiveness (>90% cure)
  - Improved dosing schedules (once-twice/day)
  - Shortened treatment duration (6-24 weeks).

Treatment and prevention of hepatitis C is now a possible – as is hepatitis C elimination.

WHO Global targets for elimination

- 80% reduction in new HCV infections by 2030
- 65% reduction in HCV-related deaths by 2030 compared with 2010

Achieving the 2030 targets will require reaching ambitious service coverage milestones

- 90% of people diagnosed by 2030
- 80% of eligible people treated and cured by 2030

Will require a multipronged approach

- Prevention – OST and NSPs
- Testing
- Treatment
- Vaccine

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Will require a multipronged approach

- Prevention – OST and NSPs
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Will require a multipronged approach

- Prevention – OST and NSPs
- Testing

Treatment and prevention

- Vaccine

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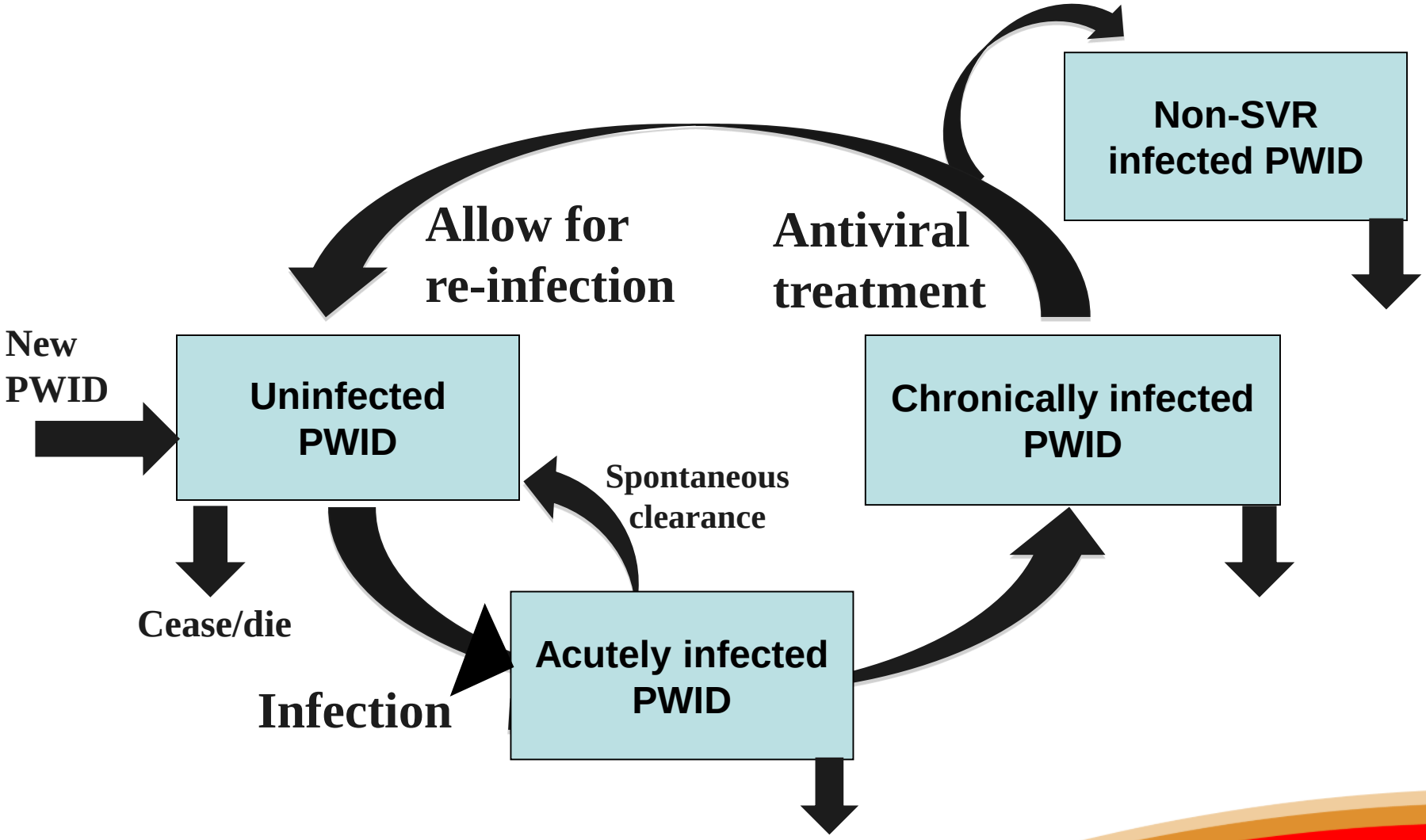
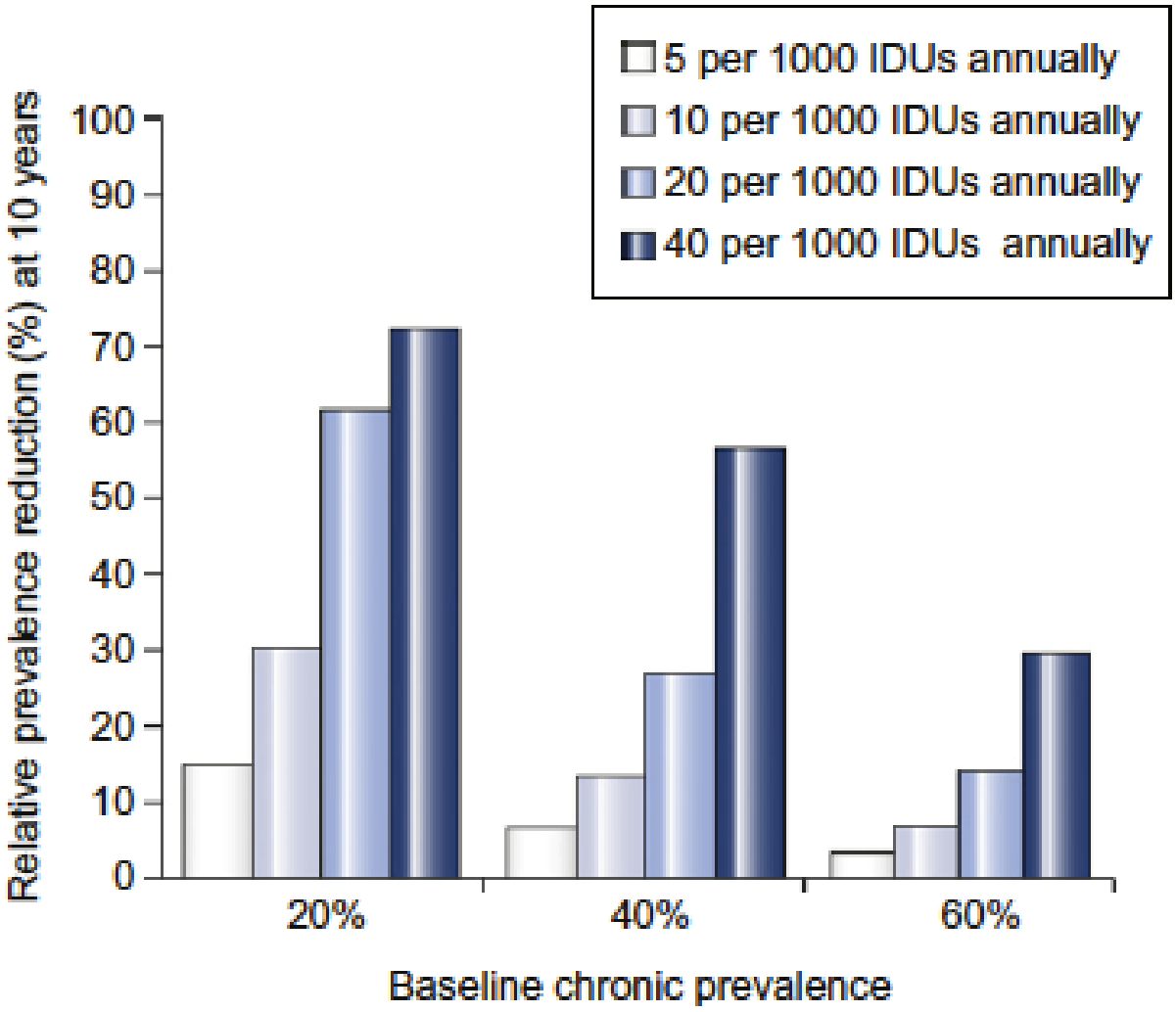
Models informing hepatitis C elimination

