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Lessons learned from Health Technology Assessment pilot projects to assess real-world evidence's usefulness in reassessments of effectiveness and value

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Our speakers

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Disclosures

Ashley Jaksa: employee with stock options in Aetion, Inc.

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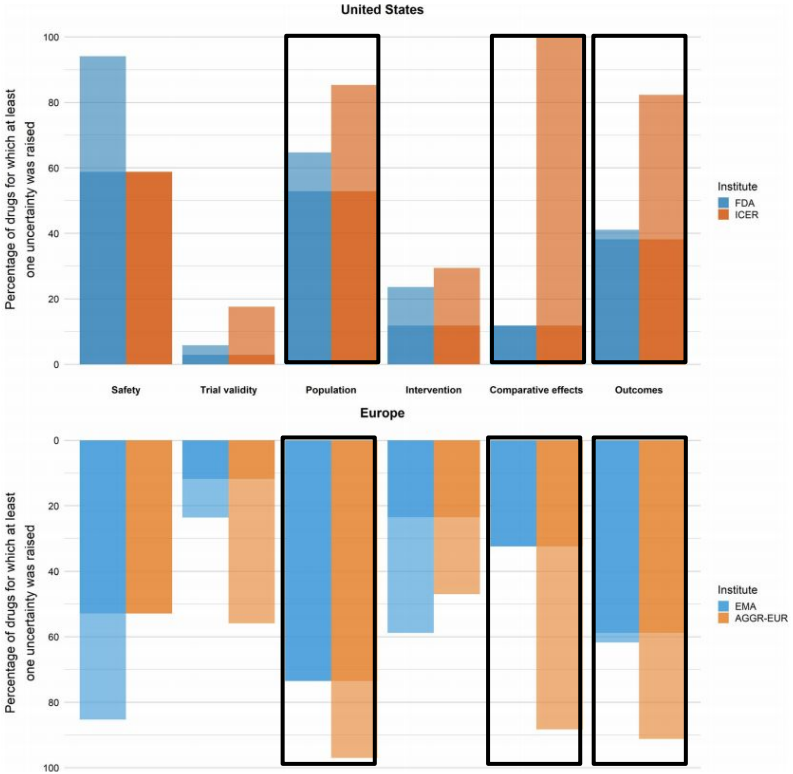
Health Technology Agencies’ shift toward lifecycle management

HTAs often cite uncertainty in clinical evidence at launch

Regulatory programs that speed up access (e.g. FDA's Accelerated Approval) have lead to less clinical evidence at time of launch and potentially more uncertainty.

- Drugs approved on at least 2 pivotal studies **decreased** 28%
- Use of surrogate endpoints **increased** 11%
- Use of single-arm studies **increased** 9.3%

Areas of uncertainty raised in the clinical evidence of approved drugs by regulators and HTA bodies in EU and US

