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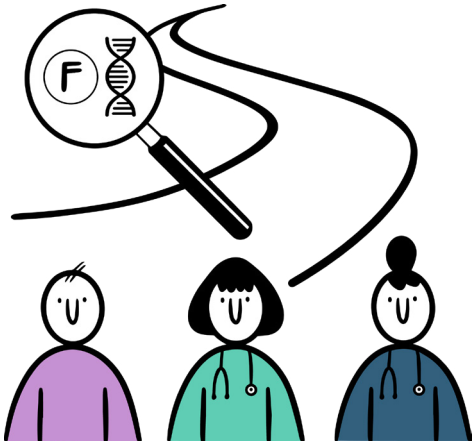
CLINICAL PRACTICE

# The journey of gene therapy in haemophilia – putting the patient at the centre of the hub and spoke model

Declan Noone, Jan Astermark, Brian O'Mahony, Flora Peyvandi, Kate Khair, Luke Pembroke, Kathryn Jenner

As gene therapy for haemophilia is now licensed in Europe, and the hub and spoke approach is widely promoted for its delivery and follow-up, it is essential that people with haemophilia (PwH) who are eligible and opt to have this treatment are enabled to obtain the maximum benefit. Ensuring the pathway that makes up the patient gene therapy journey is effective is key to achieving this. EAHAD and the EHC have recommended that gene therapy is delivered through a hub and spoke model of care to ensure that the right expertise is available throughout the various stages of the haemophilia gene therapy journey. Effective communication between hub and spoke centres is essential, and the processes that make up the journey must be understood clearly by both PwH and the multidisciplinary teams delivering their care. The starting point for this is to take each step of the gene therapy journey in turn – through initial engagement, eligibility, detailed patient education, informed decision-making, dosing, and follow up in year 1, year 2 and beyond – and to consider and identify the roles and responsibilities of the patient, the hub centre and the spoke centre. It is important that the expectations of both health care practitioners (HCPs) and patients are aligned with the key challenges and goals associated with each step. Understanding these




The patient journey in haemophilia gene therapy is complex and multifaceted, presenting challenges to the hub and spoke model of care. Understanding these from the patient viewpoint will help ensure people with haemophilia receive the information, guidance and support they need throughout their gene therapy journey.

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**from the patient point of view will help to ensure that the individual PwH treading this path receive the information, guidance and support they need from hub and spoke HCPs throughout their journey, and that they, as the patient, remain the focus of care. Visualising the journey may help to explain the gene therapy clinical pathway to PwH and could provide a useful tool for HCPs in spoke centres. Visualisation may also serve as a tool for facilitating discussion, not only in terms of initial engagement and education, but throughout the haemophilia gene therapy journey.**

**Keywords:** Haemophilia, Gene therapy, Hub and spoke care model, Patient-centred care, Decision making, Follow-up

With the first gene therapy now having conditional marketing authorisation in Europe for the treatment of severe haemophilia A in adults without a history of inhibitors and without detectable AAV antibodies, it is only a matter of time before gene therapy for haemophilia becomes more widely available. It is essential that people with haemophilia (PwH) who decide to opt to have (and are eligible for) gene therapy are enabled to obtain the maximum benefit from this treatment. Ensuring the pathway that makes up the patient gene therapy journey is effective is key to achieving this.

Preparation, administration and follow-up for gene therapy is different from other haemophilia therapies and will necessitate a new model of collaborative care [1]. The European Association for Haemophilia and Allied Disorders (EAHAD) and the European Haemophilia Consortium (EHC) have recommended that gene therapy for haemophilia in Europe is delivered through a hub and spoke model of care [2].

The hub and spoke concept is not new in haemophilia care and is, to some extent, existent within the network of Haemophilia Comprehensive Care Centres and Haemophilia Treatment Centres outlined by EUHANET [3]. For gene therapy, the hub centres should be designated haemophilia centres, and both hub and spoke must have haemophilia specialist knowledge to ensure appropriate care and follow-up [4]. This model of care means that the right expertise is available through the various stages of the haemophilia gene therapy journey. In the hub centre, there is expertise on dosing, the potential need for steroids, and aspects related to response rates, for example. The spoke, meanwhile, is likely to be the patient's trusted centre where a longstanding care relationship has developed. All of these aspects are important, but effective communication and coordination between hub and spoke centres is essential [5].

