# Validation of model

With a limited number of fitting points each with wide confidence intervals, there are numerous HCV epidemic scenarios that pass through them. 250 different scenarios were considered and the scenario below was chosen giving good fits to the available data, with a moderate growth rate for the PWID population.
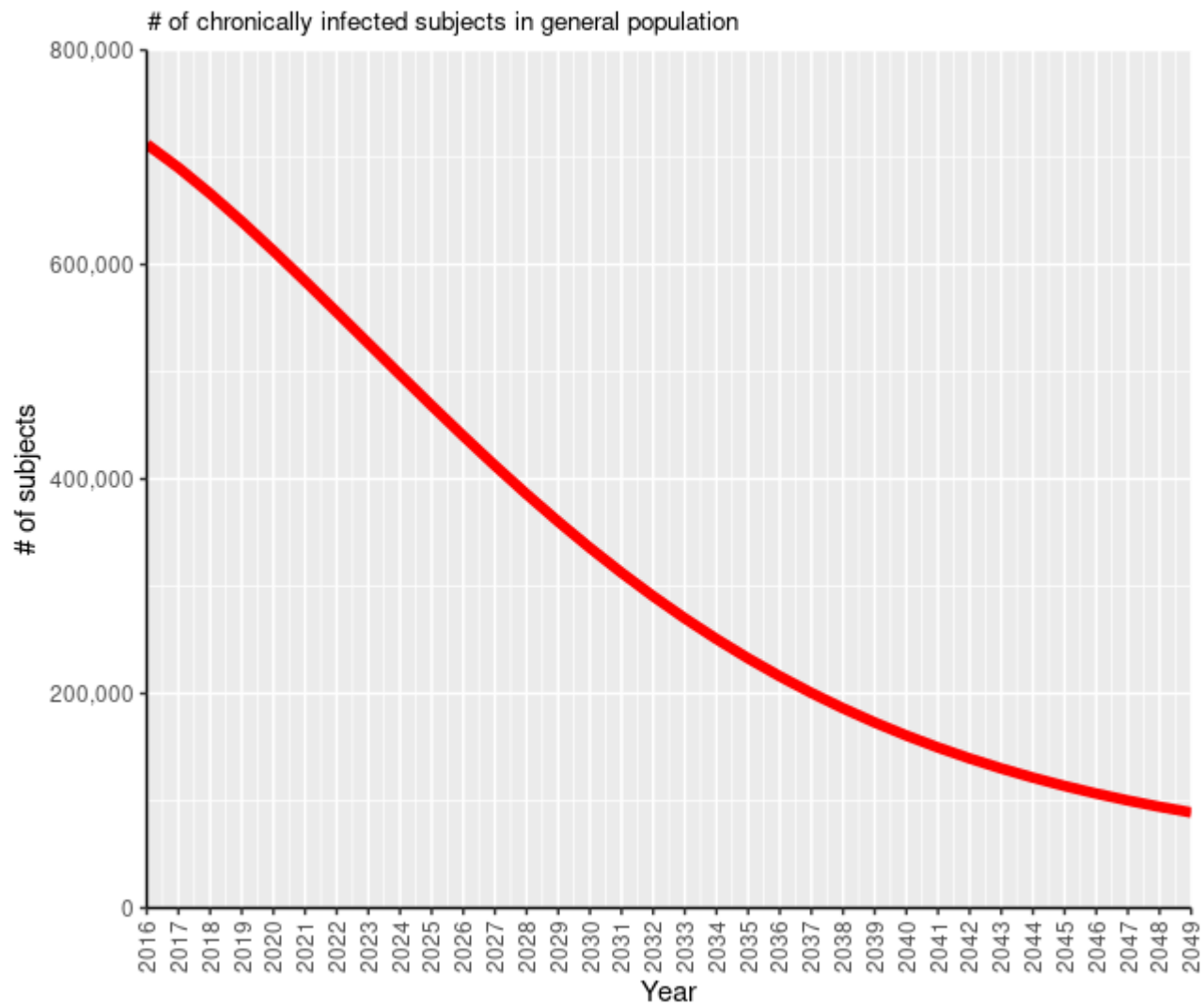
Fitting points

In 2016 there were 3.5 million subjects with HCV, 60% were in PWID and 20% in the general population. See Figures 1 and 2 confirming the actual numbers.

