HEOR

Not another value framework! Extension and implementation of a framework to capture holistic value of new medicines

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Bristol Myers Squibb™

We have an esteemed panel to lead discussion of the issues

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Principal, Market Access, Operations and HTA Specialist, Putnam PHMR, London

Moderator

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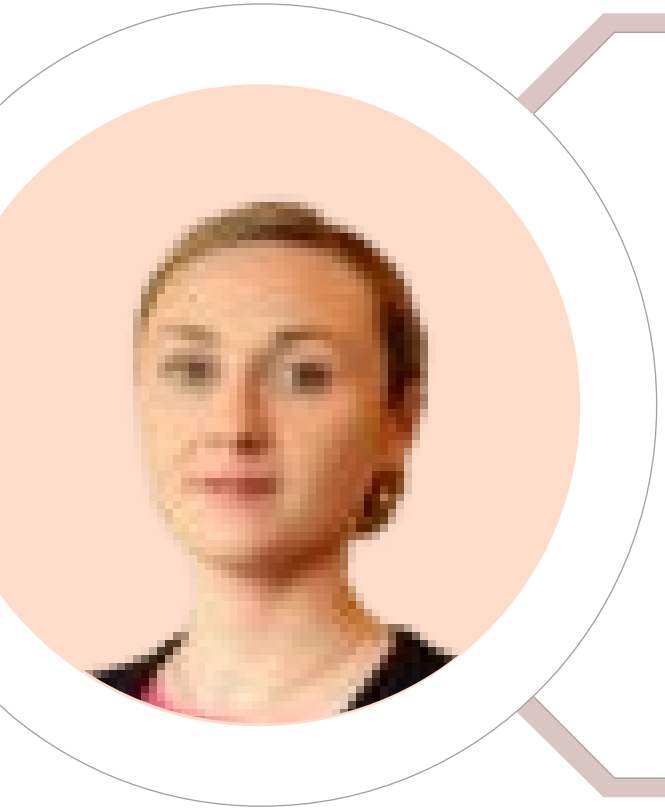


Introduction

Jasmine Farrington
Principal, Market Access, Operations and HTA Specialist, Putnam PHMR, London

Moderator

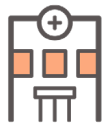
Today we aim to discuss value and value frameworks in the assessment of medicines for access and pricing

Decision-makers, particularly payers/HTA, still primarily rely on narrow healthcare perspectives using traditional elements of value (CEA, net cost) to assess innovation. ***Novel assessments are needed to reward development of medicines that bring more holistic value*** and incentivise timely patient access to these medicines

Elements of holistic value include those captured in the ISPOR Value Flower but may also include elements related to well-being of patients, carers and families, healthcare organization impact, and economy-wide effects

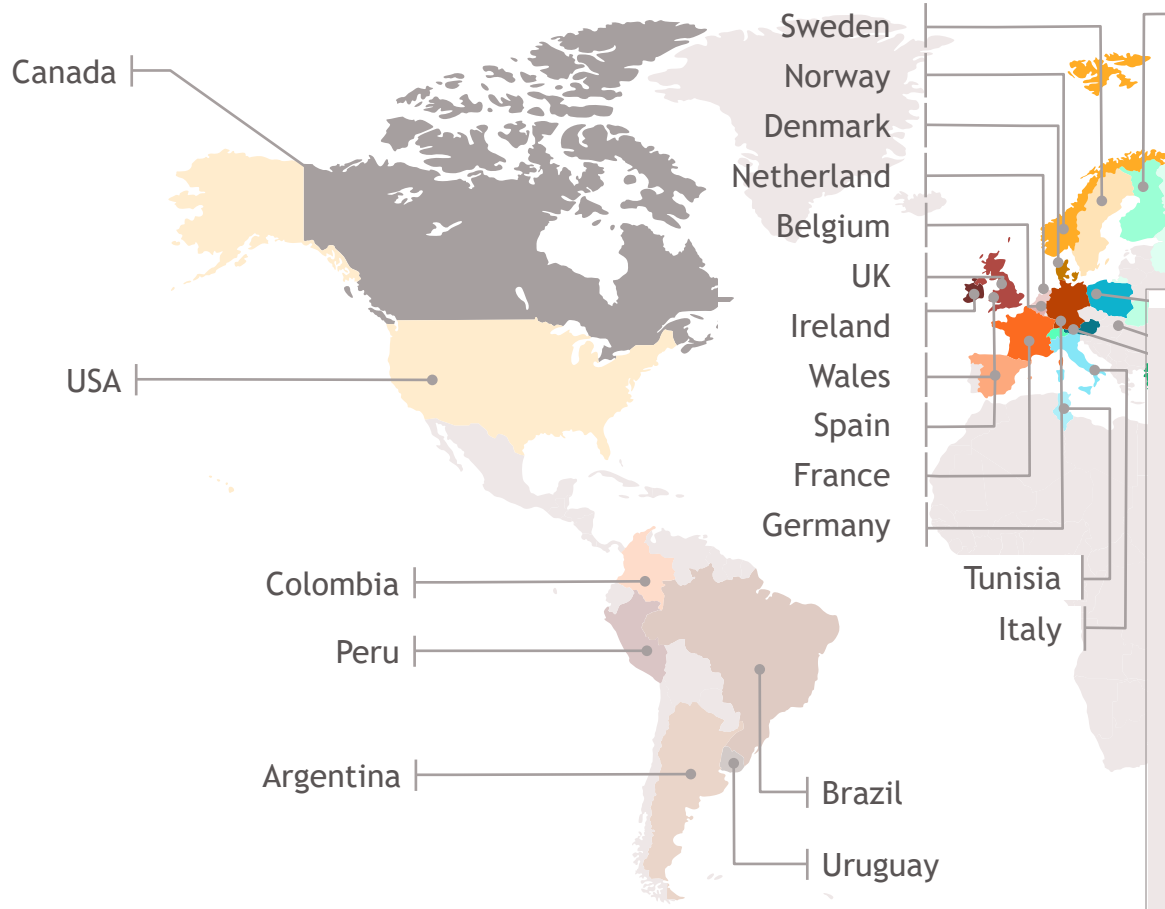
A more holistic definition of value is not routinely used mainly due to a perception of pharmaceutical companies trying to drive higher prices, a lack of credible supporting data, a belief that the impact is generally insignificant, and a compartmentalised welfare paradigm where these value elements fall outside the remit of HTA and payers

We have worked to develop a framework that aims to address each of these challenges such that additional, more holistic definitions of value can be effectively implemented where appropriate – so that ***spending on medicines can be considered as a societal investment rather than a healthcare cost centre***



The perspective assigned to most HTA bodies is narrowly focused on healthcare costs and benefits

Even where HTA bodies indicate acceptance of a societal perspective, this is limited in practice



QALY-Based

UK:
Centralized, Formal QALY-Based with thresholds

Sweden:
Centralized, Formal QALY-Based with thresholds

"Flexible"

US:
Decentralized; Little reliance on formal HTA and government outlaws QALY; **BUT** with **I.C.E.R.**— Emergence of a "value-based price" (VBP) using the QALY

France:
Centralized, Growing QALY use but no fixed threshold

Non-QALY-Based

Germany:
Centralized, Focus on relative clinical efficacy not QALY-based Heavy reliance on formal HTA as stakeholder- driven, deliberative process

