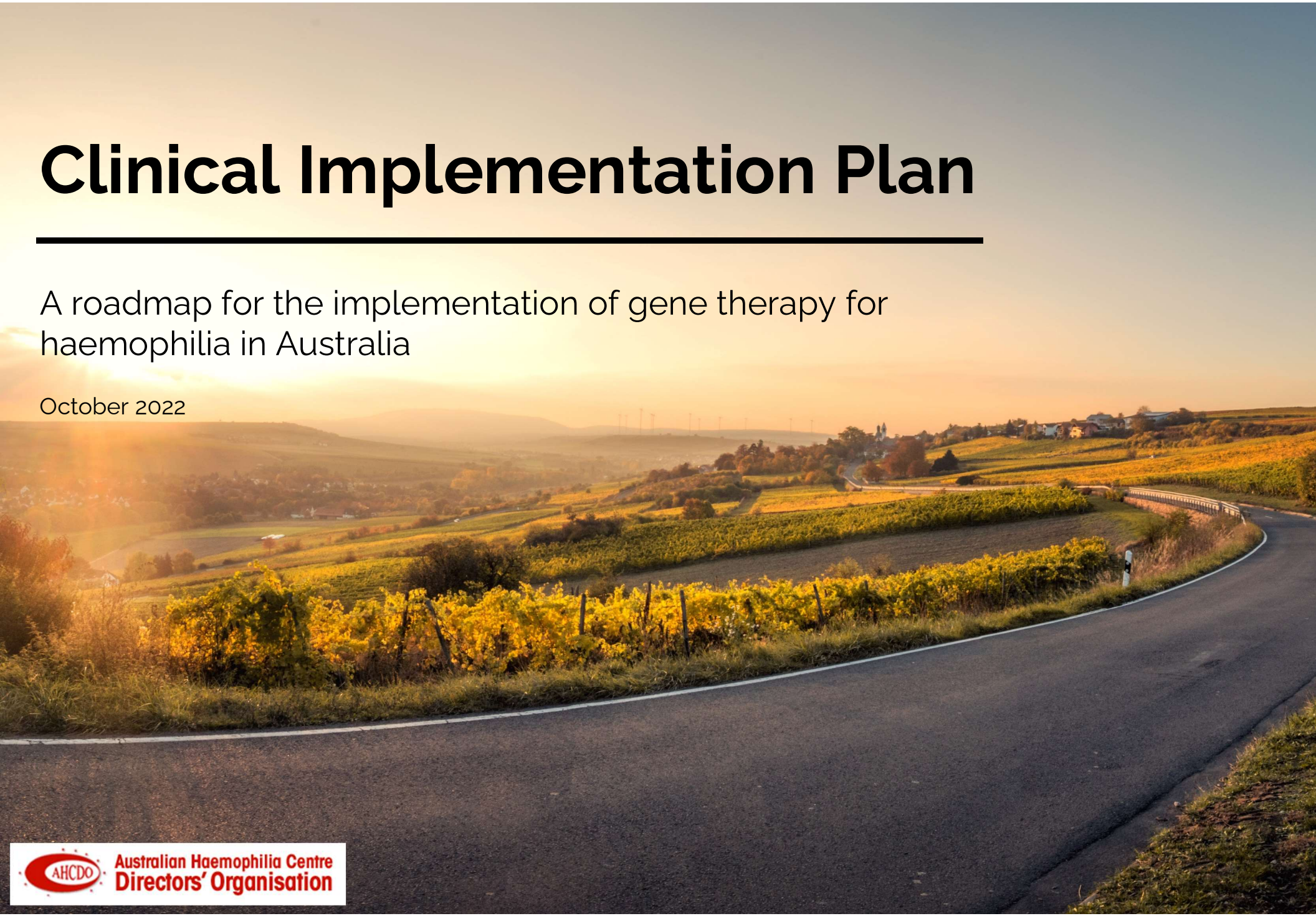
Clinical Implementation Plan

A roadmap for the implementation of gene therapy for haemophilia in Australia

October 2022



Australian Haemophilia Centre Directors' Organisation

About this Clinical Implementation Plan

Background

About AHCDO

The Australian Haemophilia Centre Directors' Organisation (AHCDO) is a national not-for-profit organisation. It brings together medical directors of Haemophilia Treatment Centres (HTCs) and other clinicians involved in the care of people with bleeding disorders.

Our role in gene therapy

Gene therapy is emerging as a potential treatment option for people living with haemophilia. Phase 3 clinical trials are well progressed, with more than 15 trials assessing various gene therapies for Haemophilia A or Haemophilia B (1).

The first gene therapy products for haemophilia are now nearing commercialisation (2). This means that, subject to satisfactory results from Phase 3 clinical trials, gene therapy is likely to become a treatment option in Australia over the coming years.

Purpose of this plan

Why has this plan been developed?

The implementation of gene therapy for haemophilia in Australia will be complex.

It will require extensive coordination and planning between Governments (both federal and state/territory), clinicians, HTCs, patients, and other stakeholders.

This Clinical Implementation Plan sets out AHCDO's position on the preferred approach to implementation of gene therapy for haemophilia in Australia, with a focus on patient need that is informed by clinical experience.

How will this plan be used?

