Economics:

Cost-effectiveness of options for Hepatitis A vaccination

Miami, 1st December 2007

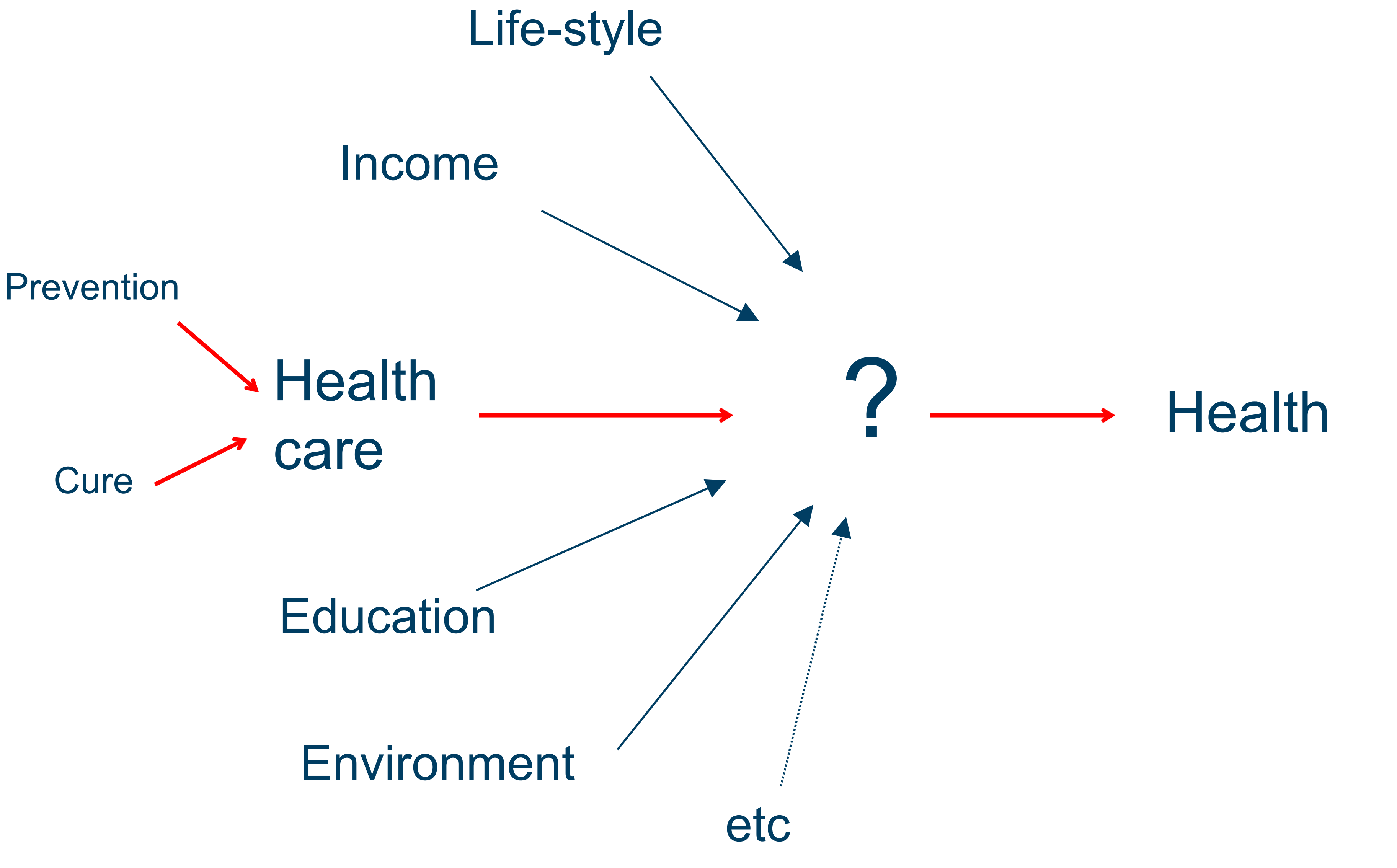
Philippe Beutels, PhD

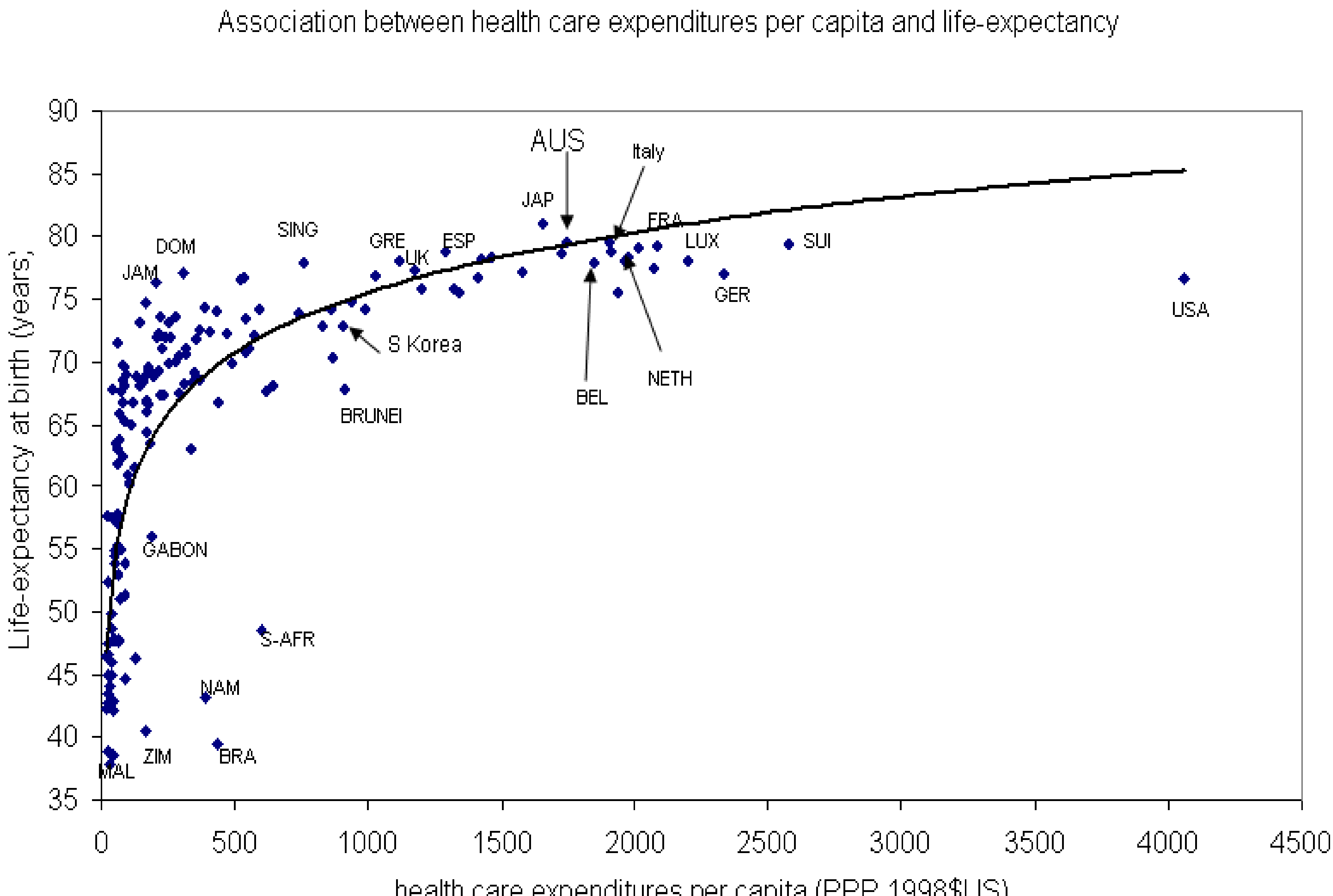
Health Economics & Modeling Infectious Diseases
Vaccine & Infectious Disease Institute

Universiteit Antwerpen

Centrum voor de Evaluatie van Vaccinaties

Economics = the study of choice
The basic health question: Health "production"





Beutels P, 2002, based on WHO and WB

What we want to know, preferably in advance ...

