ISPOR 2026
May 17-20, 2026 | Philadelphia, PA | USA

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Role of Integrated Real-World Evidence and Patient Reported Outcomes in Lifecycle HTA

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Presentation number: Podium 3817

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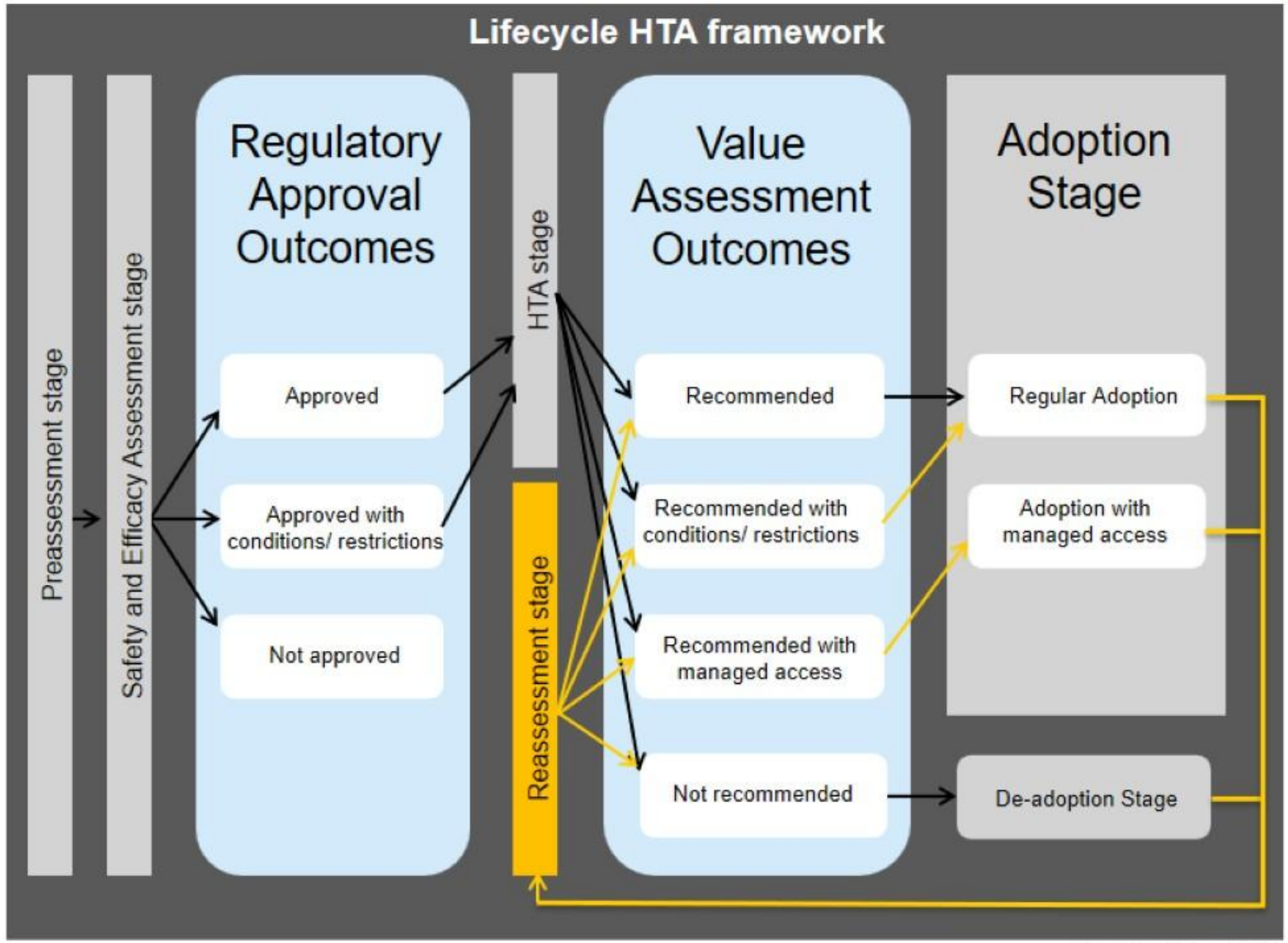
Disclosures

- All authors report employment with Evidinno Outcomes Research Inc. (Vancouver, BC, Canada)

Background

- Health technologies often launch amid clinical and economic uncertainty, making post-launch evidence generation critical for payer and regulatory decision-making[1]
- Lifecycle Health Technology Assessment (HTA) is an iterative approach that reassesses technology's value over time, using real-world evidence (RWE), patient reported outcomes (PROs) and stakeholders input[2-4]
- PROs are essential to lifecycle HTA because they capture patient-perceived treatment effects, treatment burden, and quality-of-life impacts that may not be fully reflected by clinical endpoints, particularly in chronic, rare, and high-uncertainty conditions[5]
- However, use of RWE and PROs remains challenging with regard to application and acceptance by evaluators