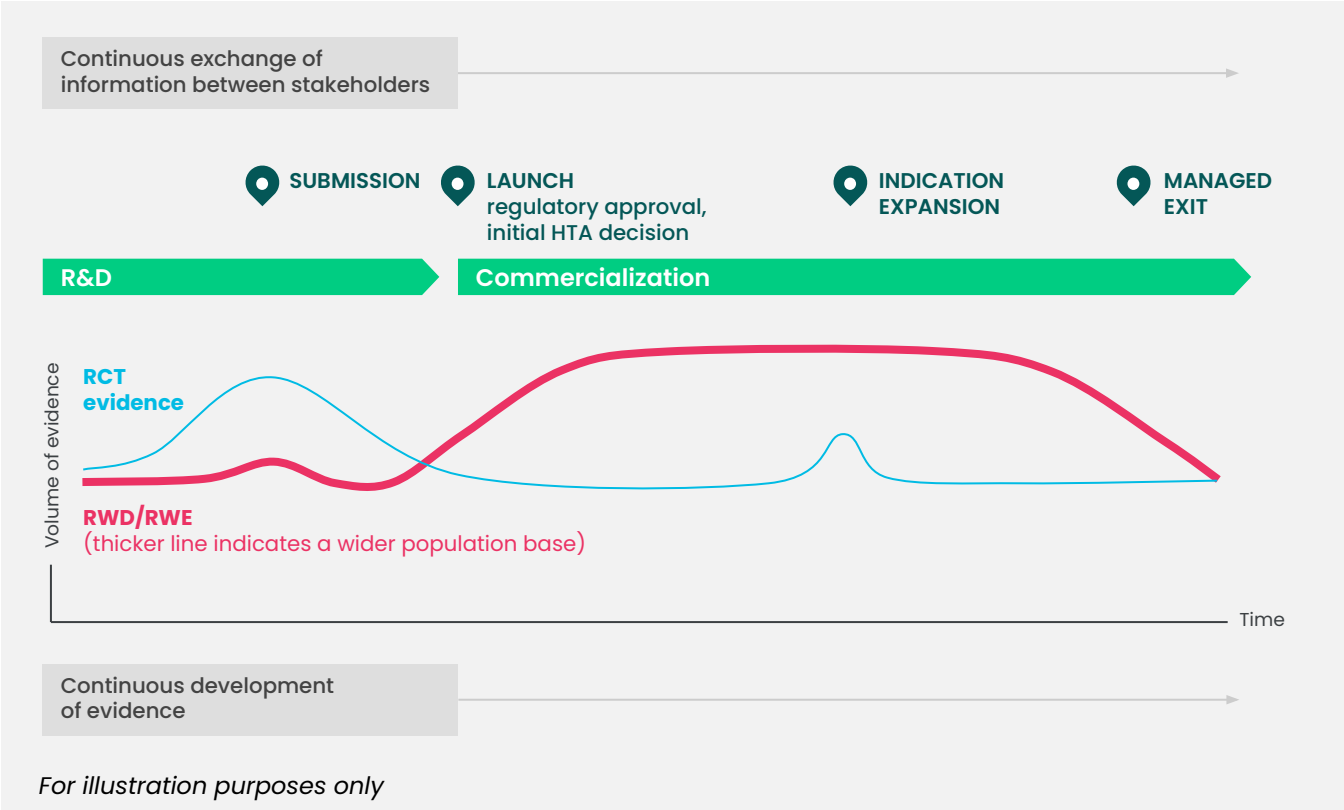


Darrow et al 2020. FDA Approval and Regulation of Pharmaceuticals, 1983-2018.
Zhang et al 2020. Assessment of Clinical Trials Supporting US Food and Drug Administration Approval of Novel Therapeutic Agents, 1995-2017
Vreman et al, 2020. Decision Making Under Uncertainty: Comparing Regulatory and HTA Reviews of Medicines in US and EU.

