Health Economics…. A New Toxicity?



"The drug itself has no side effects - but the number of health economists needed to prove its value may cause dizziness and nausea"

SPECIFICITIES OF HEALTH ECONOMICS IN THE AREA OF VACCINES EVALUATION

MJ Postma

Prof in PharmacoEconomics

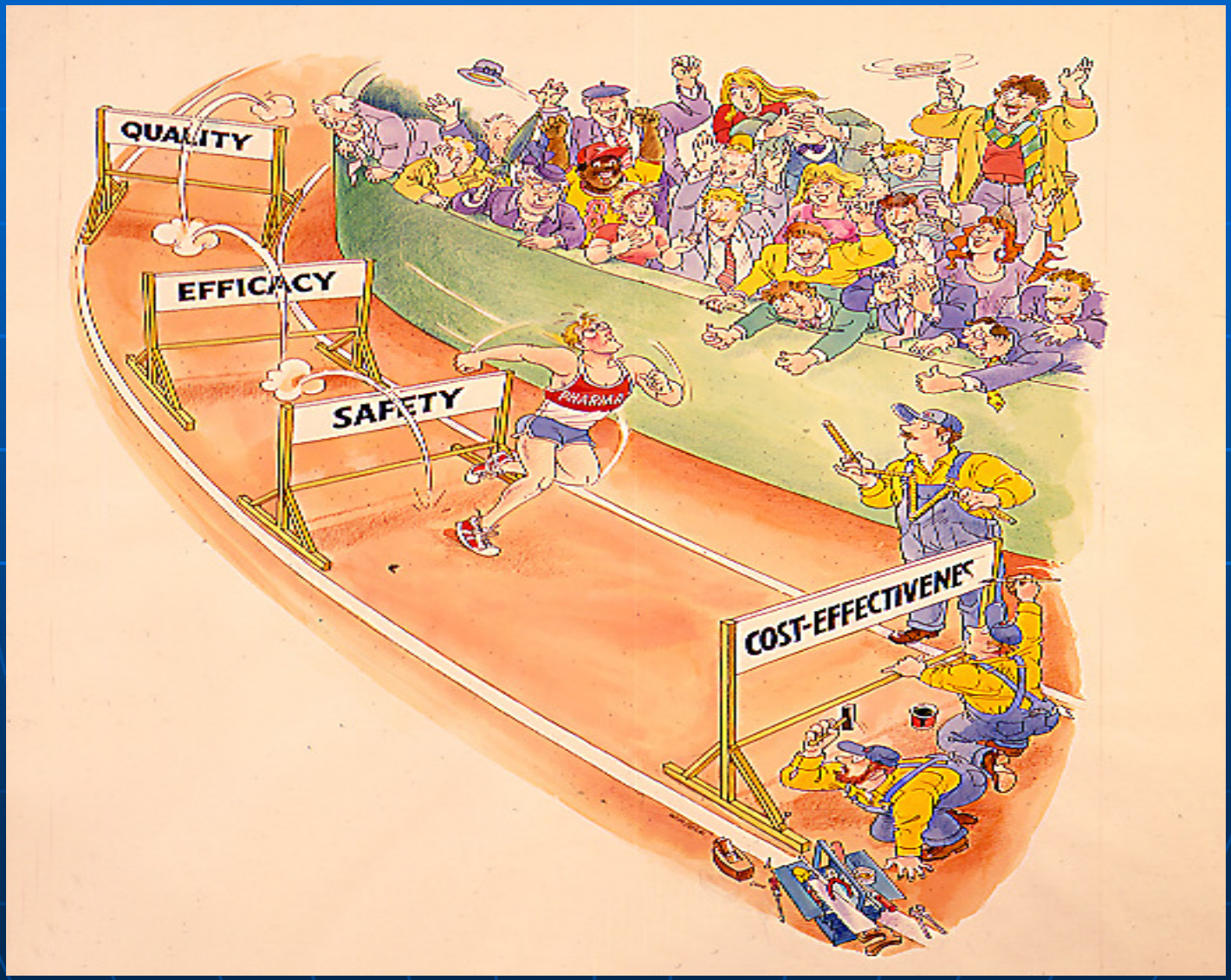
Unit of PharmacoEpidemiology & PharmacoEconomics (PE2)
Department of Pharmacy
University of Groningen

Former member of Dutch Health Council Committee on Vaccines

OVERVIEW

- Decision-making context
  - Introduction into the current Dutch landscape
  - Role of cost-effectiveness
  - Thresholds
- Guidelines
  - Discounting
  - Modeling
  - Perspective
- Examples
  - HPV
  - Influenza
  - …

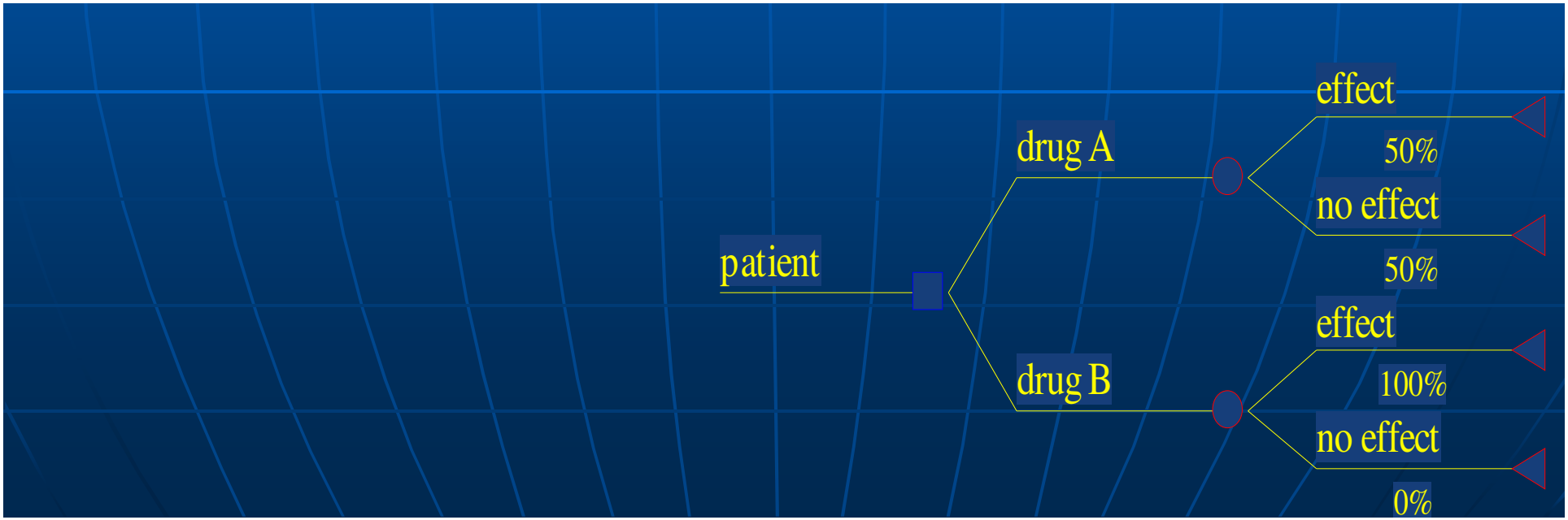
4th HURDLE IN THE DUTCH NATIONAL IMMUNIZATION PROGRAM



Available online at www.sciencedirect.com
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Vaccine 23 (2004) 470–479
Vaccine
www.elsevier.com/locate/vaccine

Economic evaluation of meningococcal serogroup C conjugate vaccination programmes in The Netherlands and its impact on decision-making

R. Welte[a,b,c,*], G. van den Dobbelsteen[c], J.M. Bos[c,d], H. de Melker[e], L. van Alphen[c], L. Spanjaard[f], H.C. Rümke[g], M.J. Postma[d]



4th HURDLE

- Hepatitis B
  - 2000 ⇨ not cost-effective
  - 2008 ⇨ cost-effective
- Meningococcal Vaccination 2001
  - 3 shots not cost-effective
- HPV, no full catch-up due to unfavourable cost-effectiveness
- Conjugate pneumococcal vaccination
  - 2001 ⇨ not cost-effective
  - 2005 ⇨ cost-effective
  - 2010 ⇨ not cost-effective

ISSUES

- General
  - How to interprete the cost-effectiveness ratio?
  - Types of costs to include: broader societal, production losses, indirect medical …
- Specific for vaccines
  - Lack of hard endpoints in trials
  - Discounting
  - Type of model to use

Funding of drugs: do vaccines warrant a different approach?

Philippe Beutels, Paul A Scuffham, C Raina MacIntyre

Vaccines have features that require special consideration when assessing their cost-effectiveness. These features are related to herd immunity, quality-of-life losses in young children, parental care and work loss, time preference, uncertainty, eradication, macroeconomics, and tiered pricing. Advisory committees on public funding for vaccines, or for pharmaceuticals in general, should be knowledgable about these special features. We discuss key issues and difficulties in decision making for vaccines against rotavirus, human papillomavirus, varicella-zoster virus, influenza virus, and *Streptococcus pneumoniae*. We argue that guidelines for economic evaluation should be reconsidered generally to recommend (1) modelling options for the assessment of interventions against infectious diseases; (2) a wider perspective to account for impacts on third parties, if relevant; (3) a wider scope of costs than health-care system costs alone, if appropriate; and (4) alternative discounting techniques to explore social time preference over long periods.