HTA organisations currently listed as members of HTAi or INAHTA

*Non currently listed by HTAi or INAHTA

Looking beyond price and healthcare sector impact means including all types of resources and effects of value to society

Without this approach, medicines with broader societal benefits will be undervalued with access delays

Sovaldi in Hepatitis C

Diagnostic testing in personalised medicine

If a societal perspective is not taken, likely outcomes include:

- Underfunding of medicines with broader societal impact
- Reduced incentives for manufacturers to develop medicines with broader societal impact
- Overall health and social outcomes may be poorer while society is less well-off

mRNA vaccines to prevent Covid-19

Combination treatments in Hematological malignancy

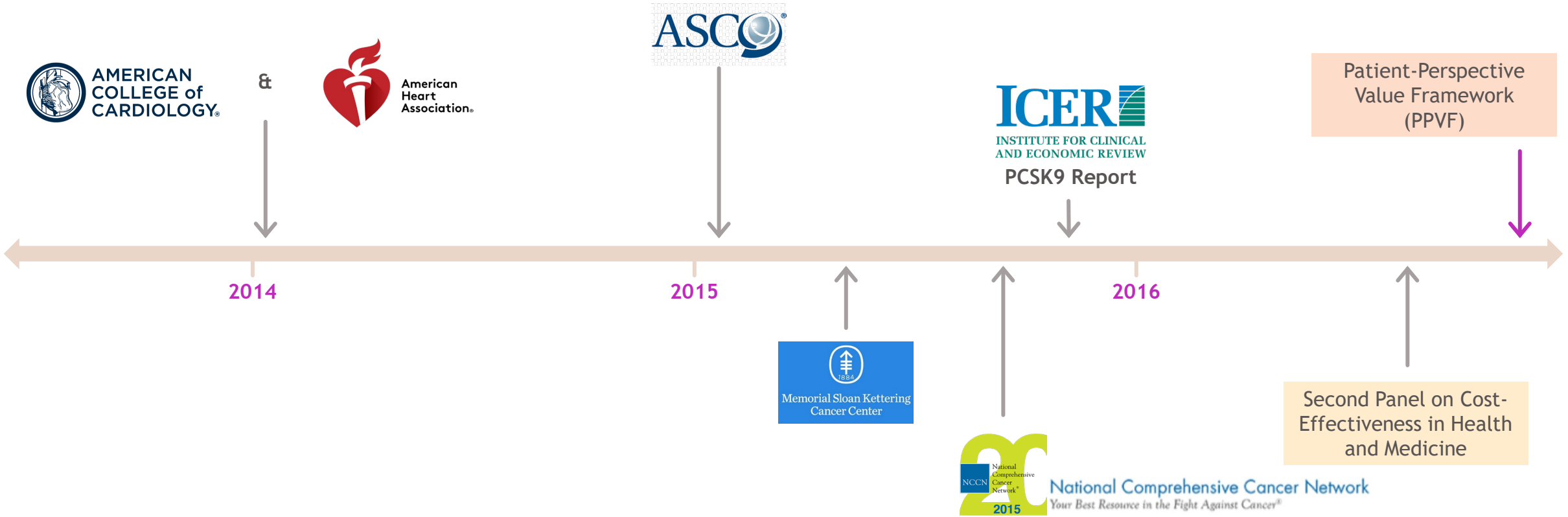
Recent examples show clear benefits of looking beyond standard value elements to understand the full value of medicines……

	Healthcare perspective	*Societal (holistic) perspective*
Covid-19	• Vaccine price • Preventing infection • Reduced hospitalisation	• Productivity gains • Scientific spillovers with mRNA used in other disease areas • Financial and health risk protection • Reduced fear of contagion • Benefits associated with reactivating most, if not all, areas of society
Immuno-oncology in cancer	• Price of immuno-oncology therapy • Improved survival and quality of life • Reduced healthcare resource use	• Productivity gains (patients/carers) • Value of hope • Real option value • Scientific spillovers • Financial and health risk protection

….while further examination may show that the benefits of looking to a societal perspective are more extensive than expected

	Healthcare perspective	*Societal (holistic) perspective*
Treatment and prevention of stroke	• Medicine price and administration • Preventing strokes and reducing mortality, improving quality of life • Reduced hospitalisation and healthcare resource use	• Productivity gains (patients/carers) • Financial and health risk protection • Reduced fear of contagion • Value of hope • Scientific spillovers
Treatment-resistant infections	• Price of medicine & administration • Improved survival and quality of life • Reduced hospitalisation and healthcare resource use	• Productivity gains (patients/carers) • Scientific spillovers • Financial and health risk protection • Improved patient satisfaction and quality of care • Improved efficiency of healthcare

There have been many value frameworks over recent years; the today's focus is valuation for access and reimbursement



The focus for this discussion is on frameworks that drive reimbursement and access through national, regional, or health benefit formulary - whether by *Cost-Effectiveness or Price Negotiation through benefit assessment*

These include ICER, NICE, and the 2nd Panel report

As you listen to the Panel, please consider two key questions

How could a holistic value assessment be implemented to capture the value of innovative medicines beyond traditional elements?

What key “distinctive” elements could be employed in a comprehensive value assessment?

Voting question 1

Q1 *Are current definitions of value sufficient to encourage innovation?*

A Yes, pharmaceutical companies are doing very well thank you very much!

B Yes, the pace of change with developments such as cell and gene therapies, immuno-oncology treatments and new treatments in Alzheimer's Disease show that innovation is doing very well!

C Yes and no – there are innovations making it to patients, but access is often delayed, while the focus of decision makers is often on price rather than value

D No – the relentless focus on price by payers and the focus on impact within health only discourages the development of medicines with a wider impact on patients, their families, and society

Voting question 2

Q2 *Why do we need another value framework?*

- **A** Unless it has a cool name or acronym, we don't!
- **B** There are a number of great value frameworks and tools – the Value Flower, the GRACE framework to name but two – but until HTAs and payers start accepting them there is no value in yet another value framework….
- **C** Existing value frameworks have added value but take a narrow healthcare perspective – new value frameworks could bring a stronger patient and systemic efficiency perspective and more focus on economy-wide effects
- **D** Current value frameworks don't incentivise the development of evidence to support the value, we need a framework and a process to do this
- **E** We just need to move towards greater use of MCDA!

