HTA SUMMIT

Building collaboration around HTA reform

November 2022

HTANALYSTS

ACKNOWLEDGEMENTS

HTANALYSTS

HTANALYSTS has been providing boutique impact measurement and communication services for over 20 years. **HT**ANALYSTS is a purpose driven organisation, working to have a powerful impact on society by driving human-centric outcomes. In healthcare this purpose is operationalised by connecting people with the best treatments in the fastest time.

Originally founded in 2002, **HT**ANALYSTS has grown to become a leader in healthcare and impact assessment consulting, providing services to the healthcare industry. In recent years, its scientific rigour has proven valuable for those outside the healthcare sector, and this has seen the company grow its capabilities to include expertise in social impact measurement, government services, healthy ageing and disability.

HTANALYSTS has extensive experience working with numerous stakeholder groups to develop a comprehensive understanding of complex topics such as health technology assessments, genomics, climate change and many public health issues.

AUSTRALIAN ISPOR COMMITTEE

ISPOR is the leading professional society for health economics and outcomes research globally. The mission of the local Australian chapter is to promote the science of pharmacoeconomics (health economics) and outcomes research. Importantly, ISPOR Australia serves as a bridge in bringing together Australasian members of industry, academia, government and other health-related organisations.

FUNDING

HTANALYSTS and ISPOR Australia would like to thank Medicines Australia's Oncology Industry Taskforce for providing funding for this event.

STEERING COMMITTEE

In order to build the key elements of the Summit, a Steering Committee was established including equal representation from industry and academia. The Steering Committee was chaired by Dr Colman Taylor (President ISPOR Australia; CVO **HT**ANALYSTS). Regular meetings were held leading up to the Summit to discuss agenda topics, potential speakers and format for the day. **HT**ANALYSTS and ISPOR Australia would like to thank the Steering Committee for their contribution to the organisation of the Summit.

Prof Paul Scuffham

Director Health Institute Queensland

Claire Parken

Head of Value and Access (Chapter Lead)
Roche

A.Prof Martin Downes

Consultancy Team Lead, Centre for Applied Health Economics

Megan Bohensky

Head of Market Access ANZ
Beigene

Prof Rachael Morton

Director Health Economics
NHMRC Clinical Trials Centre

Dr Pinky Dharmshaktu

Global Launch Capability Lead
Merck

SPEAKERS

Thirteen speakers presented at the Summit (full bios available in Appendix IV). **HT**ANALYSTS and ISPOR Australia would like to thank these individuals for their time and expertise.

Vanessa Stevens
CSL Vifor

Lucas Tocchini
Biogen

Dr Martin Snoke
Roche

Andrea Kunca
Roche Diagnostics

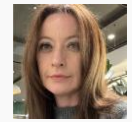
Julia Lewis
AbbVie

Rachael Anderson
AstraZeneca

Ann Single
Patient Voice Initiative

Prof Sally Pearson
University of NSW

Felicity McNeil
Better Access Australia; Perspicacite



Tiffany Boughtwood
Australian Genomics

A.Prof Haitham Tuffaha
University of Queensland

A.Prof Bonny Parkinson
Macquarie University

FACILITATORS

Breakout discussions were coordinated by six facilitators representing industry, academia, ex-Government, patients and consultancy. All facilitators joined a panel discussion at the conclusion of the day. **HT**ANALYSTS and ISPOR Australia would like to thank these individuals for their time in making the day a successful collaborative event.

Ian Noble

Director, Value Access and Policy at Amgen

Krystal Barter

Founder Pink Hope and Humanise Health

A.Prof Penny Reeves

Associate Director, Health Research Economics; HMRI

Katrina Lapham

Director Strategic Market Access & Policy, Biointelect

Renae Beardmore

Managing Director, EVOHEALTH

A.Prof Joshua Byrnes

Director Centre for Applied Health Economics Menzies Health Institute Queensland

EXECUTIVE SUMMARY

Health Technology Assessment (HTA) is used in Australia to evaluate a range of healthcare interventions, including medicines, vaccines, diagnostic tests and public health programs.

GIVEN THE IMPORTANCE OF HTA TO ACHIEVING ACCESS TO THE BEST MEDICAL INTERVENTIONS, THE FEDERAL GOVERNMENT RECENTLY AGREED WITH MEDICINES AUSTRALIA TO UNDERTAKE A POLICY AND METHODS REVIEW OF HTA IN AUSTRALIA.[1]

The review is likely to encompass many elements such as policies (e.g. how medicines are funded), processes (e.g. how evaluations take place) and methods (e.g. how value for money is determined). In order to promote discussion around key topics that will be covered in the upcoming review, a Summit was recently organised by **HT**ANALSYTS in collaboration with ISPOR Australia. The Summit was primarily targeted at industry, academia and consulting, with representation from patient advocacy groups and government.

THE PURPOSE OF THE SUMMIT WAS TO FIND COMMON GROUND ON HOW AUSTRALIA CAN REFORM HTA POLICIES, PROCESSES AND METHODS TO ENSURE PATIENTS GET ACCESS TO THE BEST TREATMENTS RAPIDLY, WHILST RECOGNISING THE GOVERNMENT'S OBJECTIVE TO ACHIEVE VALUE FOR MONEY.

A Steering Committee was formed to build an agenda for the Summit and invite speakers. The final list of topics included:

- CAPTURING THE PATIENT VOICE IN HTA
- MAKING BETTER USE OF REAL-WORLD EVIDENCE
- SECOND ORDER EFFECTS
- ACCESS TO PRECISION MEDICINE
- CONDITIONAL LISTING
- MANAGING UNCERTAINTY

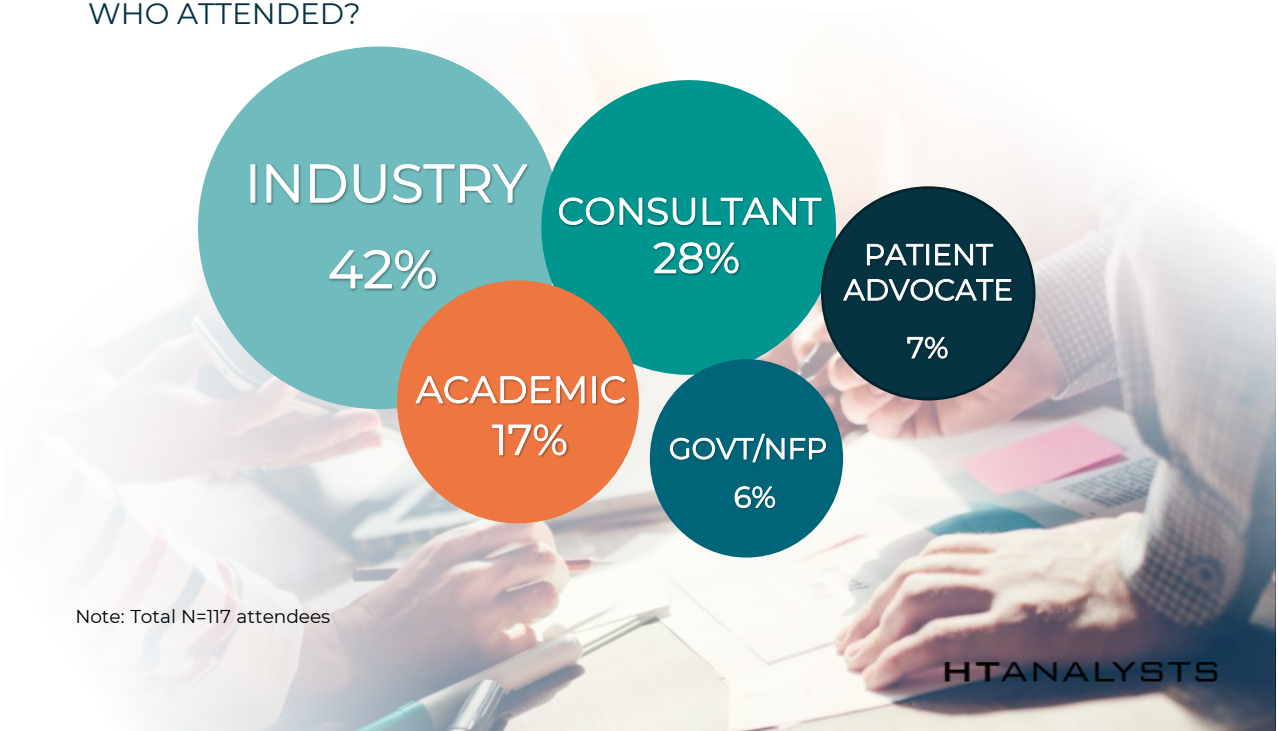
1. See Appendix II for a summary of the Strategic Agreement.

THE AGENDA WAS DESIGNED TO PROMOTE DIALOGUE AMONGST PARTICIPANTS.

Each topic was addressed by an industry speaker and a non-industry speaker, followed by breakout discussions in small groups. Each small group addressed a specific question related to the Summit topics (e.g. identifying the barriers to increasing patient involvement in the HTA process). A facilitator was assigned to each breakout group (see Acknowledgements) and provided a summary of the discussion after each breakout session.

The Summit was attended by academics, industry, patient advocates and others working in not-for-profit or Government roles.

WHO ATTENDED?

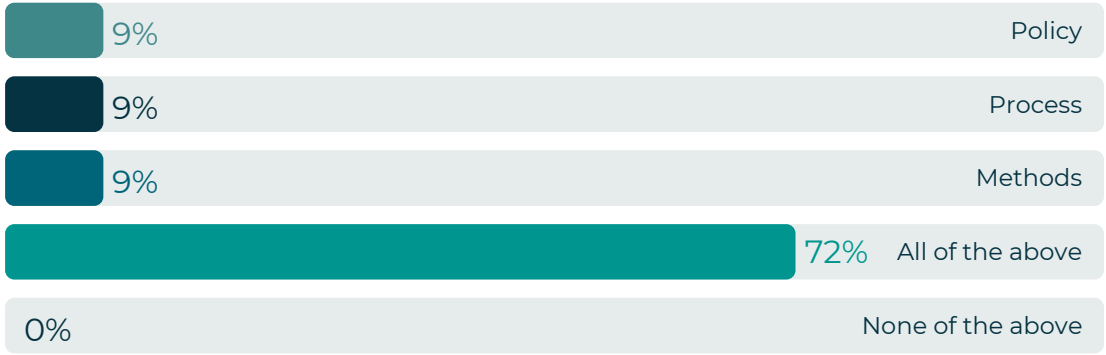


Note: Total N=117 attendees

During the Summit participants were asked to share specific words that they considered to be related to HTA, highlighting the diversity of concepts and experiences that HTA encapsulates.

Participants at the Summit were also polled on what elements need to be improved with respect to HTA in Australia. Results highlighted a significant majority of participants who thought all aspects HTA, including policy, process and methods, should be improved.

WHAT ELEMENT NEEDS IMPROVING IN HTA?



THE UK EXPERIENCE

Professor Mark Sculpher provided a keynote presentation for the Summit reflecting on the UK experience of collaboration in the HTA process.

This included being clear on the objectives of collaboration and separating collaboration around technical methods from decision making, which involves value judgements. A number of relevant principles were presented to guide collaboration including transparency, accountability, expertise and considering impacted parties.

Another important part of the presentation was an overview of the National Institute for Health and Care Excellence (NICE) decision-making process, including the use of a citizen's council and how equity considerations are now used to modify cost-effectiveness calculations.

COLLABORATION IS OFTEN ACHIEVABLE ON TECHNICAL MATTERS, HOWEVER SOME POLITICAL AREAS HAVE LESS OF A CLEAR ROLE FOR COLLABORATION. THIS INCLUDES OBJECTIVES OF THE HTA PROCESS AND THRESHOLDS FOR FUNDING DECISIONS.

TOPICS AT THE SUMMIT

PATIENT VOICE

The patient voice should be more prominent in HTA throughout the process including pre-submission, during the evaluation and after the funding decision via feedback mechanisms. However, care should be taken to ensure patient insights are captured in an equitable manner, so that people from marginalised communities or those with lower health literacy are not left out of the conversation. The process should be fit-for-purpose with transparency and a two-way dialogue as key principles.

FUTURE WORK in this area should start by addressing the pre-existing perceptions concerning the value of patient insights. For example, current perceptions around patient insights from decision makers is unknown and should be investigated. To ensure patient insights are seen as credible evidence, there is a need for robust and validated tools. A further point is that patients could be engaged outside of HTA, such as during trial design, to ensure there are relevant outcomes reported.

REAL-WORLD EVIDENCE

Inclusion of real-world evidence (RWE) was identified as an important element to get right in the HTA review, as it was perceived that this could have a substantial impact on the patient access gap. RWE influences many barriers discussed at the Summit (such as uncertainty or the conditional listing process). To improve access to RWE, jurisdictional challenges in accessing data should be confronted and it was also noted that industry also has a role in sharing data when feasible. Public trust in linked data (especially in light of recent high profile data breaches) and the workforce skills gap were noted as key barriers.

FUTURE WORK should leverage the HTA review to work towards a national dataset capturing Federal (PBS/MBS) and State/Territory (Hospital) data.

SECOND ORDER EFFECTS

There was general agreement around the need to examine second order effects in HTA, however the details of how and when this should be done needs clarification. A key risk identified was that inclusion of second order effects may increase the uncertainty in the economic evaluation, and may not actually improve the patient access gap. A key opportunity noted during discussions was the inclusion of carer wellbeing, which was considered likely to be the easiest effect to measure (i.e. through a clinical trial).

FUTURE WORK is needed to guide how and when to include second order effects in the HTA process. An idea was floated to use a pilot to test use of second order effects in the HTA process. Overall, it was felt that guidance is needed on how to collect second order effects in a robust manner and how this data is factored into decision making.

TOPICS AT THE SUMMIT

PRECISION MEDICINE

Precision medicine captures the challenges and opportunities with genetic and genomic testing, as the latter enables access for the former. There is a workforce skills shortage in many areas that slows down access. In addition, the information in this space is constantly evolving through research, yet the MBS is static and cannot be used within research. A question raised with broad applicability across other topics addressed, was whether committee decision making could follow a more defined framework, so the process is more predictable. Given the number of issues raised, it was felt that HTA may not be the best way to evaluate genetic and genomic tests, especially when multiple biomarkers are considered.

FUTURE WORK should aim to ensure consistency around terminology which some sections of the community find difficult to understand. Work is also needed to refine the HTA process (e.g. disjointed MSAC/PBAC timelines) methods (e.g. panel testing) and decision making (e.g. decision making framework). An opportunity for collaboration was identified to build knowledge and capabilities across stakeholder groups to address the workforce skills shortage.

CONDITIONAL LISTING

It was recognised that the mechanism for conditional listings (Managed Access Program; MAP) is already in place, but it is not currently being utilised effectively. A key barrier raised in discussions was that the PBAC lacked the power to offer a MAP proactively. In addition, many other barriers and risks were identified, and many themes crossed over with discussion around RWE. Some complexities that were highlighted in discussions included the interaction with multiple Sponsors in the process and the implications for pricing as well as what an exit process would look like (managed exit; MEXIT). From a patient perspective, it was noted that patients would rather have access sooner with the risk that the drug is taken away, then delayed or potentially no access.

FUTURE WORK is needed to identify why companies are not requesting MAPs in the current process. In addition the potential MEXIT process should be clarified (if the final results were not as good as initially thought). Finally, there is a need to investigate whether additional methods such as value of information would help reduce uncertainty in the process.

MANAGING UNCERTAINTY

Uncertainty was recognised as an unavoidable consequence of evaluating new medicines and technologies. There was a perception from industry that evaluators and the PBAC tend towards the most conservative parameter estimates, rather than the most likely. The identification of uncertainty needs to consider the probability and the consequences. There was general consensus that this could be reframed as risk management. Not doing anything (i.e. not recommending a drug) is also a risk, as it means experience access delays for an effective treatment. Finally industry noted a desire to have increased communication between them, the evaluator, patients and decision makers throughout the lifecycle of the submission. This would increase communication and transparency regarding the perceived risks and enable collaboration on how to manage that risk.

FUTURE WORK should develop a ‘risk matrix’ for submissions to identify areas of uncertainty and the risk they present. This could be conducted by the sponsor and the evaluator to increase transparency on how uncertainty and risk are being factored into the decision-making process. A process is also needed to enable earlier and more productive engagement between industry, evaluators, patients and decision makers.

THEMES FROM THE SUMMIT

COLLABORATION

Participants enjoyed the opportunity to discuss ideas and work towards solutions. The topics addressed in the Summit require considerable work, and therefore, the enthusiasm from the Summit should be harnessed in future forums. There were many areas identified to progress further collaborative work, such as creating robust tools to capture patient insights, defining second order effects and creating a risk matrix to manage uncertainty.

COMMUNICATION

Many of the issues arising in HTA were due to a lack of communication between Sponsors, evaluators, patients and decision makers. Processes to increase dialogue between these parties are needed. For example, a process for open communication between Sponsors and evaluators post submission lodgement was mentioned as a positive step to reduce uncertainty for decision makers.

TERMINOLOGY

HTA encompasses a number of technical terms which have different meanings across stakeholders. An example is real-world evidence, which academics perceived as observational evidence and patients perceived as feedback captured during the HTA process. Some participants (particularly patients) felt alienated by the technical jargon used among the HTA practitioners. Terminology should be clarified and simplified before the HTA review begins and this can be progressed through further collaboration.

PATIENT INVOLVEMENT

Patients should be involved in HTA, earlier and throughout the process, ensuring equality/equity across disease areas, so that people from marginalised communities or those with lower health literacy are not left out of the conversation. However considerable work is needed to improve the process, such as addressing current perceptions and building tools/processes to incorporate patient insights in an equitable and transparent manner.

ACCESS TO RWE

Improving access to RWE was identified as an important element to get right in the HTA review, as it was perceived that this could have a substantial impact on the patient access gap. RWE was considered to be important as it could help address many issues noted in the other topics discussed on the day. The HTA review was seen as an opportunity to push for better access to Government data – and an idea was put forward to advocate for the creation of a linked dataset covering Federal and State data

UNCERTAINTY AND RISK

When evaluating new healthcare technologies, uncertainty is unavoidable. Uncertainty can occur in many areas including the estimates of efficacy or safety as well as how patients are assumed to use a medicine and progress in their disease over time. To improve the efficiency of the process, uncertainty could be reframed as risk management, which incorporates the impact of the uncertainty on the funding decision. A framework could be developed to characterise risk in a consistent manner for each submission.

THEMES FROM THE SUMMIT

HTA IS BROAD, HOWEVER VALUE JUDGEMENTS ARE A SEPARATE MATTER.

HTA includes policies, processes and methods, and it is used as a tool by decision makers to make informed funding decisions. During discussions at the Summit, it was noted on several occasions that funding decisions have a political element, including what we value and prioritise as a society and how much we are collectively willing to pay to extend or improve life. It will be important for the HTA review to focus on key areas of reform that can speed up access to new medicines, whilst taking patient perspectives into account. In addition, an idea was floated to implement a decision-making framework so that decision-making is more methodical and transparent.