HTA agencies are moving toward lifecycle management

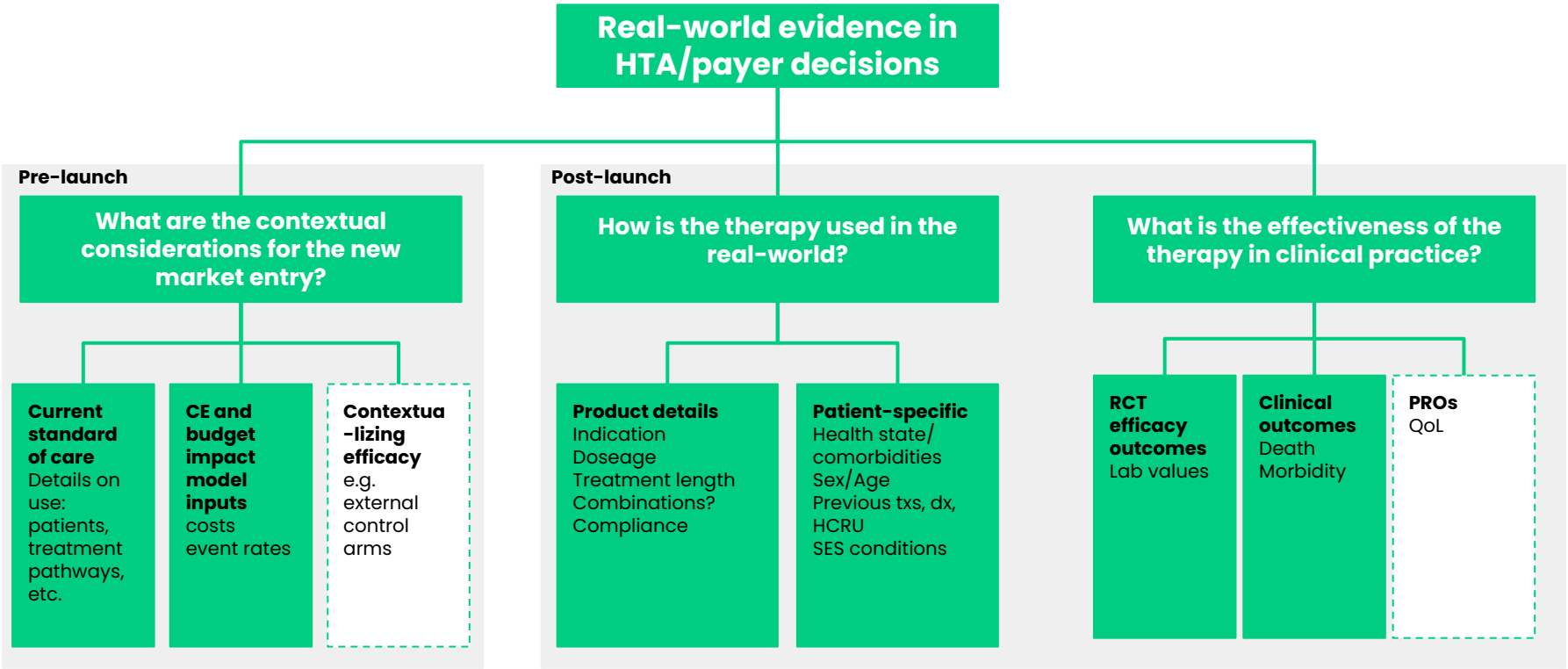
Reassessments represent **initial steps** in the shifting focus from one-time evaluations to more regular assessments across the lifecycle. For example:

- Coverage with evidence development (e.g., Cancer Drugs Fund in the UK, conditional funding in Netherlands, CMS in US)
- 5-year reassessments (HAS)



For illustration purposes only

Opportunity for RWE for HTAs/payers



Adapted from Facey, et al (2020)'Real-world evidence to support payer/HTA decisions about highly innovative technology in the EU-actions for stakeholders,' TLV's (2020) 'RWD report', and HTx (2020) 'Overview of the development of the use of RWD including a review of international consensus methods currently developed.

As needed/ if available

HTAs are piloting RWE driven reassessments

1. Determine and demonstrate the value of RWE in reassessments
2. Explore how rapid and transparent RWE could be utilized in health technology management