AHCDO is uniquely well placed to represent the perspectives of clinicians involved in haemophilia care, as well as the logistical and feasibility considerations of implementing new therapies in existing HTCs.

This Clinical Implementation Plan is being made available so that the experience and insights can be used to inform planning by Governments, industry, patient advocates. and others involved in the care of people with haemophilia.

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2. Kaczmarek, R. (2021). Gene therapy – Are we ready now? *Haemophilia*, 28(Suppl.4), 35-43.

Disclaimer

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Foreword

Professor Huyen Tran
Chairman, AHCDO

On behalf of the Australian Haemophilia Centre Directors' Organisation (AHCDO), I am pleased to share with you this Clinical Implementation Plan to help pave the way for the implementation of gene therapy for haemophilia in Australia.

Supporting people living with haemophilia

Haemophilia is a serious and lifelong genetic bleeding disorder that affects approximately 3,000 Australians. It causes internal bleeding into the joints and muscles, which can be episodic or spontaneous, and results in the development of chronic pain, arthritis and disability over time. While there are a range of effective treatment options to prevent and manage bleeds, living with haemophilia can impact significantly on a person's health and quality of life.

Gene therapy: A new treatment option?

Innovation in haemophilia care is moving at pace. Multiple gene therapies are in development that will offer another treatment option for people living with moderate to severe haemophilia. Clinical trials, both overseas and in Australia, have demonstrated that a single dose of gene therapy is safe and well tolerated for both Haemophilia A and B. There are promising signs that gene therapy is effective in significantly reducing bleeding rates, although long-term data is still being collected to inform evidence about the durability of responses to gene therapy.

Leveraging the expertise of AHCDO clinicians

AHCDO's members are specialists in the management of bleeding disorders and at the forefront of innovations in care. Our Haemophilia Treatment Centres (HTCs) are the primary point of care for people with haemophilia from the point of diagnosis (typically in early childhood) through adolescence and into their adult lives. AHCDO clinicians bring a deep understanding of patients' experience of haemophilia, as well as the challenges and opportunities associated with new treatment options such as gene therapy.

A patient-centred and clinician-led approach to implementation

Gene therapy is a new chapter in healthcare in Australia. There are many unknowns about how it will be evaluated by regulators, funded by governments and made available to patients.

In developing this Clinical Implementation Plan, AHCDO is taking a proactive opportunity to start the conversation about what the future of gene therapy for haemophilia could look like in Australia and, importantly, put patient needs and clinician experience at the centre.

3,000

Australians live with haemophilia – a serious and lifelong bleeding disorder[1]

~25%

of haemophilia cases are the severe form, which involves spontaneous bleeds that have no identifiable cause[2]

Gene therapy

targets haemophilia at its source by delivering a therapeutic version of the Factor VIII or IX gene.

1. Haemophilia Foundation Australia. 2022. Accessed from: https://www.haemophilia.org.au/about-bleeding-disorders/
2. Australian Bleeding Disorders Registry. Accessed from: https://www.blood.gov.au/sites/default/files/ABDR-Annual-Report-2019-20-FINAL.pdf

Executive Summary

Gene therapy is on the horizon as a durable treatment for Haemophilia A and B. On a global scale, the first gene therapy candidates for the treatment of haemophilia have demonstrated good results in clinical trials and are now being assessed by regulatory bodies. AHCDO expects that gene therapy will become available for Australians living with haemophilia within the next five years.

AHCDO will advocate for a nationally consistent, patient-centred and equitable approach to gene therapy. As a novel therapy, there are choices to be made about how gene therapy is made available to patients and how care is delivered. A model that leverages the expertise of our national network of Haemophilia Treatment Centres (HTCs) and national framework of care will support safe and high-quality multidisciplinary team care.

All HTCs will have a role to play in gene therapy, whether as a 'hub' site (responsible for administering gene therapy) or as a 'spoke' site (supporting patients before and after their gene therapy infusion). The 'hub-and-spoke' model is recommended for the delivery of gene therapy by leading international organisations to support patient access whilst concentrating expertise and resources. Hub and spoke centres must work in partnership so that patients can benefit from continuity of care.

Implementation of gene therapy will be complex and require national cooperation. Gene therapy is highly specialised. There are many important steps in patient care in the lead-up to receiving a gene therapy infusion and in the months or years afterwards as patients are monitored and, if required, treated for side effects. Clear roles and responsibilities, a national model of care and collaborative implementation planning will be important to prevent delays to patient access.

It is time to start preparing. Gene therapy is rapidly evolving, so we should expect that the range of therapies on offer for people with haemophilia will continue to develop. However, there are many complexities and long lead-times involved in introducing a new therapy – particularly for highly complex and specialised products such as gene therapy. AHCDO welcomes the opportunity to engage with governments, clinicians, patients, patient organisations, industry and other stakeholders to ensure that Australians living with haemophilia can access proven and effective treatments in a timely and equitable manner.

Our vision: Implementation of gene therapy in Australia

As a novel and specialised treatment, the implementation of gene therapy for haemophilia must prioritise safety and quality. AHCDO proposes a product-agnostic approach that balances the needs, preferences and quality of life of patients with the capability and capacity of Haemophilia Treatment Centres (HTCs) to safely deliver gene therapy as a standard of care treatment, informed by evidence and clinical practice.