DYNAMIC HCV TRANSMISSION MODEL



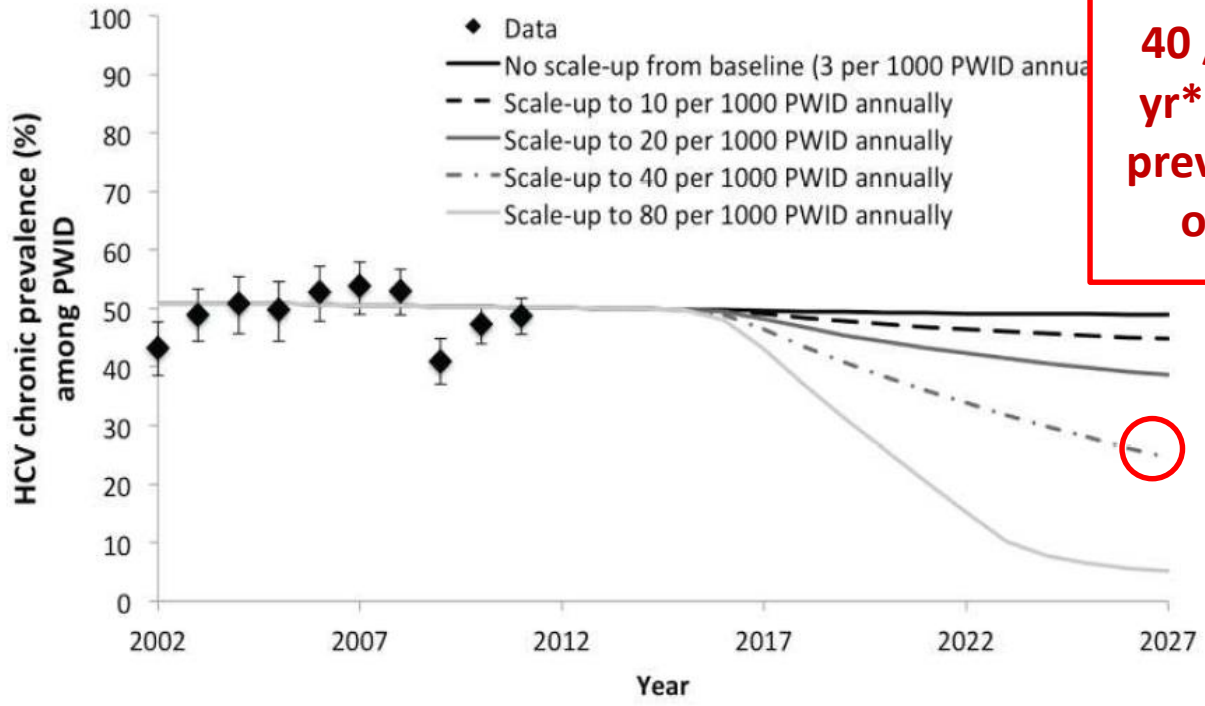
Martin et al. J Hepatology 2011; J Theoretical Biology 2011

Prevention impact results: prevalence reductions at 10 years



Martin et al. J Hep 2011

Treatment and prevention



Scale-up to treating 40 / 1000 PWID / yr* would reduce prevalence by 50% over 15 years

Chronic prevalence among PWID over time in Melbourne, Australia. Simulations show no scale-up from baseline (current treatment levels), or scale-up to 10, 20, 40, or 80 per 1000 PWID treated annually. A linear scale-up from baseline (2002 – 2007) to scaled-up rate during 2015- 2017 was modelled. HCV prevalence data points shown for comparison with 95% confidence intervals.

*Assumes IFN-free DAA with 90% efficacy, 12 week duration

Martin N, et al., Hepatology, 2013

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Social networks among PWID

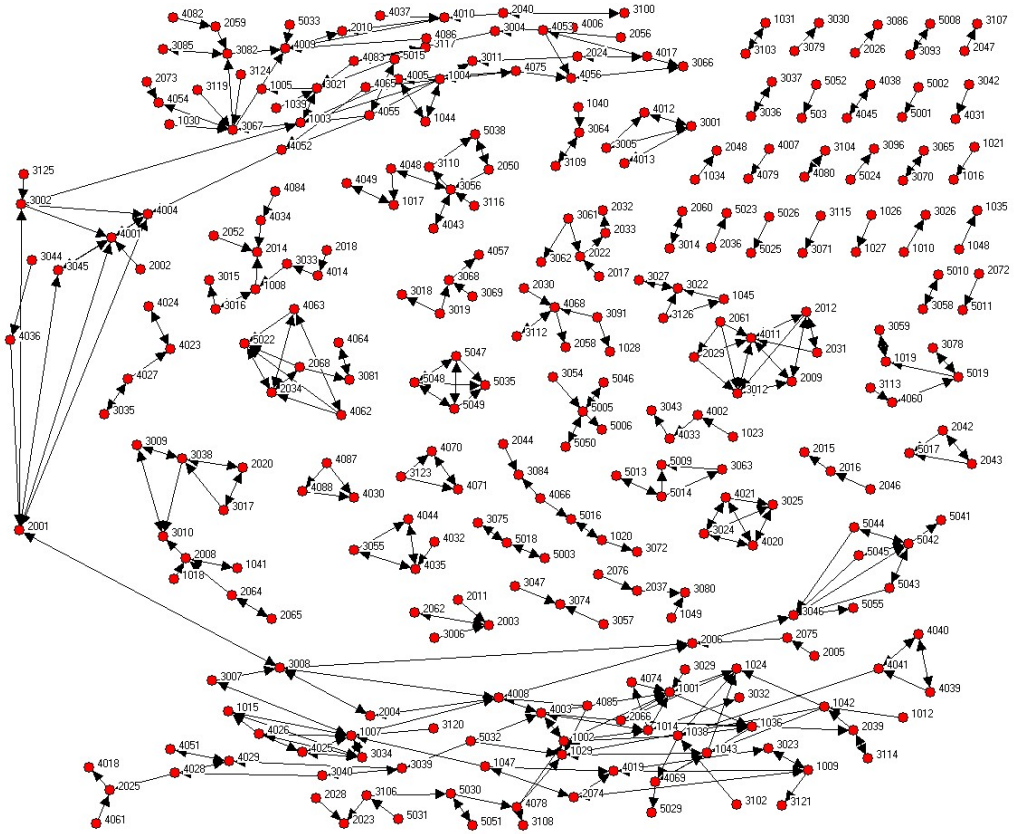
- In modelling studies, PWID are assumed to mix homogenously with all other injectors in a population

