AN ADVOCATE'S TOOLKIT TO SHAPING THE POLICY ENVIRONMENT

1 December 2021 HAAB Webinar: Discussion Report

For the final webinar in the HAAB series, the following speakers joined us for *An Advocate's Toolkit to Shaping the Policy Environment.*

- **Dr. Louis Garrison**, *Professor in the Pharmaceutical Outcomes Research and Policy Program in the School of Pharmacy, and Adjunct Professor in the Departments of Global Health and Health Services at the University of Washington*
- **Mark Skinner**, *Institute for Policy Advancements, Ltd.*
- **Jamie O'Hara**, *CEO at HCD Economics*
- **Cliff Goodman**, *Senior Vice President and Director, Center for Comparative Effectiveness Research, The Lewin Group*

Dr. Louis Garrison: Is the world ready for gene therapy?[i]

The resources, expertise and experiences needed to develop new payment models are not yet available in all countries and regions; therefore, we will need to collaborate internationally on the assessment of clinical and economic value.

In the *Haemophilia* supplement paper, authors sought to set the landscape for the following three elements of drug development: assessing the value of innovation, and the HTA (Health Technology Assessment) and payment models for such innovations. Subsequent speakers during this webinar went into further detail on each of these elements.

Scientific advancements over the last decades have meant that people with hemophilia can manage their condition, and their quality of life has improved significantly. However, patients still cannot avoid bleeding episode completely and still suffer from joint problems.

Gene therapy reverses genetic mutations that we previously thought would be incurable, offering a functional cure to people with hemophilia, making people with hemophilia indistinguishable from people without the disease. This allows people with hemophilia to more easily realize personal goals and reduces their burden on the healthcare system.

There has also been a large level of investment from the private sector in gene therapy. This level of investment was not anticipated 5 years ago.

Realistic expectations of gene therapy must be taken into consideration. The decision to undergo gene therapy is a personal one for the patient, and their physician must fully inform them of the benefits and risks; the patient's feelings towards these benefits and risks must be taken into consideration when deciding on whether to move forward with the therapy. Routine monitoring will also be required, meaning not all healthcare costs will be eliminated by undergoing gene therapy.

Some patients may also not be eligible for the therapy, for example if the patient has pre-existing antibodies against the delivering vector. There is also uncertainty around the durability of the treatment, which causes problems on the financing side of the matter.

There are also several ethical issues, regarding the unknown long-term side effects of gene therapy, as well as the impact such therapies would have on health equity between markets and economies.

Therefore, the access framework used to evaluate value in the hemophilia space must be evolved and optimized, both in the US and internationally.

These risks cause problems for both the private and public sector, and how the risks are shared between sectors over time must be considered. The concept of value must also be made more

patient-centric, to include more elements of the patient's experience and quality of life, going beyond traditional clinical efficacy endpoints.

Mark Skinner: Assessing the value of hemophilia treatment

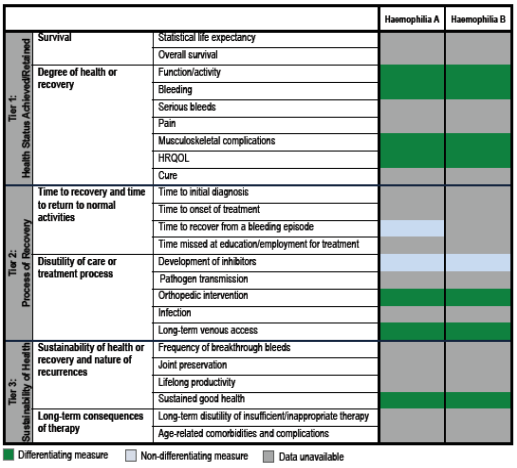
A value framework is a tool to organize information and data – they are widely used in the healthcare setting. The concept of value frameworks has emerged over the last several years, particularly when assessing value for emerging therapies. Traditional frameworks have not worked for the hemophilia community, because these frameworks rely on factors that can be counted in a clinical setting. To combat this, the value framework has emerged and will hopefully guide how we generate and collect evidence.

The value framework[ii] was initially used to analyze the value of prophylaxis but is now used to assess the value of other treatments and therapies that are emerging.