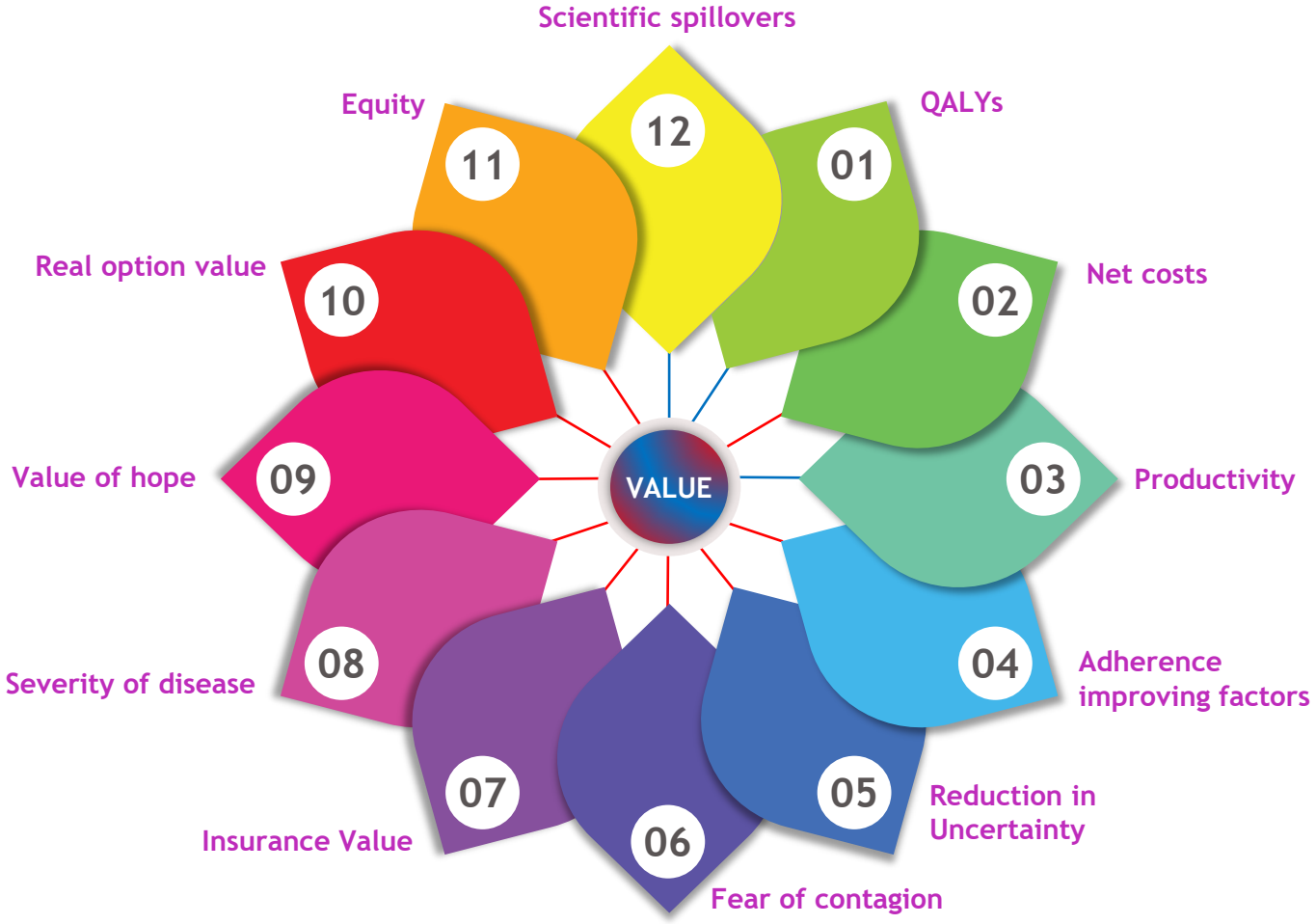
First viewpoint: Expanding our definition of value is vital!

Lou Garrison
Emeritus Professor of Health Economics at University of Washington, Seattle

Panelist

The ISPOR Value Flower is the visual representation of the output of the ISPOR Special Taskforce, aligned with the 2nd Panel outputs

The Value Flower was initially published in 2018 and has helped to drive debate since then



The ISPOR "Value Flower" outlines the importance of capturing wider elements of value **both in the numerator** (Δcosts) **and denominator** (Δbenefits) of a cost-effectiveness assessment

Experience with treatments with prospect of cure, along with the experience of pandemic, has further validated the Value Flower

The COVID-19 pandemic, as well as the Zika scare and the cascade of benefits shown in immuno-oncology, has shown the value placed on hope for cure as well as worry about disease spread

Value of hope

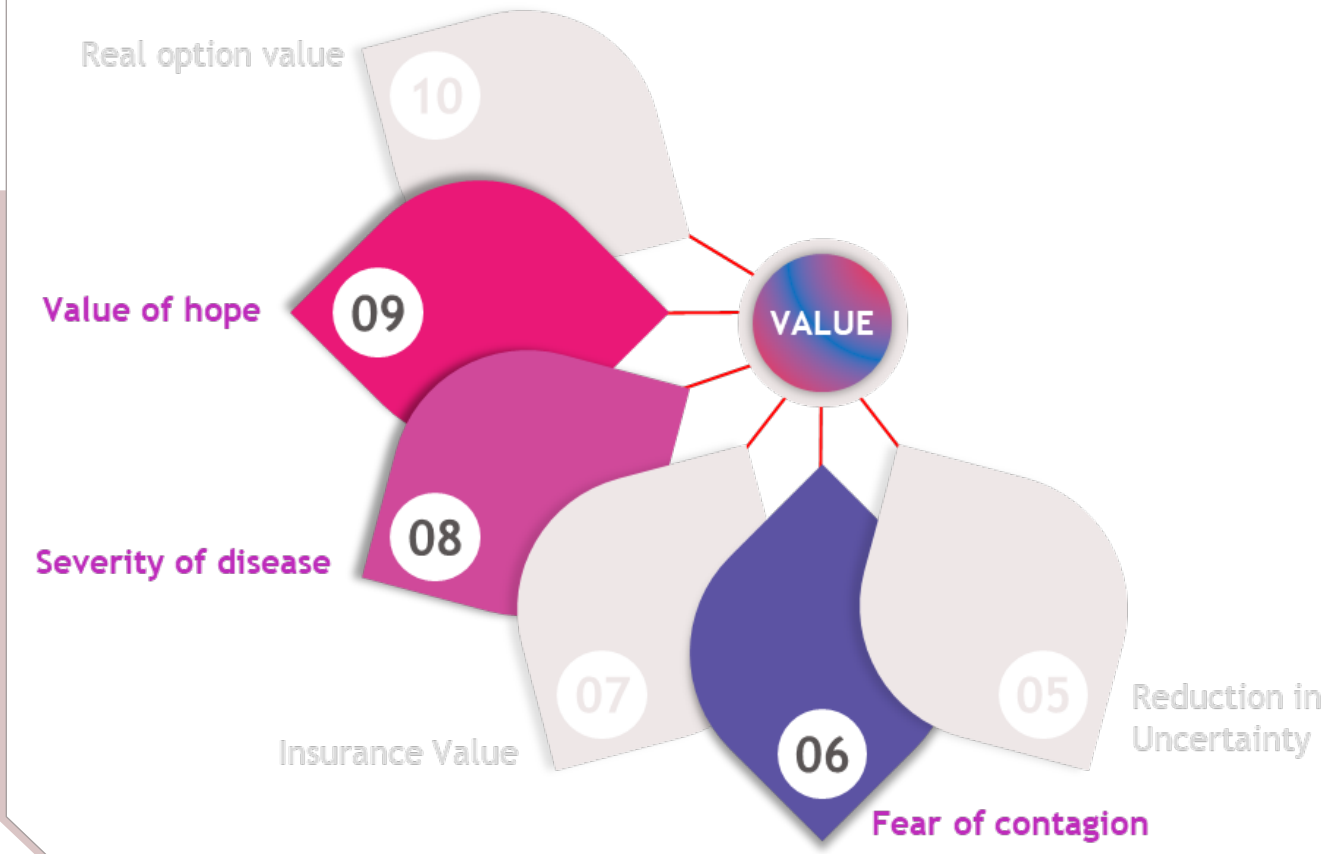
Many patients are willing to sacrifice some life expectancy for the chance for a cure