AN OPTIMAL SERVICE DELIVERY MODEL…

…IS NATIONALLY CONSISTENT

Referral pathways, patient screening, administration protocols and ongoing monitoring of gene therapy should be nationally consistent, with minimal variability between treatment centres.

…LEVERAGES EXISTING GOVERNANCE

Implementation of gene therapy should make use of the strong national framework between AHCDO, the National Blood Authority (NBA), HTCs, the Australian Bleeding Disorders Registry (ABDR) and patient representatives.

…BUILDS ON REAL-WORLD EXPERIENCE

Several treatment centres in Australia have administered gene therapy as part of clinical trials. Future implementation should make use of the expertise and infrastructure at these sites.

…IS ADAPTABLE TO INNOVATIONS IN CARE

Exponential growth in the availability of gene therapies is expected over the next decade. Implementation of gene therapy must be flexible and adaptable to future innovations.

THE IDEAL PATIENT EXPERIENCE INVOLVES…

…EQUITABLE ACCESS

There are no barriers to care for eligible haemophilia patients who wish to receive gene therapy. There must be equity of access to gene therapy, irrespective of where a patient lives.

…PATIENT CHOICE AND EMPOWERMENT

All eligible patients should be given the choice to receive gene therapy and be able to access it in a timely fashion. Patients' needs, preferences, and quality of life are put first.

…TRANSPARENT COMMUNICATION

All patients with haemophilia are informed about gene therapy by their clinicians. The risks, benefits, unknowns, follow-up commitment, and trade-offs are made transparent upfront.

…PSYCHOSOCIAL SUPPORT

The decision to undergo gene therapy is not to be taken lightly. All patients should have access to specialist psychosocial support before, during, and after a gene therapy infusion.

Making gene therapy accessible to patients

The selection of treatment sites is a key consideration for the implementation of gene therapy. AHCDO's position is that an adapted 'hub and spoke' model of service delivery is optimal for Australia to achieve a balance between facilitating patient access and concentrating expertise, resources, and costs.

What could a hub and spoke model look like in Australia?

What is a hub and spoke model?

The 'hub and spoke' model is gathering momentum internationally as an approach for delivering gene therapy.

Under the model, a selection of treatment centres become 'expert hubs' that prescribe and administer gene therapy. Other centres then become 'spokes', responsible for pre- and post-gene therapy care.

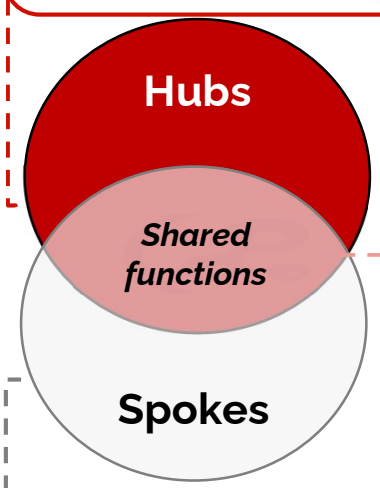
The model relies on hubs and spokes collaborating on treatment decisions and co-managing adverse events to provide safe and high-quality continuity of care to patients.

The hub and spoke model has many benefits including centralising expertise, facilitating consistent care and reducing regulatory and administrative burdens.

Full resourcing of both hubs and spokes to accommodate the introduction of a new therapy will be critical to success.

Hubs would be responsible for…

- Setting national guidance to spoke centres and patients on gene therapy for haemophilia.
- Managing supply of gene therapy including prescribing, ordering, compounding, and disposal.
- All aspects of care associated with administering gene therapy to approved patients.
- Managing immediate post-infusion side effects and co-managing adverse events with spokes.



Shared responsibility would be needed for…

- Making the decision to approve patients for gene therapy.
- Determining post-infusion monitoring and care.
- Managing and reporting adverse events.

Spokes would be responsible for…

- Assessing patients' suitability for gene therapy, including undertaking screening tests.
- Referring eligible patients to a Clinician Advisory Group to be assessed for gene therapy.
- Conducting follow-up appointments and tests with patients after their gene therapy infusion.
- Communication with patients' primary care and allied health physicians as needed.
- Providing or facilitating access to psychosocial support at all stages of gene therapy.

AHCDO'S POSITION

1.1. Gene therapy should be implemented with a 'hub and spoke' model, in line with emerging international best practice.

1.2. All adult Haemophilia Treatment Centres (HTCs) nationally should be designated as hub or spoke sites. Some hub sites will perform the roles of both hub and spoke where they are the primary point of care for haemophilia patients.