The gene therapy care pathway must be understood clearly by both PwH who consider and opt to have it and the multidisciplinary team of health care practitioners (HCPs) who are involved in this journey and deliver their care. A focus on the patient and informed shared decision-making are key, alongside understanding of the processes and different stages, the roles of hub and spoke, and the challenges associated with these.

## INITIAL ENGAGEMENT

All people with haemophilia (PwH) should have access to general information on gene therapy for haemophilia (Figure 1). Initial engagement with the concept of gene therapy creates awareness of its potential as a treatment option. This is the point at which the individual engages with basic education around gene therapy, which may come from a variety of sources including individual research, peers, and patient organisations. The discussion of gene therapy may be raised within the haemophilia centre, either through the clinical team presenting it as a treatment option or individuals asking about the concept. This may happen at a hub or a spoke, depending on where individual PwH usually receive their care. In many cases, it will be spoke clinicians who are responsible for initial communication about gene therapy [5].

While PwH may not be seeking in-depth information at the 'initial engagement' stage, it is important for members of the clinical team at spoke centres – where there is likely to be less gene therapy-specific expertise – to have enough clear, accessible information to provide a broad overview of what haemophilia gene therapy is [6]. If the conversation is initiated by a patient at a spoke centre, it may be appropriate to facilitate a discussion with an expert at the hub centre.

The aim at this stage should be for PwH to establish a good general understanding of gene therapy through clear, basic education, including an understanding of the requirements and commitment involved. However, this should not preclude a much more detailed discussion if the individual wants to go into more depth (see Detailed Education, below). In all cases, initial discussions around gene therapy should form part of a wider discussion about their overall care, including life and health goals in the short and long term, and what part gene therapy may (or may not) play in this. Alternative available therapies and new therapies likely to become available in

the near future should be part of this discussion. Ideally, hub and spoke centres should collaborate with national patient organisations around the supply of educational material about gene therapy to ensure the availability of consistent information throughout a country.

## ELIGIBILITY

Once PwH have a general understanding of gene therapy, their eligibility should be assessed if they are interested in pursuing it as a treatment option (Figure 2). Establishing eligibility before engaging in more in-depth discussion of the process and potential impacts may benefit the individual by clarifying which gene therapies they are eligible for and enabling a more detailed conversation at an earlier stage about how these compare to their current treatment.

Only those aged over 18 with severe haemophilia, without inhibitors, who do not have neutralising antibodies to AAV and do not have significant liver damage are currently eligible to have gene therapy. They will have a blood test to check for antibodies that indicate an existing immune resistance to AAV vector used to deliver the gene therapy. The blood sample will be taken at the patient's haemophilia centre (hub or spoke) for testing and analysis as a first step. Further specialised testing may be undertaken at the hub or a regional/national/international central laboratory. Information from liver and cardiac health assessments should be similarly recorded. Eligibility criteria for specific gene therapies will be governed by each product's licence. However, any existing comorbidities will also need to be considered, as they may affect the individual's ability to tolerate other medications such as steroids/immunosuppressants if they are needed.

One of the key challenges here relates to how the hub and spoke centres are networked and communicate nationally, and potentially internationally. Regardless of where blood is taken or where liver and cardiac monitoring take place, the results must be recorded in such a way that they can be accessed and reviewed by both hub and spoke multidisciplinary teams [5]. This information would also be helpful in establishing a database of people with haemophilia who may be eligible for gene therapy in the future (although retesting for AAV antibodies would also be required), and in planning and setting expectations around how treatment may be delivered. Another aspect that should also be considered is the linking of data to international registries such as the World Federation of Hemophilia (WFH) Gene Therapy Registry.

While relatively straightforward in clinical terms, the challenges associated with establishing eligibility for gene therapy for individual PwH should not be underestimated and must be addressed. Gene therapy may be considered as an option before eligibility is known, but discussion around expectations is important

**Figure 1. Initial engagement**
PwH may seek information on gene therapy from a variety of sources, including their treatment centres. Both hub and spoke clinicians must be able to provide enough clear, accessible information to enable a good general understanding of gene therapy.