Severity of disease

Greater willingness to pay for more severe diseases (beyond the QALY loss)

Fear of contagion

A psychic externality due to worry about spread of infectious disease (e.g., Covid and Zika viruses)



In the intervening years, the importance of addressing uncertainty through the ISPOR Value Flower has increased

There is particular value in addressing uncertainty and its implications for patient and family health outcomes

Insurance value

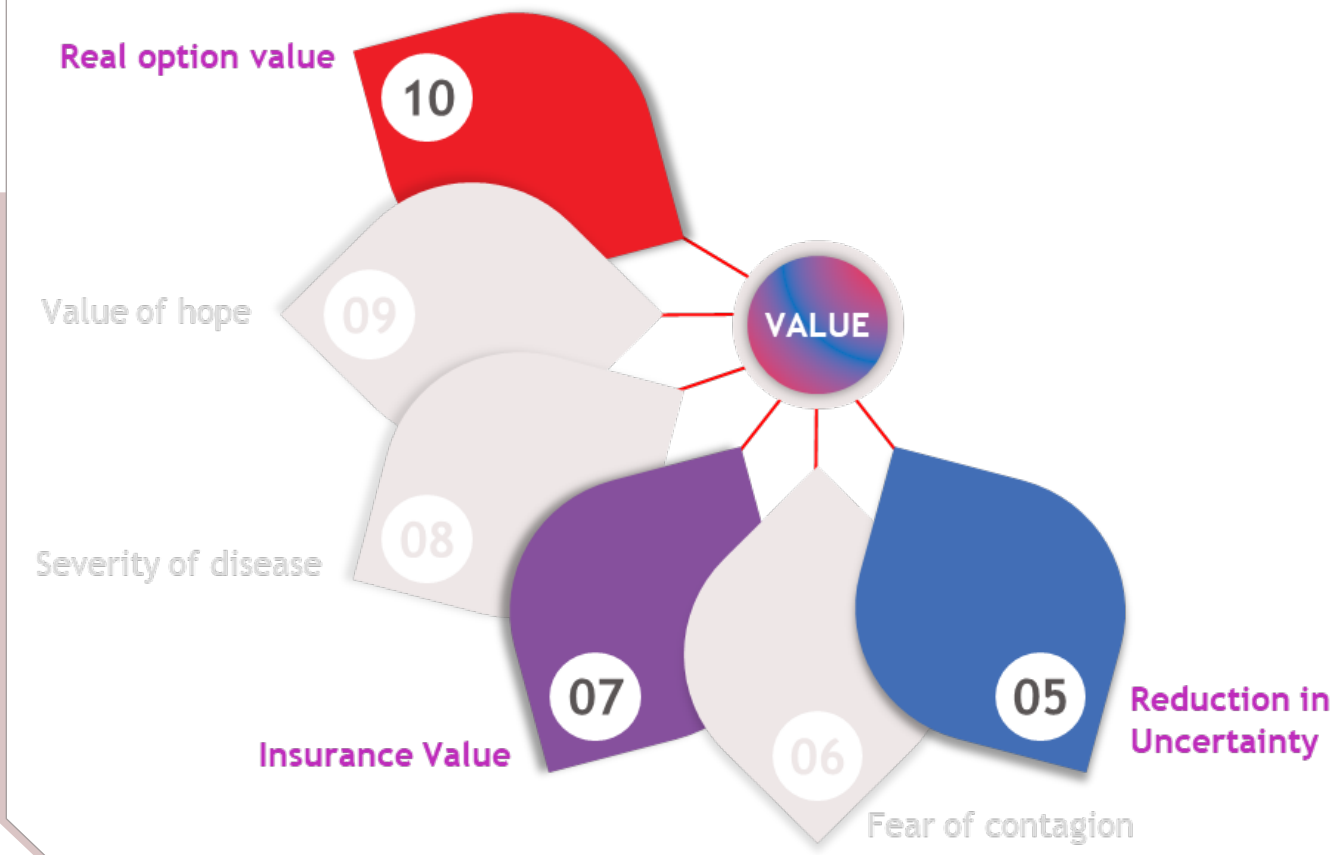
- Financial risk protection AND
- Health risk protection
- Can adjust for severity and rarity;
- In “Extended CEA” used in global health

Reduction in uncertainty due to Dx test (also called “Value of Knowing”)

- Text-drug combination more valuable
- Value in prognosis

Real option value

- Investing in a life-extending treatment provides more value in disease area with more promising pipeline



Furthermore, there is increased recognition of the importance of value elements operating at societal level

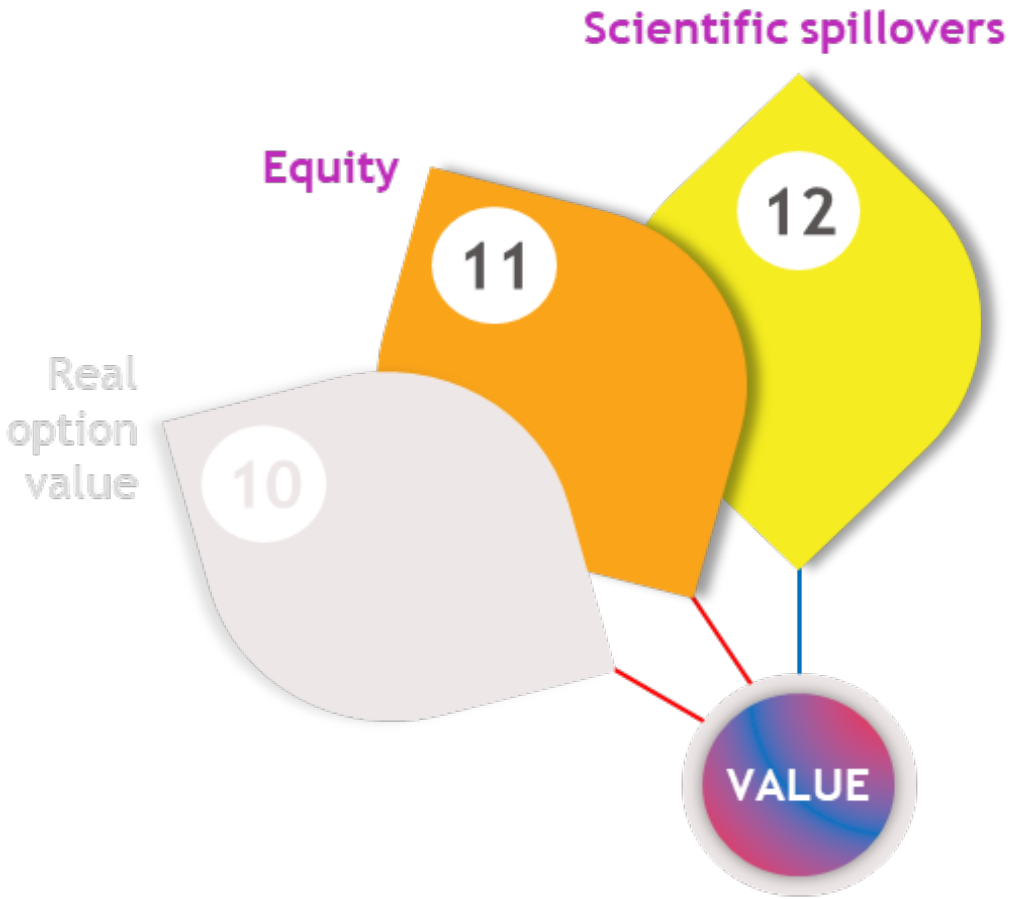
The success of mRNA vaccines in addressing the COVID-19 pandemic have shown the benefits of scientific spillovers, while the impact of uneven global vaccine distribution has shown the importance of equity

Scientific spillovers

- Knowledge externalities
- Researchers gain scientific information from each others' successful and failed trials

Equity

- High prices mean less access: The efficiency-equity trade-off
- There are multiple concepts of equity (e.g., equity of access vs. equity of outcomes)
- **Distributional CEA is new methodology (Cookson et al., 2020)**



However, there were several elements that may have been pursued in the Value Flower but were not initially included or implemented

Impact of lifetime pricing

The benefits of medicines last well beyond generic competition but price at evaluation is carried forward as though it applies for all of this period.