NICE National Institute for Health and Care Excellence

Learnings from 2022 Afib RWE Comparative Effectiveness study

ICER INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

Learnings from 2021 Hereditary Angioedema (HAE) RWE reassessment pilot

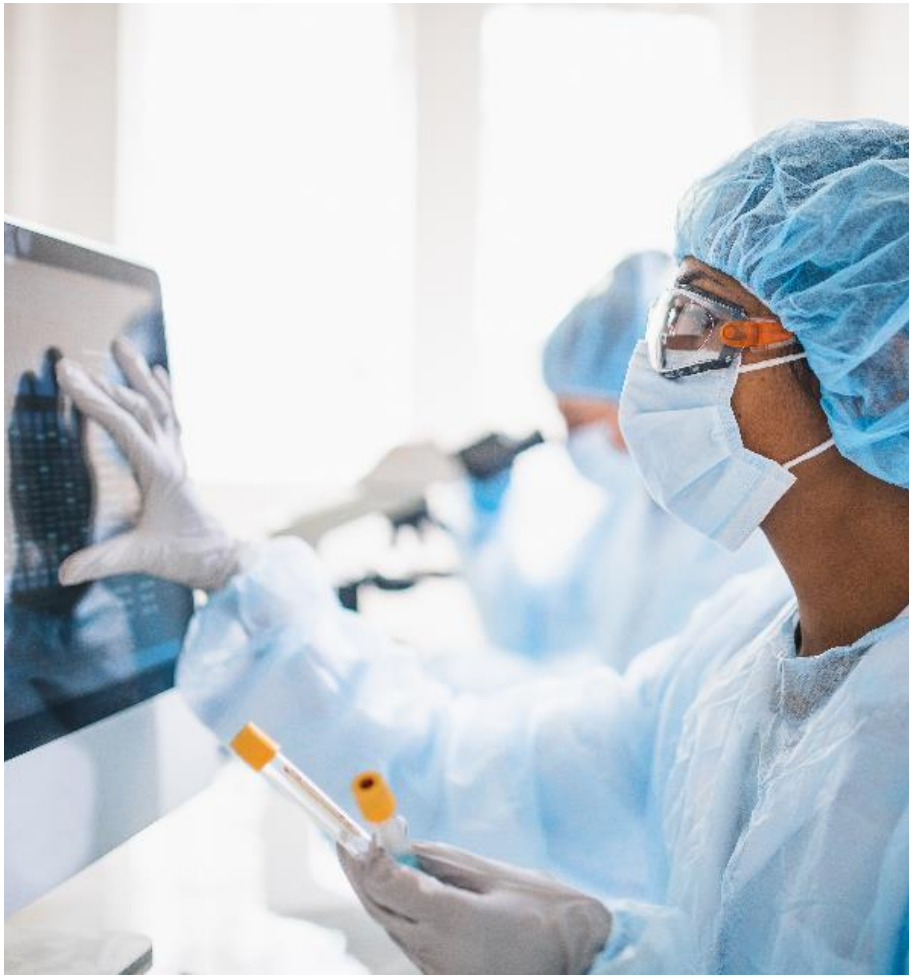
Complimenting clinical trial evidence with RWE