EFFICACY & SAFETY
"Does it work, is it safe in individuals ?"

EFFECTIVENESS
"How well does it work in the real world ?"

EFFICIENCY
"How do the costs relate to the effectiveness?"

EQUITY
"Does it (dis)advantage subgroups of the population?"

Welfare economics

Main types of economic evaluation differ in how health gains are valued

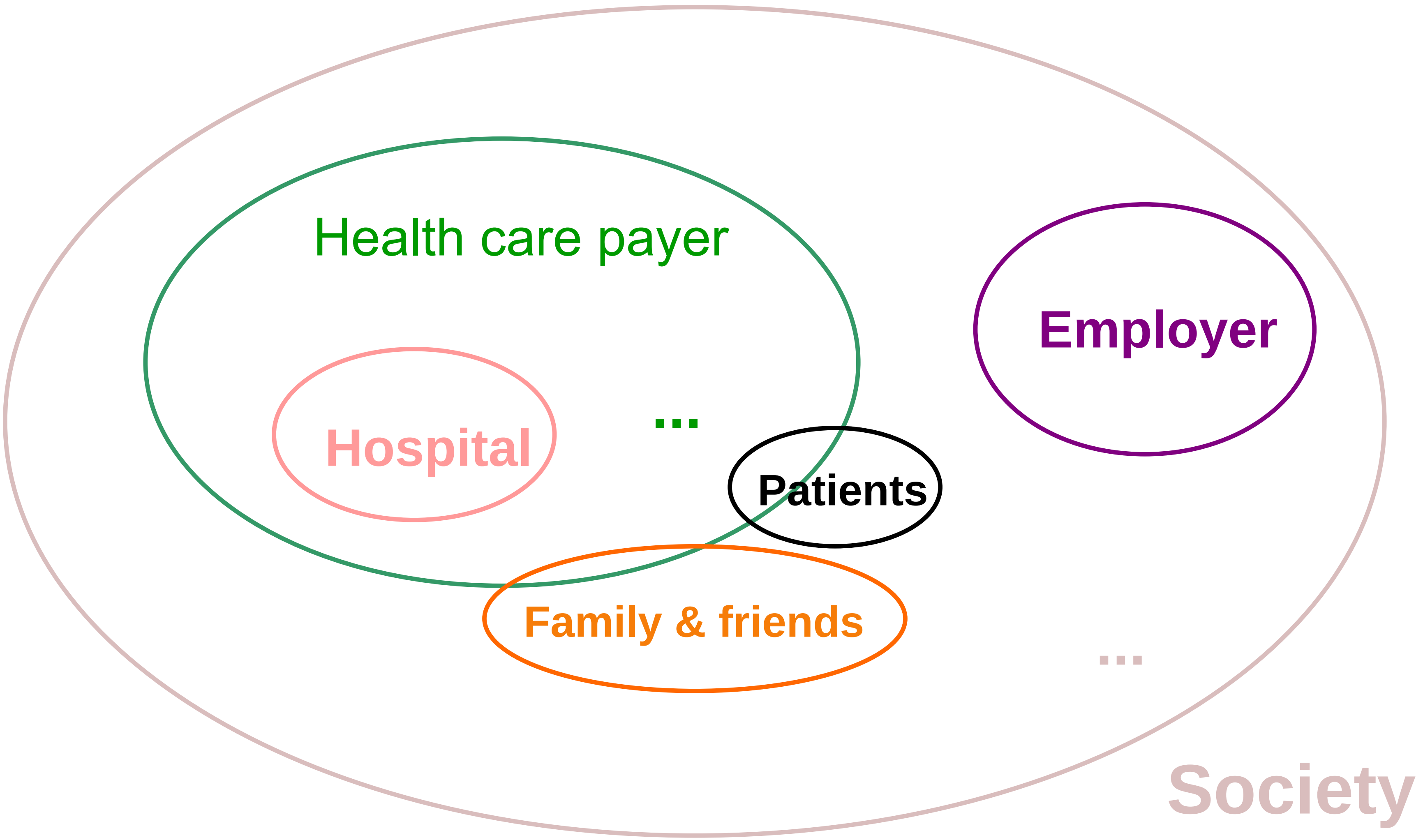
- **Cost-effectiveness analysis (CEA):**
  - in natural units (e.g., cases/hospitalisations/deaths prevented, life-years gained)

