How to quantify the value of treatments: Evidence generation to support value and access

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What we will be covering today

- Why value matters
- Tools to quantify value
- Real-World Evidence
- Integrated lifecycle strategy
- Take-home messages

How do we quantify value?

Traditionally… but there is much more

CLINICAL

- Efficacy, effectiveness
- Safety
- Treatment patterns
- Adherence

ECONOMIC

- Healthcare Resource Utilization
- Costs
- Disease burden
- Productivity loss

HUMANISTIC

Patient/caregiver reported outcomes:

- Quality of life
- Preferences
- Satisfaction

Different stakeholders have different needs

Regulators
- Safety and efficacy
- Adherence to quality standards
- Address unmet medical needs

Payers
- Cost-effectiveness evidence
- Budget impact analysis
- Real-world effectiveness

Prescribers
- Clinical efficacy data
- Guideline alignment
- Patient adherence facilitators

Patients
- Improved quality of life
- Treatment convenience & tolerability
- Affordability & access

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Why do we need to talk about “the money” in healthcare?

Healthcare Systems have been facing…

INCREASING Demand
- Longer life expectancy
- Increasing chronic patients
- Innovation

INCREASING Financial Pressures
- Limited budgets
- Public debt controls
- More expensive products

Pharma

“We have received marketing authorization for this new technology that has proved efficacy and safety in randomized clinical trials.”

PAYER

“**So What?** Wasn’t there a safe product already? Why is that supposed to be worthy of paying more? Why is that better than alternatives? Can you turn that into something important to me?”

When deciding whether a health technology should be reimbursed, payers assess its **VALUE**.
Choose technologies that outweigh their **OPPORTUNITY COST** (what’s lost by choosing them).

The History of NICE

The National Institute for Clinical Excellence (NICE) was created in April 1999. Its first appraisal was for Relenza, a Glaxo Welcome drug to treat the flu. **It did not show cost-effectiveness** and therefore, **reimbursement was not recommended**.

This decision led Glaxo Welcome's chairman to threaten that if the decision was not reversed, they would consider leaving the UK, but NICE did not reverse it.

> "That was the day that the world changed forever for the pharma industry, and I think companies got it."
>
> — Mike Thompson, chief executive of the Association of the British Pharmaceutical Industry

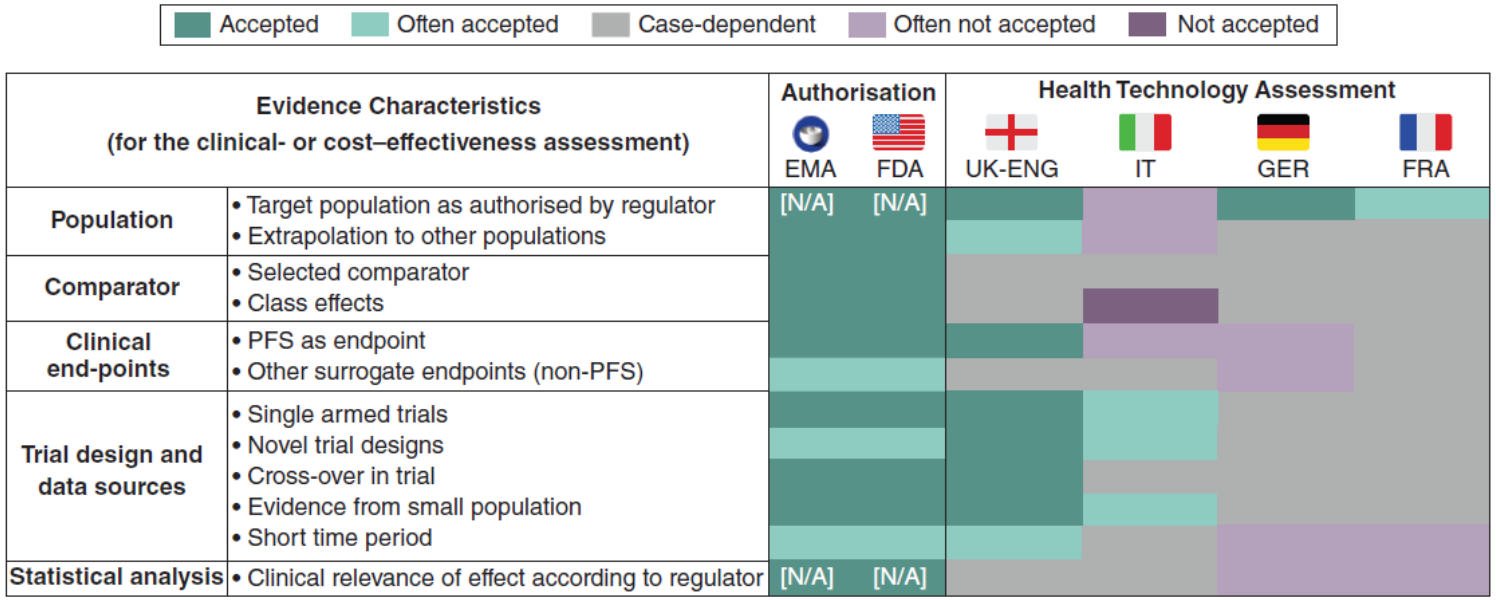
> "The industry has to accept that just because new medications are licensed does not mean that the health service wants or needs to buy them."
>
> — Professor Michael Rawlins, NICE Former Chairman

This marked the formal institutionalization of cost-effectiveness as a reimbursement criterion and shifted evidence generation needs

Regulator vs Payer

The payer has risen to become ***a key stakeholder in all major pharmaceutical markets over the last decade and is the decision-maker(s) on three key elements*:**

- ***reimbursement*** (will the new therapy be paid for at all)
- ***pricing*** (what price will be considered acceptable)
- ***patient access*** (which patients can receive the therapy).



Evidence Characteristics (for the clinical- or cost–effectiveness assessment)		Authorisation		Health Technology Assessment			
		EMA	FDA	UK-ENG	IT	GER	FRA
Population	• Target population as authorised by regulator • Extrapolation to other populations	[N/A]	[N/A]				
Comparator	• Selected comparator • Class effects						
Clinical end-points	• PFS as endpoint • Other surrogate endpoints (non-PFS)						
Trial design and data sources	• Single armed trials • Novel trial designs • Cross-over in trial • Evidence from small population • Short time period						
Statistical analysis	• Clinical relevance of effect according to regulator	[N/A]	[N/A]				

*There are fundamental differences between the type of evidence considered by **regulators** and **payers**.*