Figure 1   HCV prevalence against year for PWID population
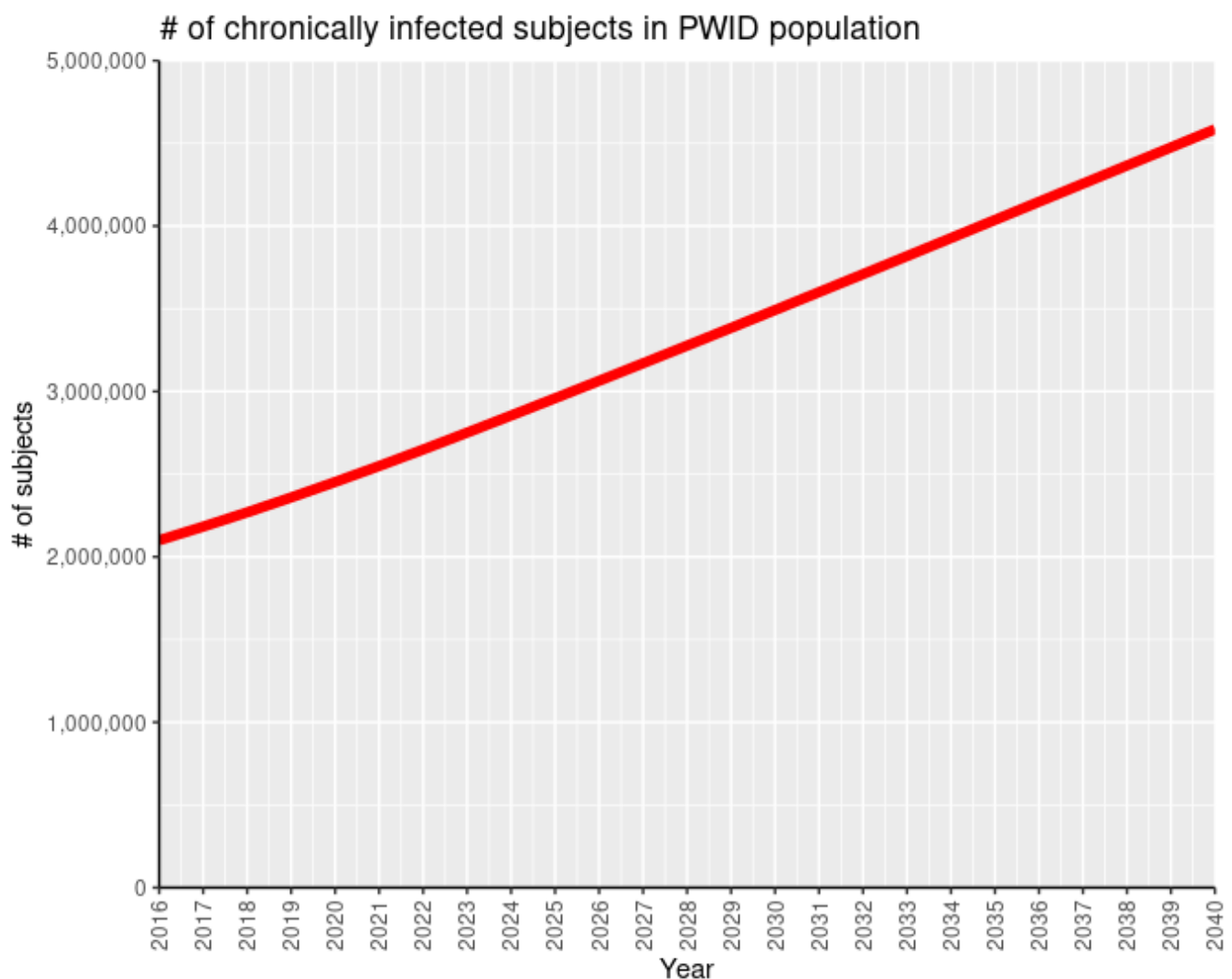
Note that the growth assumes no treatment and a growing PWID population (see Figure 3)
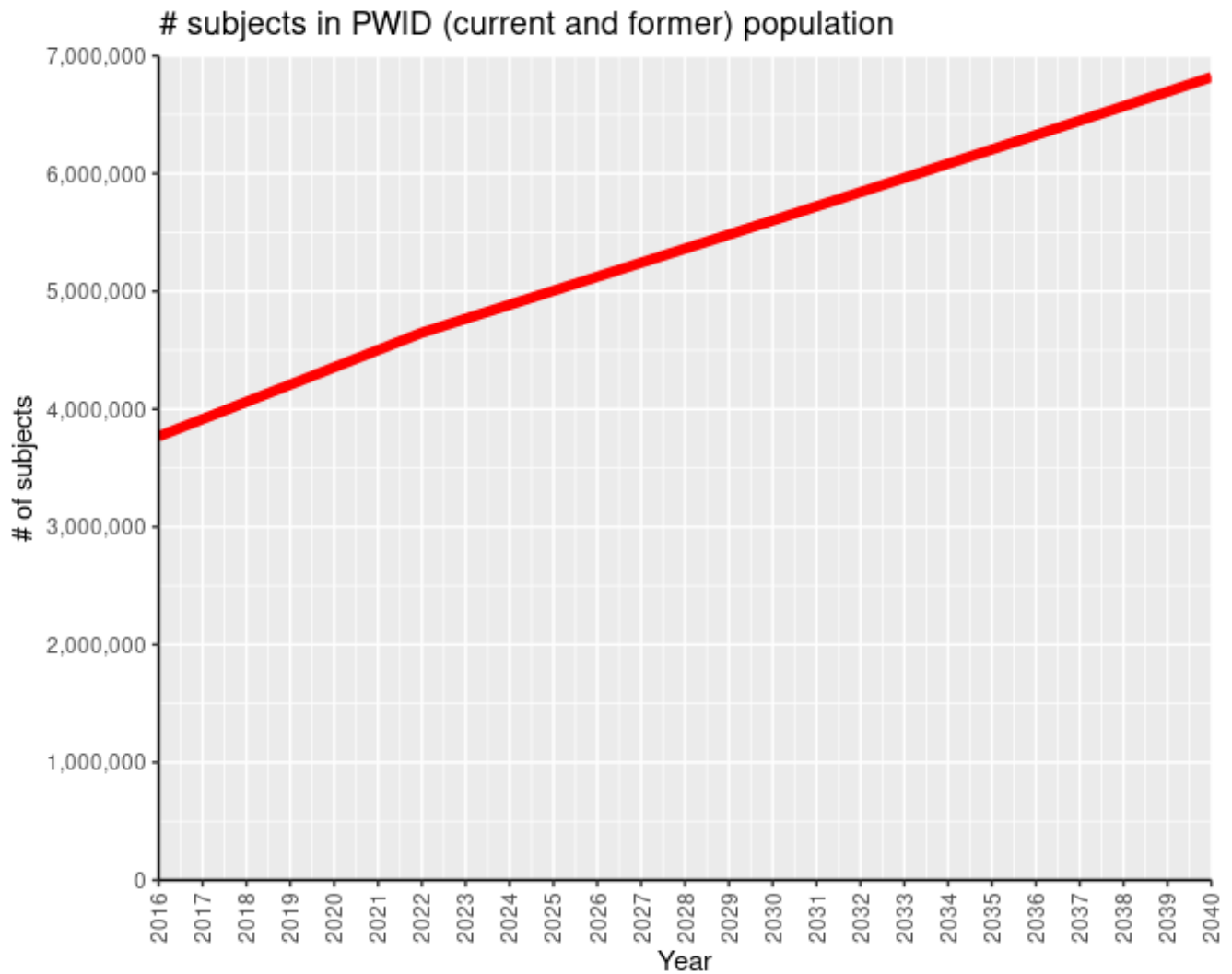
Figure 2   HCV prevalence against year for general population

