Optimal intertemporal setting of drug expenses: a case study of Hepatitis C

Pierre Dubois (Toulouse School of Economics)
Thierry Magnac (Toulouse School of Economics)

Workshop: Innovation, regulation and organization in healthcare
June 2022

Context

- Bargaining over drug prices between health authorities and pharmaceutical firms are annual without long-run commitment.
- Long-run optimal planning could generate benefits for all parties (see Alvarez, Argente and Lippi, 2021 or Assenza, Collard et al, 2021, for a recent application to Covid).
- These gains depend on diseases and drugs
- Case study: Hépatitis C and therapeutic innovations in years 2010 to inform other cases.

Hepatitis C: Structural characteristics

- Non-expansive disease at least in European countries after decades 1990-2000s
- Ineffective drug treatments before 2010 decade
- Asymptomatic cases, e.g. undetected, quite prevalent.
- Effective drug treatments introduced in 2014 although not for all virus genotypes
- New treatment more costly than the traditional one
- Other treatments introduced between 2014 and 2020 adapting to different genotypes

Objectives

- Focus on the optimal assignment of new drug treatment to some infected keeping the traditional treatment for others e.g. "Controling" an epidemy.
- Model trade-offs between expenses and future effectiveness of drugs coupling with a Susceptibles Infected Recovered model.
- Measurement of cost effectiveness in case of dynamic externalities due to infection.

Underlying dynamics: A SIR-family model

- Subpopulations: Susceptibles, s_t, infected, i_t, and unchecked infected, u_t.
- A natural remission rate
- Decreasing returns to treatment by new drug: the curing rate, or effectiveness of the new drugs, is a non-time varying increasing and concave function of expenses per patient.

Decreasing returns to treatment

- Medical justifications:
  - Heterogenous treatment effects (e.g. depend on virus genotype),
  - the organizational capacity to identify the patients who benefit the most from new treatments (i.e. the undetected)
- Economic justifications:
  - Bargaining pricing game between health authorities (HAs) and drug companies (Dubois and Magnac, 2022)
  - Expecting more effective innovations in the future

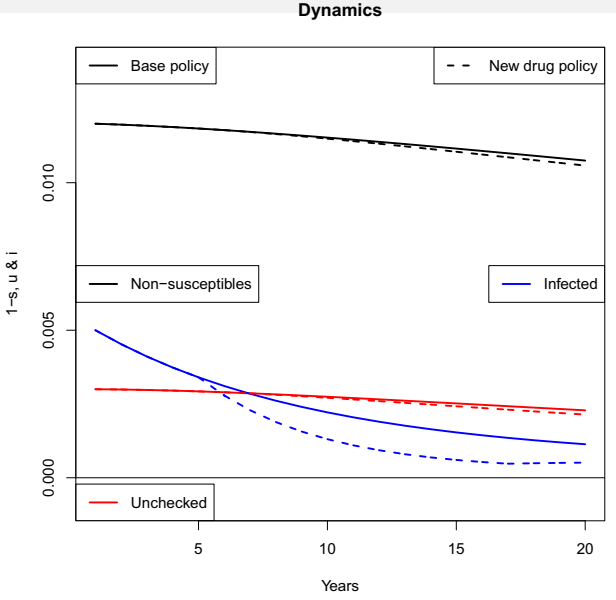
Dynamics and Social Welfare

- Absent any policy, the unique stable stationary equilibrium for a non-expansive disease is disease-free (Hethcote, 2000).
- Health Authorities devote to the new drug treatment an initial endowment $A_1 > 0$ which is depleted according to:

$$A_{t+1} = (1 + r)A_t - B_t,$$

  in which r is the interest rate and B_t are period-t expenses.
- Costs of traditional treatment also implicitly included.
- *Social welfare* : a convex cost function of infected rate written as $-v(i_{t+1}) = -(i_{t+1})^2/2$.

Simulation of SIR model



Variational calculus

The intertemporal discounted expenses are:

$$\sum_{1}^{\infty} \frac{B_t}{(1+r)^t} = A_1,$$

so that a constant budget variational analysis rests on expenses being transferred between period t and period $t+1$.

