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REALISING THE BROADER VALUE OF VACCINES IN THE UK

Ready for Prime Time?

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Simon Brassel
Margherita Neri
Lotte Steuten

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Simon Brassel
Office of Health Economics, London

Margherita Neri
Office of Health Economics, London

Lotte Steuten
Office of Health Economics, London

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Corresponding Author:
Simon Brassel
Email: sbrassel@ohe.org

OFFICE OF HEALTH ECONOMICS
CONSULTING

For further information please contact:

Professor Graham Cookson
Chief Executive, OHE
Honorary Visiting Professor in Economics at City, University of London

Tel +44 (0)207 747 1408
Email gcookson@ohe.org

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Executive Summary

The COVID-19 pandemic has revealed the broad and devastating health, economic and societal impact of a highly infectious and deadly disease, for which safe and effective vaccines are the most important exit strategy.

While initially the human suffering of COVID-19 patients made headlines, this soon proved to be only the tip of the iceberg. Consider the toll on patients' families, friends, colleagues, and other social networks; on all the healthcare staff working around the clock, wave after wave; and on the capacity of the NHS, buckling under pandemic pressures with consequences that will last for years. Then there's the disastrous economic impact, crippling economies in the UK and worldwide.

This clearly shows that an effective vaccine against this disease will have broad value to society. Value that extends well beyond 'just' preserving the health of the vaccinated individuals and avoiding the costs of treating patients with COVID-19.

The ability to generate such broad value to society is by no means unique to COVID-19 vaccines. In fact, health economists have long recognised the broad value attributes of vaccines and called for the recognition of those in vaccines value assessment. Yet, health technology assessment (HTA) approaches in the UK (as well as some other countries) limit themselves to evaluating health benefits that accrue to treated individuals and resource use within the healthcare system. As a result, vaccines and other technologies that generate broader benefits – such as maintaining healthcare capacity or labour productivity – may be undervalued and underused.

While this concern is not exclusive to vaccines, it is of special relevance to them. Our prior work on this topic exposed the gaps between vaccines' potential broader value and their recognition in England's HTA appraisals. Furthermore, our research showed that about 75% of the societal return on investment from vaccines accrues from preventing productivity losses. While the status quo of the UK's value assessment of vaccines risks undervaluation and consequently underfunding of vaccines relative to other health technologies, creating change is not trivial.

Therefore, this third report on the broader value of vaccines, as commissioned by the ABPI Vaccines Group, sets out actionable short and long term recommendations on how to drive change towards recognising and rewarding the broader value of vaccines in the UK.

Preparing the stage

We brought together an expert panel, including six academic HTA/vaccine assessment experts, two consultants with treasury and civil service experience, and one industry representative. Via a modified Delphi approach including two online survey rounds plus an expert roundtable, this panel set out to:

a) refine and prioritise the value elements that are most significant a/o likely to be incorporated into value assessments in the UK;

b) identify general and specific opportunities and challenges for considering those value elements as part of the vaccine assessment processes; and

c) explore ways to leverage opportunities / overcome barriers around data, methods, and policy advancements needed.

Revising the script

Starting from the broader value of vaccines framework, the experts prioritised *transmission value*, *impact on the vaccinee/patient productivity*, *impact on care productivity*, *impact on carer quality of life (QoL)*, and *prevention of antimicrobial resistance (AMR)*. They based their prioritisation on each value element's importance and the feasibility to incorporate the element in vaccine value assessments in England. In addition, *health system delivery value* was proposed for consideration as part of the value element *healthcare system cost off-sets*, while *enablement value* was deprioritised mainly due to a lack of a clear agreed-upon definition.

What needs to change behind the scenes

According to the expert panel, data and evidence availability is the main barrier across most broader value elements. While the Covid-19 pandemic has provided urgency and a political climate to reconsider the broader value of vaccines, there is a large consensus among experts that broader value elements should be considered for all health technologies and not be limited to vaccines. Achieving this requires thoughtful alignment of HTA data requirements, methods, and processes within England and abroad.

Lifting the curtain

The recommendations generated by this programme of work are described in the table below. We distinguish between those that are specific to vaccines and can be achieved in a relatively short timeframe. Other recommendations require a more systemic change, as well as collaboration and alignment between different stakeholders. As the Covid-19 pandemic put the spotlight on the broader value of vaccines, it is now time to prepare it for prime time.

Recommendations

Vaccines-specific, short term	Systemic, longer-term recommendations
Improve methods to capture the value of vaccines that maintain health system delivery capacity	Progress efforts towards recognition of the impact of vaccination on patient and carer productivity
Align positions between JCVI and NICE on the recognition of carer QoL	Invest in general data collection and access
Strengthen national analytical expertise and improve the collection of and access to data concerning transmission value	Broadening value frameworks and (international) alignment concerning new value elements
Develop data and tools to quantify the value of vaccines in preventing AMR development	

1 Introduction

1.1 Introduction

The COVID-19 pandemic shows that the value of an effective vaccine against a highly infectious and severe disease extends well beyond patients and the healthcare system, benefitting our society more broadly. Yet, health technology assessment (HTA) approaches, including those for vaccines, are typically limited to evaluating the health benefits that accrue to treated individuals and resource use within the healthcare system. As a result, vaccines and other technologies that generate such broader benefits may be undervalued and underused.

This issue, however clearly illustrated by the current pandemic, is not new. Health economists have long argued that vaccines and other healthcare technologies can generate substantial 'externalities', which are the benefits and costs beyond those attributable to the treated patient, both within and beyond the health system (Mauskopf et al., 2018). Large externalities that are ignored by the HTA process may lead to an inefficient allocation of healthcare resources.

OHE's previous work on this topic has shown the gaps between vaccines' potential broader value and their recognition in HTA appraisals in England (Brassel et al., 2020). To conceptualise the broader value of vaccines, we synthesised a framework of multiple value elements of vaccines based on a literature review (Bärnighausen et al., 2011; Deogaonkar et al., 2012; Jit et al., 2015; Bloom et al., 2017). Using a representative sample of ten preventative and therapeutic vaccines that are currently in development and likely to reach the UK market within the next five years, our analysis suggests that these vaccines may generate health benefits in the unvaccinated population (via herd immunity) and productivity benefits to patients and their caregivers. An overview of our framework and the definitions of the value elements is available in the following section.

Nonetheless, the Joint Committee for Vaccines and Immunisation (JCVI) and the National Institute for Health and Care Excellence (NICE) do not fully recognise most value elements within this framework when assessing preventative and therapeutic vaccines[1], respectively. For example, discrepancies exist between the value generated by vaccines and NICE's and JCVI's mechanisms to recognise vaccines' value from preventing antimicrobial resistance (AMR), enhancing the cost-effectiveness of other non-vaccines interventions, and improving productivity (Brassel et al., 2020).

The unrecognised value is substantial, as we estimated recently for the existing vaccination programmes against pneumococcal disease and human papillomavirus. From a governmental perspective, our prior analysis showed that about 75% of the total return on investment resulted from the prevention of lost productivity (Brassel and Steuten, 2020). This risks undervaluation and consequently underfunding vaccines relative to other health technologies.

Recognising the broader value of vaccines is, however, not a straightforward task. It requires a mix of advancements in data and methodological capabilities as well as policy advancements concerning the perspective of decision making and the alignment of views from different stakeholders. This project, therefore, aims to prioritise broader value elements for inclusion in HTA processes in England, to identify barriers and opportunities for doing so, and to provide recommendations or changing the status quo.

[1] *Preventative vaccines stimulate the immune system of healthy individuals to produce antibodies. Therapeutic vaccines stimulate the immune system to produce antibodies after the infection has occurred.*

1.2 Vaccines value framework and recognition by JCVI and NICE

Building on the existing literature on broader value elements relevant for vaccines (Bärnighausen et al., 2011; Deogaonkar et al., 2012; Jit et al., 2015; Bloom et al., 2017), we synthesised a framework composed of four categories of value: (1) health effects, (2) productivity-related impact, (3) health system and community health impact and (4) health system economic impact. The framework focuses on the dimensions of value that we expect to be most relevant to high-income countries[2].