- Burnet - over the past 10 years explored and modelled the impact of PWIDs' social networks on HCV transmission or clearance:
  - Injecting networks substantially impact transmission rates
  - A **"Treat Your Friends"** strategy
    - reduces the risk of HCV reinfection post-treatment
    - reduces HCV transmission through the network

- In the medium long-term this will
  - substantially reduce the overall number of PWID needing treatment
  - reduce long-term HCV prevalence and treatment costs

Rolls D et al J Theor Biol, 2012.; Rolls D, et al.. Social Networks, 2013.; Rolls D et al. Plos One 2014
Hellard et al Hepatology 2014

The role of the injecting network on hepatitis C treatment and prevention.



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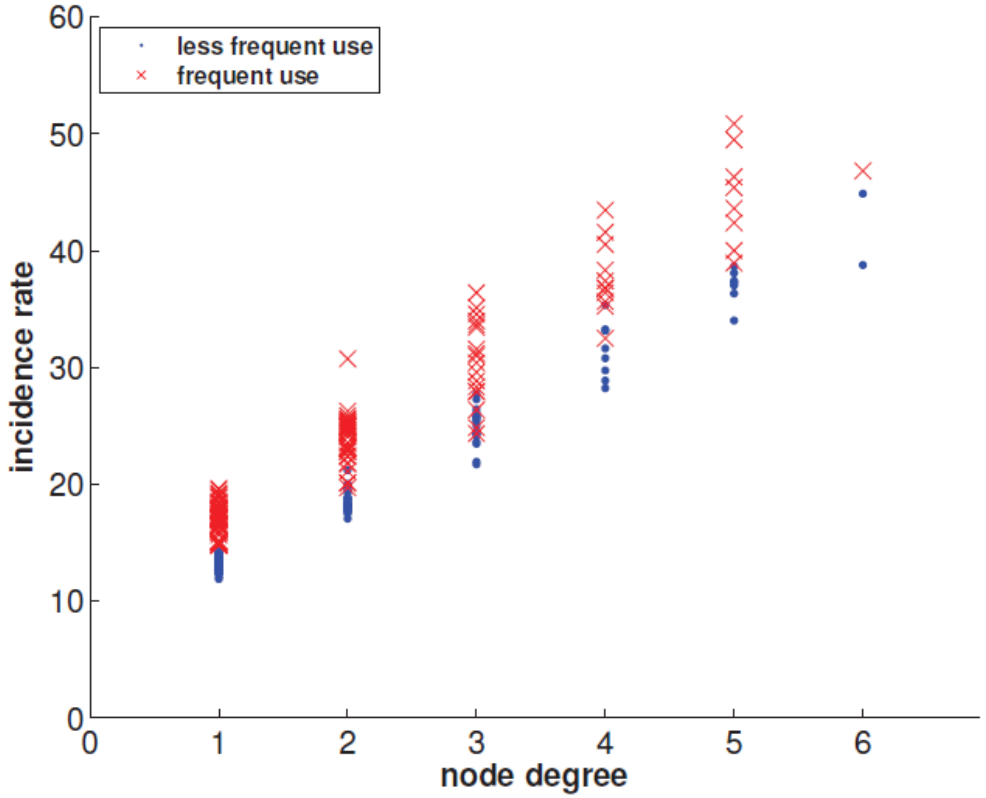
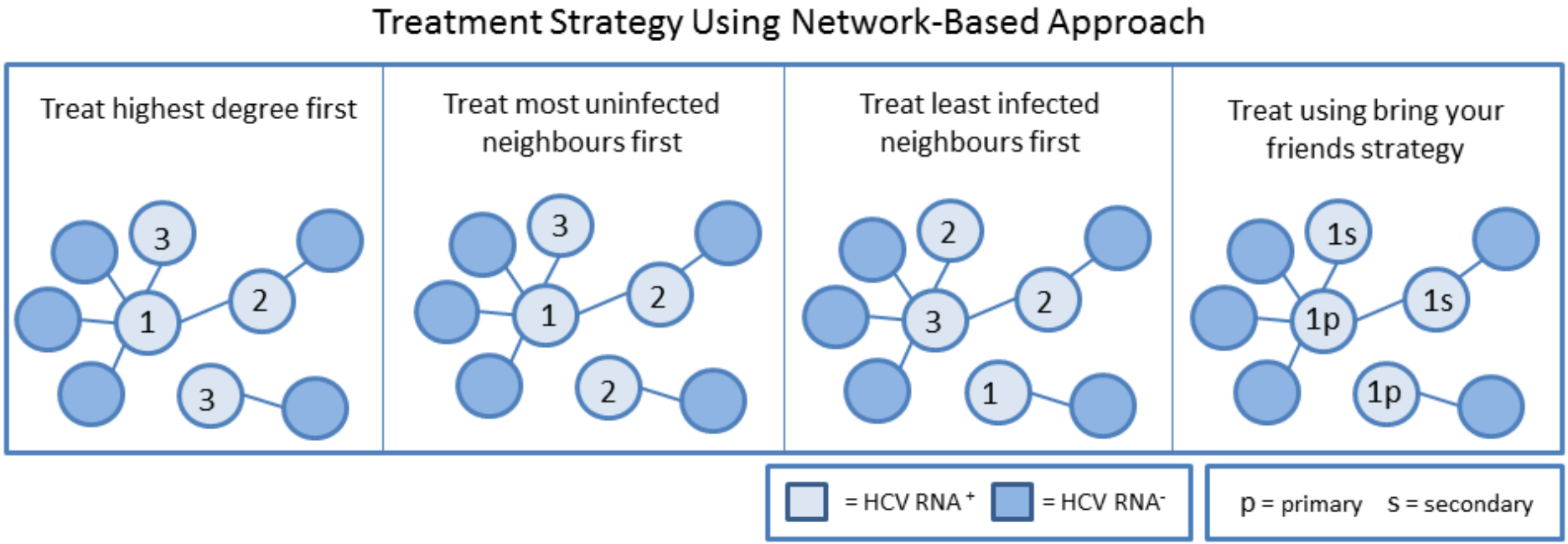
Hepatitis C incidence rate