Seamus Kent

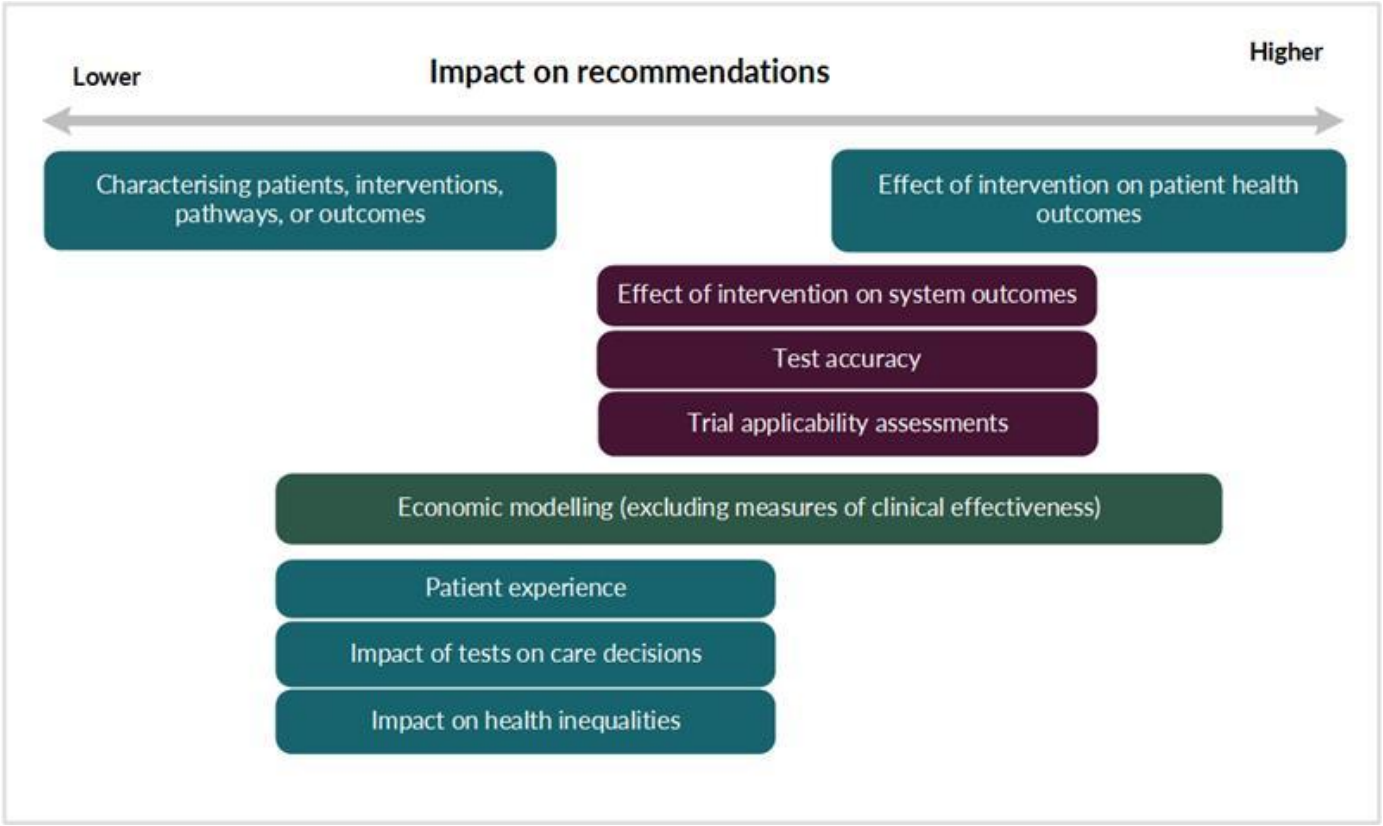
National Institute for Health and Care Excellence (NICE)