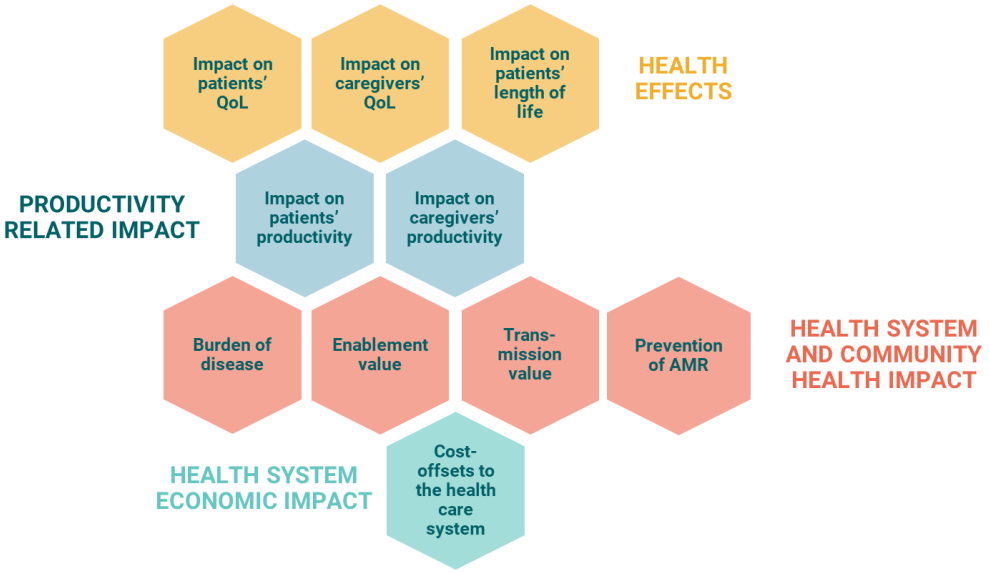

FIGURE 1: OHE VALUE FRAMEWORK
Notes: QoL = Quality of Life; AMR = antimicrobial resistance.

Health effects:

- **Impact on patients' (vaccinated individuals) quality of life (QoL)** is the effect on their physical, mental, emotional, and social functioning.
- **Impact on caregivers' QoL** is the effect on their physical, mental, emotional, and social functioning.
- **Impact on patients' (vaccinated individuals) length of life** is the impact on life expectancy or life-years saved.

[2] *An evolved version of this framework includes social equity value as part of the health system and community impact dimension, and macroeconomic effects as part of the health system economic impact dimension (Bell, Neri and Steuten, 2020). Please note that social equity and macroeconomic effects have been discussed by the panel members, especially with respect to productivity value.*

Productivity-related impact:

- **Impact on patients' (vaccinated individuals) productivity** includes the effects on work productivity due to sickness or death. This should capture the impact on lost days of work and on the level of productivity at work, both for getting vaccinated and for disease avoided.

- **Impact on caregivers' productivity** includes the effects of work on productivity due to the time spent caring for a patient.

Health system and community health impact:

- **Burden of disease** relates to the aggregate impact of disease in terms of total disability-adjusted life years (DALYs) or quality-adjusted life years (QALYs) lost in the UK. Incorporation of disease in HTA may also partly reflect societal preferences for equity.

- **Transmission value** is the impact on disease transmission patterns and associated morbidity. Vaccines for infectious diseases can have an impact on population-wide epidemiological outcomes by providing herd immunity to unvaccinated individuals.

- **Prevention of AMR** is the impact on the rate of development and transmission of resistant infections. Vaccines targeting resistant bacterial infections can reduce the transmission AMR and lower the prescription rates of antibiotics, another contributor to the development of AMR.

- **Enablement value** is the impact on the cost-effectiveness of other non-vaccine interventions. For example, vaccines may enhance the effectiveness of other non-vaccine interventions (e.g., a vaccine for patients with HIV may enable cancer treatment with chemotherapy, which is otherwise a non-recommended option in people with already weak immune systems).

Health system economic impact:

- **Cost off-sets to the health system**. Impact on medical costs borne by the health system from potential reductions in the number of GP and specialist consultations, treatment, screening interventions, and hospitalisations.

An assessment of the JCVI and NICE guidelines (Table 1) showed whether value elements of the value framework are likely to be considered in appraisals of vaccines (JCVI, 2013; NICE, 2013a).

TABLE 1: VALUE ELEMENTS CONSIDERED BY THE JCVI AND NICE

	VALUE ELEMENTS									
	Impact on the QoL of patients	Impact on QoL of carers	Impact on length of life	Productivity of patients	Productivity of carers	Burden of disease in the UK	Enablement value	Transmission value	Prevent AMR development	Cost-offsets to healthcare system
JCVI's ASSESSMENT CRITERION?	▲	▲	▲	✖	✖	▲	✖ [4]	▲	✖ [1]	▲
NICE's ASSESSMENT CRITERION?	▲	▲ [2]	▲	✖	✖	▲ [3]	✖ [4]	✖ [6]	✖ [5]	▲

▲ Likely to be considered by JCVI/NICE ✖ Not likely to be considered by JCVI/NICE

Notes: [1]The JCVI advises further research in quantifying the potential impact of vaccines in reducing the long-term burden of AMR (https://www.gov.uk/government/groups/joint-committee-on-vaccination-and-immunisation#research-recommendations); [2] Carers' impact on QoL is considered when relevant: "The perspective on outcomes [includes] all direct health effects, whether for patients or, when relevant, carers"; [3]Burden of disease is considered deliberatively. Severity is considered by means of the 'end of life' criteria, which allow a different weighting of the cost-effectiveness threshold when specific conditions are met; [4] The JCVI can, in principle consider Enablement value. However, this is often not possible due to a lack of data or because the impact of this element is expected to be small. In such cases, the enablement value may be part of the deliberative process (but not captured in the actual modelling); [5] The DHSC has announced a pilot programme of a 'volume-delinked' payment scheme, which will include a modified assessment approach of antibiotics. [6] It should be noted that NICE has no experience so far from assessing vaccination programmes and that normal health-related interventions do not create much transmission value. Consideration of transmission value by NICE may be likely if the assessment of vaccination programmes is included in their remit.

The elements of value that are currently not fully recognised by JCVI and NICE are the *impact on the productivity of patients and their carers, enablement value,* and *prevention of AMR development and transmission*. Further, *transmission value* is currently not recognised by NICE in the assessment of therapeutic vaccines. We note there may be instances where the guidelines do not formally state the inclusion of a value element, but, in practice, special allowances may be made deliberatively on a case-by-case basis. For further explanation of these, please refer to the original OHE report (Brassel et al., 2020).

1.3 Objectives and structure of this report

Building on our prior work on realising the broader value of vaccines in the UK (Brassel et al., 2020; Brassel and Steuten, 2020), this project had three objectives:

a) to refine and prioritise the value elements that are most significant a/o likely to be incorporated into value assessments in the UK;

b) to identify general and specific opportunities and challenges for considering those value elements as part of vaccine assessment processes; and

c) to explore ways to leverage opportunities / overcome barriers around data, methods, and policy advancements needed.

The remaining part of this chapter will outline the primary methods and related outcomes. Chapter 2 provides a classification and prioritisation of a refined list of value elements before focussing on the challenges posed by three selected value elements in chapter 3. We discuss the general barriers and enablers for broader value assessment in England in chapter 4. Finally, we provide recommendations on how to realise the broader value of vaccines in chapter 5 and conclusions in chapter 6.

1.4 Methods

We collected data using a modified Delphi process, which is an iterative multistage process designed to gather opinions and transform these into a group consensus (as far as possible) (Hasson, Keeney and McKenna, 2000).

A panel of subject matter experts (n=9) was recruited based on their expertise regarding vaccine assessment and general HTA processes in the UK. The expert panel included six academic HTA / vaccine assessment experts, two of whom have held or hold active roles within the JCVI, two consultants with former experience in the civil service, and one industry representative.

Our modified Delphi approach consisted of three rounds. We facilitated the first two rounds using an online survey (SurveyMonkey), and the third round through an interactive expert roundtable moderated by OHE researchers. The results from each round served as input into the consecutive round. After each survey round, participants were provided with the aggregated group responses, allowing them to inform their opinions based on these, and gradually build consensus. We give a short description of the outputs of each Delphi round below and further detail on methods used in the appendix.

The output of Delphi round one was a prioritisation of value elements according to:

- the **importance** of the value element to improving the value of assessment of vaccines,
- the availability of high-quality **evidence** related to each value element,
- The **analytical ability** to incorporate each value element into existing HTA processes.

Round two resulted in an overview of expert's opinions on key barriers and opportunities in England's current HTA environment to include broader value elements according to

- **Data & evidence** comprises all aspects of generating high-quality evidence to demonstrate the broader value of vaccines within an economic evaluation.
- **Methods & Tools** covers all methodological and analytical aspects of performing the economic evaluation itself, such as modelling approaches, the perspective of the evaluation, or required software and computing power.
- **Systemic flexibility** encompasses all systemic factors that hinder or support a potential change of the status quo of HTA of vaccines. Examples can be ring-fenced budgets or considerations for better alignment of appraisal approaches between the Health and Care sectors.
- **Political context** includes the current political climate and all stakeholders that might affect systemic change.