- For ‘frequent’ (daily) users, each additional network partner increases the incidence rate by about 6.9 infections per 100 person-years



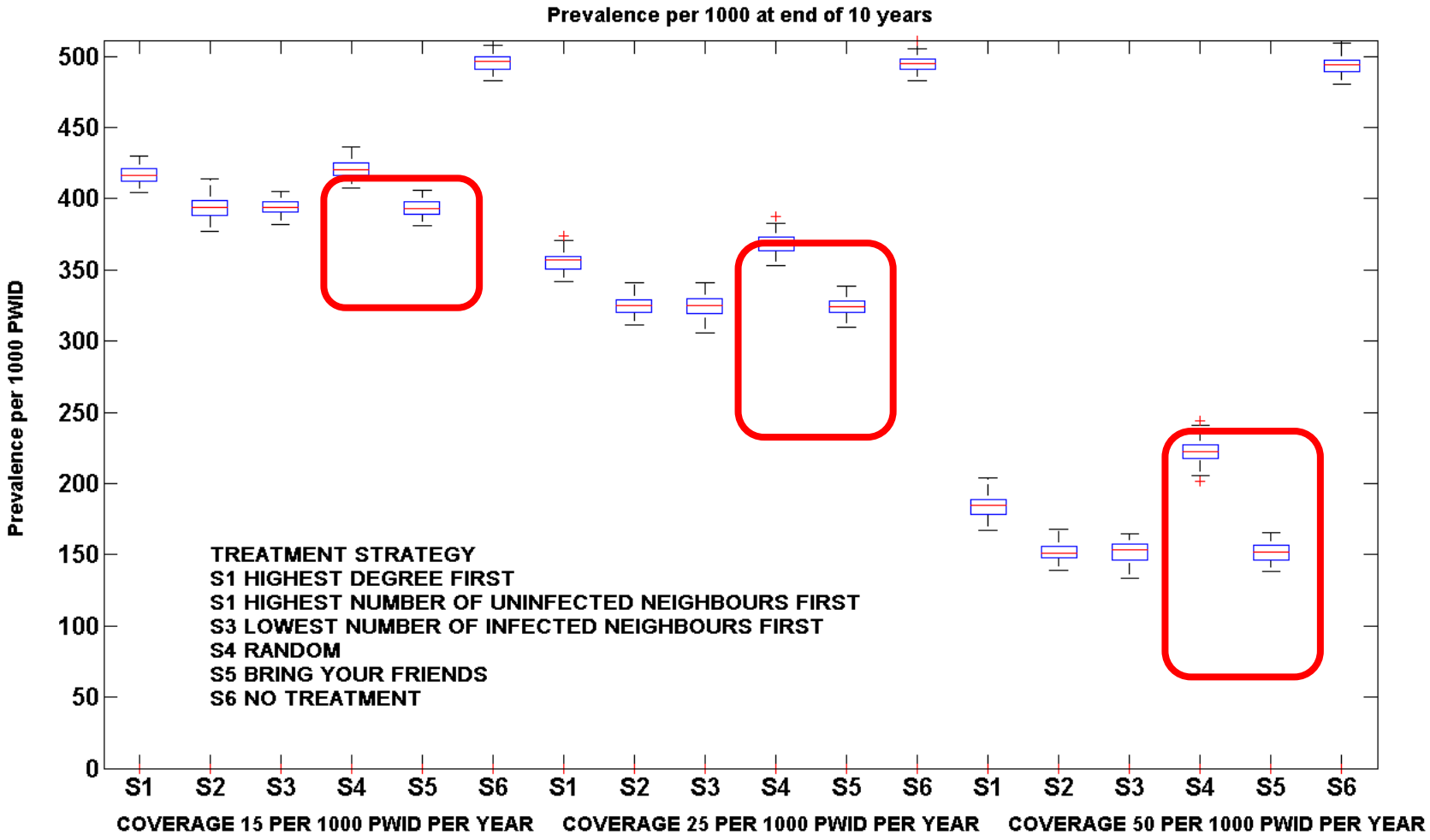
Rolls et al Theoretical Biology (2012)

