Current and future trends in HTA

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THE LONDON SCHOOL OF ECONOMICS AND POLITICAL SCIENCE

Outline

1. Some noteworthy trends on HTA across countries, funding & coverage

2. The challenges for HTA going forward

3. Thoughts on options for assessment & funding of new drugs in the future

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WP7- Methodological tools using multi-criteria value methods for HTA decision-making

Objectives	Deliverables	Policy Impact
• To develop and validate an actionable analytical framework on the determinants of HTA/funding decisions • To build a multi-criteria framework allowing for the evaluation of new technologies based on a common & transparent value metric	• An analytical framework and a toolkit outlining the determinants of HTA recommendations across settings. • A flexible evaluation framework and design techniques to structure MCDA models	• Insights for HTA policy-makers about which aspects should be considered in the evaluation of new medicines • Provide an actionable framework for HTA agencies and their committees evaluating new drugs within a common value frame

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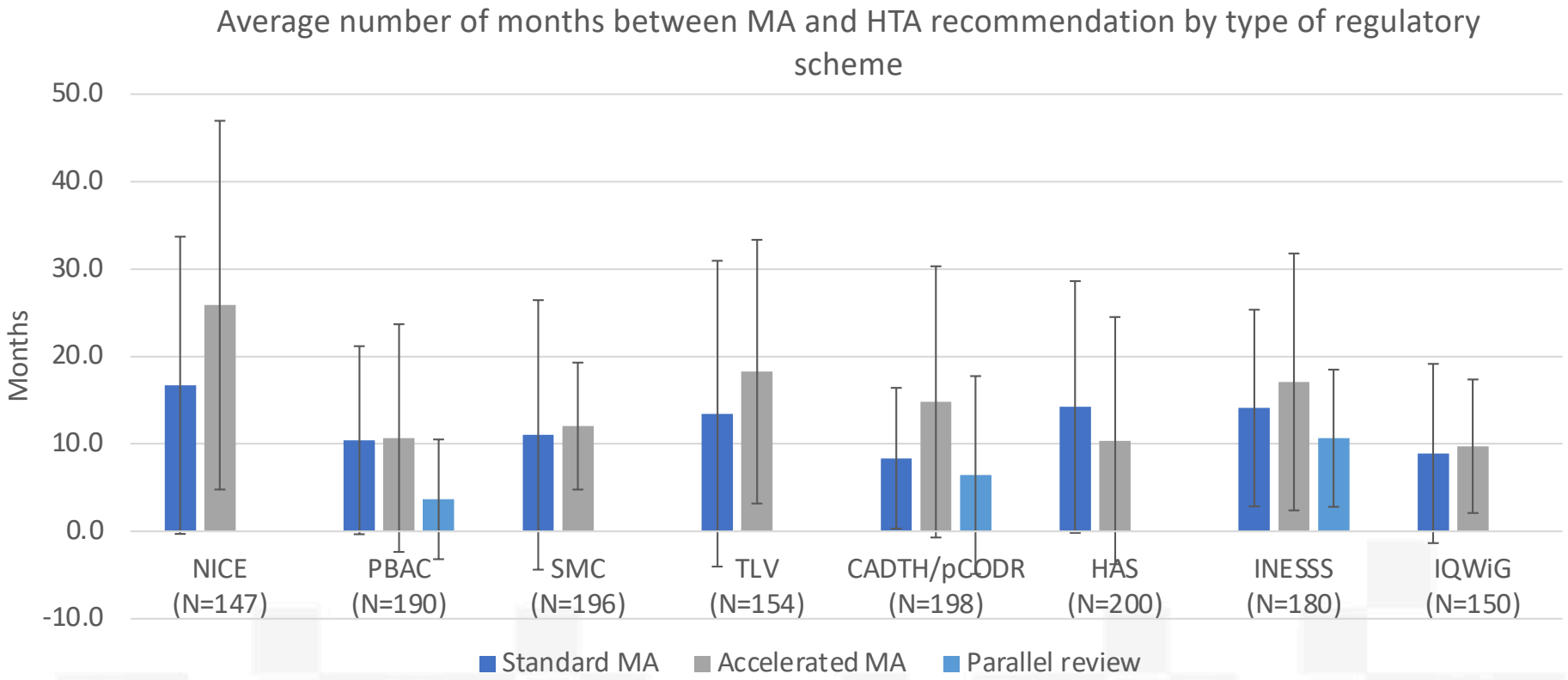
- Analysis of HTA recommendations across 8 countries: England, Scotland, France, Germany, Canada, Australia, Sweden, Quebec
- Sample of 1,415 drug-indication pairs across all indications and 8 countries
- Extensive analytical framework capturing value drivers across products