Lancet Infect Dis 2008; 8: 727–33

Centre for Health Economics Research and Modelling Infectious Diseases (CHERMID), Centre for the Evaluation of Vaccination, Vaccine and Infectious Disease Institute, University of Antwerp, Antwerp, Belgium (P Beutels PhD); School of Public Health, University of Sydney, Sydney, NSW, Australia (P Beutels); Centre for Applied Health Economics, School of Medicine, Griffith University, Logan, Queensland, Australia (Prof P A Scuffham PhD); and

Introduction

In many high-income countries, public funding of preventive vaccines is assessed based on the same criteria as the funding of curative pharmaceutical drugs. Such Immunisation, US Advisory Committee on Immunization Practices). Often, cost-effectiveness evidence for vaccines is assessed in the same manner as for any drug. Nevertheless, as we discuss below, vaccination has special

ORIGIN: RP-SYSTEM

- Since 2005 cost-effectiveness plays a role in reimbursement for new innovative drugs
  - For example, diabetes, psychotropic and haemato-/oncological drugs
  - Oseltamivir, but also HPV
  - Dutch Foundation for Health Care Insurance (CVZ)
  - NICE (SMC, KCE)
- No threshold
  - € 20,000 per QALY
  - € 80,000 per QALY
  - Assessment based on qualitative criteria
  - 11 guidelines for good pharmacoeconomic research
  - Really no threshold…??

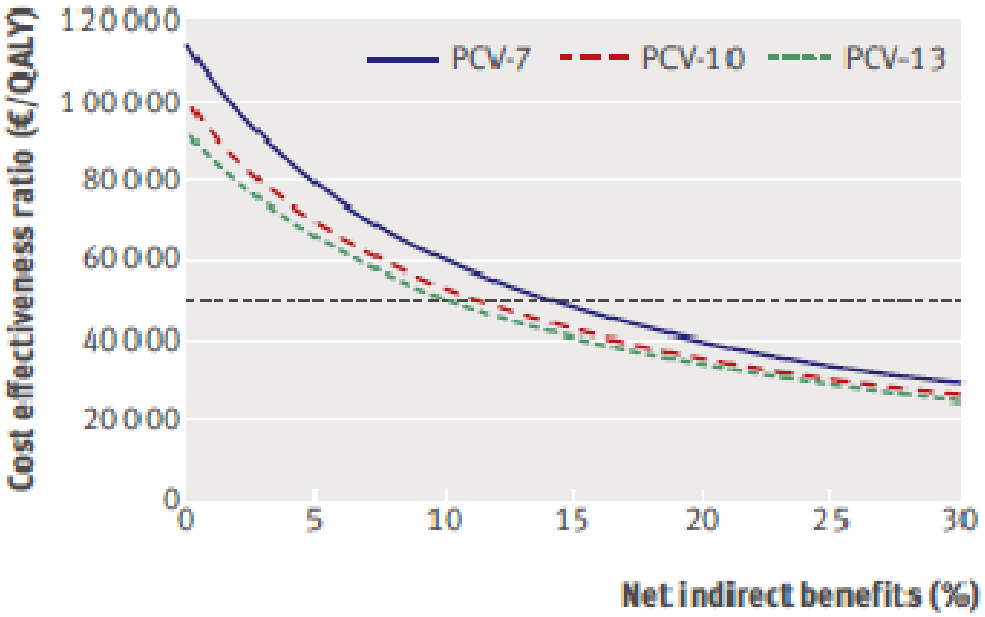


Fig 3 | The effect on cost effectiveness ratios of varying the level of net indirect effect of vaccination for individuals aged 5 years or older. The horizontal dashed line shows the threshold at €50 000 per QALY. PCV-7/10/13, seven/10/13 valent pneumococcal conjugated vaccine (3+1 dose schedule); QALY, quality adjusted life year

DAGBLAD VAN HET NOORDEN

30 november 2012 , pag. 4

'Grens noodzakelijk voor kosten gezondheidszorg'

REPORTAGE
GRENS AAN ZORGKOSTEN

- Hoogleraar: 50.000 euro per gewonnen levensjaar is redelijk
- Debat over geld verdienen aan gezondheid gaat snel over grenzen


Hoeveel mag een gewonnen levensjaar kosten?

Door Arend van Wijngaarden

Groningen De kosten van de gezondheidszorg in Nederland lopen gigantisch uit de hand en daarom moet er maar eens een grens getrokken worden, betoogde professor Maarten Postma, hoogleraar farmacie en economie aan de Rijksuniversiteit Groningen gisteren tijdens een debat. "Ik stel voor 50.000 euro per gewonnen levensjaar. Dat is een redelijke grens."

ROTAVIRUS VACCINE (KCE-RAPPORT)

Tabel I. Proportie aanvaardbare incrementele kosten-effectiviteits simulaties, gegeven de bereidheid €50000 te betalen voor een extra 'gezond levensjaar' (Quality Adjusted Life Year, QALY) (gebaseerd op 1000 simulaties). Resultaten voor vaccinatie met Rotarix® en RotaTeq® vanuit het perspectief van de betaler voor de gezondheidszorg. Scenarios waarbij geen, één of twee verzorgers per kind in rekening gebracht werden, en waarbij de last van kinderen (en hun verzorger(s)) die ziek zijn door rotavirusinfectie, maar voor wie geen medische hulp gezocht wordt, al dan niet in rekening gebracht werd.

	ROTARIX® 'geen medische hulp' niet in rekening gebracht	'geen medische hulp' in rekening gebracht	ROTATEQ® 'geen medische hulp' niet in rekening gebracht	'geen medische hulp' in rekening gebracht
geen verzorger	2%	8%	1%	2%
1 verzorger	6%	46%	1%	13%
2 verzorgers	26%	81%	6%	46%

ISSUES

- How to interprete the cost-effectiveness ratio?
- Lack of hard endpoints in trials
- Discounting
- Type of model to use
- Perspective

Volume 13 • Number 6 • 2010
VALUE IN HEALTH

Quantification of the Potential Impact of Cost-effectiveness Thresholds on Dutch Drug Expenditures Using Retrospective Analysis

Cornelis Boersma, PhD, Adriaan Broere, Maarten J. Postma, PhD Prof

Unit of PharmacoEpidemiology & Pharmacoeconomics (PE^2), Department of Pharmacy, University of Groningen, Groningen, The Netherlands

SPECIFIC FOR VACCINES

- How to interprete the cost-effectiveness ratio?
- Lack of hard endpoints in trials
- Discounting
- Type of model to use
- Societal perspective

MODELLING

- To extrapolate from intermediate endpoints to "hard endpoints"
  - Blood pressure
  - Immunogenic parameters
- Time horizon
  - From short-term trial to lifetime in the economic models following a cohort, for example, in a Markov model
  - Although long-term effects are "discounted away"