Different treatment strategies – including treat your friends strategy



Treating injecting networks

Modelling the impact of treatment on prevalence at 10 years; 80% SVR



Hellard et al Hepatology 2014

The TAP Study
(Treatment and Prevention)

A community based study measuring the impact of hepatitis C treatment on disease transmission using a networks based approach.

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TAP Study

Primary Aims

1. To measure the efficacy and feasibility of community-based treatment of PWID using SOF+LDP
2. To measure the effectiveness of treating PWID on rates of HCV primary infection and reinfection
3. To measure the effectiveness of using the “Bring Your Friends” strategy to treat PWID and their injecting networks on rates of HCV primary infection (transmission) and reinfection

SuperMIX cohort

- Over 700 PWID – nearly 300 chronic HCV
- Research team includes field based workers
- Mobile vans
- Participants engaged every 3 - 12 months (dynamic)

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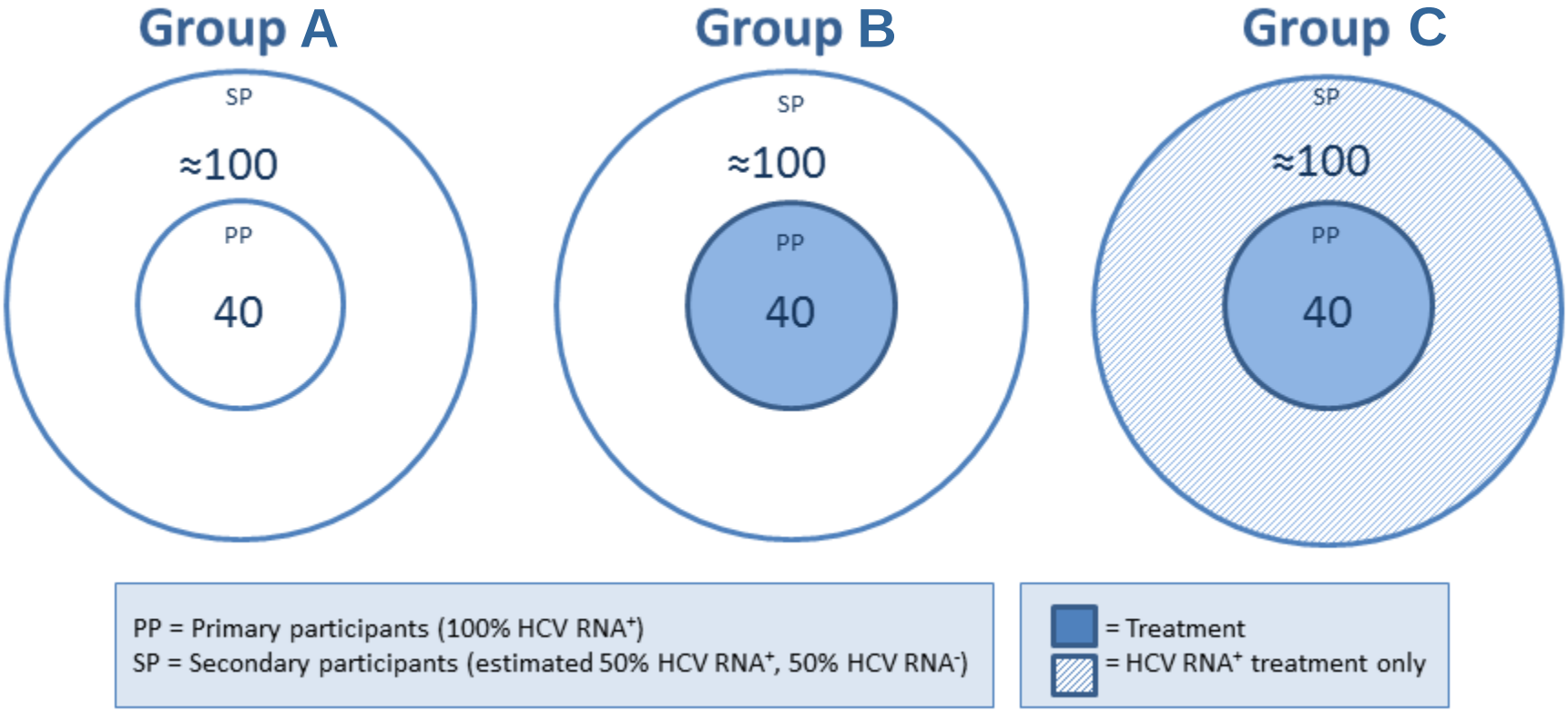
TAP study design (N=420)

