NICE's RWE Framework: for comparative effects studies

Dr. Stephen Duffield

Senior Analyst, Data and Analytics team

ISPOR EU: 07/11/2022

NICE National Institute for Health and Care Excellence

About NICE

Who are we?

We are the experts in evidence-based best practice and value for money in health and care system across England and Wales.

What do we do?

We balance the best care with value for money, delivering both for individuals and society

We drive innovation into the hands of health and care professionals to enable best practice

We are fiercely independent: our decisions are rigorous, transparent and based on evidence

NICE

NICE Vision for RWE

1. RWD access
2. Use of RWE
3. Capability building
4. Signposting
5. Partnership and research

NICE's RWE Framework

Published June 2022

Aims to:

- Increase use of RWE to fill evidence gaps and improve recommendations
- Improve quality and transparency of RWE studies that inform guidance
- Inform critical appraisal of RWE studies
- Increase trust in high-quality RWE studies

Describes

- Where and how RWE can be used to improve recommendations
- Best-practices for planning, conducting, and reporting RWE studies

Principles of evidence generation

1 Transparency

Generate evidence in a transparent way and with integrity from study planning through to study conduct and reporting.

2 Data suitability

Ensure data is trustworthy, relevant and of sufficient quality to answer the research question.

3 Methods

Use analytical methods that minimise the risk of bias and characterise uncertainty.

Transparent reporting

- enables reviewers to understand what was done
- builds confidence in the results
- allows independent researchers to reproduce the results

STaRT – RWE
DataSAT
RWE Registries
STROBE/RECORD-PE

Key content for reports:

Describe the data and methods

Demonstrate data provenance and fitness-for-purpose

Fully describe data curation, study design, and analytical methods

Report results completely

Fully describe patient exclusions, participation rates, and loss to follow-up and present all important patient characteristics by intervention or subgroup

Results of all analyses, whether planned or unplanned

Assessing data suitability (DataSAT)

Data provenance

- What was the purpose of data collection?
- What data was collected, in what settings, how and by whom?
- Data documentation and quality management
- Data governance arrangements

Fitness for purpose

Quality

- How much data is missing on key study variables (see PICO)? Why is data missing?
- How accurately is data recorded?
- How was accuracy assessed?

Relevance

- Does the data source contain all relevant study variables?
- Is the population similar to the intended population for the technology?
- Are the care settings relevant to patient care in the NHS?
- Are the sample size and follow-up sufficient to generate reliable results?

NICE

HDRUK Innovation Gateway

SPIFD

STaRT-RWE

Real-world evidence studies of comparative effects

Here we present best-practices for cohort studies (including trials using real-world data to form external control). Other study designs including quasi-experimental designs might be most appropriate for some interventions.

