

Cost-effectiveness of treatment for Hepatitis C Virus

Infectious disease modelling for HTA in R

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Background

Hepatitis C virus (HCV) is a highly infectious blood-borne virus. It is widespread in people who inject drugs (PWID), and in some settings is also prevalent in the general population due to contact with blood products through medical, dental or cosmetic treatments.

In 2016, WHO set a target of eliminating HCV by 2030.

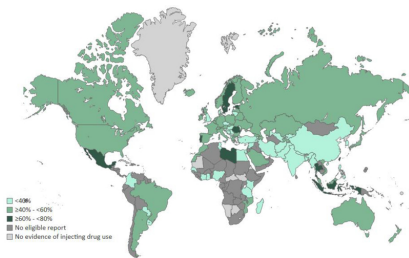


Figure 1: HCV prevalence in PWID (Grebeley et al 2019 Addiction)

Approach

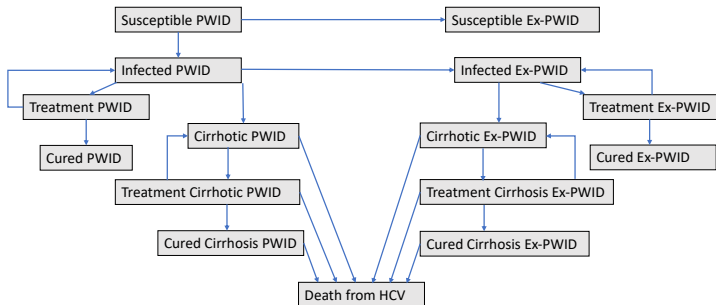
Highly effective drugs are now available to treat HCV, however, access has been limited in many low and middle-income countries.

My job involves modeling the impact and cost-effectiveness of HCV treatment in a variety of settings.

For HCV, a large impact of treatment particularly in PWID is on averted *infections*, which must be estimated with a transmission model.

Here we'll use an SIR-type transmission model to do a cost-effectiveness analysis of HCV treatment in PWID.

Model structure



Key Model Assumptions

- ▶ Transmission only occurs in PWID
- ▶ PWID leave injecting at a certain rate
- ▶ Those infected with HCV develop cirrhosis over time
- ▶ Risk of death is higher for PWID and those with cirrhosis, doesn't change after treatment, but progression to cirrhosis is prevented after treatment
- ▶ Entry into the susceptible PWID group to keep a stable population size

Research Question

What is the cost in USD per QALY gained of treating people who inject drugs for Hepatitis C, compared to no treatment in this population? Is it more cost-effective to exclude active PWID from treatment, treat PWID at the same rate, or at a higher rate, compared to the treatment rate for ex-PWID? We will look at a time horizon of 100 years or 5 years, with an annual discount rate of 3% for both costs and outcomes.

Cost-effectiveness analysis

- ▶ Assume cost of treatment is \$375
- ▶ Assume cost of care for cirrhosis is \$200/year
- ▶ Assume QALY weights:
 - ▶ Ex-PWID: Uninfected 0.94; Infected 0.77; Cirrhotic 0.55; Recovered 0.82; Recovered cirrhosis 0.61
 - ▶ PWID: $A_s - ExPWID * (0.85/0.94)$

Set initial conditions

```
#Load libraries
library(ggplot2)
library(deSolve) # differential equation solver
library(tidyverse)

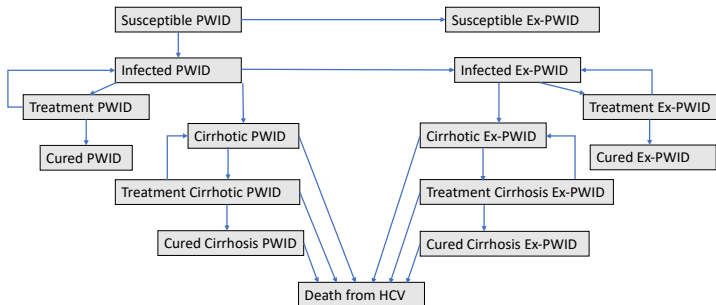
# Initial conditions

initial_values=c(SP=6000,IP=4000,TIP=0,CP=0,TCP=0,RP=0
                ,RCP=0,SX=0,IX=0,TIX=0,CX=0,TCX=0,RX=0,
                RCX=0,D=0) # assume 40% prevalence in PWID

# Time points

time=seq(from=1,to=100,by=1)
```