# of chronically infected subjects in general population

Population growth

It is unlikely that the PWID population will remain constant. The model assumes an approximate 75% increase in 25 years.
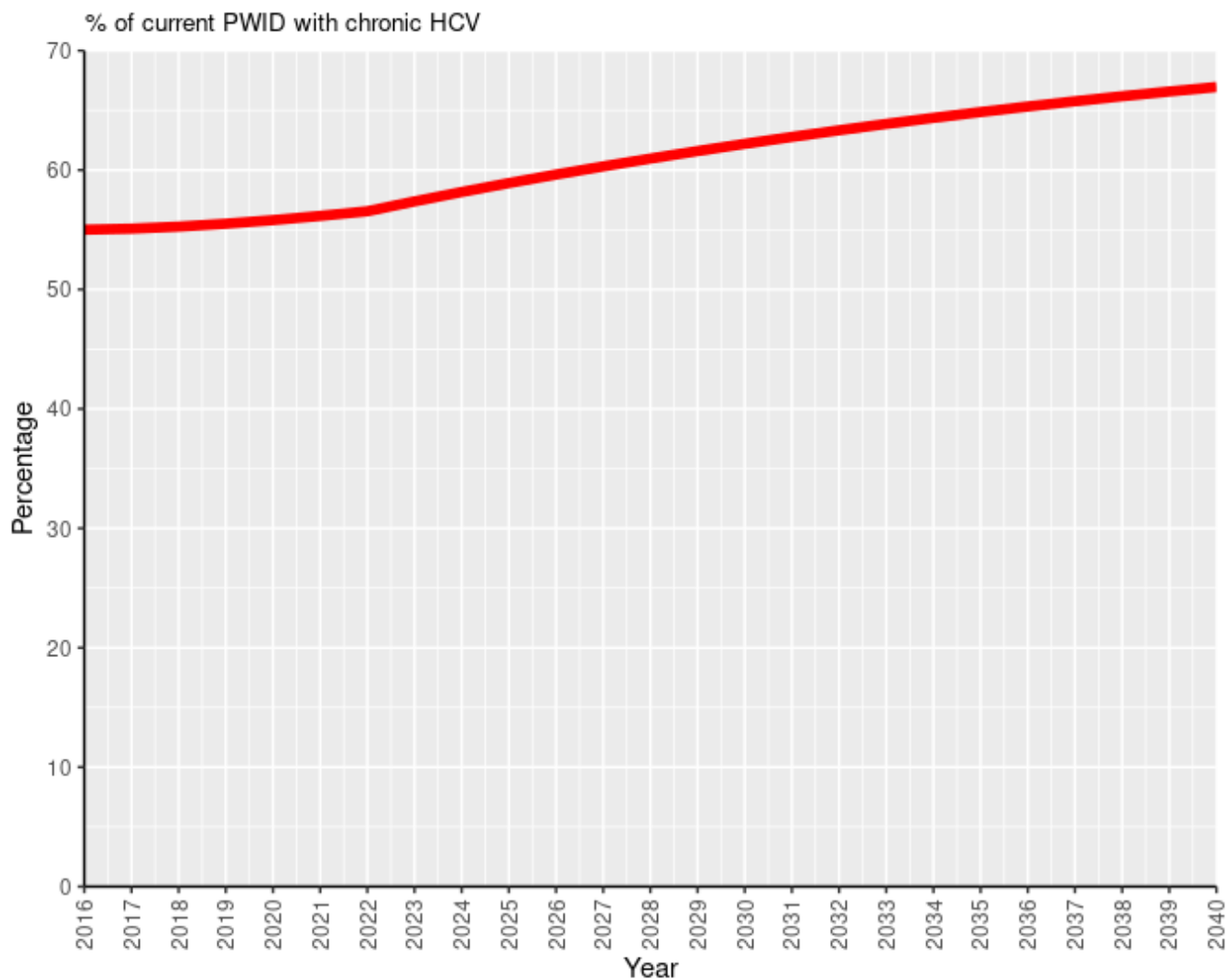
Figure 3   PWID population (includes all HCV+ and susceptible subjects)
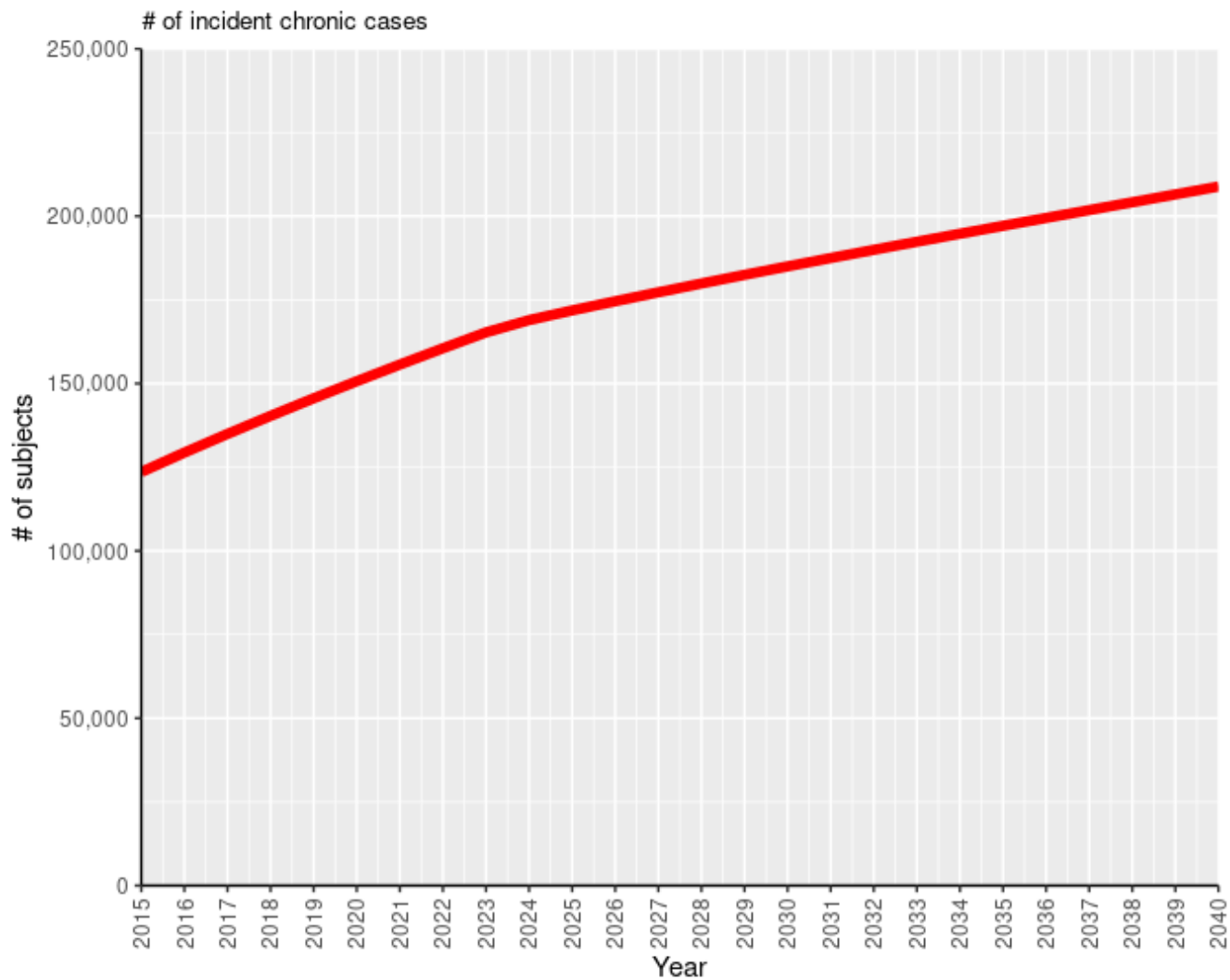
Incidence