Firstly, the evidence currently available in published literature regarding the difference between standard-half life and extended-half life was assessed as a pilot exercise. Often, the information searched for is not peer-reviewed, but available through congress posters or podium presentations. Therefore, for this paper, authors manually reviewed the results of a PubMed search to identify such non-published resources, to find pieces of evidence that were important to building the value framework.

Based on this work, the investigators evaluated the level of evidence available for a variety of value factors, as identified by patients and caregivers. Value elements were organized into three tiers and the volume of published data was evaluated. Evidence was categorized into:

- (Green) areas with evidence illustrating a differentiating measure, e.g., bleeding or function relevant to standard- and extended half-life treatment
- (Blue) areas with evidence of a non-differentiating measures
- (Grey) areas where no data is available.



This gap assessment made it clear that for many elements, evidence simply is not published. Therefore, if these elements are to be taken into consideration when evaluating the value of a treatment, it's important that evidence is published in relation to these elements to put them on the map.

This could be by encouraging sponsors to generate data with regards to these fields or encouraging them to publish the evidence that is currently sitting in the form of congress posters or podium presentations.

The value framework is a tool to effectively identify both the gaps in the literature, as well as identify the differentiating features based on what is available.

Note that the above diagram was adapted from O'Mahony B, Dolan G, Nugent D, Goodman C; International Haemophilia Access Strategy Council. Patient-centred value framework for haemophilia. *Haemophilia*. 2018 Nov;24(6):873-879.

Jamie O'Hara: Health Technology Assessment for Gene Therapy in Hemophilia[iii]

HTA bodies are in place to inform decision making in a clinical setting. The meaning of HTA varies significantly between countries and regions, with HTA board direction being legally binding in some countries.

It can be difficult to conduct a HTA on a small patient population. When considering hemophilia, a static paradigm has been observed, with a burst of innovation in recent years. This includes extended-half life products, monoclonal antibodies and gene therapies. Policy makers must be informed about the landscape and these changes, and the hemophilia advocacy community are well-positioned to provide this information.

In recent years, HTAs have introduced new thresholds for paying for rare disease, recognizing the fact that investment must be attracted into the market. Instead of applying standard processes, different approaches may be applied to rare diseases.

There are many challenges when considering HTA in hemophilia. Firstly, considering appropriate endpoints is challenging given the high heterogeneity of the patient populations. There are also high costs associated with these treatments which may surpass existing cost effectiveness thresholds, meaning assessing treatments through traditional HTA process may result in a negative ruling.

HTA bodies can be diverse, with some passing rulings that are legally binding compared to some who issue guidance. As a community, it's important to understand regionally what gaps there are and what input can be provided as patient groups and advocates to influence processes and improve access to treatment for patients.

Cliff Goodman: Designing alternative payment models for durable therapies: The Case of Gene Therapy for Haemophilia A[iv]

Authors of this paper aimed to better understand alternative payment models (APMs) in the context of hemophilia A, as well as factors that determine the appropriate APM for risk-sharing arrangements for gene therapies.

Gene therapies for hemophilia are amongst the emerging durable cell and gene therapies, though the price tag is challenging. These therapies present clinical and economic uncertainty for payers, providers, patients, patients' families and manufacturers, including physiological expression, duration of effect, patient outcomes, upfront costs, variable additional costs and the uptake among patient subgroups.

These uncertainties raise questions and interest among payers and providers, as understanding and mitigating unforeseen costs that may arise due to these uncertainties is important to these stakeholders.

There are many factors that may impact decision makers' selection of APMs. This includes regulatory status, indications of a treatment, what proportion of patients may be indicated for the treatment and how many of these will seek the given treatment. In addition, outcomes of a treatment, the extent to which outcomes can be measured and the length of time it will take a patient to arrive at a given outcome also influence the APM selected by decision makers. The durability of the response to treatment, cost per patient, timespan for analysis and regional healthcare regulations all impact decision-makers' willingness to enter into a given APM.

The entry of gene therapy for hemophilia has moved discussions away from the traditional fee-for-service payments for lifetime prophylactic replacement factor and towards the development of alternative payment strategies, as many of the existing ways to pay for healthcare may not work for innovative treatments where outcomes and costs are less certain. Multi-stakeholder collaboration is required for implementing such APMs, contingent on informed and shared decision making.