17 May 2022

NICE National Institute for Health and Care Excellence

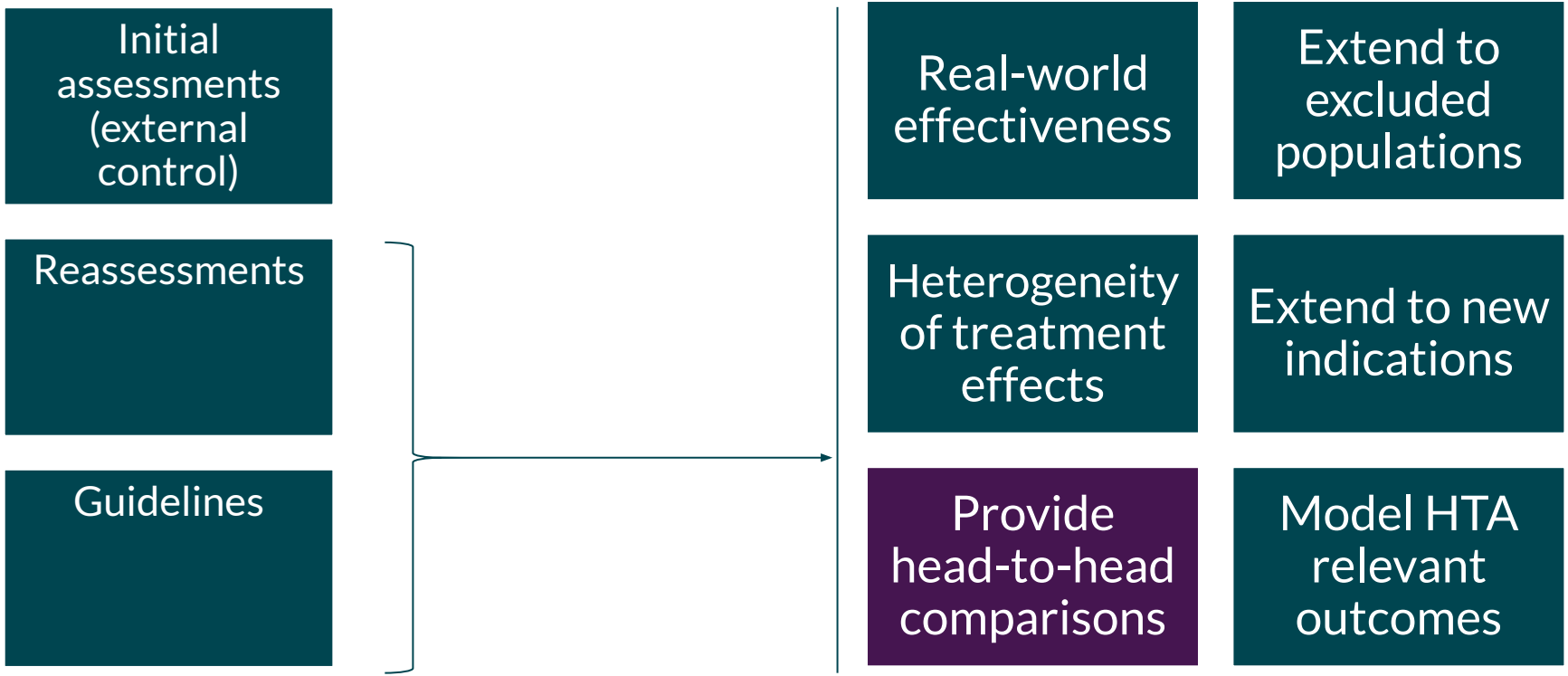


Use of real-world data in NICE guidance



NICE

Use of RWE for effectiveness

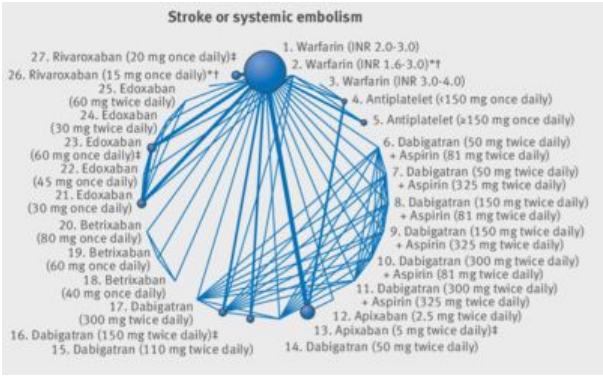


NICE

NICE recommendations about DOACs for stroke prevention

Technology evaluations

- Dabigatran 2012 (TA249)
- Rivaroxaban 2012 (TA256)
- Apixaban 2013 (TA275)
- Edoxaban 2015 (TA355)