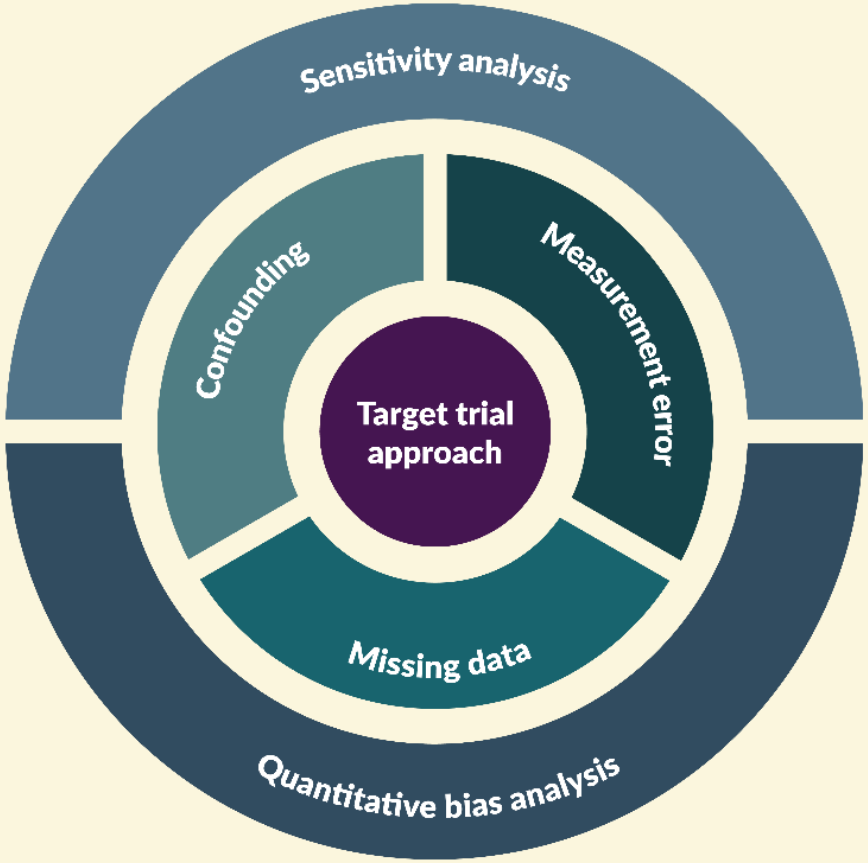
- Design studies to emulate the preferred randomised controlled trial – use a “target trial approach”
- Identify potential confounders and address these considering observed and unobserved confounding
- Consider the impact of bias from informative censoring, missing data, and measurement error – address appropriately where required
- Use sensitivity and bias analysis to assess the robustness of study findings

NICE

Target trial approach | STaRT-RWE | ROBINS-I | Bias reporting template

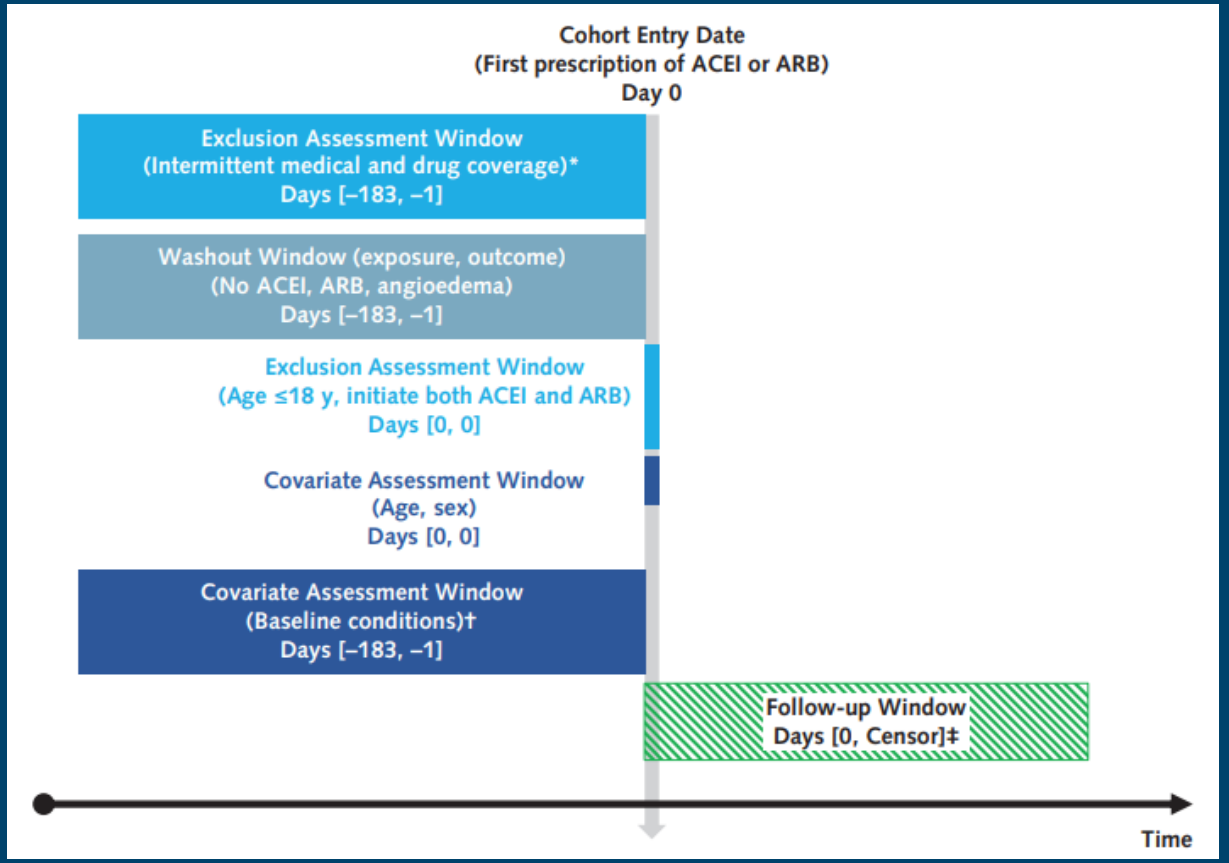
Study design – the target trial approach