In additional, growing experience with APMs across the broader field of gene therapies will enhance stakeholders' ability to design payment models to enable access to approved therapies, while managing the health of the overall population and potential financial risks.

Following the presentation, a Q&A was moderated by HAAB members Brian O'Mahony and Dawn Rotellini, providing a forum for attendees to follow up on any questions they had to the keynote presentations or any other areas they wanted Dr. Garrison and Mark Skinner's thoughts on.

The Q&A saw the following questions discussed:

Is the world ready to pay for gene therapy? Please frame your answer in relation to the US, to Europe and to low-middle income countries.

It is important to think about the USA vs Europe vs low- and middle-income countries. Economists believe that the scientific information that is embedded into these technologies is a global public 'good'. If we use that information in the US, it does not keep it from being used in South Africa for example - these are global public goods and should be financed globally.

When considering these therapies as global public goods, it's also important to note that once the innovation is created, the cost of production is relatively low. This is financed by rewarding those who invest in the innovation during the patent period and letting them monopolize the market to make the money back that was invested through the innovation period.

One-hundred billion dollars is spent a year globally on R&D, and the US picks up around 40-50% of that spend. 50 new compounds are produced a year, and these are increasingly in orphan areas such as hemophilia. We talk of rewarding the best products based on the value they create; however, it is important to think about how this creates different access problems in different systems.

When considering the fragmented healthcare system in the US, all payers are having to understand the different therapies and associated costs for these new therapies, which is a complex landscape. The cost savings for undertaking these expensive therapies with a cure outcome in the long run are also difficult to understand in a system as complicated as the US, with no one sole payer or decision maker.

In comparison, if the system has a single payer such as the NHS in the UK, it should be easier to take a longer-term view on paying for these therapies. However, when decisions are made based on annual budgets, problems arise with this multi-year valuation approach. High-cost items should be paid for over multiple years, and this is what the alternative payment mechanisms try to achieve.

How should payers change their procedures to assess treatments using a framework and how might that link to a payment model?

One of the greatest frustrations when participating in HTA meetings is the evidence and data that is important to the hemophilia community is just not available. If you read an ICER or a NICE review, for the outcomes that make a difference to lives, data is simply not available. Although a payer or a HTA agency may be willing to consider other metrics if the data is not published, then there is no way they can model it or take it into account, so it becomes purely anecdotal.

By using the rigor of the value framework and working to fill the gaps in the data it can be used by payers within their models, and not just as contextual considerations, but we can persuade the drug sponsors and developers to do a timely publication and the data will be influential.

As you move through the series of papers presented in this report's order, first assessing what data is available, then looking at how the HTA could be modified for novel technologies and then look at how they can be paid for, it's clear it all begins with the data and the value framework shows how many gaps there are in the published data.

It's clear that we have to understand what data is out there, how HTAs can assess the new therapies and how they can be paid for, and members of the community have been asking these questions for years. However, what are the next unanswered questions to start thinking about?

The difference in the therapies is not self-evident to payers and these become pieces to help us re-frame and re-structure the debate. We use these as advocacy tools, and although they become part of the formal processes, we need to understand and be as adaptable as possible to fill in the gaps. If you look at the three papers together, a strong case begins to be built that can be taken to payers and HTA bodies to show why processes must be modified for novel therapies for rare diseases in local regions.

In the medium-term, advocates must consider, has your country got the infrastructure to pay for these therapies? Does your country have the infrastructure for anything other than a one-off payment for treatments? If not, what are the barriers to this? Who will make the decision, and how can you get in the room with them to make sure your voice is heard?

Please note that all speakers' comments throughout this report do not necessarily reflect Bayer opinion.

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[i] Is the world ready for gene therapy? Garrison, L., Kleinermans, D. *Haemophilia* 2021; supp in press.
[ii] O'Mahony, B, Dolan, G, Nugent, D and Goodman, C. (2018). Patient-centred value framework for haemophilia. *Haemophilia*. 24 (6), 873-879.
[iii] Health technology assessment for gene therapy in hemophilia. O'Hara J, Neymann P, Jonsson B, *Haemophilia 2021;* supp in press.
[iv] Alternative payment models for durable and potentially curative therapies: the case for gene therapy for haemophilia A. Goodman C, Berntorp E, Wong O. *Haemophilia* 2021; supp in press.