At the conclusion of the summit, participants were asked to share their key takeaways from the day. The importance of collaboration and involving patients in the HTA process were highlighted.

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ABBREVIATIONS

DRG	Diagnosis Related Group
ESC	Economic Subcommittee
GBMA	Generic and Biosimilar Medicines Association
HTA	Health Technology Assessment
ICER	Incremental cost-effectiveness ratio
InGeNA	Industry Genomics Network Alliance
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
MADIP	Multi-Agency Data Integration Project
MAP	Managed Access Programs
MBS	Medicare Benefits Schedule
MSAC	Medical Services Advisory Committee
NDIS	National Disability Insurance Scheme
NHMRC	National Health and Medical Research Council
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
NIHSI	National Integrated Health Service Information
NMP	National Medicines Policy
PAG	Patient Access Gap
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PLAC	Prosthesis List Advisory Committee
QALY	Quality-adjusted life year
RCT	Randomised controlled trials
RWE	Real-world evidence
TGA	Therapeutic Goods Administration
TRUST	TRansparent Uncertainty ASsessmenT
UNSW	University of New South Wales
WHO	World Health Organization

INTRODUCTION

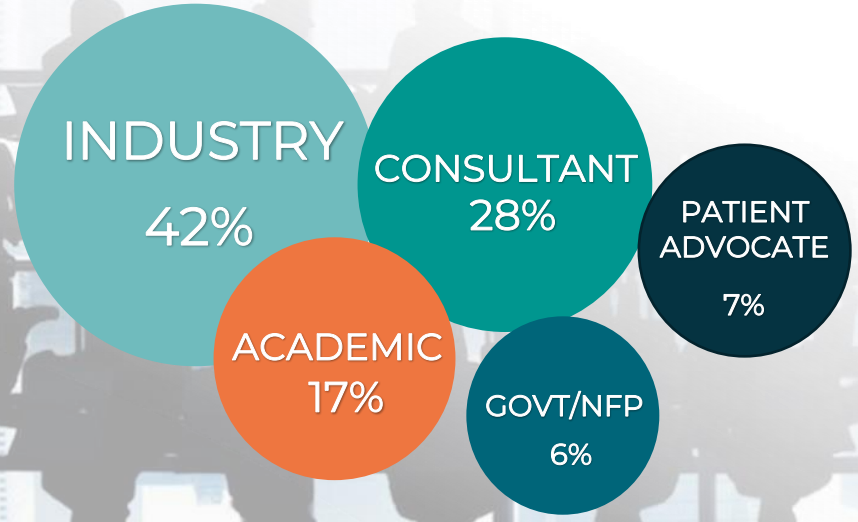
CONTEXT

As part of Medicine Australia's five-year Strategic Agreement with the Federal Government there will be an independent review of Australia's HTA policy and methods[2]. In order to promote discussion around key topics that will be covered in the HTA review, a Summit was recently organised by **HT**ANALSYTS in collaboration with ISPOR Australia.

THE PURPOSE OF THE SUMMIT WAS TO FIND COMMON GROUND ON HOW AUSTRALIA CAN REFORM HTA POLICIES, PROCESSES AND METHODS TO ENSURE PATIENTS GET ACCESS TO THE BEST TREATMENTS RAPIDLY, WHILST RECOGNISING THE GOVERNMENT'S OBJECTIVE TO ACHIEVE VALUE FOR MONEY IN PURCHASING DECISIONS.

WHO ATTENDED

The Summit was attended by representatives from academia, the healthcare industry, patient advocacies and others working in not-for-profit or Government roles. A full list of attendees is provided in Appendix III.



HOW THE AGENDA WAS CONSTRUCTED

The agenda (Appendix I) was built around six key topics which were selected from the Strategic Agreement, industry working groups and discussion amongst the Steering Committee. The final list of topics included:

- CAPTURING THE PATIENT VOICE IN HTA
- MAKING BETTER USE OF REAL-WORLD EVIDENCE
- SECOND ORDER EFFECTS
- ACCESS TO PRECISION MEDICINE
- CONDITIONAL LISTING
- MANAGING UNCERTAINTY

The Summit was headlined by Professor Mark Sculpher from the University of York. Professor Sculpher has been a member of the NICE Technology Appraisal Committee, the NICE Public Health Interventions Advisory Committee and NICE's Diagnostics Advisory Committee. He has also been involved in advising NICE on methods over many years and was involved in the recent review[3].

THE SUMMIT WAS CONSTRUCTED TO PROMOTE DIALOGUE AMONGST PARTICIPANTS.

Each topic was addressed two speakers of different backgrounds (industry and non-industry), followed by breakout discussions in smaller groups. Small group discussions were held to delve deeper into a specific question related to each topic. The breakout group discussions focused on elements such as collaboration, facilitators and barriers, and international best practice examples. A facilitator was assigned to each breakout group and provided a summary of discussions after each breakout session.

A number of pre-reads including publications and working papers developed by industry were shared prior to the Summit to promote discussion.

2. See Appendix II for a summary of the Strategic Agreement.
3. Full bio provided in Appendix IV.

WHAT IS HTA?

There are numerous definitions of HTA. A commonly used definition developed by The World Health Organization (1) is as follows:

HEALTH TECHNOLOGY ASSESSMENT (HTA) IS A SYSTEMATIC AND MULTIDISCIPLINARY EVALUATION OF THE PROPERTIES OF HEALTH TECHNOLOGIES AND INTERVENTIONS COVERING BOTH THEIR DIRECT AND INDIRECT CONSEQUENCES.

IT IS A MULTIDISCIPLINARY PROCESS THAT AIMS TO DETERMINE THE VALUE OF A HEALTH TECHNOLOGY AND TO INFORM GUIDANCE ON HOW THESE TECHNOLOGIES CAN BE USED IN HEALTH SYSTEMS AROUND THE WORLD.

HTA IS A TRANSPARENT AND ACCOUNTABLE PROCESS THAT CAN BE USED BY DECISION MAKERS AND OTHER STAKEHOLDERS TO SUPPORT THE DECISION-MAKING PROCESS IN HEALTH CARE AT THE POLICY LEVEL BY PROVIDING EVIDENCE ABOUT GIVEN TECHNOLOGIES.

IT HAS BEEN DESCRIBED AS A BRIDGE THAT CONNECTS THE WORLD OF RESEARCH TO THAT OF POLICY MAKING.

During the Summit participants were asked to share specific words that they considered to be related to HTA, highlighting the diversity of concepts and experiences that HTA encapsulates.

HTA IN AUSTRALIA

HTA is used in Australia to assess a range of interventions, including pharmaceuticals (medicines + vaccines), diagnostic tests, medical devices, surgically implanted prostheses, medical procedures and public health programs. At a Federal level, applications are adjudicated by three technology advisory committees, including: Medical Services Advisory Committee (MSAC); Pharmaceutical Benefits Advisory Committee (PBAC); Prostheses List Advisory Committee (PLAC).

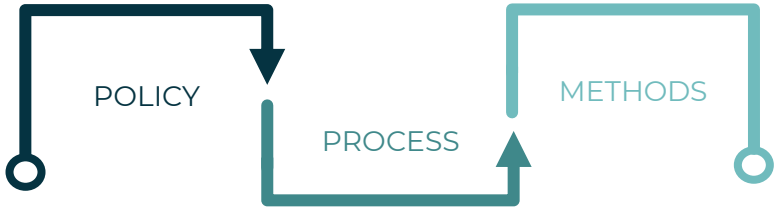
According to Australian Federal Government (2), the Australian HTA system is guided by several principles including: sustainability; transparency, accountability and independence; consultative and reflective of Australian community values; administratively efficient; flexible and fit for purpose; informed by robust and relevant evidence.

The audience at the HTA Summit were polled as to whether the use of HTA could be improved in Australia, highlighting an overwhelming majority of participants who considered improvements were needed.

WHAT ELEMENT NEEDS IMPROVING IN HTA?

REFORMING HTA

It was recognised during the Summit that reforming HTA potentially involves three key elements:



HTA in Australia is guided by specific legislation as well as umbrella policies such as the National Medicines Policy (NMP). The recently revised draft NMP (3) aims to achieve equitable, timely and affordable access to high-quality and safe medicines and medicines related services for all Australians. This vision is then actioned through legislation such as the National Health Act 1953. An excerpt from this legislation is provided below, highlighting how the PBAC should consider effectiveness and cost as part of the HTA process for medicines or vaccines.

> For the purpose of deciding whether to recommend to the minister that a drug or medicinal preparation, or a class of drugs and medicinal preparations, be made available as pharmaceutical benefits under this part, THE COMMITTEE SHALL GIVE CONSIDERATION TO THE EFFECTIVENESS AND COST OF THERAPY involving the use of the drug, preparation or class, including by COMPARING THE EFFECTIVENESS AND COST OF THAT THERAPY WITH THAT OF ALTERNATIVE THERAPIES, whether or not involving the use of other drugs or preparations.
>
> - National Health Act 1953 101 3a.

In addition, HTA in Australia involves significant process challenges, such as co-dependent technologies (e.g. test and drug combinations) and therapies for rare diseases. Finally, HTA methods encapsulate numerous potential reform opportunities such as the discount rate, methods for assessment of evidence and inclusion of second-order effects in economic modelling.

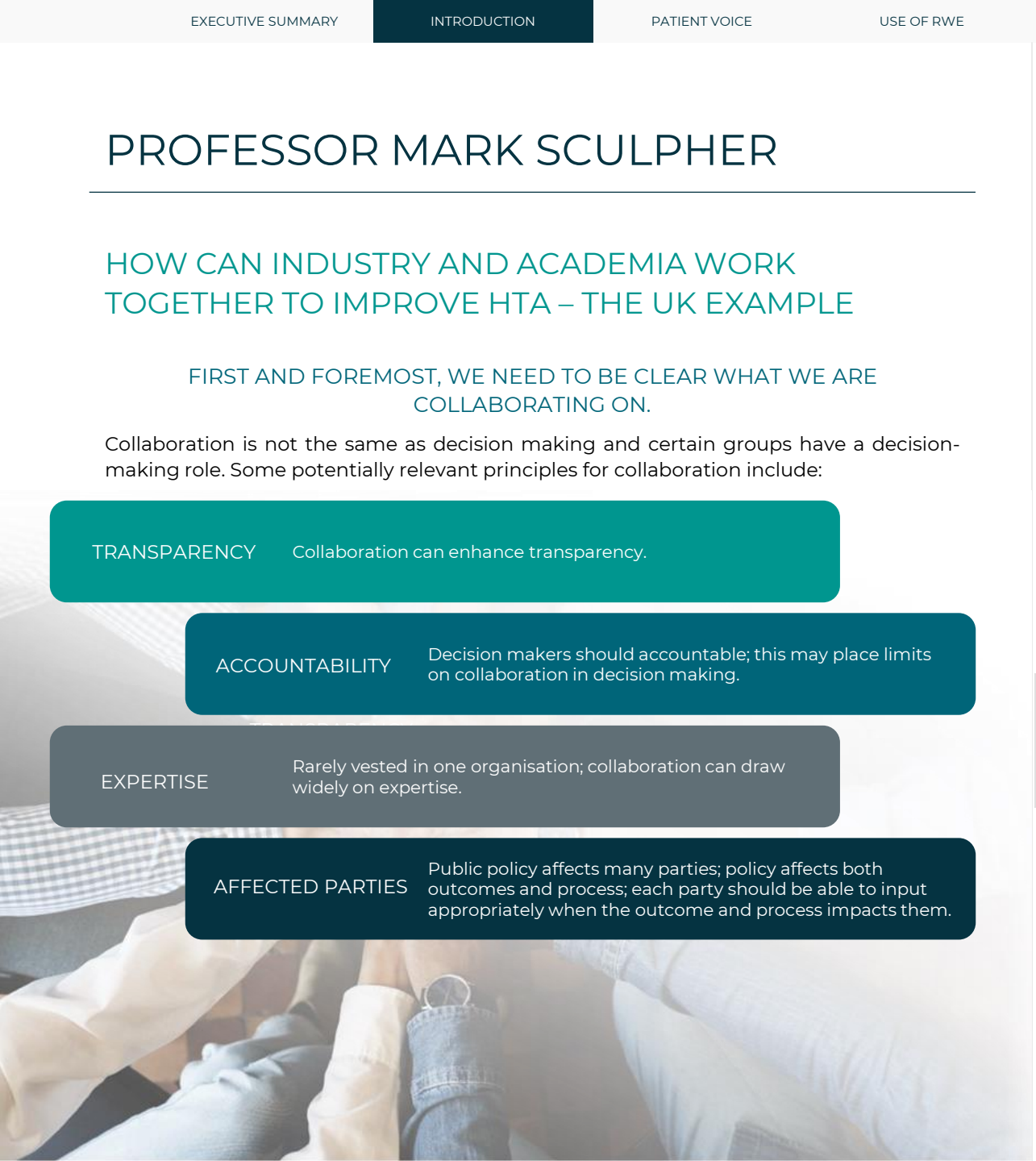
PROFESSOR MARK SCULPHER

HOW CAN INDUSTRY AND ACADEMIA WORK TOGETHER TO IMPROVE HTA – THE UK EXAMPLE

FIRST AND FOREMOST, WE NEED TO BE CLEAR WHAT WE ARE COLLABORATING ON.

Collaboration is not the same as decision making and certain groups have a decision-making role. Some potentially relevant principles for collaboration include:

TRANSPARENCY	Collaboration can enhance transparency.
ACCOUNTABILITY	Decision makers should accountable; this may place limits on collaboration in decision making.
EXPERTISE	Rarely vested in one organisation; collaboration can draw widely on expertise.
AFFECTED PARTIES	Public policy affects many parties; policy affects both outcomes and process; each party should be able to input appropriately when the outcome and process impacts them.



METHODS IS A TERM USED VERY GENERALLY, IT COVERS ELEMENTS INCLUDING DECISIONS, RELEVANT OBJECTIVES OF DECISION MAKING, EVIDENCE, PROCESS AND MODELLING.

An overview of the NICE 2020-2022 methods review was presented. The review included 12 Task and Finish groups, with over 180 people involved. NICE methods and reviews focus on making the most use of limited resources. However, it is important to consider the overall goals of NICE. Questions relating to health equity, which costs should be included (govt, patients, carers, productivity), and time horizon were raised.

ULTIMATELY THESE ARE ALL VALUE JUDGEMENTS RATHER THAN TECHNICAL JUDGEMENTS AND THERE IS NO CORRECT ANSWER.

It comes down to who is responsible. At a high level it is the elected government, but day to day responsibility is given to organisations like NICE. Decision makers will take input from a range of places and often the public's preferences are important. When considering a fair distribution of resources, the opinion of academia and industry should be considered the same as that of the general public.

The NICE Citizen's Council model was presented. The Citizen's Council is drawn from the community and has a role in thinking about the basic ethical principles under which NICE operates, its objectives, and constraints.

NICE PRAGMATISM IS DRIVEN BY POLITICAL JUDGEMENT THAT REFLECTS A DUAL OBJECTIVE. FIRSTLY, SUPPORT THE PHARMACEUTICAL AND LIFE SCIENCES INDUSTRY, AND SECONDLY, PROTECT THE NHS AND MAKE SURE THAT IT IS GETTING VALUE FOR MONEY.

NICE now has built-in process to look at modification factors for weighting incremental cost-effectiveness ratios (ICERs), such as end of life or rare disease. NICE is focused on traditional clinical trial evidence although it also sees a role for patient input to provide context.

Modelling considerations tend to be covered quite comprehensively in methods guidance. This is generally treated as a technical area, given the objectives of each system. Models are important for decision making because they can increase transparency. However, they can also increase workload and complexity.

Methods can quantify the value of perfect information. However on the basis of feedback from stakeholders, value of information was removed from the methods review.

WHEN MAKING DECISIONS, THERE IS A QUESTION REGARDING HOW TO INCORPORATE OUTCOMES AND EQUITY THAT ARE NOT FORMALLY QUANTIFIED.

For example, how should the value of innovation be included and how can we account for uncertainty. There is an opportunity for collaboration around what can be quantified and how cost-effectiveness thresholds are determined. Ultimately transparency and accountability are key in how decisions are made.

NICE re-stated that it's cost effectiveness threshold is $20-30k per quality-adjusted life year (QALY) gained, this was pre-negotiated with industry, despite the fact that there is a compelling argument that the threshold should be based on evidence including opportunity cost

HTA has numerous facets, some more suitable for collaboration than others. The broadest type suitable for collaboration is technical.

THE BOUNDARY BETWEEN TECHNICAL VALUE JUDGEMENTS AND DECISIONS HAS BECOME SOFTENED.

Some of the most political areas have a less clear role for collaboration. This includes objectives of the HTA system and cost-effectiveness thresholds.

CONSIDERATIONS FOR AUSTRALIA

Prof. Sculpher concluded with some reflections on the NICE HTA review, and how this might be considered in Australia. Some key questions were raised:

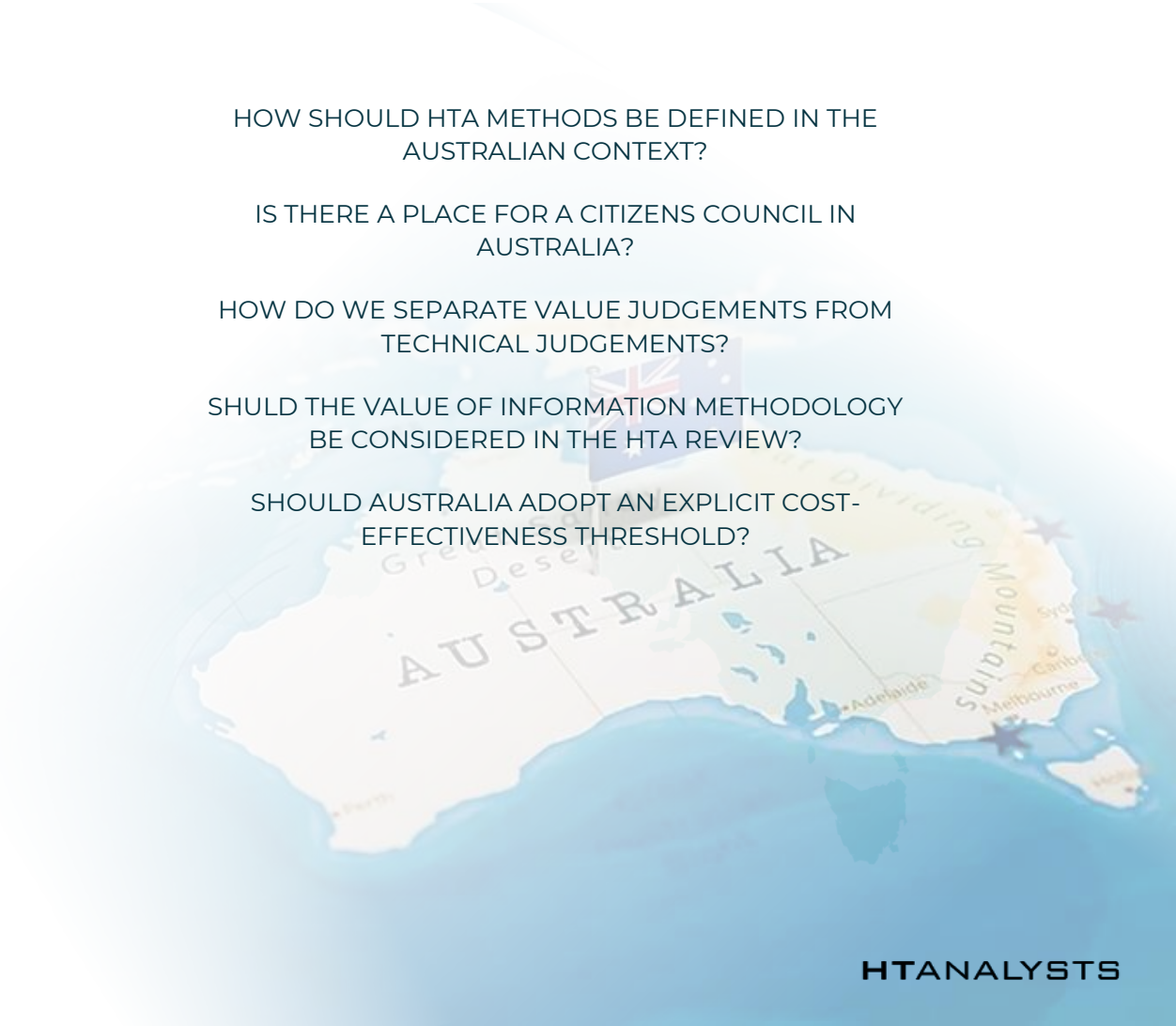
HOW SHOULD HTA METHODS BE DEFINED IN THE AUSTRALIAN CONTEXT?