In round three, experts discussed the results of the previous rounds to ultimately arrive at a consensus-view of whether and why including a specific prioritised value element in HTA would be considered:

- an **easy win:** a value element that is important and has a high probability of being accepted.
- An **important challenge:** a value element that is of such importance that extra effort and changes are justified to overcome high barriers that prevent its inclusion.
- An **unlikely success:** a value element for which inclusion is not very likely to succeed.

2 Revising the script – Prioritising the Broader Value of Vaccines

This section summarises the prioritisation and refinement of broader value elements put forward for recognition in HTA processes in England.

2.1 The importance, evidence, and ability to incorporate broader value elements

The Delphi process's first round focused on the six value elements from the original framework currently not fully considered during the HTA process for vaccines in England. These are transmission value, impact on the patients' productivity, impact on caregivers' productivity, impact on the caregivers' quality of life (QoL), enablement value, and prevention of antimicrobial resistance (AMR) development and transmission.

Figure 2 shows the group's views on the **importance** of each value element for broadening the value assessment of vaccines (represented by the colour of each bubble), the availability of high-quality **evidence** (shown on the horizontal axis), and today's **analytical ability** (shown on the vertical axis) to incorporate each value element into existing HTA processes.

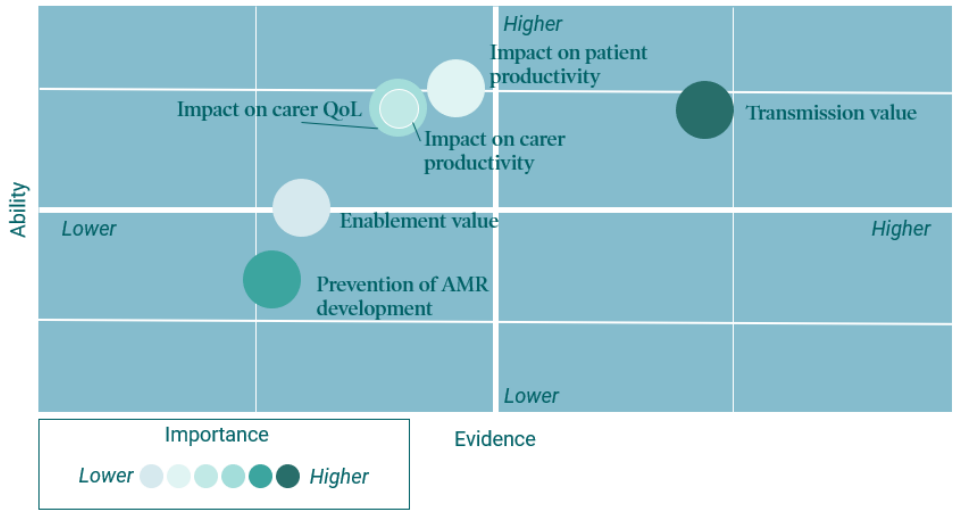

FIGURE 2: IMPORTANCE, AVAILABILITY OF EVIDENCE AND ANALYTICAL ABILITY CONCERNING EACH VALUE ELEMENT.
Note: The visualisation is based on the weighted average of numerically-coded Likert scale data. The mapping of evidence and ability represents the absolute weighted average while we derived the colour coding of importance from ranking the related weighted-average for each value element.

In the following, we describe the group's view on each value element of the broader value framework that is currently not (consistently) considered in the HTA of vaccines in England.

Transmission value

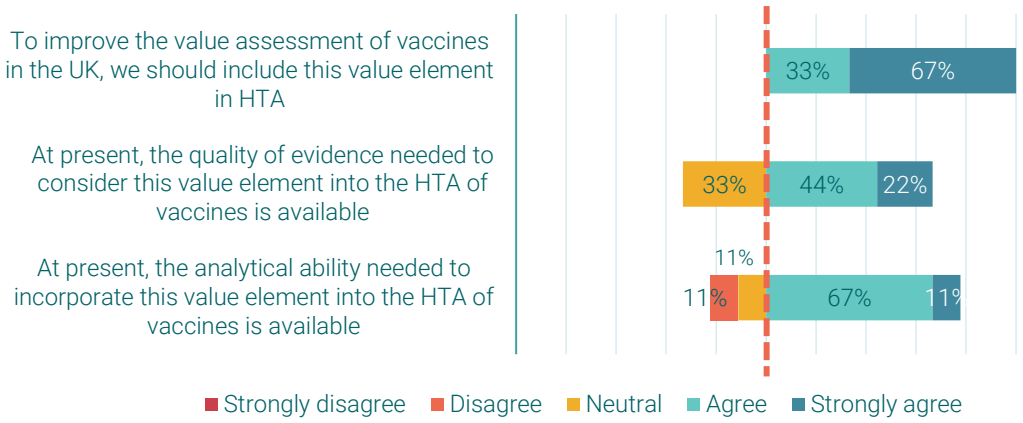

FIGURE 3: TRANSMISSION VALUE - PANEL MEMBER'S VIEW ON IMPORTANCE, AVAILABILITY OF EVIDENCE, AND ANALYTICAL ABILITY.

The element *transmission value* holds a unique position. All panel members (100%) consider it important, and a clear majority (66% and 78% respectively) agreed that today's analytical ability and evidence base are sufficient to include the value element into HTA routinely.

Modelling transmission value for an HTA requires dynamic disease models, which are more complex than the static models used for most HTAs. Such complexity is challenging as there is still a shortage of health economists with the relevant skillset.

Impact on the patients' productivity

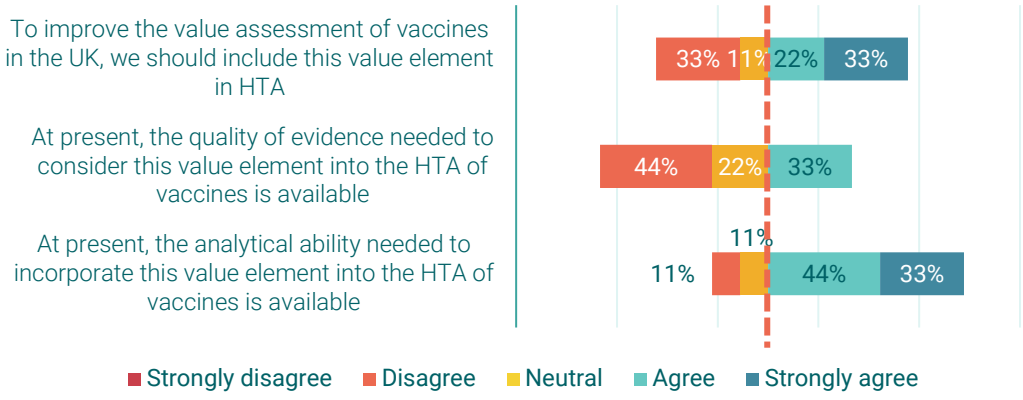

FIGURE 4: IMPACT ON THE PATIENTS' PRODUCTIVITY - PANEL MEMBER'S VIEW ON IMPORTANCE, AVAILABILITY OF EVIDENCE AND ANALYTICAL ABILITY.

The slight majority (56%) of the panel members agreed that considering *productivity of patients* is important with a few (33%) believing it less important and one panel member being neutral. This value element should encompass productivity losses incurred for getting vaccinated and potential short term side effects of that such as aches and flu-like symptoms and potential productivity gains accrued from avoiding or reducing the severity of the disease vaccinated against. 11% of respondents were neutral about the importance of this value element, and 33% consider it not to be important. They noted that including this value element is challenged by a lack of data and evidence. At the same time, the vast majority (77%) of the panel members agreed that, when given the data, the necessary analytical methods to quantify productivity are available today.

Panel members discussed that inclusion of productivity value would require careful equity considerations to prevent funding bias towards those health technologies that prevent disease and/or death in individuals with higher earning potential. Additionally, some panel members noted that a critical requirement for incorporating productivity would be to reconsider the health economic evaluation decision-context. They highlighted the need to change the evaluation perspective from a health system perspective to a societal perspective, and, consequently, the need to reassess the cost-effectiveness threshold.

