The contribution of injecting drug use as a risk factor for hepatitis C virus transmission globally, regionally, and at country level: a modelling study

Adam Trickey[1,2], Hannah Fraser[1], Aaron G Lim[1], Amy Peacock[3], Samantha Colledge[3], Josephine Walker[1], Janni Leung[3,4], Jason Grebely[3], Sarah Larney[3], Natasha K Martin[5,1], Matthew Hickman[1,2], Louisa Degenhardt[3], Margaret T May[1,2], Peter Vickerman[1,2]

[1] Population Health Sciences, University of Bristol, UK
[2] NIHR Health Protection Research Unit in Evaluation of Interventions, UK
[3] UNSW Sydney, Australia
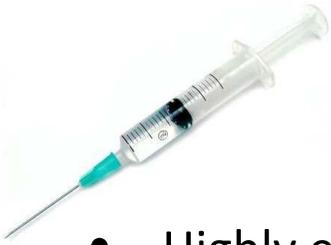[4] Centre for Youth Substance Abuse Research, University of Queensland, Australia
[5] Division of Infectious Diseases and Global Public Health, University of California San Diego, USA

LISBON ADDICTIONS 2019

University of BRISTOL

Hepatitis C virus epidemic

- Highly effective direct acting antivirals (DAAs) have been developed as treatment for hepatitis C virus (HCV) infection
- An estimated 71 million people are infected with HCV globally[1]
- The WHO has set targets to eliminate HCV by 2030
  - Includes reducing incidence by 80% from 2015 levels

- HCV is highly prevalent (>30%) among people who inject drugs (PWID)[2]
- Proportion of adults that are PWID in most countries is low (<0.5%)[2]
- Generally assumed role of IDU to HCV transmission important mostly in high-income countries[3]
- In low- and middle-income countries it is thought most HCV transmission is due to other routes[3]
  - Eg. Unsterile medical injections and unscreened blood transfusions

1: Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Blach, 2017
2: Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. Degenhardt, 2017
3: Epidemiology of hepatitis C virus infection. Alter, 2007

Aim

- We aimed to estimate the percentage of infections prevented if HCV transmission due to IDU were removed from 2018-2030:
    - Country-level
    - Regionally
    - Globally

Methods

- A dynamic, deterministic HCV transmission model simulated country-level HCV epidemics among:
  - PWID
  - the general population

- Accounted for:
  - population growth
  - ageing
  - demographics
  - disease progression
  - injecting drug use
  - vertical transmission
  - historical treatment numbers

Model parameterization

- Demographic information: UN datasets
- Key parameters and bounds from various systematic reviews:
  - HCV prevalence among general population[1]
  - HCV prevalence among PWID[2]
  - Proportion of adults that are PWID[2]
- **Countries included if data were available on all three key parameters**
- Model accounted for uncertainty in parameters

1: Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Blach, 2017
2: Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. Degenhardt, 2017

Key model assumptions

- Decreasing HCV epidemics among general population (around 1%) per year[1]
- (due to evidence from countries with 2 surveys)
- Stable HCV epidemics among PWID[2]
- Stable proportion of adults that are PWID[2]
  - (except in Eastern Europe and Sub-Saharan Africa: increasing)

- These assumptions were investigated in many sensitivity analyses

1: Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Blach, 2017
2: Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. Degenhardt, 2017

Analyses

- Models for each country projected the HCV epidemic to 2030 (baseline projections)
  - 1000 runs for each country

- The population attributable fraction of HCV transmission (incidence) due to IDU in each country, regionally, and globally, was estimated – the **tPAF**
  - This is the percentage of transmission that would be avoided if the extra transmission due to IDU removed

- To do this, the baseline model fits for each country were re-run with the transmission risk due to IDU set to zero from 2018 onwards
  - Compared vs baseline projections

- Generalised linear regression models used to determine what country-level factors are associated with the tPAF of HCV due to IDU