In 2016 a fitting point of 55% of the current PWID population was used, confirmed in Figure 4.

Figure 4   Percentage of current PWID with chronic HCV from fitting point

The absolute incidence is difficult to measure via survey and many of the estimates are obtained form modeling. This model also includes a period prior to 2016 of increased incidence of HCV infection within the US. Figure 5 shows the absolute HCV incidence predictions from 2016 to 2040, assuming no changes to the baseline treatment levels (which are implicitly models via parameter and model fitting).

Figure 5   Number of incidents cases among PWID population

The 2015 figure is close to the upper bound of the estimate from Heffernan (the relevant estimate is the gray line with the gray shaded 95% confidence intervals. Heffernan does not assume an increase in HCV incidence between 2010 and 2018 and assumes a constant PWID population.

Note the incidence of HCV in the general population is very low and will have a negligible effect.

Heffernan, A., Cooke, G. S., Nayagam, S., Thursz, M. & Hallett, T. B. Scaling up prevention and treatment towards the elimination of hepatitis C: a global mathematical model. *The Lancet* **393**, 1319–1329 (2019).
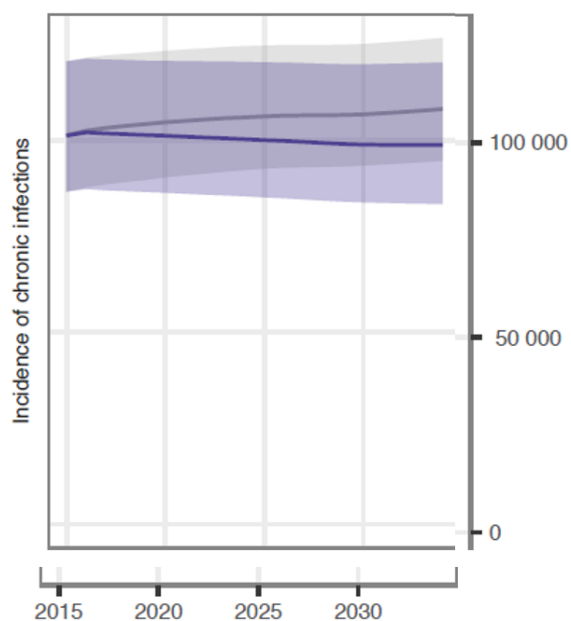
Mortality

Stages DC,HCC and post Liver transplant are assumed to incur additional liver related mortality above the baseline population mortality rates.