*Adapted from Kirwin et al. (2022)[6] [doi:10.1016/j.jval.2021.11.1373]

HTA: Health Technology Assessment; PRO: Patient-reported outcome; RWE: Real-world evidence

Objective

To evaluate how major HTA agencies integrate RWE and PROs within lifecycle HTA processes to address post-launch uncertainty

HTA: Health Technology Assessment; PRO: Patient-reported outcome; RWE: Real-world evidence

Methods

Literature Search

- A targeted review of publicly available appraisal and reassessment documents from NICE, HAS, CDA-AMC, and ICER (2021-2025) was conducted
- Included evaluations demonstrated **one or more lifecycle feature** (managed-access or scheduled re-evaluation, evidence-update requirements), and **documented real-world evidence (RWE)/ patient reported outcome (PRO) use**

Analysis

- A standardized analytic matrix compared
  - PRO instrument presence
  - RWE source categories
  - Patient & equity considerations
  - Managed-access frameworks
  - Cost-effectiveness reassessment
  - Stopping or continuation rules
- These elements were examined as interconnected components through which post-launch evidence informs lifecycle HTA decisions

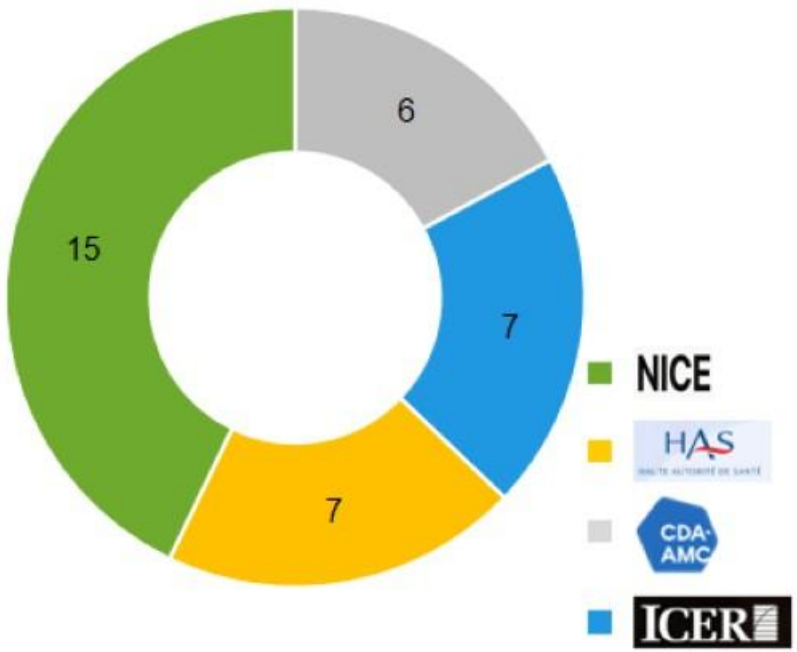
Conceptual framework illustrating how RWE and PROs are translated into lifecycle HTA decisions

CDA-AMC: Canada's Drug Agency; CE: Cost-effectiveness; HAS: Haute Autorité de santé; HTA: Health Technology Assessment; ICER: Institute for Clinical and Economic Review; NICE: National Institute for Health and Care Excellence; PRO: Patient-reported outcome; RWE: Real-world evidence

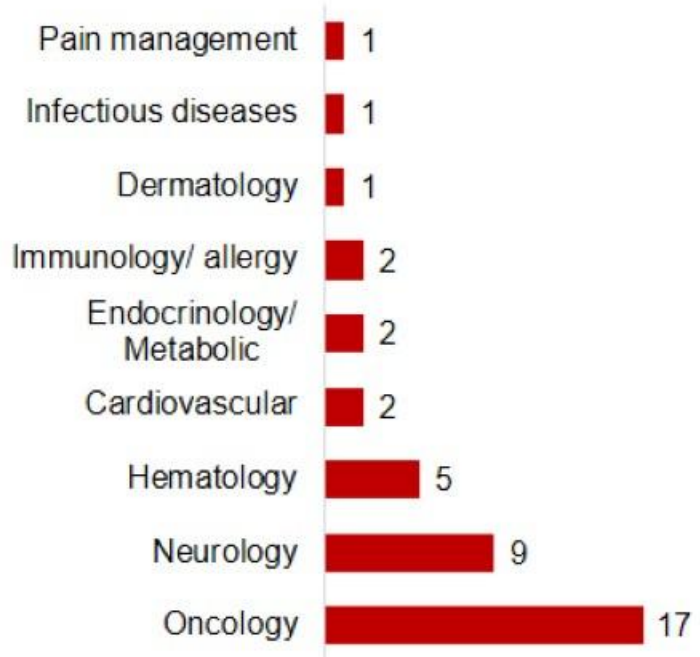
Results: Appraisals Included Across HTA Bodies