Define model equations as a function



Define model equations as a function (1/3)

```
# SIR model function
```

```
sir_model <- function(time,state,parameters){  
  with(as.list(c(state,parameters)),{
```

```
# force of infection assuming only transmission in PWI
```

```
NP=SP+IP+TIP+CP+TCP+RP+RCP
```

```
lambda=beta*((IP+TIP+CP+TCP)/NP)
```

```
B = muP*NP + muX*(SX+IX+CX+TIX+TCX+RX+RCX) # births
```

Define model equations as a function (2/3)

```
dSP= B -lambda*SP - tau*SP - muP*SP
# birth (non HCV deaths), - infection, cessation, death
dIP= lambda*SP + (1-svr)*tl*TIP -treat*treatP*IP - zeta*IP
# +infection, failed treatment, - treatment, -progression,
dTIP= treat*treatP*IP - tl*TIP - muP*TIP # treatment, - lea
dCP= -(treat*treatP+muC+muP+tau)*CP + zeta*IP + (1-svr)*tl*
# +progression, failed treatment, -death, - treatment, - c
dTCP= treat*treatP*CP - tl*TCP - muC*TCP - muP*TCP
dRP= svr*tl*TIP - muP*RP - tau*RP# recovered, death, cessa
dRCP = svr*tl*TCP - muP*RCP -muC*RCP - tau*RCP
```

Define model equations as a function (3/3)

```
dSX= tau*SP - muX*SX
dIX= tau*IP - muX*IX - treat*IX + (1-svr)*tl*TIX
dTIX= - muX*TIX + treat*IX - tl*TIX
dCX= tau*CP - muX*CX - muC*CX - treat*CX
      + (1-svr)*tl*TCX
dTCX= - muX*TCX - muC*TCX + treat*CX - tl*TCX
dRX= tau*RP - muX*RX + svr*tl*TIX
dRCX = tau*RCP - muX*RCX - muC*RCX + svr*tl*TCX

dD= muC*(CP+RCP+TCP+CX+TCX+RCX) #don't track non-HCV d

return(list(c(dSP,dIP,dTIP,dCP,dTCP,dRP,dRCP,dSX,
             dIX,dTIX,dCX,dTCX,dRX,dRCX,dD)))
}
)
}
```

What are those parameters?

No treatment scenario

```
# Baseline parameters
parameters=c(
  treat=0, # baseline rate of treatment
  treatP=1, # scaling factor for treating PWID
  beta=0.3, # transmission rate per contact per year
  tl=1/0.25, # rate of leaving treatment
  svr=0.95, # cure rate
  muC=1/20, # death rate with cirrhosis
  muX=1/70, # death rate for exPWID
  muP=1/40, # death rate for PWID
  zeta=1/20, # progression to cirrhosis
  tau=1/20 # average injecting duration of 20 years
)
```

Model scenarios

Change parameters to model different scenarios:

- ▶ No treatment: $\text{treat}=0$
- ▶ Treat all equally: $\text{treat}=0.2$, $\text{treatP}=1$
- ▶ Treat PWID at higher rate: $\text{treat}=0.2$, $\text{treatP}=3$
- ▶ Treat Ex-PWID only: $\text{treat}=0.2$, $\text{treatP}=0$

Note: doing it this way, the total treatment numbers will be different in each scenario

Solving the differential equations

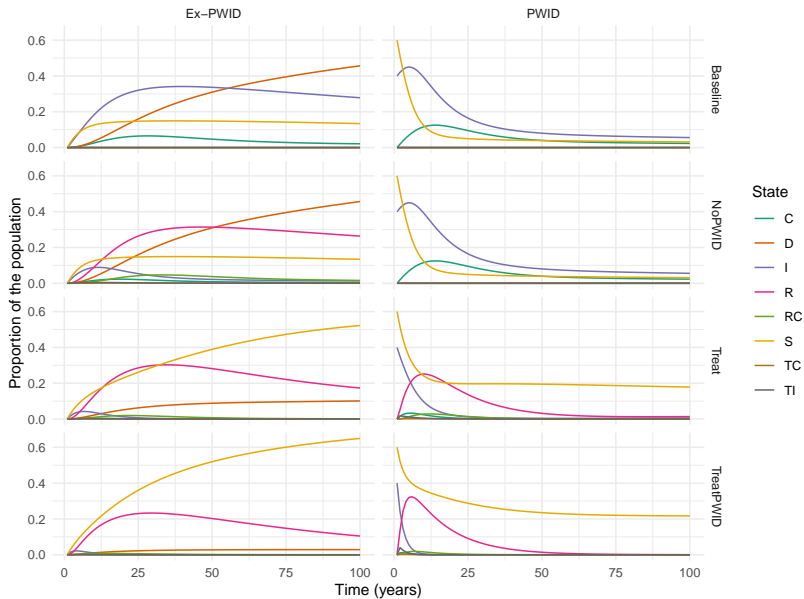
#Solving the differential equations

```
output<-as.data.frame(ode(y=initial_values,  
                           func = sir_model,  
                           parms=parameters,  
                           times = time))
```

```
output_treat <- as.data.frame(ode(y=initial_values,  
                                  func = sir_model,  
                                  parms=parameters_treat,  
                                  times = time))
```