1. Time to funding recommendation



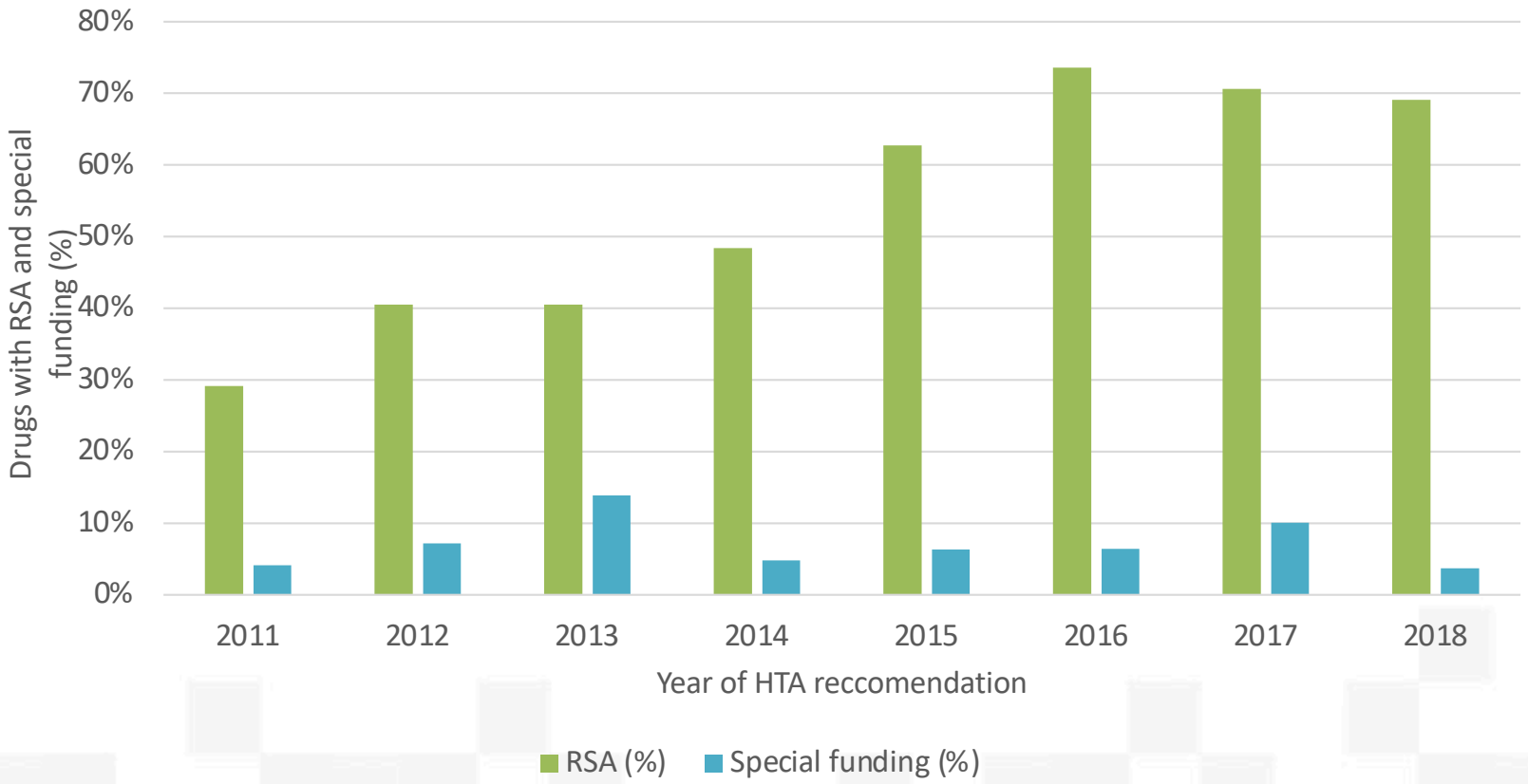
- **Significant variations exist across countries**, but there is **no strong impact** of accelerated approval scheme on the time to coverage recommendation by HTA bodies.
- The implementation of **parallel reviews** in a number of settings (Canada and Australia), has an impact on the time to coverage recommendation. Some European countries implement similar practices in their jurisdiction (e.g. UK for oncology drugs)

Source: The authors based on information extracted from publicly available HTA reports.
Note: CADTH: Canadian Agency for Drugs and Technologies in Health; IQWIG: Institute for Quality and Efficiency in Health Care; TLV: The Dental and Pharmaceutical Benefits Agency; HAS: Haute Autorité de Santé; NICE: National Institute for Health and Clinical Excellence (NICE); PBAC: Pharmaceutical Benefits Advisory Committee; SMC: Scottish Medicines Consortium; pCODR: pan-Canadian Oncology Drug Review.

2. Clinical restrictions

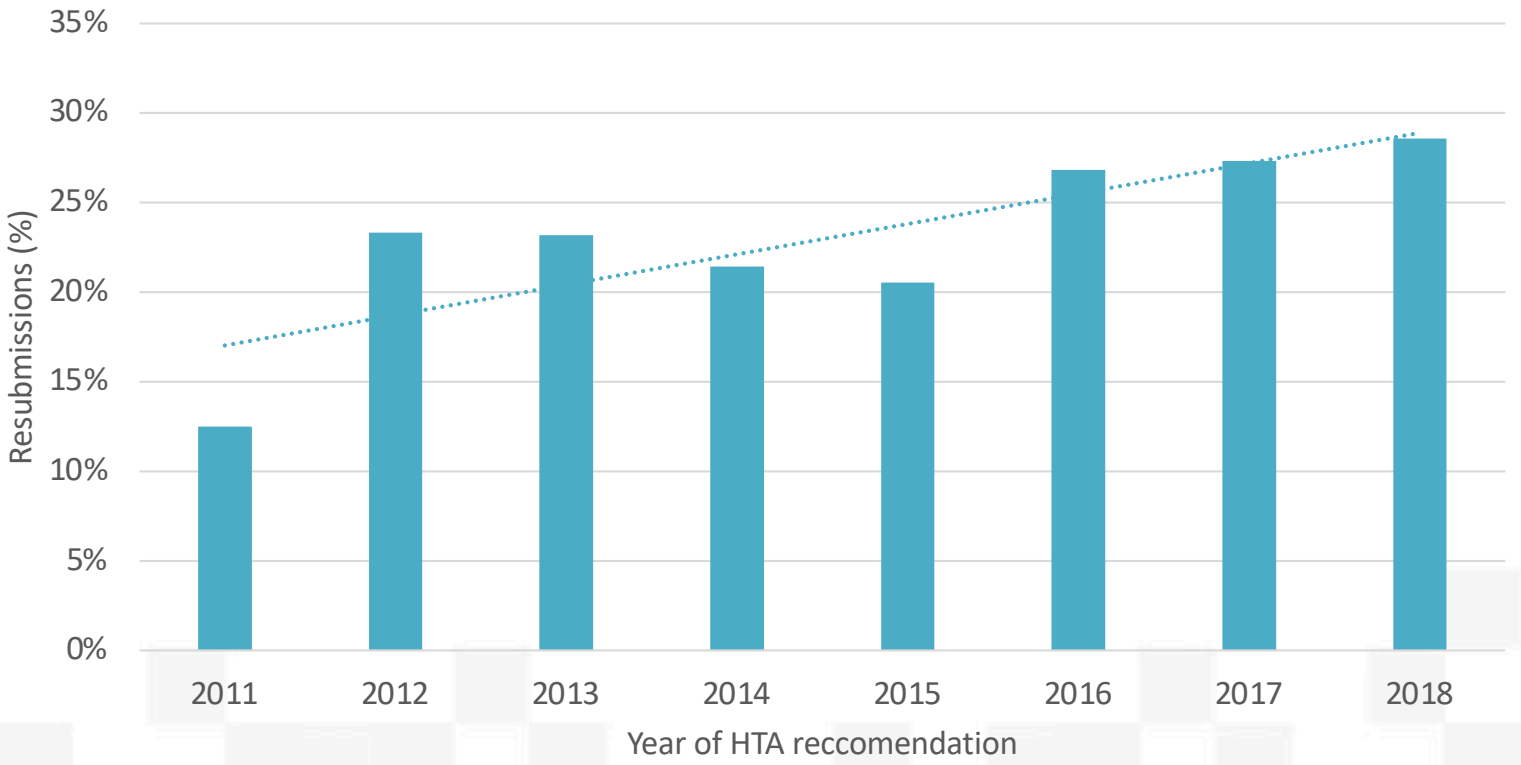
- **Clinical Restrictions:** may relate to the use of the medicine in patient *sub-populations* that are likely to benefit most, in a certain *dosing or setting* or if it is related to country specific administrative provision
- Restrictions at sub-population level constitute **restrictions on the approved indication**