Economy-wide effects

Impacts on sectors beyond healthcare build upon assessments of equity and scientific spillovers as key benefits to society not routinely captured.

Healthcare organisation impact

Treatments that improve the efficiency of the healthcare system, or allow effective treatments to be implemented without delay, add actual value to treatments.

Caregiver and patient wellbeing related to uncertainty

The increased prospect of future cures or effective treatment, or patient access to care through improved pathways, improve patient and caregiver wellbeing even if not currently measured in QoL.

Despite strong foundations, implementation of holistic value has been slow

Decision makers and HTA agencies have provided at best, limited incentives to produce evidence to support broader value elements, while manufacturers have only slowly begun to generate this type of evidence.

Problem

Limited incentive to generate extra evidence – Payers and HTAs don't consider them part of the value base!

Payers sometimes argue that although additional elements do represent value, they are outside the payer remit.

If this causes delayed or denied access, people blame excessive prices and not systemic failure.

Solution?

Clearly define additional elements of value relevant to decision makers

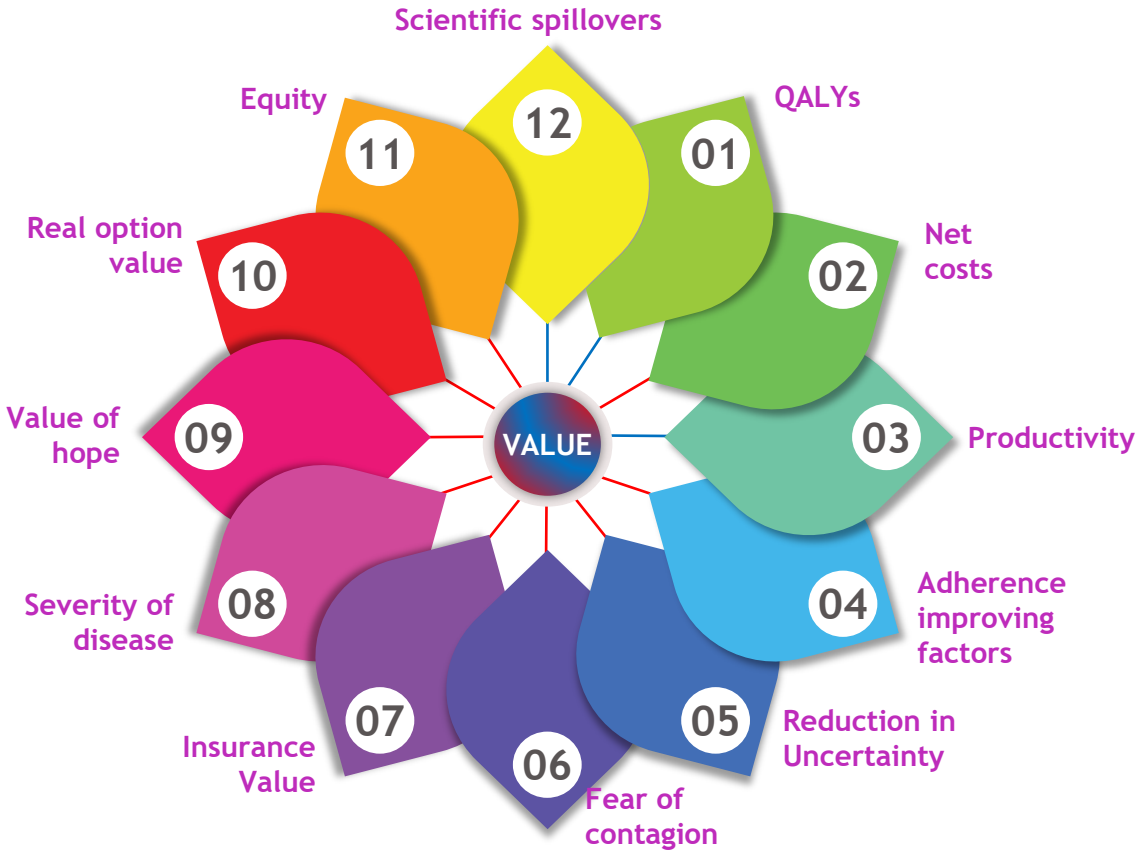
Agree on key elements for a particular medicine and the evidence needed to support these value elements from a boarder societal perspective

Expand the remit of decision makers to ensure that this evidence is considered in the value assessment

Voting question 3

Q3 *With the exception of QALYs and net costs, what are the most important additional value elements in the Value Flower?*

Open text answers to form wordcloud



Voting question 4

Q4 ***Beyond the Value Flower, what additional elements of Value should be prioritised?***

- **A** None – the Value Flower has it all
- **B** None – the Value Flower is already too extensive
- **C** Efficiency of healthcare systems
- **D** Patient well-being within healthcare systems
- **E** I have no idea…
- **F** These are terrible options – what should be prioritised is…

This should be an open text answer – if they like one of the first five options, they can put the corresponding letter. If they want the sixth, just type in the priority

Second viewpoint: We already have all the tools we need!

Isabelle Durand-Zaleski
Professor in Public Health,
Health Economics and Health Services Research Unit, Paris

Panelist

HTAs and payers are assigned a healthcare perspective; they must act within this remit when assessing costs and benefits

Why?

We take an extra-welfarist approach – the maximisation of health is most important! The WHO does take a broader view…

Really?

Yes! Countries like France and Germany have Bismarckian systems – disconnect between social insurance and budgets

What about others?

Even in countries like the UK, there is a preference to keep health budgets separate from other budgets

A practical point

If budgets are constrained, it is hard to anticipate how a new medicine will displace resources previously used for other patients

Nonetheless, HTA bodies and access decision makers may consider additional value elements if appropriately measured

Well-targeted therapies with effective diagnostics (Value of knowing) (France)

Defining impact of treatment as clinical, not economic impact

All must be supported by robust evidence

Distributional CEA to integrate equity (UK)

Integrate impact of extending life until more efficacious therapy (real option value)

For value elements to be accepted, there must be evidence that potential savings from a new technology are:

A Real; and

B Re-allocated as they should

Strong and relevant supporting evidence is always needed!

Payers often think…

Every medicine's value increases massively, so ICER thresholds are simply reduced

Most measurable value is already captured in a healthcare perspective, so holistic value makes little difference

Manufacturers will try to increase thresholds, not reduce prices….