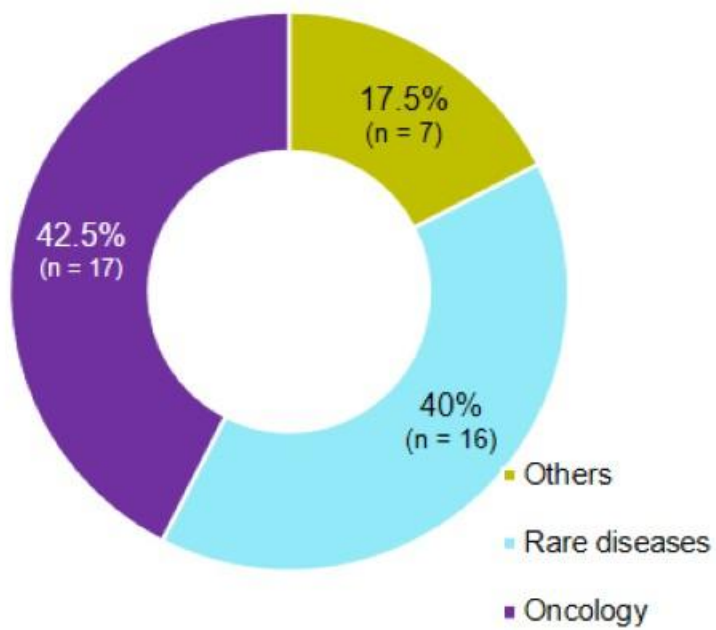
- Forty appraisals focusing on RWE and PRO to inform lifecycle assessments were included: NICE (n = 15), HAS (n = 12), ICER (n = 7), and CDA-AMC (n = 6)
- The majority involved oncological (n = 17), neurological (n = 9), and hematological indications (n = 5). Around 40% (n = 16) targeted rare diseases

Number of appraisals across HTAs



Number of appraisals across therapeutic areas





HTA: Health Technology Assessment; PRO: Patient-reported outcome; RWE: Real-world evidence

Results: PRO Integration in Lifecycle Assessments

PROs are routinely considered in HTA deliberations

- Public reporting of PRO instruments was inconsistent
  - Specified PRO instruments: 25/40 appraisals (63%)
  - Unspecified instrument: 15/40 appraisals (37%)

Types of PRO measures reported

- Generic HRQoL utilities (most frequently reported)
  - EQ-5D appears most frequently (n=19)
  - Used mainly for economic modeling
- Disease-specific PROs (selective, indication-driven)
  - Functional and neurodevelopmental scales in rare diseases (e.g., HFMSE, CHOP-INTEND, MFM32, SMAIS)
  - Symptom-specific scales in pain and dermatology (e.g., NRS/VAS, DLQI, POEM)

PRO role importance is contextual

- PROs led to the primary decision where primary clinical endpoint was not met
- Across agencies and therapeutic areas, PROs are most often used to:
  - Contextualize disease burden
  - Inform committee deliberations
  - Support patient and clinician testimony
  - Contribute to value narratives
- This is consistent across:
  - Oncology
  - Rare diseases
  - Metabolic and pain indications