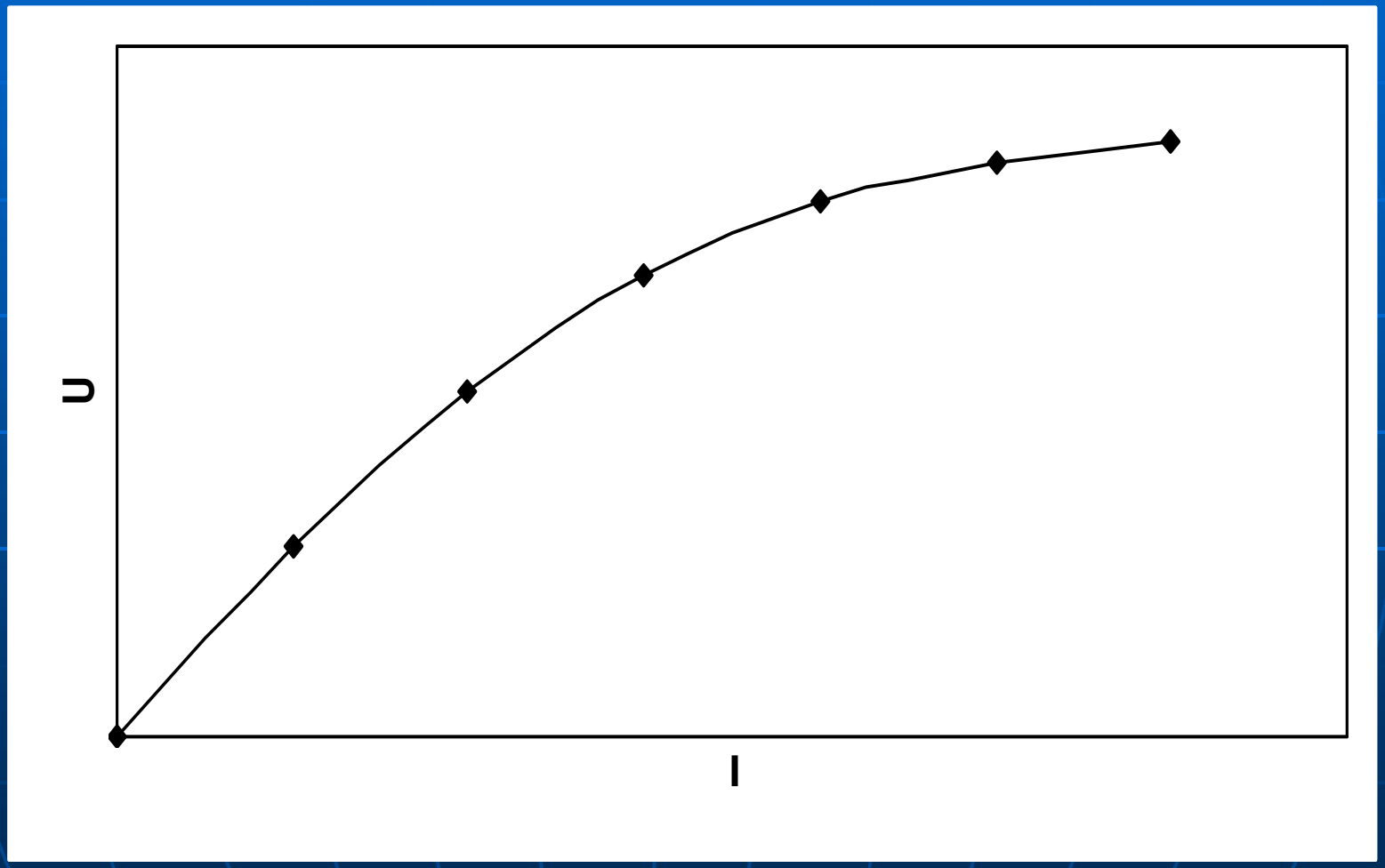
SPECIFIC FOR VACCINES

- How to interprete the cost-effectiveness ratio?
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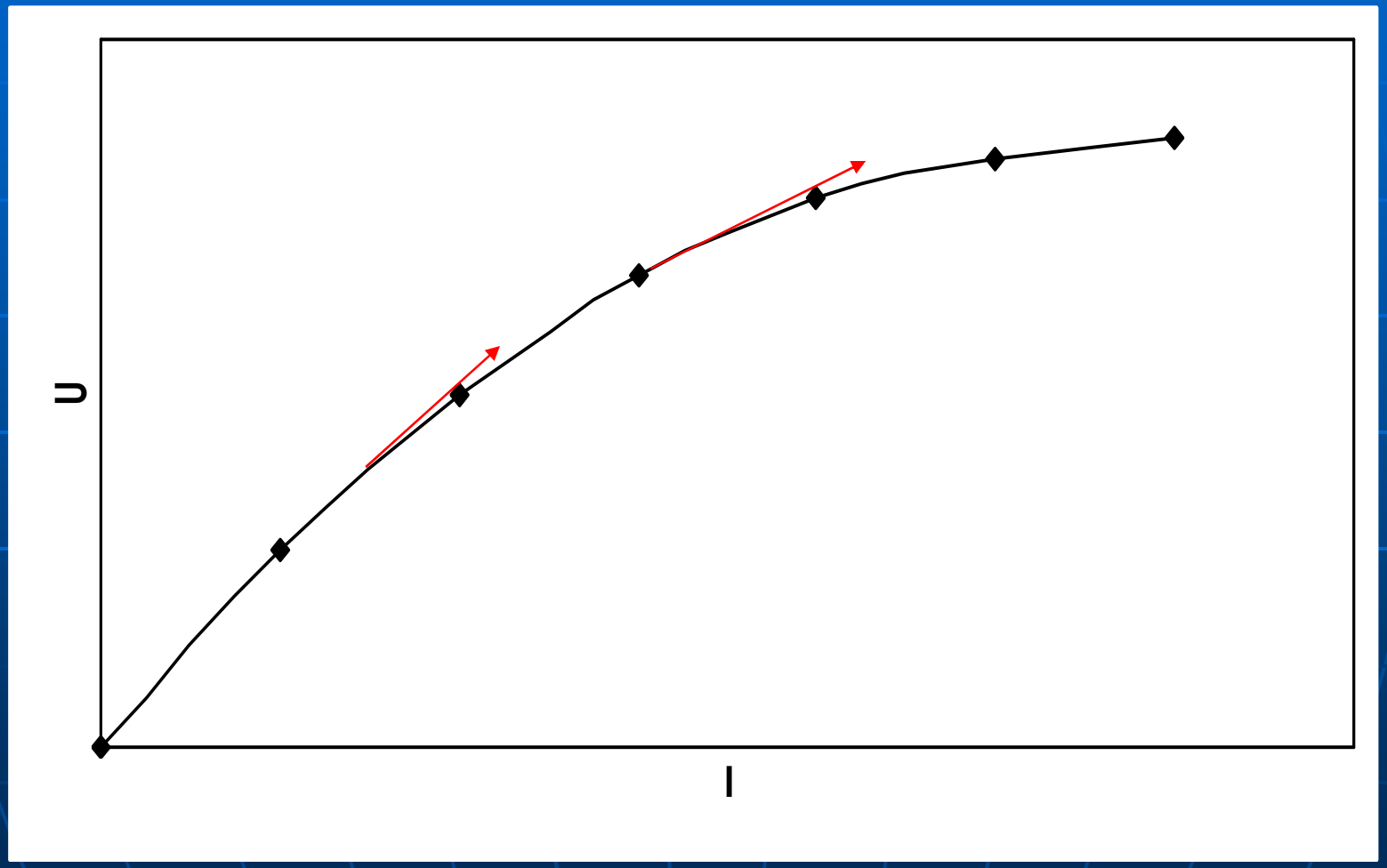
DISCOUNTING

- Rationale for discounting is time preference
- €100 (t=0) is preferred over €100 (t=1)
- €100 (t=0) = €100*(1+*r*) (t=1)
- Netherlands: r=4%
- The exact rate is derived from real rate-of-return on investment
- Discount rate comes over and above the deflator
- Discounting relates to real economic growth (90%) and uncertainty (10%)
- Also applied to life years (and QALYs) related to growth in life expectancy