Impact on the caregivers' QoL

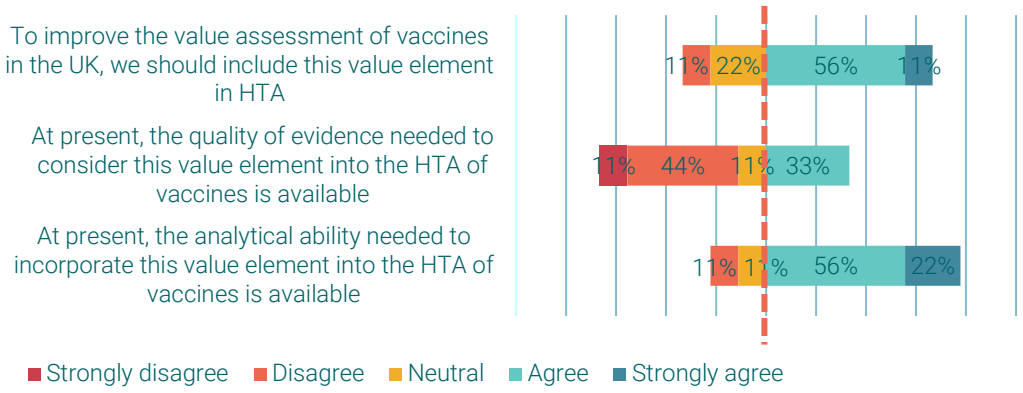

FIGURE 5: IMPACT ON THE CAREGIVERS' QOL - PANEL MEMBER'S VIEW ON IMPORTANCE, AVAILABILITY OF EVIDENCE, AND ANALYTICAL ABILITY.

A majority (67%) of panel members considered the *impact on caregivers' quality of life* as important, but many (55%) also noted this to be challenging due to limited evidence. However, if the evidence were available, the members consider today's appropriate analytical methods to be adequate.

Impact on caregivers' productivity

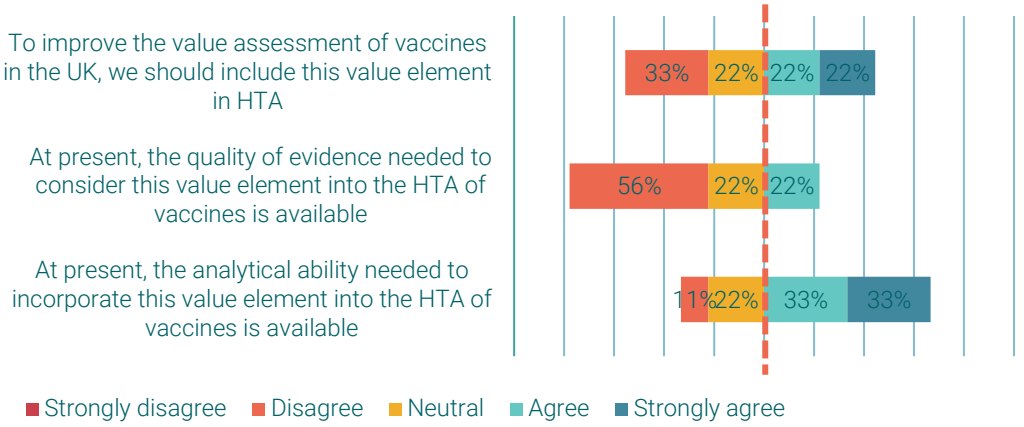

FIGURE 6: IMPACT ON THE CAREGIVERS' PRODUCTIVITY - PANEL MEMBER'S VIEW ON IMPORTANCE, AVAILABILITY OF EVIDENCE, AND ANALYTICAL ABILITY.

Concerning the importance of this value element, opinions diverged: a third of respondents did not deem the caregiver's productivity as important, while 22% were neutral, and 44% consider it to be important. A slight majority (56%) disagrees that today's data availability is sufficient to include the value element. At the same time, 66% think today's analytical ability to include the value element is adequate.

Respondents agreed that recognising the *impact on caregivers' productivity* faces similar constraints as patients' productivity. These include a shortage of high-quality data, equity concerns, and setting methodological standards across all health technologies.

Prevention of AMR

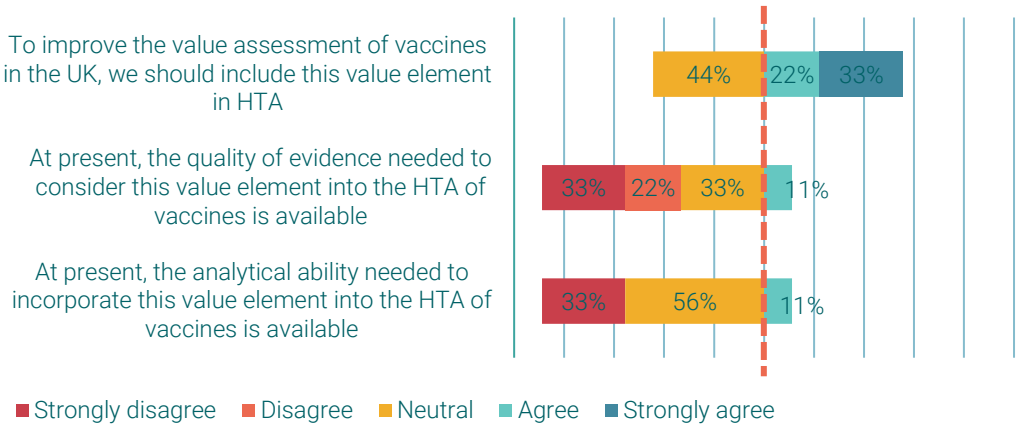

FIGURE 7: PREVENTION OF AMR - PANEL MEMBER'S VIEW ON IMPORTANCE, AVAILABILITY OF EVIDENCE, AND ANALYTICAL ABILITY.

While many panel members (55%) deem *prevention of AMR development* an important value element (with the remaining respondents being neutral), only 11% considered the current evidence or methods to be fit for incorporating this value element.

Specific barriers for recognising this value element include modelling complexity and challenges in generating high-quality evidence of the causal chain linking vaccines to a reduction of antibiotics-usage and finally to improved health outcomes.

Enablement Value

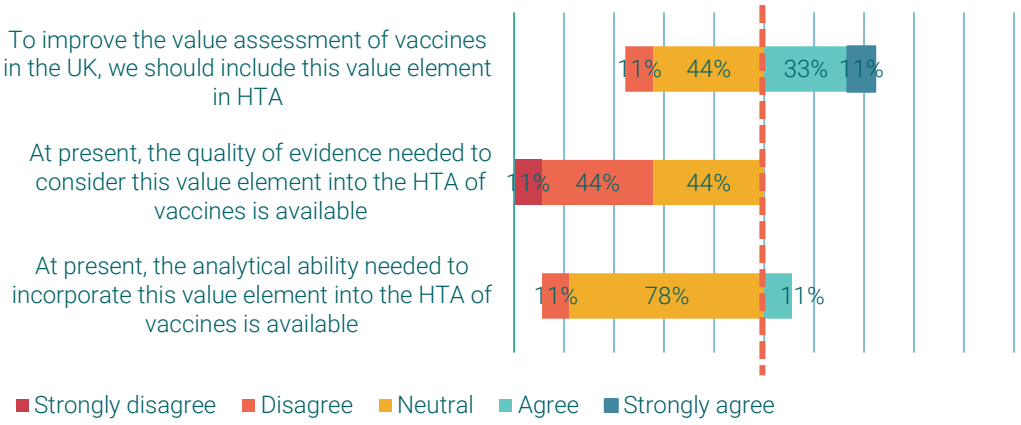

FIGURE 8: ENABLEMENT VALUE - PANEL MEMBER'S VIEW ON IMPORTANCE, AVAILABILITY OF EVIDENCE, AND ANALYTICAL ABILITY.

There was a divergence in opinion concerning *enablement value,* with 44% agreeing that the value element is important, while 44% were neutral, and 11% disagreed on its importance. Also, many panel members (55%) do not consider the relevant evidence to be currently available, and only 11% were positive that the analytical ability to incorporate this value element is there.

Overall, this value element ranked lowest in almost all three categories. One reason for this beyond evidence and analytical ability is that the literature is unclear about its precise definition.

2.2 Additional broader value elements

To further develop our framework and ensure the list of value elements considered in this project was as comprehensive as possible, we asked the expert panel whether there would be added value elements to consider. They suggested the following four value elements:

- **Macroeconomic value** that goes beyond individual productivity and captures the link between vaccination and a countries economic growth.
- **Fear of contagion value**: defined by ISPOR as the per-capita value of avoiding fear and anxiety associated with the risk of future spread of disease in the vaccinated & unvaccinated population. Fear can be quantified using survey methods designed to elicit the individual's willingness to pay to eliminate the possibility of exposure.

- **Health service delivery value**, which captures the value of maintaining healthcare delivery through a reduction of pressure on regular services (e.g., flu vaccinations that help manage winter surge capacity).