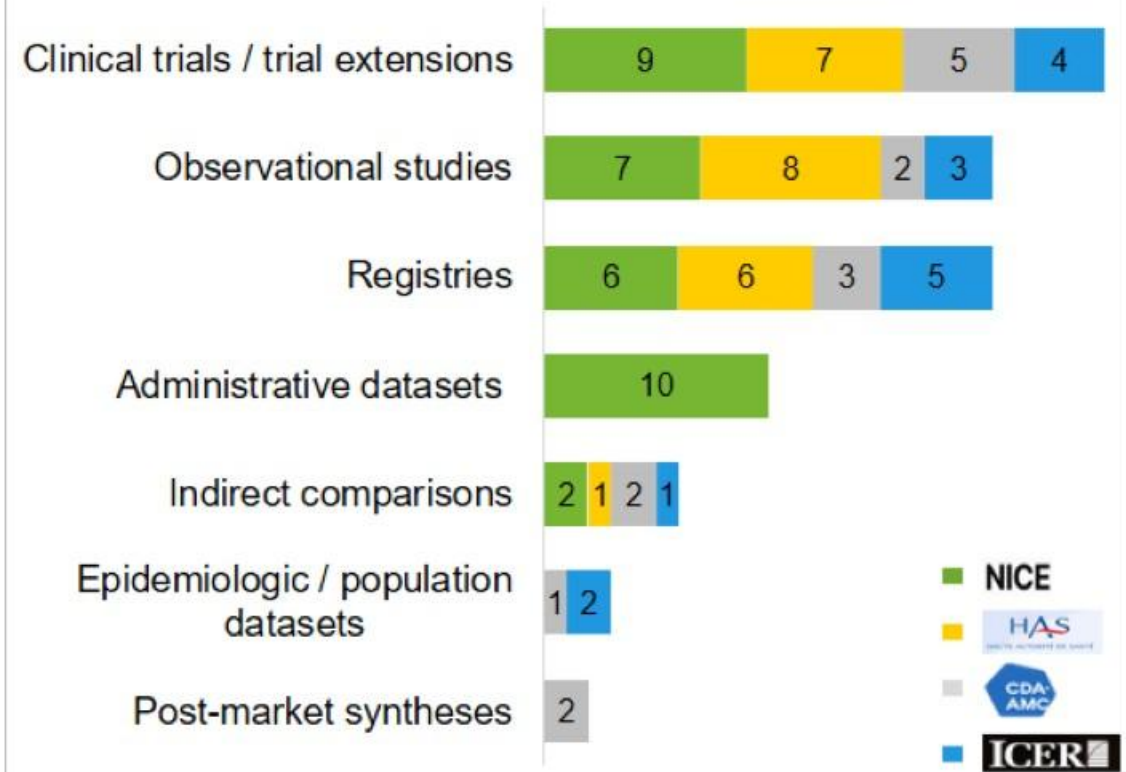
CHOP-INTEND: Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders; DLQI: Dermatology Life Quality Index; EQ-5D: EuroQol 5-Dimension questionnaire; HFMSE: Hammersmith Functional Motor Scale–Expanded; HINE-2: Hammersmith Infant Neurological Examination, Section 2; ITQoL-SF47: Infant and Toddler Quality of Life Questionnaire – Short Form 47; KCCQ-23: Kansas City Cardiomyopathy Questionnaire-23; MFM32: Motor Function Measure-32; NRS/NPRS: Numeric Rating Scale / Numeric Pain Rating Scale; POEM: Patient-Oriented Eczema Measure; QoL: Quality of life; RULM: Revised Upper Limb Module; SMAIS: Spinal Muscular Atrophy Independence Scale; SPID: Sum of Pain Intensity Differences; VAS: Visual Analog Scale.

RWE Sources Used Across HTA Appraisals

RWE sources are highly heterogeneous

- Across 40 appraisals, multiple RWE sources were often used within the same evaluation, reflecting layered evidence strategies rather than single-source reliance
- There is no single dominant RWE source across HTA agencies
- Registries and administrative datasets are disproportionately used for advanced therapies and oncology, reflecting:
  - Long-term uncertainty
  - Durability concerns
  - Safety and implementation complexity
- RWE is most often used to contextualize or resolve uncertainty, rather than to replace trial evidence at initial appraisal

RWE sources used across HTA appraisals



Rapid regulatory approvals (e.g., CMA) often rely on immature trial data, shifting evidence generation post-launch and increasing reliance on RWE in HTA.

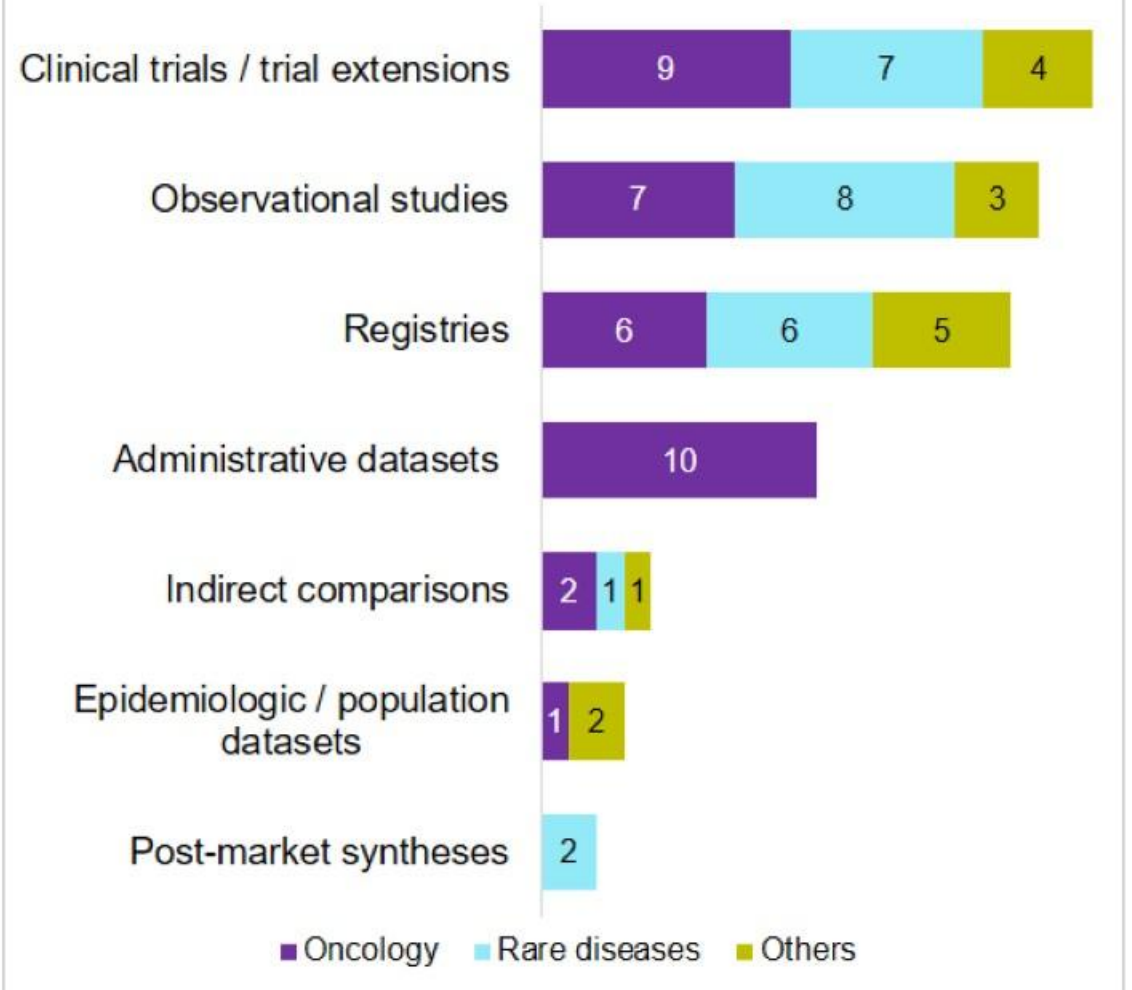
CMA: Conditional Marketing Authorization; HTA: Health Technology Assessment; RWE: Real-world evidence

