Implementation of New Health Care Technologies

Past, Present and Future

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OSLO UNIVERSITY HOSPITAL

Outline

- **Defining** Health Technologies and Implementation
- **Past** - Emergence of Health Technology Assessment
- **Present** - Changing Landscape of Evidence
- **(Near) Future** - Challenges and Opportunities
- **Summing up**

Defining health technology

- A health technology can be a test, device, medicine, vaccine, procedure, program, or system.[1]

1. O'Rourke, B. et al. (2020). The new definition of health technology assessment: A milestone in international collaboration. *Int J Technol Assess Health Care*.
2. Icons made from www.onlinewebfonts.com

Defining implementation

- The process by which health technologies, following **evidence generation**, **evaluation** and **decision-making**, are adopted into clinical practice and become **accessible** to patients.

Past (1883-1999)

Emergence of Health Technology Assessment

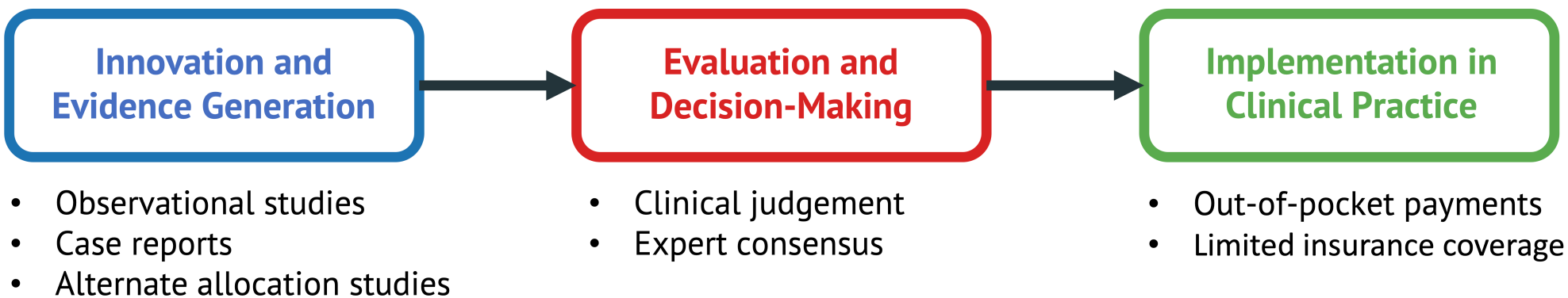
Historical expansion of health coverage

- **1883**: Bismarck introduces first insurance-based health system in Germany
  - Example followed by Western and Central European countries by 1930's
- **1948**: The tax-funded National Health Service (NHS) established in the UK following Beveridge's 1942 report
- **1965**: U.S. introduces Medicare and Medicaid to improve health care access for elderly and low-income

Tulchinsky, T. H., & Varavikova, E. A. (2014). A History of Public Health. In *The New Public Health* (pp. 1–42). Elsevier.

Implementation of new health technologies in the early 1900's

- Technologies introduced in the early 1900's include antibiotics, vaccines, electrocardiograph



Thalidomide tragedy

- Thalidomide was a widely used drug during the late 1950s and early 1960s to treat nausea in pregnant women.
- In 1961, a link between thalidomide and severe birth defects was found
- Estimated that over 10,000 children worldwide were born with malformations due to thalidomide

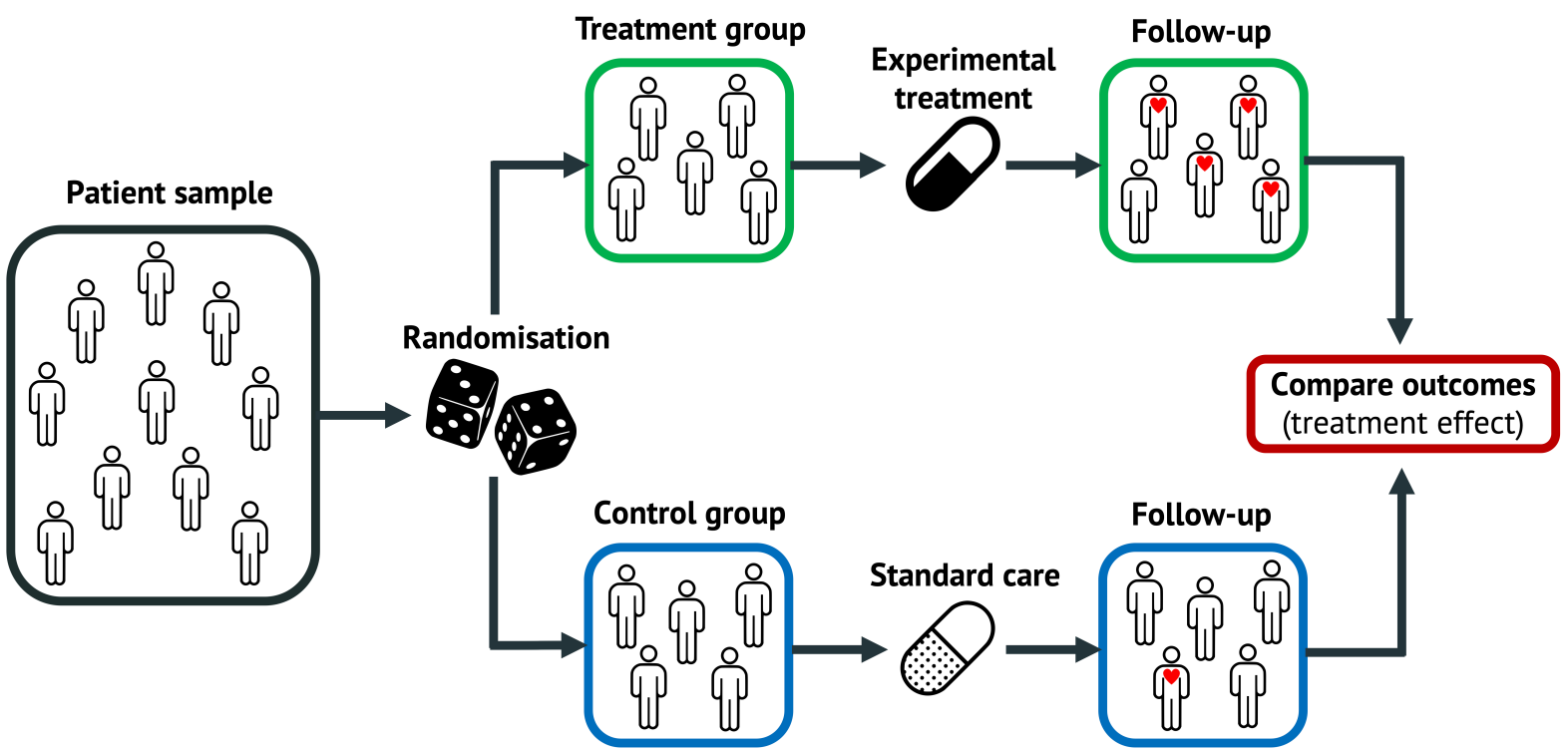
Kim, J. H., & Scialli, A. R. (2011). Thalidomide: the tragedy of birth defects and the effective treatment of disease. *Toxicological sciences*.

The 1962 Drug Efficacy Amendments in the U.S.

- The Kefauver-Harris Drug Amendments were enacted in 1962 in the U.S. in response to the thalidomide tragedy
- New law required drugs to demonstrate not only safety but also **effectiveness** prior to approval by the U.S. Food and Drug Administration (FDA)
- FDA approval requires evidence from well-controlled studies, reinforcing the role of the **Randomised Controlled Trial (RCT)**

The Randomised Controlled Trial (RCT)

- The RCT has become the **gold standard** for identifying **treatment effects**
  - The 1948 British Medical Research Council's trial of streptomycin for tuberculosis is often cited as the first proper RCT