If manufacturers don't believe in holistic value enough to generate evidence, why should HTAs?

It is the **responsibility of manufacturers** to justify the value of medicines with robust and relevant supporting data.

Supporting data must be relevant – not all value elements need a clinical trial!

Even evidence considered low on the hierarchy may be relevant – for example, establishing the impact of stigma in certain conditions may require a survey

The inclusion of economy-wide effects is more difficult to support from an HTA perspective

Can HTA bodies or payers can effectively reward manufacturers for impacts that may be unintended, indirect or unmeasurable? Again, it comes down to hard evidence!

What are economy-wide effects?	These include scientific knowledge and spillovers in R&D, health equity, and impacts on other sectors like education, environment, criminal justice, etc.
Why are these considered difficult?	In most cases, the impact can only be truly observed following the introduction of a new medicine
Is it really that hard?	Even for years after the entry of a new medicine, spillovers in R&D or impacts on other sectors can be intangible, difficult to measure, and indirect

Voting question 5

Q5 ***The defined perspective and lack of remit to consider holistic value is a good reason to exclude the consideration of broader benefits: Yes or No - and why?***

Open text answers (up to 6 words) to form wordcloud

Examples may include:

- Yes, healthcare budget, healthcare value
- Yes, otherwise no consistency between assessments
- No, too much value excluded
- No, medicine prices investment not cost
- No, public money funds societal outcomes
- No idea, but controls prices!

Voting question 6 (two answers can be provided)

Q6 ***Why don't manufacturers generate the required evidence to support the benefits obtained from more holistic value?***

A Too lazy – they are difficult to measure, and it is hard work to do so

B Too scared – manufacturers know that it is unlikely that results will change too greatly and prefer to complain about the exclusion of holistic benefits rather than measure these holistic benefits

C Too futile and expensive – they know that HTA bodies and payers will never accept these holistic value measures and so prefer to concentrate on evidence that has a higher return on effort and investment

D Too unimaginative – they don't take the time and effort required to work with other stakeholders to develop evidence that can be used to influence these other stakeholders

E We just need to move towards greater use of MCDA!

Third viewpoint: New framework to address different needs

Jose Diaz
WW HEOR – HTA Strategy & Affordability Lead at Bristol Myers Squibb, London

Panelist

Disclaimer

The views and opinions expressed as part of this presentation are those of the author and do not necessarily reflect the official policy or position of BMS

Special Acknowledgement to Bill Malcolm - **Senior Director – BMS WWHEOR Economic & Predictive Modeling (EPM) Lead**

We have proposed a framework that looks beyond the HTA perspective that also focuses on implementation

Includes aspects of patient wellbeing, healthcare system efficiency, and economy-wide effects in value

A defined approach to identifying the evidence to support additional value elements to an appropriate standard

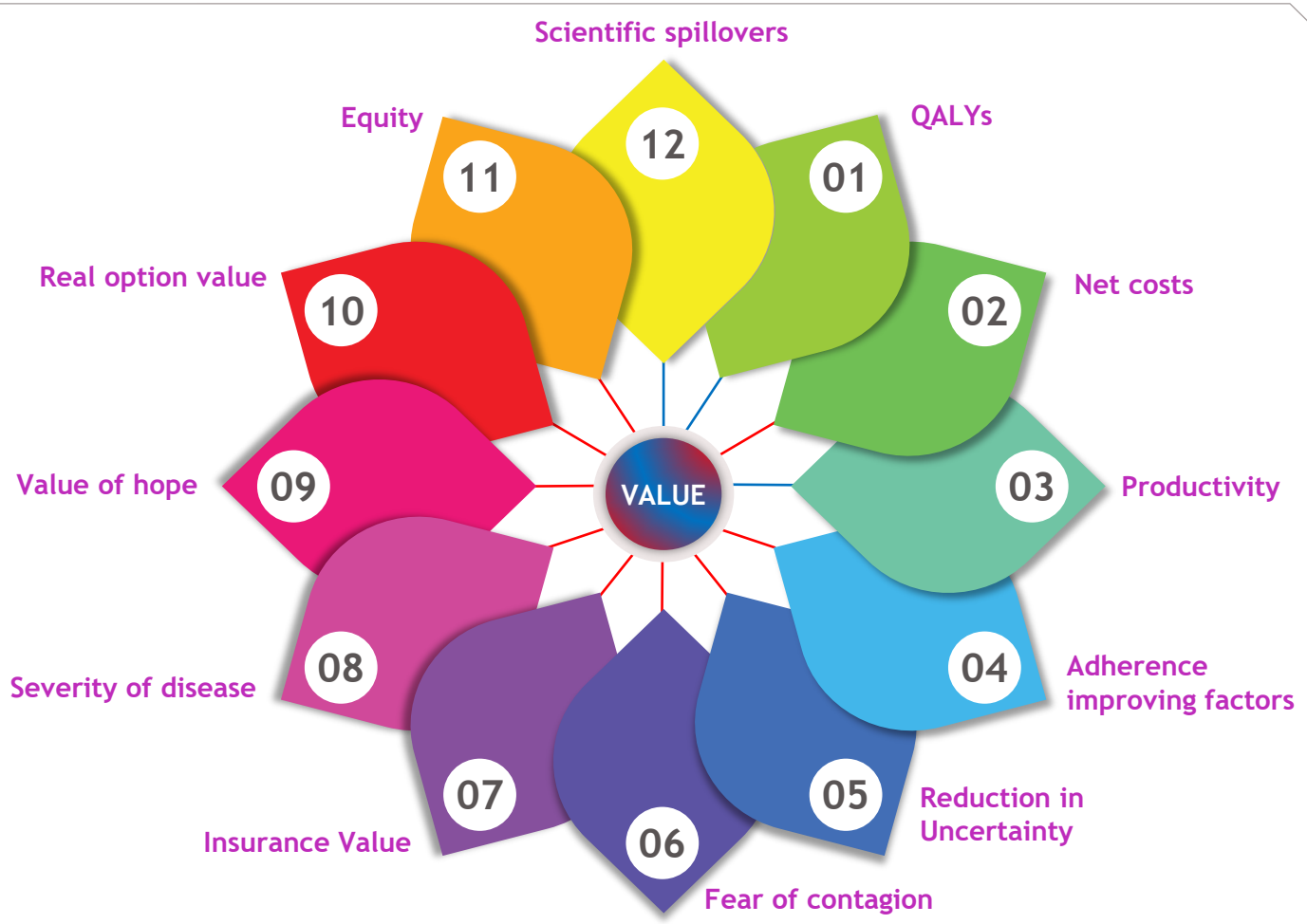
A defined process for multi-stakeholder involvement in the identification, prioritisation and implementation of societal value elements

There has been limited uptake for the Value Flower and it still focuses primarily on economic evaluation

This framework builds upon existing Frameworks to broaden value definition, identify evidence needs, and include external stakeholders

This is a necessary first step to drive better understanding of benefits beyond healthcare and the need to reward these

We propose to move from the foundations of the ISPOR Value Flower…



The ISPOR "Value Flower" outlines the importance of capturing wider elements of value **both in the numerator** (Δcosts) **and denominator** (Δbenefits) of a cost-effectiveness assessment