Contribution of IDU to HCV 2018-2030

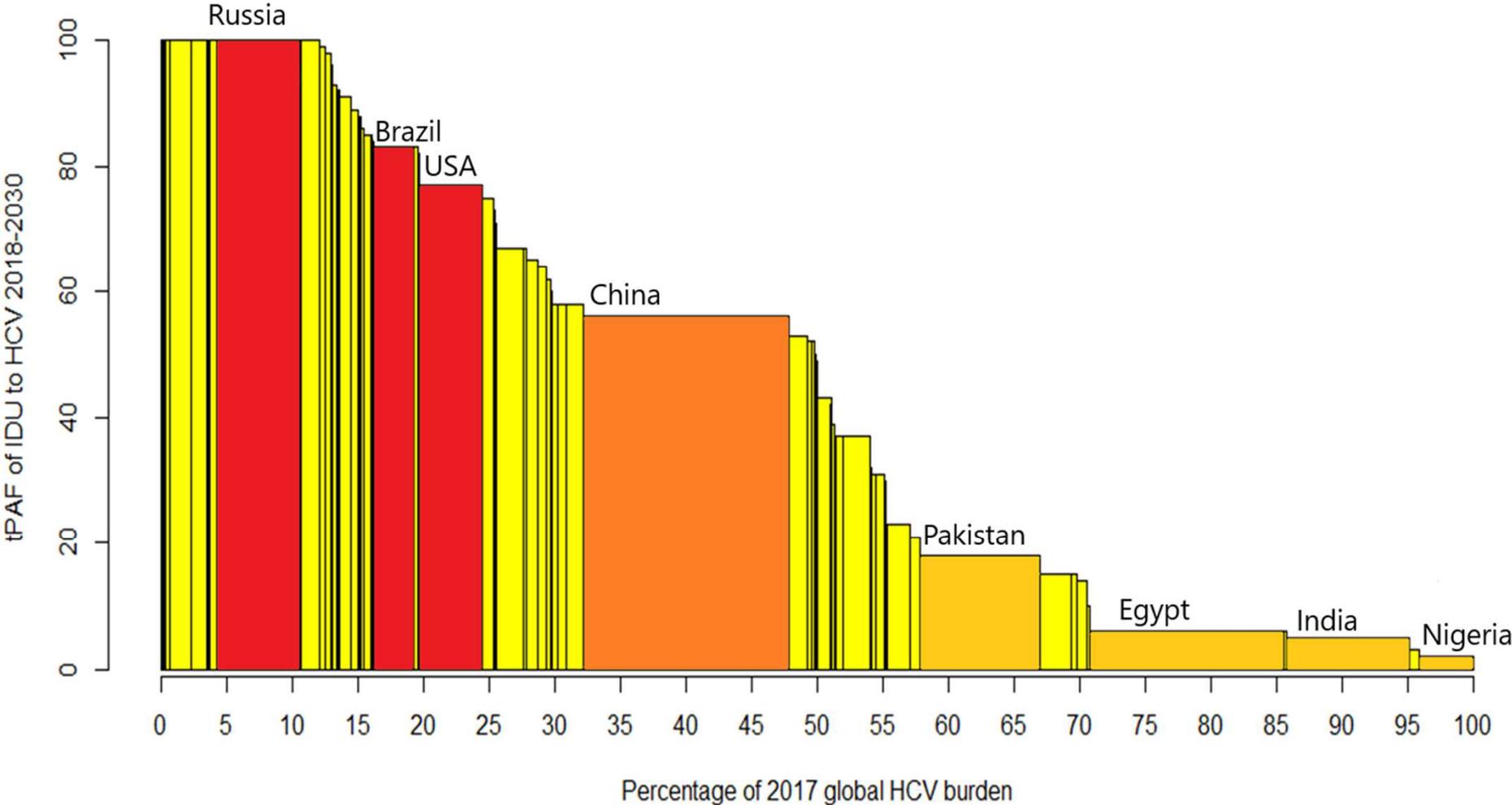- Successfully calibrated