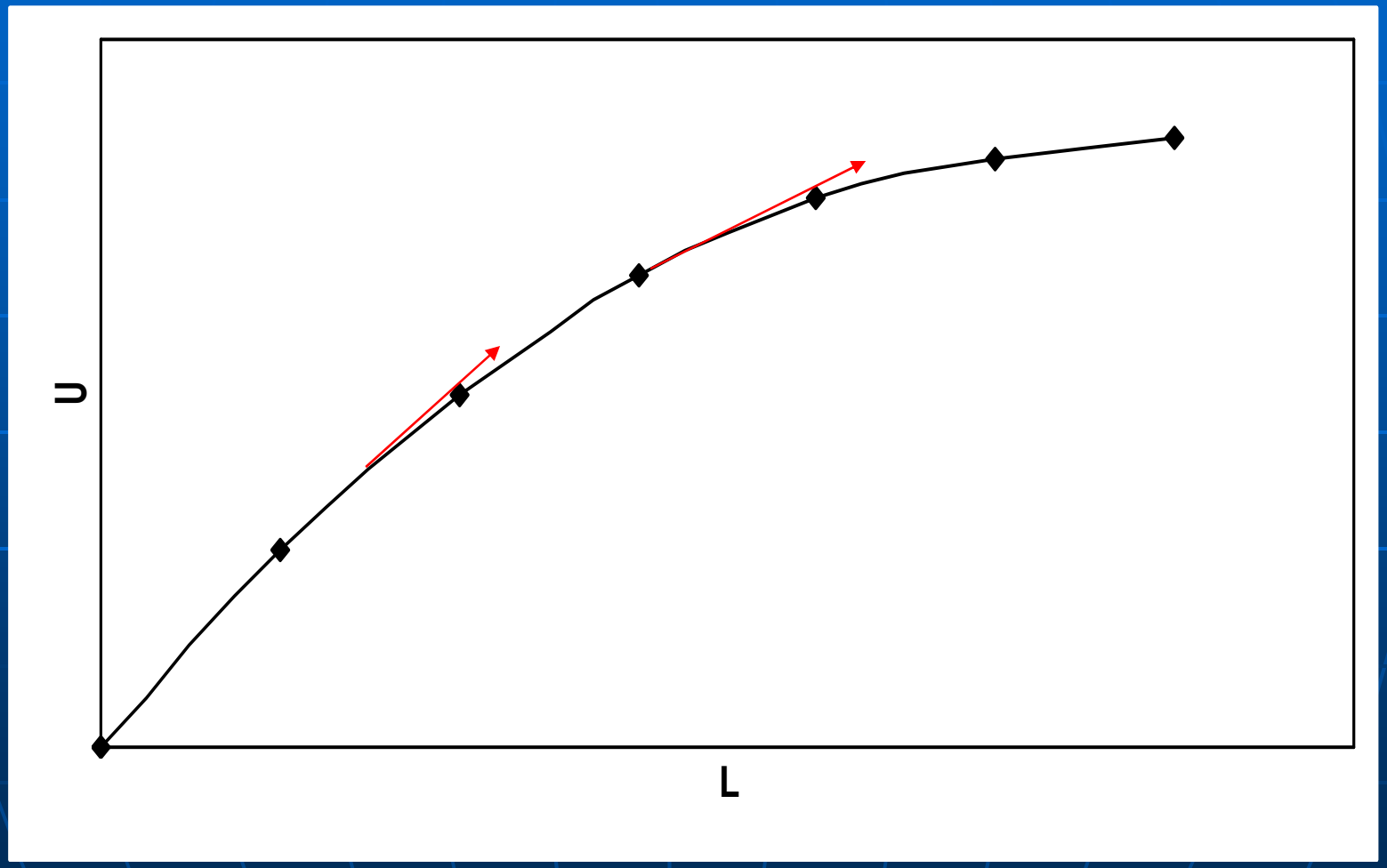
MICRO-ECONOMICS



MICRO-ECONOMICS

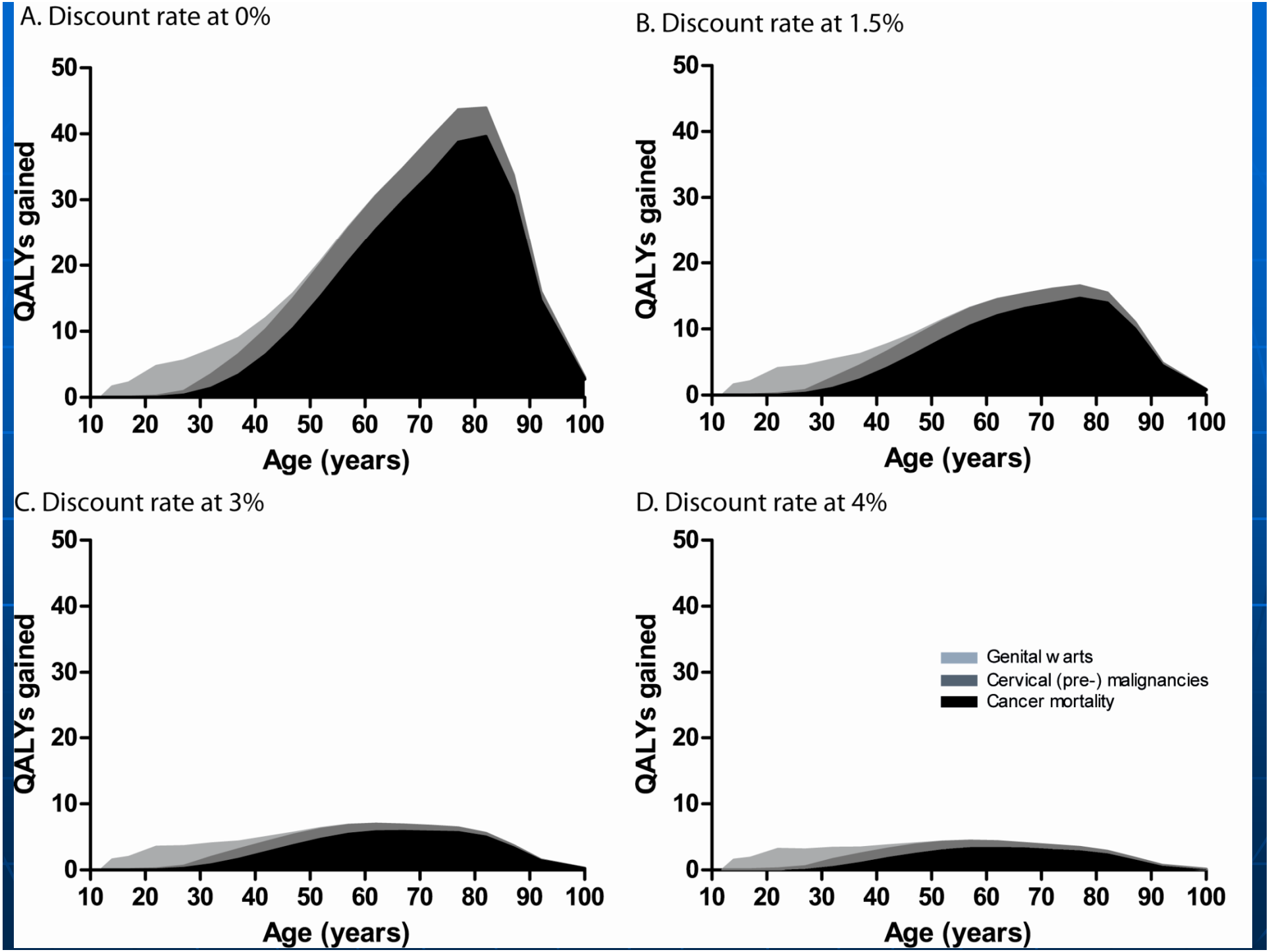


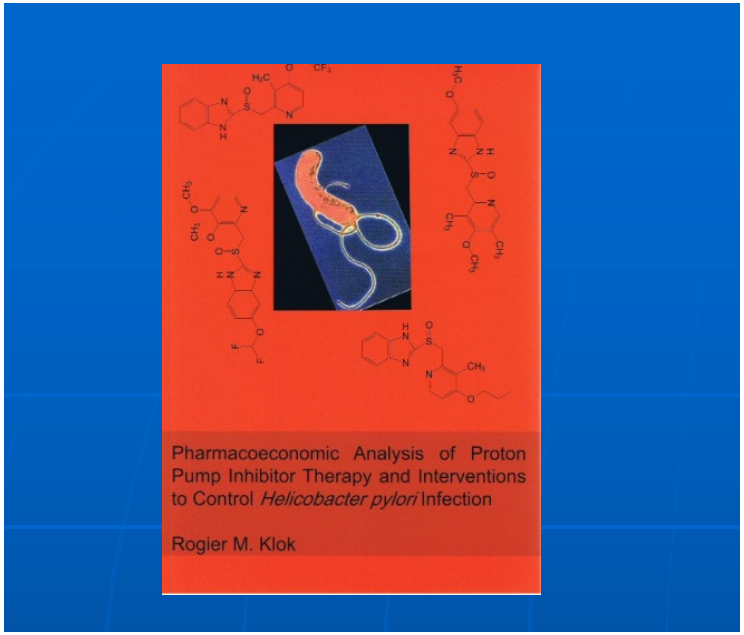
MICRO-ECONOMICS



DISCOUNTING

- Developed for money, but also applied to health
  - 1 life year (t=1) = 1/1.04 life year (t=0)
  - 1 life year (t=2) = $1/1.04^2$ life year (t=0)
  - …
  - 1 life year (t=80) = $1/1.04^{80}$ life year (t=0)
- 80 ⇨ 20


A. Discount rate at 0%
B. Discount rate at 1.5%
C. Discount rate at 3%
D. Discount rate at 4%
QALYs gained
Age (years)
0
10
20
30
40
50
10
20
30
40
50
60
70
80
90
100
Genital warts
Cervical (pre-) malignancies
Cancer mortality



Education and de

Summary points

New National Institute for Health and Clinical Excellence guidelines change the discount rates for costs and effects from 6% and 1.5% respectively to 3.5% for both

This change gives a lower weight to future health effects and may worsen the cost effectiveness ratio, especially for preventive interventions

Differential discounting is more appropriate when non-monetary outcomes like QALYs are used

NICE should return to a 1.5% discount rate for effects

Need for differential discounting of costs and health effects in cost effectiveness analyses

Werner B F Brouwer, Louis W Niessen, Maarten J Postma, Frans F H Rutten

The decision of the National Institute for Health and Clinical Excellence to abandon differential discounting of future health is a step backwards and could change funding decisions

SPECIFIC FOR VACCINES

- How to interprete the cost-effectiveness ratio?
- Lack of hard endpoints in trials
- Discounting
- Type of model to use
- Societal perspective

DISCOUNTING

- NL
  - Costs: 4%
  - Health: 1.5%
- Most countries do equal discounting
- Differential discounting
  - NL
  - Belgium
  - Estonia
  - Swiss
- Constant or decreasing?

Intervention

Infectious disease

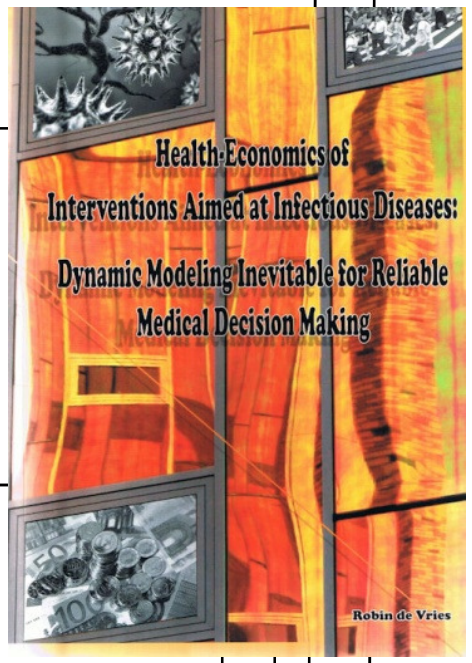
Non-infectious disease

Transmission of pathogen* between humans

No transmission of pathogen* between humans (e.g. tetanus, rabies)

Intervention has influence on susceptibility to infection or transmission of infection

Intervention has no influence on susceptibility to infection and transmission of infection (e.g. therapeutic interventions)



Interventions in groups which contribute significantly to the transmission of the infection

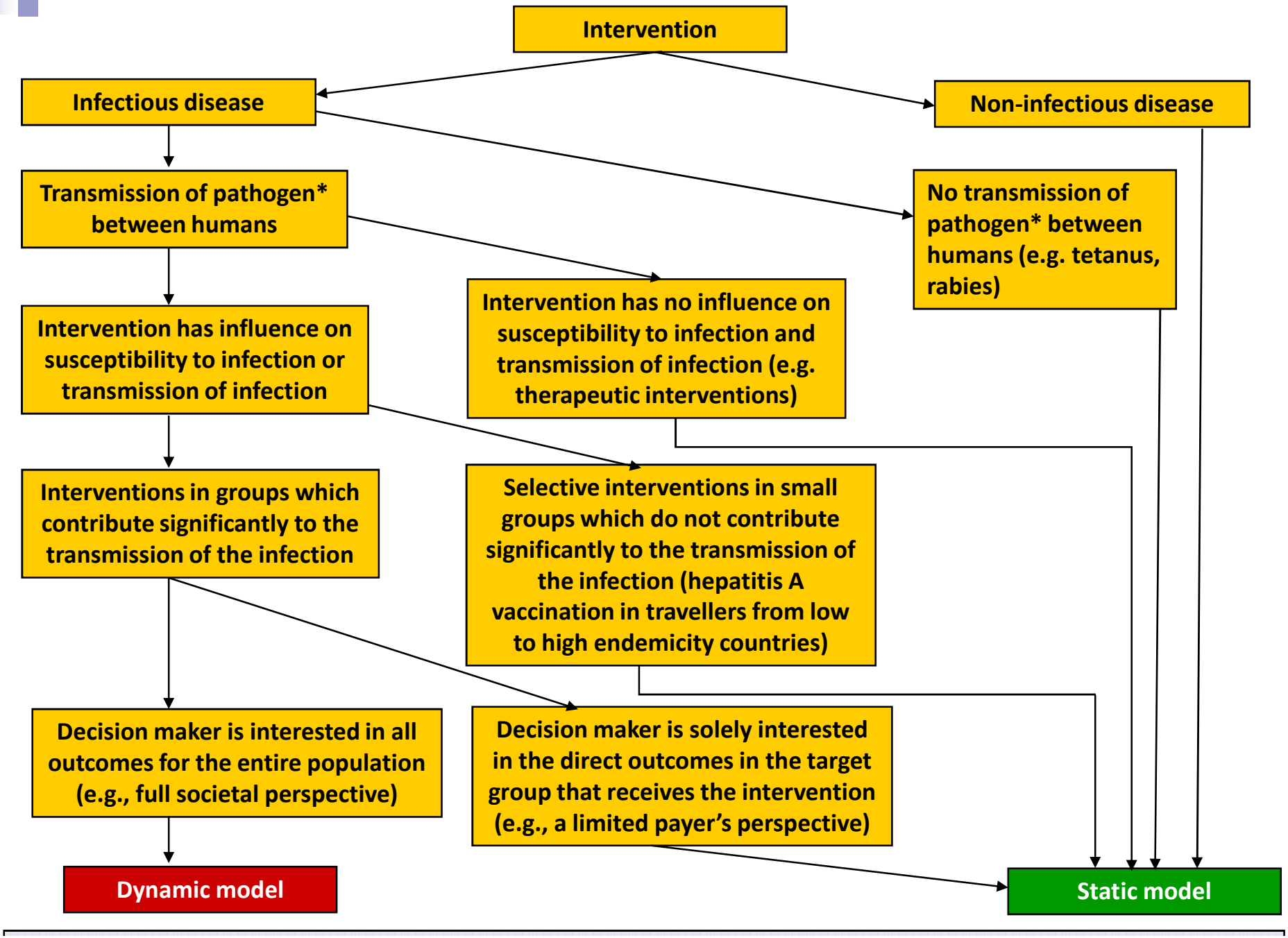
Selective interventions in small groups which do not contribute significantly to the transmission of the infection (hepatitis A vaccination in travellers from low to high endemicity countries)