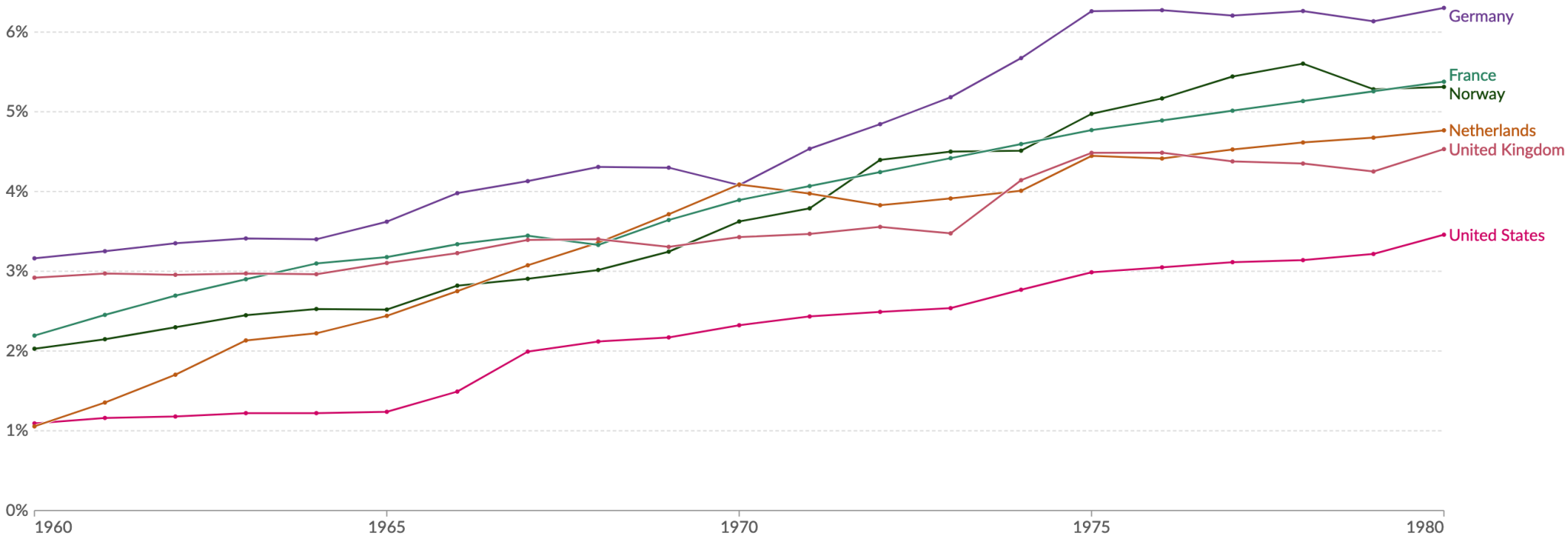
Government health expenditure as a share of GDP, 1960 to 1980

This metric captures spending on government funded health care systems and social health insurance, as well as compulsory health insurance.

Our World in Data

Table | Map | Chart

Edit countries and regions | Settings



Play time-lapse | 1880 | 2021

Data source: Our World In Data based on Lindert (1994), OECD (1993), OECD Stat – Learn more about this data

Note: Health spending includes final consumption of health care goods and services (i.e. current health expenditure). This excludes spending on capital investments.

OurWorldInData.org/financing-healthcare | CC BY

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Reasons for rising health expenditure

- **Introduction of new health technologies**
  - E.g. laboratory tests, medical imaging technologies (CT, MRI, ultrasound), pacemakers, renal dialysis machines
- **Aging**
  - As people live longer, the prevalence of age-related disease increases
- **Changing patterns of disease**
  - Shift from infectious to chronic and non-communicable diseases
- **Increasing demand for health care services**
  - Partly due to health insurance reducing financial barriers for consumers

Beginnings of Health Technology Assessment

- Need for **cost control**, and **greater efficiency** in particular use of new health technologies[1]
- **1976:** Report by the U.S. Office of Technology Assessment (OTA):
  - *"Development of Medical Technology: Opportunities for Assessment"*
- **1987:** Establishment of the Swedish Council on Technology Assessment in Health Care
- **1991**: European Health Ministers identified **Health Technology Assessment** as a key tool to improve the management of scarce resources[1]

1. Banta, D. (1997). Introduction to the EUR-ASSESS report. *Int J Technol Assess Health Care*.

Health Technology Assessment (HTA)

is a multidisciplinary process that uses explicit methods to determine the **value of a health technology**[1] at different points in its lifecycle. The purpose is to **inform decision making** in order to promote an equitable, efficient, and high-quality health system[2].

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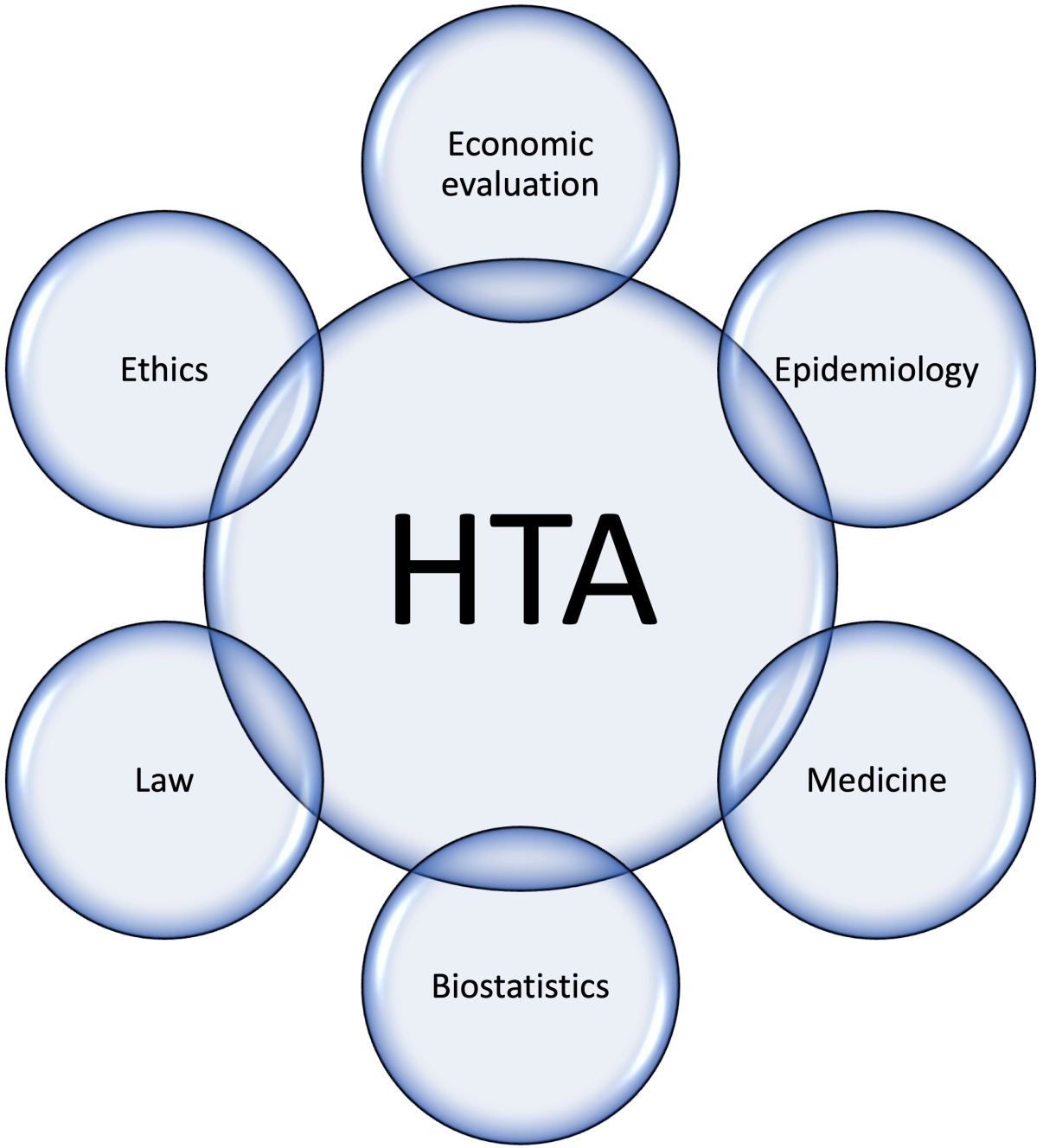
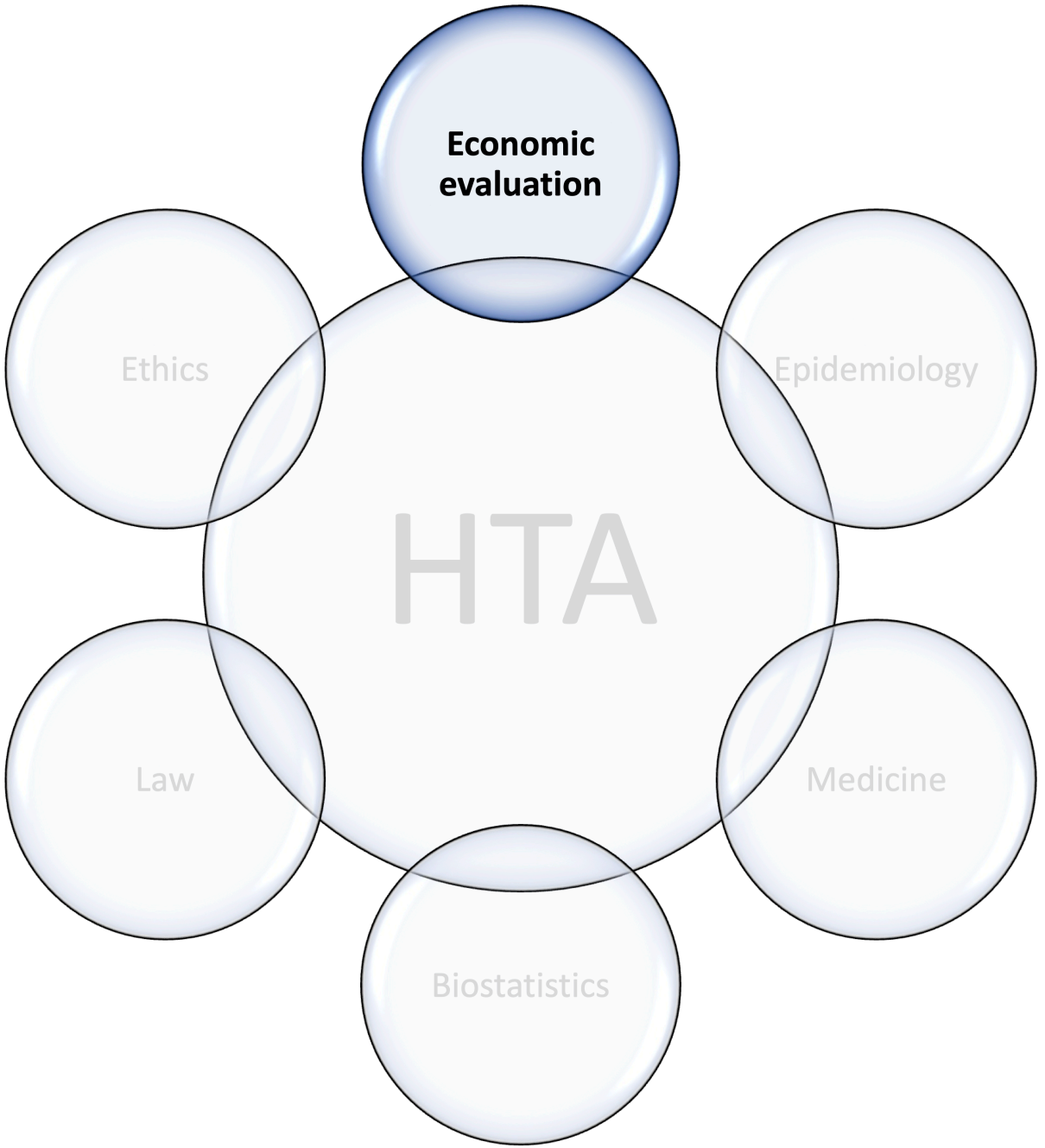
2. O'Rourke, B. et al. (2020). The new definition of health technology assessment: A milestone in international collaboration. *Int J Technol Assess Health Care*.