for all 88 countries with data (85% of world's population)
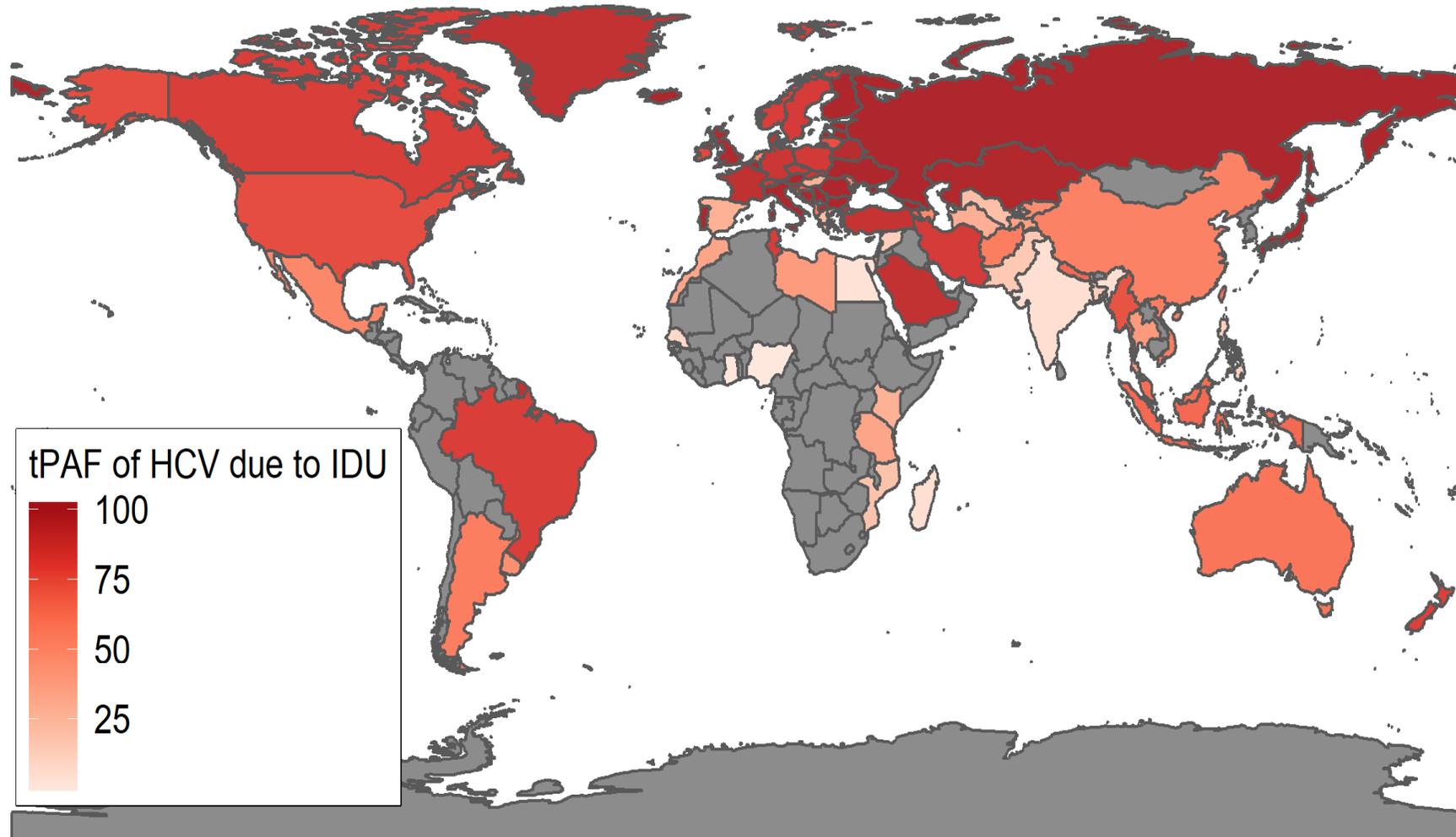