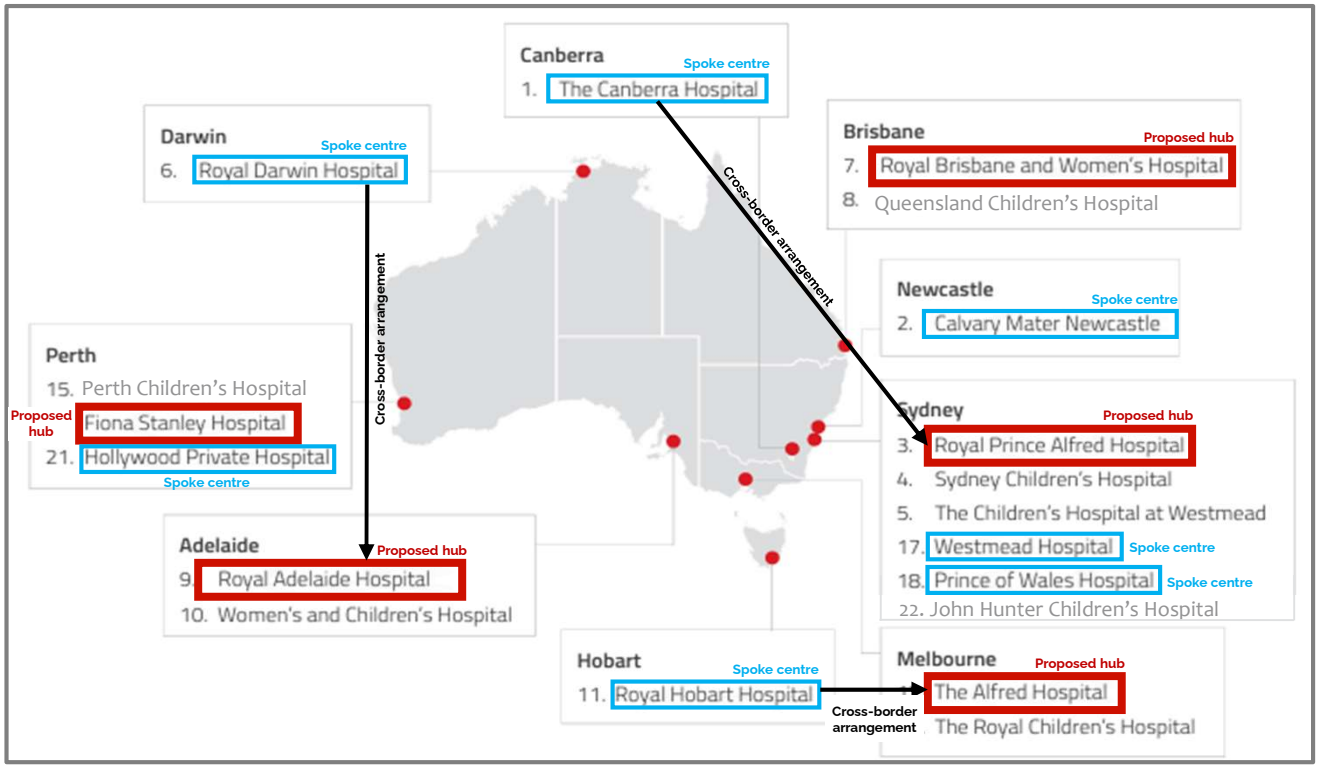
1.3. Hubs should provide national guidance to inform patient selection, monitoring and other elements of care.

1.4. Hub and spoke centres must work in partnership to ensure continuity of care to patients receiving gene therapy.

1.5. Identification of hubs and spokes should focus initially on adult treatment sites, although it is noted that gene therapy could become an option for paediatric patients in the future.

Proposed approach to site selection

AHCDO's assessment of current Haemophilia Treatment Centres (HTCs) as potential gene therapy sites



Commentary: This map shows AHCDO's proposed distribution of hub and spoke centres for gene therapy for haemophilia across Australia. It applies the principle of selecting one expert 'hub' per State/Territory for the treatment of adult patients. Paediatric treatment centres have been excluded from consideration, as much longer lead-times are anticipated for regulatory approval for gene therapy among patients aged younger than 18 years.

AHCDO'S POSITION

2.1. There should be one hub per State/Territory to balance patient access with the high costs of setup and ongoing delivery.

2.2. There must be equitable access for patients from spoke centres to access hubs, including cross-border arrangements.

2.3. The first hub sites should be clinical trial sites that already have the requisite infrastructure and expertise for gene therapy:

- Royal Brisbane & Women's Hospital (QLD)
- Royal Prince Alfred Hospital (NSW)
- The Alfred Hospital (VIC)
- Royal Adelaide Hospital (SA)
- Fiona Stanley Hospital (WA)

2.4. If sufficient funding, resources and expertise can be secured, **all States and Territories should be able to establish one gene therapy hub** in the future.

Considerations in patient selection

For people living with haemophilia, the choice to undergo gene therapy will be a significant decision. In addition to the eligibility criteria set out by manufacturers and regulators, AHCDO believes there are several factors that should be considered by clinicians when assessing the suitability of gene therapy for patients.

Eligibility criteria

Based on restrictions that have been applied in clinical trials, AHCDO expects that the below eligibility criteria may be applied to gene therapy for haemophilia in Australia:

- Adult male patients with moderate to severe haemophilia.
- No pre-existing immunity to AAV vectors.
- No active hepatitis.
- No severe liver or lung disease.

A history of factor inhibitors has been an exclusion criteria in many clinical trials, though AHCDO considers that this may be eased in future.

Additional factors in assessing patient suitability for gene therapy

Identity and mental health
Undergoing gene therapy can have a material impact on a patient's sense of self as a person with haemophilia, as well as their sense of connection to the broader haemophilia community.

Tolerance of uncertainty
Gene therapy requires patients to tolerate uncertainty about how long therapeutic effects will be sustained, given lack of long-term data about durability.