- *Primary participants*: n = 120
  - SuperMIX participants with evidence of HCV
    - HCV RNA+ at screen
- *Secondary participants*: n = 300
  - *Primary participants* will be asked to invite their current injecting partners
  - Data from the Networks study suggests that:
    - PWID have an average of 2.5 current injecting partners.
    - 50% of secondary participants will have HCV infection (150/300).



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Statistical analysis and power

- Approximately 130 participants allocated to receive HCV treatment - 40 primary participants from Group 2 and 40 primary participants and 50 secondary participants from Group 3.

- Assuming that 75% (100 of the 130) of participants undertake HCV treatment the 95% confidence interval for an SVR of 90% is 82.38 to 95.10.

Statistical analysis

- Based on Networks and SuperMiX – expected rate of primary infection of 12.8 per 100 person years and a rate of re-infection of 28.8 per 100 person years - or a minimum of 4.27 primary infections (95% CI 2.57, 6.67) per group and a minimum of 12.96 incident reinfection events per group.

- Powered to detect a minimal reduction in reinfection incidence of
  - 5.55 reinfections per 100 person years Group C compared with Group B
  - 10 reinfections per 100 p-y in Group C compared with Group A.
  - 10.5 reinfections per 100 p-y in Group B compared with Group A

Other research objectives

- Dynamic transmission modelling, network modelling
- Health service utilisation and cost-effectiveness
- Qualitative research
- Behaviour change in association with treatment
- HCV sequencing, linked transmission and viral evolution

Progress to date

- Screened - 103 60 primaries, 43 secondaries
- 82 enrolled; 21 non eligible
- Randomized – 54
- Two third on treatment

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Anticipated challenges for the TAP Study

- Recruitment – people's willingness to undergo treatment?
- Willingness of participants injecting partners to participate and undergo treatment?
- Deferred treatment group – will this be acceptable to participants?
- Changes in injecting behaviour and risk in the SuperMIX cohort
- Frequency of follow up – will it be achievable?
- Treatment compliance?

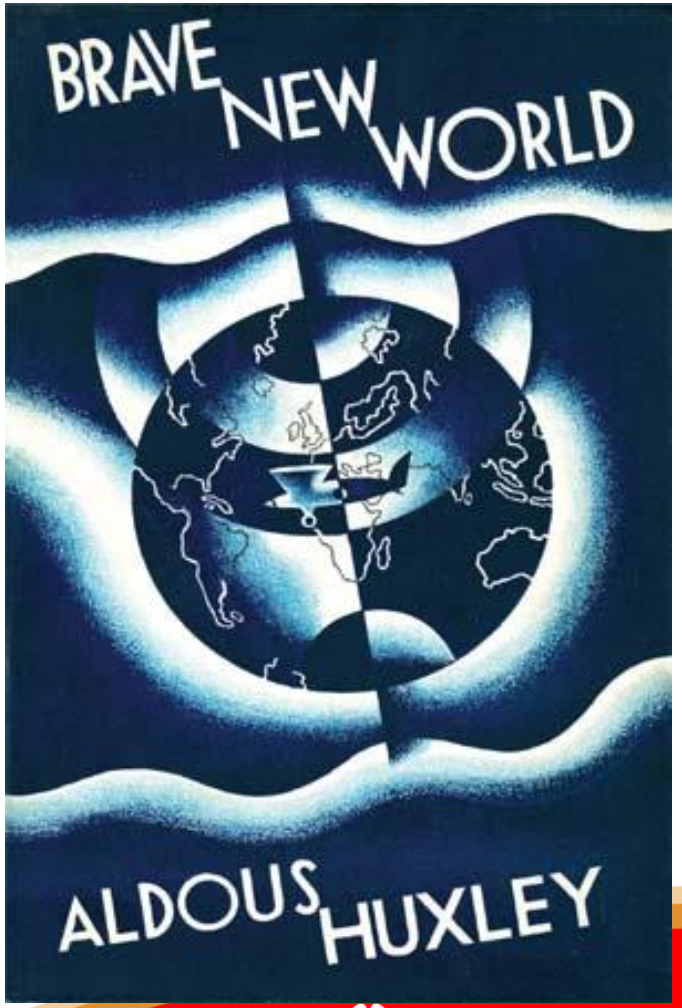
Actual challenges for the TAP Study

- Most participants who are eligible are interested and willing to have treatment
- Changes in injecting behaviour and risk in the SuperMIX cohort - a number of HCV RNA positive SuperMIX participants have stopped injecting or no longer injecting with others
- To date – no major issue with the deferred treatment group – mindful this may change with PBS listing
- Frequency of follow up – still yet to reach this stage
- Treatment compliance – important to be clear about the medication and that not likely to interact with drugs or OST