…to a Value Garden that includes rarely used elements of the Value Flower and additional key elements of societal value

Additional patient-focused and system-focused elements of value are pivotal in assessing societal value

Commonly used

- QALYs
- Net costs
- Adherence improving factors
- Uncertainty reduction
- Productivity
- Fear of contagion
- Value of insurance
- Disease severity
- Value of hope
- Real option value
- Equity
- Scientific spillovers

Rarely used

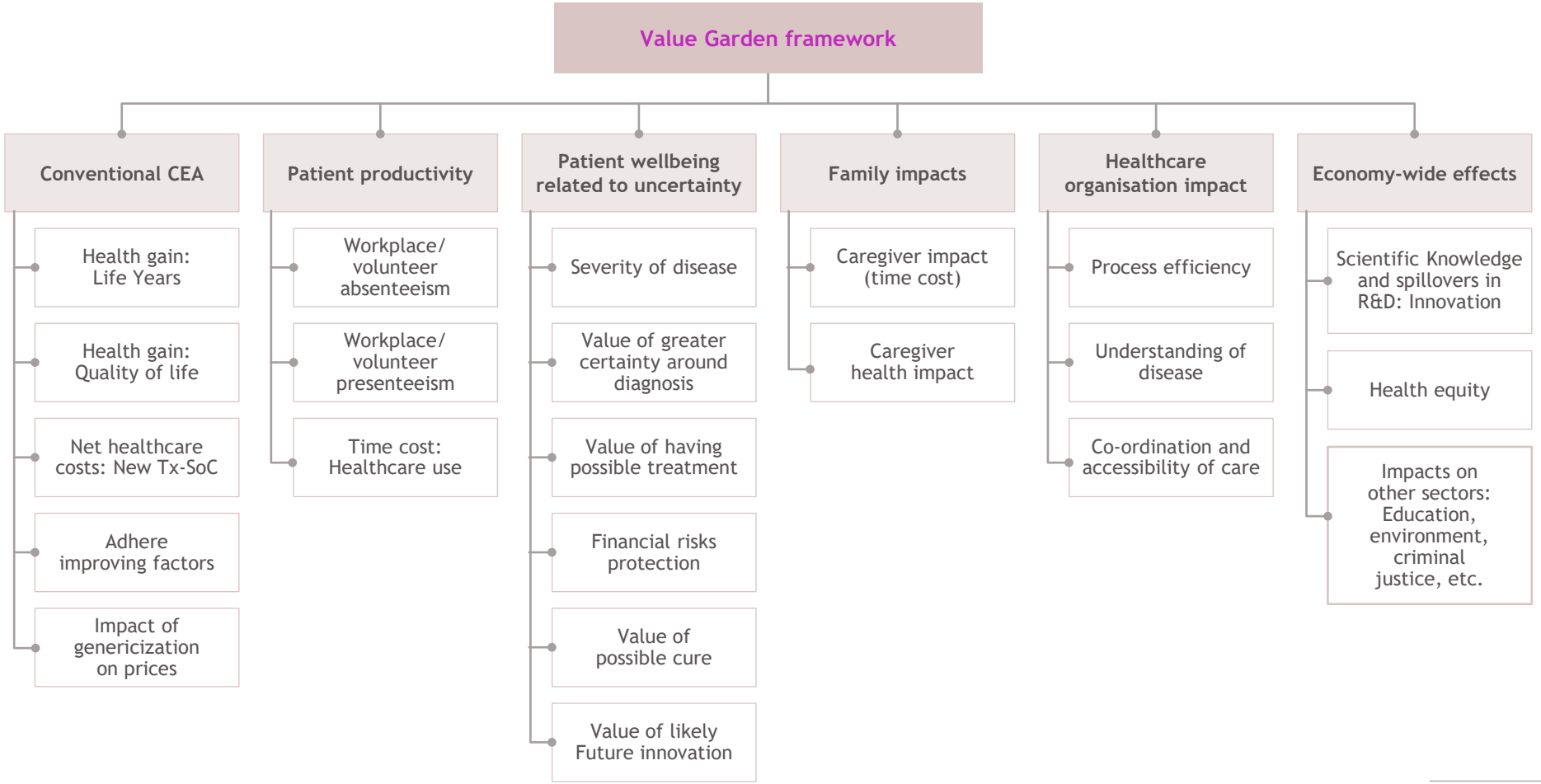
New flowers in the garden

Very seldom used

- Productivity paid work by caregivers and family members
- Productivity unpaid work by patients, caregivers and family members
- Health impact on caregivers as a result of the caregiving
- Social well-being and stigma
- Patient understanding of disease — *Patient focussed*
- Affordability — *Patient focussed*
- Quality and healthcare service delivery — *Process/ efficiency focussed*
- Process efficiency and reduction in waste and inefficiency — *Process/ efficiency focussed*
- Co-ordination and accessibility of care — *Process/ efficiency focussed*

The additional value elements are organised into six core buckets

These buckets incorporate the impact of lifetime pricing and the impact of treatment beyond the patient and the healthcare system



The six defined core buckets are:

- Conventional CEA
- Patient productivity
- Patient wellbeing related to uncertainty
- Family impacts
- Healthcare organisation impact
- Economy-wide effects

These buckets represent an update on the Value Flower and extension beyond conventional CEA

The minimum and optimal levels of evidence for each element must be defined according to the needs of each assessment

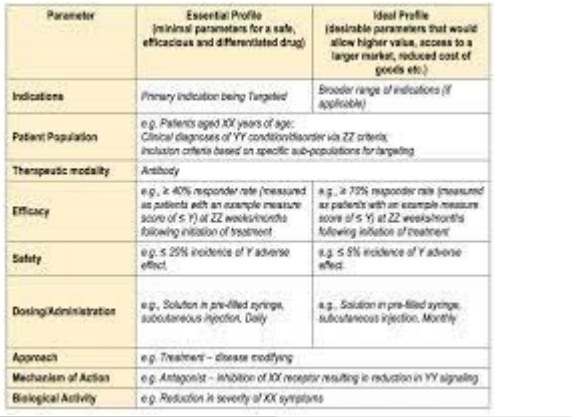
The definition and agreement on minimum and optimal evidence drives the success of the Value Garden

Value element	Source of evidence
● **Conventional CEA (health outcomes, costs, adherence)**	• Quantitative strongly preferred • Clinical trial (health outcomes, adherence, drug schedules) • Real-world evidence (healthcare resource use, unit costs)
● **Patient productivity**	• Clinical trial or RWE (absenteeism, presenteeism through WPAi) • Patient surveys to understand time impact of treatment
■ **Patient well-being**	• Willingness to pay and/or discrete choice experiments • Mathematical models (real option value and financial and health risk protection) • Patient surveys
● **Family impacts**	• Clinical trial or RWE (absenteeism, presenteeism through WPAi, utility and health impacts of caregiving) • Patient/caregiver dyad surveys to understand caregiver impact
● **Healthcare organisation**	• Time and motion studies • Real-world studies showing impact of new treatment on systems • Expert interviews outlining links between new Tx and efficiency
■ **Economy wide effects**	• Full-economy models and/or distributional CEAs • Expert panel discussion where impact of scientific innovation is assessed, areas of additional impact highlighted