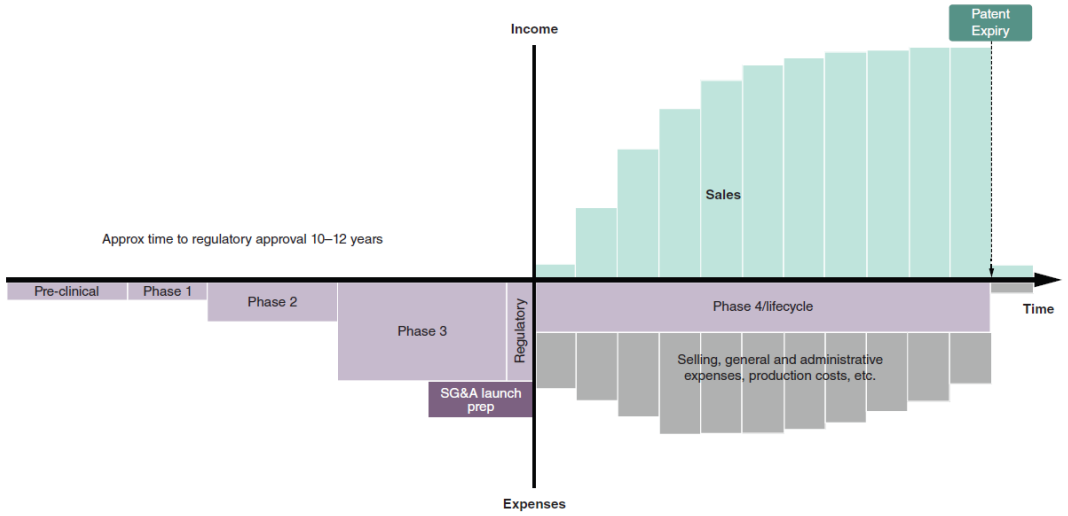
- ***Regulators** focus on safety, efficacy, internal validity and benefit-risk*
- ***Payers/HTA** focus on opportunity cost, external validity, cost-effectiveness and affordability*

*Evidence generation needs to be multi-dimensional and show **clinical benefit and value to healthcare systems** to ensure patients get access to new therapies and can only be achieved through strong evidence of*

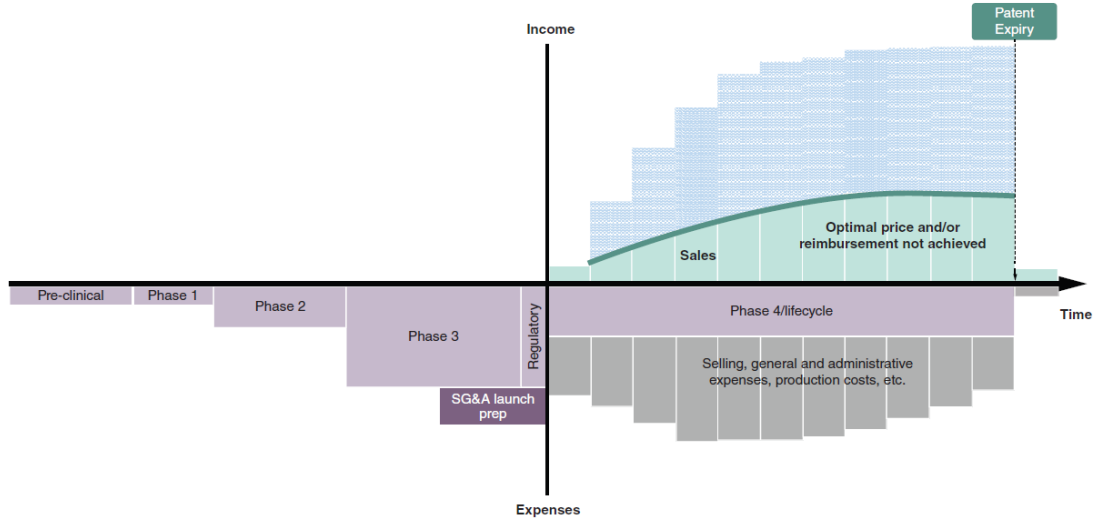
Ramagopalan et al. ***J. Comp. Eff. Res.*** (2025) e250036

Impact of market access in financial cashflow in drug development

Overview of typical financial cash flows in drug development



The impact of poor market access on financial cash flows in drug development.



Evidence generation needs to be planned from very early stages to ensure value and access

Ramagopalan et al. ***J. Comp. Eff. Res.*** (2025) e250036

Specific tools for evidence generation to support value and access

Health Economics Outcomes Research and Real-World Evidence

Health economics

- Cost-Effectiveness Analysis
- Budget Impact Models
- Cost-Minimization Analysis
- Cost-benefit

Outcomes Research

- Trial data analyses
- Literature reviews
- Meta analyses
- Indirect Treatment Comparisons

Real-World Evidence

- RWE Database analyses (retrospective)
- RWE primary data collection (prospective/retrospective)
- Surveys

Integration needed in current HTA

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Evidence driving pricing & reimbursement

Country	Key Decision-Maker(s)	Primary Evidence Requirements
UK	*NICE*	*Clinical effectiveness;* ***Cost-Effectiveness (QALYs); Budget Impact***
Germany	IQWiG → G-BA	Additional clinical benefit; Comparator data; Price negotiation
France	HAS (SMR/ASMR); CEESP; CEPS	Clinical benefit rating; **Cost-Effectiveness (QALYs); Budget Impact**
Italy	AIFA	Clinical value; **Cost-Effectiveness (QALYs)**; Budget Impact; Managed Entry Agreements
Spain	MoH / Interministerial Pricing Committee	Clinical data; **Budget Impact**; Increasing **Cost-Effectiveness (QALYs)** use
USA	CMS; Private Payers; PBMs	Clinical outcomes; Real-world evidence; **Budget/Affordability**
Canada	CADTH → pCPA	Clinical effectiveness; **Cost-Effectiveness (QALYs); Budget Impact**
Australia	PBAC	Comparative effectiveness; **Cost-Effectiveness (QALYs); Budget Impact**
Japan	MHLW / Chuikyo	Clinical benefit; **Cost-Effectiveness; Budget Impact**
China	NHSA	Clinical value; Strong price focus; **Budget Impact**; Local evidence
Brazil	CONITEC	Clinical evidence; **Cost-Effectiveness (QALYs); Budget Impact**

Centralized EU-level Joint Clinical Assessment of relative clinical effectiveness and safety vs appropriate comparator(s). Applies initially to oncology medicines and ATMPs (from Jan 2025), expanding to orphan medicines (2028) and all centrally authorized medicines (2030).

EU HTA Regulation 2021/2282; NICE Methods Guide; IQWiG General Methods; HAS Economic Evaluation Guidelines; CADTH Reimbursement Review; PBAC Guidelines; HIRA Positive List System literature; CONITEC HTA framework (peer-reviewed publications).

Budget Impact Model (BIM)

WHAT?

Aims to investigate the financial impact of adopting a new intervention or technology.

HOW?

1. Narrow down the overall population to the actual population of interest
2. Calculate the cost of illness for the population with and without the new medication
3. Budget impact is then calculated as: $Cost_{alternative\ scenario} - Cost_{base\ case}$

Uncertainty generally managed through deterministic sensitivity analysis (DSA)

WHEN?