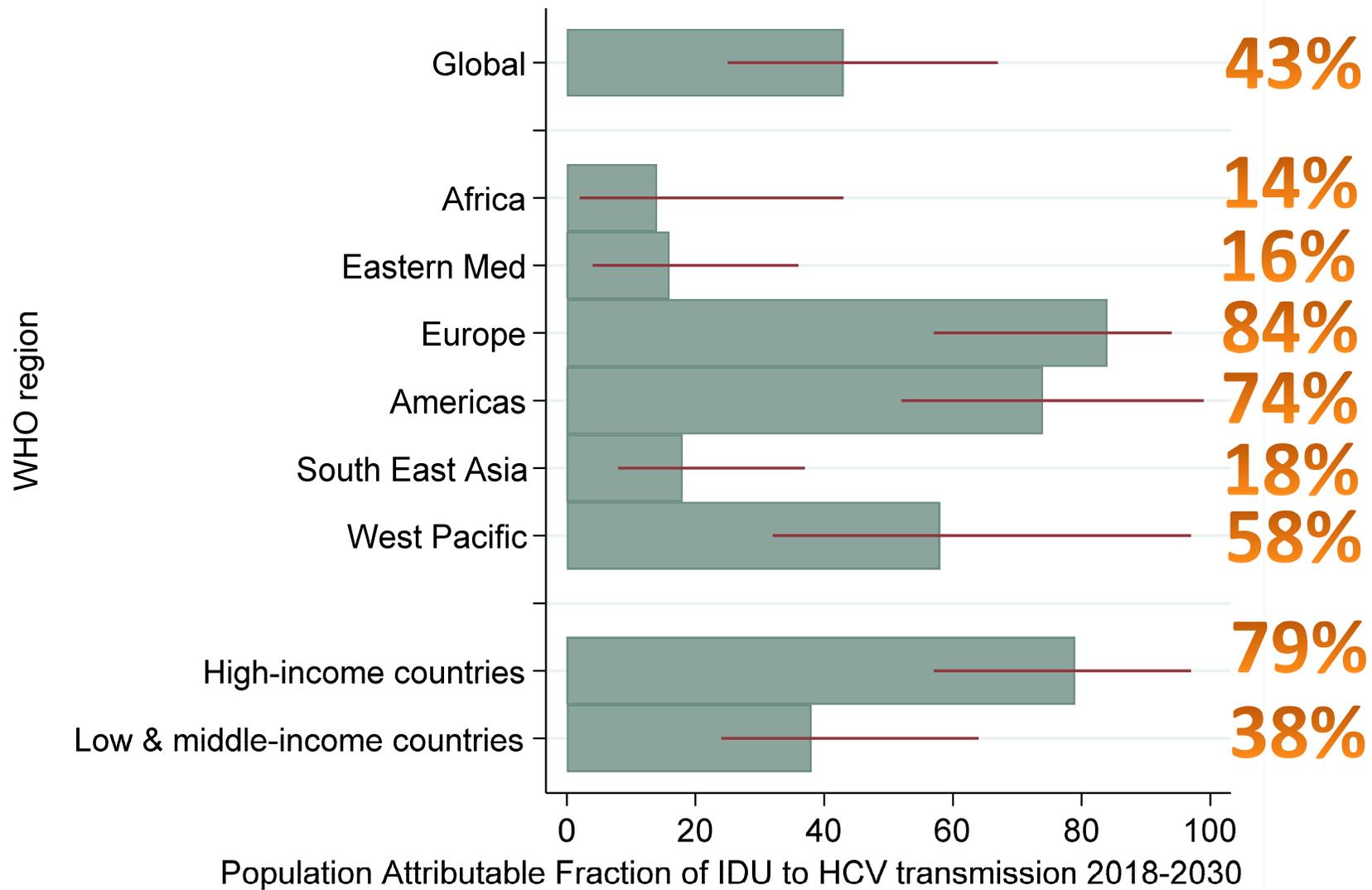*Countries in grey were not included in the model due to missing data

