Real World Evidence *The HTA Perspective*

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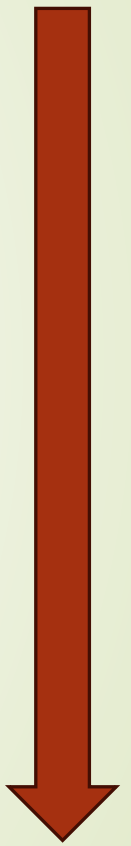
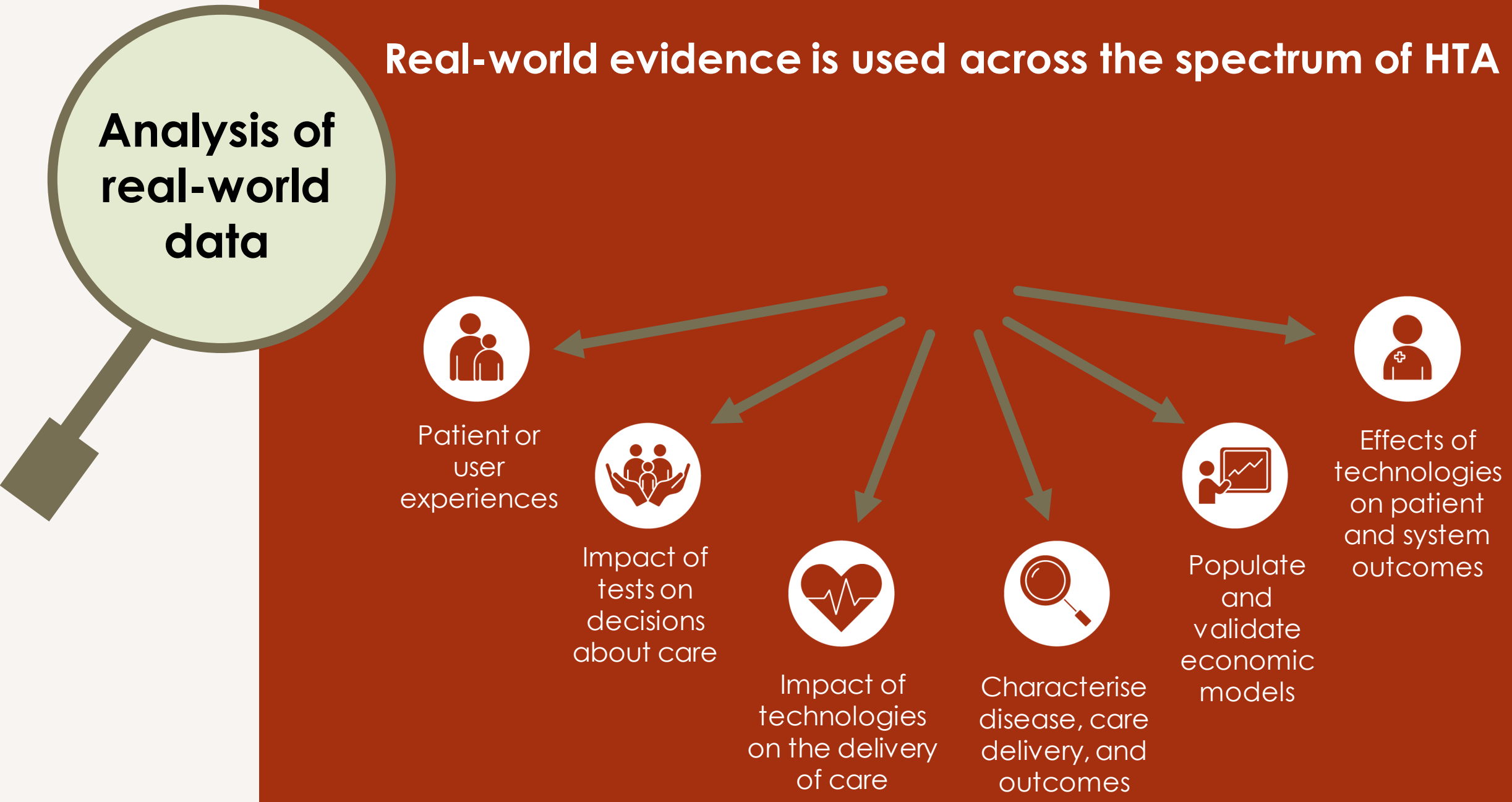
What data matters for HTA?

- **Characterising patient populations**, subgroups of interest, treatment effect modifiers
- **Financial**: real costs, unexpected costs
- **Treatment usage**, duration, dosing
- **Sequencing** of treatment, subsequent or adjunctive therapies
- **Long-term outcomes** data (final, non-surrogate)
- **Clinically-important outcomes**, clearly defined, outcomes in subgroups
- **Reasons for treatment discontinuation**: progression, adverse events
- **Relative treatment effects**, compared to standard of care



Real-world evidence is used across the spectrum of HTA



Trust

Data quality

Risk of bias

Limited transparency

Complexity

Challenges in making greater use of RWE

Assessing real world data suitability

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 framework)? 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?