BIAs are developed to inform those who manage health care budgets to help answer the following question:

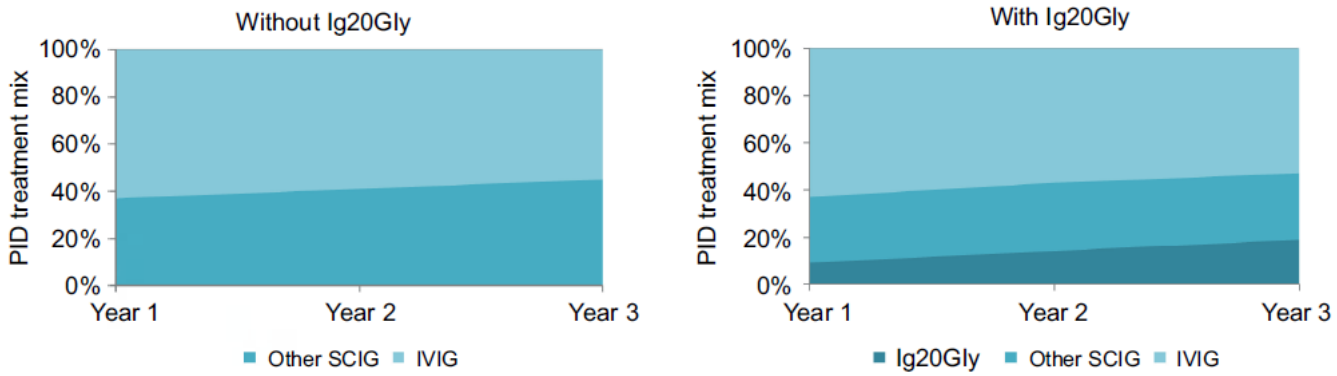
"Can we afford this?"

Sullivan SD, et al. Budget impact analysis—principles of good practice: report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force. Value in health. 2014 Jan 1;17(1):5-14.

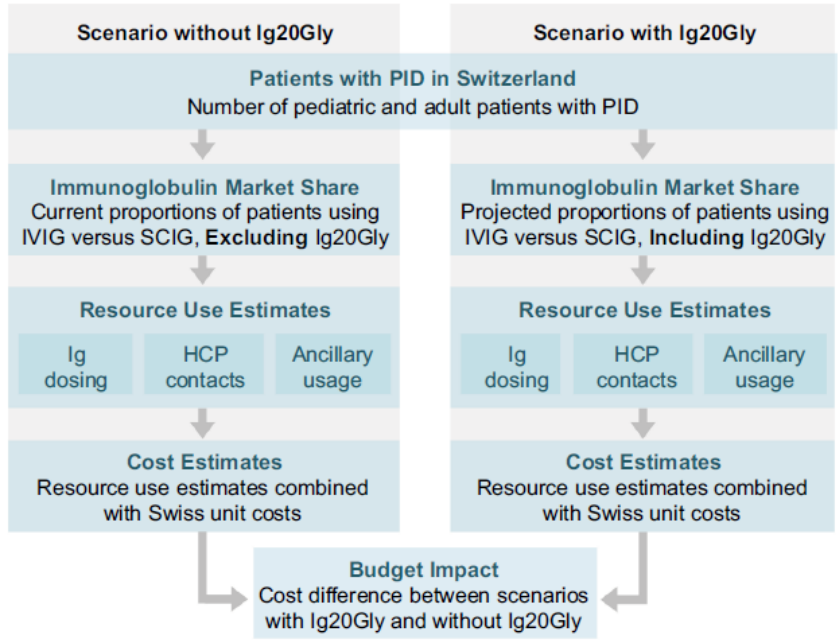
Budget Impact Model (BIM): example

Objective: Evaluate the budget impact of the introduction of a new subcutaneous Immunoglobulin in patients with Primary immunodeficiency in **Switzerland**

Treatment Scenarios



Budget Impact Model Schematic



Pollock R et. al. Clinicoecon Outcomes Res. 2018 Apr 10;10:223-229.
PIDD: Primary immune deficiency disease

Cost-Effectiveness Analysis (CEA)

WHAT?

CEAs are used to compare the relative costs (cost) to the health outcomes (effect) of different interventions.

HOW?

It is expressed in terms of a ratio where the denominator is the gain in health outcomes (years of life, premature births averted, sight-years gained, avoided heart attacks) and the numerator is the cost associated with the health gain:

$$ICER = \frac{C_A - C_B}{E_A - E_B}$$

Uncertainty is managed through probabilistic and deterministic sensitivity analysis (PSA)

WHEN?

When there is enough clinical and economic data for one intervention versus comparators and there is a clear **cost-effectiveness threshold**.

It allows answering the question: ***"is this intervention good value for money?"***

ICER: Incremental Cost-Effectiveness Ratio

A Special Kind of CEA: Cost-Utility Analysis (CUA)

What are utilities and what's the point of measuring QALYs?

Measuring effectiveness in usual units, makes it difficult to compare cost-effectiveness across different therapeutic areas

QALY stands for Quality-Adjusted Life Years and is a generic outcome that considers both the years of life gained and the quality of life gained.

QALY = Years of life gained x **utility**

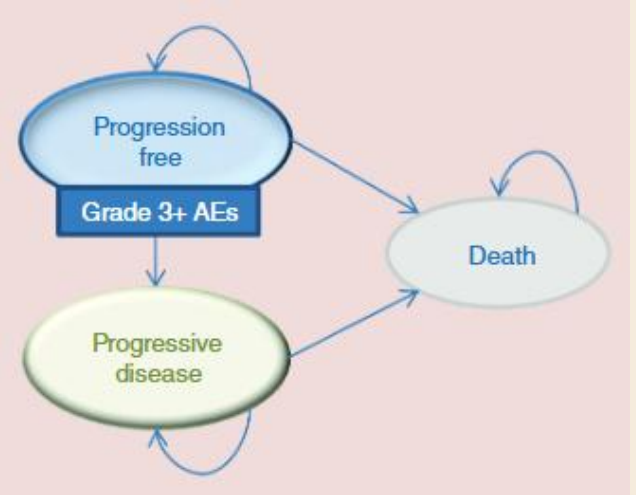
$$ICUR = \frac{C_A - C_B}{QALY_A - QALY_B}$$

ICUR: Incremental Cost-Utility Ratio

Cost-effectiveness analysis: example

Objective: Cost-effectiveness of pembrolizumab versus chemotherapy as first-line treatment in PD-L1-positive advanced non-small-cell lung cancer in the USA

Cost-effectiveness model structure



Time horizon: Lifetime (10–20 years)

Results

Table 4. Base-case results.

	Chemotherapy	Pembrolizumab	Incremental pembrolizumab vs chemotherapy
Life years	1.73	2.33	0.60
Quality-adjusted life-years	**1.28**	**1.77**	**0.49**
Incremental cost–effectiveness ratio			
Cost per life-year gained			US$106,617
Cost per quality-adjusted life-year gained			**US$130,155**

Huang M, Lopes GL, Insinga RP, Burke T, Ejzykowicz F, Zhang Y, Feliciano JL. Cost-effectiveness of pembrolizumab versus chemotherapy as first-line treatment in PD-L1-positive advanced non-small-cell lung cancer in the USA. Immunotherapy. 2019 Dec;11(17):1463-1478. doi: 10.2217/imt-2019-0178. Epub 2019 Nov 18. PMID: 31738117.

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Indirect Treatment Comparison (ITC)

WHAT?

ITCs aim to generate indirect evidence around the comparative clinical outcomes of different health technologies.

HOW?

1. Perform SLR to identify evidence of competing interventions
    - A vs C
    - B vs C
2. Evaluate the evidence to ensure comparability among studies and interventions
3. Perform statistical tests to generate indirect evidence of A vs B
4. Validity will be mostly driven by the comparability of the trials

WHEN?