IS THERE A PLACE FOR A CITIZENS COUNCIL IN AUSTRALIA?

HOW DO WE SEPARATE VALUE JUDGEMENTS FROM TECHNICAL JUDGEMENTS?

SHULD THE VALUE OF INFORMATION METHODOLOGY BE CONSIDERED IN THE HTA REVIEW?

SHOULD AUSTRALIA ADOPT AN EXPLICIT COST-EFFECTIVENESS THRESHOLD?



01 CAPTURING THE PATIENT VOICE

KEY THEMES AND FUTURE WORK

PROMINENCE

The patient voice should be more prominent throughout the HTA process including pre-submission, during the evaluation and after the funding decision.

EQUALTIY/EQUITY

Care should be taken to ensure equality and equity of voice, so that people from marginalised communities or those with lower health literacy are not left out of the conversation.

TRANSPARENCY

To ensure the best outcomes for patients in an equitable and efficient health system, HTA should use transparent, inclusive and suitable processes to inform timely new and ongoing healthcare investment.

TWO-WAY

Including the patient voice should be a two-way endeavour, not simply providing patients with a summary of information once an application has been submitted and asking them to provide consumer comments.

PLACE OF THE PATIENT VOICE

If we are going to embed the patient voice, we need to tackle our assumptions, the place of the patient voice and what it can contribute.

COLLABORATION

There is a need for robust and validated tools to capture the patient voice, so that this evidence is seen as credible. This is an opportunity for collaboration between industry, academia, and patient representatives.

ASSUMPTIONS

What are the current assumptions around patient insights from decision makers?

How do these need to be modified?

EARLY ENGAGEMENT

Is there scope to engage patients earlier in the product lifecycle?

Could patients be involved in trial design to have them define the outcomes that matter to them?

ANN SINGLE

EVIDENCE PRESENTED IN THE HTA APPLICATION DOES NOT CONTAIN ALL ASPECTS OF IMPORTANCE TO PATIENT LIVES.

The evidence needs to be interpreted with lived experience and expertise to understand relevance in the proposed setting. “Patients have knowledge, perspectives, and experiences that are unique and contribute essential evidence for HTA and decision making” (4).

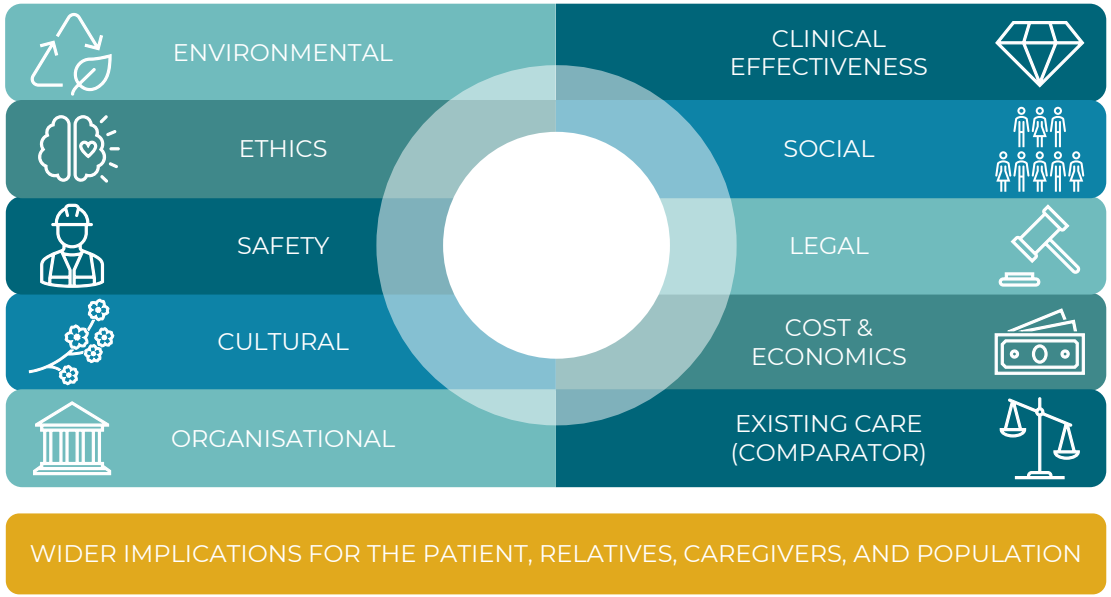
WITHIN THE CURRENT PROCESS WE HEAR THE PATIENT VOICE QUITE LATE IN THE PRODUCT LIFECYCLE, OFTEN ONLY DURING AN HTA APPRAISAL, AND IT TENDS TO BE ONE-WAY.

A common push back is that patients are biased and don’t understand the process. The way the process is currently structured, there is a risk that we prioritise certain types of knowledge over others.

IN AN OPTIMAL HTA PROCESS, PATIENT INTERACTION WOULD BE DYNAMIC AND FREQUENT, WITH OPPORTUNITIES FOR A TWO-WAY DIALOGUE BEFORE A SUBMISSION, DURING THE EVALUATION AND AFTER A DECISION IS MADE.

Currently written submissions have become the typical medium for patients to provide feedback in the HTA process. However, some HTA bodies have been pushing for more dialogue in place of written feedback. Questions remain about how to best include robust research into patients’ needs, experiences and preferences, such as qualitative evidence syntheses and patient preference studies, while balancing the need to obtain feedback against the burden of being involved in the process.

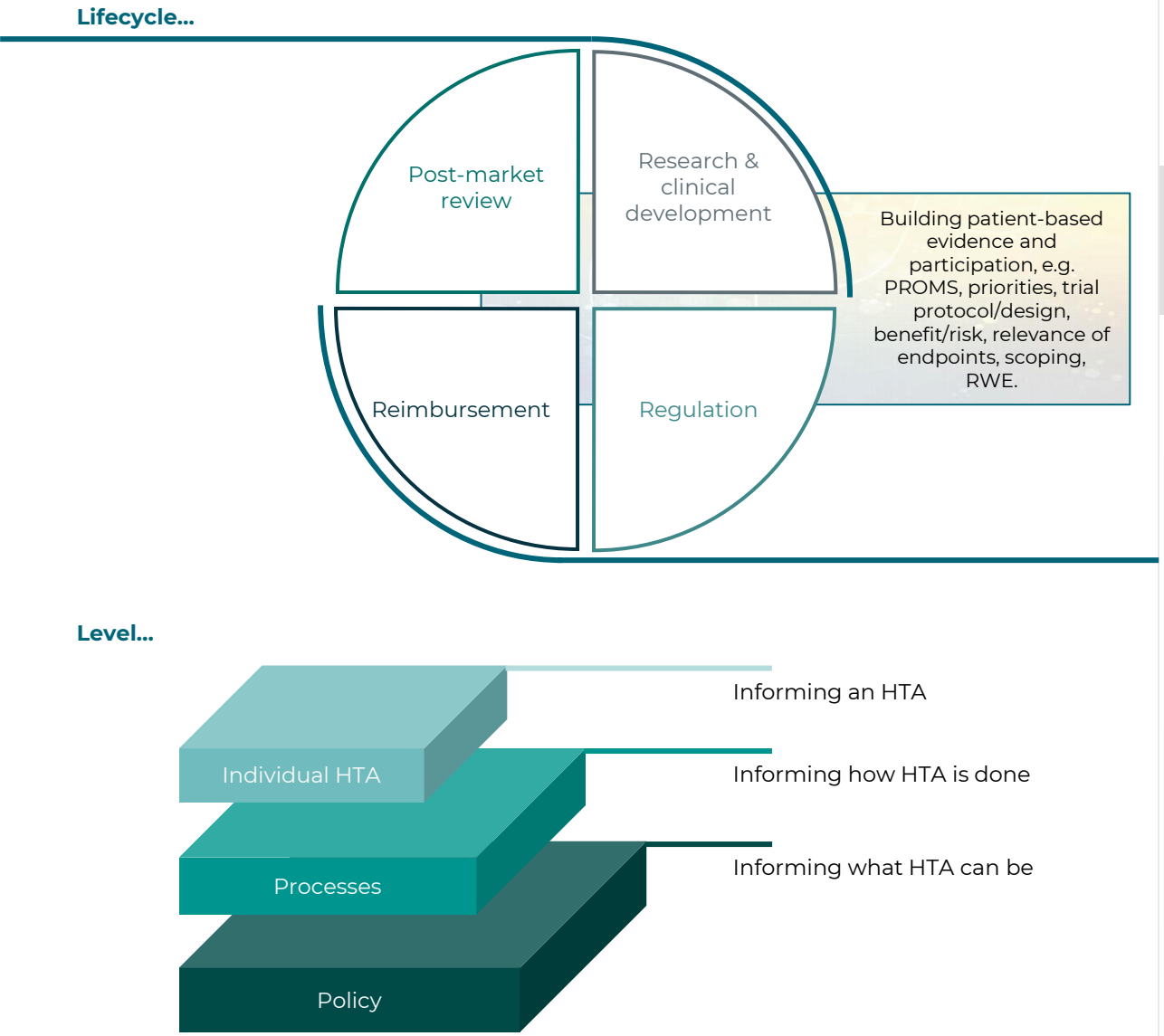
FIGURE 1: Dimensions of value (5)



HTA IS A VALUE-LADEN ENTERPRISE, REGARDLESS OF WHETHER PATIENTS ARE INVOLVED.

The overall value you determine depends on the domains you consider (5) and there are ethical assumptions underpinning all the questions considered in these domains (6). Overall value may vary depending on the perspective taken, the stakeholders involved and the decision context.

FIGURE 2: Learning with patients throughout a product lifecycle, developed from (7-9)



Patients could be involved in a medicine's lifecycle before the HTA process begins – including advising on trial design and endpoint selection. This involvement can then shift to inform the scope of HTA, how it is done and what an assessment can achieve. For example, in Scotland, the patient involvement network wanted a process for ultra-orphan drugs and were very involved in what was included. Internationally, agencies are learning what HTA is and what it can be for patients. This includes greater interaction with regulators and learning how to use RWE and early access.

TO ENSURE THE BEST OUTCOMES FOR PATIENTS IN AN EQUITABLE AND EFFICIENT HEALTH SYSTEM, HTA SHOULD USE TRANSPARENT, INCLUSIVE AND SUITABLE PROCESSES TO INFORM TIMELY, NEW AND ONGOING HEALTHCARE INVESTMENT.

It should be acknowledged that patients are diverse and we need to include diversity in the HTA process. "A key question however is whether current HTA processes may be incommensurable with the use of patient-based evidence and whether we need to address the epistemological assumptions that currently create a range of barriers to its use" (10).

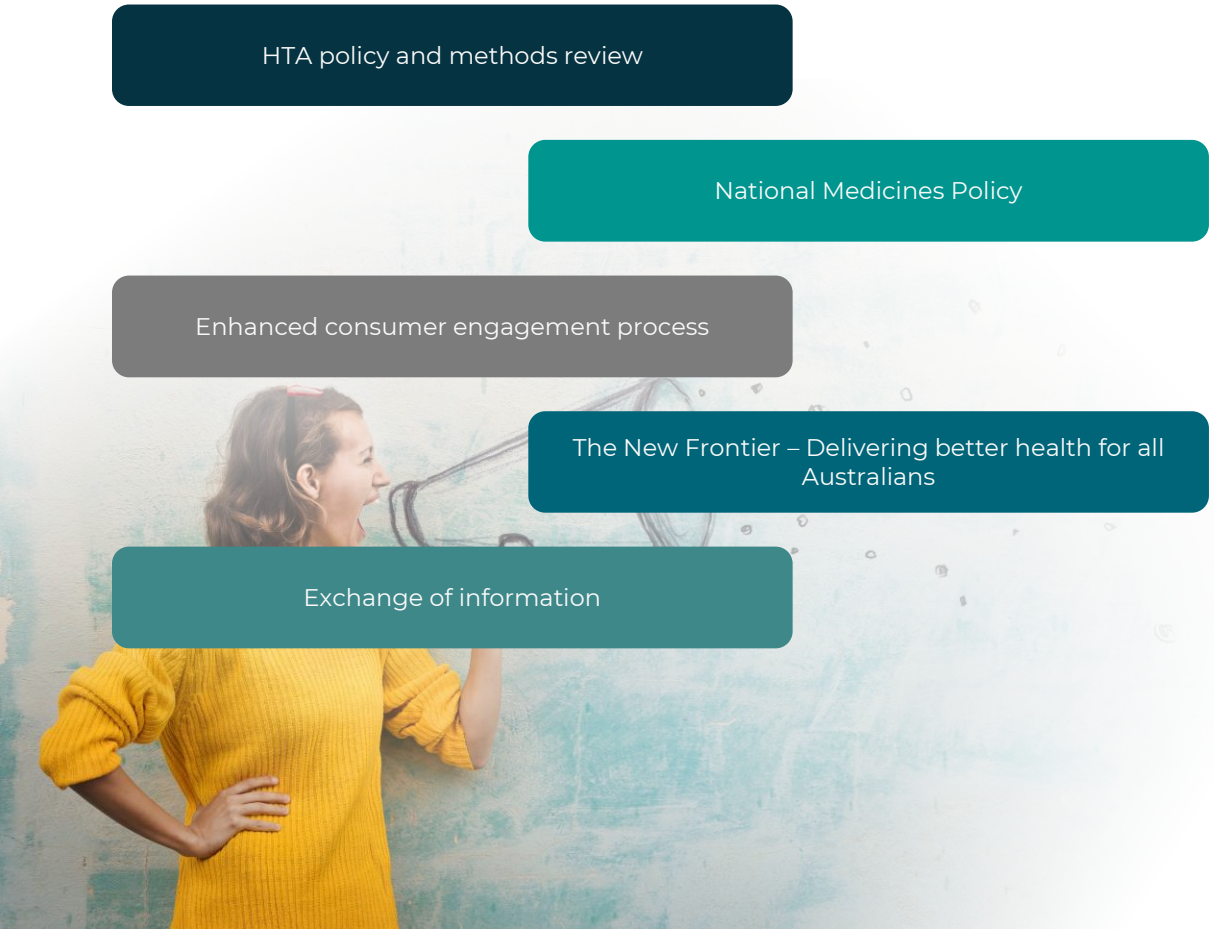
IF WE ARE GOING TO EMBED THE PATIENT VOICE, WE NEED TO TACKLE OUR ASSUMPTIONS, THE PLACE OF THE PATIENT VOICE AND WHAT IT CAN CONTRIBUTE.

VANESSA STEVENS

PATIENT INTERACTION SHOULD BE EARLY, MORE OFTEN AND MORE PROMINENT.

We need to improve the depth and breadth of patient involvement in HTA and beyond.

FIGURE 3: An overview of the changing environment



Exchange of information during a HTA evaluation shouldn't just be between the Sponsor and the evaluator or decision makers.

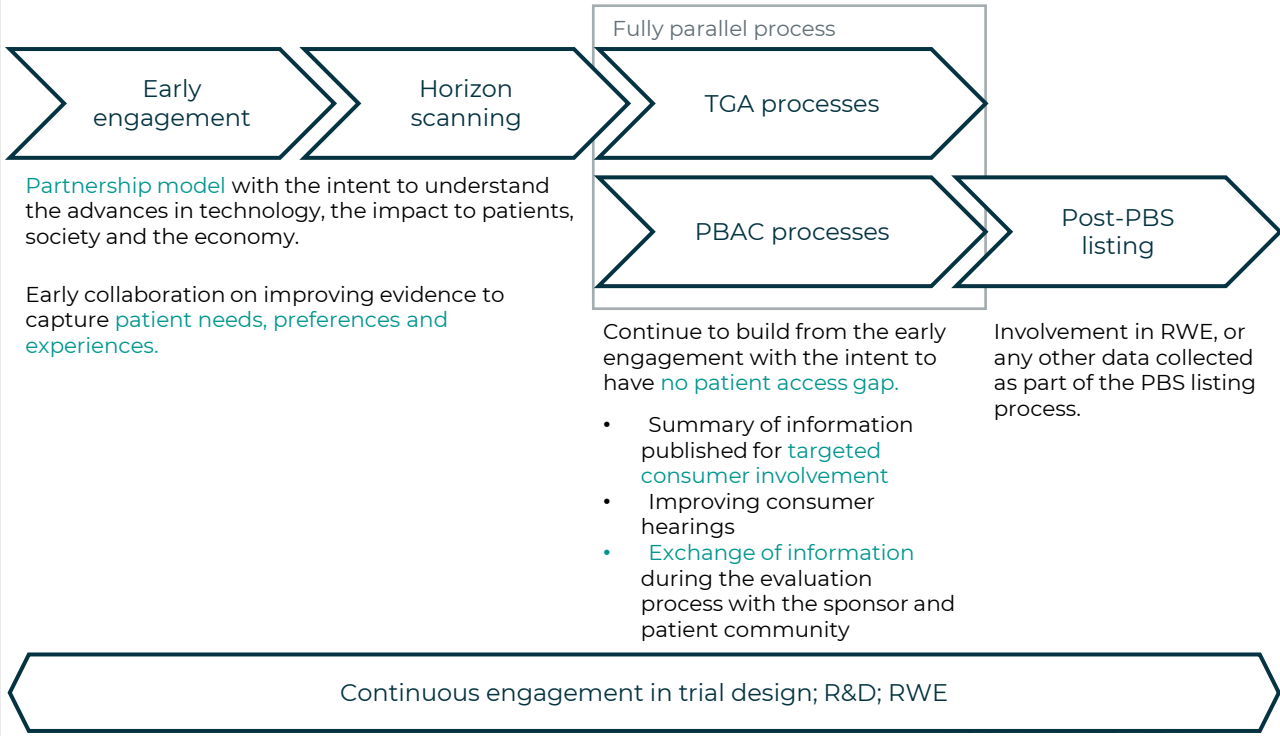
PATIENTS SHOULD BE INCLUDED IN THIS EXCHANGE AS WELL.