- **Non-health enablement value**, the disease-specific value that allows society to do things that would not be possible otherwise. Examples include increasing time spent outside (e.g., the malaria vaccine) or the freedom to travel (e.g., the yellow fever vaccine).

We then asked the panel members to repeat their ranking of the value elements' importance using the extended list of ten value elements. Figure 9 shows that the original value elements' relative ranking position did not change significantly after considering the extended list. While most of the new value elements were ranked as relatively low importance *(non-health enablement value*, *macroeconomic value*, and *fear of contagion*), the group ranked *health system delivery value* third overall. Panel members acknowledged this ranking was in part motivated by the current Covid-19 pandemic, which pushed the limitation of health service capacity into the spotlight. However, seasonal outbreaks such as respiratory syncytial virus (RSV) infections in infants that can hinder a whole paediatric ward's operation were given as another example where health system delivery value would be relevant.

Based on these results, we focused on the six selected elements from the value framework plus *health system delivery value* and excluded *non-health enablement value*, *macroeconomic value,* and *fear of contagion* from further discussion.

Round 1		Round 2
Transmission value		Transmission value
Impact on patient productivity		Impact on patient productivity
		Health system delivery value
Impact on carer Quality of Life (QoL)		Impact on carer Quality of Life (QoL)
Impact on carer productivity		Impact on carer productivity
Prevention of Antimicrobial resistance (AMR) development		Prevention of Antimicrobial resistance (AMR) development
		Fear of contagion Value
		Macroeconomic Value
Enablement value		Enablement value
		Non-health enablement value

FIGURE 9: RANKING ACCORDING TO IMPORTANCE WITH AND WITHOUT ADDITIONAL VALUE ELEMENTS.
Note: Additional value elements were added from respondents during round 1 and added to the ranking exercise in round 2.

2.3 Prioritisation of value elements

From the list of seven value elements, we asked each panel member to select motivate their choice of three elements of which:

- one 'easy win' (i.e., a value element that is important and has a high probability and feasibility of being incorporated),

- one 'important challenge' (i.e., a value element that is of such importance that extra effort and changes are justified to overcome the barriers that prevent its inclusion); and

- one 'unlikely success' (i.e. a value element whose inclusion is not very likely to succeed).

As Figure 10 shows, a majority (56%) of panel members considered *transmission value* an 'easy win'. This was motivated by the importance of this value element, while the barriers concerning the collection of relevant data and the development of methods were seen as relatively low. The remaining 44% (n=4) of the respondents attached considered *patient productivity* to be an 'easy win', mentioning the existence of data collection and analysis tools as the main reason for their choice.

There was less agreement on the 'important challenges'. 33% chose *health system delivery value* as an important challenge considering that COVID-19 demonstrated the magnitude of health loss occurring when health system capacity does not keep up with the demand for services. *Transmission value* received 22% of the vote due to the significant modelling and data-gathering challenges. Another 22% of panel members considered *the prevention of AMR* as an important challenge, motivated by the UK Government's dedicated strategy to tackle AMR. The *impact on the productivity of patients* was put forward by one panel member (11%) and *impact on carer QoL* by another (11%).

Enablement value (44%), *prevention of AMR* (33%), and *impact on the productivity of patients* (22%) were considered 'unlikely successes'. The choice for *enablement value* to be an unlikely success was motivated by the lack of a clear and agreed-upon definition. While considered an *'important challenge'* by some, *prevention of AMR* was considered an unlikely success by others because establishing a causal effect between vaccination and reduction in AMR was considered problematic with current data and methods. Regarding *productivity value,* respondents mentioned failed past attempts to appropriately incorporate this in HTA as a reason to consider this an unlikely success in the (near) future.

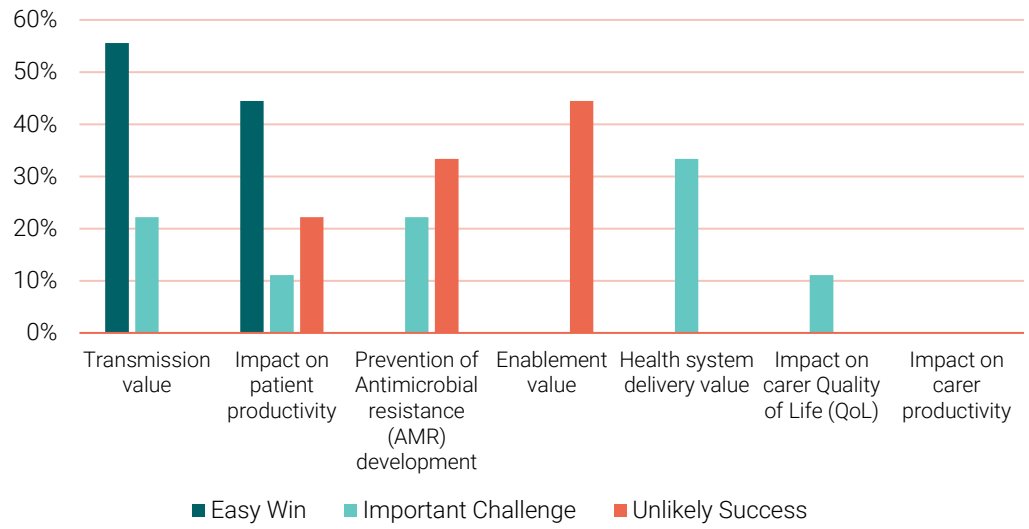

FIGURE 10: DIFFERENTIATION OF VALUE ELEMENTS.

3 Spotlight on three 'important challenges'

This section summarises the discussion on the three value elements that the panel members chose to prioritise in light of their importance as well as the feasibility of overcoming the related barriers, which are *impact on patient productivity*, *prevention of AMR,* and *health system delivery value.*

3.1 Impact on patient productivity

A prerequisite for the inclusion of patient (and carer) productivity in HTA of vaccines is the appropriate perspective of evaluation. In England, the HTA of vaccines and other health technologies is undertaken from a health system's perspective, in which resource allocation decisions aim to maximise utility within the budget constraints of the healthcare system. Consensus existed among the panel experts that a change in HTA perspective to include value elements beyond health outcomes and health system costs should apply to all health technologies rather than exclusively to vaccines. Such a change would require structural revisions and allocation of budget across public sectors. As such, its success will rely on support from multiple decision-making bodies (Treasury, Department of Health and Social Care, NICE). Also, depending on what the cost-effectiveness threshold represents, be it the consumption value of health or the marginal cost-effectiveness of current spending, there may be a need to re-estimate the cost-effectiveness threshold level when changing the HTA perspective[3]. An in-depth discussion of estimating cost-effectiveness thresholds is outside the scope of this paper, and further reading is recommended (Vallejo-Torres et al., 2016; Hernandez-Villafuerte, Zamora and Towse, 2018; Brouwer et al., 2019).

A second challenge stressed by the panel experts concerning productivity effects relates to equity concerns. Health technologies that mainly benefit population groups with higher earning potential would, ceteris paribus, generate larger productivity gains than those in lower-income populations or among those who mostly carry out unpaid work (Brassel, Neri and Steuten, 2020). So far, equity considerations in the HTA of vaccines have been made on a case-by-case basis as part of a deliberation process. For example, equity played a key role in the decision to add the human papillomavirus (HPV) vaccine to the immunisation schedule for both adolescent girls and boys in England (DHSC, 2018). However, a uniform approach across all health technologies for considering productivity effects may require a more formal method to incorporate equity in decision-making. Existing approaches to value productivity while considering equity use average national earning values by age group, like in the Netherlands (Ministerie van Volksgezondheid, 2016). Equity, however, is a broader concept, which may consider multiple dimensions beyond differences in income, including the ability to benefit from treatment, life expectancy, or rarity of disease (Soares, 2012). Hence, developing a quantitative approach to consider equity is a complex task, but recent research in distributional cost-effectiveness analysis of health technologies may provide promising options (Love-Koh et al., 2019; Cookson et al., 2020). The panel experts indicated that the NICE methods review proposal to introduce a 'modifier' for health inequalities might create some momentum to find a solution for the outstanding methodological questions (NICE, 2020).

According to the panel experts, the practical measurement of productivity effects should also consider the scope of productivity losses from vaccination and potential data gaps. The former is likely to arise due to the productive time lost to receive an additional vaccine. The magnitude of this

[3] *Please note that a re-estimate of the cost-effectviness threshold may not only be necessary when including productivity value but to some degree also when including any other value element in the objective function.*

effect could vary widely depending on the population group receiving the vaccine (e.g., children, adults, elderly) as well as the delivery strategy. In terms of data, countries that routinely include productivity effects in HTA have experienced challenges in the past in obtaining good quality data on work absences. The necessary data requirements should, therefore, be carefully evaluated.