RWE Source Distribution Across Therapeutic Areas

RWE source use reflects therapeutic area-specific evidence needs and availability

- **Oncology appraisals** more frequently use administrative datasets and registries, consistent with established national RWE infrastructures
- **Rare disease appraisals** more frequently use registries and observational RWE, often supplementing small or single-arm trial evidence
- Clinical trials and extensions remain foundational across all therapeutic areas, but are layered with different RWE sources depending on context
- **Other therapeutic areas** use narrower RWE inputs, mainly observational or epidemiologic, with limited lifecycle integration

RWE sources across therapeutic areas

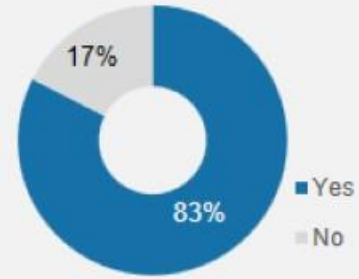


RWE: Real-world evidence

Patient-reported & Real-World Equity Informing HTA Reassessments

Patient-reported and real-world equity input

- Explicitly identified in 33 of 40 (83%) evaluations, indicating widespread acknowledgment of equity-relevant issues across HTA decisions



Primary ways patient equity considerations were incorporated

Patient- and caregiver-reported outcomes and experiences

- Burden of disease
- Treatment logistics
- Caregiver impact and quality of life

RW treatment access and burden

- Travel to specialist centers (e.g., CAR-T, gene therapy)
- Treatment complexity and monitoring burden
- Eligibility constraints and pathway positioning

Population-level equity evidence from RW use

- Underserved or historically marginalized populations
- Pediatric and ultra-rare disease populations
- Disparities in baseline access to care

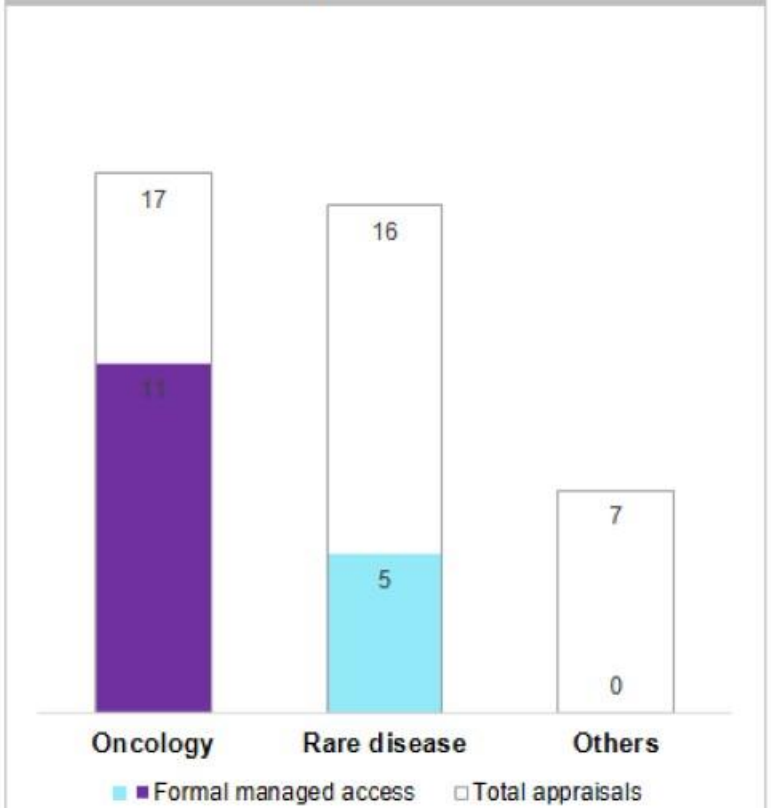
CAR-T: Chimeric Antigen Receptor T-cell therapy; HTA: Health technology assessment; RW: Real-world