Patients are a diverse population and we need to capture that diversity, as well as needs, preferences and experiences.

We envisage a partnership model where different experiences are gathered from different stakeholders early and frequently. The Sponsor could provide patient groups or other stakeholders with a summary of information, including evidence and the funding question.

After registration or reimbursement we need to think about how best to close the loop with patients, by explaining what the restrictions are, especially if it's a restricted population, to continue engagement for broadening access.

FIGURE 4: Overview of potential engagement model



BREAKOUT GROUP DISCUSSIONS

How can industry, academia and other stakeholders work together to increase the patient voice in HTA?

- Industry engages clinicians early in the product lifecycle, and patients should be engaged at the same time to understand their lived experience.
- There is an opportunity for collaboration between industry and academia in developing a framework to enable meaningful engagement with patients. This includes validated measures to capture patient preference and the outcomes that matter to patients, so that the patient voice can be incorporated into decision-making in a rigorous way.
- Patient organisations should be proactive in engaging industry, initiating the contact and ensuring their voice is heard in decision-making.
- Concerns were raised about transparency and issues regarding commercial-in-confidence information that industry may not want to share with patients. There is a need to challenge what industry are comfortable sharing. Despite this, it was noted that patients don't care about the price of a medicine, they want to know what the assumptions are and whether these reflect their lived experience.
- How does the patient voice get incorporated: does it have to be written, or can it be verbal?

What measures should be put in place to improve the use of (or encourage the development of) evidence that captures or is informed by patients' needs, preferences and experiences for HTA?

- Patient and consumer engagement can be elite, only including certain types of patients who are confident enough to be in the room.
- There needs to be a standardised regulatory mechanism for including the patient voice.
- It was explained that bringing patients in is converting their truth into evidence.

What concerns or barriers about involving patients or communities in your research?

- Cost and timeliness.
- There is a need to demonstrate the impact that patient evidence is having on decision-making, otherwise it may become difficult to convince people to get involved.
- When including patients, it is important to consider elements such as health literacy, which may impact the representativeness of the patients being included. This has the potential to impact health equity if the most unwell, marginalised and remote communities are not being included.
- Robust methods need to be developed to extract good quality data.
- Mechanisms to manage tension, disagreements and trust. Information sharing is also a concern.
- Patient needs and unmet needs are demand side factors, while what comes through the medicine pipeline is often determined by supply side factors from global companies.

02

USE OF REAL-WORLD EVIDENCE

HTANALYSTS

KEY THEMES AND FUTURE WORK

PROMINENCE

Inclusion of RWE was identified as an important element to get right in the HTA review, as it was perceived that this would have a substantial impact on the patient access gap.

JURISDICTION

Jurisdictional challenges were noted; data linkage between federal (PBS, MBS) and state/territory (hospital) data was an important element to improving the use of RWE.

ROLE FOR INDUSTRY

Industry has a role in sharing data when feasible.

TRUST

Public trust in linked data (especially in light of recent high-profile data breaches) was a concern.

PATIENT-CENTRIC

Data governance needs to be patient-centric.

WORKFORCE

A workforce skills gap and getting the right skills to analyse RWE was noted as a significant limitation.

OPPORTUNITY

Overall, a significant amount of work is needed to improve the use of RWE – however the HTA review is an opportunity to make progress.

NATIONAL DATASET

The HTA review provides an opportunity to work towards a national dataset capturing federal (PBS, MBS) and state/territory (hospital) data.

LUCAS TOCCHINI

Randomised controlled trials (RCTs) are the gold standard design to generate evidence with a low risk of bias, but they are not a perfect source of evidence and can have low external validity. RWE can be considered useful in specific situations, such as when it is not ethical or not feasible to run an RCT.

RWE IS ACCEPTED IN AUSTRALIA,
BUT THE EXTENT TO WHICH IT IS CONSIDERED IS VARIABLE.

There is a lack of guidance about the use of RWE, which leads to inconsistent decisions. In addition, a lack of access to linked data limits Sponsors from creating robust RWE in Australia. We need a high-level framework that could be used across the HTA committees as well as the TGA.

Many professional associations have issued best practice guidelines for the analysis of RWE (such as the Food and Drug Administration, European Medicines Agency and ISPOR HARPER - HARmonized Protocol Template to Enhance Reproducibility).

TO ENABLE USE OF RWE, WE ALSO NEED MORE INVESTMENT IN INFRASTRUCTURE AND THERE IS A CASE TO INCREASE INDUSTRY INVOLVEMENT AND ACCESS.

We propose co-designing a set of principles that allows RWE to be incorporated into the HTA process. This should include aspects such a data provenance, transparency, potential bias, descriptions around the types of observational data, and example situations where it could be used to inform decision making.

There are currently linked datasets available, however these datasets are not fit-for-purpose for use in the HTA process.

MADIP	Combines information on health, education, government payments, income and taxation, employment, population over time. Projects must be in the public interest. Confidentiality is a condition of access.
NIHSI	State/territory, national administrative data sets, MBS, PBS, residential aged care, national death index. Can be used to inform planning, monitoring and evaluation.

FIGURE 5: Overview of MADIP data sharing model (11)

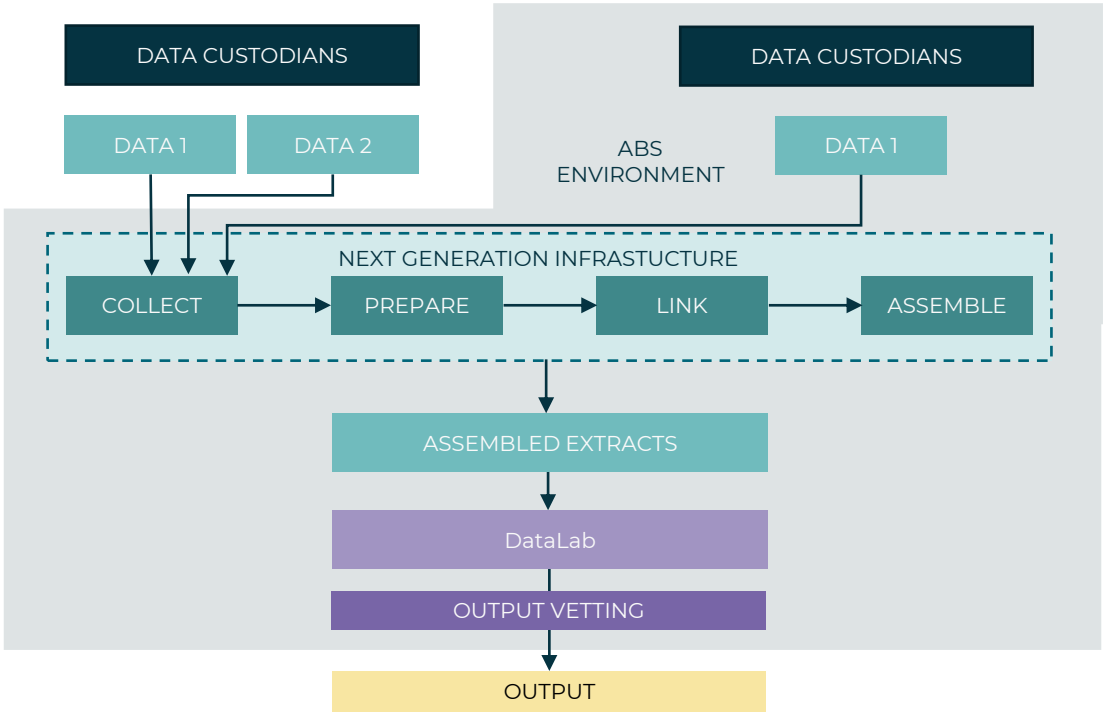
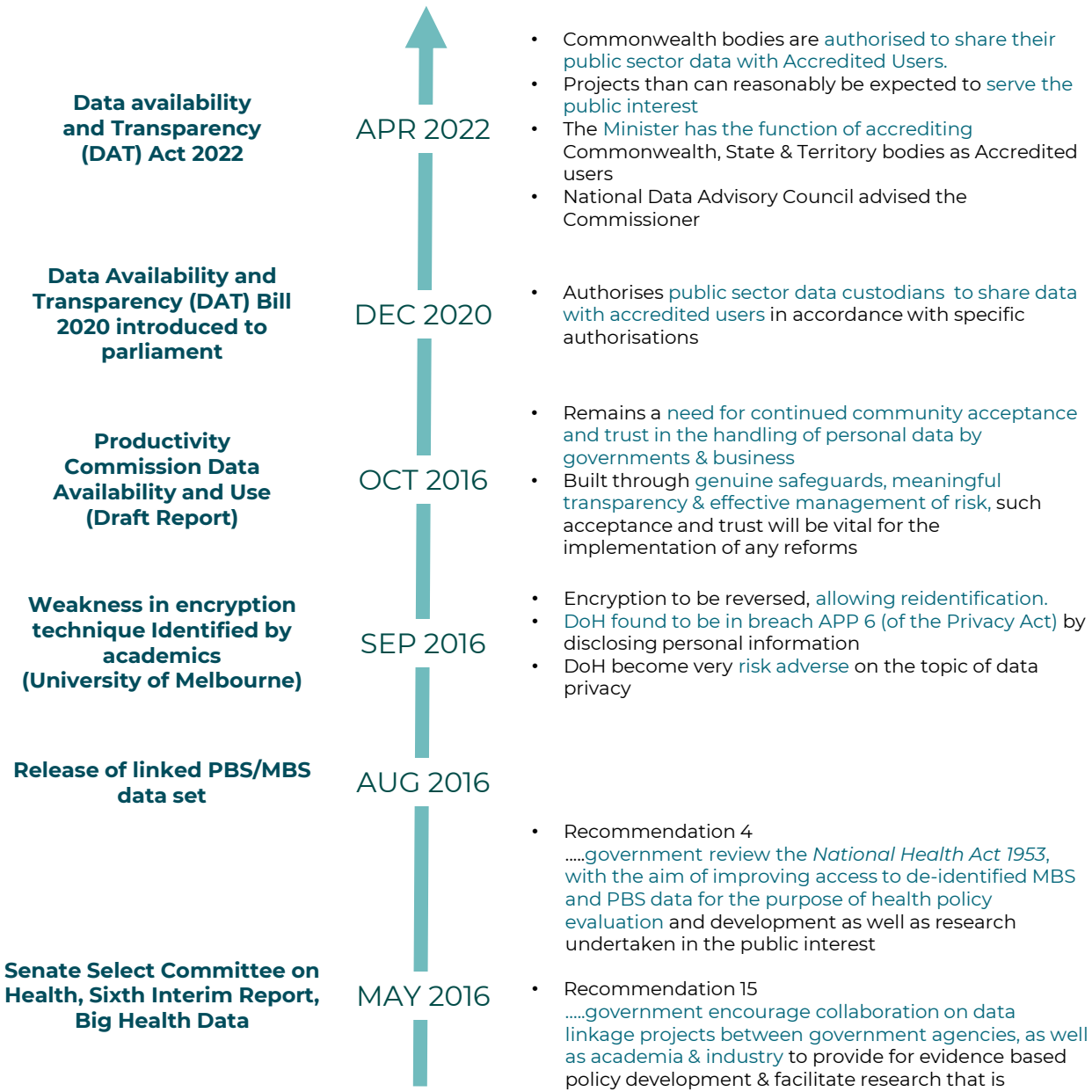


FIGURE 6: Summary of key milestones for Federal health data access



There are several potential use cases for RWE in HTA, including:

- informing natural history data or untreated controls,
- primary evidence for difficult to study diseases,
- supporting data inputs in terms of applicability or extrapolation,
- post-market in terms of expanding indications,
- to inform Managed Access Programs (MAPs), and
- to understand the relationship between the outcome measure and the modelled outcome.

However, currently a lack of access and patchy linkage data limits Sponsors from generating robust RWE.

There is a complicated history related to publicly available linked datasets in Australia.

IN AUGUST 2016, A LINKED DATASET COMBINING PBS AND MBS DATA WAS RELEASED. HOWEVER, A WEAKNESS IN THE ENCRYPTION TECHNIQUE WAS IDENTIFIED AND THIS HALTED ANY PROGRESS.

The recent Data Availability and Transparency Act 2022 authorises the public sector data custodians to share data with accredited users, however it is unclear what this will achieve.

Overall, RWE can help decision making by reducing uncertainty. Australia is investing in capturing this data, and a case can be made that a HTA submission is in the public interest. However, comprehensive multiple linked datasets are needed to support timely access to medicines/treatments and for post market reviews.

PROFESSOR SALLIE PEARSON

What are the best sources of RWE?

BEST VS WHAT WE USE ARE NOT THE SAME THING

- In academia we use anything we can access
- We have an aspiration around the types of data we want but need to be pragmatic
- The best data source depends on the question you want to ask
- Linked data sets are not going to solve all of our problems

What are the barriers stopping use of RWE?

- Public trust is paramount
- Nuanced communication about the issues and solutions
- Access to fit-for-purpose data and timing of access

THERE IS WORK TO DO AROUND PROMOTING LEGITIMACY OF RWE AND ROBUSTNESS OF METHODS

- Exposure data (PBS/MBS) is held by Federal Government, compared to outcome data (hospitalisation, deaths) which is held by the states – linkage takes time and resources across both jurisdictions
- Workforce with requisite skills to analyse data is a challenge
- Tradition and attitudes to RWE remains a barrier

How do we move this forward?

- Academics, industry and government don't necessarily have equitable access but have similar questions

WE NEED TO ACKNOWLEDGE A SHARED GOAL BETWEEN ALL STAKEHOLDERS

- Better knowledge sharing within and between sectors, transparency is a key limitation
- Need to develop FAQs around the difference between data sets, particularly for the public and why the benefits of pulling data together outweigh the risk of identification

Is the HTA review an opportunity to harness different groups to get progress in this space?

RWE IS A BIT OF A BROAD TERM THAT WOULD INCLUDE VARYING LEVELS OF STUDY QUALITY, AND IF WE WANT TO IMPROVE THE USE OF RWE WE NEED TO BE CLEARER ABOUT WHAT THAT ACTUALLY MEANS .

BREAKOUT GROUP DISCUSSIONS

What facilitators can be leveraged to increase the use of RWE in HTA?

- We have a shared goal between government, industry and patients around improving use of evidence and using data to inform decision making.
- There needs to be a conversation and a different mindset on how we can use RWE in HTA.
- Frameworks should be developed for when RWE should be used.
- Equity considerations could be a trigger to accept RWE in HTA.
- Having a public discussion around benefits of RWE and how data can benefit everyone.
- We should be leveraging what already exists and using networks of practitioners to build on this where possible.
- Data governance needs to be patient centric.
- Information symmetry would better facilitate the use of RWE. Currently, the Department of Health have more in-depth access to claims data, which means that the Department and industry are not necessarily 'talking the same language' during negotiations.

What methods should the HTA review look at to increase the use of RWE?

- RWE used to be called observational research. Moving forward, there is a need to define what RWE is when it is being used in HTA.
- Methods should be developed for the use of registries in HTA submissions.
- It would be helpful to have databases where RWE has previously been used in HTA, to increase transparency.
- Guidance for where to use RWE (for example, during reimbursement submission vs post-market) would be useful.
- There should be greater collaboration between the people who design RWE databases, decision-makers, and people who use the data.
- Early dialogue and agreement are needed regarding what RWE will be used for and how it will fill evidence gaps in the submission.

How should we use RWE in HTA?

- Routinely collected data sets are often used.
- RWE is useful for getting historical data, but it is harder to use for experimental design.
- RWE can be used to look backwards after a decision has been made.
- RWE could be used to support the validation of models or other assumptions.

What international examples should the HTA review look at?

- NICE
- France
- FDA guideline and clinical trial transformation
- Nordic countries were identified as having good use of linked data.
- Challenges were also identified including diversity and inclusion in relation to data. There is a need to look at barriers to inclusion in data sets.

What barriers need to be removed to increase the use of RWE in HTA?

- The hierarchy of evidence is still widely used, which limits the use of RWE as it is considered low quality or highly biased.
- There is a need to develop workforce skills to interpret data being generated.
- The cost of developing, maintaining and interpreting registries and RWE studies is a limitation.

How can industry and academia work together to increase use of RWE in HTA?

- Collaboration in the design and development of a national data set that is considered to be robust and is of benefit to the public. This data set should include PBS, MBS, hospital data which requires collaboration across jurisdictions (federal and state).

03 SECOND ORDER EFFECTS

KEY THEMES AND FUTURE WORK

OPPORTUNITY

The inclusion of carer wellbeing is a key opportunity, and this is likely to be the easiest second order effect to measure.

GUIDANCE

Guidance is needed on how to collect second order effects in a robust manner, and how this data is factored into decision making.

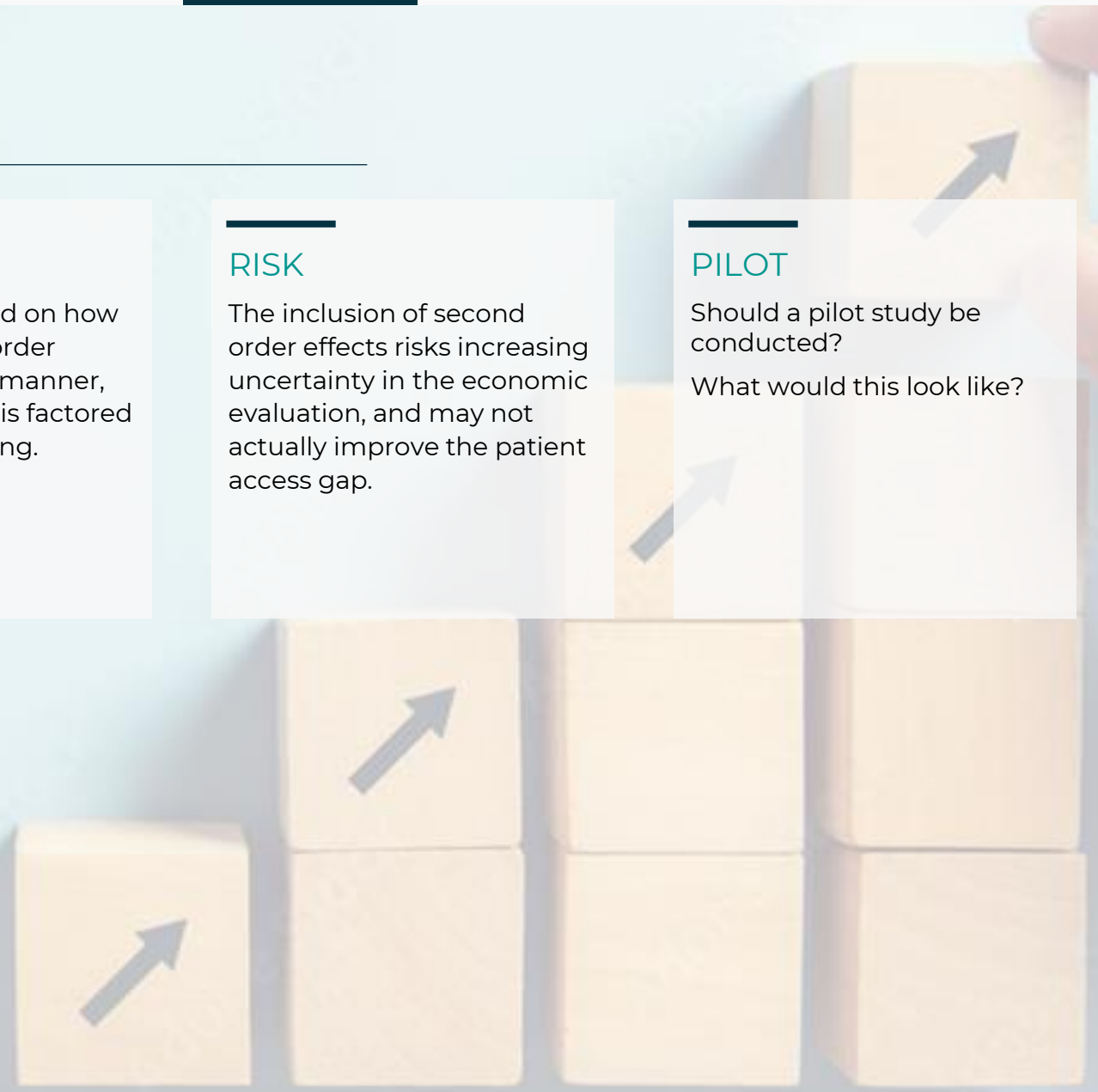
RISK

The inclusion of second order effects risks increasing uncertainty in the economic evaluation, and may not actually improve the patient access gap.