Economic evaluation
Ethics
Epidemiology
HTA
Law
Medicine
Biostatistics


Economic evaluation
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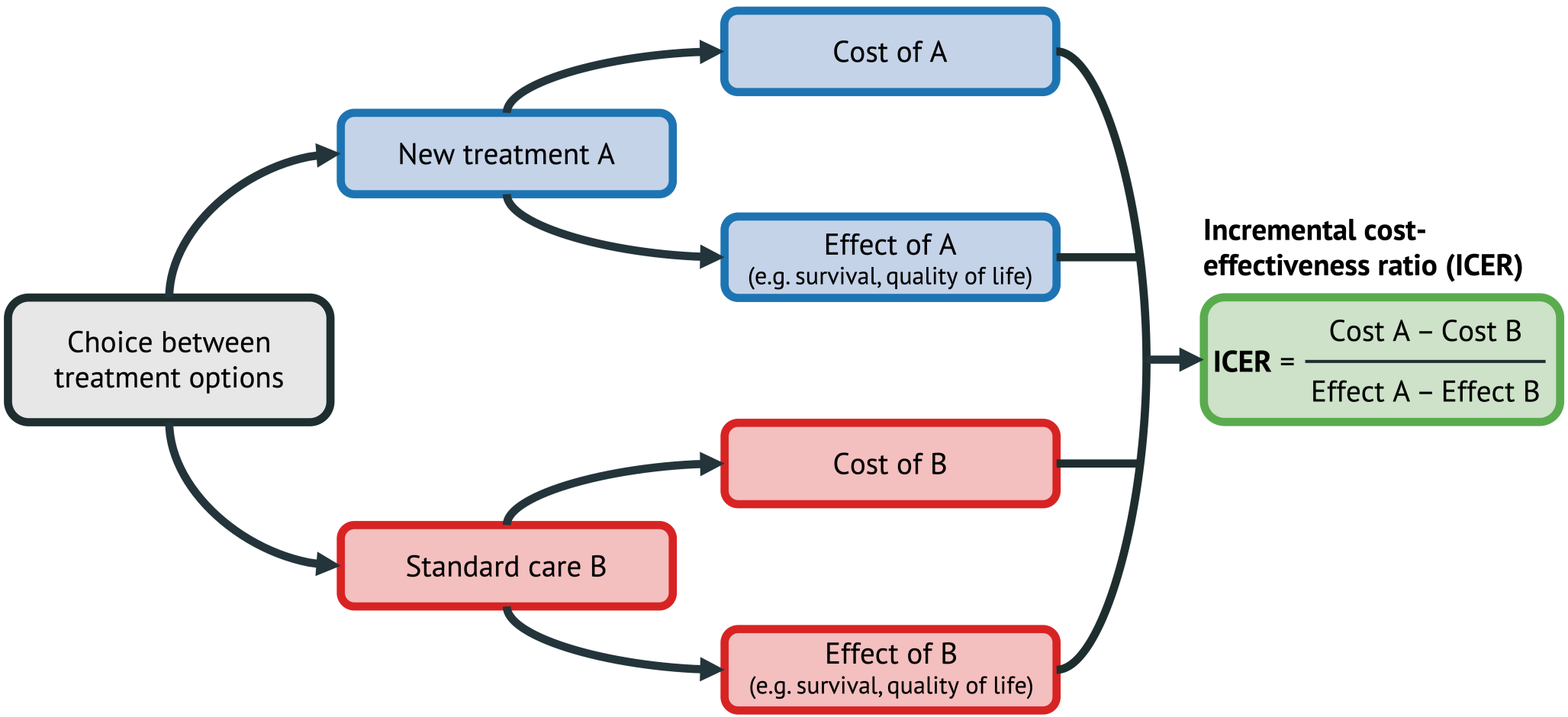
Economic evaluation

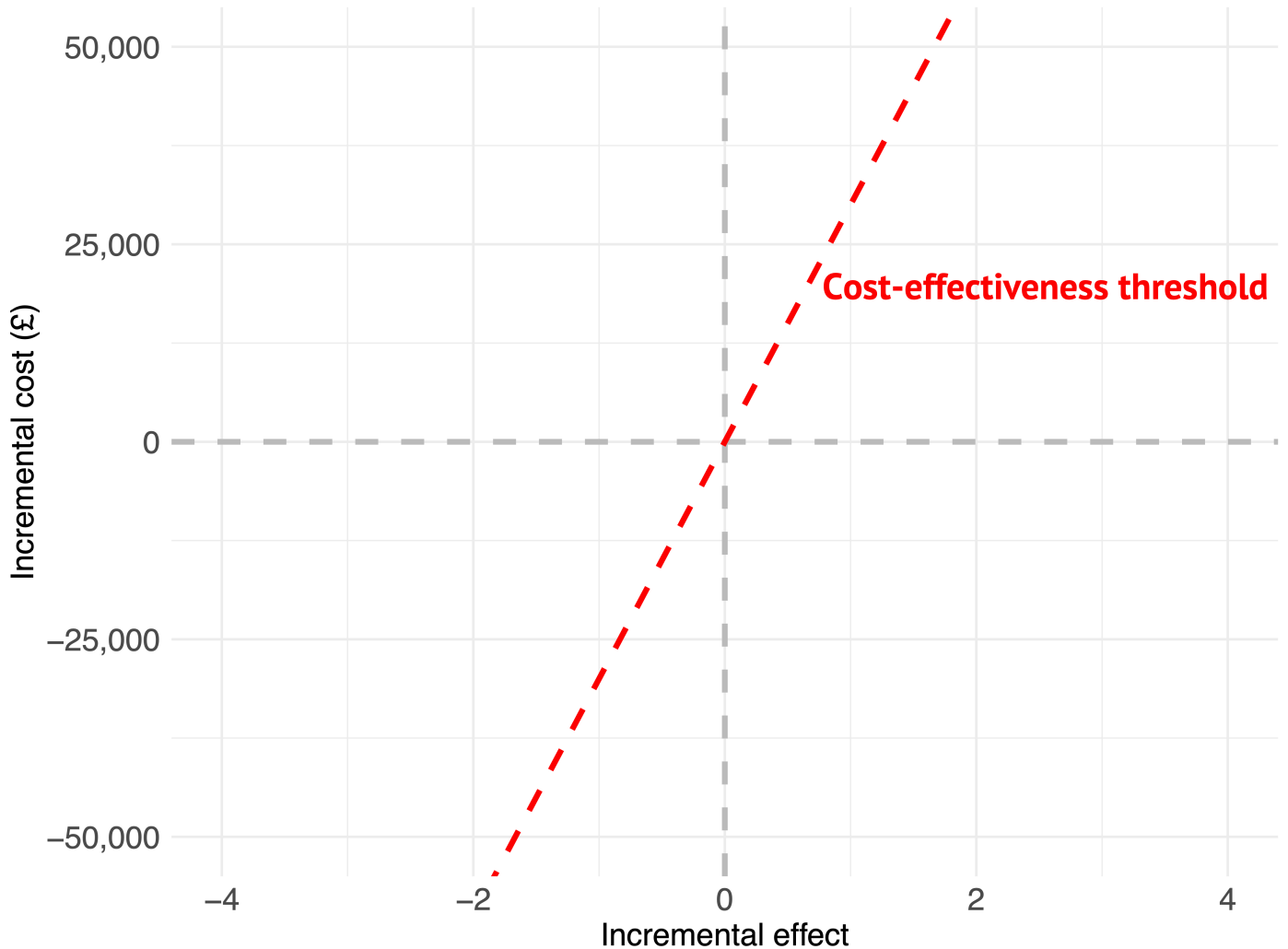
- Economic evaluation is the comparative analysis of alternative courses of action in terms of both their **costs** and **outcomes**[1]