# Each country's percentage of global HCV burden (2017) vs Contribution of IDU to HCV transmission 2018-2030 (tPAF)

Regional contribution of IDU to HCV 2018-2030

*Red lines are 95% credibility intervals

Association with current percentage of infections among PWID

R squared = 0.87

tPAF of HCV due to injecting risks 2018-2030

Percentage of prevalent infections among PWID in 2017
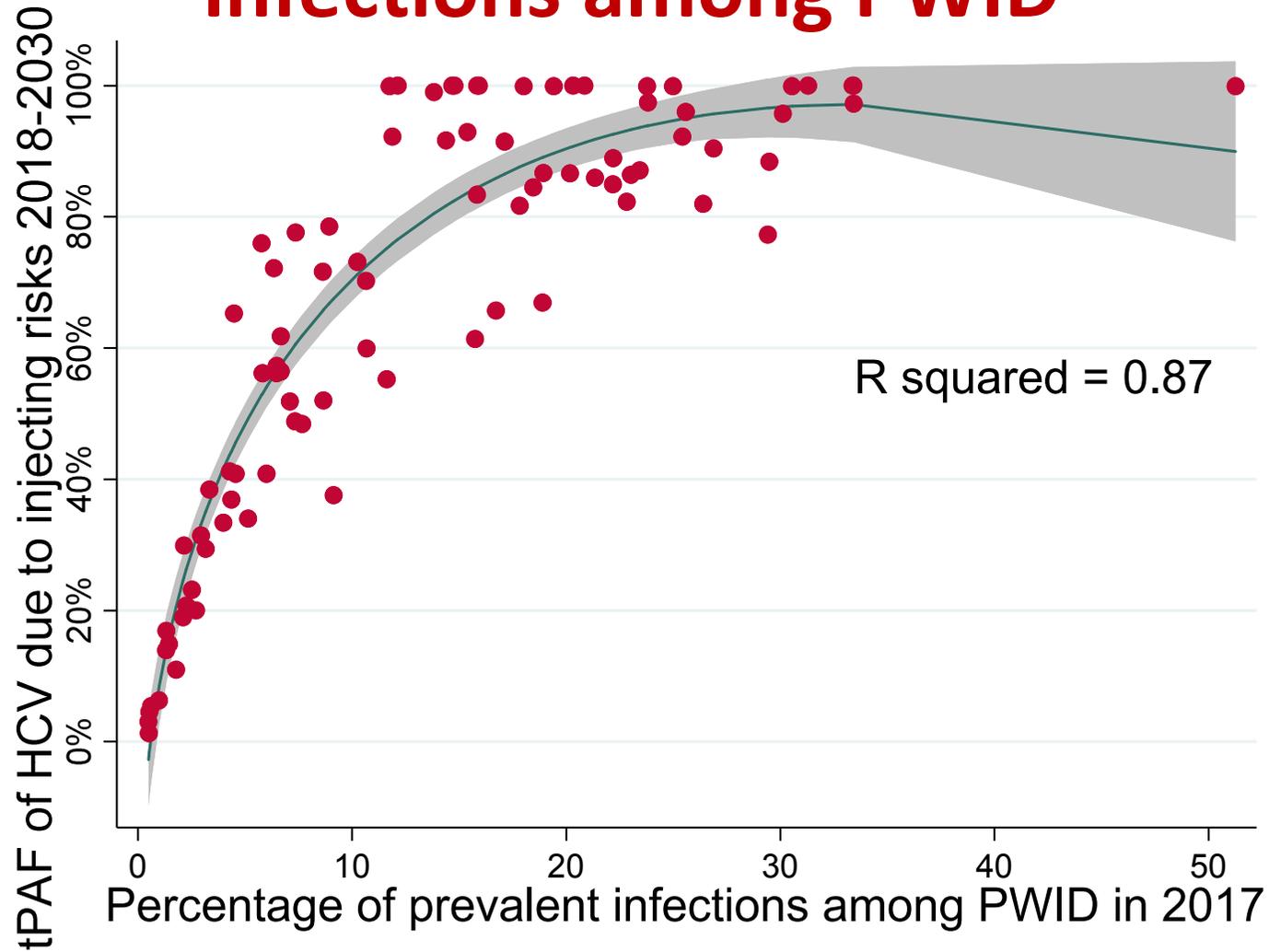
No other multivariable associations found with the tPAF

Sensitivity analyses

- Various sensitivity analyses tested assumptions

- Most had very little effect on the tPAF

- Largest changes occurred when:
  – Assuming a stable general population HCV prevalence over time (33% tPAF)
  – Varying epidemic trajectories by region (30% tPAF)

Limitations

Caution: Numbers

- Taking data from disparate sources can create imprecise results but overall trends should be robust
- **Data!**
  - Data unavailable for many countries (particularly Africa)
  - Not necessarily high quality data
- Migration not included – lack of data
- Assumptions about directions of epidemics:
  - Only 3 countries had 2 robust, comparable general population estimates
  - Investigated in sensitivity analyses

Key results and conclusions

- **43% (25%-67%)** of incident HCV infections would be prevented from 2018-2030, globally, from removing all extra transmission due to IDU
- Varies regionally
- 79% in high-income countries
- 38% in low- and middle-income countries

- Unsafe injecting practices among PWID contribute substantially to incident infections globally
- Any intervention that can reduce transmission among PWID will have a pronounced effect on country-level incidence
  - OST, NSP, treatment as prevention

- Published in Lancet Gastroenterology and Hepatology:

- I have no conflicts of interest to disclose.

NHS

National Institute for Health Research