PILOT

Should a pilot study be conducted?

What would this look like?



DR MARTIN SNOKE

Second order effects are the 'flow on' impacts of a policy or medicine that affect the broader economy, beyond just the patient and the health care system.

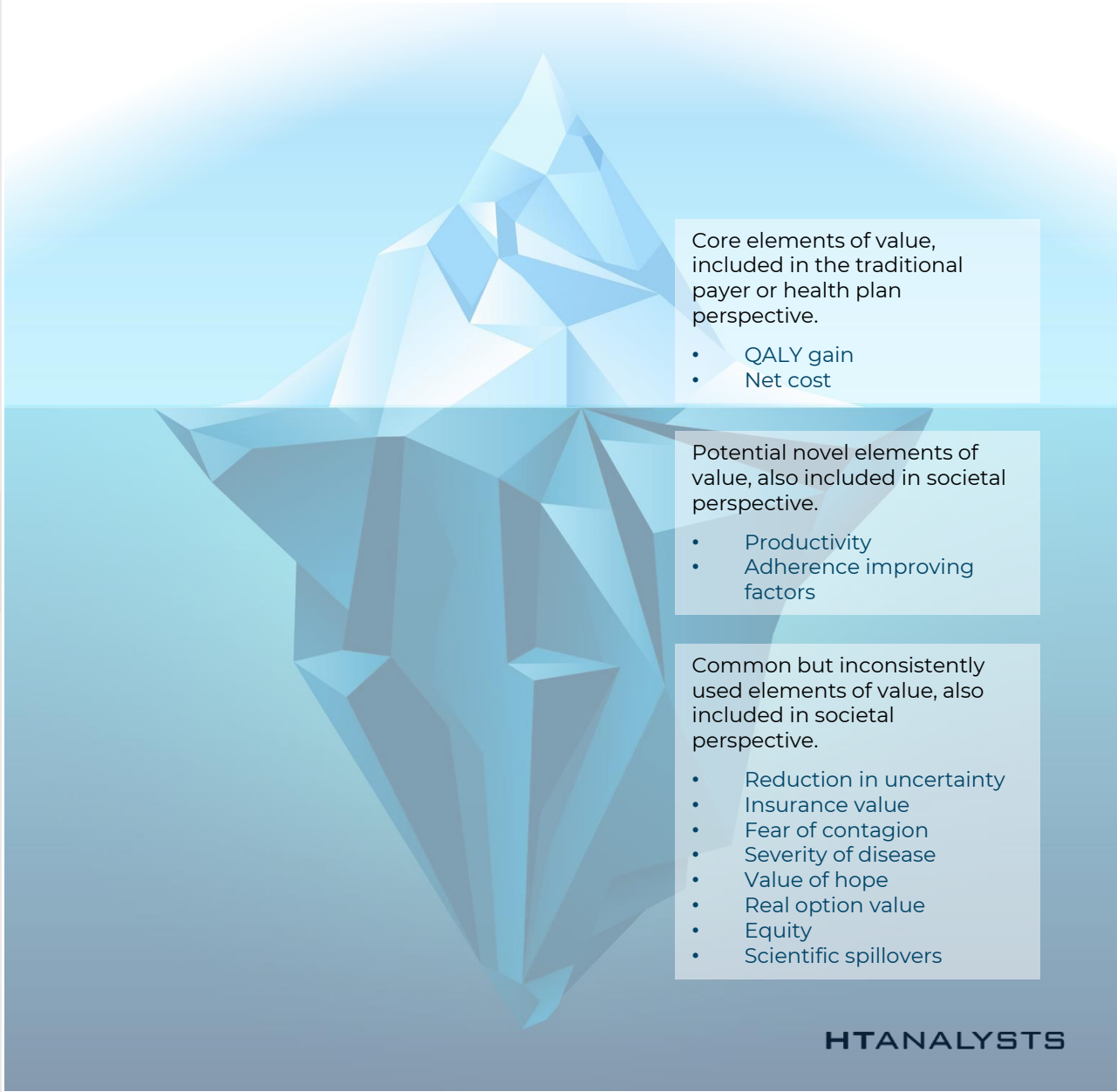
AS A GENERAL RULE, THESE ARE NOT INCLUDED IN POLICY COSTINGS, WHICH ONLY CONSIDER THE DIRECT BEHAVIOURAL/HEALTH IMPACTS.

The reason these impacts are usually not included is due to the uncertainty in estimating the magnitude of effect, timing of the effects, and that the size of the effect is expected to be small relative to the primary impact.

Currently, second order effects such as the value of hope, improvements in productivity, and carer burden are not included in economic evaluations used in HTA, and decision makers typically consider the direct patient outcomes and cost to the Federal PBS and MBS budgets.

INDUSTRY IS PROPOSING THAT SECOND ORDER EFFECTS SUCH AS BROADER HEALTH SYSTEM COSTS AND IMPACTS ON CARERS SHOULD BE INCLUDED IN HTA.

FIGURE 7: ISPOR value flower (12), adapted



In the future, this could be broadened further to include societal impacts such as productivity, tax revenue, education and carer replacement costs. Internationally, the most common second-order effect to be considered is carer outcomes.

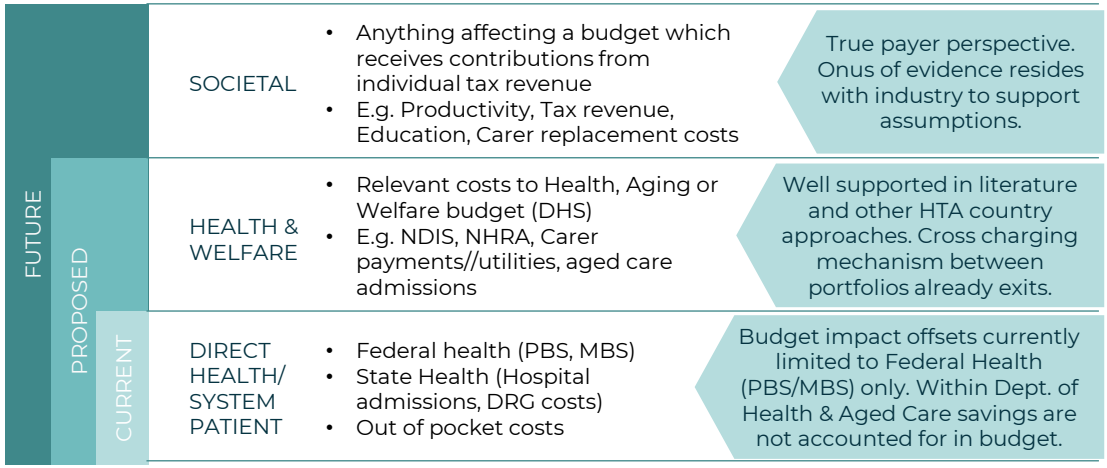
The current approach to second order effects in the PBAC guidelines excludes these effects from the base case analysis, although there is the potential to present these as supplementary analyses.

Potential future opportunities were identified to include second-order effects in a broader economic evaluation, and broader budget impact calculation. However, there is a need for further clarity on how these analyses are used in the overall decision-making process.

THERE IS AN OPPORTUNITY FOR INDUSTRY AND ACADEMIA TO WORK TOGETHER TO CONSIDER THE TYPES OF SECOND ORDER EFFECTS AND MODELS THAT WOULD BE MOST COMPELLING FOR HTA.

There is also a question about whether there should be certain circumstances in which second order effects are considered in the base case, for example conditions identified as a National Health Priority, conditions that have direct and substantial impact on carers, and conditions that affect productivity.

FIGURE 8: Proposal for consideration of second order effects in HTA



INTERNATIONALLY, THE INCLUSION OF SECOND ORDER EFFECTS IS INCONSISTENT AND LARGELY DEPENDENT ON THE PERSPECTIVE OF THE ECONOMIC EVALUATION.

FIGURE 9: International perspectives

	COSTS	OUTCOMES
AUS	Patient or Healthcare provider	Patient
ENG	NHS + Personal social services	Patient + carer
CAN	Publicly funded healthcare	Patient + carer
FIN	Patient + family (travel, productivity, social services)	Patient + family
AUT	Societal	Societal
BEL	Payer + community + patient	Societal
FRA	Collective	Anyone whose health is affected, including public
NOR	Patient + family (travel and time)	Patient + carer
DEN	Resource utilisation (overheads + productivity)	Patient
GER	Direct + indirect, medical + non-medical	Patient

FELICITY MCNEIL

THE PROBLEM WE ARE AIMING TO SOLVE IS THE PATIENT ACCESS GAP.

Results from a time to event analysis indicate that the average time from TGA registration to subsidised listing is over 430 days. For certain submissions, where the price is higher than the comparator (and requires a cost-effectiveness evaluation), the time from registration to subsidised access is over 750 days. Second order effects could be an impediment to timeliness of access.

Industry has proposed developing agreed criteria where second order effects could be included in the evaluation and develop methodologies for inclusion of second order effects in HTA. In effect a societal return on investment captured in a new health survey for matters beyond the patient experience.

FIGURE 10: Overview of Australian health priorities

National Health Priorities
Cardiovascular health, cancer control, injury prevention & control, mental health & diabetes mellitus
7.2 – 12.1M Australians

Draft Australian Cancer Plan population priorities
In addition to Aboriginal & Torres Strait Islander people, priority population groups identified in the ACP include:
Lesbian gay, bisexual, transgender, intersex, queer and asexual (LGBTIQA+) people; People from culturally and linguistically divers (CALD) backgrounds; People living with disability; People living in lower socioeconomic areas; People living with a mental illness; Older Australians; Adolescents & young adults; Children; People living in rural and remote areas

Counting the cost the true value of investing in cancer treatment
A societal return on investment based on a higher value placed on value of life and impacts such as: capacity to care, missed milestones, & avoided costs such as alcohol & drug rehabilitation; displacement, trauma, funeral costs, costs to carers & families

Contemplate who misses out in these scenarios?
Does it *improve equality* of access?
Does it *improve time* for access?

IF WE PRIORITISE CERTAIN DISEASES, THE RISK IS THAT OTHERS ARE LEFT BEHIND. THE FOCUS SHOULD BE ON EQUALITY OF ACCESS AND TIME TO ACCESS.

Second order effects are already included and considered by the PBAC, and there is a question as to why companies don't include this data in submissions. As companies try to increase price by including second order effects, they increase uncertainty in the model which increases risk of rejection.

Overall, this is not an easy topic to include in the HTA review. A risk is that the government will want to recoup second order effects that are not realised if they are claimed as a cost offset in the modelling.

We need KPIs in the system for access and companies need transparency in how decisions are made.

EVERY INDIVIDUAL'S HEALTH IS A PRIORITY TO THEM REGARDLESS OF WHAT A NATIONAL HEALTH PRIORITY FOCUS IS.

BREAKOUT GROUP DISCUSSIONS

What methods should the HTA review look at regarding the inclusion of second order effects?

- Methods should be developed to inform how to collect data on second order effects in a robust and consistent manner.
- Clear guidance is needed on how second order effects are factored into decision-making.
- There is a need for transparency to identify when and where second order effects are best used in HTA.

How can we increase alignment regarding the use of second order effects in HTA modelling?

- Need to understand stakeholder concerns.
- Opportunities to pilot the inclusion of second order effects should be identified.
- Clinical trials could build in carer quality of life measurements as an outcome to ensure more robust, prospective data collection of second order effects to be used in HTA.

What international examples should the HTA review look at?

- Countries where second order effects are more likely to be included are those countries where health is seen as broadly impacting the economy.
- Second order effects could also include the value of innovation (UK and Japan noted as examples).

How can industry and academia work together on this topic?

- The key area identified for collaboration was defining second order effects, and when and how to include them in HTA.

How should second order effects be defined?

- Being too broad could be counterproductive if it increases uncertainty.
- Second order effects might not be relevant for every product.
- We need to identify the 'low-hanging fruit' for second order effects first, what will be easy to define and measure?
- Could this be done through a pilot?

What are the risks of including second order effects?

- The main risk is that inclusion of second order effects could result in adding another hurdle and actually increase time to access.
- Second order effects also risk increasing uncertainty.
- Assuming that there is a limited health budget, will the inclusion of second order effects actually improve access?

04 PRECISION MEDICINE

KEY THEMES AND FUTURE WORK

WORKFORCE

There is a workforce skills shortage in many areas that slows down access.

DATA SHARING

There is a perception that industry captures a lot of data through clinical trials that could be shared more broadly. Additionally, results from tests conducted through the MBS cannot currently be used for research.

HTA FRAMEWORK

It was not clear whether the HTA framework was the most appropriate method to assess genomic technologies.

DECISION MAKING FRAMEWORK

Work needs to be done to develop a framework to inform committee decision making for genomic tests.

TIMELINES

MSAC/PBAC timelines are currently disjointed and should be better aligned.

COLLABORATION

A working group should be established between academia and industry to build knowledge and capabilities.

GUIDANCE

Better guidance for panel testing is needed.

CLARITY OF TERMS

Need to clarify definitions of terms such as precision medicine.

TIFFANY BOUGHTWOOD

The Australian health ecosystem is extremely complex with shared responsibility for health delivery and multiple decision makers.

THE GENETIC AND GENOMIC ECOSYSTEM IN AUSTRALIA ADDS AN ADDITIONAL LAYER OF COMPLEXITY, INCLUDING THE EVOLUTION OF TRADITIONAL CLINICAL ROLES AND EVOLUTION OF THE MODELS OF HEALTHCARE DELIVERY.

Generally, progressing genetic and genomic clinical and diagnostic practice requires applications to the MSAC.

An example of an MSAC application for genetic/genomic testing is the Australian Reproductive Genetic Carrier Screening Study (Application number 1637). Overall MSAC did not support the application but recognised there was a high unmet clinical need. In addition, MSAC noted there was a need to resolve the current inequity of access. An analysis of the public summary document for this application highlighted several elements that would need to be addressed in a resubmission. This ranged from ethical considerations to societal acceptance to clinical considerations and infrastructural issues related to national implementation. MSAC also asked the Department to investigate whether funding and implementation would be more appropriate as a population screening program.

THE BREADTH OF INFORMATION REQUESTED BY MSAC RAISES QUESTIONS REGARDING HOW FIT-FOR-PURPOSE THE HTA PROCESS IS FOR GENETIC AND GENOMIC TESTS.

Genetic and genomic clinical practice is evolving constantly as research progresses at a rapid pace. However, to align with MSAC timelines, there is often a need to submit to MSAC application while research is still ongoing.

THIS HAS IMPLICATIONS FOR GENE LISTS INCLUDED IN PANEL APPLICATIONS, WHICH CAN EVOLVE OVER TIME WITH RESEARCH.

Overall, there could be better linkages between genetic and genomic clinical practice (determined via the MBS) and research. In particular, genetic and genomic research priorities could be informed by submission evidentiary requirements. Ongoing evaluation of items could also be better linked with research priorities. Currently we cannot use data derived from MBS tests to enrich secondary research.

FINALLY, WE SHOULD ALSO CONSIDER THE DYNAMICS OF COMMITTEE DECISION MAKING IN THE HTA PROCESS, AND WHETHER A CONSENSUS VIEW IS REPRESENTED, AND COLLECTIVE DECISION REACHED.

Should we be looking at a model where members submit their preliminary deliberations prior to meeting with the committee, to support improved committee dynamics and the achievement of collective outcomes?

FIGURE 11: The Australian genomics landscape

ANDREA KUNCA

There are many different stakeholders in the genomics industry that may have different objectives. The vision of the Industry Genomics Network Alliance (InGeNA) is to realise the full potential of genomics to personalise healthcare. This organisation brings together genomics industry stakeholders to facilitate collaboration.

PRECISION MEDICINE RELIES ON BROAD, CONSISTENT AND AFFORDABLE ACCESS TO GENOMIC TESTING. THIS LARGELY RELIES ON MBS LISTING WHICH RELIES ON THE HTA PROCESS.