Managed-access Frameworks Utilized by HTAs

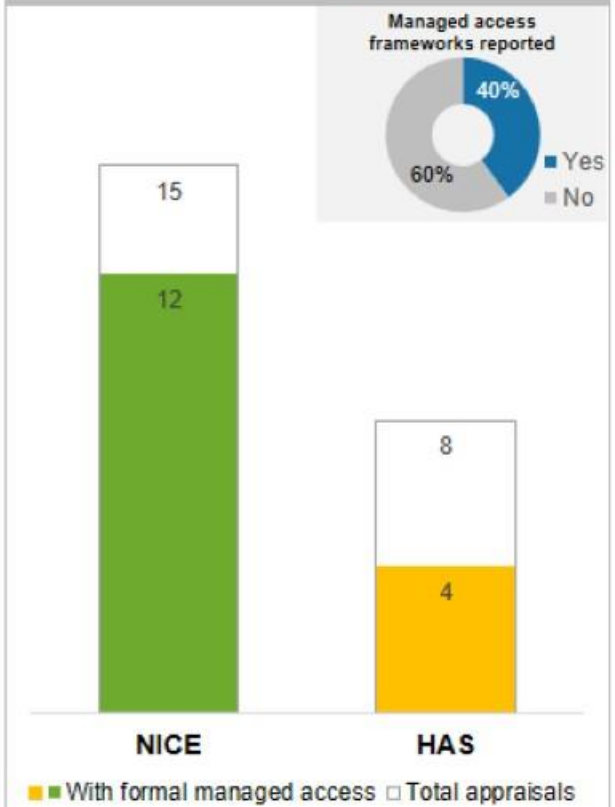
Formal managed-access frameworks

- Formal lifecycle mechanisms were identified in 16 of 40 (40%) HTA evaluations, indicating explicit structural adoption of lifecycle HTA approaches
- **NICE** implemented through:
  - Managed Access Agreements (MAAs)
  - Cancer Drugs Fund (CDF)
  - Highly Specialized Technologies (HST) arrangements
- **HAS** implemented primarily via:
  - Early Access linked re-evaluation pathways
  - Restricted-scope reimbursement with planned reassessment

Managed access frameworks across therapeutic areas



Managed access frameworks across HTA appraisals



Although no formal lifecycle frameworks were identified for CADTH and ICER:

- CADTH frequently applied: Conditional reimbursement; Post-Market Drug Evaluation (PMDE)
- ICER* routinely: Signaled future reassessment; Linked recommendations to anticipated evidence maturation

CDF: Cancer Drug Fund; HST: Highly Specialized Technologies; ICER: Incremental Cost-effectiveness ratio;; MAA: Managed Access Agreement; PMDE: Post-Market Drug Evaluation . *Note ICER is not a formal HTA body (yet)

Levers in Cost-effectiveness Reassessment Decisions

Stopping or continuation rules

- **Stopping rules**: structured, predefined criteria used to determine when a technology's evidence generation phase should end, and a formal reassessment should be initiated to decide on continued reimbursement, restriction, or disinvestment
- **Continuation rules**: structured mechanisms designed to determine whether a technology should continue to be reimbursed, used, or adopted based on new evidence, often following a period of conditional approval
- Stopping or continuation rules were applied in 29/40 (73%) evaluations; prominently by NICE and HAS (examples below)

NICE

- Fixed treatment duration (e.g., 2-year stopping rule in oncology)
- Stop on progression or loss of benefit
- Continuation criteria specified within CDF/ MAA decisions

HAS

- Short-term reassessment checkpoints (e.g., 6-month weight-loss thresholds)
- Scope-restricted continuation criteria
- Early Access-linked discontinuation rules