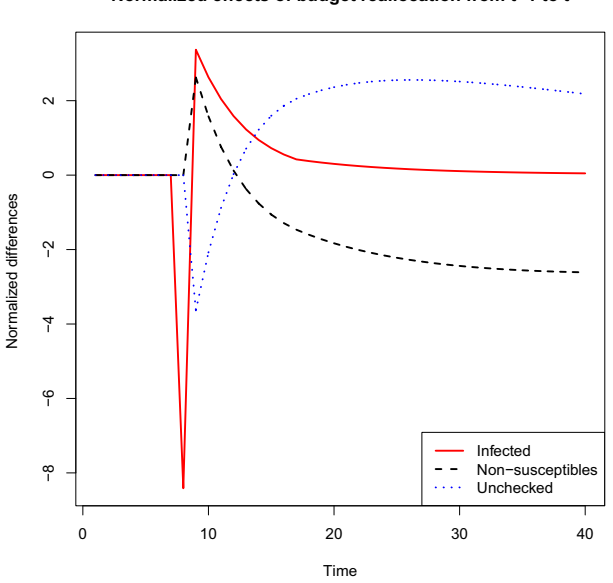
$$dB_t = dB > 0; dB_{t+1} = -(1+r)dB.$$

Reallocation of budget from t+1 to t

- Infection decreases in period t and increases in period $t+1$
- Indirect benefits on the share of susceptibles and undetected
- Complicated dynamic effects of these variations in expenses
- Impossible to derive clear cut predictions because these effects could balance each other.

$\Longrightarrow$ use simulations and calibrate results using French aggregate data about Hepatitic C

Simulation of variational budgets



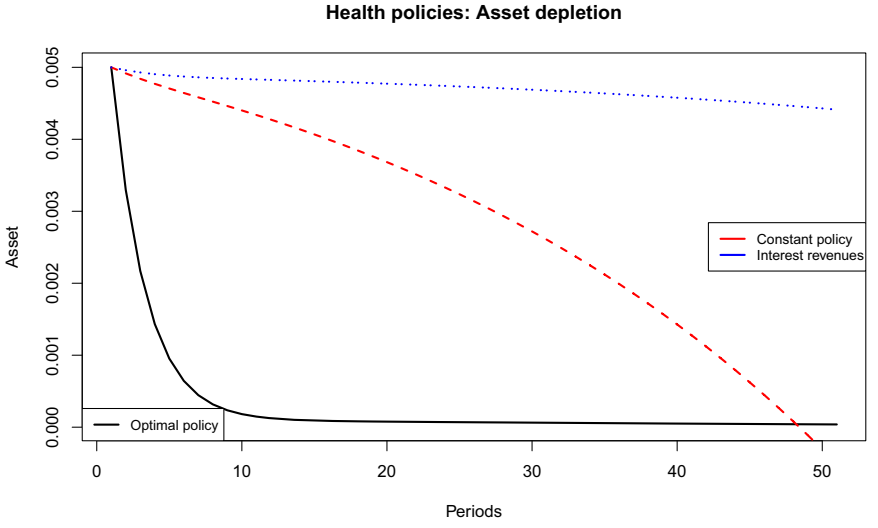
Optimal budget policy

- Timing of expenses by the Health Authorities across time
- Dynamics of infection defined by the epidemiological model
- *Optimal control* of infection