When there is no direct head-to-head evidence between a health technology and other real-world comparator(s) (e.g. only RCT evidence available for a health technology is against placebo or standard of care). Often required by HTA agencies (e.g. NICE), that provide guidelines on methodology.

Indirect Treatment Comparison (ITC): Example

Objective: Conduct a network meta-analysis of CAR T-Cell therapies for the treatment of large B-cell lymphoma using salvage chemotherapy as a common comparator

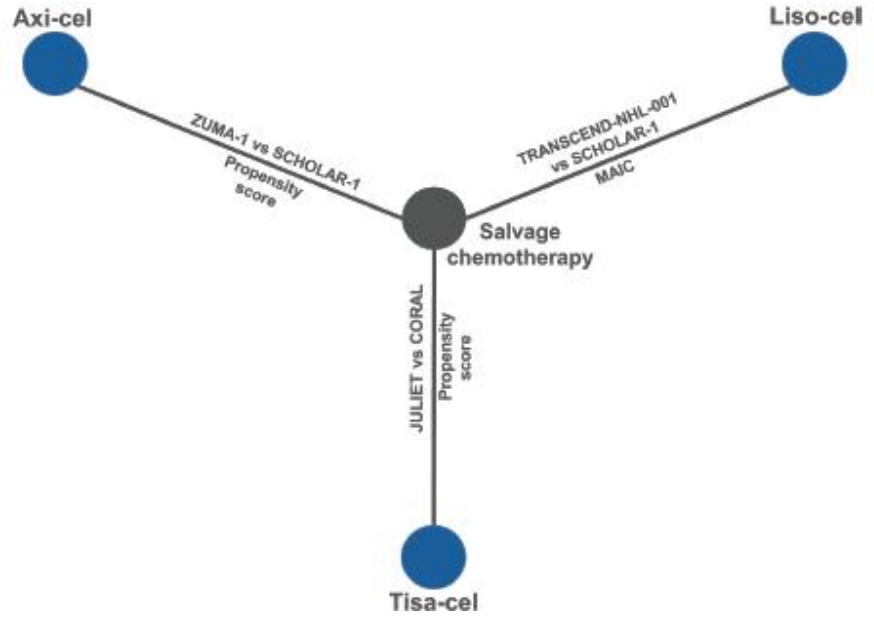

Table 2. Network meta-analysis results using the primary network.

	OS (HR, 95% CrI)	ORR (OR, 95% CrI)	CR (OR, 95% CrI)
Compared to salvage CT:			
Axi-cel vs salvage CT	**0.27 (0.19, 0.38)**	**9.29 (5.18, 18.16)**	**8.57 (4.95, 15.00)**
Liso-cel vs salvage CT	**0.50 (0.40, 0.60)**	**7.06 (4.71, 10.73)**	**12.89 (8.06, 20.87)**
Tisa-cel vs salvage CT	**0.57 (0.44, 0.73)**	**1.66 (1.05, 2.61)**	–
Between CAR T-cell therapy comparison:			
Axi-cel vs liso-cel	**0.54 (0.37, 0.79)**	1.32 (0.64, 2.89)	0.67 (0.32, 1.39)
Axi-cel vs tisa-cel	**0.47 (0.26, 0.88)**	**5.63 (2.66, 12.54)**	–
Liso-cel vs tisa-cel	0.87 (0.42, 1.78)	**4.26 (2.33, 7.93)**	–

Axi-cel, axicabtagene ciloleucel; CAR T-cell therapy, chimeric antigen receptor T-cell therapy; CrI, credible interval; CR, complete response; CT, chemotherapy; liso-cel, lisocabtagene maraleucel; ORR, overall response rate; OS, overall survival; SoC, standard of care; tisa-cel; tisagenlecleucel.

Oluwole OO, et al. Expert Rev Anticancer Ther. 2024 Jun;24(6):457-465.

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Real-World Data (RWD) & Real-World Evidence (RWE)

While often used indistinctively, RWD and RWE are different yet linked concepts

> "RWD is data relating to patient health status and/or the delivery of healthcare routinely collected from a variety of sources."
>
> — Definition of RWD According to the U.S. Food and Drug Administration (FDA)

> "RWE is then generated by the analysis of RWD providing clinical evidence about the usage and potential benefits or risks of a medical product."
>
> — Definition of RWE according to the FDA

The use of real-world data (RWD) to generate real-world evidence (RWE) within healthcare systems is growing significantly as stakeholders face pressure to satisfy the needs of a changing industry.

1. Ji, Mingham, et al. "Key Takeaways from FDA's Framework for Real-World Evidence for Pharmaceuticals." Covington Digital Health, Covington and Burling LLP. December 13, 2018. www.covingtondigitalhealth.com/2018/12/key-takeaways-from-fdas-framework-for-real-world-evidence-for-pharmaceuticals/

Evolution of RWD & RWE over the years

Pre-2010

Mostly observational studies

2010-2015

Focus on post-marketing safety, early EHR data use

2016-2020

FDA & EMA formalize RWE pathways

2020-present

Surge in data volume, AI/ML integration, pandemic-driven use

Key drivers for RWE adoption

- Explosion in digital health data (EHRs, claims, genomics, wearables)
- Big data platforms, cloud infrastructure, AI/ML tools including NLP, causal inference methods
- Supportive regulatory landscape (FDA, EMA, PMDA)
- COVID-19 and urgent need for rapid, scalable data sources
- Rising costs of clinical trials and potential for RWE to improve RCT efficiency
- Value-based healthcare

Key applications of RWD & RWE

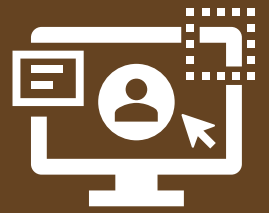
Area	Use case
Epidemiology & Public Health	Understanding disease patterns, burden of illness, vaccine effectiveness
Pharmacovigilance	Real-time safety monitoring
Market access	HTA submissions, payer negotiations, comparative effectiveness
Clinical Trials	Synthetic control arms, patient recruitment, protocol optimization
Regulatory	Label expansions and post-marketing surveillance

Types of RWE studies

Data collection:
- Primary data collection (surveys, observational studies)
- Secondary data use (database analysis of claims or EHR data)

But, most importantly, may also be classified based on **study design**

Study design (most common):
- Cross-sectional study
- Case-control studies
- Cohort study
  - Prospective
  - Retrospective



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How to select the best data source

The data source to be selected will depend on:

1. The research question 2. The resources available, level of complexity

	Survey	Database Study	Observational Study
Treatment patterns	++	+++	+
Cost of illness	+	+++	+
Healthcare resource use	+	+++	++
Treatment effectiveness	-	++	+++
Treatment safety	-	++	+++
Patient Reported Outcomes	+/-	-	+++
HCP opinion	+++	-	+

Increased resources, complexity

Claims vs EHR – how do they compare?