Challenges beyond the TAP Study if we are to successfully eliminate hepatitis C

If TAP works – we need to ensure:

- the outcomes translated into a broader response – costs v cost effectiveness
- People have real choice and are not be "rail-roaded" into treatment
- Funds are not diverted from effective harm reduction programs



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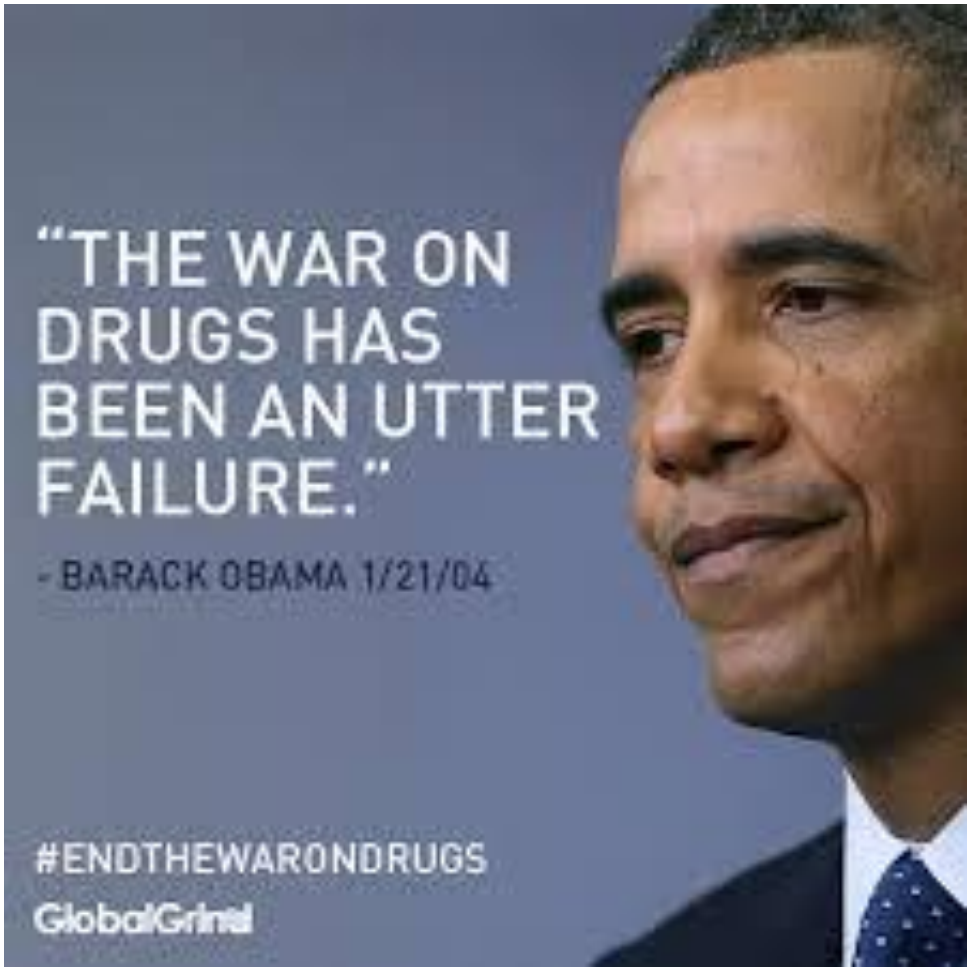
Stigma and discrimination



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Treatment and prevention - and hepatitis C elimination

- HCV elimination as a public health problem is possible but we need to treat people who drive transmission as well as those with chronic infection
- In most developed & some developing countries this is PWID
- The advent of DAAs offers us the opportunity to dramatically scale up treatment
- Need to identify the best and most cost effective models of care to do this
- At the same time we must not forget the importance of harm reduction – OST and NSP
- Also – a vaccine would be very handy!

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The Networks Study and MIX Study participants

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- **Joe Doyle, Rachel Sacks Davis, Peter Higgs**,, **Paul Dietze**, Mark Stoove, Campbell Aitken, Emma McBryde, Tim Spelman, Damien McCarthy
- Sally von Bibra, Leona Burke, Josie Lupi, Shelley Cogger, Emma Woods, Arthur Truong, Deane Quelch, Dan O'Brien
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