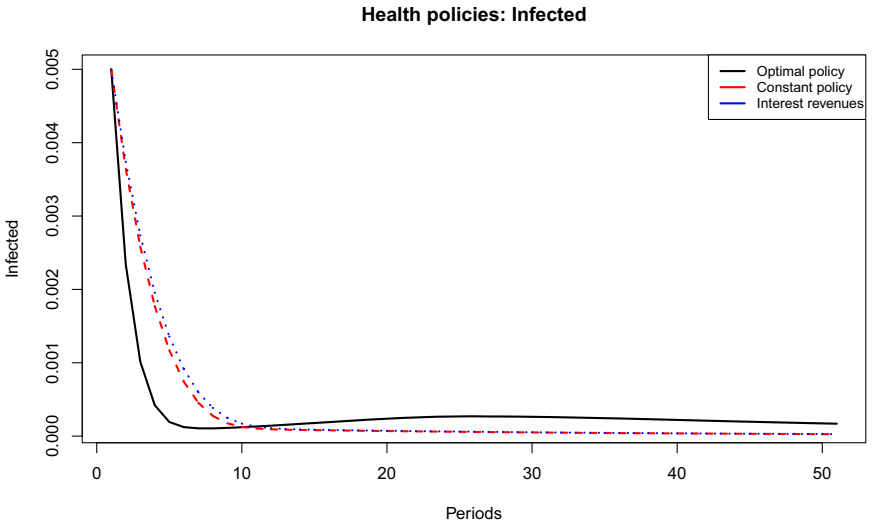
Simulations

- Empirical model solved by backwards induction
- Dependent on various hypotheses: e.g. preferences for the present.
- Comparison of optimal policy with:
  - a " conservative" policy of consuming interests of the endowment for the treatment
  - a constant policy every period

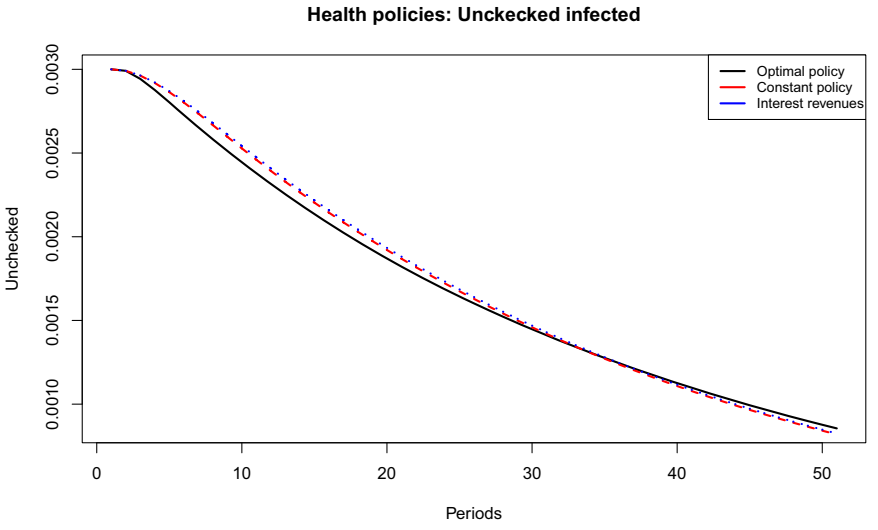
Results : Expenses



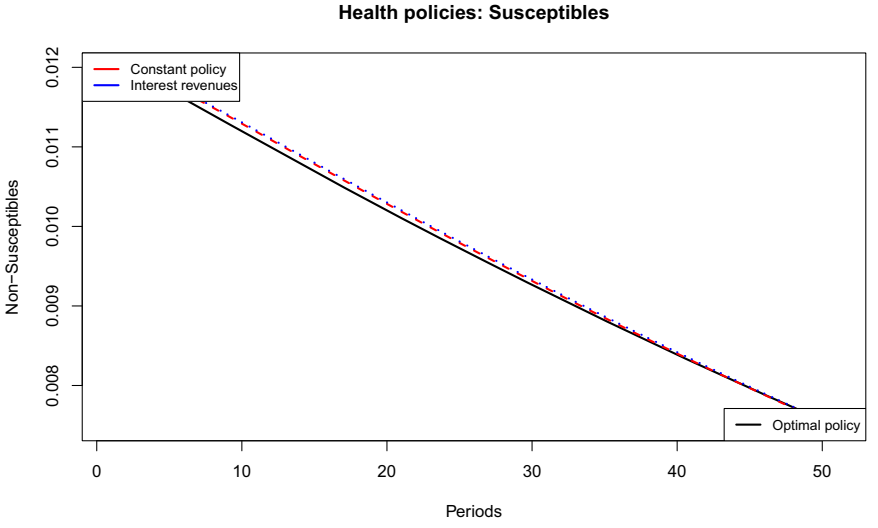
Results : Infected



Results : Unchecked



Results : Non-Susceptibles



Conclusion

- In the case of a disappearing epidemic like Hepatitis C, an equal budget policy is dominated by a front loaded policy
- This result is calibrated on the Hepatitis C case study. Difficult to prove its external validity.
- Depends on the main trade-off: spending more today implies not only less infection tomorrow and some dynamic externalities, but also less effective cures.
- No feed back on the innovation process