● Ex-ante ■ Ex-post or ex-ante

When implementing the BMS Value Garden, one size does not fit all

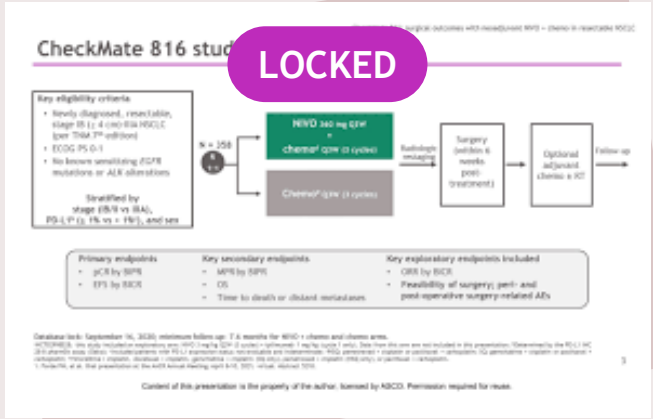
Effective implementation requires an understanding of which value elements are relevant for a disease or treatment and the supporting evidence required



Parameter	Essential Profile (minimal parameters for a safe, efficacious and differentiated drug)	Ideal Profile (desirable parameters that would allow higher value, access to a larger market, reduced cost of goods etc.)
Indications	Primary indication being Targeted	Broader range of indications (if applicable)
Patient Population	e.g. Patients aged XX years of age; Clinical diagnoses of YY condition/disorder via ZZ criteria; Inclusion criteria based on specific sub-populations for targeting	
Therapeutic modality	Antibody	
Efficacy	e.g., ≥ 40% responder rate (measured as patients with an example measure score of ≤ Y) at ZZ weeks/months following initiation of treatment	e.g., ≥ 70% responder rate (measured as patients with an example measure score of ≤ Y) at ZZ weeks/months following initiation of treatment
Safety	e.g. ≤ 25% incidence of Y adverse effect.	e.g. ≤ 5% incidence of Y adverse effect.
Dosing/Administration	e.g., Solution in pre-filled syringe, subcutaneous injection, Daily	e.g., Solution in pre-filled syringe, subcutaneous injection, Monthly
Approach	e.g. Treatment – disease modifying	
Mechanism of Action	e.g. Antagonist – inhibition of XX receptor resulting in reduction in YY signaling	
Biological Activity	e.g. Reduction in severity of XX symptoms	

Development of Target Product Profile for medicine

Discussions on priority value elements and required evidence should take place early in the drug development process with a cross-functional group of experts



Finalisation of pivotal trial design

Step 1

Determine the relevant value elements for a new medicines and related evidence needs

Step 2

Convene a multi-stakeholder panel to review and prioritise holistic value elements

Step 3

Finalise evidence planning and generate evidence to support holistic value elements

This process addresses the challenges with previous value frameworks while ensuring a pragmatic approach to assessment

Insufficient inclusion of holistic value

- Builds upon existing Value frameworks
- Incorporates additional value elements relating to patient wellbeing, healthcare system efficiency, and economy-wide effects
- Moves beyond a strict HTA perspective to incorporate elements important to patients to healthcare system operability

Generation of appropriate supporting evidence

- Identifying minimal and optimal evidence to support each value element
- Incorporation of Value Garden into internal company value and evidence planning

Process for ensuring multi-stakeholder alignment

- Engages multi-stakeholder experts to refine and prioritise value elements – not all flowers in the Value Garden will be needed for every assessment
- Supports planning and acceptance of evidence well ahead of HTA submission
- Involves decision makers outside HTA to ensure all perspectives are captured

Voting question 7

Q7 ***Do the proposed methods of collecting evidence, including through qualitative methods where appropriate, meet decision maker needs?***

A No, unless the evidence is coming from a clinical trial or well-conducted meta- analysis, it will not be enough

B No, I can just about accept the use of RWE in assessments, but qualitative data are just not acceptable!

C Yes and no – it will greatly depend upon the quality of evidence once collected and the disease area itself, but it is possible

D Yes – it is important to match relevant evidence to the relevant part of a research question, and we should look at the most effective way to address any question, using any evidence that is available and interpreted appropriately

Voting question 8

Q8 ***How would credibly generated and reported evidence support the inclusion of more holistic value elements?***

Post as many words or short phrases as you can in 30 seconds, even if that is just:
“We just need to move towards greater use of MCDA!”

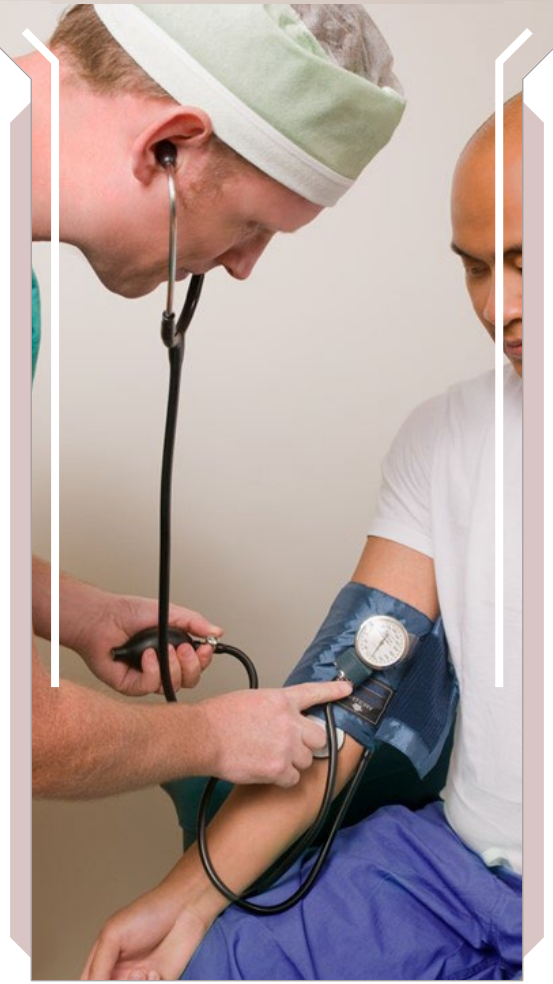
Time for discussion!

Discussion points

What is the real need for an expanded definition of value for medicines? Is it driven by the pharmaceutical industry to justify higher prices, is it needed to incentivise innovation, or will it actually have a limited impact on most drugs and be Much Ado About Nothing?

Are there any elements of value missed from the new Value Garden – or any elements that are not at all relevant? Is it possible to measure the holistic value elements using the approaches proposed – Would these be accepted by decision makers in any case and how would the acceptability be enhanced?

What would be the key driver(s) of success for a new framework such as the Value Garden: Generation of robust evidence, broadening of decision-maker remit, acceptance that it may disadvantage/reduce prices of some medicines – or a miracle?



What would it take to give incentives to manufacturers to produce strong supporting evidence for holistic value elements – If companies develop the evidence, will decision makers accept?

Is this an either/or proposition – Can the standard approach using QALYs with healthcare perspective be a first step to widening the perspective to a societal perspective with input from policy makers/ politicians/HCPs/PAGs/Media/General public?

Now that we have had this great discussion, let's repeat the last voting question

Final

How would credibly generated and reported evidence support the inclusion of more holistic value elements?

Post as many words or short phrases as you can in 30 seconds, even if that is just:
"We just need to move towards greater use of MCDA!"