	Claims	EHR
What is it?	Information submitted by healthcare providers to payers to receive reimbursement for services rendered to patients	Digital documentation of patient health information generated throughout clinical care
Variables captured	• Demographics – age, gender, location, **insurance details** • Diagnoses – ICD diagnosis codes • Procedures – CPT and HCPCS procedure codes • Medications – NDC codes, dose, **number of prescription refills** • **Costs – total and itemized costs, amount paid by payer and patient responsibility**	• Demographics – age, gender, **race, ethnicity, language** • Medical history – conditions, diagnoses, allergies, immunizations, procedures • Medications – prescriptions, dosing instructions • **Vital signs – blood pressure, heart rate, weight, height** • **Lab test results** • **Radiology images** • **Clinical notes – physician notes, discharge summaries**
Limitations	• Diagnosis/procedure codes and prescription records are driven by reimbursement rather than clinical context, and may be inaccurate or incomplete • Inability to track individuals who change payers over time. • Variable data quality and completeness across sources. • Biased sampling based on specific payer population. May not represent the general population.	• Incomplete or missing records if providers fail to properly document encounters or if patient receives care at multiple healthcare networks • Difficulty normalizing data across disparate EHR systems due to lack of common standards • Biased datasets dependent on specific health system • Requires data science skills to analyze unstructured notes and documents and clinical background to appropriately interpret notes • More resource intensive data extraction/processing vs claims

Claims Data vs EHRs- Distinct but United in Real-World Research - Nashville Biosciences
Available from: https://nashbio.com/claims-data-vs-ehrs/

Some key players in the RWD / RWE ecosystem

TriNetX	• A global health research network offering de-identified patient data from EHRs across 200+ healthcare organizations. • Used by pharma for feasibility studies, clinical trial design, and retrospective RWE generation • It incorporates a **user-friendly tool** that allows for simple **analysis without programming** requirements
Truveta	• Aggregates EHR data from a growing alliance of U.S. health systems. • Focused on providing clean, normalized datasets enriched with **AI** for precision analytics
Flatiron Health	• Specializes in oncology data from EHRs and structured abstraction. • Partnered with the FDA to explore RWE in cancer treatment
Optum	• Offers large claims and EHR datasets. • Has **robust analytic tools** and is widely used in HEOR and payer strategy
IQVIA	• Integrates RWD from multiple sources and provides advanced analytics. • Offers hybrid solutions that combine RWE with traditional trial models
Panalgo	• Comprehensive dataset incorporating EHR data, claims and labs to support various analytic needs • Incorporates a **self-service analytic platform** tool that eliminates the need for complex programing and an **AI tool that enables data exploration through NLP**
Komodo	• One of the most comprehensive de-identified, patient level data healthcare data in the US (330+ patient journeys) including claims, EHR and labs • It incorporates a **user-friendly tool that allows for simple analysis** without programing and includes **AI support to help generate the cohort**

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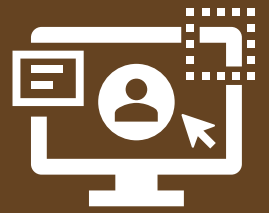
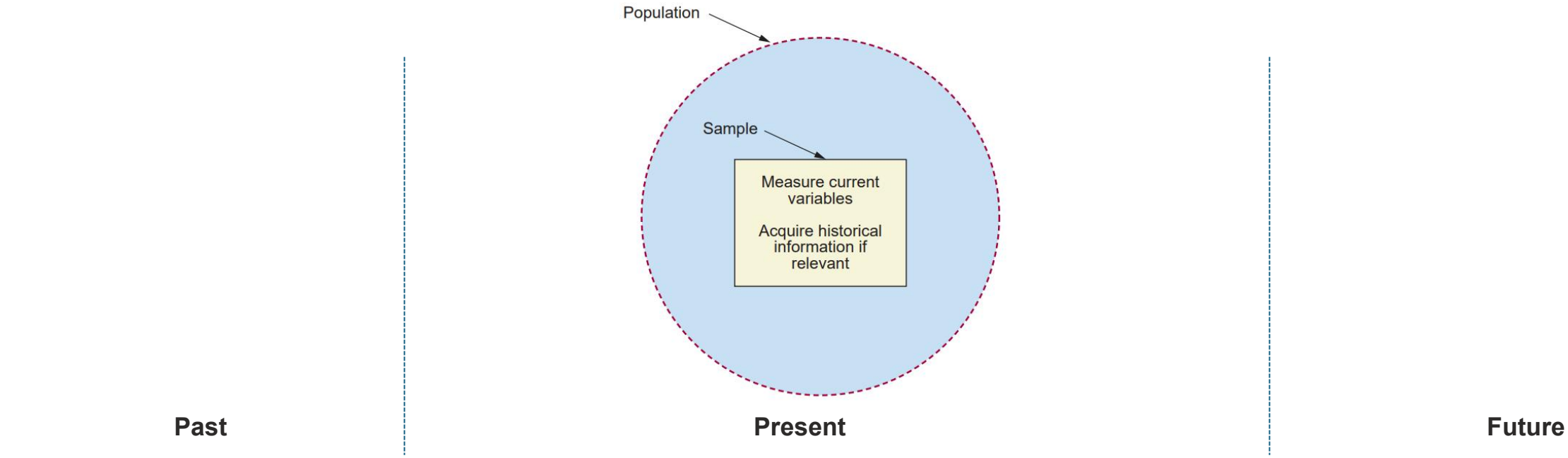


Cross-sectional studies

Description: In a cross-sectional study **all the measurements are made at about the same time**, with **no follow-up period ("snapshot")**. Cross-sectional designs aim to describe variables and their distribution patterns. Exposure and outcome are measured simultaneously. They can provide information about the prevalence of an outcome/disease. It may be used to generate hypothesis.

Research question: What is the **prevalence** of AATD within patients with COPD?

Design scheme



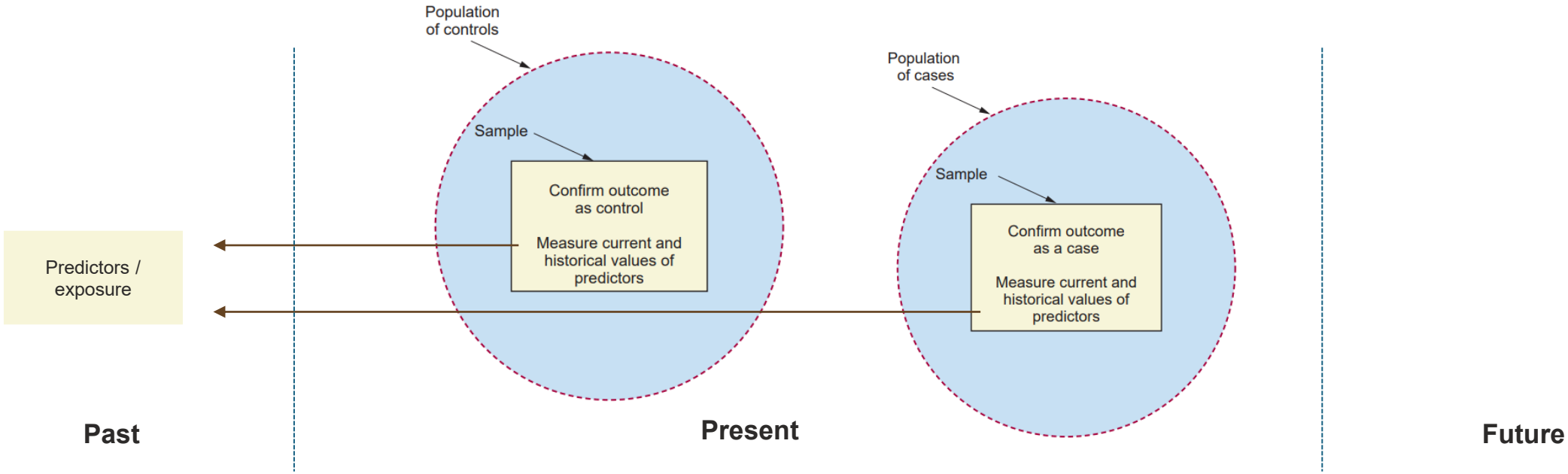
Taur SR. Perspect Clin Res. 2022 Jan-Mar;13(1):12-16.
Hulley et al. Designing Clinical Research 4th edition. Wolters Kluwer Lippincott Williams & Wilkins. 2013