Commitment to follow-up
Gene therapy will require frequent follow-up appointments to monitor outcomes and detect side effects. This commitment is intensive for the first twelve months.

Possible need for steroids
Gene therapy patients may need to undergo steroid treatment in response to adverse events. Steroids can significantly impact mood, appetite, sleep and other functions.

Lifestyle impacts
Gene therapy can require patients to make lifestyle changes, including adherence to contraception for a period of time and abstaining from alcohol to reduce the risk of adverse events to the liver.

Timing of gene therapy
Gene therapy can only be given once at this current time. Patients should consider the best timing based on their circumstances, expected benefits, and possibility of new therapies becoming available.

AHCDO'S POSITION

3.1. All eligible patients who make an informed decision to undergo gene therapy should be able to receive it.

3.2. Treating clinicians must inform patients about the logistical, psychosocial, and lifestyle implications of receiving gene therapy.

3.3. Treating clinicians should work with eligible patients to identify the optimal timing for gene therapy that best suits the patient and their circumstances.

3.4. Gene therapy will not be a treatment option for every patient. Many eligible patients may not be suited for, or willing to undergo, gene therapy. Its use in each patient must be assessed in relation to all available therapies.

AHCDO's proposed model of care

In this Clinical Implementation Plan, AHCDO has put forward a proposed model of care that prioritises patient safety, timely access, and feasibility across the existing network of Haemophilia Treatment Centres.

Key steps in the proposed model of care

Stage	Description	Hub activity	Spoke activity	Shared activity
Identification	Identification of haemophilia patients that are eligible to undergo gene therapy. This stage includes patient education and initial discussions about risks, benefits, side effects, and the end-to-end treatment process.		✓	
Screening	Assessment of relevant clinical factors against eligibility criteria to inform the decision to proceed with gene therapy.		✓	
Decision	Patients provide enhanced consent to undergo gene therapy. Clinician approval to treat with gene therapy is facilitated via a Clinician Advisory Group with hub and spoke representatives.			✓
Supply	Prescription, ordering, storage, and compounding (if applicable) of gene therapy products.	✓		
Administration	Administration of gene therapy to eligible haemophilia patients as a day procedure (with option of overnight stay if clinically indicated or if travel home exceeds 3 hours), including pre-infusion preparations and post-infusion monitoring.	✓		
Monitoring	Twelve months of testing (initially on a weekly basis) and monitoring for patients who have received gene therapy, with check-ups at regular intervals thereafter. This stage also includes management of adverse events should they occur.		✓	✓[1]

[1] Routine patient monitoring will be primarily managed by spoke centres. Should any adverse events arise, a shared care approach between the hub and spoke site will be needed.

AHCDO'S POSITION

4.1. The model of care should leverage good practices from clinical trials, making use of existing expertise and resources.

4.2. Hub sites will be responsible for prescribing, ordering, and administering gene therapy.

4.3. Spoke sites will remain the primary point of care for patients with haemophilia. They will oversee pre-care and post-care for gene therapy patients.

4.4. Shared care will be required for the decision to treat with gene therapy and for **managing adverse events** post-infusion.

4.5. Expert hubs and spokes must work in partnership to manage monitoring, follow-up and any adverse events.

4.6. Patient education and psychosocial support must be a core focus – before, during and after gene therapy.

Model of care

Gene therapy for haemophilia in Australia

	Identification	Screening	Decision	Supply	Administration	Monitoring
Patient actions	• Discuss gene therapy with their haematologist. • Understand risks, benefits, prognosis, side effects, and commitment to follow-up.	• Undergo an eligibility assessment. • Complete screening for factor inhibitors, liver function, hepatitis & adeno-associated virus (AAV) immunity. • Access psychosocial support to inform decision.	• Review patient information and consent forms. • Complete a four-week 'cooling off period' from confirmation of eligibility. • Provide enhanced consent to undergo gene therapy.	• Agree a date and location to receive gene therapy with the hub centre. • Advise the hub if travel and accommodation is required.	• Attend the infusion clinic at a hub site on the agreed date. • Receive pre-infusion care, gene therapy infusion and post-infusion monitoring. • Overnight hospital stay if clinically indicated or if significant travel from hub.	• Attend appointments (initially weekly) at their spoke centre • Weekly monitoring of factor levels, vector shedding and liver function. • Access psychosocial support if needed
Spoke centre actions	• Provide information on gene therapy in the context of all treatment options at annual patient reviews. • Discuss risks, side effects and potential adverse events. Manage patient and family expectations.	• Assess and discuss patient suitability and eligibility. • Perform screening tests. • Arrange access to psychosocial support. • Provide information and education about gene therapy to the patient.	• Provide patients with detailed documentation (e.g. consent form, information sheet, FAQs). • Participate in a national Clinician Advisory Group to recommend the patient for gene therapy.	• Review and sign-off on the hub's Patient Treatment and Monitoring Plan.	• Remain available to the hub for planning and treatment decisions pre- and post-infusion.	• Conduct patient monitoring for 12 months (weekly, then regular intervals). • Engage the treating hub to co-manage adverse events. • Participate in fortnightly call with treating hub. • Provide or facilitate access to psychosocial support.
Hub centre actions		• Provide advice to spoke centres on eligibility and patient suitability. • Define and communicate screening requirements to spoke centres.	• Lead a Clinician Advisory Group to assess patients for gene therapy. • Develop and maintain key patient information and consent documents and share with spoke centres.	• Write prescription for gene therapy for eligible patients. • Place order to manufacturer and manage compounding, storage, and disposal. • Develop a Patient Treatment and Monitoring Plan for joint sign-off by the spoke centre.	• Administer pre-infusion medications (e.g. steroids). • Administer gene therapy, including clinical observations and immediate post-infusion monitoring. • Provide post-infusion advice to patient.	• Provide treatment summary to the spoke centre. • Participate in a fortnightly call with treating spoke. • Available to co-manage adverse events with spoke. • Develop guidance on managing adverse events, including commencement of corticosteroids with abnormal LFTs.
Data and reporting	• Draw on the Australian Bleeding Disorders Registry (ABDR) to identify eligible patients.	• Screening results to be recorded in the ABDR.	• Patient consent and Clinician Advisory Group decision to be recorded in the ABDR.	• Product, dosage and dates to be recorded in the ABDR for each patient.	• Infusion details and clinical observations to be recorded in the ABDR for each patient.	• Monitoring data, adverse events and long-term quality of life measures to be recorded in the ABDR.