Decision maker is interested in all outcomes for the entire population (e.g., full societal perspective)

Decision maker is solely interested in the direct outcomes in the target group that receives the intervention (e.g., a limited payer's perspective)

Dynamic model

Static model


Intervention
Infectious disease
Non-infectious disease
Transmission of pathogen* between humans
No transmission of pathogen* between humans (e.g. tetanus, rabies)
Intervention has influence on susceptibility to infection or transmission of infection
Intervention has no influence on susceptibility to infection and transmission of infection (e.g. therapeutic interventions)
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Dynamic model
Static model

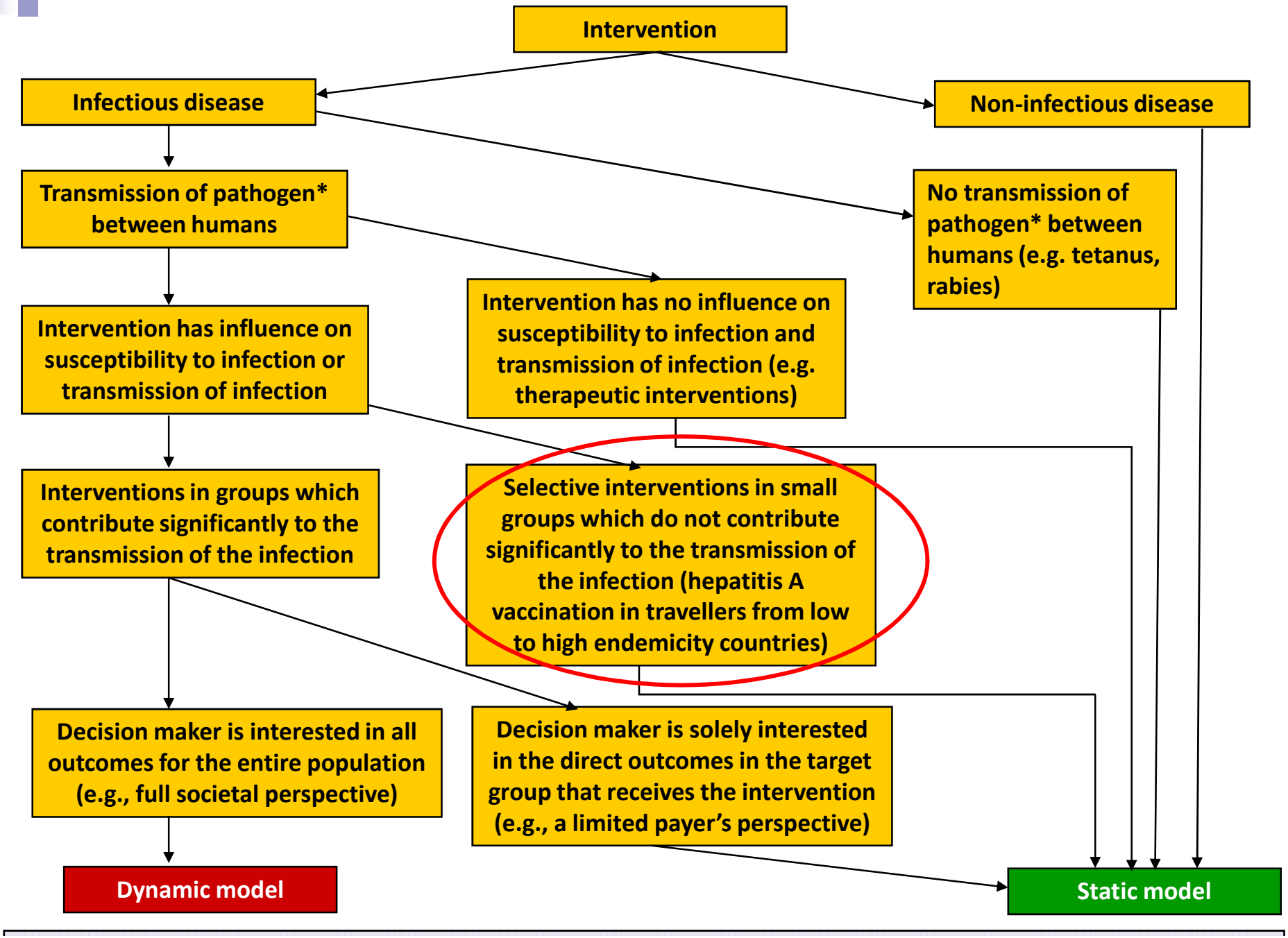
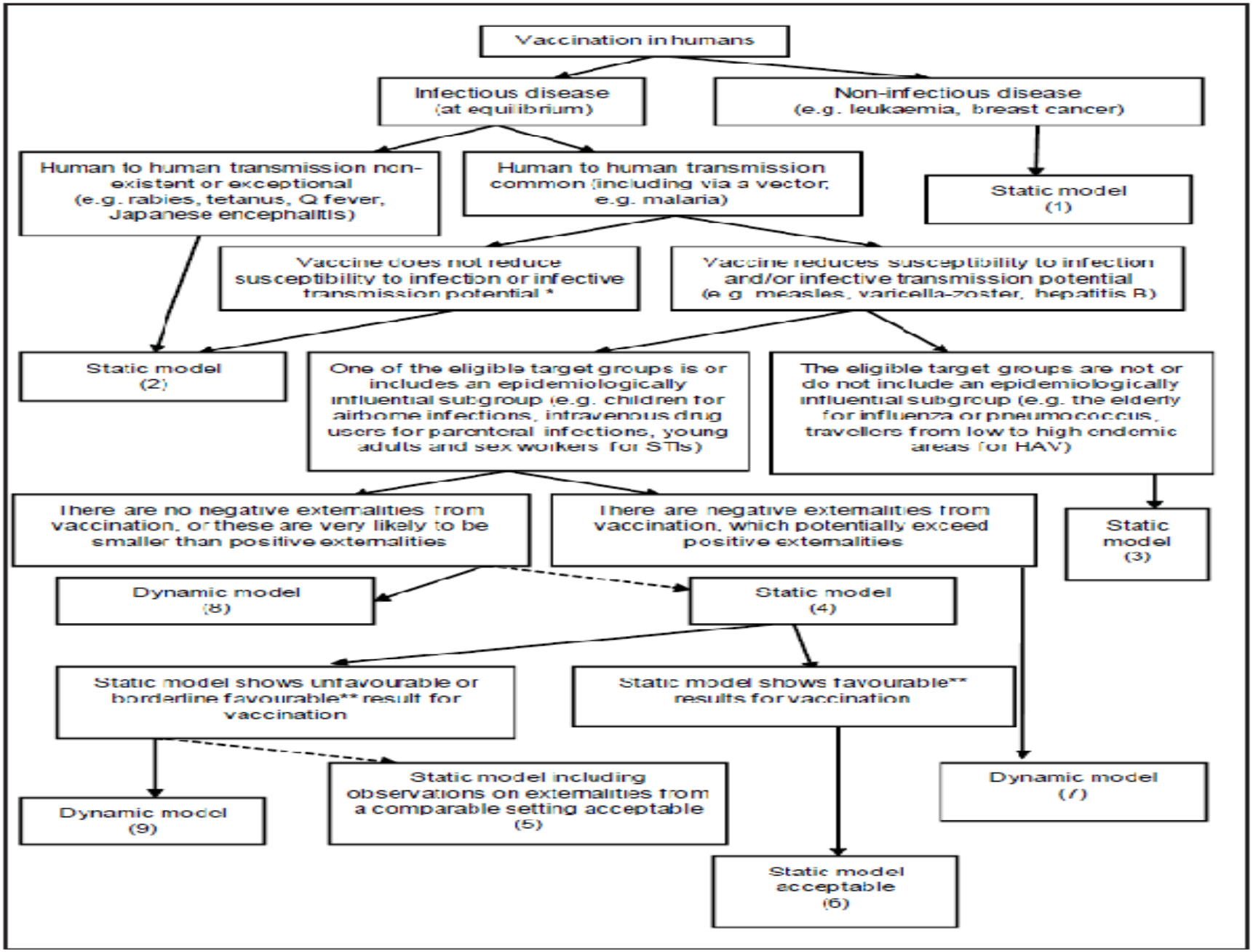

Intervention
Infectious disease
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Dynamic model
Static model

Figure 3: Flow chart to help determine when dynamic or static models are appropriate



STATIC MODEL

- Constant force of infection / chronic disease
- No herd immunity

- Modellers
  - Keep it as simple as possible
  - However, grasp all essentials

- Used
  - Cocooning in pertussis
  - Initially in pneumococcal

Clinical Therapeutics/Volume 32, Number 8, 2010

Cost-Effectiveness Analysis of Various Pertussis Vaccination Strategies Primarily Aimed at Protecting Infants in the Netherlands