3. Economic restrictions



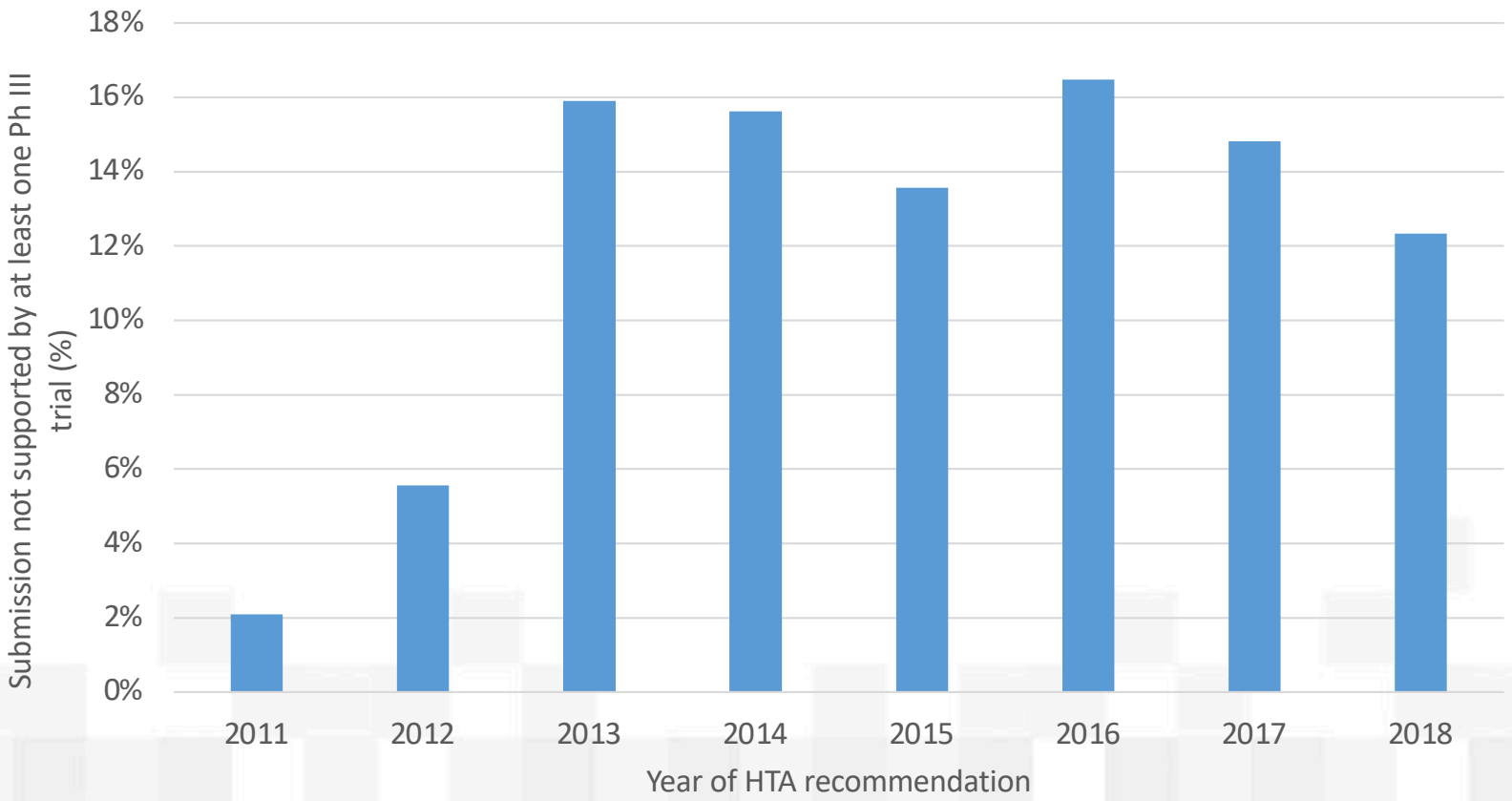
Economic restrictions: may relate to the presence of a *risk sharing agreement (RSA)* or *other special funding arrangement* [non-risk-sharing] (e.g. CDF, new drug funding programme (NDFP), exceptional access programme (EAP), among others)

