# Modelling Hepatitis C virus infection and treatment impact through serological surveillance data

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## 1 A Global Health Challenge

- Hepatitis C is a blood-borne virus that can cause life-threatening liver damage over time.
- In the UK, the Hepatitis C virus (HCV) is primarily transmitted through the sharing of drug-injection equipment, making people who inject drugs (PWID) a key at-risk group.
- From 2015 to 2022, the number of people living with chronic HCV infection in England has fallen dramatically in the general adult population by 51.6% and is now estimated at 62,600 [1].

## 2 New Treatment, New Hope

- The advent of effective new treatments for HCV in 2015 has transformed the landscape for HCV control.
- This has enabled the formulation of an elimination strategy led by the World Health Organisation (WHO) based on a reduction in HCV incidence.

Incidence is the rate at which new cases of a disease occur in a specified population during a defined time period - it measures the risk of contracting the disease.

Monitoring incidence directly is challenging – cross-sectional biobehavioural serosurveys, which capture information on infection status and duration of exposure, provide a means to estimate incidence indirectly and can be conducted serially to track changes over time.

## 3 Evidencing Elimination

Needle Exchange Points

- The unlinked anonymous (UAM) survey annually monitors blood-borne viruses among PWID in England, Wales and Northern Ireland.
- PWID are recruited at needle exchange points to participate in the UAM survey – this involves taking a dried blood-spot (DBS) sample and completing a biobehavioural questionnaire.
- DBS samples are tested for antibody (Ab) and ribonucleic acid (RNA) status – this can be leveraged to differentiate between current and past HCV infections.
- This information facilitates the development of a multi-state model characterising HCV transmission dynamics.

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Primary incidence rates among recent initiates rose between 2011 and 2022, from 0.21 (95% CrI: 0.20–0.22) to 0.32 infections per person-year (95% CrI: 0.30–0.33), coinciding with increased needle-sharing behaviour - conversely, rates among long-term injectors declined.

Multi-state models serve as robust tools to monitor progress toward WHO elimination goals and inform public health strategies.

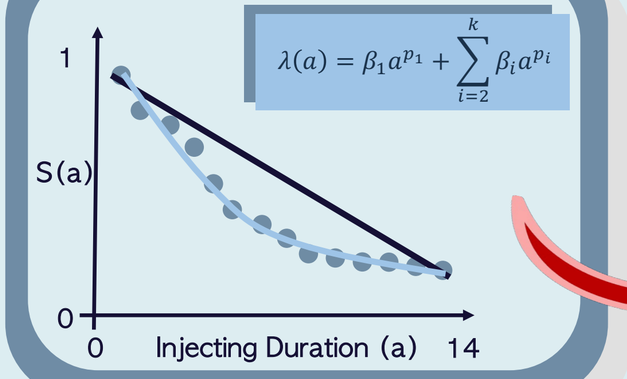
Spontaneous clearance rates are higher than widely reported - consistent with studies including RNA-negative individuals.

Key Findings

HCV Working Groups

Aim 1: Flexibly model transition parameters

- Transition parameters are modelled over time at risk (a) and calendar time (t) – information obtained from the biobehavioural questionnaire.
- Fractional polynomials [2] are chosen from a suite of flexible model parametrisations [3] to model the transition parameters.

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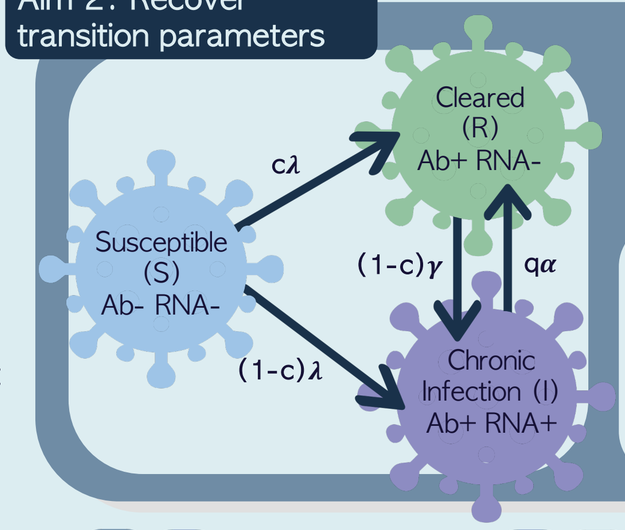
Biostatistician (me)

Aim 2: Recover transition parameters




The multi-state model is governed by a system of ordinary differential equations.

$$\frac{dS}{dt} = -\lambda S$$

$$\frac{dI}{dt} = (1-c)(\lambda S + \gamma R) - q\alpha I$$

$$\frac{dR}{dt} = c\lambda S + q\alpha I - (1-c)\gamma R$$

$\lambda$: primary incidence rate
$\gamma$: reinfection rate
$c$: spontaneous clearance rate
$\alpha$: treatment uptake rate
$q$: sustained virologic response rate

- The multi-state model is implemented within a Bayesian framework – integrating external information to inform our prior beliefs about the unknown parameters.

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[1] Hepatitis C in England 2023. https://www.gov.uk/government/publications/hepatitis-c-in-the-uk/hepatitis-c-in-england-2023.
[2] Royston, P. and Altman, D.G., 1994. Regression using fractional polynomials of continuous covariates: parsimonious parametric modelling. *Journal of the Royal Statistical Society Series C: Applied Statistics*, *43*(3), pp.429-453.
[3] Egan, C., Harris, R.J., Mitchell, H.D., Desai, M., Mandal, S. and De Angelis, D., 2024. Analysing HCV incidence trends in people who inject drugs using serial behavioural and seroprevalence data: A modelling study. *International Journal of Drug Policy*, p.104469.

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