- Principles behind economic evaluation
  - **Resources are scarce**; there is a limited amount of time, labor, money and materials to allocate to health care
  - **Scarcity necessitates choices** about which health technologies to fund from available resources
  - **Choices have an opportunity cost**; i.e. the health gains that could have been achieved elsewhere with the same levels of investment

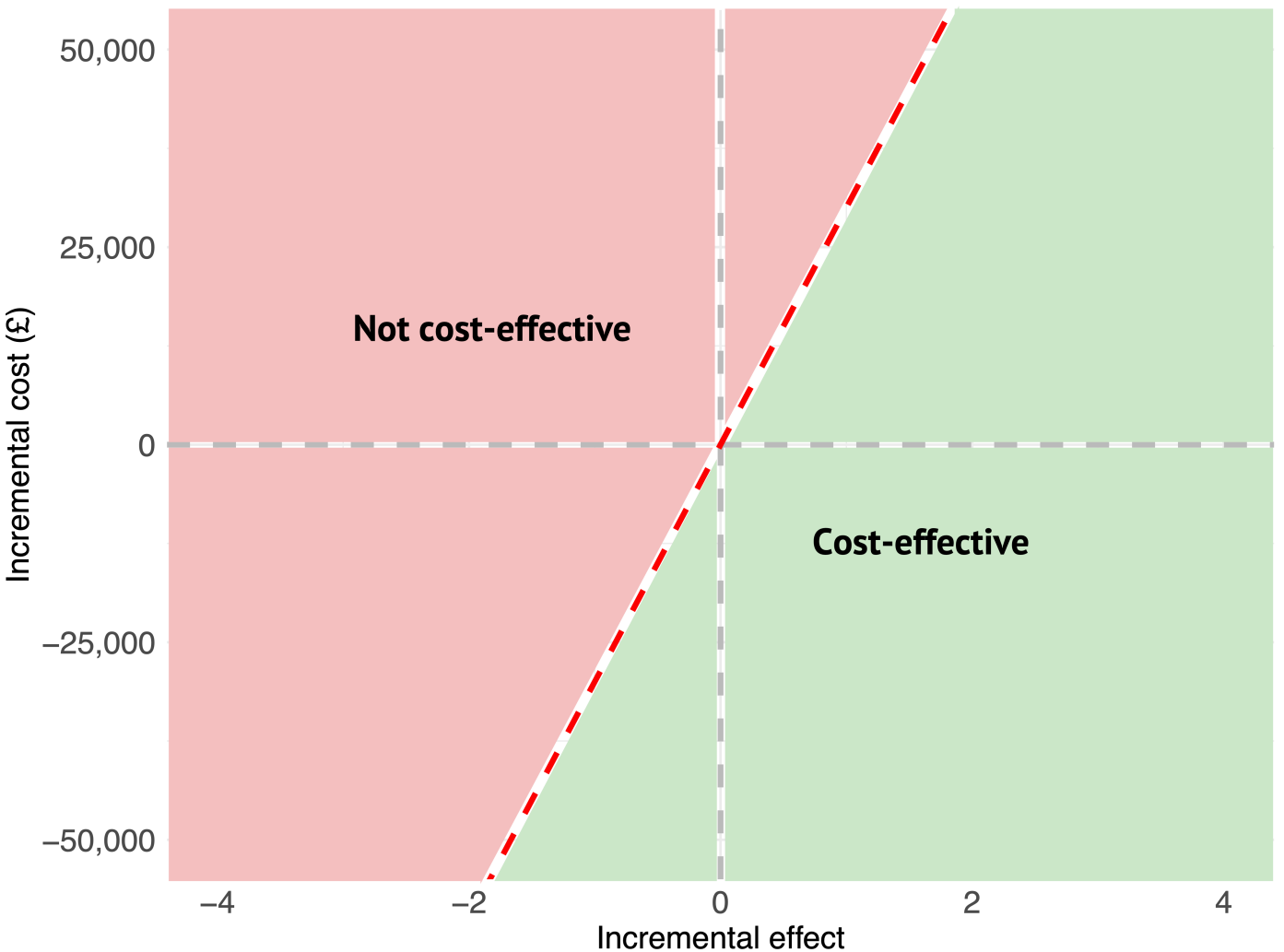
Cost-effectiveness



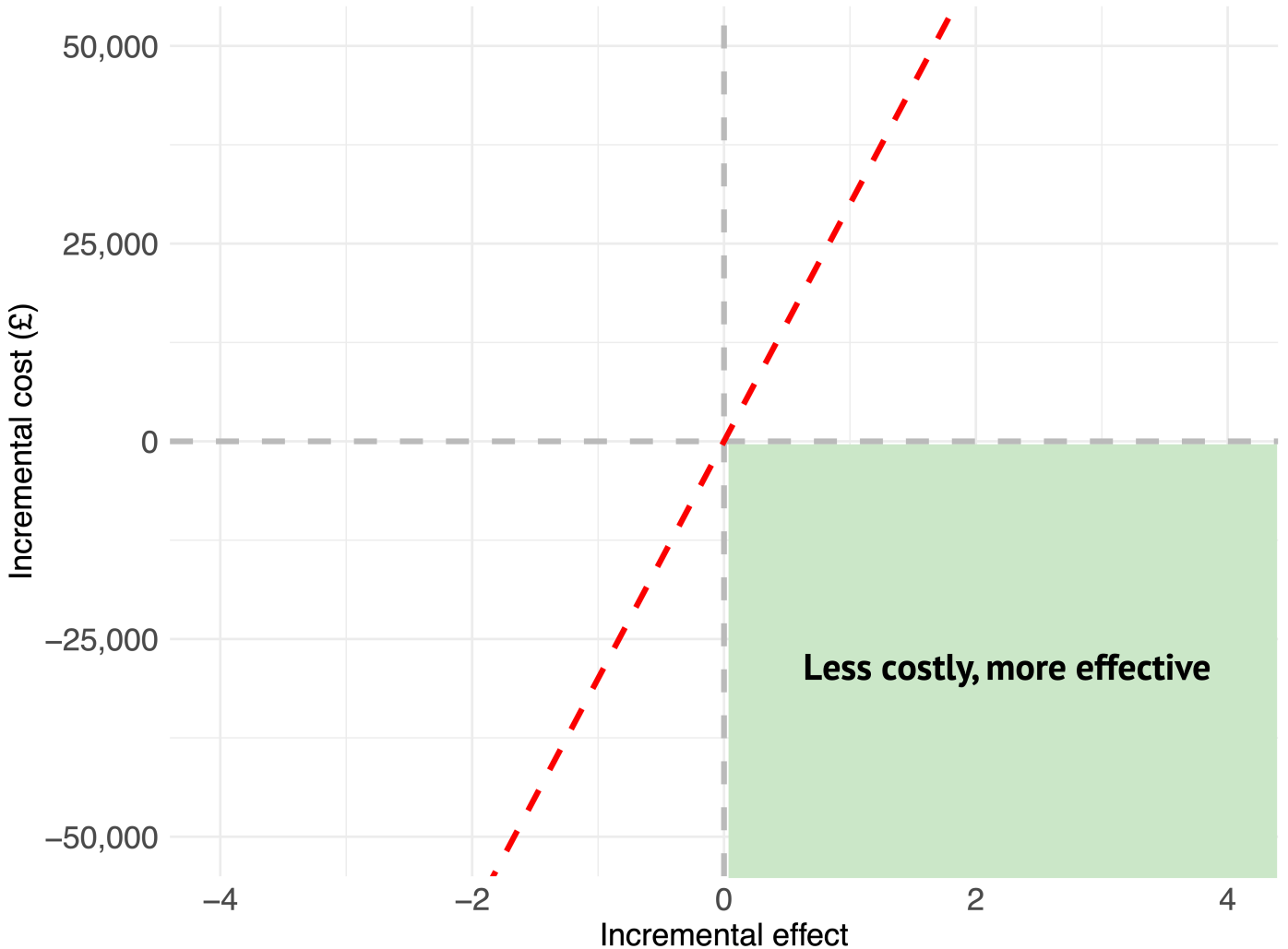
Cost-effectiveness plane



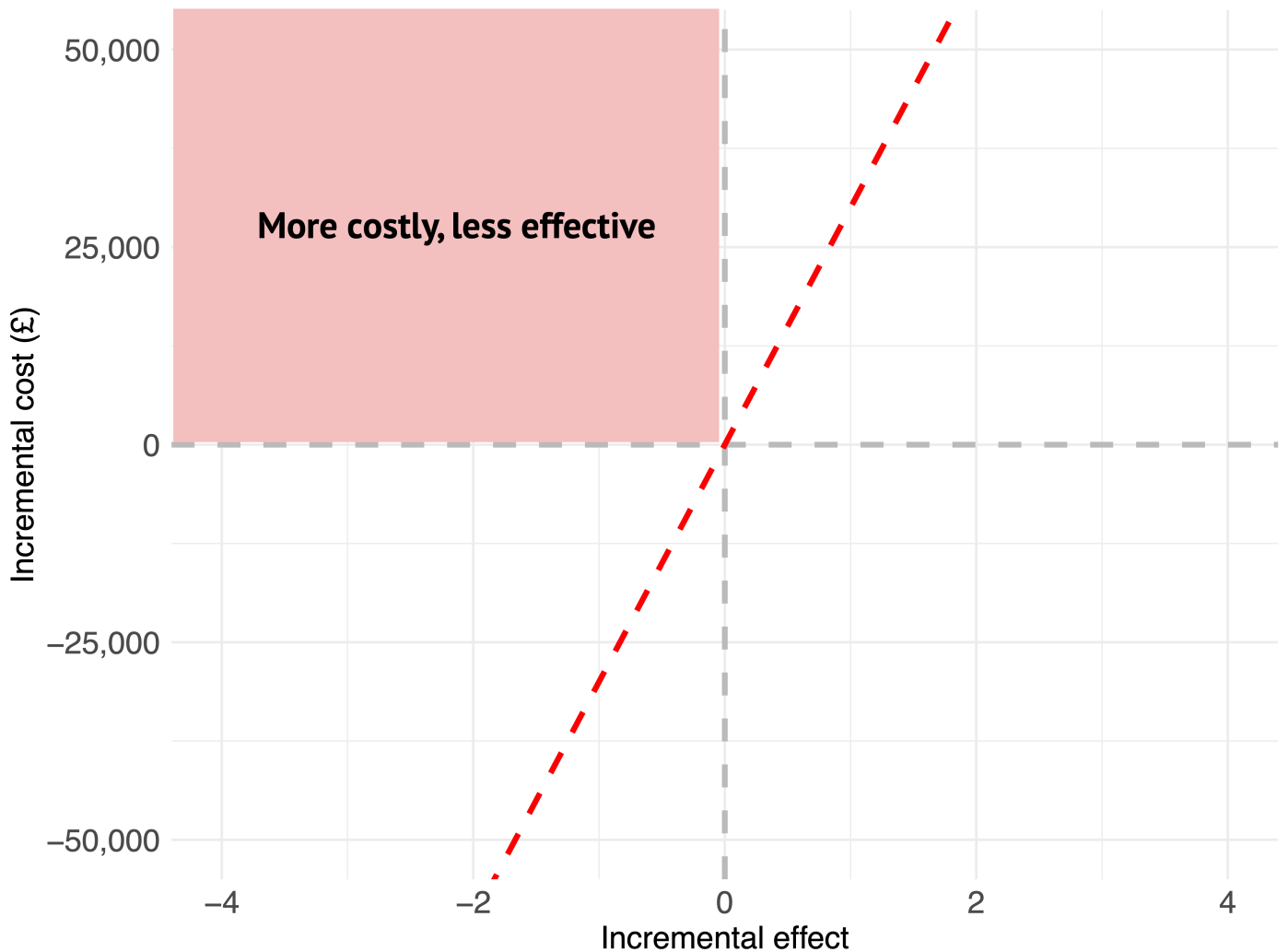
Cost-effectiveness plane



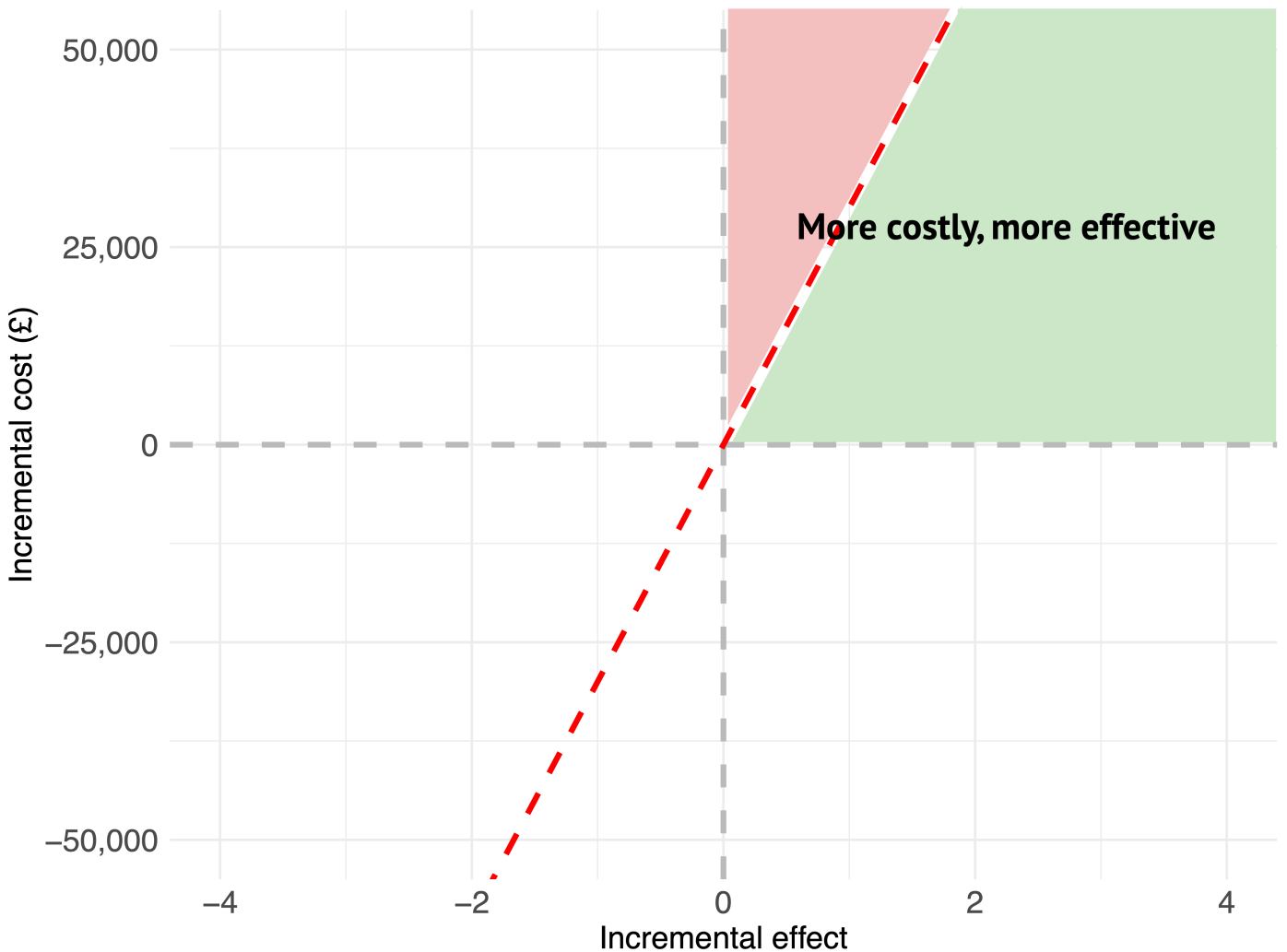
Cost-effectiveness plane



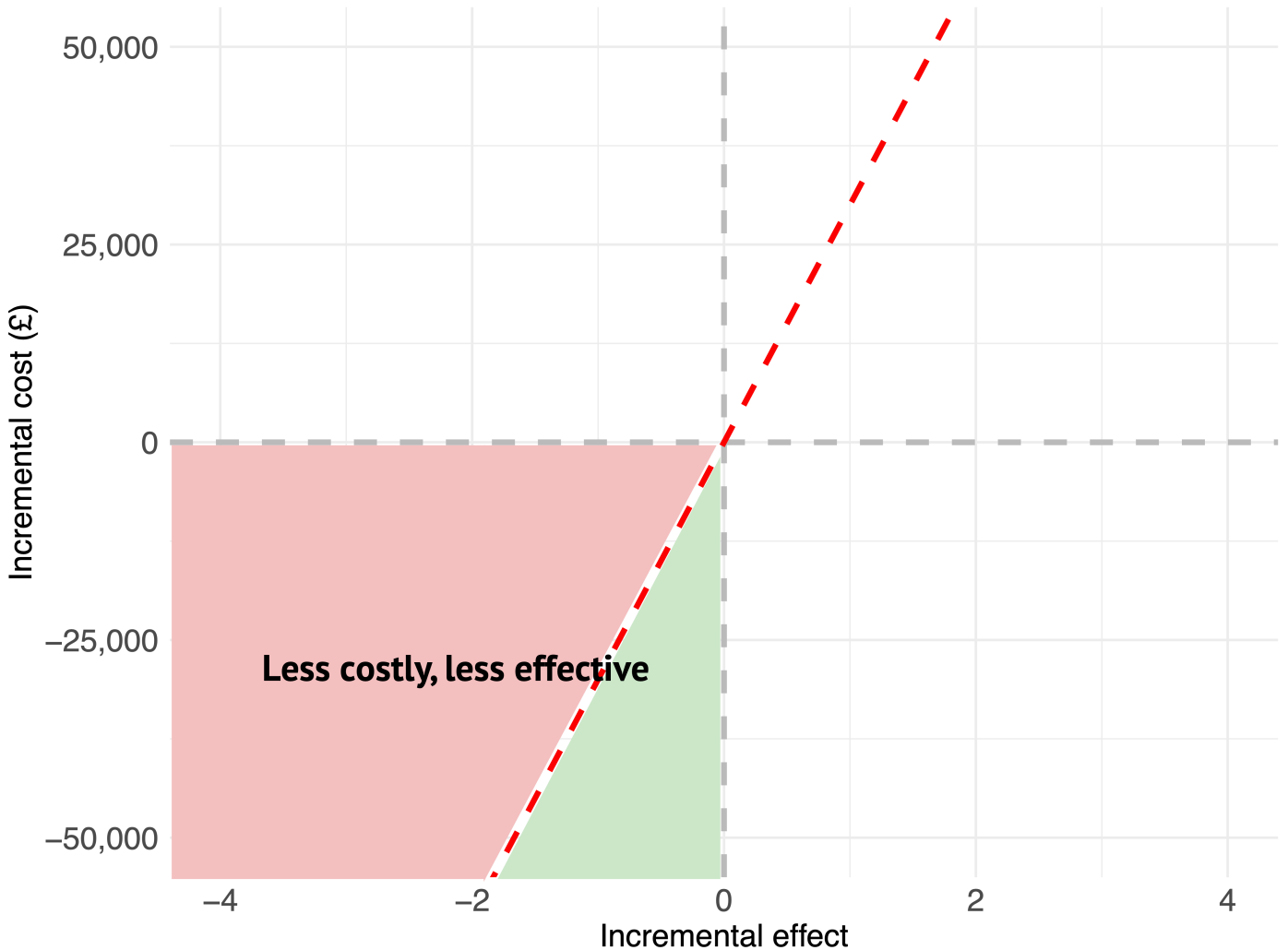
Cost-effectiveness plane



Cost-effectiveness plane



Cost-effectiveness plane



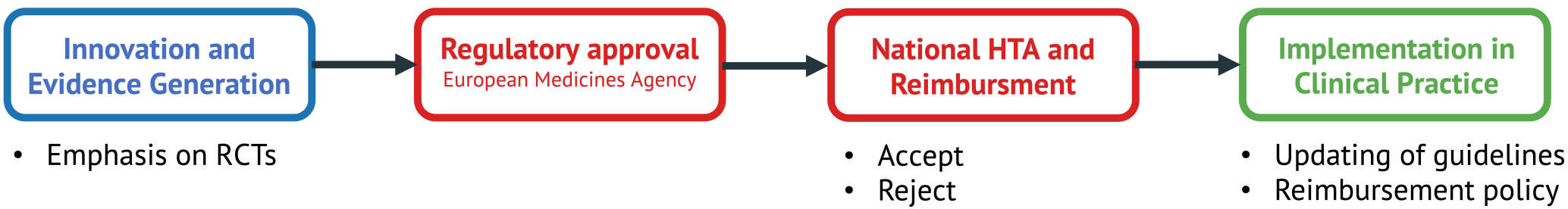
Economic evaluation in health care decision making

- **1993:** Economic analyses are formally required as part of submissions to the Australian Pharmaceutical Benefits Advisory Committee
  - Policy soon adopted by many other countries
- **1999**: Establishment of the National Institute for Health and Care Excellence (NICE) in the UK