Note: In Australia, hub centres will also fulfil the responsibilities of spoke centres for some patients. For example, the Royal Prince Alfred Hospital in NSW could be a gene therapy treatment hub for all patients in NSW. It would also fulfil the responsibilities of a spoke centre for those patients who ordinarily receive care at the hospital's Haemophilia Treatment Centre.

Enablers of success

The successful introduction of gene therapy for haemophilia will require that all elements of governance, training, data, reporting and other operational activities are considered and adequately funded. Key areas of focus are identified below.

CLINICAL GOVERNANCE

As a novel therapy, strong clinical governance will be required to ensure the safe and efficient implementation of gene therapy. Key considerations include:

- Establishment of a national advisory and decision-making forum with representation of all States and Territories (which could be led by AHCDO to guide and oversee a nationally consistent implementation of gene therapy.
- There is a strong national governance framework for managing bleeding disorders that fosters collaboration between AHCDO, HTCs, National Blood Authority (NBA), Haemophilia Foundation Australia (HFA), and others. Where possible, efforts should be made to integrate gene therapy within this framework.

CLINICIAN EDUCATION

Haemophilia patients access care from various clinicians and allied health staff through the comprehensive care model. Educating the multidisciplinary care team about gene therapy will be important for consistency and safety.

- All those involved with care for haemophilia patients should be equipped to support patients undergoing gene therapy, but only haematologists need to be able to direct care.
- Hubs will be well placed to set national guidance on the best approach to implementing the model of care. Additional resourcing will be needed to upskill hub and spoke staff.
- Partnerships with key organisations such as patient advocates and professional clinical groups will be important to promote education and share key messages.

DATA AND REPORTING

The ability to capture, assess and learn from patient data will be critical to inform clinical decisions and service planning. Data and reporting needs must be considered early in implementation.

- The Australian Bleeding Disorders Registry (ABDR) is used daily by clinicians in the management of haemophilia patients. It captures treatment information and informs understandings of prevalence and incidence.
- The ABDR is AHCDO's preferred platform for monitoring gene therapy. It is anticipated that a new module would need to be built to support data capture, ordering, and event reporting.
- As a novel therapy, consideration should be given to long-term patient outcome data including quality of life measures.

FUTURE-PROOFING THE MODEL

The field of gene therapy is moving at a fast pace, which will have ongoing implications for clinical practice and patient selection. Implementation of gene therapy must be designed with adaptability in mind.

- In the coming years, gene therapy may become available for new populations, such as paediatric haemophilia patients. This would impact the demand for gene therapy.
- Similarly, gene therapies may become available for other conditions in Australia. This may have implications for service delivery, site selection, and knowledge sharing between sites.
- While AHCDO's current vision is for there to be one gene therapy hub per State/Territory, the optimal service delivery model may vary based on future take-up and demand.

AHCDO'S POSITION

5.1. The introduction of gene therapy should leverage the existing national framework for managing haemophilia.

5.2. The Australian Bleeding Disorders Registry (ABDR) should be used as the primary source to capture patient data and outcomes associated with gene therapy.

5.3. A national approach to clinician education should be considered to support national consistency, development of specialist knowledge and patient safety.