"The goal of observational research is to emulate the ideal target trial"



Intuitive	Transparent	Incorporates Estimand fwk
Generalisability assessments	Selection & time-related bias	Outcomes & Detection bias
Confounding bias	Informative censoring	Sensitivity analysis & unmeasured confounding

Study design diagrams



Schneeweiss S, Rassen JA, Brown JS, Rothman KJ, Happe L, Arlett P, Dal Pan G, Goettsch W, Murk W, Wang SV. Graphical depiction of longitudinal study designs in health care databases. Annals of internal medicine. 2019 Mar 19;170(6):398-406.

NICE

Analysis - missing data & measurement error

Impact depends on:

- Size of problem (and direction of error)
- Variables affected
- Mechanism (across groups, over time?)

Measurement error

Differential - Incorporated into analysis (e.g. calibration)

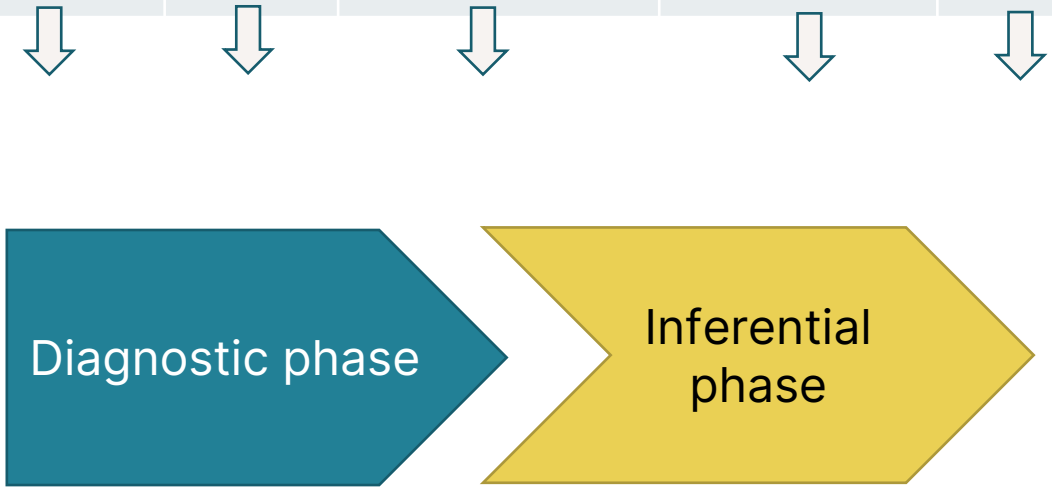
Random – Impact varies: exposures; continuous or categorical outcomes

Missing data:

- Complete records
- Advanced methods (imputation, IPW, MLE)
- Sensitivity/bias analysis