  → no valuation, just counting

- **Cost-utility analysis (CUA):**
  - in combined measure of morbidity and mortality (e.g., Quality-Adjusted Life Years (QALYs) gained)

- **Cost-benefit analysis (CBA):**
  - in monetary terms (€,$, ...)

Perspective: Viewpoint of the analysis



Beutels P, 2005

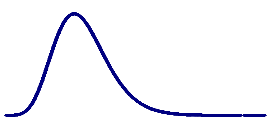
ICER: incremental cost-effectiveness ratio

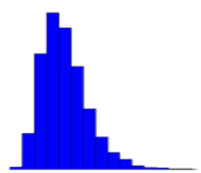
$$\frac{\Delta \text{ COST}}{\Delta \text{ QALY}} = \text{ICER}$$

-Choice of comparator : current practice and next best alternative option

- **→ Doing nothing**
- **→ Targeted vaccination (single option)**
- **→ Targeted vaccination (combination of options)**

incorporating parameter uncertainty: data driven distributions on ALL parameters





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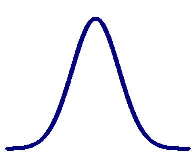


eg:

- Risk of clinical disease
(→ serology + rate of underreporting)
- Indirect (time) costs

Specific issues for economic evaluation of vaccines

- Herd immunity
- Often short-lived illness (often in very young children), which causes extra familial care and work loss, for which valuation methods lack credibility and acceptability
  - Quality of Life assesment
  - Indirect time cost estimates
- Very sensitive to analytical time span and assumptions regarding time preference (discounting)
- Some infections are eradicable
- Some emerging infections (eg, SARS, pandemic influenza) would have a major macroeconomic impact that goes beyond lost productivity of sick people

Valuing time

- (Leisure) time to the individual
  - Leave unvalued in Cost-Utility Analysis (i.e. with QALYs)
    - mortality: is included in life-years gained
    - morbidity: should be included in quality adjustment
  - Put a $ value on in Cost-Benefit Analysis
    - willingness to pay (revealed or stated preference studies)
    - human capital method (assumes you value your time at what you earn)
- (Productive) time to society

Valuing indirect costs of productivity losses

- Absence from paid work:
  - human capital approach = production losses valued at value of wages
  - friction cost method = amount depends on time span organizations need to restore production levels.
    - Lost workers/working time not irreplaceable – the only cost is interim losses.
    - Friction costs < traditional production losses

[• Impaired productivity at paid work
  - measure suboptimal productivity by questionnaire
- Impaired productivity at unpaid work
  - valued by replacement costs (e.g. average wage rate of professional housekeeper)]

Most country-specific guidelines on economic evaluation want direct health care costs per QALY gained as criterion

The epidemiological consequences of childhood vaccination

- **The force of infection declines**
  - Force of infection = probability a susceptible person is infected per unit of time
- **The average age at infection increases**
- **The interepidemic period increases**

Childhood vaccination increases the average age at infection

Three causes:

1. Cohort effect: only leads to an increase in **proportion** of adult cases
2. + Waning immunity: only secondary vaccine failures. Can increase **number** of adult cases [if force of infection greater at older ages]
3. Herd immunity: can lead to an increase in **number** of adult cases [if effective coverage is not sufficiently high]. Eg, rubella and CRS in Greece

But with Hep A:

- **this happens without vaccination too**
  - **The infection is not at endemic equilibrium in many settings**
  - **Will increased susceptibility fuel large outbreaks?**

herd immunity

- Implications for effectiveness, efficiency and equity
- difficulties for modelling

MODEL UNCERTAINTY

- Static model:
  - Typically deterministic Markov model, for a single ageing cohort
  - Force of infection independent of proportion infectious at each time point
  - Herd immunity can only be introduced in the model based on observations from a similar setting
- Dynamic model:
  - Typically deterministic population based model, with constant total population size over time
  - Force of infection recalculated as a function of the proportion of infectious people at each time point
  - Herd immunity impact is a built-in part of the model

→The underlying infectious disease transmission process is modelled
→Needs data or assumptions on mixing patterns and duration of infectivity
→Not part of traditional toolbox of health economists and epidemiologists

Modelling practices for economic evaluations

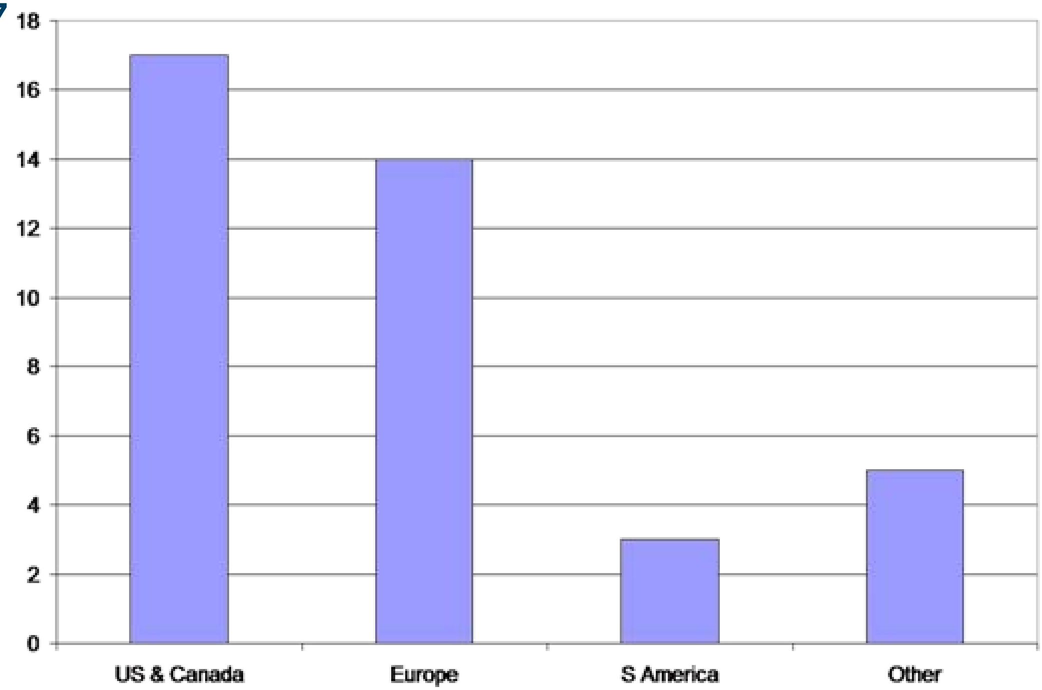
Review	Static models	Dynamic models
Hepatitis B (Beutels, Health Econ 2001)	**19**	**2**
Pneumococcal conjugate vaccination (De Graeve & Beutels, PharmacoEconomics 2004; Beutels et al, Vaccine 2007)	**20**	**0**
Varicella-zoster (Thiry et al, PharmacoEconomics 2003)	**16**	**3**
Meningococcal C vaccination (Welte et al, PharmacoEconomics 2005)	**13**	**1**
Human Papilloma Virus (Newall et al, Lancet Infect Dis 2007)	**3**	**1**