Figure 6 Liver related deaths from general and PWID population

Number of liver related deaths (DCC,HCC,LT)
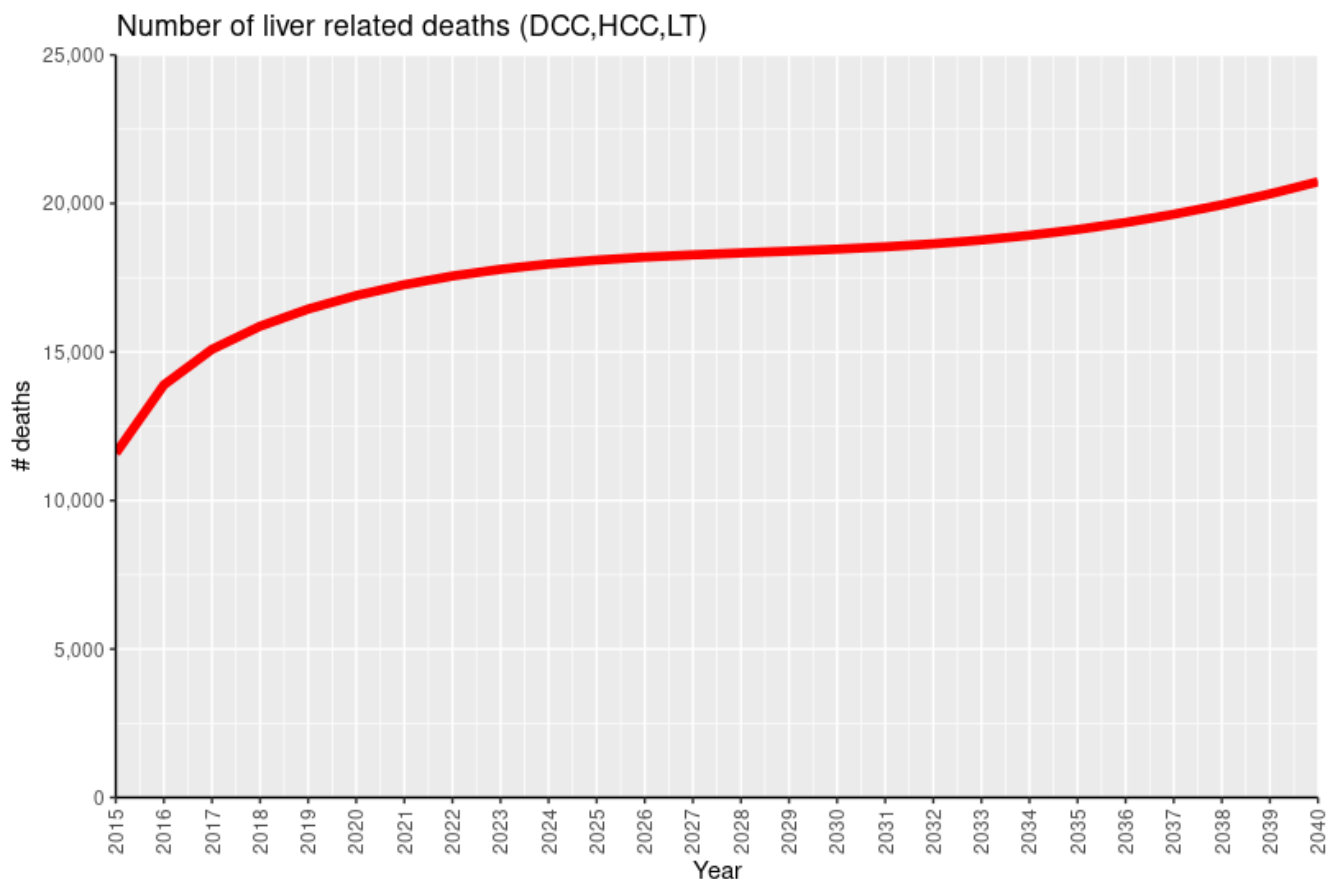
The estimates from Heffernan are higher (gray line) than those shown above. The reason for this is that Heffernan included the F4 stage with a yearly probability of death of 0.03 as a liver related death.

Repeating Figure 6, but also including deaths from F4 as incurring a higher liver related mortality, then give a similar number of deaths.