Case-control studies

Description: Case–control studies are **retrospective and identify one group of subjects with a disease or outcome** (**cases**) and another one without it (**controls**) then **looks backward to find differences in predictors or exposures** that may explain why the cases got the disease/outcome and the controls did not. Outcome is ascertained before exposure. They can primarily inform association causal inference requires strong design and analytic methods. They can be hypothesis-generating.

Research question: Is there an **association** between myocardial infarction and exposure to non-steroidal anti-inflammatory therapies?

Design scheme



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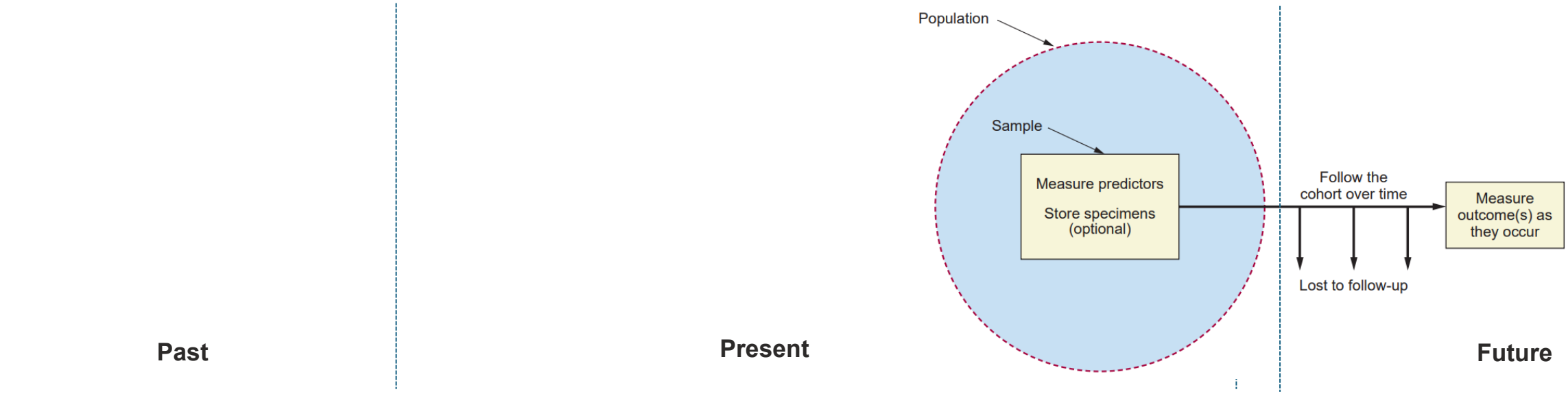
Prospective cohort study

Description: Prospective cohort studies require the **identification of a sample of patients (cohort)** that are **followed up over time and measures exposures (predictors) that may *predict* subsequent outcomes** in the future to evaluate the association. The fact that predictors are measured before the outcome, strengthens the process of inferring a causal association. It also allows estimating **incidences**. It allows association between **multiple exposures** (or predictors) and outcomes.

Research question: Do patients with multiple myeloma exposed to BsAbs have a **greater risk** of infections than untreated patients?

Design scheme



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Retrospective cohort study

Description: The design of a retrospective cohort study differs from that of a prospective one in that the assembly of the cohort, baseline measurements, and follow-up have all happened in the past. This type of study is only possible if adequate data about the predictors are available on a cohort of subjects that has been assembled for other purposes, such as an electronic clinical or administrative database

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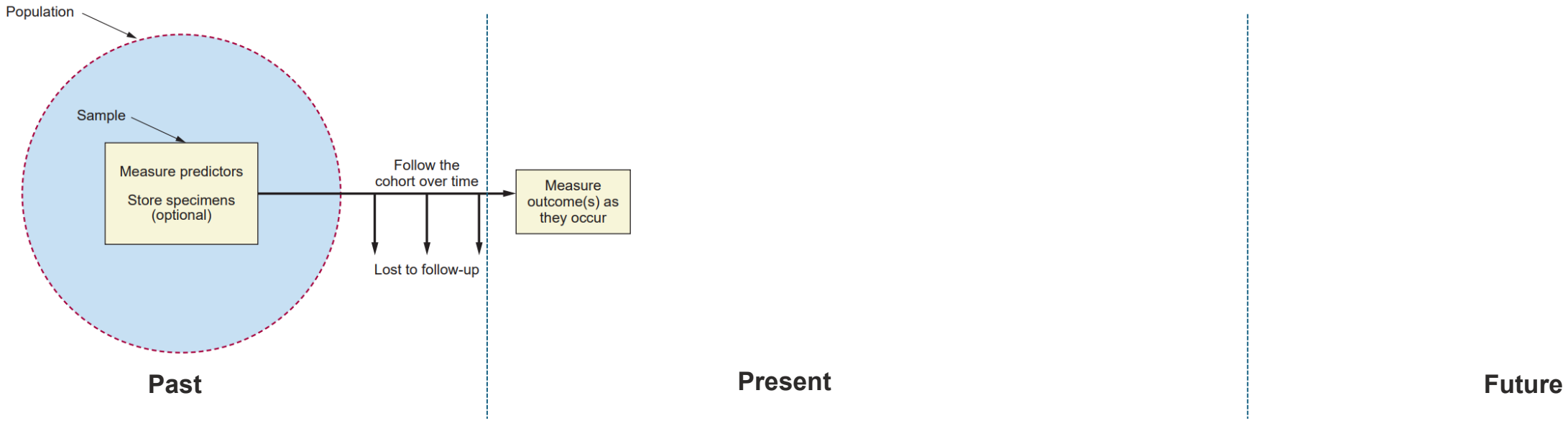
Design scheme



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Other RWE study design approach

- **Nested case-control study**
- **Target-trial emulation framework**
- **Within subject designs** (time-stable confounding already adjusted for)
    - Case crossover design
    - Self-controlled case series
    - Self-controlled risk interval
    - Pre-post self-control design