  - NICE's technology appraisal guidelines and methods are internationally recognized

Present (2000 - 2023)

Changing Landscape of Evidence

Implementation of new pharmaceuticals in Europe by early 2000's



- **Key difference** between regulatory approval and HTA and reimbursement:
  - Regulatory approval focuses on assessing the **benefit/risk ratio** of treatments
  - HTA and reimbursement decisions require estimating the **absolute magnitude** of treatment benefits and costs over a patient's **lifetime** to determine the value of a treatment

Accelerated licensing of new pharmaceuticals

- The European Medicines Agency (EMA) introduced **accelerated licensing mechanisms** for new pharmaceuticals
  - Including ‘conditional marketing authorization’ in 2006 and ‘adaptive pathways’ in 2014
- Consequently, HTA and reimbursement now more often depend on:
  - Non-randomised evidence and real-world data
  - Immature survival data (i.e. absence of long-term data on survival outcomes)
  - Surrogate outcomes
- These trends are especially pronounced for new **cancer treatments**, which represent **454 (48%)** of 943 NICE technology appraisals since 2000

Consequences of less comprehensive evidence

- **Uncertainty about the treatment effect**
  - Uncertainty about whether and to what extent a new treatment improves survival and quality of life
- **Uncertainty about cost-effectiveness**
  - Greater uncertainty about whether the treatment benefit justifies the additional cost
- **Increased risk of wrong reimbursement decisions**
  - I.e. paying for a technology that does not provide good value to the health care system

Concerns about added value of new treatments

European Journal of Cancer 182 (2023) 23–37

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Belgian observational survival data (incidence years 2004–2017) and expenditure for innovative oncology drugs in twelve cancer indications

Mattias Neyt [a,*], Carl Devos [a], Nancy Thiry [a], Geert Silversmit [b], Cindy De Gendt [b], Nancy Van Damme [b], Diego Castanares-Zapatero [a], Frank Hulstaert [a], Leen Verleye [a]

[a] *Belgian Health Care Knowledge Centre (KCE), Belgium*
[b] *Belgian Cancer Registry (BCR), Belgium*

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KEYWORDS
Antineoplastic agents;
Therapies;
Investigational;
Technology;
High-cost;
Observational study