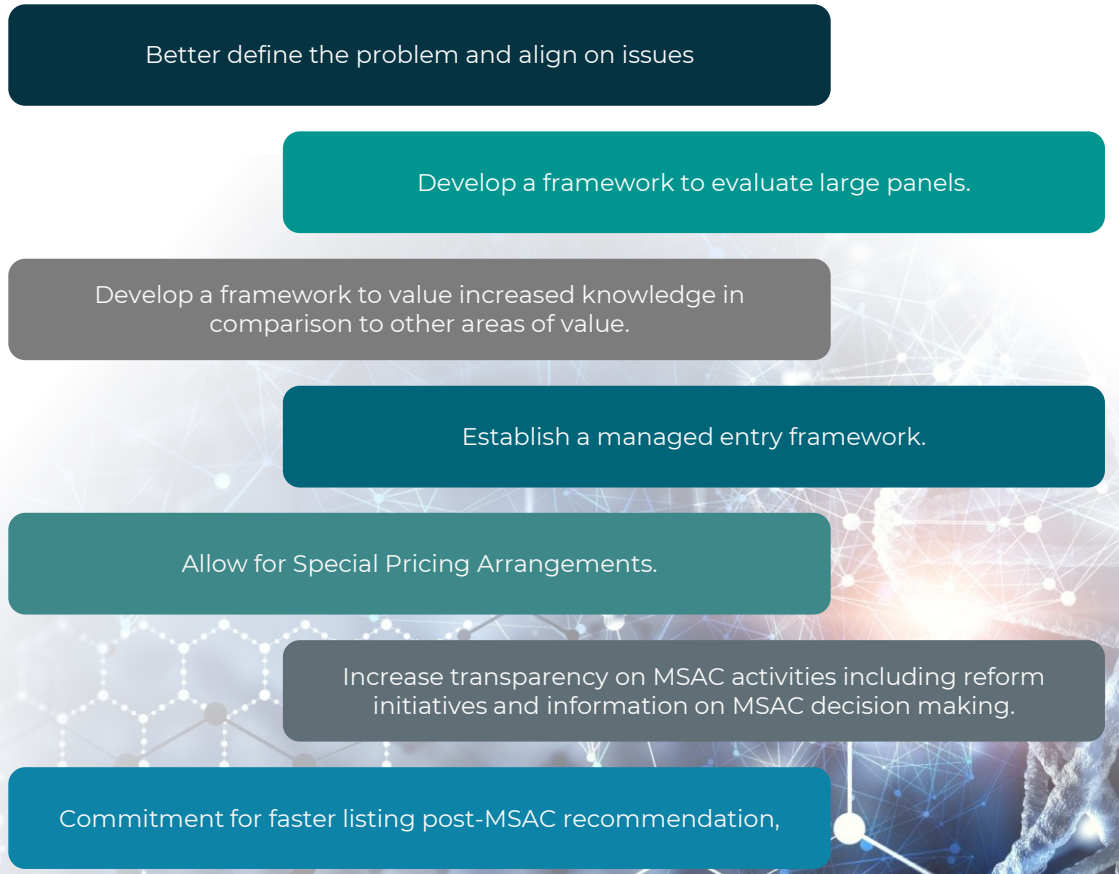
There are numerous challenges relating to the HTA for genomic tests. The InGenA White Paper included several phases of research starting with a systematic review of the literature, followed by multiple rounds of stakeholder consultations. A review of MSAC recommendations identified several barriers including uncertainty, clinical utility, cost-effectiveness, place of testing in pathway as well as positive and negative impacts of testing.

STAKEHOLDER CONSULTATION REVEALED A LACK OF ALIGNMENT ON CHARACTERISING THE KEY CHALLENGES.

In addition it was recognised that there is a significant access delay, even after a positive MSAC recommendation.

The White Paper identified several key recommendations moving forward.

FIGURE 12: Recommendations from InGenA White Paper (14)



The Bouttell et al publication(13) (included in pre-reading material), identified challenges that relate to genetic testing. Five genomic specific issues included heterogeneity of tests and platforms, increasing stratification of disease, measuring personal utility, impact of incidental findings and spillover effects of testing into relatives – how far do we go?

It is clear there are issues at the level of the MSAC and post-MSAC processes and we should be building on what has been done to date. However, these need to be better defined to get alignment and buy-in to address comprehensively. Effort should be focused in the areas which are responsible for slowing down patient access now or have the potential to do so as genomics evolves in the future.

WE NEED TO GET AN UNDERSTANDING OF THE HTA METHODS AND PROCESS ISSUES IN AUSTRALIA AND ACHIEVE SOME LEVEL OF ALIGNMENT ON THE ISSUES.

In addition, there were issues identified relating to the reimbursement and funding structures. Collaborating to create a shared purpose will be key to defining what we need to do, clarity about what it will achieve, and lastly how we will work to achieve this.

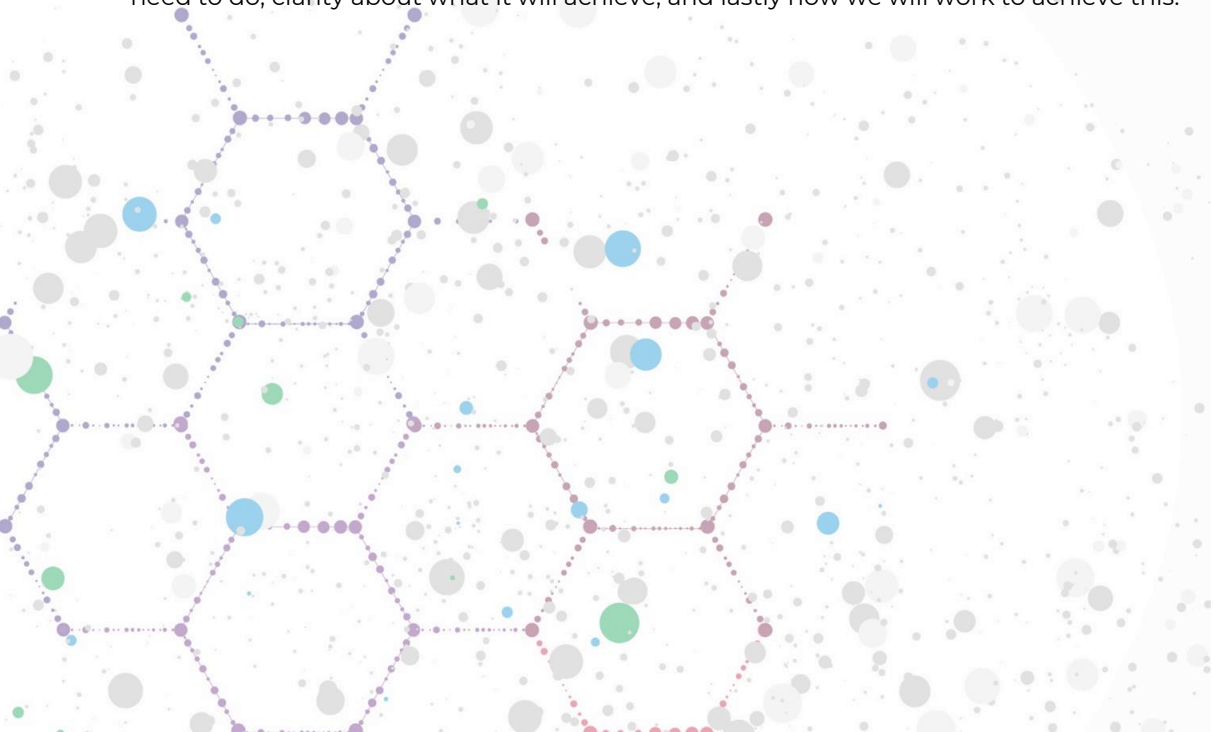


FIGURE 13: Bouttell et al (15) – Author's views on the 5 genomic specific issues

HETEROGENEITY	Heterogeneity of tests and platforms makes it difficult to identify cost and resource use, and measure effectiveness. Current methods are feasible for interventions and comparators in a narrow setting, but this is not appropriate for genomic tests.
STRATIFICATION	Increasing stratification of disease reduces patient populations, making generation of evidence of effectiveness more difficult. Economic evaluation techniques may need to evolve alongside clinical trials.
PERSONAL UTILITY	Measuring personal utility may be difficult as tools to estimate QALYs may not be sufficiently sensitive to capture all aspects valued by patients and families. Methods development is required, when cost-utility analysis is undertaken, the broader elements of value could be qualitatively considered.
INCIDENTAL FINDINGS	The impact of incidental findings on short- or long-term patient management outcomes. Methods may need to evolve, but this is currently seen as a theoretical challenge as all results must be interpreted and reported for use by clinicians.
SPILLOVER EFFECTS	The spillover effects of testing on reproductive decisions or family members to take action to alter their health outcomes. Current methods can incorporate health impact for current and future family members. Valuing impact on reproductive decisions my require methods development.

BREAKOUT GROUP DISCUSSIONS

What are the priority areas for the HTA review regarding genomics and precision medicines (noting Bouttell as a key ref)?

- The capability and capacity of Department of Health & decision-making committees needs to be enhanced.
- Disjointed PBAC and MSAC processes should be aligned.
- The review should be clear about the definition of precision medicine? Does it include things like personalised medicine and gene therapies?
- Methods for valuing the long-term benefits of precision medicine should be developed.
- There is a need to develop guidelines for how HTA should consider gene panel testing.
- There was a question regarding whether HTA is the right process for precision medicine, or whether there are other frameworks that should be drawn on.
- There is a need for adaptive decision making and recognition of increasingly complex therapies in this space.

How can industry and academia work together to increase efficiency with respect to HTA evaluations of genomics and precision medicine? What would be required?

- Unlike overseas, it was noted that there is a perceived conflict of interest between academics in Australia working with industry.
- We need to be more transparent and work out how we can better work together.
- Industry has access to lots of good information captured in trials, but they don't share it with academics.
- More education and platforms for upskilling academics are needed.
- A working group between industry and academia for building and sharing knowledge could be developed.
- More communication & early identification of issues at PICO/PASC phase to maximise acceptability of the application (two-way discussion with stakeholders early on), would be beneficial.

What international examples should the HTA review look at (such as the UK)? How are things done differently?

- Precision medicine is a constant area of change, and international solutions may not fit the Australian context.

What are potential solutions to speed up the assessment of genomics/precision medicines through the HTA process?

- There are two elements that need to be considered: submissions coming in & the review/evaluation side.
- If we speed up submissions, what other elements might slow down as a result? Will this actually result in faster access?
- We need clarity and guidelines on what works well, including looking at best practices from overseas.

How can we improve committee dynamics and decision making?

- There is a lot of expertise, asking more people gets better information.
- The goal is to get the best outcome for patients.
- The workload for committee members is substantial. There is a need to build the capacity of the system.
- Developing decision frameworks could be useful.

05 CONDITIONAL LISTING

KEY THEMES AND FUTURE WORK

MECHANISM

A mechanism for conditional listing (i.e. MAPs) is already in place, but it is not currently being utilised effectively.

PBAC AUTHORITY

The PBAC do not currently have the power to offer a MAP, they can only accept one if the sponsor proposes it.

PATIENTS

Patients would rather have access sooner with the risk that the drug is taken away, than face delayed or no access to treatment.

DOMINO EFFECT

There is a need to consider the potential domino effect on subsequently listed medicines. If the price comes down after more data is collected, how will this impact the price of other drugs?

BARRIERS

Many barriers and risks can be identified. These often cross over with the issues of RWE.

SUBMISSION BARRIERS

There is a need to identify why companies are not requesting conditional listing.

Is the cost of submission a factor given the perceived low chance of success?

MANAGED EXIT

How does a managed exit take place is the final results are not as good as initially thought?

VALUE OF INFORMATION

Would additional methods such as value of information analysis help reduce the risks?

JULIA LEWIS

Conditional listing can broadly be considered as coverage alongside evidence development. On the PBS, Managed Entry Schemes (2011-2015) or Managed Access Programs (MAPs) (2015 onwards) currently provide a mechanism for conditional listing. Conditional listing via MAPs can cover products with otherwise unacceptable clinical or economic uncertainty, in areas of high unmet clinical need. If the PBAC determines that a MAP is appropriate, then key areas of uncertainty are identified along with the evidence required, timeframe for providing this evidence, and potential consequences of the evidence.

DESPITE A MECHANISM FOR CONDITIONAL LISTING EXISTING IN AUSTRALIA SINCE 2011, THERE HAS BEEN LIMITED UPTAKE – WITH ONLY FOUR ONCOLOGY PRODUCTS AND FOUR CYSTIC FIBROSIS PRODUCTS LISTED ON THIS BASIS.

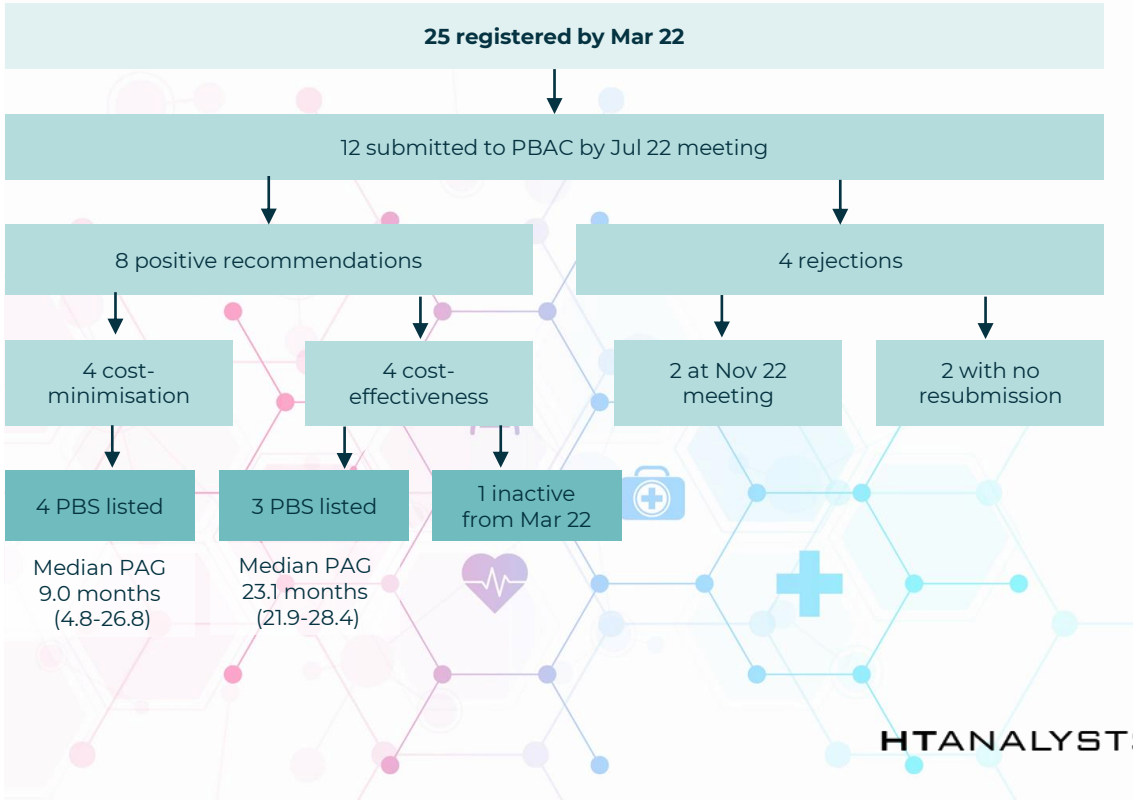
From a registration perspective, the Therapeutic Goods Administration (TGA) have had a provisional pathway available since 2018. This pathway provides time-limited registration for products where the benefit of early listing outweighs the risk of early data. Eligibility criteria for this pathway include that the product treats a serious condition, that it has a favourable comparison against existing options, that it represents a major therapeutic advance, and that the sponsor plans to submit comprehensive clinical data when it becomes available. This pathway enables medicines to become available up to two years sooner than with the standard pathway and has had strong uptake, with 62 provisional designations since 2018, including 29 non-COVID products.

Addressing the discrepancy between provisional TGA approval and conditional reimbursement of medical products was identified as a key area for improvement in "The New Frontier – Delivering better health for all Australians: Inquiry into approval processes for new drugs and novel medical technologies in Australia" (16). Provisional or interim reimbursement was identified in 29 submissions to the inquiry, and the PBAC chair Andrew Wilson noted this as a significant problem. The inquiry recommended that the PBAC be given the authority to authorise MAPs, aligned with the TGA provisional registration pathway. The current Strategic Agreement (2022-2027) between Medicines Australia and the Department of Health also acknowledges the need to complement the TGA provisional listing pathway to ensure timely access to treatment.

DESPITE THE MECHANISM CURRENTLY IN PLACE, AN ANALYSIS OF THE 25 NON-COVID TGA PROVISIONAL DESIGNATIONS THAT WERE REGISTERED BY MARCH 2022 FOUND THAT LESS THAN HALF (N=12) HAD BEEN SUBMITTED TO THE PBAC BY JULY 2022.

As of November 2022, of 12 PBAC applications of non-COVID TGA provisional designations that were registered by March 2022, 8 received positive recommendations (four based on cost-effectiveness and four based on cost-minimisation), and four had been rejected. Of those that had been recommended based on a cost-effectiveness model, 3 were PBS listed with a median patient access gap of 23.1 months. Of those recommended based on a cost-minimisation model, 4 were PBS listed with a median patient access gap of 9.0 months. This highlights a need to understand the discrepancy between the TGA provisional designation and the PBAC MAP processes.

FIGURE 14: Analysis of non-COVID TGA provisional designation production/indication pairings



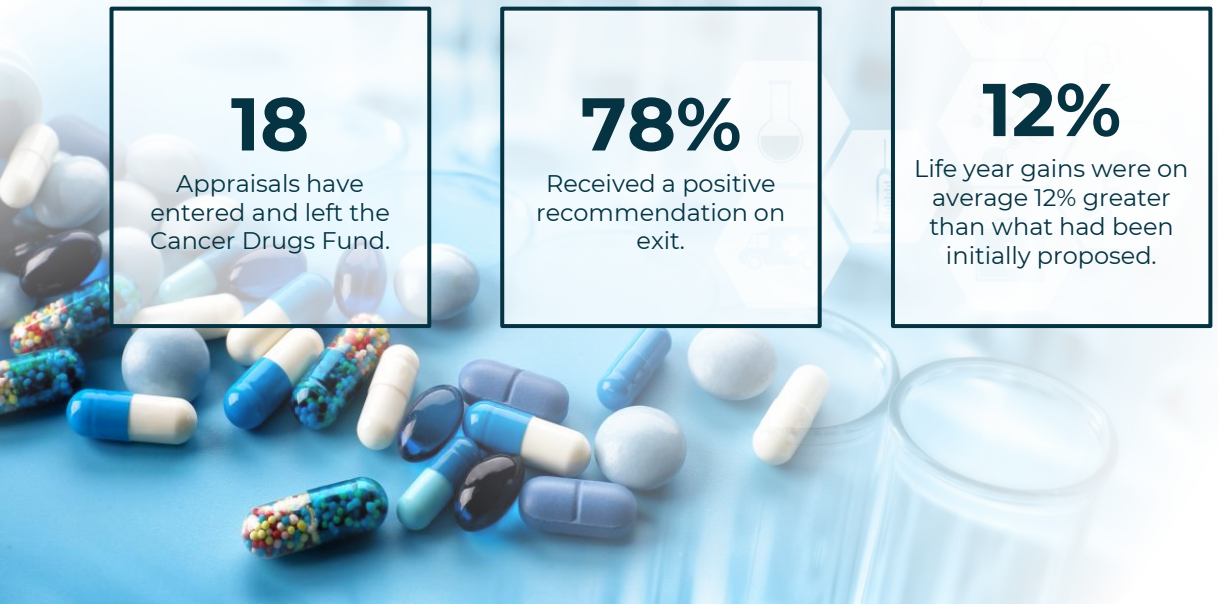
MAPS ARE PERCEIVED TO BE A LENGTHY AND RESOURCE INTENSIVE PROCESS, OFTEN REQUIRING MULTIPLE PBAC SUBMISSIONS TO RECEIVE A RECOMMENDATION.

Future-proofing MAPs is of concern, as there were no examples of a price increase in any of the MAPs examined, even when additional evidence demonstrating improved effectiveness became available. Even in MAPs, there remains a low tolerance for uncertainty, as the PBAC is bound to recommend based on a cost-effective ICER.