4. Resubmissions



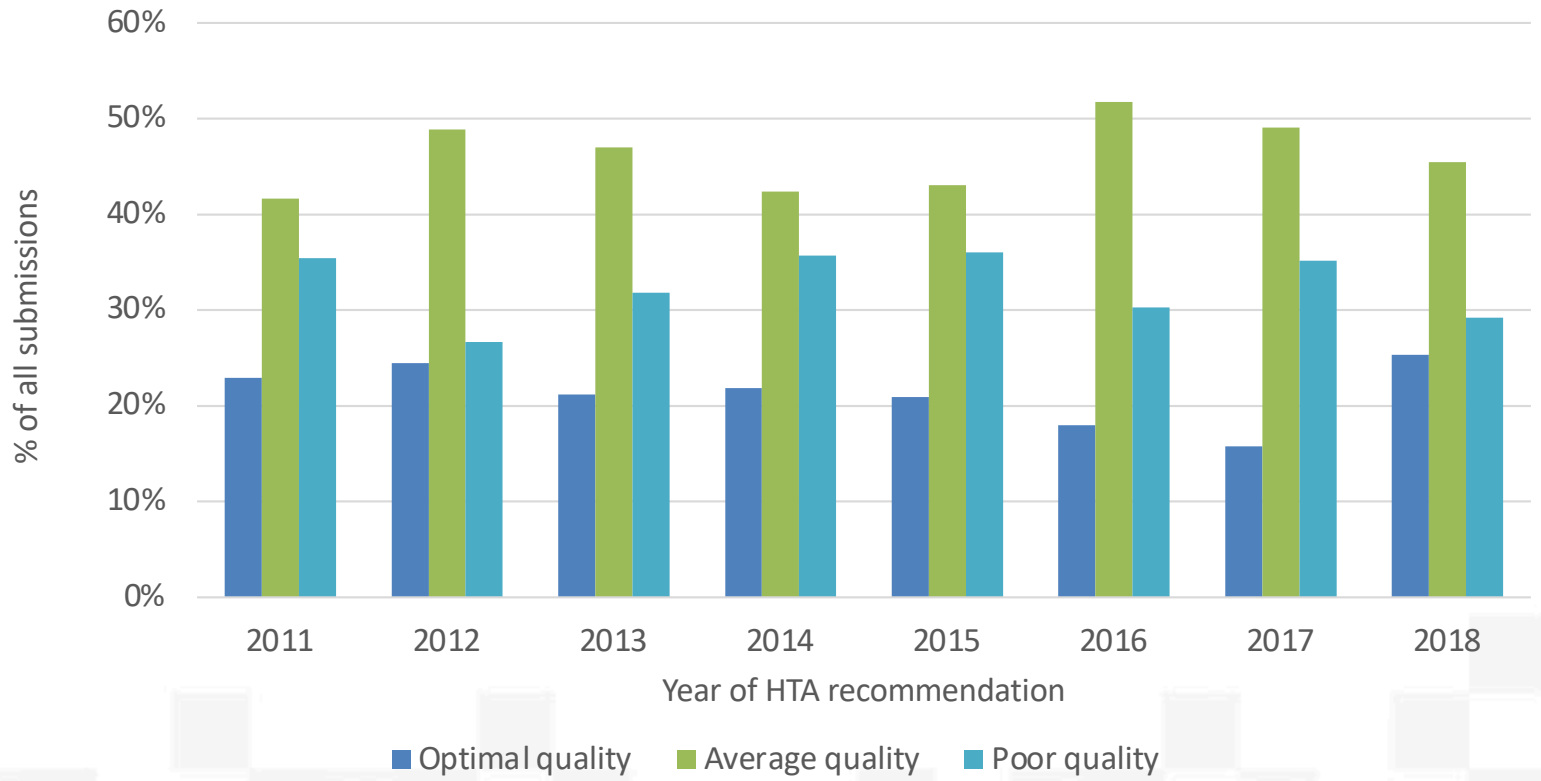
- **Resubmissions**, following a previous rejection, typically range between 20-25% of all HTAs in the study countries
- In the vast majority of cases, resubmissions result in coverage with restrictions (“LWC”)

5. Evidence supporting submission other than phase III trial



- Submissions to HTAs supported by clinical evidence other than a Phase III RCT account for approx. 14% of all cases