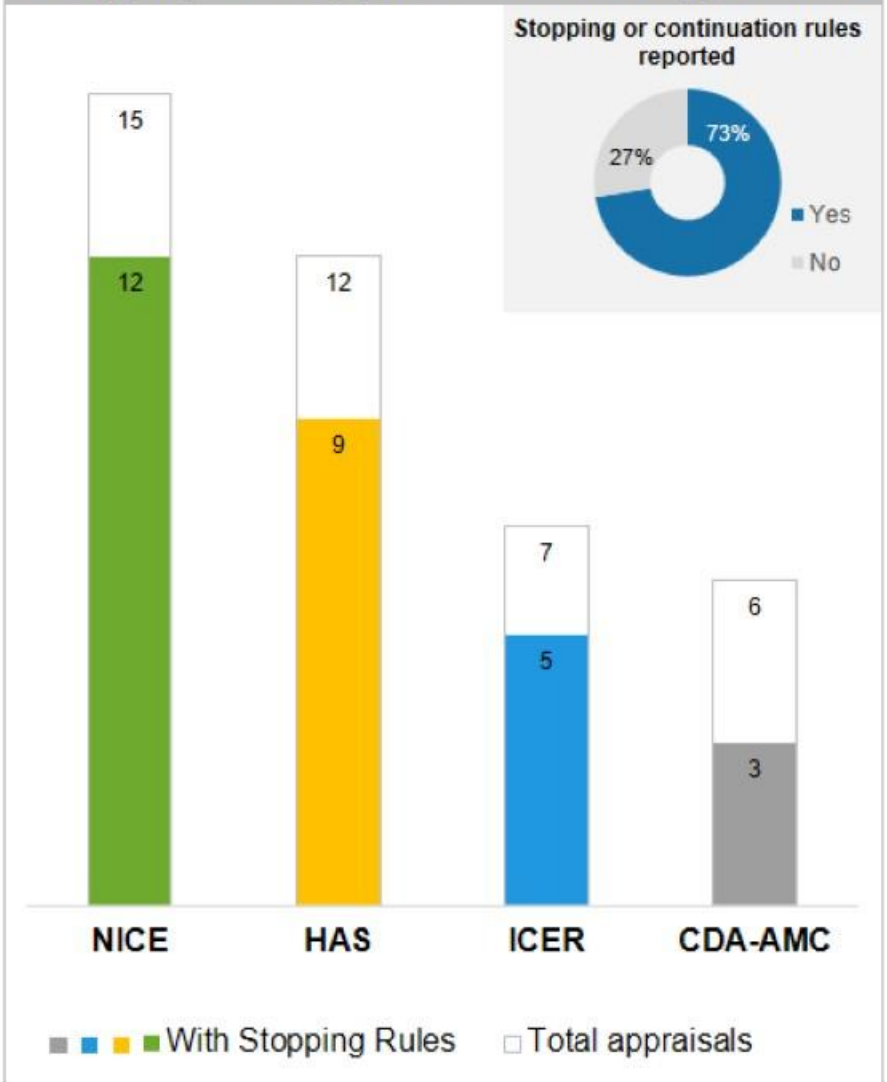
ICER

- Conditions tied to reassessment of value
- Evidence-maturity or durability thresholds

CDA-AMC

- Initiation and renewal conditions
- Implicit continuation requirements rather than formal stopping rules

Stopping rules applied across HTA appraisals



CDF: Cancer Drug Fund; HTA: Health technology assessment; MAA: Managed Access Agreement

Post-Launch Controls: Cost-Effectiveness Reassessment (1/2)

Post-approval cost-effectiveness reassessments leverage mature clinical, RWE, and PRO data to resolve uncertainty and update value conclusions.

Reasons for CE reassessments	
Mature survival or treatment durability data	Oncology (CDF exits) Gene and cell therapies
Resolution of key model uncertainties	OS extrapolation Treatment duration assumptions
Comparator repositioning	New entrants Head-to-head evidence emergence
Price or commercial arrangement changes	Managed access exits Outcomes-based agreements
Incorporation of real-world effectiveness and PRO data	

Reassessment focused on updated ICERs or value conclusions, rather than de novo re-appraisal