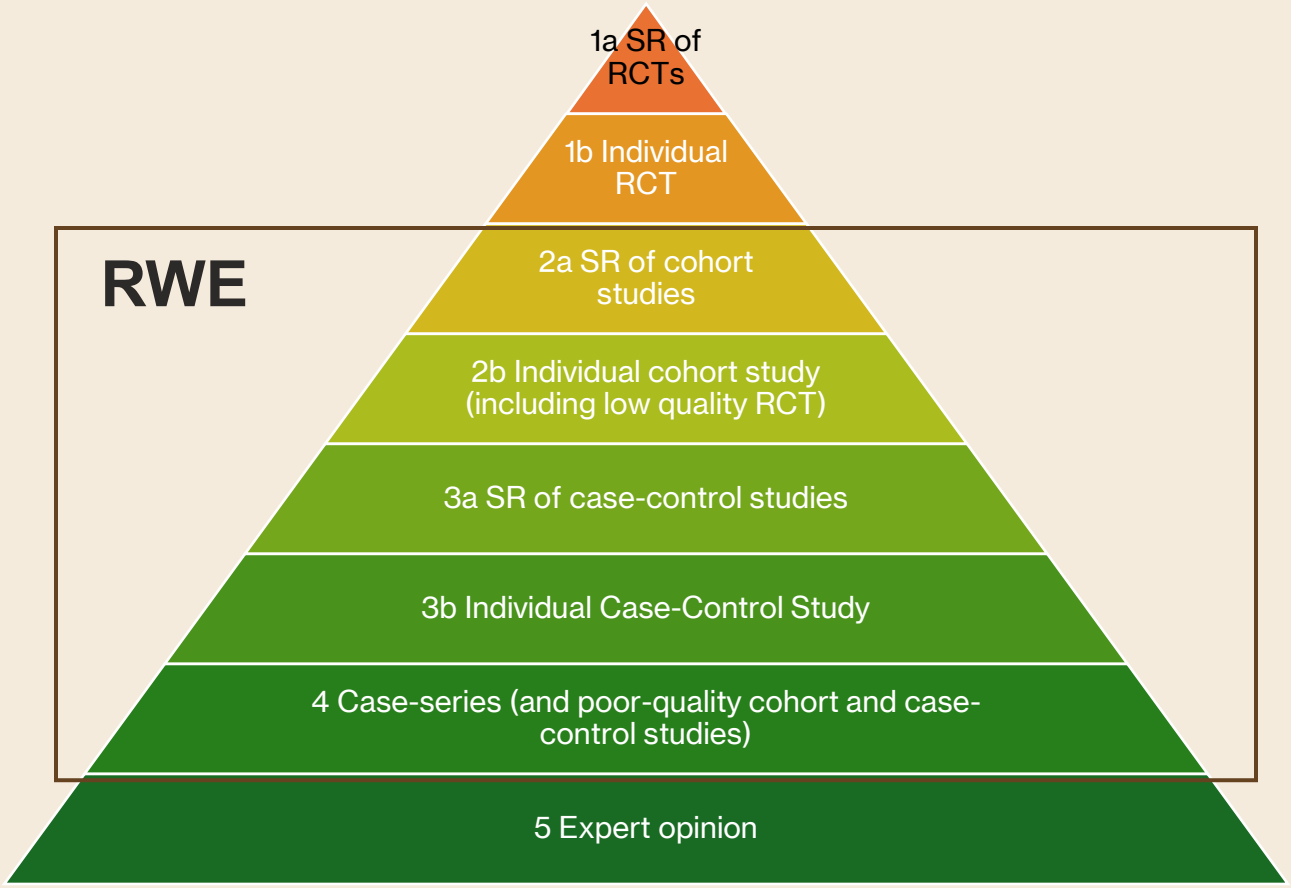
Accuracy vs generalizability

	Accuracy	Generalizability
Focus	Internal validity	External validity
Threads	• ***Bias (systematic error)*** • Precision (sampling or random error, not enough sample)	Lack of population representativeness
Importance	Ensures estimate is close to true effect	Ensures findings are useful in practice
Improved by	Rigorous study design, adjustment for confounders, larger sample size	Diverse data sources, representative populations

Key strength of RCT

Key strength of RWE

Where RWE stands in traditional evidence pyramid based on internal validity



Adapted from: Oxford Centre for Evidence-based Medicine levels of evidence table. Available from: www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009

New trends in RWE

Synthetic Control Arms

Use of external or synthetic control arms from EHR or registry data supports trials in rare diseases and oncology, accelerating timelines.

AI and Machine Learning Integration

AI techniques like natural language processing extract detailed clinical features from unstructured healthcare data for advanced RWE analytics.

Advanced Causal Inference Methods

Causal inference methods such as propensity score matching improve validity by addressing confounding in observational RWE studies.

Regulatory Framework Evolution

Global regulatory agencies are issuing guidance to integrate RWE in label expansions, post-marketing, and safety evaluations.

Use of RWE in Regulatory Decision-Making

Country/ Region	Agency	Main Uses of RWE	Key Guidance
USA	FDA	Post-marketing safety; **Label expansions; External controls**; Rare AE detection	FDA RWE Framework (2018); 21st Century Cures Act
EU	EMA	PASS studies; **Conditional approvals; Special populations; DARWIN EU**	EMA RWE Reflection Paper; DARWIN EU
UK	MHRA	Safety surveillance; ILAP; **Early access schemes**	MHRA RWE Guidance; ILAP Framework
Canada	Health Canada	Lifecycle regulation; Post-authorization monitoring; **Label updates**	Health Canada RWE Framework (2019)
Japan	PMDA / MHLW	Post-marketing surveillance; Registry monitoring	GPSP Regulations
China	NMPA	**Conditional approvals**; Rare disease data; Pilot RWE programs	NMPA RWE Technical Guidelines

References: FDA RWE Framework (2018); 21st Century Cures Act; EMA RWE Reflection Paper; MHRA Guidance; Health Canada RWE Framework; NMPA Technical Guidelines.

FDA considers RWE may fit some of the following uses

- Characterizing the **natural history** of a disease
- Help determine **sample size, selection criteria**, and study **endpoints** when **planning an interventional study**
- Selecting **suitable study participants** to include in an **interventional study** (e.g., randomized trial)
- **Identifying biomarkers or clinical characteristics** that are associated with a relevant clinical outcomes to inform a clinical trial
- Supporting, **in appropriate clinical circumstances, inferences about safety and effectiveness** in the context of:
  - A non-interventional study **evaluating a drug received during routine medical practice** and captured by the registry
  - An **externally controlled trial** including registry data as an external control arm

FDA Decision Alerts | Real-World Evidence | Aetion
Panalgo - RWE Use Cases Booklet – Website
U.S. Food and Drug Administration (fda.gov)
Jaksa A, et al. Value Health. 2022 Dec;25(12):1967-1976

DARWIN EU operationalizes real-world evidence (RWE) for regulatory decision-making at the European Union level

Background:
- EMA-coordinated federated RWE network.
- Established following HMA/EMA Big Data Task Force recommendations.
- Aligned with the European Medicines Agencies Network Strategy and the European Health Data Space (EHDS).

Objectives:
- Provide high-quality, timely RWE for regulatory decision-making.
- Support lifecycle regulation (authorisation through post-market surveillance).
- Enable rapid, federated analytics across European healthcare databases using a common data model.

Status:
- Operational with a dedicated Coordination Centre since 2024.
- Federated network of 40+ data partners covering tens of millions of patients.
- Supports EMA scientific committees and post-authorisation studies.