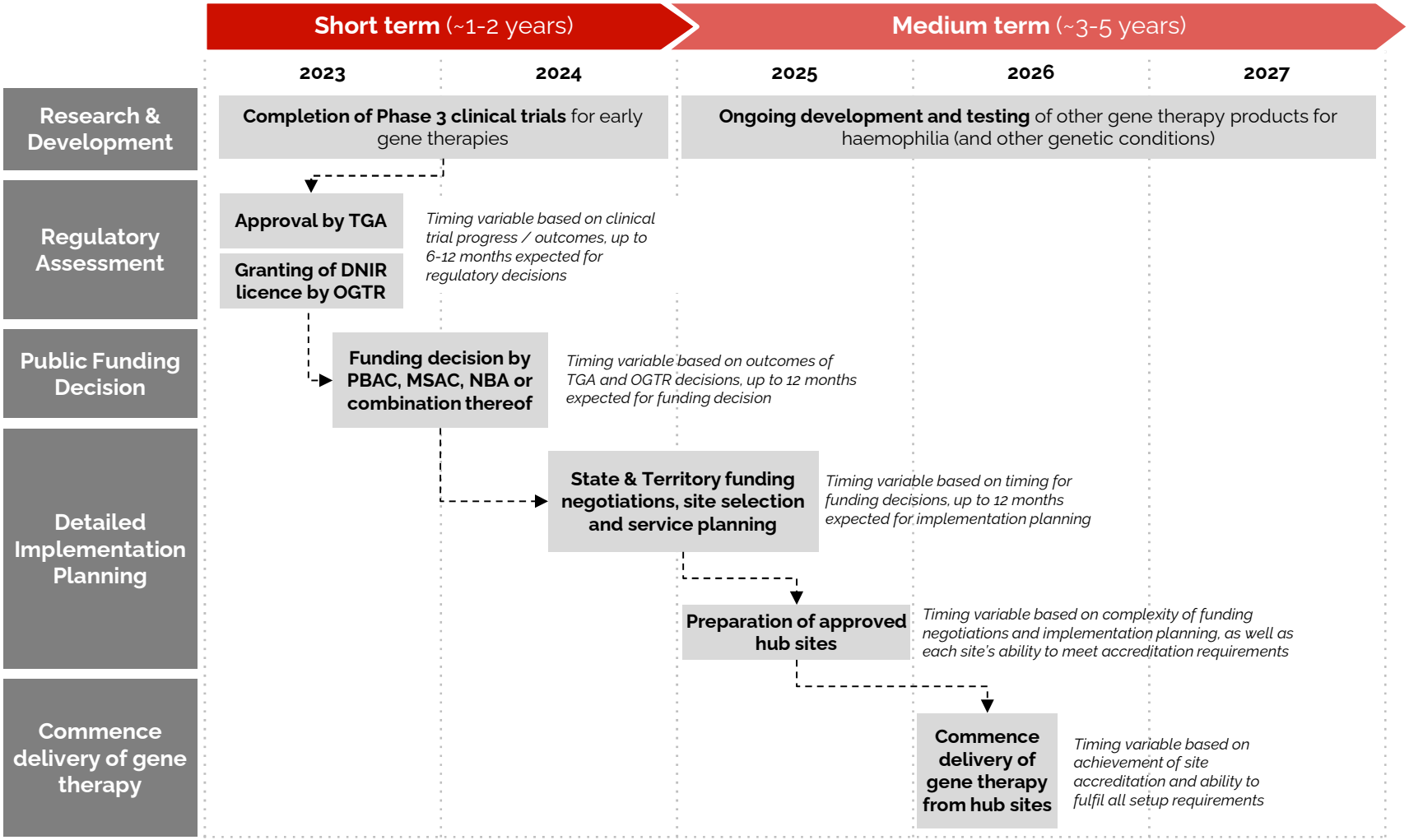
5.4. Gene therapy is a fast moving field. **The initial model must be scalable and adaptable to future changes**.

Acronyms

DNIR = Dealing Not Involving Intentional Release
MSAC = Medical Services Advisory Committee
NBA = National Blood Agreement
OGTR = Office of the Gene Technology Regulator
PBAC = Pharmaceutical Benefits Advisory Committee
TGA = Therapeutic Goods Administration

Key implementation milestones

There remains uncertainty about the introduction of gene therapy for haemophilia in Australia, with numerous products in development and completion of Phase 3 clinical trials still underway. However, based on progress to date in Australia and internationally, AHCDO assesses that implementation planning for gene therapy will span up to the next five years.



Preparing for implementation

In the short to medium term, AHCDO anticipates that the following tasks will be required to enable the implementation of gene therapy in Australia. We welcome the opportunity to work with other stakeholders to refine our understanding as implementation planning progresses.

	AHCDO	Haemophilia Treatment Centres (HTCs)
Shorter term (1-2 years)	**Monitor developments in gene therapy research** • Conduct ongoing horizon scanning of progress internationally. • Develop a consensus statement on gene therapy and its proposed place in practice. • Develop a briefing paper to inform Health Technology Assessments (HTA) that sets out which patients are expected to benefit most from gene therapy. **Develop clinical governance framework for gene therapy** • Establish a sub-committee to advise on the national implementation of gene therapy. • Design Terms of Reference for gene therapy Clinician Advisory Groups. • Define requirements for data collection and reporting, including adverse events. **Prepare the haemophilia treatment landscape for gene therapy** • Implement changes to the Australian Bleeding Disorders Registry (ABDR). • Lead a patient acceptability survey and population sizing to inform patient volumes. • Map high-level resourcing, equipment and funding requirements for gene therapy. • Assess the capacity of HTCs to deliver gene therapy (patients per week). • Develop an education and training strategy to upskill HTC staff in gene therapy. • Provide communication updates to the patient community and patient advocates. • Develop transition plans to support a shift from clinical trials to routine care at hubs.	• Provide input to, and support for, design and planning activities being undertaken by AHCDO.
Medium term (3-5 years)	**Undertake detailed implementation planning** • Refine the model of care for gene therapy for haemophilia (with stakeholders). • Develop detailed clinical guidelines for use of gene therapy for haemophilia. • Develop patient information and education resources for nationwide use. • Develop templates and forms (e.g. enhanced consent, checklist) for nationwide use. • Develop clinical procedure documents for nationwide use. **Support the introduction of gene therapy in Australia** • Establish a Clinician Advisory Group to assess patients for gene therapy. • Coordinate national quarterly adverse event reporting for gene therapy,	**Prepare hub sites** • Establish or transition gene therapy facilities including labs, pharmacies, and Office of Gene Technology Regulator (OGTR) licences. • Achieve site accreditation to deliver gene therapy. • Implement processes and procedures in line with national guidance provided by AHCDO. • Establish formal communication protocols to support shared care of gene therapy patients with spoke sites. **Prepare spoke sites** • Implement processes and procedures in line with AHCDO guidance.