THANKS

Please send comments to

Pierre.Dubois@tse-fr.eu
Thierry.Magnac@tse-fr.eu

The SIR model

$$\Delta s_{t+1} = -\beta(i_t + u_t)s_t + \nu(1 - s_t). \tag{1}$$

$$\Delta u_{t+1} = \beta(i_t + u_t)s_t - (\zeta + \nu)u_t, \tag{2}$$

$$\Delta i_{t+1} = \zeta u_t - (\rho_t + \nu)i_t, \tag{3}$$

Curing rate

- The rate at which infectives can be cured is denoted ρ_t. It might be decomposed into a natural remission rate $\rho^{(0)} \ll 1 - \nu$ – the before 2014 treatment effect – and the effect of the new drug.
- The curing rate, or effectiveness of the drug, ρ_t, is a function of expenses per patient that incur health authorities, say b_t, in each time period,

$$\rho_t = \rho(b_t) \in [\rho^{(0)}, 1 - \nu]$$

where $B_t = b_t i_t$ are total expenses.

Calibration of parameters

References:

- Roudot-Thoraval (2021): Review of characteristics of the infection in Europe and the world. Also, Hill et al. (2017) for European data.
- Specific French data : Meffre et al., (2010), Brouard et al., (2019), Bottero et al., (2016).

Main calibrated values:

- Pre-2014 initial values of $u_0 + i_0 = 0.8\%$, and $s_0 = 99.2\%$.
- The rate of detection $\zeta = 0.03$ so that the ratio of $i_0/(u_0 + i_0)$ equal to roughly 60%, and $u_0 = 0.3\%$ and $i_0 = 0.5\%$.
- The incidence rate in Western Europe is estimated $\beta \simeq 0.01$ (Hill et al. 2017) in agreement with the decrease between 1994 and 2011.
- The mortality rate, ν, is set to 0.0125
- The frequency of being treated, $\rho = 0.1$, Roudot-Thoraval (2021).

Algorithm: Details : First Step

For different starting values $z_0 = (s_0, u_0, i_0)$ on a grid of values, denoted $z_0^{(s)}$, covering the initial values of the processes we are interested in. We then forward simulate $\{z_t^{(s)}\}_{t \geq 1}$ using the SIR model, in *the absence of a policy* until T is sufficiently large and we evaluate $W_0^{(T)}(z_0^{(s)})$ as:

$$W_0^{(T)}(z_0^{(s)}) = \sum_{t=0}^{T} v(i_t) = -\sum_{t=0}^{T} \frac{(i_t)^2}{2}.$$

We test the stability of $W_0^{(T)}(z_0^{(s)})$ with respect to T and choose T such that :

$$d(W_0^{(T)}(z_0^{(s)}), W_0^{(T+1)}(z_0^{(s)})) = \frac{1}{\#\{z_0^{(s)}\}} \left(\sum_{z_0^{(s)}} \frac{(W_0^{(T)}(z_0^{(s)}) - W_0^{(T+1)}(z_0^{(s)}}{\frac{1}{\#\{z_0^{(s)}\}} \sum_{z_0^{(s)}} W_0^{(T)}(z_0^{(s)})} \right.$$

with an ε_{TOL} sufficiently small.

Simulation of the optimal policy

1. Absent any policy, simulate the value function $W_0^{(T)}(z_0^{(s)})$ for large horizon T on a grid for state variables $z_0^{(s)}$. Approximate this value function by a quadratic function. T is chosen such that the difference between subsequent value functions are close to zero
2. On a grid of budget resources, defined bt $A_0^{(s)}$, simulate the value function $V_0^{(T)}(x_0^{(s)})$ on a grid for state variables $z_0^{(s)}$ and $A_0^{(s)}$ in which the endowment is exhausted in k periods.
3. The less costly policy is the one whereby HAs consume the interest rates of their endowment. The most costly policy is the one whereby the HAs also consume their endowment.
4. Approximate this value function by a quadratic function. T is chosen such that the difference between subsequent value functions as a function of k are close to zero since there is a single fixed point.