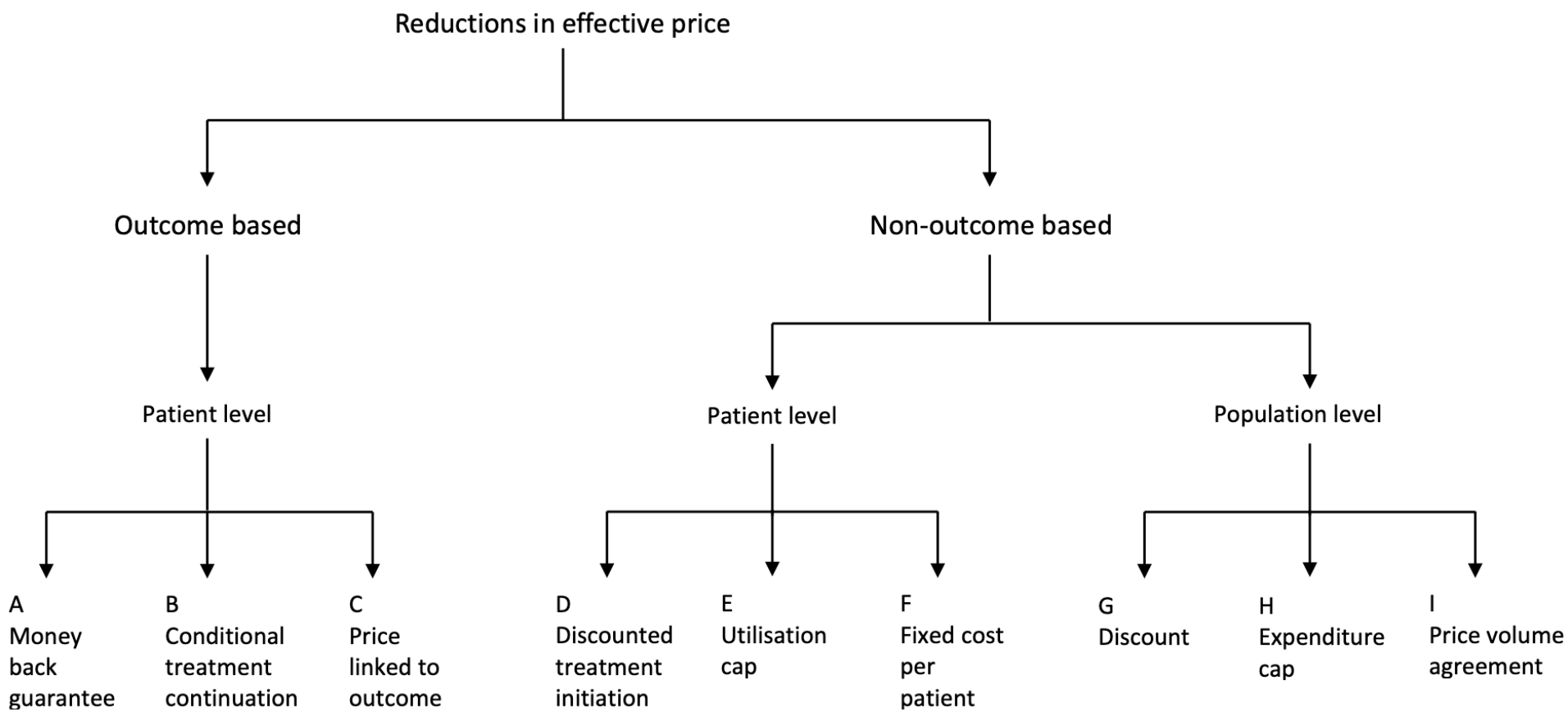
Abstract ***Background:*** The Food and Drug Administration and European Medicines Agency typically approve market access for cancer drugs based on surrogate end-points, which do not always translate into substantiated improvements in outcomes that matter the most to patients, i.e. survival and quality of life. These drugs often, also, have a high price tag. We assessed whether there was an increase in cancer drug expenditure for a broad selection of indications, and whether this correlates with increased overall survival.
Methods: This cohort study used Belgian Cancer Registry data from 125,692 patients (12 cancer indications, incidence period 2004–2017), which was linked to reimbursement and survival data. This reliably represents the Belgian situation. One-to-five year observed survival probability, median survival time, oncology drug expenditure and mean oncology drug cost per patient were reviewed.
Findings: In almost all indications, total expenditure and average treatment cost for oncology drugs increased over the years (2004–2017). In contrast, mixed findings are observed for the evolution in overall survival probability and median survival time. While an absolute improvement in the 3-year survival probability of about 10% is noticed in non-small-cell lung cancer and chronic myeloid leukaemia, improvements in about half of the other indications are limited or even absent.
Interpretation: The Belgian observational data indicate that assuming 'innovative' oncology drugs always add value in terms of improved survival is often unjustified. The literature also highlights the problem of using surrogate end-points, and the lack of comparative evidence

Managed entry agreements

- **Managed Entry Agreements (MEAs)** are schemes that allow access to new health technologies under conditions that aim to **reduce the risk** of making a wrong reimbursement decision

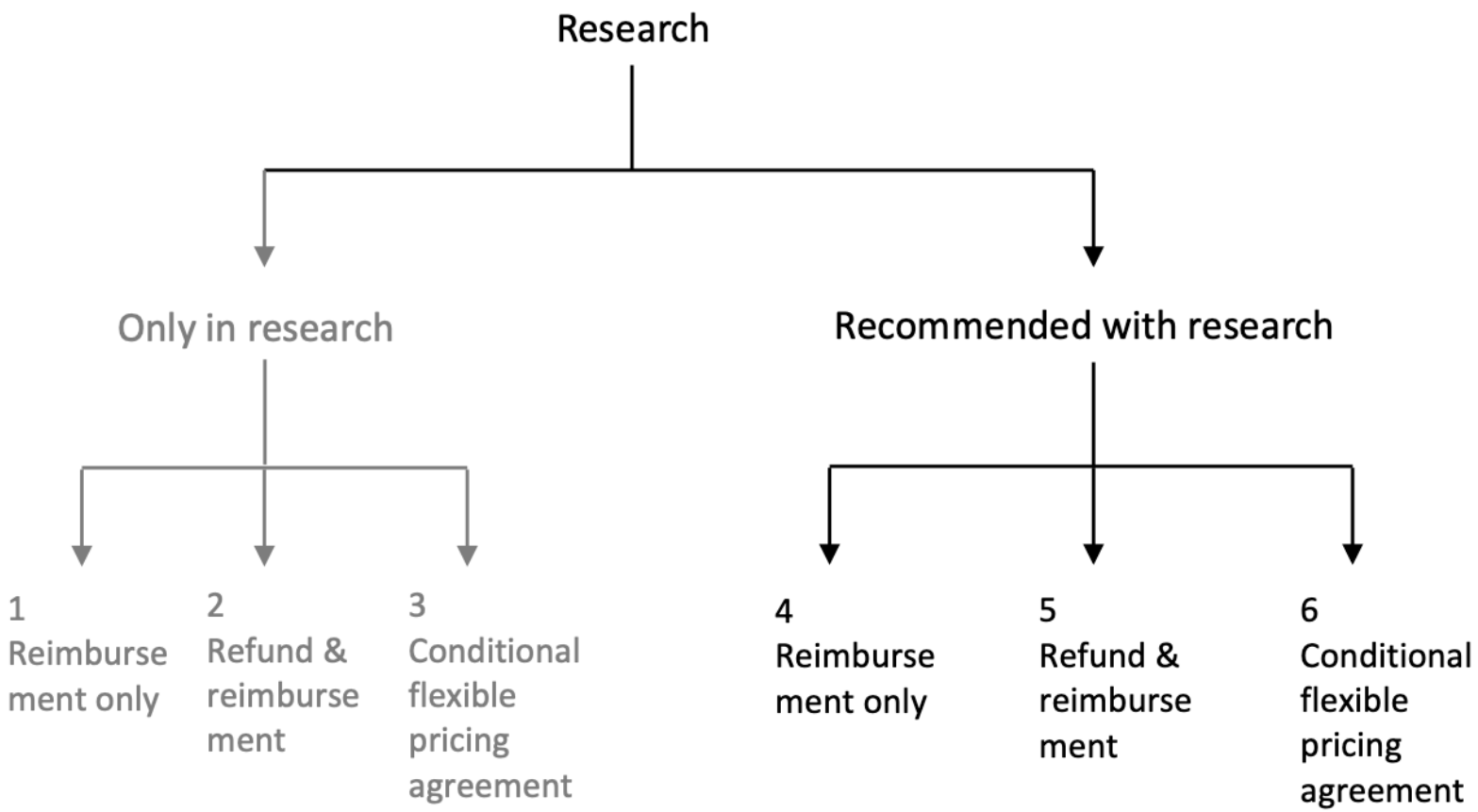
- **MEAs** can be categorised into:
  - Price reduction schemes
  - Research schemes

Price reduction schemes



Grimm, S. et al. (2016). Framework for analysing risk in health technology assessments and its application to managed entry agreements. *University of Sheffield*.

Research schemes



Grimm, S. et al. (2016). Framework for analysing risk in health technology assessments and its application to managed entry agreements. *University of Sheffield*.

The multiple sclerosis scheme in England

- Initiated in 2002, the scheme provided patient access to disease-modifying treatments for multiple sclerosis conditional on a 10-year monitoring study
  - Price review would take place at 2-year intervals if the observed benefit was less than predicted
- Despite the first analysis reporting no evidence of improved patient outcomes, funding for β-interferon continued
  - Furthermore, results were not published until 2 - 5 years after data became available
- NHS could have saved £250 million by 2010
  - if an assessment and price review had been completed after the first 2 years

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McCabe, C. et al. (2010). Continuing the multiple sclerosis risk sharing scheme is unjustified. *BMJ*.