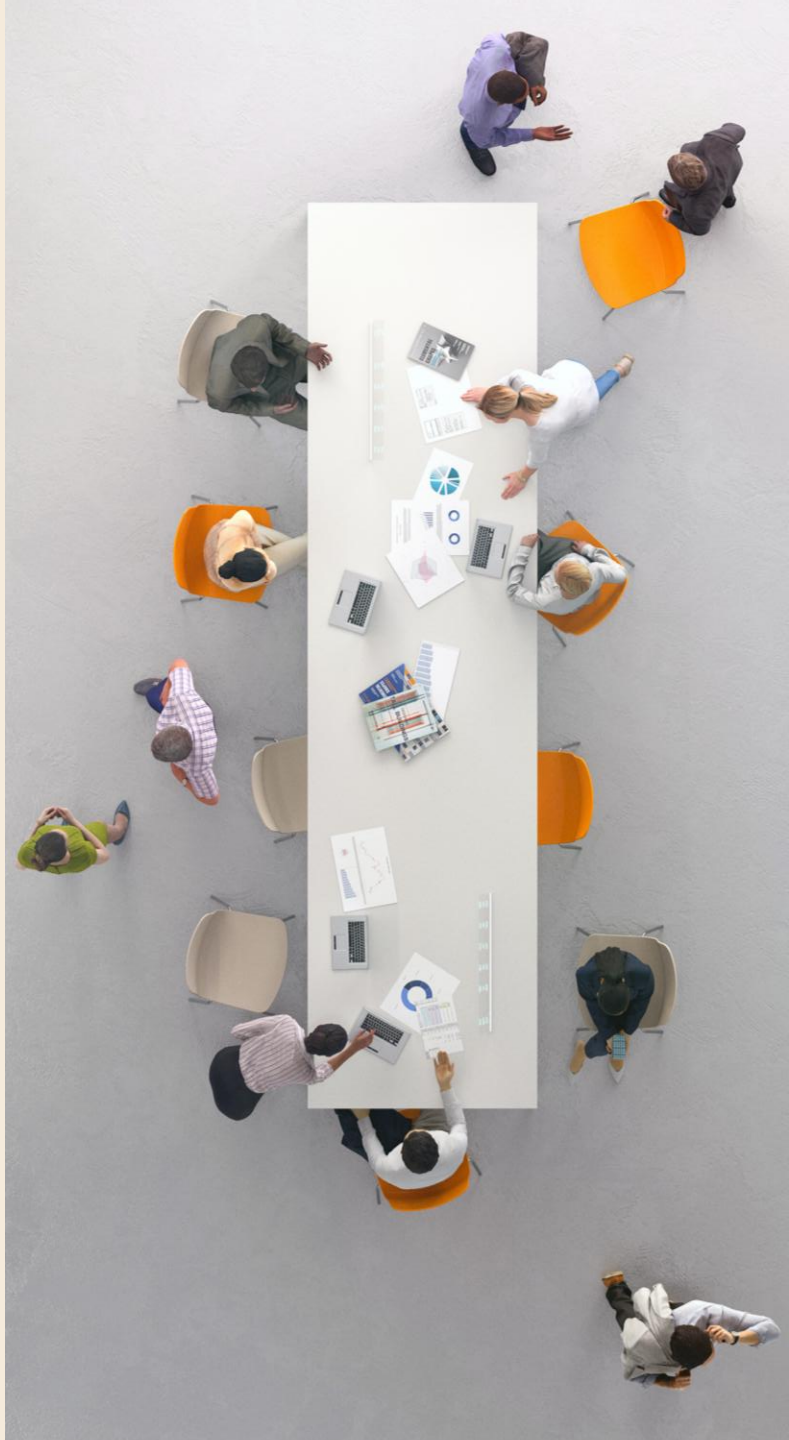
Strategic implications for industry or academia:
- Increasing regulatory reliance on RWE for lifecycle decisions.
- Greater scrutiny of post-authorisation safety and effectiveness evidence.
- Need for pre-specification, protocol transparency, and data standardisation.
- Potential indirect influence on HTA through shared data infrastructure and methodological convergence.

References: EMA. Data Analysis and Real World Interrogation Network (DARWIN EU); EMA Press Release (2022) on DARWIN EU Coordination Centre; European Medicines Agencies Network Strategy to 2025; DARWIN-EU.org updates.

Use of RWE in HTA Decision-Making

Country/ Region	Agency	Main Uses of RWE	Key Guidance
UK	NICE	Survival extrapolation**; External controls**; Utilities; **Resource use**; Managed Access	NICE RWE Framework (2022); NICE Methods Guide (2022)
Germany	IQWiG / G-BA	Contextual benefit assessment; Registry data; Reassessment	IQWiG General Methods; GSAV legislation
France	HAS / CEESP	Post-listing reassessment; Effectiveness; **Economic inputs**	HAS Real-World Studies Doctrine
Canada	CADTH	**Indirect comparisons**; **Survival validation; Model inputs**; Reassessment	CADTH RWE Guidance (2022)
Australia	PBAC	Managed entry schemes; Model validation; Utilization refinement	PBAC Submission Guidelines
EU	EU HTA CG	Post-JCA uncertainty reduction; **Complementary evidence**	Regulation (EU) 2021/2282

References: FDA RWE Framework (2018); 21st Century Cures Act; EMA RWE Reflection Paper; MHRA Guidance; Health Canada RWE Framework; NMPA Technical Guidelines.



Let’s recap

Health Economics Outcomes Research and Real-World Evidence

Health economics

- Cost-Effectiveness Analysis
- Budget Impact Models
- Cost-Minimization Analysis
- Cost-benefit

Outcomes Research

- Trial data analyses
- Literature reviews
- Meta analyses
- Indirect Treatment Comparisons

Real-World Evidence

- RWE Database analyses (retrospective)
- RWE primary data collection (prospective/retrospective)
- Surveys

Integrated evidence generation

R&D / Clinical development

- Quantify target population
- Characterize the disease
- Support planning of trial for a more efficient enrolment
- Determine sample size, selection criteria, endpoints
- Identify biomarkers, patient characteristics
- Early economic model to assess likelihood of reimbursement

Regulatory / registration

- Evidence on effectiveness / safety that can support a label indication
- Generate an external control group for a single-arm clinical trial
- Develop a natural history study to assess external validity of a trial
- Literature review to support submission

Clinical guideline recommendation

- Evidence on effectiveness / safety that can support a label indication
- Literature review
- Meta-analysis of randomized clinical trials
- Subgroup analysis from trials

P&R

- Support value dossier
- Assess cost-effectiveness or budget impact
- Burden of disease and treatment patterns (SoC)
- Literature review
- Meta-analysis of randomized clinical trials
- Indirect treatment comparison
- Subgroup analysis from trials

Launch

- Quantify target population
- Assess unmet need
- Stratify target population based on effectiveness, safety, patient or HCP preferences
- Generate value story

Post-market / maturity

- Understand patient journey
- Support market forecast based on RWE
- Generate evidence on effectiveness, safety, impact on healthcare resource utilization and patient reported outcomes
- Develop cost calculators / tools to support value story and approach customers

Take-home messages

- Value is multi-dimensional and context-specific
- Clinical approval ≠ market access
- Evidence strategy must begin before Phase III
- RWE is now integral to regulatory and HTA decisions
- Methodological rigor determines credibility
- Integrated evidence planning drives sustainable access

Thank you