Key implementation risks and mitigations (1/2)

#	Risk	Description	Likelihood	Impact	Rating	Proposed mitigations
1	**Regulatory and funding approval**	Gene therapy does not become accessible to patients in Australia within expected timeframes due to: • Delays to, or failure to achieve, regulatory approval of gene therapy products by the Therapeutic Goods Administration (TGA) and/or Office of the Gene Technology Regulator (OGTR). • Delays to, or failure to secure, public funding for gene therapy.	Possible	Major	**High risk**	• Monitor clinical trial progress and international developments to identify potential obstacles early. • Early engagement with government.
2	**Real-world efficacy**	Gene therapy does not deliver expected therapeutic results for patients with haemophilia, either in the short term or over the long term.	Possible	Major	**High risk**	• Manage expectations about gene therapy, including communication of risks and unknowns.
3	**Cost of delivering gene therapy**	States & Territories do not have sufficient budget to fund the cost of establishing hubs and/or funding cross-border arrangements.	Possible	Moderate	**Medium risk**	• Early engagement with State & Territory Governments to support budget allocation and service planning.
4	**Failure to achieve accreditation**	Hub sites are unable to secure accreditation to deliver gene therapy.	Unlikely	Moderate	**Low risk**	• Leverage experience from participation in clinical trials. • Share knowledge and insights between hubs. • Understand and prepare for requirements early.
5	**Capacity of hub sites to deliver gene therapy**	Hubs are unable to meet patient demand due to capacity limits (noting early and indicative estimates that hubs could typically support a throughput of ~1-2 patients receiving gene therapy each week).	Possible	Moderate	**Medium risk**	• Model expected patient volumes to inform resourcing decisions.
6	**Capability to deliver gene therapy**	• Hubs lack the specialist expertise, knowledge, skillsets or operational resources (e.g. procedures) to safely deliver gene therapy. • Spoke lack knowledge, skills or operational resources (e.g. procedures) to monitor and support patients who have received gene therapy.	Unlikely	Major	**Medium risk**	• Develop national guidance to support hubs & spokes. • Leverage expertise built from clinical trials.

Key implementation risks and mitigations (2/2)

#	Risk	Description	Likelihood	Impact	Rating	Proposed mitigations
7	**Resourcing impacts of gene therapy**	Sites are unable to meet resourcing demands for gene therapy, including: • Commitment by haematologists, hepatologists and other specialists. • Experienced lab, pharmacy and technical staff. • Nursing staff to oversee patient monitoring. • Psychosocial resources for mental health support.	Likely	Major	**High risk**	• Early identification of resourcing requirements to safely deliver gene therapy • Develop a national workforce plan to support recruitment and retention • Seek additional government funding to cover necessary skillsets
8	**Timely access to gene therapy**	Patients are unable to receive timely access to gene therapy due to bottlenecks resulting from manufacturing, supply or clinic capacity.	Unlikely	Moderate	**Low risk**	• Estimation of patient volumes to inform capacity planning • Negotiations and service agreements with manufacturers
9	**Communication breakdowns between sites**	Hub and spoke sites lack efficient and/or effective mechanisms for communicating and information sharing about patients who have received gene therapy, with impacts on continuity or quality of care.	Unlikely	Major	**Medium risk**	• Establish formal mechanisms nationally for facilitating hub and spoke collaboration • Make use of nationally accessible systems and registries (e.g. (Australian Bleeding Disorders Registry) ABDR)
10	**Limited or fragmented access to data**	There is limited or fragmented access to decision, operational and outcome data relating to patients who have received gene therapy, resulting in inefficient processes and potential reporting gaps.	Possible	Moderate	**Medium risk**	• Early identification of data and reporting needs • Implement new module and/or other upgrades to ABDR to support gene therapy • Make use of nationally accessible systems and registries (e.g. ABDR)

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AHCDO Gene Therapy Working Group

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- Associate Professor Chris Barnes, VIC
- Dr Julie Curtin, NSW
- Dr Liane Khoo, NSW
- Dr Simon Brown, QLD
- Dr Stephanie P'Ng, WA
- Dr Tina Carter, WA

Stakeholder interviews

- Haemophilia Foundation of Australia (HFA)
- NSW Health
- Office of the Gene Technology Regulator (OGTR)
- Therapeutic Goods Administration (TGA)
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