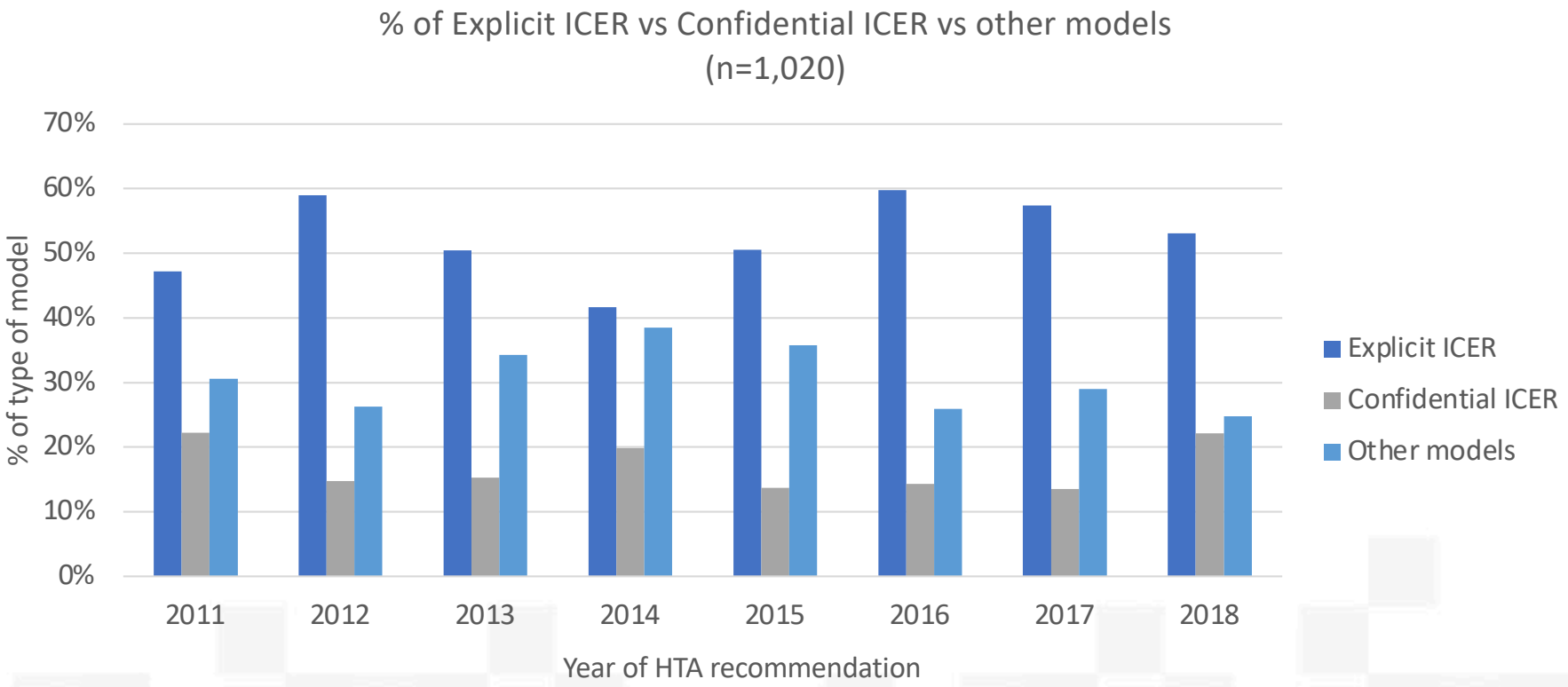
6. Quality of evidence supporting HTA submissions



Overall quality of clinical evidence presented in the HTA submission combining the occurrence of one or multiple issues related to (a) the design of the study, (b) the comparator used in the study and (c) the follow up period.

- "**High quality"** of data refers to no issue in any category
- "**Average Quality"** of data refers to cases when there are issues in one of the categories
- "**Poor quality"** refers to cases when there are issues in more than one category.