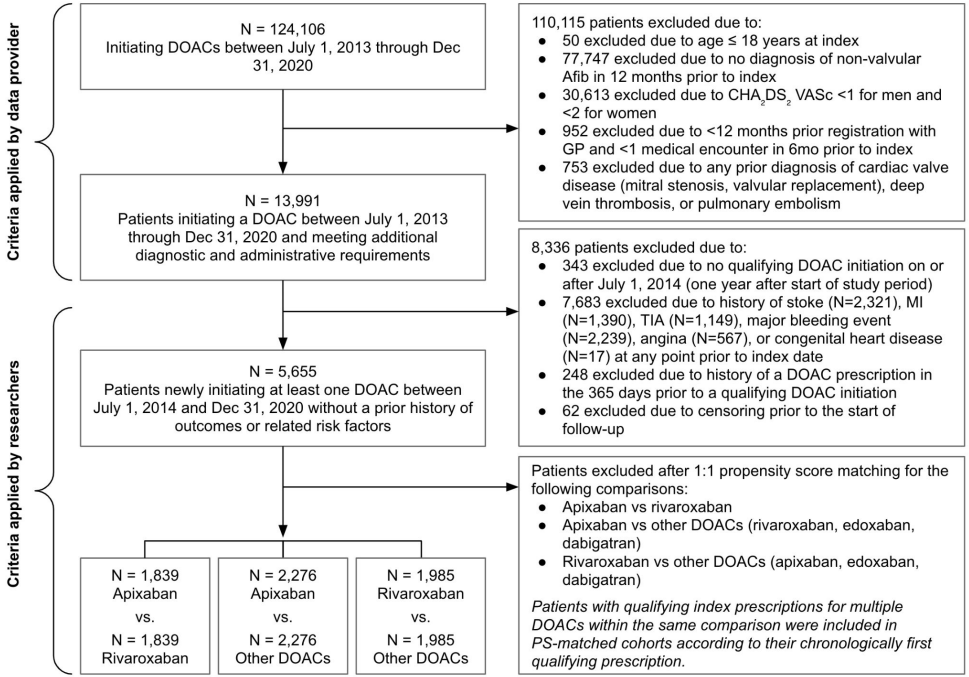


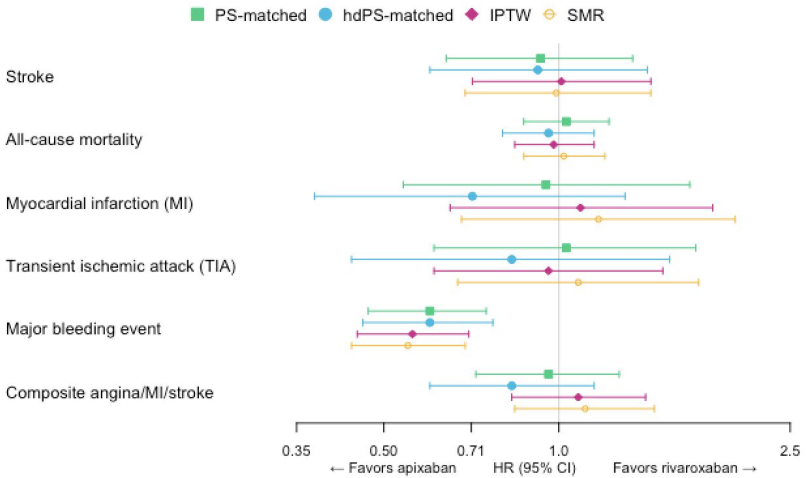
Lopez-Lopez et al 2017, BMJ

Decision making

- Reliant on indirect comparisons
- No evidence of differences in stroke incidence by DOAC
- Substantial differences in trial characteristics creates uncertainty in the indirect comparisons

Case study: Head-to-head comparisons of DOACs for stroke prevention in patients with AF





HR = hazard ratio; CI = confidence interval; PS = propensity score; hdPS = high dimensional propensity score; IPTW = inverse probability of treatment weighting; SMR = standardized mortality ratio weighting.

PS model accounts for age, gender, CHA2DS2 VASc score, year of treatment initiation, and the following diagnoses and treatments in baseline: non-major bleeding events, anemia, diabetes, hypertension, heart failure, osteoporosis/hip fracture, malignant neoplasm, acute kidney injury, chronic kidney disease, asthma/copd, dementia, aspirin, antiplatelets other than aspirin, warfarin, antianemic preparations, NSAIDs, opioids, SSRIs, antidepressants other than SSRIs, antiepileptics, antipsychotics, benzodiazepines, lipid lowering drugs, insulin, antihyperglycemics other than insulins, antihypertensives, antiarrhythmics, nitrates cardiac vasodilators, cardiac stimulants, gastrointestinal protective agents, bisphosphonates and other agents affecting bone structure, systemic corticosteroids, antineoplastics, systemic antibiotics, systemic antivirals, vaccines/immunoglobulins

Patients were followed until occurrence of outcome, death, end of patient registration, or end of study period (12/2020).

NICE

The future role for RWE on comparative effects in HTA assessments?

- There is a clear potential for RWE to augment trials and answer additional questions in the post-marketing setting
- High-quality research can be done on a reasonable timeframe
- We need better access to high-quality data through federated networks or other secure environments

When should a HTA body commission or undertake a real-world evidence study to complete existing RCT or observational studies?