Heffernan includes the whole population – in the scenario in this document 20% of the HCV+ population are not modeled. Also as previously mentioned an incidence trend increase and growing PWID population are included in this model.
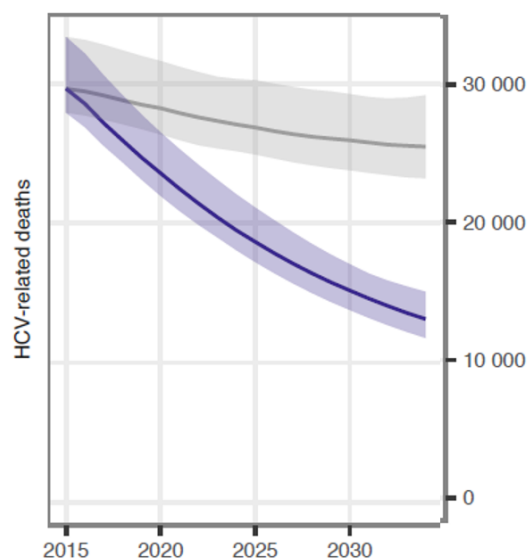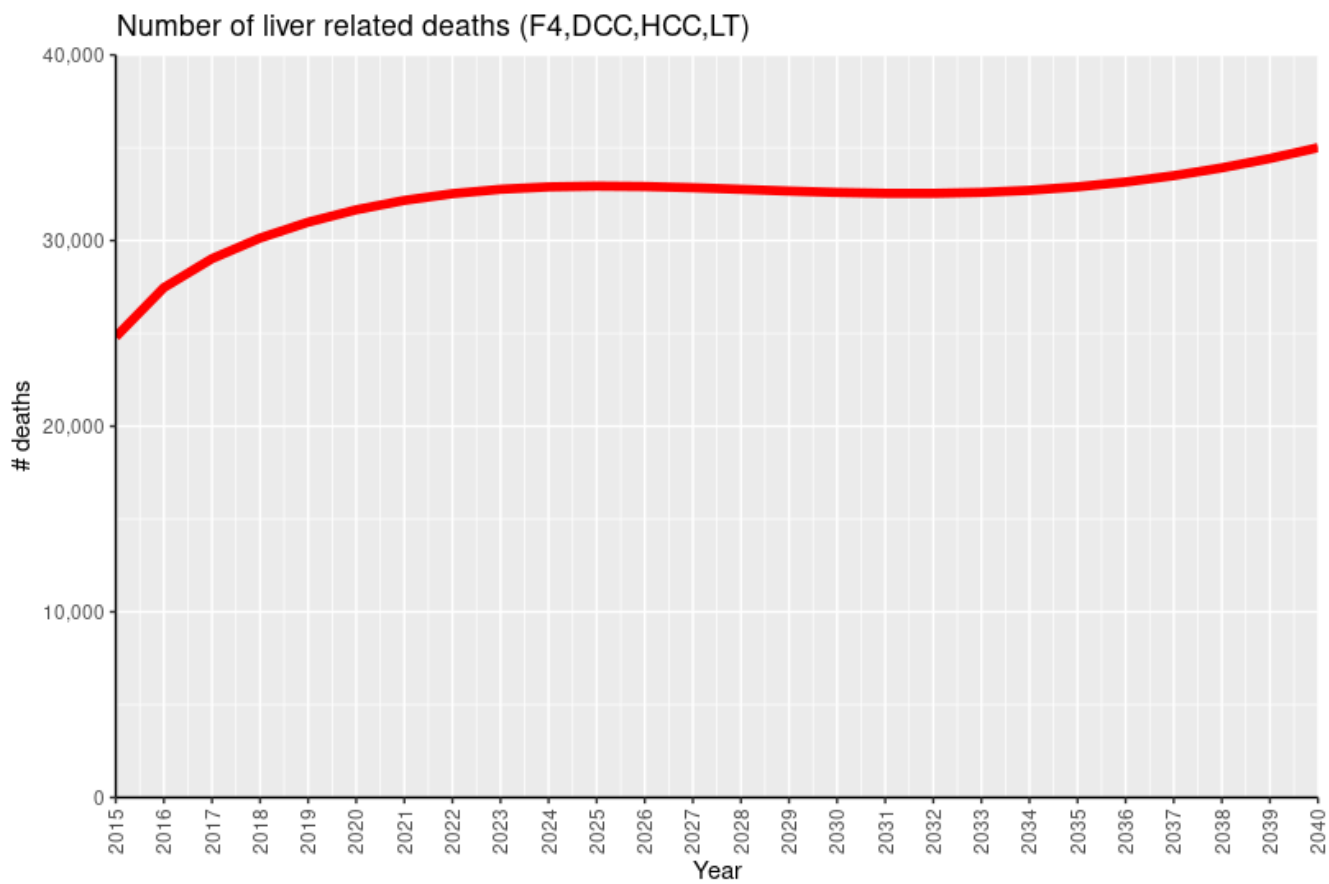
Figure 7   Liver related mortality including the stage **F4**