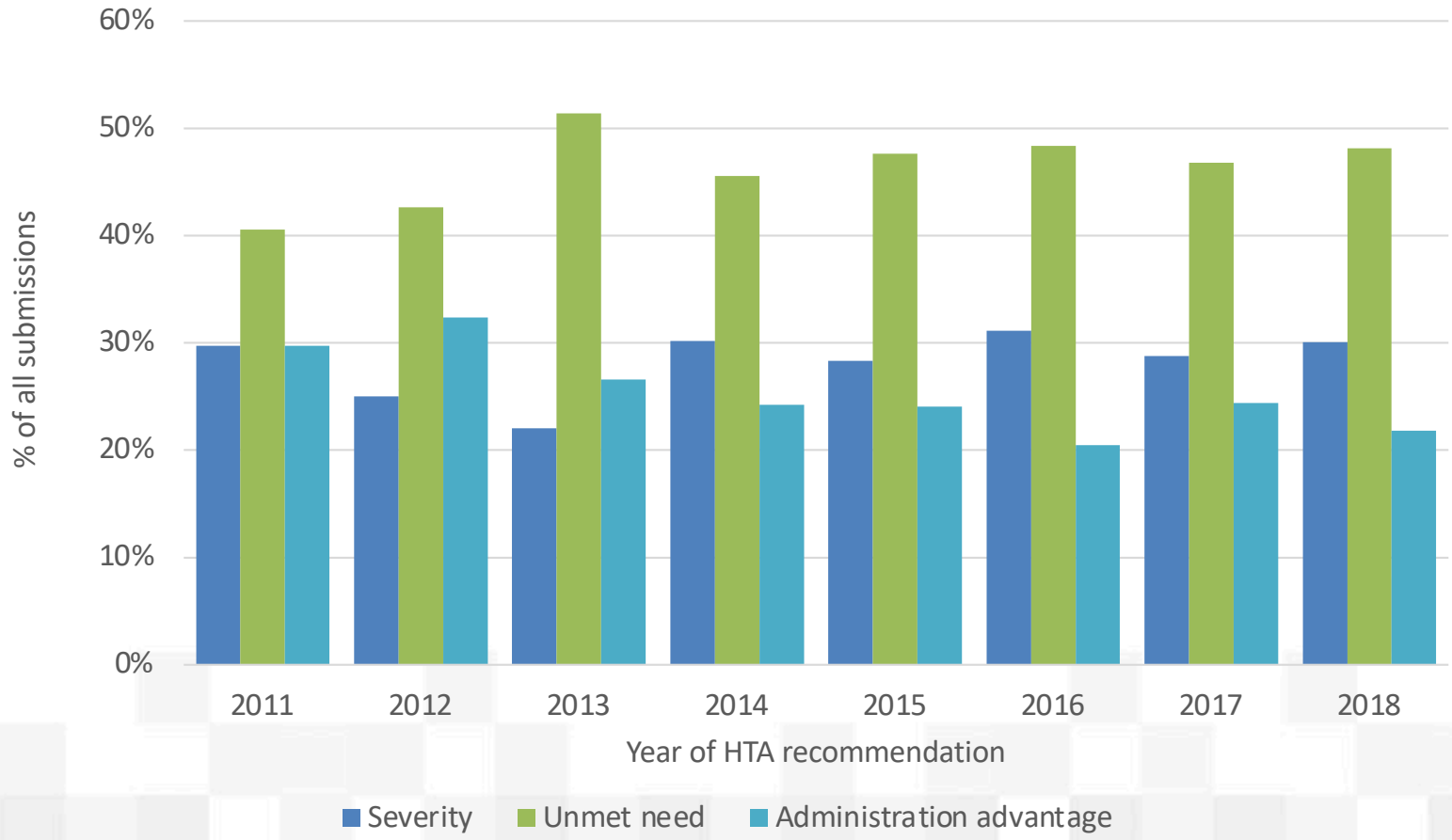
7. Economic evidence



- The variable considers wheatear a cost-utility analysis was conducted and the ICER was publicly available or other model were submitted by the manufacturer.
- France and Germany are excluded from this comparison as economic analysis does not form part of their assessment

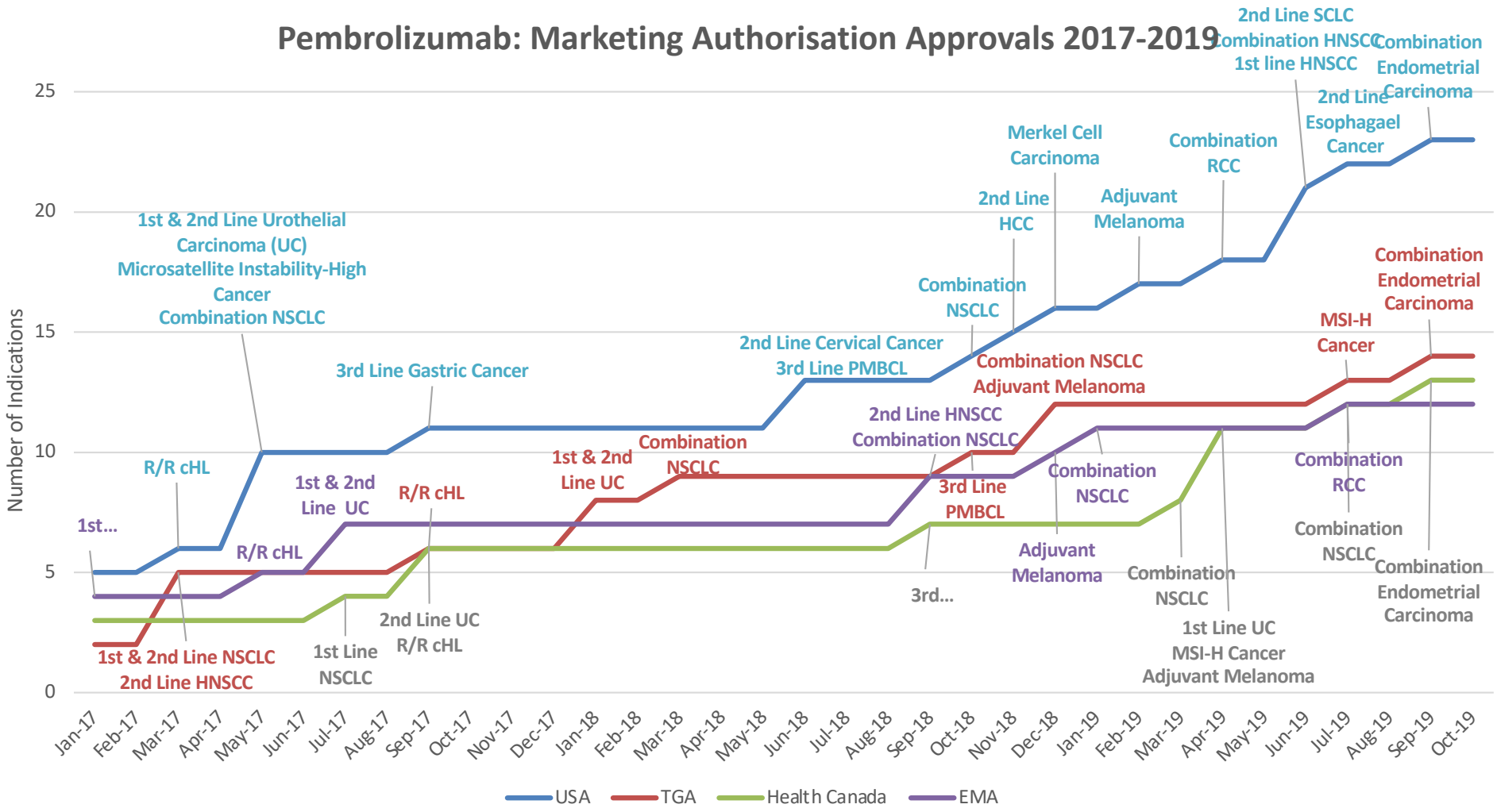
Note: [1] "Other models" do not necessarily relate to cost-effectiveness or cost-utility analysis, but could be cost-minimisation or cost analysis.[2] Excluding France and Germany, where economic evidence does not constitute an essential part of the assessment process. *Source:* The authors based on information extracted from publicly available HTA reports

8. Key social value judgements considered by HTA agencies



- The likely impact of a number of **social value judgements** was considered.
- **Severity**, **unmet need**, **administration advantage** was explicitly recognized by HTA agencies in **30%** of all cases (severity), **48%** (unmet need) and **25%** (administration advantage)

9. Number of indications is increasing, but there is no portfolio approach to pricing; how do we use HTA?



Source: LSE database.

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General Challenges

1. High levels of clinical uncertainty at the time of approval

- RCTs often unfeasible or unethical in the context of less common, rare and serious diseases, often leading to regulatory approval based on single arm trials with historical controls.
- Limited data on long-term clinical efficacy. Are cell and gene therapies actually cures?