Analysis - addressing confounding

	Tx group	Unmatched controls	Matched controls	SMD
Age				
Gender				



Covariate selection

Pre-identification
Consider relevant variables
Outline causal assumptions

} Expertise, Literature review, ?ML

Outline causal assumptions

Bias due to inappropriate adjustment

Time-varying confounding

Propensity score methods

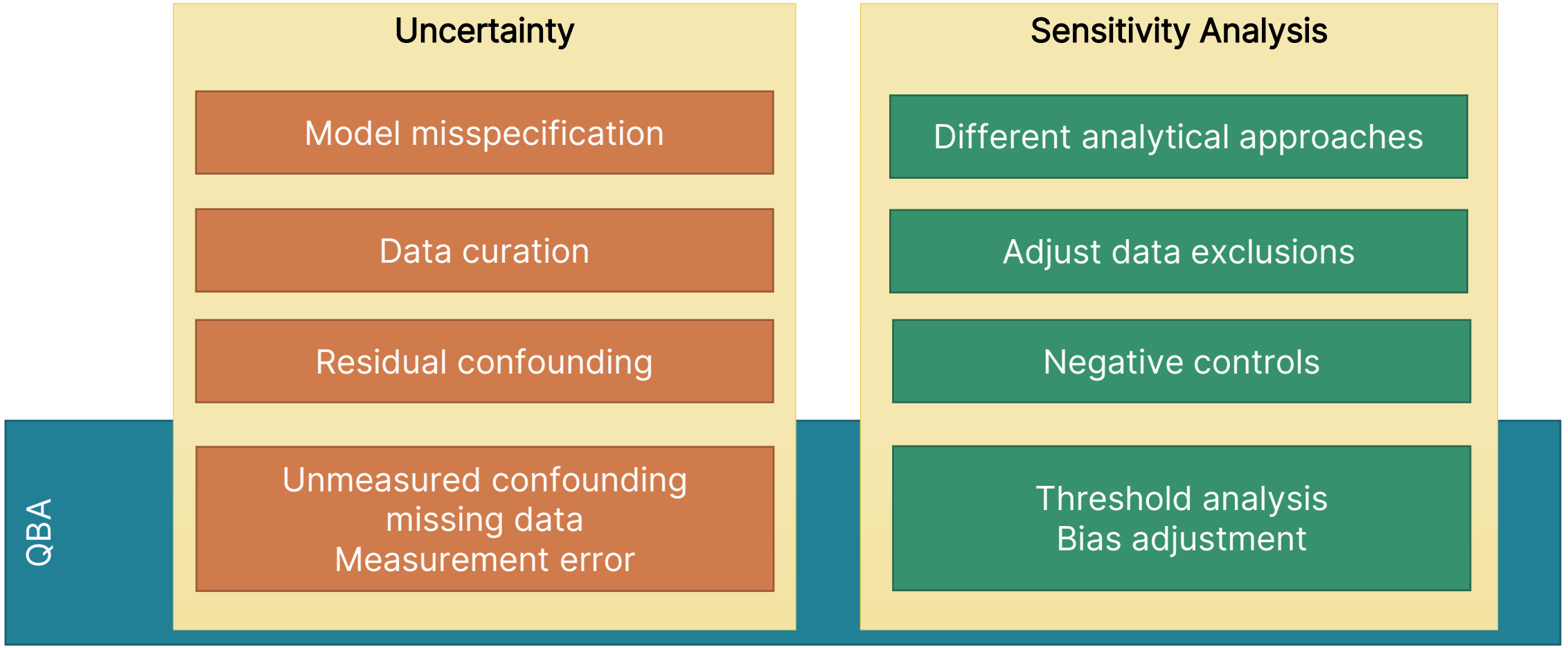
Balance assessments: diagnostic and inferential phases

Reporting: absolute values of each variable and standardised differences before and after PSM

NICE

Assessing robustness

Focus on areas where the impact of bias, assumptions, uncertainty are greatest – justify choice, pre-specify where possible



Summary

- NICE's RWE Framework **describes best-practices** for planning, conducting, and reporting real-world evidence studies
- **Numerous tools are referenced** to help operationalize these best practice principles,
- Principles for comparative effects studies, include:
  - Prespecify where possible
  - emulate the preferred randomised controlled trial
  - Consider the impact of bias from informative censoring, missing data, and measurement error – address appropriately
  - Identify potential confounders and address these considering observed and unobserved confounding
  - Use sensitivity and quantitative bias analysis to robustness of findings

NICE

NICE National Institute for Health and Care Excellence

Thank you