NICE

Real-World Evidence's Usefulness in a Reassessment of Value

Jon Campbell, PhD

SVP for Health Economics

ICER
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Disclosure

- ICER's funders are available online: https://icer.org/who-we-are/independent-funding/
- ICER's value assessments are free from financial conflicts of interest from life science companies and insurers
- Views are my own

ICER Uses Real-World Evidence in Assessments

- Patient Lived Experience
- Other Potential Benefits and Contextual Considerations
- Cost-Effectiveness
  - Natural history, costs, and quality of life associated with different health states (Alzheimer's)
  - Modeling relative effects of treatments to real-world patient populations (high cholesterol)
  - Defining outcomes of "usual care" for single-arm trials (multiple myeloma)

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Observational Real-World Evidence Update

Prophylaxis of Hereditary Angioedema with Takhzyro and C1 Inhibitors: Effectiveness and Value

August 24, 2021

Case Study Methods

- In 2018, review of treatments for long-term prophylaxis against acute attacks in patients with hereditary angioedema (HAE)
- 2018 cost-effectiveness analysis sensitive to baseline severity
- Observational RWE Update: Nationally-representative insurance claims analysis provided baseline attack frequency
  - We continued to rely on RCT evidence to estimate relative reductions in attacks

Case Study Results

- Claims analyses suggested that those initiating preventative therapy had 1.88 attacks per month (vs. 3.39 per month from trials)
- 0.3 to 0.5 QALYs gained (vs. 0.8 to 1.3 QALYs gained)
- Cost-effectiveness findings suggested higher discounts to achieve value-based pricing

Case Study Discussion

- Impacts are case specific
- Observational RWE shifted the absolute (not relative) benefits
  - comparative clinical effectiveness and cost-effectiveness implications

My View of Observational RWE

- RWE remains vital to HTA as a complement to data from rigorous trials
- Reassessments may be strategic rather than routine

Acknowledgements and Future Directions

International Journal of Technology Assessment in Health Care

www.cambridge.org/thc

Commentary

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Key learnings from Institute for Clinical and Economic Review's real-world evidence reassessment pilot

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Abstract

Health technology assessment (HTA) agencies are considering adopting a lifecycle approach to assessments to address uncertainties in the evidence base at launch and to revisit the clinical and economic value of therapies in a dynamic clinical landscape. For reassessments of therapies post launch, HTA agencies are looking to real-world evidence (RWE) to enhance the clinical and economic evidence base, though challenges and concerns in using RWE in decision-making exists. Stakeholders are embarking on demonstration projects to address the challenges and concerns and to further define when and how RWE can be used in HTA decision making. The Institute for Clinical and Economic Review piloted a 24-month observational RWE reassessment. Key learnings from this pilot include identifying the benefits and challenges with using RWE in reassessments and considerations on prioritizing and selecting topics relevant for RWE updates.

Acknowledgements and Future Directions

- Topic Selection:
  - Can RWE influence decisions?
  - Prioritize actionable opportunities
- Feasibility:
  - What can be validly addressed using RWE
  - Can bias be appropriately controlled?

Real-World Evidence's Usefulness in a Reassessment of Value

Jon Campbell, PhD

SVP for Health Economics

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Industry Perspective

Polling Questions and Q&A

Polling Question 1

We discussed RWE cost-effectiveness model inputs and comparative effectiveness demonstration projects from ICER and NICE, respectively. What are priority use cases where HTAs should develop RWE guidance? **Rank these in order of most (1) to least important (4).**

- External control arms (ECAs)
- Synthetic data
- Nuances in generating RWE for med device
- Digital therapeutics

Polling Question 2

What is the most important trigger for a reassessment? **(Select 1)**

- Level of uncertainty in the initial clinical or economic assessment
- Newly published evidence (e.g., RCT)
- Environmental shifts (e.g., new market entries that change treatment paradigm)
- Time (e.g. 5 year reassessment)
- Other

Q&A

Thank you for joining.

Questions? Contact us.

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