Internationally, more than half of OECD countries have performance-based agreements, and a trend is observed that countries are moving away from coverage with evidence development and towards pay-for-performance on an individual patient level. Conditional listings are used most commonly in England via the Cancer Drugs Fund. In this mechanism, NICE can recommend managed access if the medicine has the plausible potential to be cost effective, new evidence that would support the recommendation is expected from ongoing trials or could be collected in practice, and data can be collected in a reasonable timeframe.

The Innovative Medicines Fund was launched in June 2022, and aims to build on the success of the Cancer Drugs Fund.

FIGURE 15: Analysis of Cancer Drugs Fund appraisals (17)



18
Appraisals have entered and left the Cancer Drugs Fund.

78%
Received a positive recommendation on exit.

12%
Life year gains were on average 12% greater than what had been initially proposed.

FIGURE 16: Enablers for successful conditional listing framework

FRAMEWORK	Clear, transparent, predictable, co-developed
EARLY MANAGEMENT	Early, reliable advice with consumer engagement
MANAGEMENT OF UNCERTAINTY	Early data more readily accepted, with a plausible and mutually acceptable initial price band that poses no barrier to uptake
REASSESSMENT	Clear definition and agreement of parameters – balance between flexibility and certainty
DATA COLLECTION	Appropriate expectations about feasibility of data collection; no extraneous data collection
RISK SHARING	Predictable and manageable risk around future price impact including comparators; no/partial payback if data less positive
EXIT FROM SUBSIDY	Clear expectations and dispute resolution process; shared responsibility for patient maintenance on treatment

A. PROF HAITHAM TUFFAHA

WHILE, IN THEORY, MAPS PROVIDE A FLEXIBLE PATHWAY THAT ENABLE FASTER ACCESS, IN REALITY, THE MAJORITY OF THE TIME THEY ARE USED AS A LAST RESORT.

When considering a MAP, there are a number of factors to weigh up:

FIGURE 17: Considerations when establishing a MAP

- Is a MAP the most appropriate way forward?
- What evidence is required and how will it be collected?
- Who is responsible for collecting, reviewing, analysing, and reporting data?
- What are the expectations and assumptions for the evaluation of the MAP?
- Will the benefits of collecting more information justify the additional cost of the agreement?

A REVIEW OF PRODUCTS NOT INCLUDED IN MAPS FOUND THAT THE MAIN REASONS THE PBAC DID NOT RECOMMEND A MAP RELATED TO FEASIBILITY OF DATA COLLECTION AND THE LIKELIHOOD THAT THE ADDITIONAL DATA GATHERED WOULD SUFFICIENTLY REDUCE UNCERTAINTY.

FIGURE 18: Recommendations for establishing a MAP

INVOLVE STAKEHOLDERS in the development and implementation of coverage with evidence development

OBJECTIVE CRITERIA AND METHODS are needed to systematically examine the need for and value of a MAP

CLEAR, TRANSPARENT AND BALANCED conditions governing the map to address the expectations of stakeholders

CONTINUOUS EVALUATION AND IMPROVEMENT of the scheme to ensure that it serves its intended purpose

MANAGED EXIT SCHEMES could be used to manage the consequences of potential de-listing

VALUE OF INFORMATION ANALYSIS SHOULD BE CONSIDERED WHEN ESTABLISHING A MAP, TO ESTIMATE THE EXPECTED VALUE OF ADDITIONAL EVIDENCE TO REDUCE UNCERTAINTY.

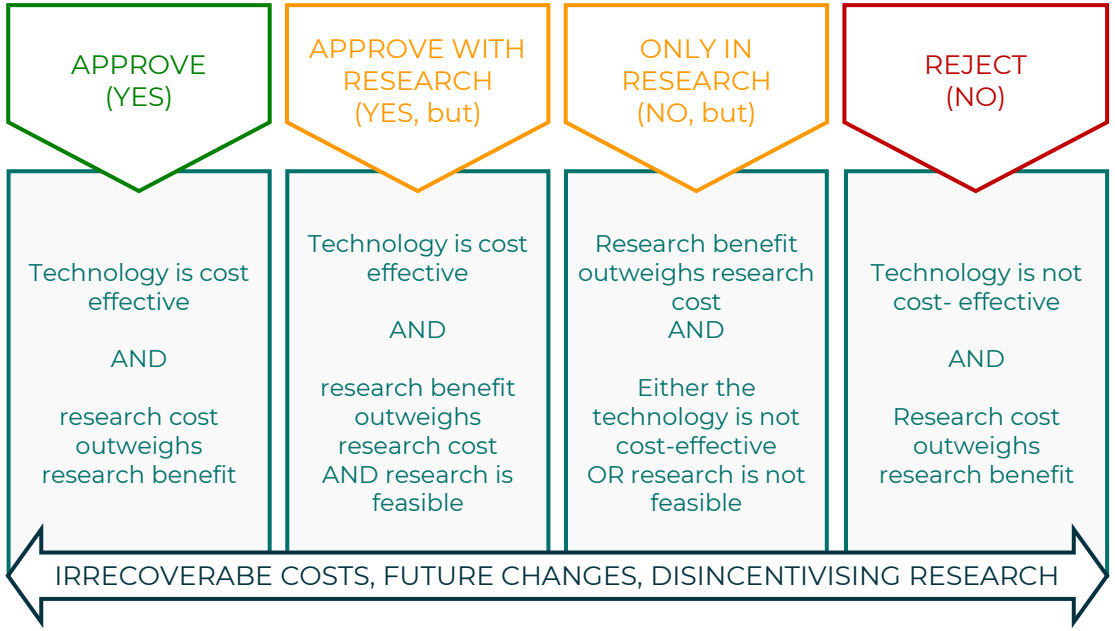
This analysis considers the probability of the decision (based on existing evidence) being wrong, the consequences of the wrong decision, the size of the population expected to benefit, and the life-time of the intervention.

FIGURE 19: Value of information analysis

EXPECTED VALUE OF PERFECT INFORMATION	Is additional evidence required?
EXPECTED VALUE OF PERFECT PARAMETER INFORMATION	What should we focus on?
EXPECTED VALUE OF SAMPLE INFORMATION	How much uncertainty is expected to be reduced?
EXPECTED NET BENEFIT OF SAMPLING	Is additional data collection worthwhile?

Value of information frameworks can help to inform decisions regarding managed access, by answering questions relating to cost-effectiveness, the potential value of conducting additional research, and the type of uncertainty that may be resolved by additional research. These frameworks would provide a systematic approach to MAPs.

FIGURE 20: Overview of value of information frameworks



BREAKOUT GROUP DISCUSSIONS

How do the PBAC guidelines need to change to facilitate conditional listing?

- A fee waiver for PBAC submissions based on TGA provisional registration was proposed. This could work in a similar way to the fee waiver for orphan drug submissions.
- There may need to be changes made to the National Health Act, to allow the PBAC to consider factors other than cost-effectiveness for conditional listing.
- A pathway or decision tree could be added to the guidelines, addressing different types of uncertainty and providing a recommendation for which mechanism is most appropriate to address this uncertainty (e.g. risk share agreement or managed access program).
- There is a need to consider the potential domino effect on medicines subsequently listed if the price changes or the medicine is de-listed at the end of a managed access program.

What are the methodological barriers to conditional listing as part of HTA?

- Each stakeholder (sponsors, PBAC, patients) may have a different objective. There may also be trust issues between the various stakeholders.
- The barriers to the use of real-world evidence were also considered to apply here.
- Challenges related to the data collection were also noted. In particular, questions were raised relating to whether the nature of the evidence that is able to be collected would resolve the uncertainty, and concerns about what would happen if data collection turned out to not be feasible, especially in the time frame required.

What products would benefit from a conditional listing policy?

- Examples of disease areas that would benefit from conditional listing were rare diseases, those with poor prognoses, and diseased affecting children.
- There would need to be confidence that the data would 'stack up' to the initial claim, and that data collection would be feasible.
- Additional data collection should be mindful of the potential burden that this would put on to patients.

What methods should the HTA review look at regarding conditional listing?

- The methods for conditional listing are already in place, however there is a need to utilise them more effectively.
- Conditional listing inherently will involve a level of risk, and there should be clear dialogue between the stakeholders to understand the level of risk that parties are willing to accept.

What international examples should the HTA review look at?

- The Cancer Drugs Fund and Innovative Medicines Fund in the UK were the best examples available internationally.
- It was also noted that the PBAC have ongoing collaboration with NICE.

What is the role of patients in conditional listing?

- This question was framed as *"would you rather have early access with the risk that it is taken away, or wait until there is certainty?"*
  - It was perceived that patients would do anything to get access sooner.
- The role of the patient was more focused on advocacy and defining the outcomes that matter to them in the additional data collection.

06 MANAGING UNCERTAINTY

KEY THEMES AND FUTURE WORK

RISK

Uncertainty is unavoidable and could be reframed as risk.

MOST CONSERVATIVE

Industry perceives that evaluators and the PBAC tend towards the most conservative parameter estimates, rather than the most likely.

RISK MANAGEMENT

There is a need to consider the likelihood of an uncertainty occurring and the consequences if it does occur. This reframes uncertainty as risk management.

DELAYED ACCESS LEADS TO POORER HEALTH OUTCOMES

While the conversation is often framed around the risk of recommending something that is not cost-effective – not doing anything (i.e. not recommending or deferring) is also a risk, as patients experience access delays for an effective treatment or they may miss out on treatment entirely. This results in poorer allocation of resources if the treatment is, in fact, cost-effective.

COMMUNICATION

There is a desire for increased communication between Sponsors, evaluators, patients and the Department throughout the HTA submission lifecycle.

RISK MATRIX

Development of a risk matrix for submissions could identify areas of uncertainty and associated risk. More communication between the Sponsor and evaluator will increase transparency on how uncertainty is being considered.

ENGAGEMENT

How does earlier and better engagement between industry, evaluators and decision makers take place?

A. PROF BONNY PARKINSON

UNCERTAINTY IS UBIQUITOUS IN HTA, AS VERY FEW PARAMETERS ARE COMPLETELY CERTAIN.

However, some parameters are more uncertain than others, and can have substantial impacts on HTA. Examples of these very uncertain elements can include things such as survival benefit, quality of life, duration of efficacy, and future health costs. Uncertainty is widely explored in health-economic academic literature, including methods for categorising, measuring, presenting, assessing, and managing uncertainty.

FIGURE 21: Types of uncertainty

PARAMETER UNCERTAINTY
What is the true parameter value? This type of uncertainty can arise due to imprecision due to sampling, choice of data source, and assumptions due to data availability.

METHODOLOGICAL UNCERTAINTY
Departures from guidelines. This type of uncertainty can arise due to policy or academic debate.

STRUCTURAL UNCERTAINTY
How the economic model is constructed. This type of uncertainty can arise due to trial limitations or lack or transparency in modelling decisions.

GENERALISABILITY
Is the trial applicable to the Australian setting? This type of uncertainty can arise due to trials generally not being conducted in Australia.

DESPITE THIS, THE PRIMARY ISSUE FROM A HTA PERSPECTIVE IS NOT UNCERTAINTY – IT IS RISK.

Risk relates to the effect of uncertainty on objectives (18). For HTA, the implicit objective is to maximise society's welfare by utilising resources in the most effective way possible. Uncertainty can lead to an inaccurate assessment of relative value which leads to incorrect funding decisions, thereby reducing societal welfare. This applies to both recommendations (i.e. recommending a therapy that is not cost-effective) and rejections (i.e. not recommending a therapy that is cost-effective).

THE ISO (18) FRAMEWORK PROVIDES A METHOD FOR SYSTEMATICALLY THINKING ABOUT RISK.

FIGURE 22: Overview of TRUST tool for assessing uncertainty (19)

		IMPACT ON COST-EFFECTIVENESS		
		Uncertainty not reflected in PSA?	Uncertainty not explored in scenario analysis?	High impact on cost effectiveness?
ASPECTS	Context/scope			
	Model structure			
	Selection of evidence			
	• Effectiveness • Relative effectiveness • Adverse events • Utilities • Resource use & costs			
	Implementation			
	Outcomes			

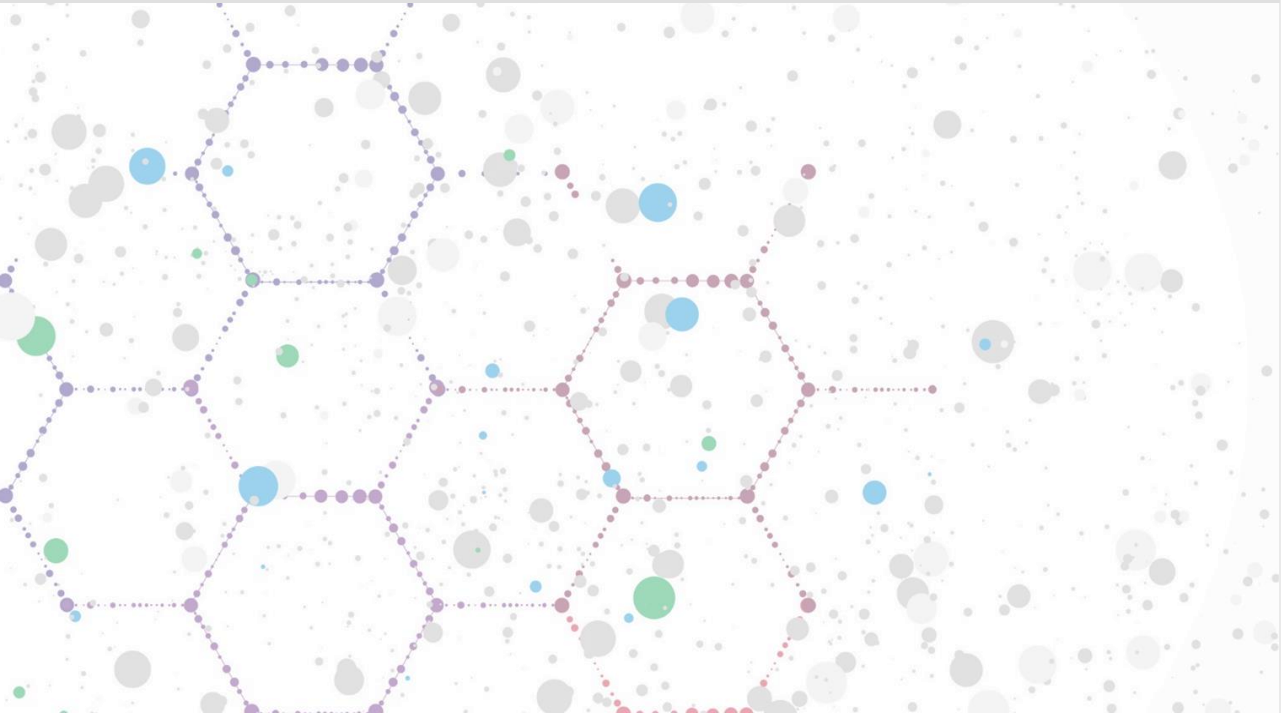
Grey cells are unlikely combinations

The ISO framework (18) outlines several steps, including:

- risk identification and its impact on outcomes,
- the likelihood of those outcomes occurring,
- whether and how risk can be managed,
- recording and reporting decisions relating to risk,
- monitoring and reviewing risks, and
- communicating issues relating to risk.

This framework can also be applied to HTA.

THE TRUST TOOL (19) FOR ASSESSING UNCERTAINTY MAY HELP TO BETTER SYSTEMATICALLY IDENTIFY RISKS AND THEIR IMPACT IN HTA. HOWEVER, THERE CONTINUES TO BE A NEED TO IMPROVE HOW WE THINK ABOUT UNCERTAINTY AND RISK IN HTA.



KEY QUESTIONS FOR THE HTA REVIEW INCLUDE:

How can we better identify risks?

How can we better analyse risks?

How can we better evaluate risks to inform decisions?

How can we better inform how and when we need risk treatment?

How can we better communicate risks to stakeholders?

RACHAEL ANDERSON

THERE IS A NEED TO BETTER MANAGE UNCERTAINTY IN HTA, AS IT IS THE FUNDAMENTAL CAUSE OF ACCESS DELAYS.

While the PBAC and evaluators tend to focus on the risk of listing a medicine that is not cost-effective, there is also a risk associated with delaying or denying access to a medicine that is cost-effective.

THERE IS ALSO A TENDENCY TO FOCUS ON THE MOST CONSERVATIVE ESTIMATES OF NET BENEFIT, RATHER THAN THE MOST LIKELY.

FIGURE 23: Proposal to improve the management of uncertainty in HTA

Estimates of net benefit and utilisation that are 'most probable' rather than 'most conservative'

- Introduce a systematic approach to improve the way in which ICER uncertainty and its component uncertainties are characterised, explored and presented within a PBAC submission and evaluations

Consultations designed to reach consensus and avoid delayed decision-making

- Introduce opportunities for engagement between sponsors, evaluators and decision-makers to broadly agree on a submission analysis plan and to address issues raised in evaluation

Risk management arrangements that can be monitored and adjusted

- Risk management plans that do not simply transfer undue risk to the Sponsor

BREAKOUT GROUP DISCUSSIONS

What HTA methods can the HTA review look at to reduce uncertainty in HTA?

- There needs to be an early dialogue by stakeholders to characterise the uncertainty and associated risk. This could be done based on the lifecycle approach for a product, taking on more uncertainty soon to get quicker access.
- Public summary documents should better characterise uncertainty, providing increased transparency on how uncertainty and risk were considered in the decision-making process.
- Additional guidance and clarification in the National Health Act regarding what the PBAC are required to consider. Presently, the PBAC tend to consider the most conservative estimates rather than the most plausible.

How should risk be communicated to stakeholders?

- For patients, it is important to consider their risk appetite, which will be influenced by their health literacy and life experiences. Ultimately, it will be a personal decision.

What are the steps required to build technical guidance for managing uncertainty in HTA?

- Uncertainty should be reframed as risk management, as uncertainty is unavoidable.
- A more formal process for how risk is quantified in HTA could be considered, for example via a risk matrix. This matrix would consider things like the types of risk, size of the consequences, and the likelihood of those consequences occurring.

What are the facilitators to reducing uncertainty in HTA?

- Increasing the opportunities for engagement between the sponsor, evaluator and decision-maker could facilitate reductions in uncertainty.
- This could be in the form of considering uncertainty at a pre-submission meeting, or by increasing the time available to respond to the evaluator commentary or the ESC report to enable better engagement and consultation. It was acknowledged that increasing the response time could increase the submission timeline.

What are the barriers to reducing uncertainty in HTA?

- Sometimes the information required to reduce uncertainty does not exist. This is particularly the case for financial and utilisation uncertainty, for example epidemiological estimates.
- For cost-effectiveness, there needs to be a discussion about where the risk should lie and who should bear the risk.
- Transparency on how submissions are being reviewed, including more open conversations between sponsors, evaluators, patients and decision-makers, is needed.

How can we better identify and analyse risk?

- Risk should be identified early in the submission process. Qualitative analyses may be required to explain the likelihood of an identified risk and the potential impact of this risk. This could then be compared to a risk appetite for key stakeholders and decision-makers.