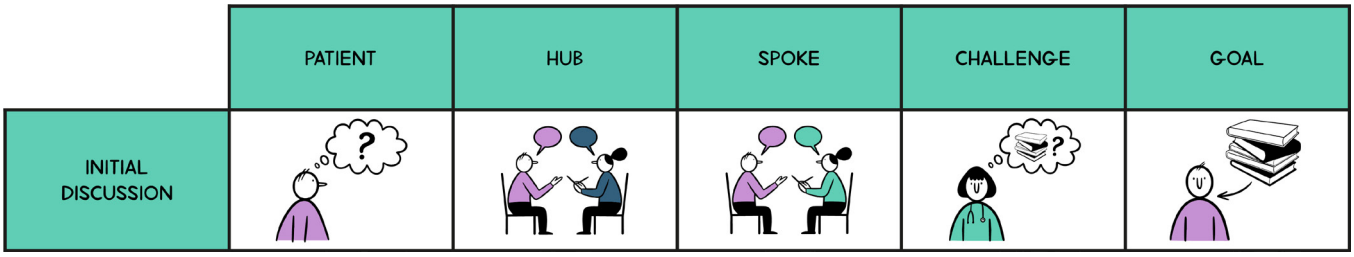
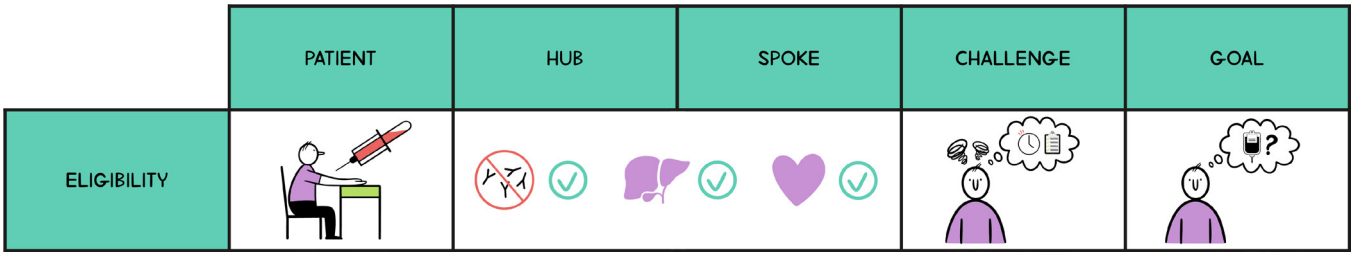



**Figure 2. Eligibility**
When establishing eligibility for gene therapy, a blood sample will be taken from the patient to check for antibodies to the AAV vector, and liver and cardiac health. This can be a challenging and potentially stressful time for PwH but enables decisions around future treatment.



– PwH must understand that there are reasons why it may not currently be possible for them to have gene therapy [7]. PwH who find that they are not eligible for gene therapy may need additional support. This may be a challenge for the individual's treatment centre, which will usually be the spoke.

The goal at this stage is to enable the individual to identify a direction for their future treatment, whether this means confirming eligibility for gene therapy, understanding the potential range of response to a particular type of gene therapy, or understanding they are not eligible for the gene therapy treatments that are currently available.

## DETAILED EDUCATION

Once eligibility is established, in-depth education is key in ensuring that PwH and their families are empowered to participate fully in the decision-making process and make fully informed decisions about their treatment [8,9] (Figure 3). Comparisons and discussions around alternative therapeutic options that are available or likely to become available in the near future should form a core part of this [10]. Partners could also be included in these conversations as they may be impacted in the choice to have gene therapy [8].

Managing expectations around the efficacy and effects of gene therapy is essential [11]. The potential benefits should be explained based on the existing body of evidence of the specific gene therapy, but its limitations should be understood. It is important that PwH are aware that there is no way to know how an individual will respond to gene therapy and/or how long its effects may last in the body. Potential side effects should be discussed alongside known and unknown complications and strategies that may be used to mitigate these [12,13]. This should include possible adverse events that may arise as a result of mitigation strategies, i.e. from use of steroids [9]. The irreversible nature of gene therapy must also be clearly understood.