2. High upfront costs

- Prices in excess of $2 million for one time use are with us already
- Budget constraints will become more problematic over time (10% of US citizens have a rare disease linked to a genetic defect)

3. High manufacturing and distribution costs: barriers

- Delivery and manufacturing process is very complex and highly regulated.
- Process can take several weeks between sample collection, transportation to and from manufacturing facilities, the manufacturing process and administration of the product.
- Manufacturing and administration facilities must be accredited limiting industrial scaling of the process (e.g. only 7 hospitals in England accredited to administer CAR-Ts).

How do we deal with expensive new products? What role for HTA?

Therapy	FDA	EMA	Clinical Evidence	Price (USD)	Outcome
Glybera (alipogene tiparvovec)	N/A	Exceptional circumstances	3 phase III trials, under 30 patients enrolled	$1.2 million	- Withdrawn, lack of demand (under 5 years of market authorization in Europe) - Original manufacturer went bankrupt
Strimvelis (GSK-2696273)	N/A	Orphan Drug	Phase I/II trial, 12 patients (additional monitoring status – patients enrolled in long-term registry)	$648,000	- Sold by manufacturer due to lack of demand - Less than five patients treated since market authorization
Kymriah (tisagenlecleucel); 2 indications	Priority Review, Breakthrough Therapy	Priority Medicines Scheme (PRIME)	2 single arm phase II trials (79 & 115 patients); Adverse events for 95% of patients; 81% remission for all; 51% ORR for B-cell lymphoma	$475,000	- Outcome-based payment model with rebate for null treatment effect - Reimbursed in several countries, incl. USA< UK, Germany
Luxturna (voretigene neparvovec-rzyl)	Priority Review, Breakthrough Therapy, Orphan Drug (2017)	Orphan Drug (2018)	Open label phase III RCT, 41 patients; 100-fold statistically significant improvement in vision; 93% of patients had improved vision at end of trial	$850,000 ($425,000 per eye)	- Outcome-based payment model with rebate for null treatment effect
Zolgensma (onasemnogene abeparvovec)	Fast Track, Priority Review, Breakthrough Therapy, Orphan Drug (2019)	CME, PRIME, Orphan designation (May 2020)	Phase I open label trial, 12 patients; 75% of patients report improved motor function	$2.1 million	- Amortized payment plan for health insurers over five years - 100 doses available through a managed-access program (lottery system for countries which the drug is not yet approved)

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Financing options for expensive drugs (1)

1. Amortization, Installments and Annuities

- Spreading large upfront cost into installments payed over time.
- Used in multiple industries including housing (mortgages) and banking (interest rates and loans).

2. Outcomes-based Payments (OBP)

- Payment for a therapy is contingent upon performance of a therapy in a pre-specified clinically meaningful endpoint
- Simplest form is a one year milestone-based contract (appropriate for disease with meaningful clinical endpoints over 12 months – e.g. Kymriah)
- More comprehensive models involve multiple years with payments spread over time based on achievement of pre-specified performance criteria (Higher degree of risk-sharing, but may be problematic in many settings)

Financing options for expensive drugs (2)

3. Reinsurance and Stop-Loss Policies

- Insurance providers purchase reinsurance or stop-loss from another insurance company.
- Financial risk of “curative” therapies is transferred to the reinsurance company, which pools risk over a much larger scale
- Already used for healthcare financing in USA (e.g. organ transplants)

4. Third Party Financing

- Financial institutions (banks, hedge funds, private equity firms) enter into payment agreement with patients and health insurers.
- Manufacturers are provided with upfront payment from the financial institution, which receives payments from the health insurer over time.

5. Intellectual Property Based Payment Models

- **Prize funds** - provided for successful development of a product in exchange for intellectual property rights
  - Enhanced & continued royalty option on top of prize
- **Subscription models** – licensing agreement for unlimited use of a product over a specified period of time

Other important issues and options to consider at HTA and funding level

1. Provisions around time-to-coverage negotiations **(*access accelerator with clauses*)**

2. Need for health systems to be *demand-driven* rather than *supply-led* **(*paying for outcomes plus*)**

3. Budget-setting as a risk-mitigation strategy **(*price as a theoretical concept*)**

4. Evidence generation and assessment through collaboration

5. Public and private funding of R&D **(*safeguarding public interests*)**

1. Provisions around time-to-coverage negotiations

- HTA not necessarily to blame; negotiation phase often too long and discussion on uncertainty mitigation complex; consider:

a) Implementing parallel review processes
b) Additional evidence generation (with cross-border collaboration)
c) Capping the length of time negotiations last
d) Consider compassionate use programmes for therapies under negotiation
e) Insurance to provide signal that negotiations are time-limited; consider voluntary licenses?

2. Need for health systems to be demand-driven rather than led

- May be necessary to have an explicit and ex ante determined needs assessment strategy
- This means becoming more demand-led rather than supply-driven, which implies setting benchmarks

a) For chronic conditions one such benchmark could be the cost of illness (both direct and indirect)
   i. can aid in cost-effectiveness analysis
   ii. helpful in measuring the potential savings of averting a case of or mitigating the costs of an illness
b) New therapies to benchmark against aspects of societal "burden" they are addressing appropriately monetized (RoI approach)
c) Product premia to be compared against cost-of-illness

3. Budget-setting as a risk-mitigation strategy

- Cost-effectiveness helpful as a starting point in negotiations regarding coverage

a) Negotiating based on a historically-set budget with forward-looking adjustments is much more meaningful (including PVAs or O-B RSAs)
b) Relevance of “price” as a variable diminishes
c) Confidentiality is necessary

4. Evidence generation and assessment

- Robust evidence needs to be produced to ensure that there are indeed meaningful clinical benefits despite significant uncertainties. This needs to take place across borders

a) Countries taking the lead in admitting such products to reimbursement can contribute important primary evidence on their effectiveness for the common good.
b) Registries, can be used where evidence from different countries and systems can be generated and leveraged.
c) Registries can be set up pro-actively, so that evidence on effectiveness becomes available within a reasonable timeframe.