Choosing between static and dynamic models for hepatitis A

- For **targeted** strategies
  - target groups without epidemiological influence (eg, HCW, HCV patients, IDU, MSM, military) in the rest of the population :
    - static models
  - target groups with an important epidemiological influence (eg, travellers from low to high endemic areas?):
    - static models ONLY IF:
      - the resulting ICERs favour vaccination
      - estimates on herd immunity are available from a comparable setting and are integrated in the model
  - **Otherwise, a dynamic model is needed**
- For **universal** strategies
  - static models ONLY IF:
      - estimates on herd immunity are available from a comparable setting and can be introduced in the model
  - **But really, a dynamic model is more relevant for any analysis of universal vaccination in any area of endemicity**

HAV economic evaluations literature search

- 39 published up till 2007
  - Universal options:
    - Infants
    - Children
    - Pre-adolescents
  - Targeted options:
    - Health Care Workers
    - Travellers
    - Military
    - Hepatitis C patients
    - Food handlers
    - Contacts of cases
    - Prisoners



Baseline cost-effectiveness of targeted vaccination options with monovalent hepatitis A vaccine

	Health outcome measure	Vaccinate all	screen + vaccinate
HCW	per QALY (US)	$65000	$20,000-$135,000
HCW	per case averted (France, Ireland)	$35,000 – $130,000	$19,000-133,000
Travellers	per case averted (BE, Europe, FR)	$9000-$90,000	$10,000-56,000
Military	per case prevented (NL, UN)	Cost-saving to $110,000	cost-saving
Hepatitis C patients	per QALY gained (US)	$5 million	$65,000
Food safety workers	per LY gained (US)	Cost-saving to $20,000	na
Contacts of cases	per case prevented (France)	Cost saving to $1500	na
Immigrant children	per case averted (Amsterdam)	$15,000	na

Often refined according to expected levels of immunity and risk of infection.
Eg, travellers by travel frequency, hepatitis C patients by age