Examples of Influential uses of RWE at NICE

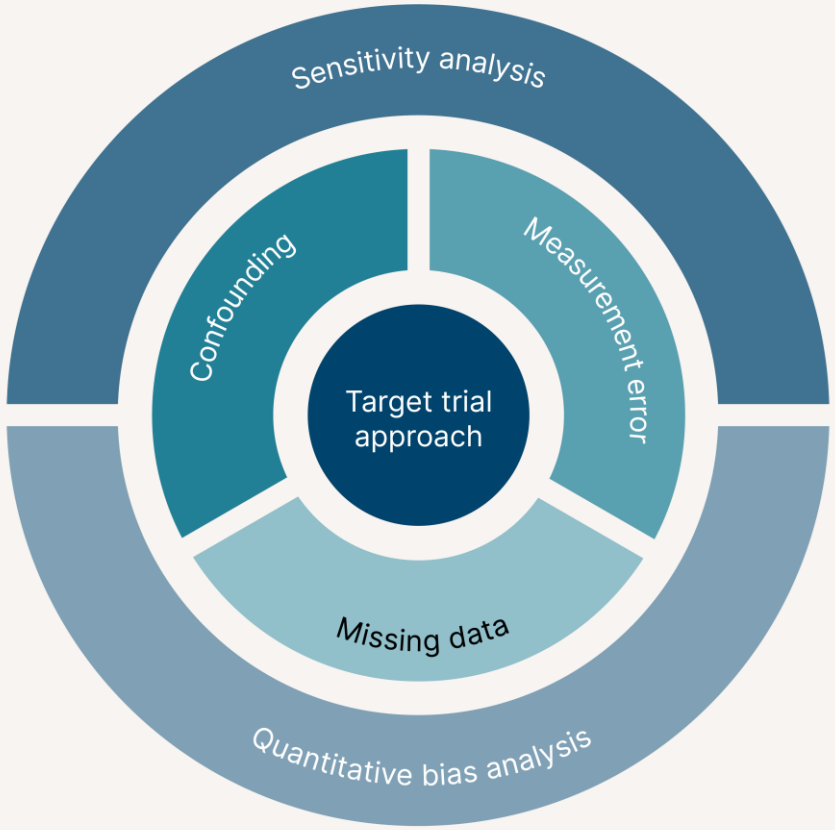
RWE use discussed by NICE committee	Appraisal
To demonstrate the generalisability of trail evidence to the UK population for patient characteristics	TA904, TA883
To estimate cost-per-use for diagnostic technology	DG48
To estimate baseline event rates, in modelling, to which relative effects from trial data are applied	TA897
To demonstrate an early signal of value for conditional recommendation of a digital therapy	HTE9
To scrutinize or support extrapolated outcomes in economic modelling	TA883, TA870, TA864, TA801
To enable effectiveness, or cost-effectiveness estimation for an important subpopulation	TA880, HST23
To provide reassurance that outcomes observed in key trial data are reflected in routine practice	TA872
As the main source of comparative effectiveness evidence	HST22, TA855, TA850
To estimate dose in clinical practice, and therefore, costs	TA866, TA808
To estimate rates of complications beyond the duration of available trial data and health state transition probabilities in economic modelling	TA860, TA804
To provide supportive evidence for an uncertain indirect treatment comparison	TA816

Duffield S, Jónsson P. The real-world impact of National Institute for Health and Care Excellence's real-world evidence framework. Journal of Comparative Effectiveness Research. 2023 Aug(0):e230135.

Real-world evidence studies of comparative effects

Real-world evidence can be used in the absence of trial evidence or to answer broader questions about the effects of interventions in routine settings

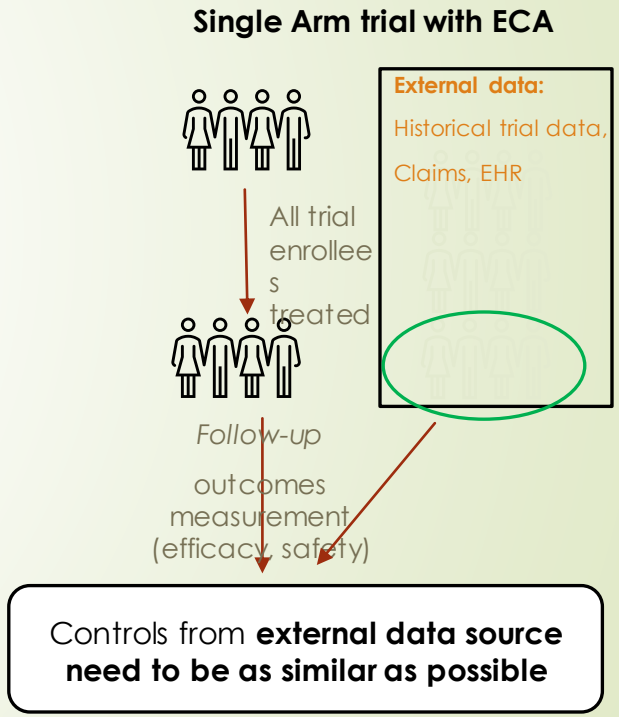
Below is best-practices for cohort studies - including trials using real-world data to form external control.