5. Public and private funding of R&D

- Public (30%), private (60%) and NGO (10%) investment contribute to drug R&D
- As R&D is a sunk cost, what matters to innovators is overall return on investment and profitability

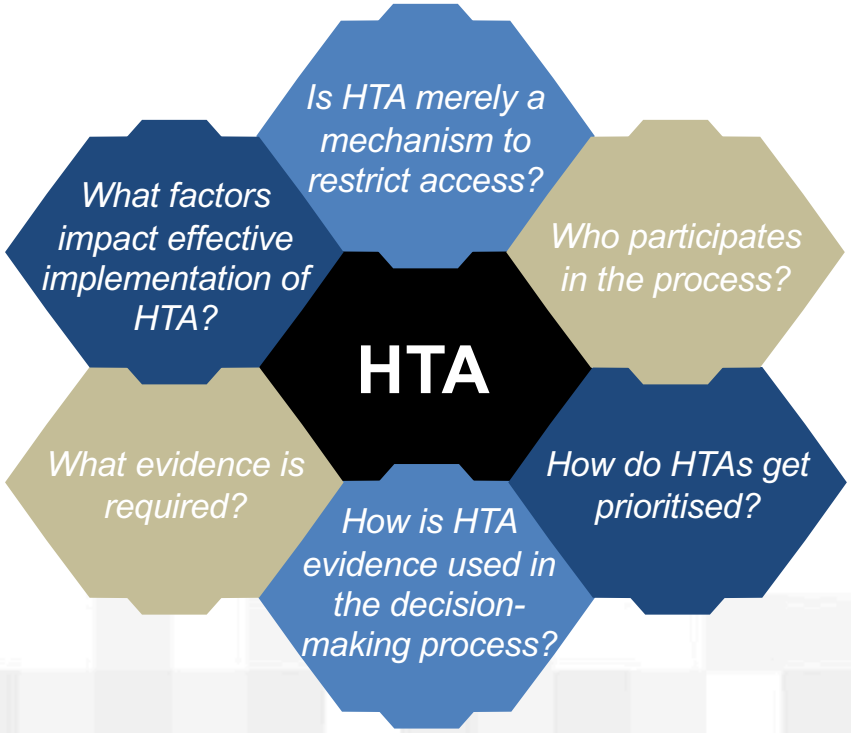
a) Balancing act required, esp. where publicly funded R&D has been important in development
   - This may have implications for pricing

b) Tradeoff: Consider dynamic effects explicitly as part of the assessment process

Concluding remarks:
The uptake and use of HTA has been increasing;
HTA Challenges **(2000s)**

While HTA systems increasingly play a role in supporting decision-making, they are not without controversy. Questions abound surrounding the following issues, among others:

- Role of HTA in decision-making and priority-setting;
- What evidence is used;
- Methods employed during the assessment process, incl. costs, metrics, comparators;
- Impact on innovation and access;
- Role of stakeholders

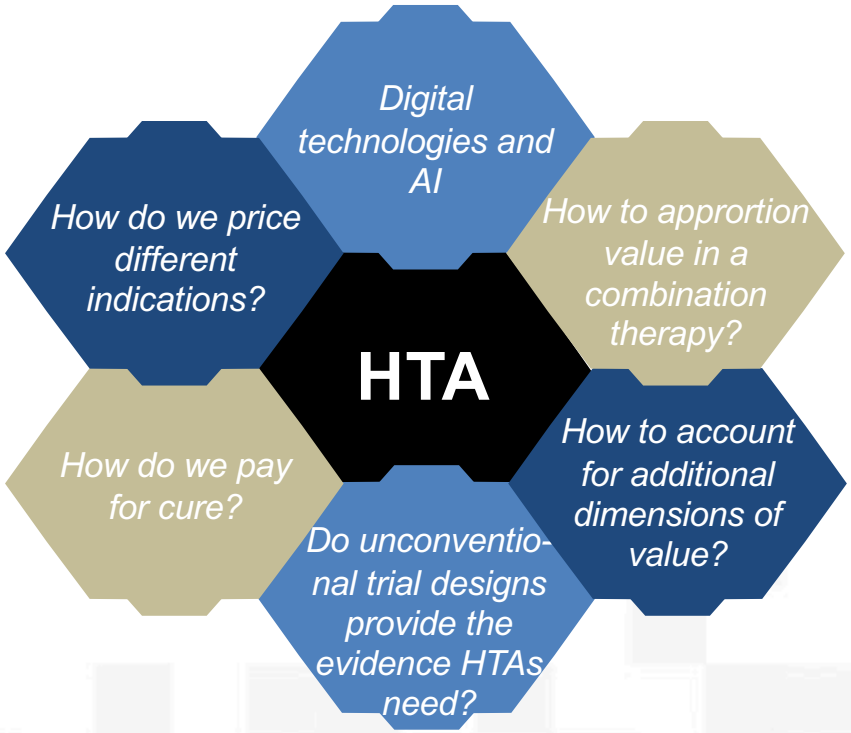


Concluding remarks

The uptake and use of HTA has been increasing! HTA Challenges **(2020 and beyond)** that local decision makers need to address

An increasing number of challenges have cropped up and challenge conventional HTA models and paradigms, including:

- Accelerated access pathways and perception by HTAs;
- Value is multi-dimensional and explicit incorporation of value beyond costs and effects is missing;
- Apportionment of value in different components of a combination;
- Indication-based pricing;
- Unconventional trial designs (e.g. single arm trials) are increasingly used;
- Payment of specialty care and cure



Addressing the challenges of HTA will require collaborative work across settings, HTA agencies and health systems to identify commonly accepted solutions