THE FINAL PANEL

HTANALYSTS

PANEL DISCUSSION

The panel commenced with some of their reflections on the day. From a patient perspective, it was noted that while patients may struggle to understand the HTA jargon and process, they should still be included.

PATIENTS ARE HOPEFUL ABOUT THE HTA REVIEW, BUT THERE IS A NEED FOR CLEAR GOALS.

There was a perception amongst some of the panellists that academia and industry can be combative, and while there is still much work to be done, the discussions on the day were a good start.

WHILE THERE IS OFTEN A FOCUS ON WHAT IS DONE OVERSEAS, THERE IS NOT A SINGLE MODEL THAT WE CAN COPY AND PASTE IN AUSTRALIA, AS IT WILL LACK THE SPECIFIC CONTEXT REQUIRED TO WORK.

Much of the conversation throughout the Summit focused on guidelines, and the need for greater direction. Guidance can help to remove some types of uncertainty and should be process oriented and outcomes focused.

WHILE INDUSTRY AND ACADEMIA ARE OFTEN KEPT APART, COLLABORATION COULD HELP THE TWO GROUPS IN UNDERSTANDING EACH OTHER.

While the health system is preparing for the implementation of genomics and precision medicine, the decision-making process needs to keep up. At this stage, the HTA process is ill-prepared to assess new genetic and genomic innovations efficiently.

Collaboration was one of the main themes of the day, and this should also include patients as early in the process as possible.

IT WAS NOTED THAT YEARS AGO, HEALTH ECONOMISTS STRUGGLED TO HAVE HEALTH ECONOMIC OUTCOMES SUCH AS THE EQ-5D INCLUDED IN TRIALS BUT NOW THEY ARE ROUTINELY COLLECTED.

Future opportunities for patient involvement could follow the same path.

PANEL DISCUSSION

The resubmission process was highlighted throughout the summit as the main cause of access delays. A 'gamification' or strategic decision-making was thought to occur on both sides (industry and PBAC). Adding opportunities throughout the submission process for communication and collaboration between the sponsor, evaluator and decision makers to resolve key issues could help to reduce the need for resubmissions and reduce time to listing.

THE INCLUSION OF RWE WAS IDENTIFIED BY ONE PANELLIST AS THE MOST IMPORTANT TOPIC TO 'GET RIGHT' IN THE UPCOMING HTA REVIEW.

While clinical trials are still considered the gold standard in terms of evidence, they often do not capture what is happening in the real world and what matter to patients. Including the patient voice is essential, and the process around how patients are included matters.

PATIENTS NEED TO BE CONSIDERED AS INDIVIDUALS, NOT A HOMOGENOUS GROUP, AND IT IS IMPORTANT TO ENGAGE A VARIETY OF PATIENTS TO ENSURE REPRESENTATIVENESS.

The HTA review is an important opportunity to reform the HTA system in Australia, rather than just making tweaks to the existing system. As a result of the COVID-19 pandemic, people appear to be upskilled in understanding healthcare and the value of a strong health system.

THIS PRESENTS AN OPPORTUNITY TO HAVE A PUBLIC DEBATE ABOUT HOW DECISIONS ARE MADE AND WHAT WE VALUE AS A SOCIETY.

The shared vision of the HTA review and all stakeholders should be faster, equitable access for patients. The resulting process should be transparent, accountable, adaptable and long-lasting.

APPENDICES

HTANALYSTS

APPENDIX I – SUMMIT AGENDA

MORNING SESSIONS

TIME	TOPIC	SPEAKER
8:00-8:10	Welcome	Dr Colman Taylor
How can industry and academia work together – the UK example		
8:10-8:40	Academic perspective	Prof Mark Sculpher
8:40-9:00	Questions and discussion	
Capturing the patient voice in HTA		
9:00-9:15	Non-industry perspective	Ann Single
9:15-9:30	Industry perspective	Vanessa Stevens
9:30-9:50	Break-out discussion	Led by facilitators
How can we make better use of RWE for HTA?		
9:50-10:05	Industry perspective	Lucas Tocchini
10:05-10:20	Academic perspective	Prof Sallie Pearson
10:20-10:40	Break-out discussion	Led by facilitators

TIME	TOPIC	SPEAKER
Second-order effects – what should be included in economic evaluations?		
11:10-11:25	Industry perspective	Dr Martin Snoke
11:25-11:40	Non-industry perspective	Felicity McNeill
11:40-12:00	Break-out discussion	Led by facilitators
Speeding up access to precision medicine – how can we do things better?		
12:00-12:15	Academic perspective	Tiffany Boughtwood
12:15-12:30	Industry perspective	Andrea Kunca
12:30-12:50	Break-out discussion	Led by facilitators

Lunch break

AFTERNOON SESSIONS

TIME	TOPIC	SPEAKER
Faster access through conditional listing – is this achievable?		
1:50-2:05	Industry perspective	Julia Lewis
2:05-2:20	Academic perspective	A.Prof Haitham Tuffaha
2:20-2:40	Break-out discussion	Led by facilitators
Managing uncertainty – how can we do it better?		
2:40-2:55	Academic perspective	A.Prof Bonny Parkinson
2:55-3:10	Industry perspective	Rachael Anderson
3:10-3:30	Break-out discussion	Led by facilitators

TIME	TOPIC	SPEAKER
3:30-4:00	**BREAK**	
4:00-4:30	Panel session	Facilitators
4:30-5:00	Discussion	

Conclusion

APPENDIX II – HTA POLICY AND METHODS REVIEW

The Commonwealth has entered into new Strategic Agreements with Medicines Australia and the Generic and Biosimilar Medicines Association (GBMA). The new agreements build on the Pharmaceutical Benefits Scheme (PBS) New Medicines Funding Guarantee, introduced in 2020.

The new agreements will further improve and safeguard access to new medicines through:

- Equitable and sustainable access to the most effective medicines, including highly specialised, expensive and at times lifechanging medicines, through the PBS
- An Enhanced Consumer Engagement Process to facilitate enhanced consumer and patient engagement through the PBAC assessment process
- Continuous improvement of health technology assessment processes for listing new medicines on the PBS to ensure they keep pace with the rapid advancement of health technology, remain world class, and keep pace with rapid advances in medicine enabling them to be marketed and funded in Australia as they emerge.
- A new Medicines Supply Security Guarantee which will bolster medicine supply to Australian patients. The Medicines Supply Security Guarantee is designed to help protect Australian patients, pharmacists, and prescribers from the impact of the increasing number of global medicines shortages by implementing mandatory stock levels for certain critical high-volume medicines
- Supporting the medicines industry who will benefit from stability and certainty for investment in new medicines, and providing certainty around health technology assessment processes
- Supporting the work of pharmacists, prescribers and other healthcare workers by protecting the supply chain and reducing workloads and inconvenience created by medicines shortages
- Commitments from the medicines industry to an improved statutory pricing system for PBS medicines which will generate net savings of approximately $1.9 billion, to be invested in new PBS medicines listings
- Supporting the Australian medicines industry, including pharmaceutical manufacturers, wholesalers, compounders, hospital pharmacies, community pharmacies and consumers through continuous Government investment in new medicines

Clause 5 of the agreement commits to continuous evaluation and improvement. This starts with a policy and methods eview of HTA covering the following key areas:

- Selection of comparators
- Methods for rare diseases and alternative funding pathways
- Methods for new and emerging technologies
- Methods for evaluating new meds and vaccines
- Use of RWE for evaluation
- Managing clinical, economic and financial uncertainty
- International work sharing

At the time of writing, a Reference Committee had been established and terms of reference were in the process of being negotiated.

APPENDIX III – SUMMIT ATTENDEES

NAME	INSTITUTION
Alice Morgan	AstraZeneca
Alicia Norman	Macquarie University
Alison Hayes	Sydney University
Allan Wu	Merck
Amanda Elsome	Gilead
Amanda Ruth	Apellis
Andrea Kunca	Roche
Andrew Thirlwell	Pfizer
Ann Single	Patient Voice Initiative
Anne-Maree Englund	Medicines Australia
Anthea Bill	HMRI
Anton Pak	University of QLD
Antonio Canale	Macquarie University
Bao Nguyen	University of QLD
Belinda Wood	Gilead
Belinda Surjadi	AbbVie
Blake Angell	The George Institute
Bonny Parkinson	Macquarie University
Brandon Jones	Janssen
Bronwyn West	CaPPRe
Bronwyn Fitzgerald	Alexion
Claire Parken	Roche
Colman Taylor	HTANALYSTS
Constanza Vargas	UTS
Daniel Thut	Bayer
Daniel Tan	Roche
David Cain	Astellas
Diedre Mackechnie	Patient Advocacy Alliance
Dominic Tilden	THEMA
Douglas Millar	Commercial Eyes

NAME	INSTITUTION
Duncan O'Brien	Janssen
Duncan Purvis	Organon
Eliana Della Fiora	The Department of Health
Elizabeth Seil	Macquarie University
Elizabeth Desomer	Medicines Australia
Emily Skillin	Medicines Australia
Fei-Li Zhao	Beigene
Felicity McNeill	Perspicatice
Fiona Tigar	Biogen
Fiona Savio	Amgen
Francis Dehle	HTANALYSTS
Franz Pichler	BioIntelect
Franz Pichler	BioIntelect
Gabrielle Bietola	AstraZeneca
Gabrielle Reppen	Lilly
George Moawad	Commercial Eyes
Gregory O'Toole	Concord Pharmaceutical Consulting
Haitham Tuffaha	University of QLD
Hansoo Kim	Griffith
Heather Wrightman	Medicines Australia
Ian Noble	Amgen
Irene Deltetto	HTANALYSTS
Jean Spinks	University of QLD
Jerome Higgins	MSD
Jo Atkins	Commercial Eyes
John Paul Delos Trinos	UNSW
Josh Bowen	Roche
Josh Ciardi	HTANALYSTS
Joshua Byrnes	Griffith
Julia Lewis	Abbvie

APPENDIX III – SUMMIT ATTENDEES

NAME	INSTITUTION
Kate Applegarth	MSD
Kathy Cargill	Abbvie
Kathy Tannous	UWS
Katrina Lapham	BioIntelect
Kim Edmunds	University of QLD
Krystal Barter	Humanise Health
Kylie Earle	Sanofi
Laurie Axford	CaPPRe
Lei Si	The George Institute
Lisa Julian	Lilly
Louise Larkin	Lilly
Lucas Tochhini	Biogen
Margaret Jorgensen	HTANALYSTS
Mark Sculpher	University of York
Martin Snoke	Roche
Mary Lou Chatterton	Monash
Matthew Frith	Amgen
Melinda Flowers	Amgen
Mia Mudge	THEMA
Michelle Burke	Cell Therapies
Mike Stephens	Naccho
Moin Ahmed	Sydney University
Monica Saba	Bayer
Natalie Betts	Roche
Oona Reardon	Pulse Economics
Oxana Chiotelis	Deakin
Penny Reeves	HMRI
Peter Murphy	Novartis
Petrina Keogh	Medicines Australia
Plum Stone	Rare Cancers Australia

NAME	INSTITUTION
Qunfei Chen	Macquarie University
Rachael Anderson	AstraZeneca
Rebecca Stratford	AstraZeneca
Renae Beardmore	Evo Health
Richard De Abreu Lourenco	UTS
Richard Norman	Curtin
Robert Stringer	Pharmalex
Robin Bell	Newcastle University
Roxanne Maurin	HTANALYSTS
Sallie Pearson	UNSW
Samuel Vigors	UTS
Samuel Vigors	UTS
Sara Pantzer	Simtrak
Sarah Bridge	Bayer
Scott Brydon	Vifor
Shabnam Valiya	Novartis
Sheena Arora	UTS
Silva Zavarsek	Deakin
Simon Fifer	CaPPRe
Simon Fifer	CaPPRe
Simone Leyden	Telix
Simone Leyden	Telix
Sophie Schultz	Takeda
Therese Franklin	Novo Nordisk
Thomas Lung	The George Institute
Tiffany Boughtwood	Murdoch Childrens Research Institute
Valda Anne Struwig	Pfizer
Vanessa Stevens	Vifor
Varinder Jeet	Macquarie University
Will Sierakowski	THEMA
Zachary Tirrell	Macquarie University

APPENDIX IV – SPEAKER BIOS

PROFESSOR MARK SCULPHER

Mark Sculpher is Professor of Health Economics and Director of the Centre for Health Economics, University of York. He is also Co-Director of the Policy Research Unit in Economic Evaluation of Health and Care Interventions, a programme of research for the UK Department of Health and Social Care funded by the National Institute for Health Research (NIHR).

Mark has been a member of the NICE Technology Appraisal Committee, the NICE Public Health Interventions Advisory Committee and NICE's Diagnostics Advisory Committee. He has also been involved in advising NICE on methods over many years. Mark has also advised the UK House of Commons Health and Social Care Select Committee, as well as health systems internationally on health technology assessment methods including those in France, Ireland, Japan, Singapore, Germany, Portugal, Taiwan and New Zealand. He has been a member of the Commissioning Board for the UK NHS Health Technology Assessment Programme, the UK NIHR /Medical Research Council's Methodology Research Panel and the UK Department of Health's Policy Research Programme's Commissioning Panel. He served as President of ISPOR.

ANN SINGLE

Ann Single is the Coordinator and an Advisory Committee Member of the Patient Voice Initiative (Australia) and internationally chairs the Health Technology Assessment international (HTAi) Patient and Citizen Involvement Interest Group. She is co-editor of the first book in the field, Patient Involvement in Health Technology Assessment (2017). Ann recently accepted an invitation to serve as a patient representative on the Reference Committee for the Australian Government's HTA Policy and Methods Review.

VANESSA STEVENS

Vanessa is Director of Patient Access and Innovation Policy of Vifor Pharma Australia and New Zealand. Vanessa is a qualified health economist with over 18 years' experience in market access related activities, both from a Federal Government and Industry perspective. The experience expands across a wide range of therapeutic areas and different geographies, including Global and Regional roles. Vanessa has successfully led the development of innovative value platforms for a broad portfolio (ranging from nanomedicines to orphan designated medicines and vaccines), demonstrated the ability to generate evidence to address unmet needs and to engage with external stakeholders to develop a high-quality health system that is focused on patients.

APPENDIX IV – SPEAKER BIOS

LUCUS TOCCHINI

Lucas is the Head of Market Access at Biogen ANZ. He is a member of the Health Economics Working Group (since 2020). Prior to working for industry Lucas worked in health economics consultancy, and is a registered Pharmacist.

PROFESSOR SALLIE PEARSON

Sallie Pearson is the Professor of Health Systems in the School of Population Health at UNSW. She is also the Director of the NHMRC Medicines Intelligence Centre of Research Excellence (MI-CRE), a collaborative research program with investigators based across nine Australian universities and scientific advisors from six leading international academic institutions. MI-CRE's primary purpose is to develop a coordinated approach to accelerate real-world evidence development for medicines policy decision makers. Sallie is a leading authority in the conduct of population-based research using routinely collected data and has led national and international studies leveraging 'big health data' to generate real-world evidence on the use, benefits and safety of prescribed medicines. In 2021, she received the Health Service Research Association of Australia and New Zealand Distinguished Investigator Award.

DR MARTIN SNOKE

Dr Martin Snoke is the Head of Corporate and Public Affairs at Roche Products. A policy expert with over fifteen years experience in the Commonwealth Department of Health, Parliamentary Budget Office and Medicines Australia, he is passionate about advocating for improved healthcare ecosystems that support patients access to innovative medicines and healthcare technologies.

FELICITY MCNEIL

Felicity is a co-founder and chair of Better Access Australia, a not for profit that contributes to the public policy debate in Australia through research, publications, public discussion and advocacy. Better Access Australia recognise that Australia's health, disability and social services systems (the social sector) work best when all parties, public, private and not-for-profit, engage in good faith with the existing systems and processes, and that each party's contribution is recognised and valued.

Felicity has over 20 years' experience in the federal Government sector, including 12 years in the Department of Finance and 7 years in health including as CEO of the Organ and Tissue Authority and head of the Pharmaceutical Benefits Division and Office of Health Protection.

For the past 5 years she has managed her own consultancy companies providing strategic advisory and regulatory services in the health, agriculture and critical infrastructure sectors domestically and globally. She was recently appointed to the board of ASX-listed company, BTC Health.

Her work at Better Access Australia is voluntary and represents about 35% of her work.

ANDREA KUNCA

Andrea is a pharmacist with over 30 years' experience in the healthcare sector, including 20 years as a senior executive in the Department of Health and seven years in the health technology industry. She has led numerous high profile reforms to pharmaceutical and medical device reimbursement and regulation and has represented both the industry and Government nationally and internationally.

APPENDIX IV – SPEAKER BIOS

TIFFANY BOUGHTWOOD

Tiffany Boughtwood is the Managing Director of Australian Genomics, an Australian Government initiative supporting genomic research and its translation into clinical practice through broad engagement and a collaborative national approach. Tiffany has 25 years' experience in molecular biology and management: leading academic and diagnostic genomic programs; collaborating internationally in genetic and genomic research; and consulting in health genomic implementation. She has served on the World Economic Forum Global Future Council for Biotechnology and the WHO Collective Global Network for Rare Disease; is an advisor to the UAE Genomic Program and is a founding Director of the Childhood Dementia Initiative.

JULIA LEWIS

Julia is currently the Head of Market Access, Immunology at AbbVie. A pharmacist by training, she has worked in medical and reimbursement-related roles in the pharmaceutical industry for the past 10 years.

A.PROFESSOR HAITHAM TUFFAHA

Haitham Tuffaha is the Acting Director and an Associate Professor at the Centre for Business and the Economics of Health at The University of Queensland. He also leads Health Technology Assessment for the Centre, which involves the economic evaluation of health interventions. He has pioneered the application of Value of Information analysis in Australia as an innovative approach to ensure clinical trials are efficiently designed and prioritised to maximise return on investment.

A. PROFESSOR BONNY PARKINSON

Associate Professor Bonny Parkinson is a health economist at the Macquarie University Centre for the Health Economy (2022). She has also worked at the University of Technology Sydney as a Research Fellow, AstraZeneca in the United Kingdom as a senior health economist, Access Economics in Canberra as a senior economist, and the Social Policy Evaluation and Research Centre at the Australian National University as an Assistant researcher. She currently co-leads a team of researchers conducting evaluations of submissions to the Pharmaceutical Benefits Advisory Committee (PBAC) and researching economic evaluation methodology. She has been involved in over 50 evaluations of submissions to the Pharmaceutical Benefits Advisory Committee (PBAC) since 2009, and has also conducted evaluations of submissions to the Medical Services Advisory Committee (MSAC).

RACHAEL ANDERSON

Rachael Anderson is the Head of Market Access & Pricing at AstraZeneca. Rachael's career in the pharmaceutical industry spans more than 20 years with Wyeth, Pfizer and now with AstraZeneca. Over the past 16 years, Rachael has held a role in market access or health economics with responsibility for PBAC submissions and the PBS listing of targeted oncology treatments, chronic illness, and specialty medicines. Rachael has a Master of Public Health and a Science Degree with Honours in Biochemistry.

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