Tjalke A. Westra, MSc[1]; Robin de Vries, PhD[1]; Johannes J. Tamminga, PhD[2]; Christophe J. Sauboin, MSc[3]; and Maarten J. Postma, PhD[1,4]

[1]Unit of PharmacoEpidemiology & PharmacoEconomics, Department of Pharmacy, University of Groningen, Groningen, the Netherlands; [2]Health Outcomes, GlaxoSmithKline, Zeist, the Netherlands; [3]Global Health Economics, GlaxoSmithKline Biologicals, Wavre, Belgium; and [4]Department of Epidemiology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands

Results: In the base-case analysis, cocooning and maternal immunization were found to be effective in reducing the incidence of pertussis among infants (123 and 174 infant cases were expected to be prevented, respectively). Furthermore, cocooning and maternal immunization were estimated to be cost-effective from a payer's perspective (€4600 [US $6400]/QALY and €3500 [$4900]/QALY, respectively) and even cost-saving from a societal perspective (savings of up to €7200 [$10,100] and €5000 [$7000], respectively). Sensitivity

DYNAMIC MODELLING

- Describing/simulating the spread of disease in populations
- Herd immunity

- Other effects
  - Negative effects
  - Age shift
  - Serotype replacement

- Age shift
  - VZV
  - Pertussis

DYNAMIC MODEL

Susceptible → Infected → Susceptible (SIS)

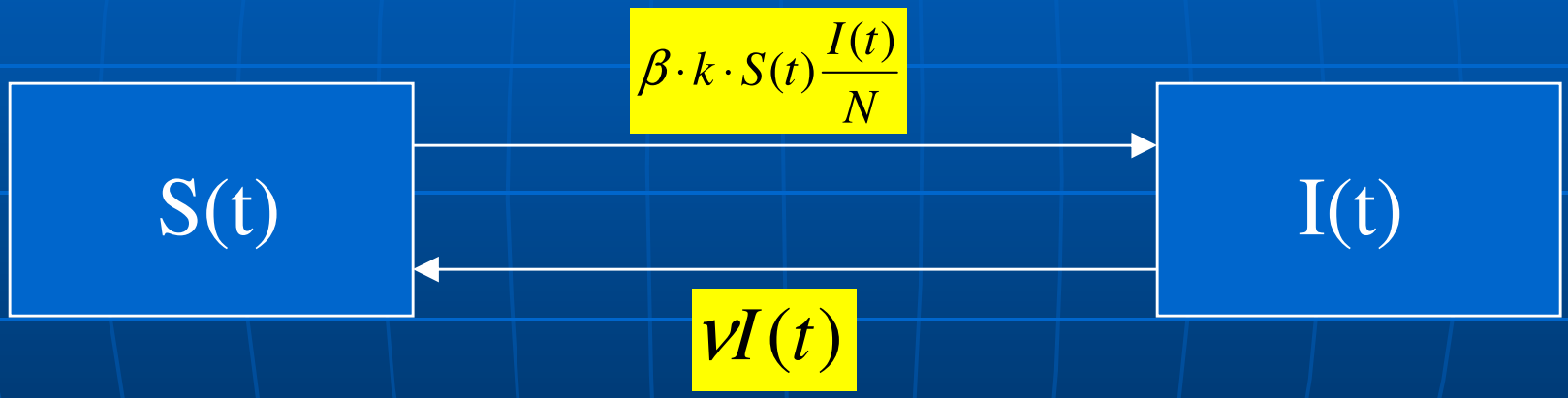
$$\frac{dS}{dt} = -\beta \cdot k \cdot S(t)\frac{I(t)}{N} + \nu I(t)$$

$$\frac{dI}{dt} = \beta \cdot k \cdot S(t)\frac{I(t)}{N} - \nu I(t)$$

S(t) = number susceptible
β = transmission parameter
k = number of partners

I(t) = number infected
v = recovery rate
N = total population

DYNAMIC MODEL



$$\frac{dS}{dt} = -\beta \cdot k \cdot S(t) \frac{I(t)}{N} + \nu I(t)$$

$$\frac{dI}{dt} = \beta \cdot k \cdot S(t) \frac{I(t)}{N} - \nu I(t)$$

Nieuwe uitdagingen voor de farmaco-economie

Introductie HPV-vaccin

Met de recente introductie van Gardasil en de verwachte registratie van Cervarix tegen humaan papillomavirus, rijst de vraag naar de kosteneffectiviteit van vaccinatie tegen baarmoederhalskanker, en naar de beste vaccinatiestrategie.

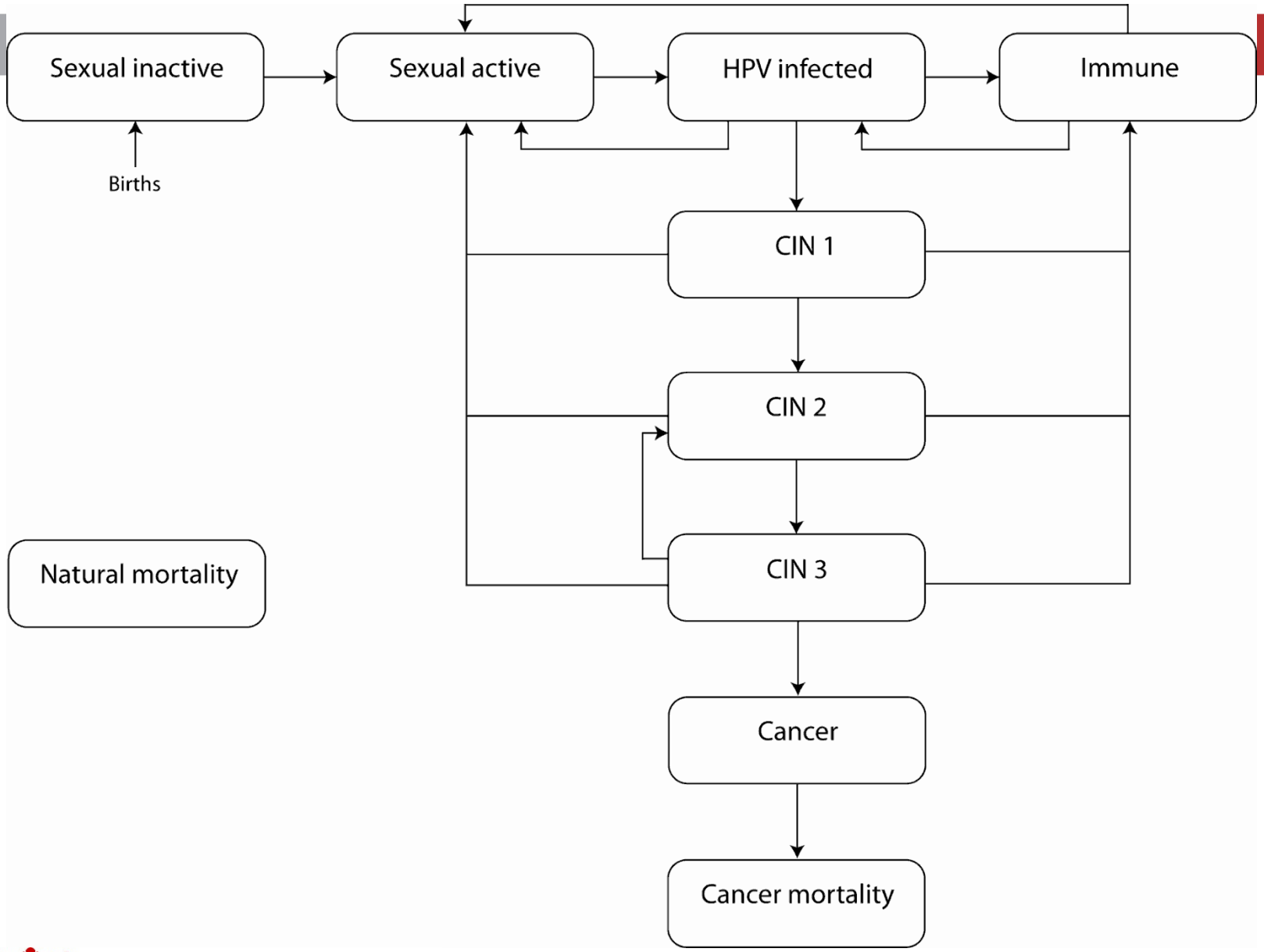
Tekst | *Maarten Postma, Hans Nijman, Toos Daemen, Ate van der Zee, Jan Wilschut*