3.2 Prevention of AMR

The value element *Prevention of AMR development* is well aligned with the current UK government priorities, including the "5-year action plan for antimicrobial resistance 2019 to 2024" (GOV.UK, 2019). This plan has multiple ambitions, including reducing resistant infections, strengthening stewardship, improving surveillance, and boosting research on tackling AMR. For this reason, the expert panel found this value element to be particularly relevant to consider for consistent incorporation in HTAs of all technologies that may help to tackle AMR, including vaccines.

Measuring the impact of new health technologies on AMR development and transmission poses significant challenges. In the specific case of vaccines, the expert panel highlighted two sources of complexity when estimating the impact on AMR from reducing the (appropriate and inappropriate) use of antibiotics for treating infections. First, it will be necessary to estimate the size of the avoided antibiotic usage thanks to a particular vaccine. Second, the usage avoided needs to translate into a long-term reduction in the AMR development rate and transmission. Research attempting to quantify this value for vaccines (Chae et al., 2020), new antimicrobial drugs (Rothery et al., 2018), and diagnostics is beginning to emerge (Steuten et al., 2018).

While research on the development of quantitative methods is ongoing, the expert panel suggested that the NICE methods review include proposals that could foster the recognition of value from preventing the transmission and development of AMR (NICE, 2020). One example is the proposal to formalise the role of expert elicitation in HTA. The current NICE methods guidance suggests that expert elicitation can be used when there is a lack of data for cost-effectiveness analyses, although preferred methods to do this are not specified (NICE, 2013b). Existing research on HTA of technologies tackling AMR has recommended the usage of expert elicitation when the quality of data on model parameters (e.g., transmission rates, rate of AMR development) is not optimal (Rothery et al., 2018; Neri et al., 2019; Morton et al., 2019).

Considering the need to familiarise HTA decision-makers with considering AMR prevention value in the appraisals and understand how best to do this, the expert panel suggested a similar approach as the mock-appraisal for CAR-T technologies (NICE, 2016). In the CAR-T case, a dedicated expert panel considered hypothetical evidence and data on CAR-T technologies, highlighted potential issues with HTA methods and decision frameworks, and came up with potential solutions to these. A similar exercise within JCVI or NICE was recommended to help to identify where an adaptation of the methods may be necessary.

Finally, the panel discussed the method for pricing the value of AMR reduction or prevention. They suggested informing the pricing of the marginal improvement in AMR by considering the counterfactual, which would be the cost of untreatable resistant infections.

3.3 Health System Delivery Value

The value of preserving health system delivery capacity is represented by the opportunity cost of healthcare that is missed or delayed when the health system reaches its operational capacity. The expert panel agreed that consideration of health system delivery value depends on the appropriate evaluation of the health systems cost off-sets. This may be particularly relevant for some infectious

diseases that are likely to put pressure on the health system capacity due to their seasonality (e.g., flu, RSV), risk of an outbreak (e.g., rotavirus), or pandemic (e.g., Covid-19).

Among the main challenges currently hindering the recognition of health system delivery value, the expert panel identified appropriate measurement and availability of data. To measure this value element, it is necessary to calculate the savings that vaccines could generate in terms of the size of the investments in health system resources made for pandemic preparedness and health-related quality of life (i.e. from excess deaths or lost QoL because of missed or delayed health care). The measurement of health system delivery value may be complicated by the fact that the counterfactual is not observed, although it can be estimated.

Research to understand and quantify the current health system capacity will also be needed. The recent experience with Covid-19, for example, has turned the spotlight on the health system in terms of intensive care units (ICUs) capacity and their cost. In addition, knowledge of other components of the health system that may be subject to pressure from vaccine-preventable diseases is needed for a comprehensive evaluation. A first step to guide the collection of data to demonstrate health system delivery value would be to identify the health system's components which, in previous outbreaks, suffered the most. Overall, the expert panel agreed that if the research agenda is shaped well, the measurement of this value element will be a feasible target.

4 Behind the scenes – general disablers and enablers

4.1 Barriers and Opportunities

The Delphi process's first two rounds provided insight into the general barriers and opportunities to broaden value assessment in England. As shown in Figure 11, most panel members (78% in Round 1 and 100% in Round 2) considered availability of data and evidence to be a barrier. Regarding methodology, the view shifted from 44%, considering this as a barrier in Round 1 down to 11% in Round 2 (the shift being absorbed in the neutral category). Systemic factors that prevent changes to the way HTA is done was considered a barrier by 78% of respondents, up from 44% in Round 1. A clear shift occurred regarding political context being considered an opportunity in Round 2 by 67% of all respondents, up from 33% in Round 1.

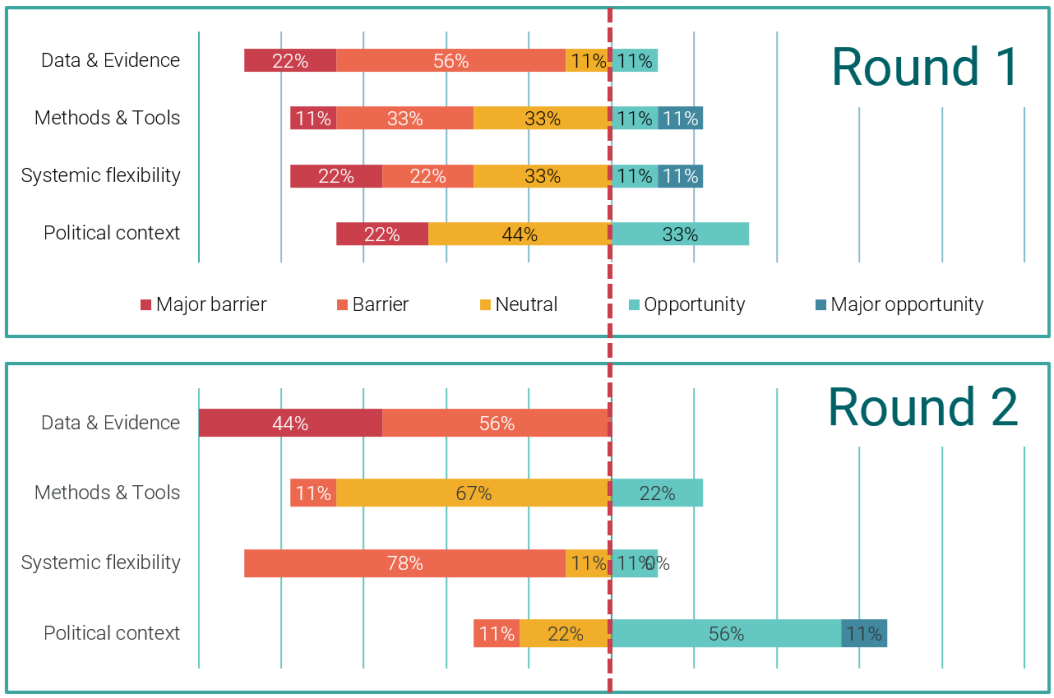

FIGURE 11: GROUP VIEW ON GENERAL BARRIERS AND OPPORTUNITIES

In the following, we summarise the results and discussion from the three Delphi rounds by category:

Data & evidence
According to the participants, the availability and quality of data vary between different value elements. An example is transmission value, where high-quality data on social and biological processes is required. Initiatives like the UK Clinical Practice Research Datalink (CPRD), a real-world research service supporting public health and clinical studies, or the Hospital Episodes Statistics Data Dictionary demonstrate the UK's strong capability concerning data collection. However, data access, especially for the industry, is currently considered to be too restricted.

Methods & tools
The panel members were relatively confident that it is possible to generate the required evidence with appropriate methods and tools if data collection and especially data access are improved. However, given the increased complexity of dynamic disease models required to predict an infectious disease outbreak, more experts are needed with these specific skill sets. This expertise is not only necessary to develop suitable models but also to appraise them. Hence, the current shortage of expertise hinders a constructive debate as only a few academics are involved in the most influential research. There is little headroom for a discussion about what is good and not good value for money with narrow scope for an appropriately insightful review or challenge.

Systemic flexibility
Many inert factors hinder systemic change of the value of assessment of vaccines. The underlying reasons are often linked to siloed stakeholders, discrepancies in methods guidelines, and resistance to change.

For example, the historical separation between NICE and the JCVI poses challenges, particularly for economic principles underpinning the methods. For the most part, those advising the JCVI are not health economists. Better representation of the various disciplines needed for HTA would improve effective communication, shared understanding, and harmonisation of methods.