Individual circumstances and treatment goals should be considered as part of education around gene therapy. The decision as to whether to have gene therapy should be aligned with life choices [13] – for example the timing of having children. While an individual may be interested in gene therapy, it may not be an appropriate time to pursue it as a treatment option. Committing to an initially intensive follow-up regimen must be a consideration – the need for numerous hospital visits during initial monitoring may cause difficulties with employers. The request to share data on outcomes is also a commitment, and it is important that PwH considering gene therapy understand the benefit of sharing data over the long term with repositories such as the WFH Gene Therapy Registry [14]; i.e., building knowledge and answering questions around long-term safety and efficacy.

Many PwH rely on the care team at their treatment centre as their key source of information about new haemophilia treatments, and both hubs and spokes will be involved in this stage of the patient gene therapy journey. Clinicians and HCPs at hubs and spokes must be prepared to assist in answering clinical questions about gene therapy [1,6]. As the centre of haemophilia gene therapy expertise, the hub should take the lead in gene therapy education. To ensure that individual PwH are fully supported, information about patient gene therapy discussions should be shared between hub and spoke based on a structured approach. While national authorities may take the lead in how this is planned at country level, it is important that PwH have access to the same level of information and detail about gene therapy, delivered in a systematic way, regardless of where they are located nationally. In all cases, any text-based educational/information materials should be available in the local language.

PwH should have the opportunity to speak with as many people as they feel necessary to gather the information they need to make an informed

**Figure 3. Detailed education**
In depth education is key to ensuring that individual PwH are able to make an informed decision about whether or not to have gene therapy. Hub and spoke centres must both be prepared to answer clinical questions; structured information on discussions should be shared between hub and spoke. This step should be considered alongside that for 'Informed Decision' (Figure 5).

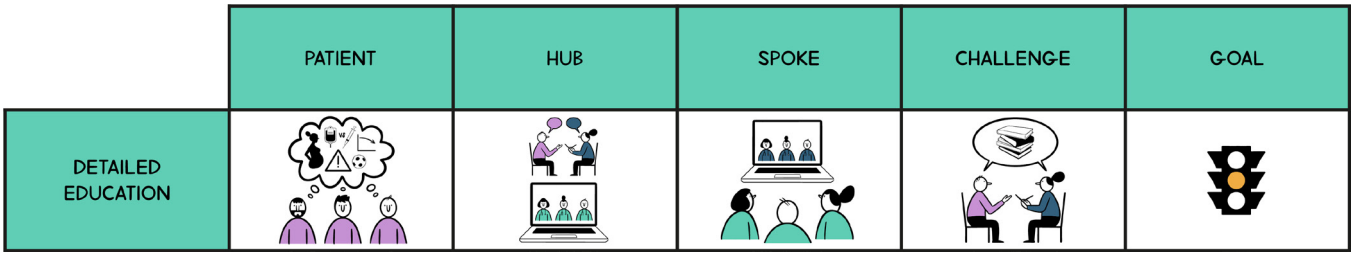


Figure 4.
Core information needed by people with haemophilia before making an informed decision on gene therapy. Where the information provided is text-based, this must be available in the local language.

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|---|
| Comparison of individual expectations of gene therapy with other available or potential therapies (coming in the next 2–5 years) |
| Understanding of the potential response to gene therapy and what this may mean, including the possibility of no response |
| Understanding of how long a response to gene therapy may last |
| Awareness of other medications that may be needed if gene therapy is undertaken |
| Awareness of current known risks of gene therapy and consideration of how these weigh up against potential benefits |
| Understanding that there are potential unknown risks with gene therapy for which there is currently no or limited information |
| Understanding of the need to commit to an initially intensive follow-up regimen and the benefit of sharing outcome data in the long term |

decision about whether to have gene therapy. While conversations with clinicians are key, patient organisations and peers also play a valuable role. Opportunities for discussion between PwH considering gene therapy and those who have had gene therapy should be supported and enabled by hubs and spokes. Having larger patient populations, hubs will be best placed to establish peer-to-peer groups where both positive and negative experiences of gene therapy can be shared. Individuals who have received gene therapy and who have the ability to provide peer support should be identified and invited by their clinical team or patient organisation. It is important that those who step into this role are confident in sharing their subjective experience in a balanced non-influential way, and that they are aware of the broad array of outcomes that are possible. This will require some degree of collaboration between the peer support candidates, patient organisations and clinical teams.