Model results

Number in each compartment over time



Assign costs and QoL weights to each compartment (1/2)

```
treatcost <- 375
cirrhosiscost <- 200

QoL <- c(0.94,0.77,0.77,0.55,0.55,0.82,0.61)
# Ex-PWID: Uninfected 0.94; Infected 0.77; Cirrhotic 0.55;
#Recovered 0.82; Recovered cirrhosis 0.61
# treatment as infected
QP <- (0.85/0.94)

outputEE <- outputAll
```

Assign costs and QoL weights to each compartment (2/2)

```
# costs
outputEE$treatcost <- (outputEE$TIP + outputEE$TIX
                        + outputEE$TCP
                        + outputEE$TCX)*treatcost

# outcomes
outputEE$QALY.X <- rowSums(
  t(apply(outputEE[,3:9],1,function(x){x*QoL})))
```

Add discounting

```
## discount
discounting <- function(years,value,rate,baseyear) {
  time <- years - baseyear
  out <- value/(1+rate)^time
  return(out)
}

outputEE$costD <- discounting(outputEE$time,
                             outputEE$tot.cost,0.03,1)
outputEE$QALYD <- discounting(outputEE$time,
                             outputEE$QALYs,0.03,1)
```

Calculate ICER

```
## calculate mean ICER
pop = 10000
TotalCE <- outputEE %>% group_by(Scenario) %>%
  summarise(costD=sum(costD)/pop,DALYD=sum(DALYD)/pop,
            QALYD=sum(QALYD)/pop) %>% arrange(QALYD)
TotalCE$diffcost <- c(NA,diff(TotalCE$costD))
TotalCE$diffQALY <- c(NA,diff(TotalCE$QALYD))
TotalCE$ICER <- TotalCE$diffcost / TotalCE$diffQALY
```

Results

> TotalCE

A tibble: 4 x 8

	Scenario	costD	DALYD	QALYD	diffcost	diffQALY	diffDALY	ICER
	<chr>	<dbl>	<dbl>	<dbl>	<dbl>	<dbl>	<dbl>	<dbl>
1	Baseline	721.	12.0	20.6	NA	NA	NA	NA
2	NoPWID	753.	11.7	20.9	32.5	0.332	-0.332	97.8
3	Treat	274.	7.02	25.5	-479.	4.63	-4.63	-103.
4	TreatPWID	116.	5.35	27.2	-158.	1.67	-1.67	-94.8

> TotalCEshort

A tibble: 4 x 7

	Scenario	costD	DALYD	QALYD	diffcost	diffQALY	ICER
	<chr>	<dbl>	<dbl>	<dbl>	<dbl>	<dbl>	<dbl>
1	Baseline	21.7	0.596	3.23	NA	NA	NA
2	NoPWID	23.3	0.595	3.23	1.60	0.000826	1937.
3	Treat	36.0	0.565	3.26	12.6	0.0304	416.
4	TreatPWID	42.6	0.527	3.30	6.59	0.0378	174.

> |

Each row is incremental to the row above

Discussion

- ▶ Important to use a model which accounts for infectious disease transmission (new cases or re-infection) when evaluating costs and impacts of interventions for infectious disease with ongoing transmission
- ▶ In this simplified case, treating the people who are involved in disease transmission makes treatment cost saving
- ▶ With a chronic disease like HCV, costs and outcomes are seen over a long time period

Next steps

- ▶ In a model like this we'd normally run many iterations to allow for uncertainty in parameters, and fit uncertain model parameters to observed data
- ▶ Other questions could be explored by tweaking this model, such as
 - ▶ Allowing for reduced transmission in Ex-PWID,
 - ▶ Prioritizing treatment to patients with or without cirrhosis,
 - ▶ Different treatment costs for different groups

Further reading

- ▶ Pakistan
[https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(20\)30003-6/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30003-6/fulltext) (done in Matlab)
- ▶ Cambodia
<https://onlinelibrary.wiley.com/doi/full/10.1111/liv.14550>
(Markov model)
- ▶ Map source
<https://onlinelibrary.wiley.com/doi/epdf/10.1111/add.14393>
- ▶ QALY weight source
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4914770/>