Furthermore, effective decision-making requires consistent methods across all health technologies that achieve the same aims. One example is a decision problem between a therapeutic and preventative approach targeting the same disease. Hence, HTA methods should avoid treating vaccines differently than any other health technology. From this, it follows that any methodological change for vaccines needs to be the product of a system-wide change across all health technologies. This also includes an alignment of discount rates, acknowledging that high discount rates can have a particularly large impact on the cost-effectiveness of vaccine programmes (Jit and Mibei, 2015) and other technologies where there is a long delay between the delivery of care and the health effects being accrued. Changing to a 1.5% discount rate as proposed in the NICE Methods Review would, therefore, be welcomed.

To facilitate change while maintaining consistency, the Health and Care Appraisal Working Group that advises the Department of Health and Social Care and its arm length bodies on the cost-benefit and cost-effectiveness of programmes would be well-placed to harmonise methods where possible.

Political context
There is a window of opportunity to achieve change due to Covid-19 pandemic heightening the awareness of infectious diseases. The severity of infectious diseases is often not understood well enough, in part as a consequence of decades of effective immunisation. The great loss of lives and health due to Covid-19 brought their impact to the centre stage.

The economic fallout has left its mark on the country's global economy for years to come. The pandemic exposed and further widened the existing inequality in British society, which needs to be addressed by future measures and policies (Marmot and Allen, 2020). With COVID-19 vaccines being developed and approved in record time, vaccination technology is in the spotlight to contribute to solving some of the most urgent healthcare challenges. The resulting momentum may be used to highlight the broader value of vaccines and the opportunity to build trust between industry, policymakers, and the public.

4.2 How to assess the value of vaccines

When deciding on the way forward, a crucial question is whether the evaluation of vaccines should conform with the NICE methods for all other health technologies or if some diversity between

approaches could be allowed. As shown on the left panel in Figure 12, most of the expert panel considers transmission value (89%) and the prevention of AMR (55%) as mainly relevant to vaccines but not to other technologies. Aside from a diverted opinion on enablement value, most respondents agree in considering all other value elements as being of relevance to vaccines and other health technologies alike. For example, non-vaccine treatments of Alzheimer's disease have a similar potential on carer QoL. Also, every treatment that prevents fatal disease within the working population affects patient productivity.

Consequently, the expert panel recommended that HTA should emphasise transmission value and the prevention of AMR when valuing vaccination relative to other health technologies (see right panel of Figure 12).

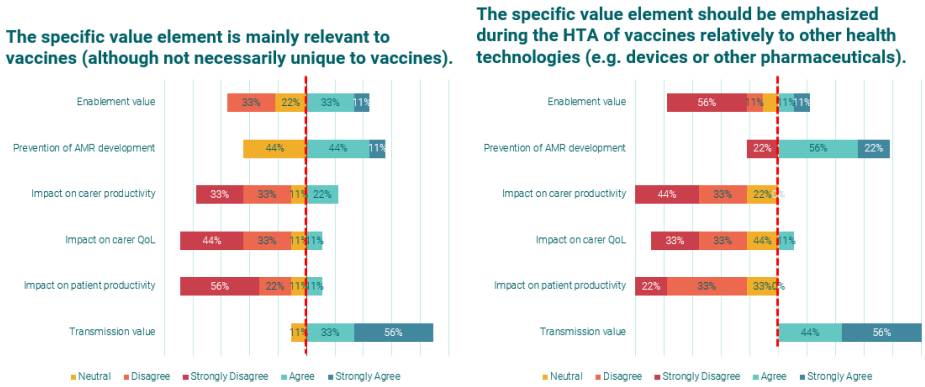

FIGURE 12: RELEVANCE OF VALUELEMENTS AND THE NEED FOR EMPHASIS

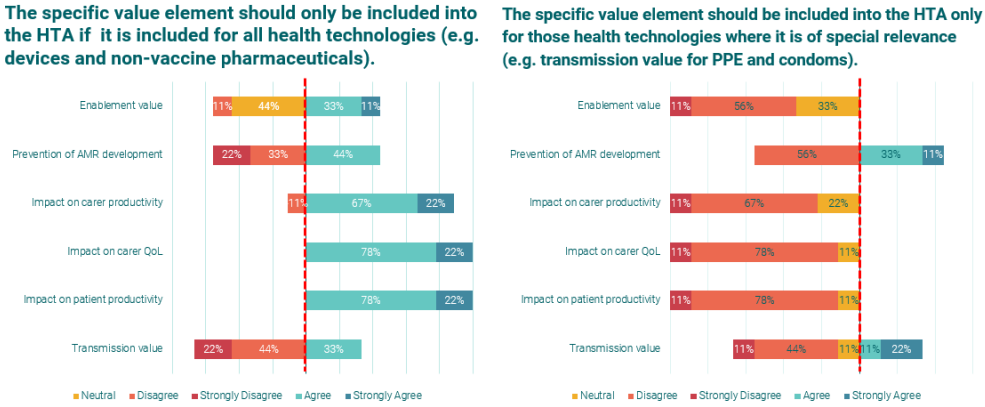

FIGURE 13: TREATMENT OF VALUE ELEMENTS RELATIVELY TO OTHER HEALTH TECHNOLOGIES

In line with this group response, the left panel of Figure 13 shows that the experts would only advise to include productivity value for patients and carers and impact on carer QoL if HTA methods would consider these value elements for all health technologies. The experts seem to be more open to making exemptions for vaccines concerning transmission value (66%) and the prevention of AMR (55%). There is considerable disagreement on how to treat enablement value.

The right panel of Figure 13, shows that some experts would agree with incorporating transmission value and prevention of AMR only for those technologies deemed to be of high relevance to the overall value proposition. However, the vast majority of the participants rejected this approach for these and other value elements.

5 Lifting the curtain - Realising the broader value of vaccines

This section sets out our recommendations for realising the broader value of vaccines in England, informed by the experts' majority view as elicited via a modified Delphi process. We frame the recommendations within two categories:

Category 1 *recommendations are most relevant to* ***vaccines*** *and face little systemic hurdles. Their implementation's main requirements are improved data collection and access and the development of methods and tools. These recommendations are achievable within a relatively* ***short time*** *horizon.*

Category 2 *recommendations require more* ***systemic changes*** *in the existing HTA processes and should apply to all health technologies due to the need to harmonise methods. These will typically require a* ***longer-term*** *view to accomplish.*

5.1 Vaccines-specific, short term recommendations

Improve methods to capture the value of vaccines that maintain health system delivery capacity

The value of maintaining health system capacity can be captured as part of the *cost-offsets to the health care system* if the opportunity costs of relevant healthcare resources are measured correctly. This value element is recommended for more consistent and comprehensive inclusion in HTA as it is strongly relevant to vaccines against infectious diseases that can paralyse (parts of) the healthcare system due to their seasonality or risk of an outbreak. To better measure the value of maintaining sufficient health system delivery capacity, we need a clear definition of what health system capacity entails and methods for measuring its opportunity costs.

Align positions between JCVI and NICE on the recognition of carer QoL

Vaccines often target infectious diseases and/or diseases that threaten the very young and the very old. Hence, the impact of vaccines on the QoL of carers can be significant. NICE already allows for assessing carer QoL in its appraisals (Pennington and Wong, 2019). However, this is currently not reflected by the approach of the JCVI. Hence, JCVI's explicit and pragmatic recognition of carer QoL aligned with NICE's methods and improved guidance to reduce uncertainty concerning the generation of related evidence generation may be enough to move the needle.

As the need for consistency in HTA requires alignment of practices across all health technologies, we recommend that the Health and Care Appraisal Working Group within the DHSC should be involved in efforts to appropriately and consistently incorporate the full value of vaccines and other technologies.

Strengthen national analytical expertise and improve the collection of and access to data concerning transmission value

A significant source of vaccines' value stems from generating positive externalities beyond the vaccinated individuals when the target disease is infectious. The value element is not unique to

vaccines. However, few other health technologies generate comparable levels of transmission value. While the JCVI considers *transmission value* in its advice to UK health departments, NICE is currently less likely to reflect this in its methods formally. To provide the required level of evidence for consideration in NICE's HTA, it requires investment in the generation of high-quality data and related access for innovators and evaluators. There is also a need to broaden the expertise to build the related dynamic disease models and interpret their results.

Develop data and tools to quantify the value of vaccines in preventing AMR development

As AMR is acknowledged as one of the most urgent threats to our society's health and economic well-being, the UK government is investing in a national action plan to tackle AMR. While vaccines have great potential to contribute to this goal, causal evidence of vaccines' impact on preventing AMR is complex to generate and comes with substantial uncertainty. The complexity of the challenge, however, should not diminish the efforts to overcome it. Rather, sufficient investment in data and methods development is called for in the near future. While the development of suitable data and methods is underway, in the short-term, flexibility is recommended in assessing this value element, e.g. by allowing for evidence generation through the expert elicitation as proposed in the NICE methods review.