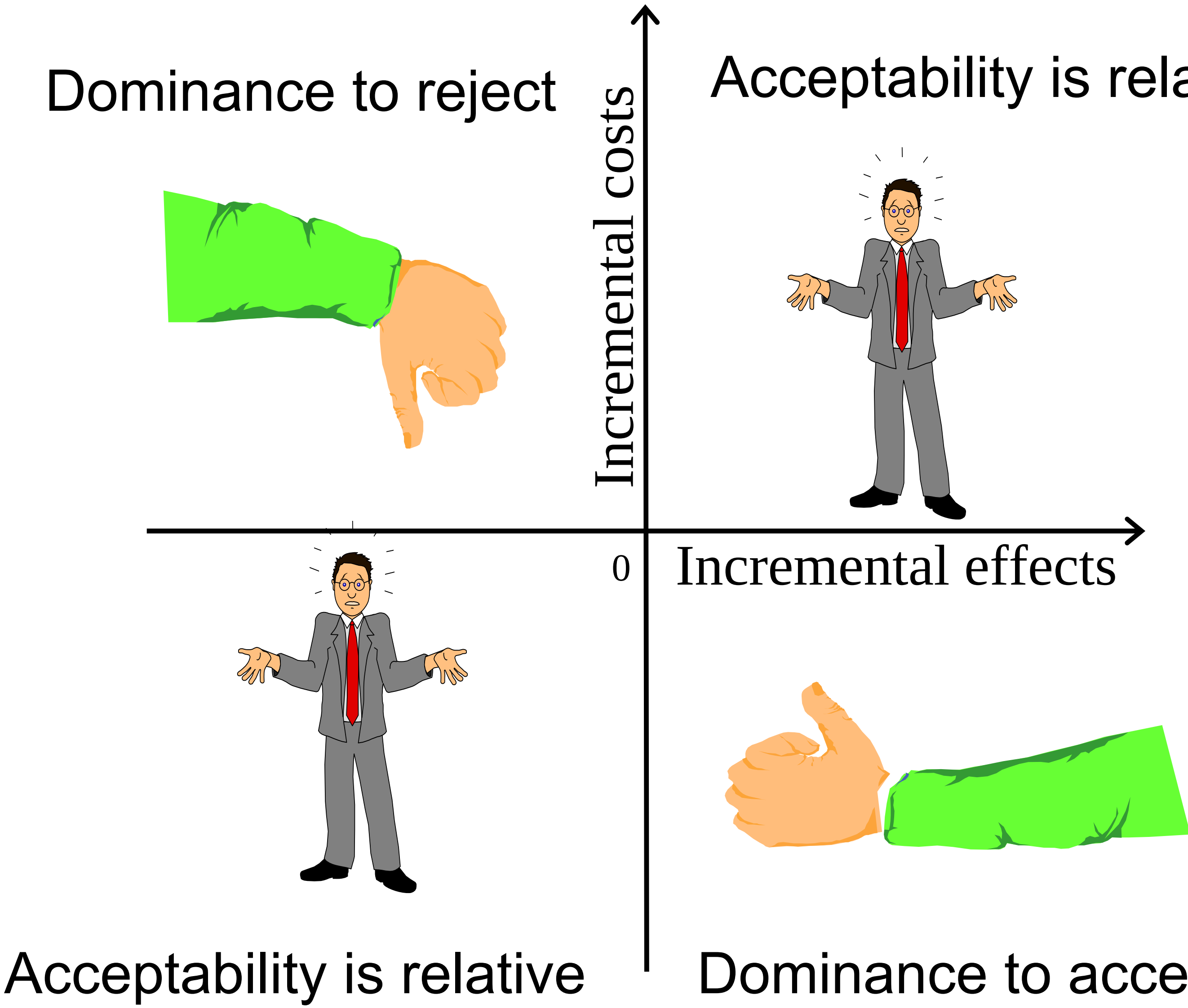
Universal HAV vaccination

- universal vaccination vs no vaccination (without herd immunity)
  - $10,000 to 133,000 per QALY gained (US)
  - Cost-saving to $5000 per QALY (Argentina)
  - Cost-saving (Spain) to $20,000 per QALY (Canada)

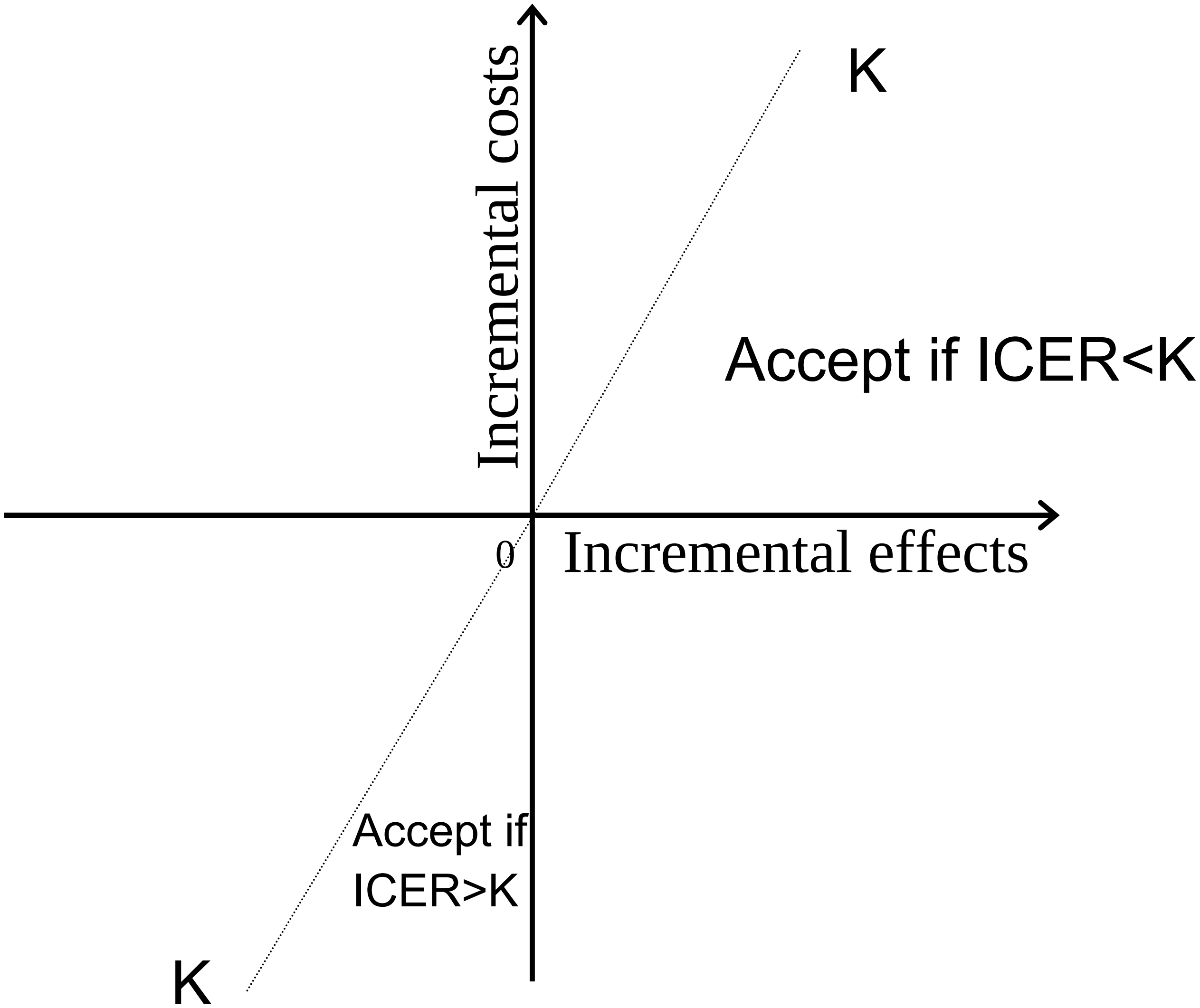
Universal HAV vaccination accounting for herd immunity