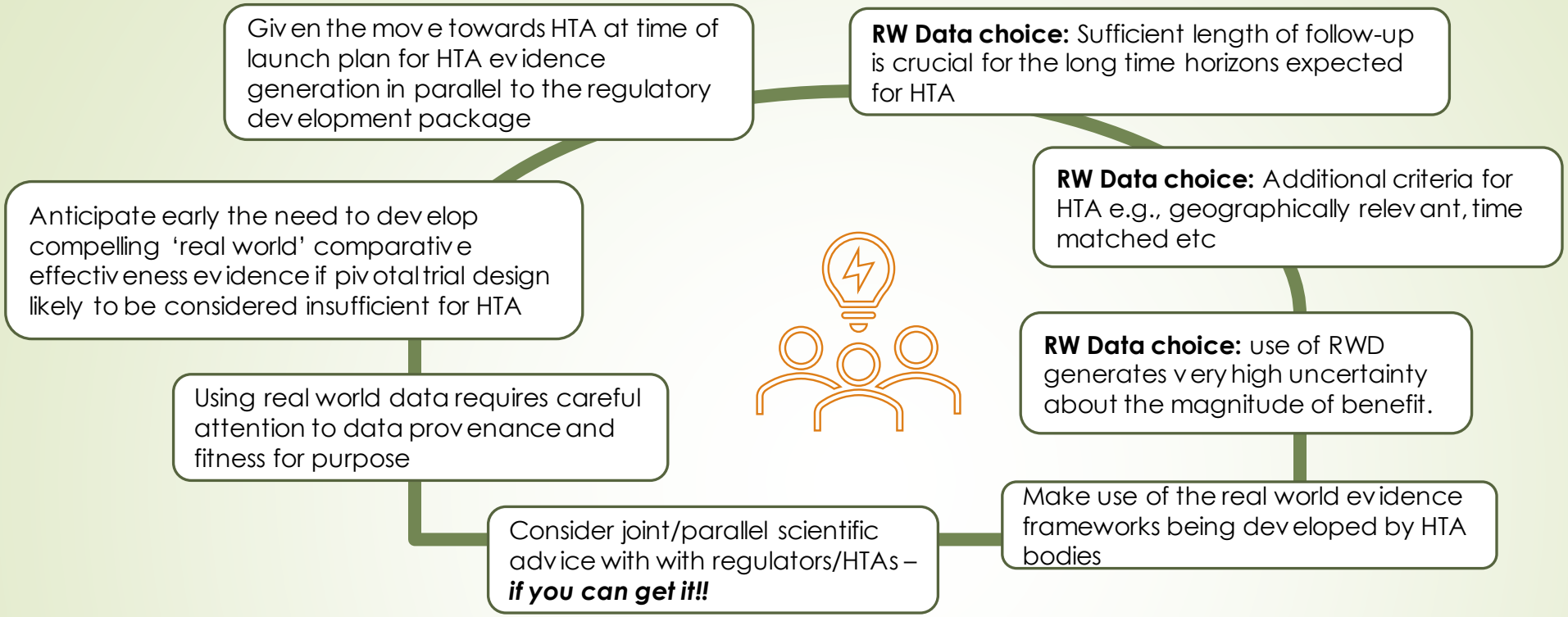


- Design studies to emulate the preferred randomised controlled trial – use a "target trial approach"
- Identify potential confounders and address these considering observed and unobserved confounding
- Consider the impact of bias from informative censoring, missing data, and measurement error – address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

Use Case: Real world data for External Control Arms

- Company conducting a single arm phase III trial for a rare cancer
- Can a suitable, fit-for-purpose external control arm data source be found?
- Does the data set contain the right outcome measures?
- What about time bias?
  - Very difficult to identify a real world ECA data set that has had the same clinical management as the trial cohort
  - This is crucial for robust comparative effectiveness assessment





Summary – use of real world evidence with HTA audiences in mind

Acknowledgments

- This Presentation has been developed in part from material provided by the National Institute for Health and Care Excellence and from Genesis Research
- With thanks from Pall Jonsson and Stephen Duffield at NICE and Alexandra Sosinsky at Genesis Research
- NICE Real World Evidence Framework Document
  - https://www.nice.org.uk/corporate/ecd9/chapter/overview