5.2 Systemic, longer-term recommendations

Progress efforts towards recognition and productivity value for patients and carers

It is recommended to progress the efforts for incorporation of *productivity value for patients and carers* in HTA, as these are considered to be of high importance to vaccines and other health technologies. The related tools and methods to quantify these value elements need further development. Notably, their inclusion raises equity concerns. Hence, new techniques, such as distributional cost-effectiveness analyses, are required to assess each technology's equity impact under evaluation. The NICE methods review proposal to introduce a 'modifier' for health inequalities might also create momentum to address such methodological questions (NICE, 2020).

Incorporating productivity value for all health technologies also requires a fundamental move away from the health system perspective on HTA. The way forward might make use of incremental steps, starting with agreeing on a set of standards to measure productivity value and provide practical guidance on how to calculate the cost of absenteeism, presenteeism, and unpaid work (Krol and Brouwer, 2014). We would also recommend including a second reference case for all health technologies that allow the inclusion of productivity value and other broader value elements consistent with a societal perspective.

Invest in general data collection and access

High-quality data and evidence are crucial to realising the broader value of vaccines in the long term. The UK can build on existing data sources and data collection processes, but room for improvement exists, especially for data on infectious diseases. Furthermore, if future health economic models are to consider the broader value elements, such data need to be accessible to all stakeholders involved, including industry. Such concerted efforts to improve data collection and access will be beneficial beyond the realm of vaccines. They are the foundation for progressing health technologies and care models to fight future disease, monitor effectiveness and improve population health. Therefore, we reinforce the recommendation from our previous work to proactively steer, incentivise, and improve the necessary data infrastructure in England.

Broadening value frameworks and (international) alignment concerning new value elements

The inclusion of a broader value element will result in broader value frameworks applied to most health technologies in the long term. Some health technologies will only produce insignificant value on specific elements (e.g. transmission value in case the underlying disease is non-infectious) and might therefore be ignorable.

Action from individual nations is unlikely to create sufficient incentives for stakeholders and notably manufacturers to bear the additional costs of data collection and model development to incorporate broader elements of value. Therefore, all stakeholders involved are recommended to discuss the need for broader value recognition and share best practices at an international level to align HTA agencies and create sufficient incentives for the industry to help develop the evidence on the broader value of vaccines.

6 Conclusion

Realising the broader value of vaccines requires the incorporation of various value elements that are currently not consistently considered as of HTA processes in England. This study's results allowed us to prioritise, from our previously developed vaccine value framework, several value elements based on their importance and the feasibility in terms of data and analytic ability required for considering these. These value elements are *transmission value*, *impact on the vaccinee/patient productivity*, *impact on carer productivity*, *impact on carer quality of life (QoL)*, *and prevention of antimicrobial resistance (AMR).* In addition, health system delivery value was proposed for consideration as part of the value element *healthcare system cost off-sets*. *Enablement value* was deprioritised mainly due to a lack of a clear agreed-upon definition.

According to the experts, the availability of data and evidence is the main barrier across most broader value elements. Progress is made on analytic tools and methods, and also the NICE methods review provides potential opportunities for inclusion of some broader value elements though more systemic change is required. While the Covid-19 pandemic has provided urgency and a political climate to reconsider the broader value of vaccines, there is a large consensus among experts that broader value elements should be considered for all health technologies and not be limited to vaccines. Achieving this requires thoughtful alignment of HTA data requirements, methods, and processes within England as well as abroad. It also requires sufficient incentives to invest in the required data collection and evidence generation. Finally, a shared understanding of the implications of broader value assessment on, for example, cost-effectiveness thresholds, discount rates, equity, and other fundamental aspects of HTA is needed.

As Covid-19 put the spotlight on the broader value of health technologies, notably those of vaccines, it is now time to prepare for their appearance at the centre stage of HTA.

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Appendix

We implemented the modified Delphi process through two round of an online survey (SurveyMonkey) leading to a virtual roundtable that was facilitated and moderated through OHE researchers.

Delphi Round 1

To differentiate the value elements, we initially asked participants to anonymously rate and rank each value element[4] on a 5-point Likert-scale concerning three main themes:

- Importance of the value element to improving the value of assessment of vaccines
- Availability of high-quality evidence related to each value element
- Technical ability to incorporate each value element into existing HTA processes

Additionally, we collected qualitative data by asking the participants to describe their underlying thought process using for each value element.

To gain more general insights on how the broader HTA environment would need to change to enable the assessment of the added value elements, we further asked participants to classify four general categories as either opportunities or barriers to changing the status quo of value assessment of vaccines in England. The categories were defined as follows:

- **Data & evidence** comprises all aspects of generating high-quality evidence to demonstrate the broader value of vaccines within an economic evaluation.
- **Methods & Tools** covers all methodological and analytical aspects of performing the economic evaluation itself, such as modelling approaches, the perspective of the evaluation, or required software and computing power.
- **Systemic flexibility** encompasses all systemic factors that hinder or support a potential change of the status quo of HTA of vaccines. Examples can be ring-fenced budgets or considerations for better alignment of appraisal approaches between the Health and Care sectors.
- **Political context** includes the current political climate and all stakeholders that might affect systemic change.

Finally, we asked participants to add any value elements that might have been missed in our original value framework. The respondents had seven days to complete the survey.

Delphi Round 2

In the second round of the virtual Delphi, participants were asked to repeat the ranking exercise according to the three themes, after being provided with the aggregated group responses from round 1. We then asked how the aggregated group response from round 1 might have affected their response in round 2.

[4] *Please note that we excluded those value elements (impact on quality of life, impact on length of life and cost-offsets to the health system) that are already included in the existing HTA methods in the UK.*

We also asked participants to name any specific challenges related to the themes 'evidence' and 'technical ability' and to name solutions how those challenges could be overcome.

Finally, we repeated the classification exercise that requires to classify four categories ('Data & Evidence', 'Methods & Tools', 'Systemic flexibility' and 'Political context') as either barriers or opportunities to realise the broader value of vaccines in the UK. However, in addition to the first round, we now asked participants to name solutions that might help to overcome the related general barriers.

As in round 1, the respondents had seven days to complete the survey.

Roundtable

The round table served as and an additional third instance of the modified Delphi process and was facilitated during one afternoon in November 2020. We split the discussions into two larger sections focussing either on specific value elements or, more generally, on how to create an HTA environment that enables the assessment of those broader value elements. Before each group exercise, the aggregated group response was presented to the participants.

During the first session, we asked each participant to pick value element that they considered either

- an **easy win:** a value element that is important and has a high probability of being accepted.
- An **important challenge:** a value element that is of such importance that extra effort and changes are justified to overcome high barriers that prevent its inclusion.
- An **unlikely success:** a value element for which inclusion is not very likely to succeed.

Participants were then asked to prioritise three value elements for a moderated group discussion that focussed on sharpening solutions to overcomes specific challenges related to each VE.

The second session focussed on more general opportunities and barriers related to the status quo of how vaccines are valued in the UK. Again, opinions from panel members were elicited using a moderated discussion.

The results over all three rounds of the modified Delphi approach were then analysed by OHE researchers serves as the main knowledge base for the rest of this report.

About us
Founded in 1962 by the Association of the British Pharmaceutical Society, the Office of Health Economics (OHE) is not only the world's oldest health economics research group, but also one of the most prestigious and influential.

OHE provides market-leading insights and in-depth analyses into health economics & health policy. Our pioneering work informs health care and pharmaceutical decision-making across the globe, enabling clients to think differently and to find alternative solutions to the industry's most complex problems.

Our mission is to guide and inform the healthcare industry through today's era of unprecedented change and evolution. We are dedicated to helping policy makers and the pharmaceutical industry make better decisions that ultimately benefit patients, the industry and society as a whole.

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- Evaluation of health care policy
- The economics of health care systems
- Health technology assessment (HTA) methodology and approaches
- HTA's impact on decision making, health care spending and the delivery of care
- Pricing and reimbursement for biologics and pharmaceuticals, including value-based pricing, risk sharing and biosimilars market competition
- The costs of treating, or failing to treat, specific diseases and conditions
- Drivers of, and incentives for, the uptake of pharmaceuticals and prescription medicines
- Competition and incentives for improving the quality and efficiency of health care
- Incentives, disincentives, regulation and the costs of R&D for pharmaceuticals and innovation in medicine
- Capturing preferences using patient-reported outcomes measures (PROMs) and time trade-off (TTO) methodology
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Registration Office Southside, 105 Victoria Street, London SW1E 6QT