Number of liver related deaths (F4,DCC,HCC,LT)

Non-liver related mortality estimates

The base line mortality age stratified rates from **Xu** are shown here:

Table 1   Base line mortality rates in the US (2018)

Parameter	Value	Units
20 -24 year old	0.702	per 1000 years
25 -29 year old	1.288	per 1000 years
30 -34 year old	1.288	per 1000 years
35 -44 year old	1.947	per 1000 years
45 -54 year old	3.959	per 1000 years
55 -64 year old	8.8867	per 1000 years
65 -74 year old	17.833	per 1000 years
75 -84 year old	43.861	per 1000 years
85+ year old	134.4507	per 1000 years

Alvai estimates on average a 5 year reduction in life expectancy for populations with a non-drug related HCV diagnosis. Using **PHE** mortality tools a 5 year reduction in life expectancy from the age of 20 on-wards is equivalent to a 30% increase in the mortality rates in Table 1. Consequently for the general population and former PWID population the background mortality rates were taken as 1.3 * the mortality rates in Table 1.

The mortality rates in the current PWID were estimated using the former to current multipliers taken from Scott.

The age related life expectancy for the three groups, base, general population/former PWID and current PWID were calculated using the PHE methodology and are shown in Figure 8.

Figure 8   Age related life expectancy for HCV model
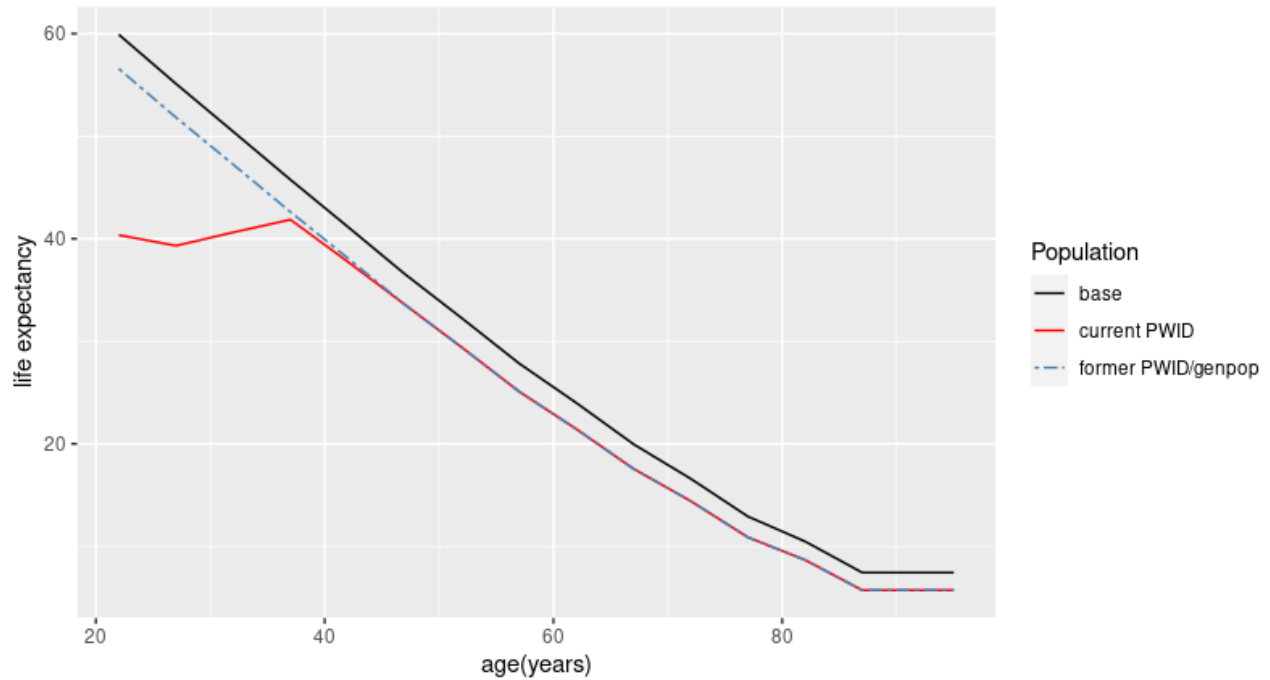
Xu: Mortality in the United States 2018. NCHS data brief NO 355, January 2020
Alvai: Lower Life expectancy among people with HCV. Journal of Viral Hepatitis,
2014, 21, e10-e18
PHE: https://CRAN.R-project.org/package=PHEindicatormethods June 2020