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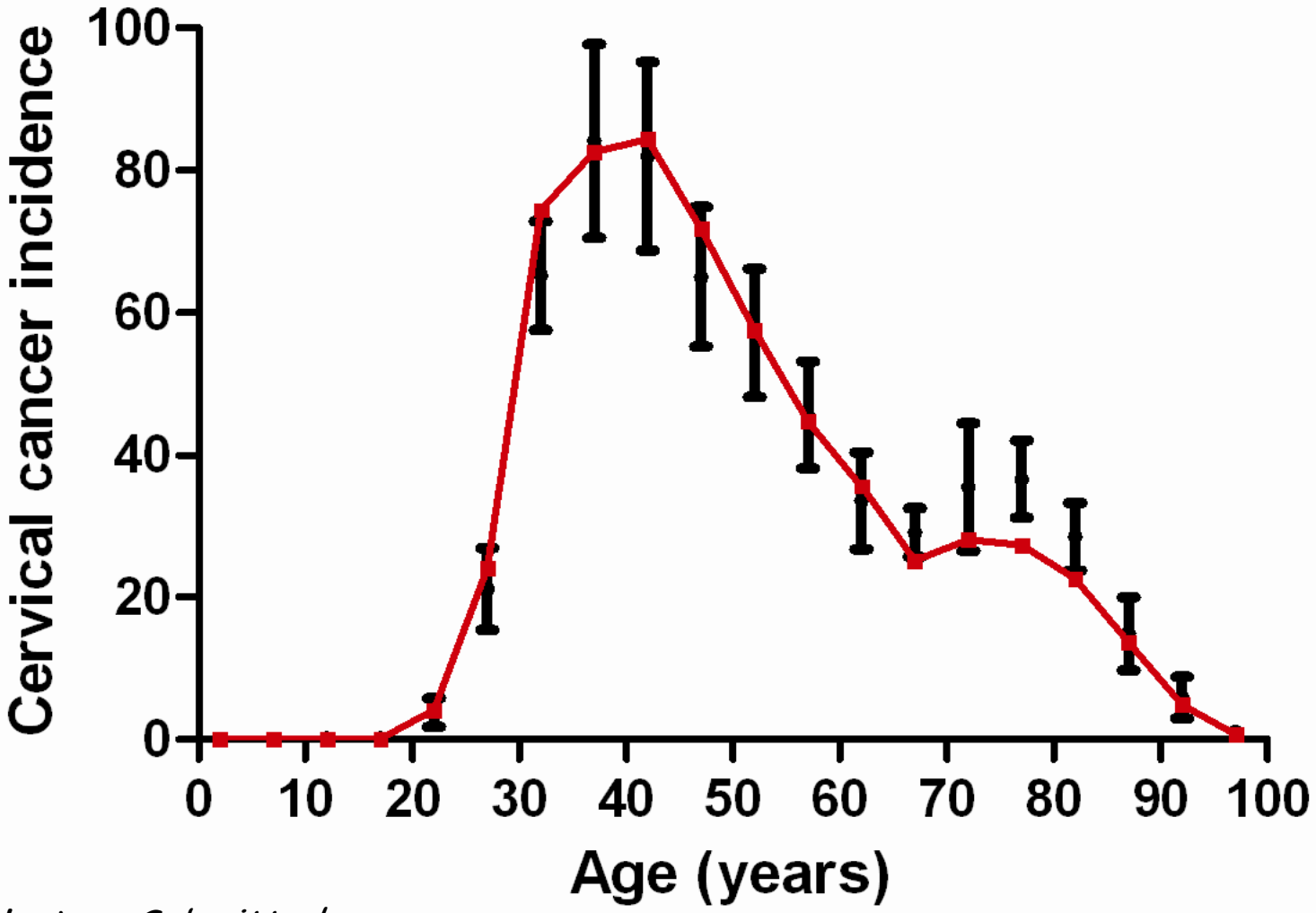
HPV-VACCINE

- HPV-vaccination in NL
  - 12 year-old girls
  - Bivalent vaccine was selected after tendering
  - Catch-up up-to-and-including 16 years
  - On top of successful screening program
- Unexpected low coverage of HPV vaccination at 50%
- Model calibration on
  - HPV-incidence for a sentinel study
  - National cancer registries



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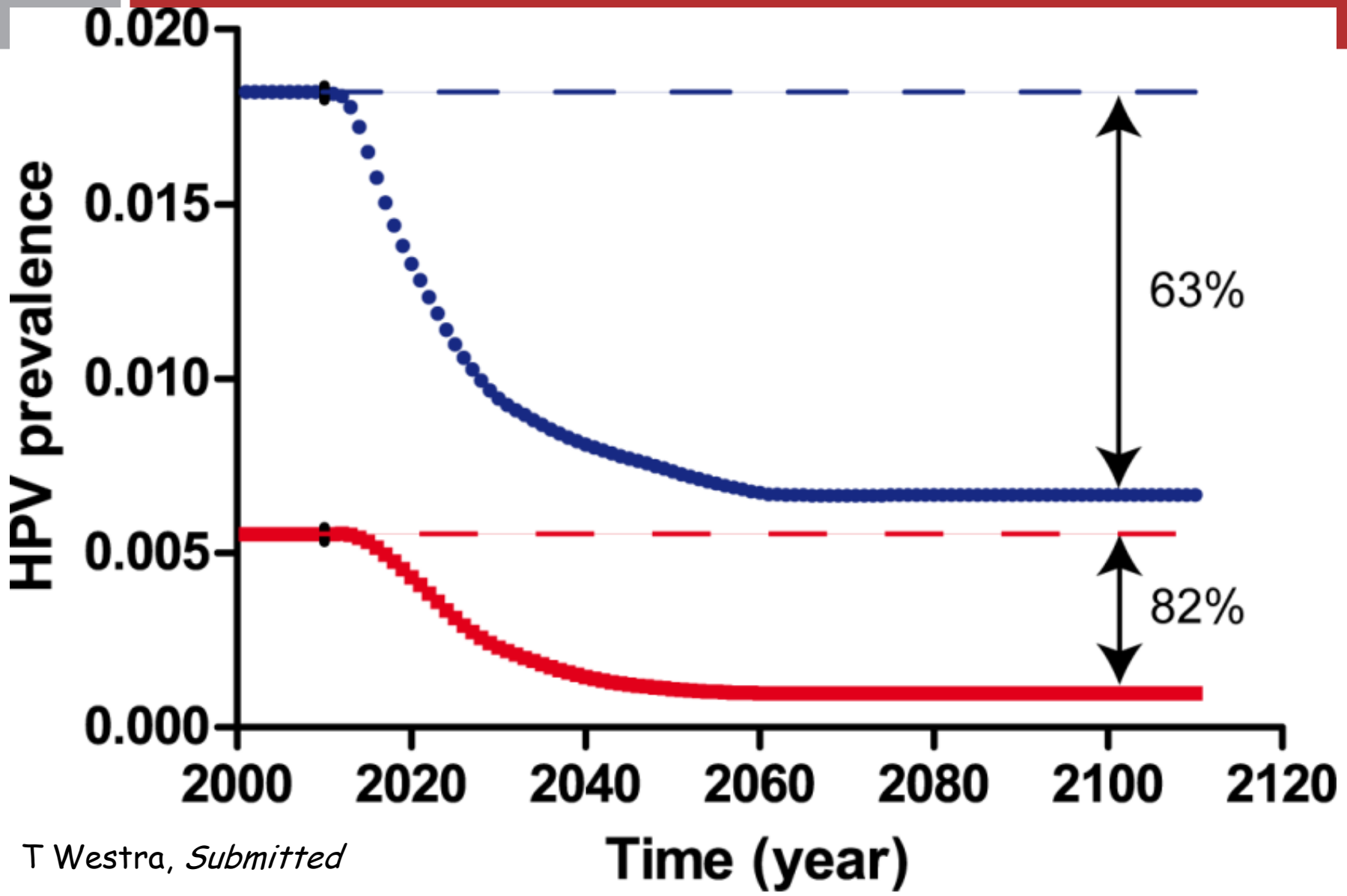
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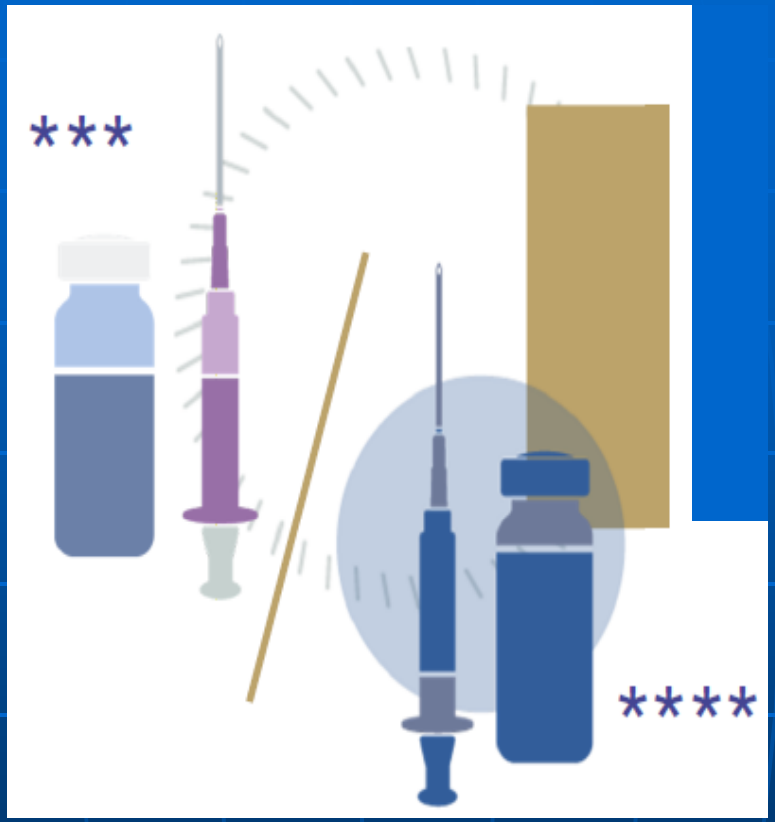