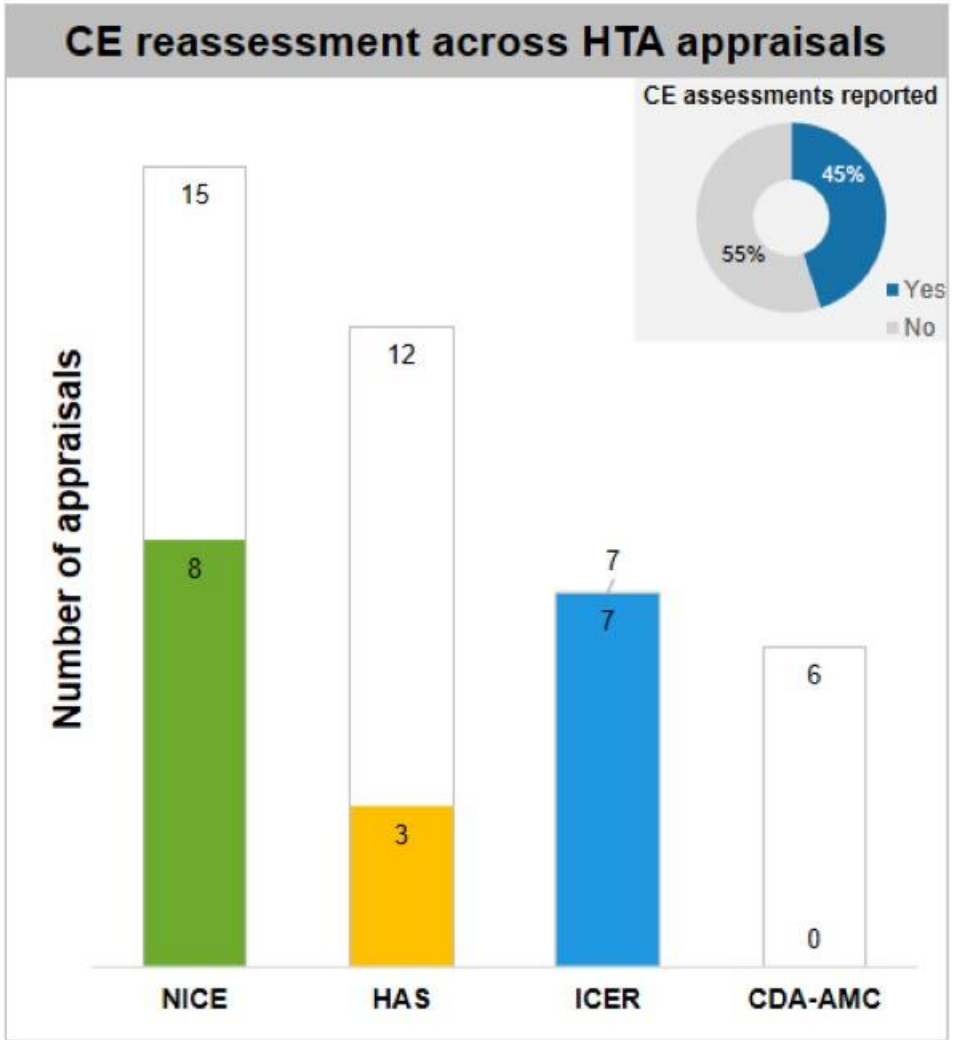
CDF: Cancer Drug Fund; CE: Cost-effectiveness; ICER: Incremental Cost-effectiveness ratio; MAA: Managed Access Agreement; PRO: Patient reported outcomes; RWE: Real-world evidence

Post-Launch Controls: Cost-Effectiveness Reassessment (2/2)

- Formal cost-effectiveness (CE) reassessments were reported in 18/40 (45%) evaluations, indicating active post-launch cost management across HTA systems

HTA agency-level distribution

- **NICE:** 8/15 (53%) evaluations involved CE reassessment, most commonly via Cancer Drugs Fund exits or Managed Access Agreement reviews
- **HAS:** 3/12 (25%) evaluations included scheduled CE re-evaluations, typically linked to Early Access or restricted-scope approvals
- **ICER:*** 7/7 (100%) evaluations underwent formal CE reassessment through public evidence and value updates
- **CDA-AMC:** 0/6 (0%) evaluations involved formal CE reassessment mechanisms



*Note ICER is an independent US-based HTA body and not a governmental decision-maker; its assessments are non-binding and do not restrict market launch or reimbursement following FDA approval..

Overall Comparison Across HTA agencies

- All HTA agencies apply lifecycle principles, but implementation varies markedly in formality and structure
- RWE is used across all agencies, but preferred sources differ (administrative datasets, registries, observational data)
- Patient input and equity considerations are widely acknowledged, yet remain primarily qualitative and deliberative, rather than formal decision rules

NICE ICER

NICE and ICER exhibit the strongest lifecycle orientation, with systematic post-launch evidence review and cost-effectiveness reassessment

HAS
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HAS applies lifecycle controls selectively, mainly through restricted scope, Early Access pathways, and scheduled re-evaluation

CDA-AMC

CADTH relies on conditional reimbursement and post-market evidence generation, without formal reassessment frameworks

HTA: Health Technology Assessment; PRO: Patient-reported outcome; RWE: Real-world evidence

Discussion and Conclusion

- **RWE and PROs are essential for managing post-launch uncertainty**, particularly for therapies approved with immature trial evidence
- **PROs consistently anchor patient-centered value across HTA decisions**, sometimes influencing outcomes when clinical endpoints fall short
- **RWE complements trial evidence heterogeneously**, informing real-world effectiveness, safety, and durability, especially in oncology and rare diseases
- **Formal managed-access and reassessment pathways translate post-launch evidence into concrete decisions**, where RWE and PRO integration most consistently occurs
- **Together, RWE and PROs enable incremental, lifecycle-based value refinement rather than de novo reassessment**

RWE and PROs are essential enablers of post-marketing drug development, supporting evidence maturation, uncertainty reduction, and dynamic value reassessment across the HTA lifecycle.

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Any questions

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Acknowledgments

- The authors would like to thank Otto Lam for assistance with the initial development of presentation materials.

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Abbreviations

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