- Based on a static model, adjusted with observed herd effects:
  - US (Armstrong et al, 2007):
    - Without herd: $32000 with herd $1000 per QALY gained
- Based on dynamic models
  - Germany (Diel et al, HEPAC 2001):
    - Universal Vaccination versus travel vaccination: $110,000 per case averted (hep A/B)
  - Argentinia (Lopez et al, J Gastroeneterol 2007):
    - Universal vaccination versus no vaccination cost-saving, robust to “background” annual decline in force of infection of 1% to 2%
  - Canada (Bauch et al, Vaccine 2007)
    - ...see later presentation

The cost-effectiveness plane



Decisions relative to willingness to pay for a QALY



Australia (PBAC) acceptability

- NHMRC Guidelines:

		Evidence on Effectiveness	
		High	Low
Evidence on Costs	Strong	Recommend if <EUR 40,000 per QALY	Recommend if <EUR 20,000 per QALY
		Do not recommend if >EUR 60,000 per QALY	Do not recommend if >EUR 40,000 per QALY
	Weak	Recommend if <EUR 20,000 per QALY	Recommend if <EUR 20,000 per QALY
		Do not recommend if >EUR 40,000 per QALY	Do not recommend if >EUR 20,000 per QALY

- If total budget impact < EUR 6 million annually = PBAC decision; otherwise ministerial decison

Other thresholds:

- NICE recommendations (UK):
  £20,000 to 30,000 per QALY = threshold above which it would be increasingly likely to reject a technology on grounds of cost-**in**effectiveness.
- NL: Euro 20,000 per QALY gained
- USA: ? $50,000 per QALY gained
- Canada: ? 25,000-75,000 Can$/QALY

Many countries don’t have an explicit threshold

In sum

- Economic evaluation and modeling are not exact science
  - **helps** policy making
- HAV is cost-effective for target groups with sufficiently high risk exposure (determined by local epidemiology, and behaviour)
- Few published studies set outside North America for universal strategies
- Cost-effectiveness of universal strategies are inconclusive, but the most recent and most relevant analyses are more favourable for the vaccine , particularly those with low vaccination costs (often replacing HBV vaccine with combined hep A/B vaccine where the schedule allows this).