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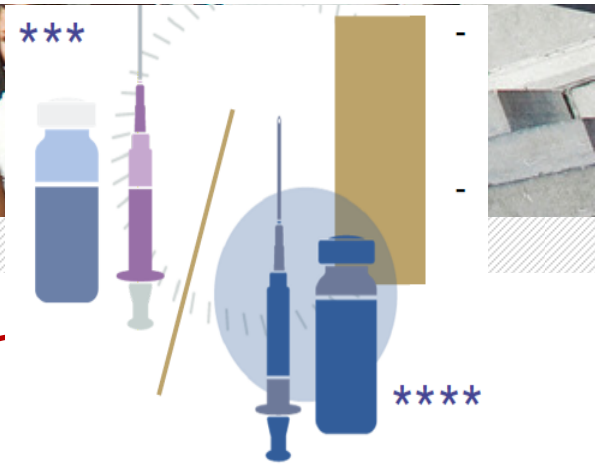
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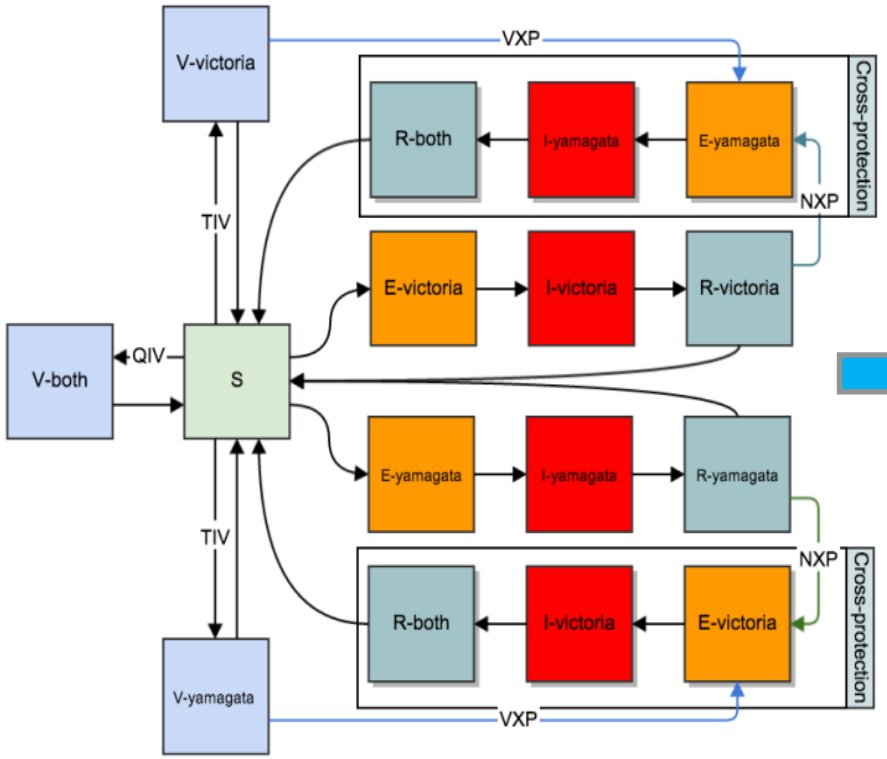
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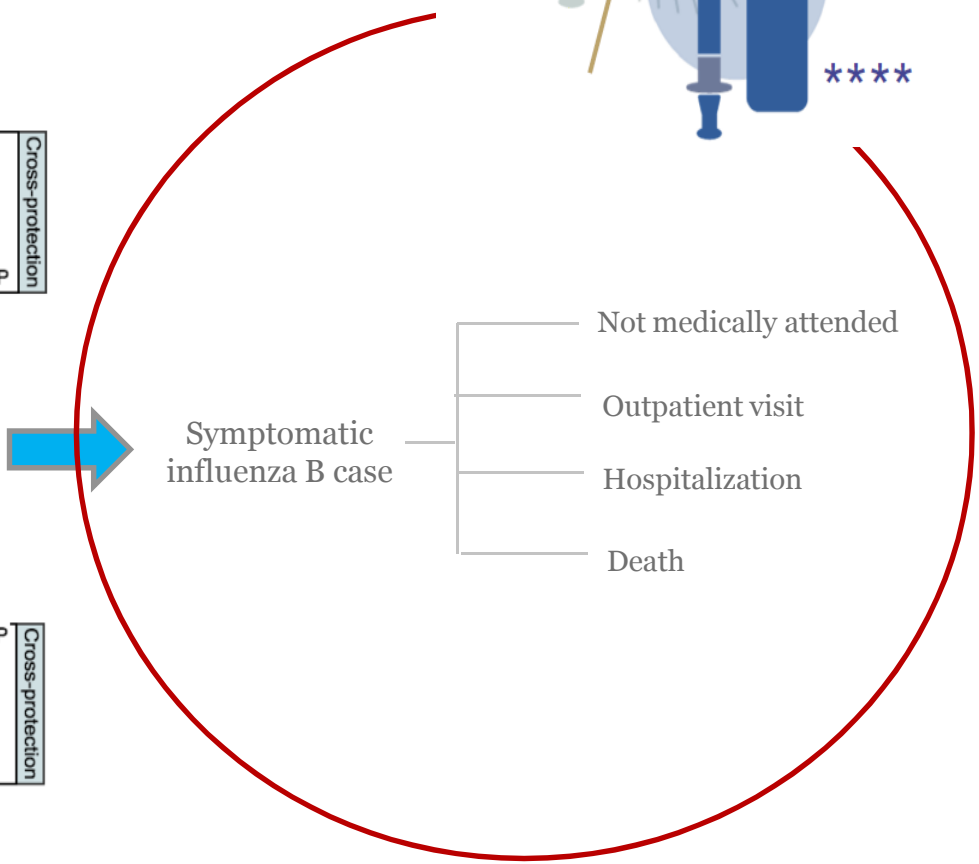


QIV

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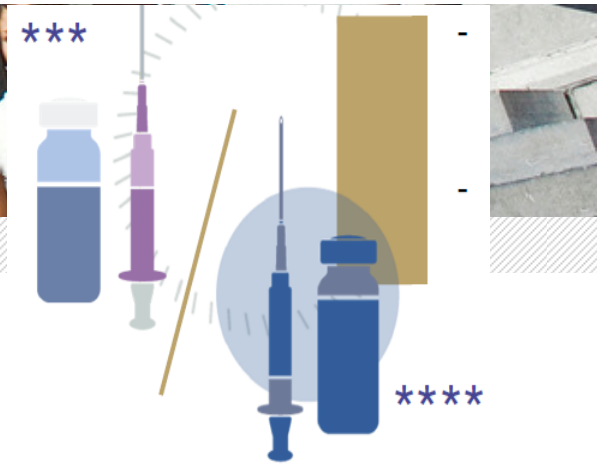


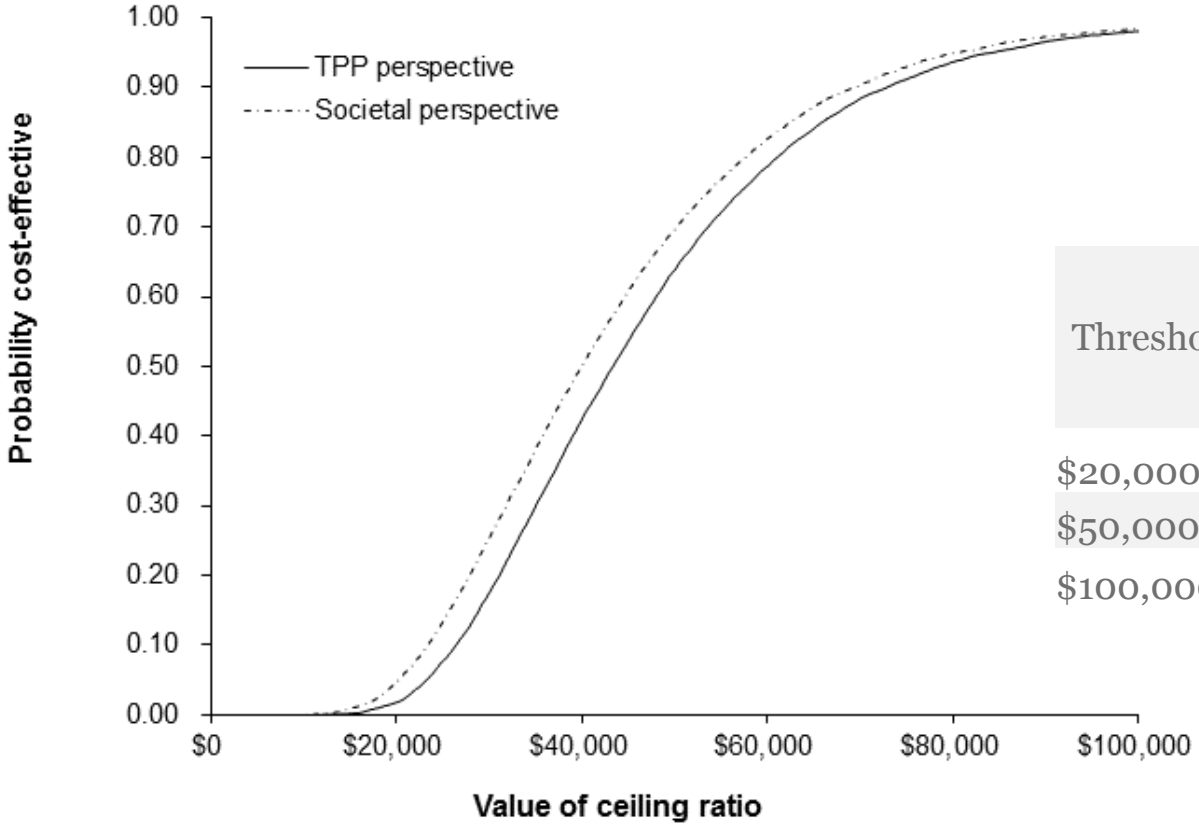


Epidemiological model

Economic model

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Threshold ($/QALY)	% of Simulations Cost-effective	
	TPP	Societal
$20,000	2%	5%
$50,000	64%	70%
$100,000	98%	99%

GUIDELINES

- How to interprete the cost-effectiveness ratio?
- Lack of hard endpoints in trials
- Discounting
- Type of model to use
- Societal perspective

SOCIETAL PERSPECTIVE

- As opposed to TPP (NICE)
- All benefits and losses, irrespective of who gains and loses
- Morbidity (sickness leave) and mortality (life years lost)
- Friction costs vs. human capital
- Double counting

SUMMARIZING

- Role of health economics
  - NIP
  - RP
- Discounting
  - Do
  - Differential or not?
  - Decreasing or constant?
- Dynamic models and beyond
  - As simple as possible
  - As complex as required, often the case
  - However, major investment
- Perspective
  - Differs per country, inclusive specific method used