Cancer Drugs Fund in England

- **2010:** Introduction of the Cancer Drugs Fund (CDF) in England
  - Provided patient access to new cancer drugs that had either not been appraised by NICE or had not been recommended
  - Created unsustainable financial pressure without evidence of patient benefit
- **2016:** Revision of the CDF
  - Purpose is to facilitate **early patient access** to promising but uncertain new cancer drugs while **additional data** are being collected
  - Highlighted the role of **real-world data** to address uncertainties

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Kang, J., & Cairns, J. (2023). “Don’t Think Twice, It’s All Right”: Using Additional Data to Reduce Uncertainty Regarding Oncologic Drugs Provided Through Managed Access Agreements in England. *PharmacoEconomics.*

Cancer Drugs Fund's impact on uncertainty

- **Immature survival data** are an important source of clinical uncertainty
  - This has largely been addressed by longer follow-up of patients in ongoing clinical trials

- **Real-world data** have not been widely used in CDF review appraisals and have done little to reduce uncertainty

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Kang, J., & Cairns, J. (2023). "Don't Think Twice, It's All Right": Using Additional Data to Reduce Uncertainty Regarding Oncologic Drugs Provided Through Managed Access Agreements in England. *PharmacoEconomics.*

Experiences with MEAs in Belgium

- MEAs were most commonly initiated due to a **lack of evidence on treatment benefits** and in the presence of **immature survival data**
- MEAs have not led to the collection of relevant additional evidence
- MEAs have provided early access with lower confidential prices
  - Unclear whether negotiated prices are in line with added value of new treatments
- Difficult to discontinue reimbursement once a drug has been approved through a MEA

Neyt, M. et al. (2020). An evaluation of managed entry agreements in Belgium: A system with threats and (high) potential if properly applied. *Health Policy*.

Experiences with MEAs in the Netherlands

- Only 1 out of 12 drugs has been processed within the envisioned 4-year period
- Collected data was of insufficient quality to answer a third of research questions
- For 6 of 12 finalized drugs, continued reimbursement was conditional on yet further evidence generation
- For 2 of 12 finalized drugs, advice to discontinue reimbursement has not been implemented

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Makady, A. et al. (2019). Implementing managed entry agreements in practice: The Dutch reality check. *Health Policy.*

VALUE IN HEALTH 20 (2017) 118–125

Available online at www.sciencedirect.com

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journal homepage: www.elsevier.com/locate/jval

The Challenge of Conditional Reimbursement: Stopping Reimbursement Can Be More Difficult Than Not Starting in the First Place!

E.J. van de Wetering, PhD[1], *Job van Exel, PhD*[2,*], *Werner B.F. Brouwer, PhD*[1]

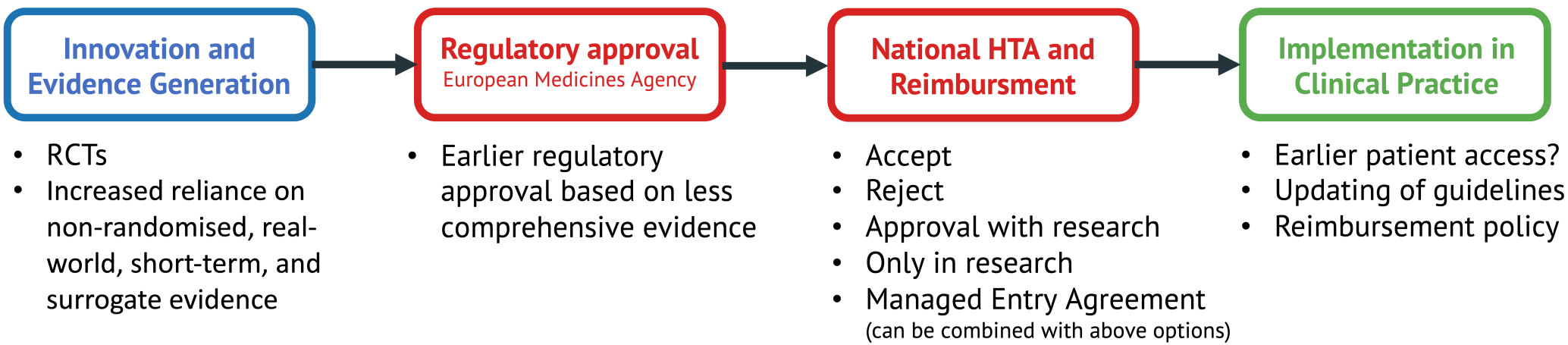
[1]*Institute of Health Policy and Management, Erasmus University Rotterdam, Rotterdam, The Netherlands;* [2]*Erasmus School of Economics, Erasmus University Rotterdam, The Netherlands*

ABSTRACT

Background: Conditional reimbursement of new health technologies is increasingly considered as a useful policy instrument. It allows gathering more robust evidence regarding effectiveness and cost-effectiveness of new technologies without delaying market access. Nevertheless, the literature suggests that ending reimbursement and provision of a technology when it proves not to be effective or cost-effective in practice may be difficult. **Objectives:** To investigate how policymakers and the general public in the Netherlands value removing a previously reimbursed treatment from the basic benefits package relative to not including a new treatment. **Methods:** To investigate this issue, we used discrete-choice experiments. Mixed multinomial logit models were used to analyze the data. Compensating variation values and changes in probability of acceptance were calculated for withdrawal of reimbursement. **Results:** The results show that, ceteris paribus, both the general public (n = 1169) and policymakers (n = 90) prefer a treatment that is presently reimbursed over one that is presently not yet reimbursed. **Conclusions:** Apparently, ending reimbursement is more difficult than not starting reimbursement in the first place, both for policymakers and for the public. Loss aversion is one of the possible explanations for this result. Policymakers in health care need to be aware of this effect before engaging in conditional reimbursement schemes.

Keywords: allocation decisions, compensating variation, conditional reimbursement, coverage with evidence development, discrete-choice models, medical technologies.

Implementation of new pharmaceuticals in Europe - present



- HTA processes and reimbursement decision options vary between countries

(Near) Future

Challenges and Opportunities

Future challenges and trends

- Evidential uncertainty is likely to further increase with further development of
  - Precision medicine leading to smaller patient groups
  - Advanced therapy medicinal products (ATMP), including ‘one-shot’ genetic treatments with curative potential, immuno-oncology and tumor-agnostic drugs
  - Accelerated regulatory approval based on on non-randomised, real-world, short-term and surrogate evidence

- Global spending on cancer drugs expected to increase from $218 billions in 2023 to $440 billions by 2028[1]
  - Driven by broader and longer use of therapies, including expected launch of 100 new drugs

1. IQVIA Global Drug Spend Report 2024

Opportunities - EU regulation 2021/2282 on HTA

- From January 2025, Member States' HTA agencies should:
  - Conduct **Joint Clinical Assessments** of new medicines and certain high-risk medical devices
  - Engage in **Joint Scientific Consultations** to advise technology developers on clinical study designs that generate appropriate evidence

- Harmonization of HTA across EU countries provides opportunities to
  - strengthen the position of HTA agencies to require appropriate evidence
  - ensure consistency between assessments and improve predictability for manufacturers
  - reduce the burden of the increasing number and complexity of assessments
  - adopt important methodologic developments
  - joint learning by sharing experiences

Success factors for MEAs

- Can decision uncertainty be reduced by further data collection?
- Can relevant clinical or economic outcomes be clearly defined and measured?
- Are the timelines for the MEA reasonable?
- Is the collection and analysis of data easily implementable and affordable?
- Are there clear decision rules following the data collection and analysis?

Drummond, M. (2015). When do performance-based risk-sharing arrangements make sense? *The European Journal of Health Economics.*

When to consider ‘Only in Research’

- The new technology is **not cost-effective** given current evidence
- Conditional approval **removes incentives** to collect or submit additional evidence
- Conditional approval is **challenging to reverse** and/or may encounter substantial **reversal delays**
- There are **high upfront treatment costs** that could be avoided by delaying the decision (chronic conditions only)

Opportunities for ‘Value of Information analysis’

- Value of information methods quantify the expected value of reducing uncertainty through additional data collection

- Value of information analysis can be useful to:
  - **identify key drivers** of decision uncertainty and **guide the design** of studies that are likely to satisfy HTA requirements
  - determine **when evidence is sufficient** to justify routine commissioning
  - compare the value of **alternative MEAs**
  - incentivize manufacturers to **reduce the price** or invest in **better evidence**

Other methodological opportunities

- Structured expert elitation[1]
  - To provide additional information when empirical evidence is lacking
- Improving the design and analysis of real-world data studies
  - E.g. Target Trial Emulation approach[2]
- Enhancing survival extrapolations by incorporating external evidence and expert opinion
  - E.g. using flexible Bayesian methods[3]

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1. Bojke, L.et al. (2022). Reference Case Methods for Expert Elicitation in Health Care Decision Making. *Medical Decision Making.*

2. Gomes, M., et al. (2022). Target Trial Emulation for Transparent and Robust Estimation of Treatment Effects for Health Technology Assessment Using Real-World Data: Opportunities and Challenges. *PharmacoEconomics.*

3. Jackson, C. H. (2023). survextrap: A package for flexible and transparent survival extrapolation. *BMC Medical Research Methodology.*

Summing up

- **HTA and economic evaluation**
  - have emerged as useful tools to guide the implementation of new health technologies
- **Recent changes to the regulatory landscape of pharmaceuticals**
  - have increased uncertainty about cost-effectiveness, and led to the introduction of MEAs
- **Collaboration across national HTA agencies**
  - could enable setting evidence standards and harmonizing assessments
- **Important role for value of information analysis**
  - to determine the need for collecting additional data before making a reimbursement decision