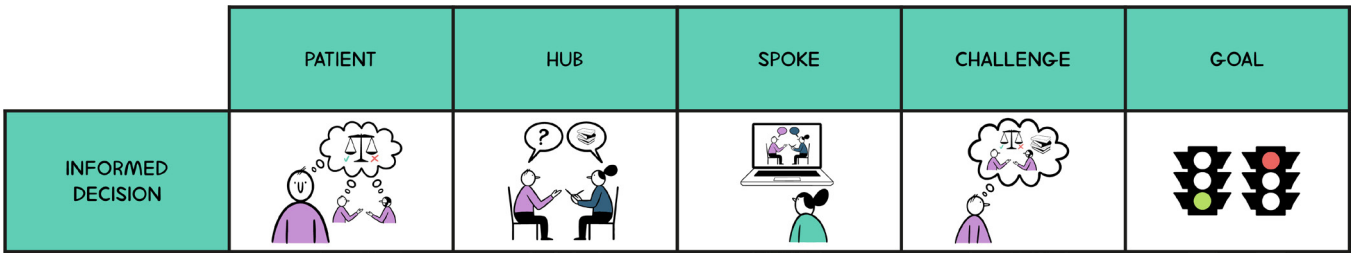
There are challenges for hubs, spokes and PwH at this stage in the patient gene therapy journey. For clinicians, these are centred on ensuring that the information they provide enables individual PwH to make a truly informed decision about whether to have gene therapy [15,16]. In addition to having appropriate knowledge, it is essential that clinicians and HCPs, at hub centres in particular, are able to communicate this in way that patients understand [6,10]. The corresponding challenge for PwH is ensuring that they have enough information, and that they understand it enough, to go on to have the discussions that will enable to them to make an informed decision about whether to have gene therapy (Figure 4).

## INFORMED DECISION

For the patient, informed decision-making is potentially the most difficult part of the haemophilia gene therapy journey (Figure 5). This stage should be considered alongside the education stage. Although the goal is to arrive at a decision, the means of doing so is a process that should take as long it needs to, however long that is, and must never be rushed [9,10]. There are risks and uncertainties to consider, and with current technology, gene therapy for haemophilia is once-only treatment – a decision made now could potentially rule PwH out of other gene therapies going forward.

Weighing up the benefits will require support from HCPs at both hub and spoke, with the hub again taking the lead as the centre of expertise. The approach should be representative of true shared decision-making [1,17], based on structured, open and honest conversation to ensure, as far as possible, that

Figure 5. Informed Decision
The process of informed decision-making should centre on enabling PwH to weigh up the benefits and risks of gene therapy. This should be supported by both hub and spoke, with information on discussions shared between them. Conversations with peers who have had gene therapy can be helpful as part of the education that supports this informed decision-making. This step should be considered alongside that for 'Detailed Education' (Figures 3 and 4).





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the benefits and risks to each individual are clear. It is important that results of the discussion are shared with the spoke to ensure that HCPs at the individual's 'home' treatment centre are also fully aware and able to best support them. Conversations involving both hub and spoke should be considered.

The challenge for the individual considering gene therapy is to bring the information they have to a point where they feel comfortable to make a decision; for hubs and spokes, as with the education stage, it is ensuring that they have enough accessible and understandable information, and supporting and helping them through their decision. The range of outcomes must be fully understood, and PwH must realise that it is as acceptable not to go ahead with gene therapy as it is to agree to it [18].

At the point where an individual has decided they want to go ahead with having gene therapy, it is essential that their care team ensures that they are certain. The challenge for the patient lies, of course, in making their decision; for hub and spoke, it is supporting and enabling them to do this and ensuring that it is personal decision based on clear understanding of the process and what the individual believes is right for them.

In the SHARE approach to shared decision-making developed by the Agency for Healthcare Research and Quality (AHRQ) in the US, the final step is evaluation of the decision and it is recommended that the decision is revisited and reviewed after a period of time [19]. As gene therapy is a one-time, irreversible treatment, this step is critical. As part of the evaluation process, discussion and even challenging of the decision by a psychologist or patient advocate may be prudent. Encouraging the individual to sign a non-binding agreement on their decision is also an option. While the discussion around the decision is likely to take place at the hub, both hub and spoke must be involved in this process.

## DOSING

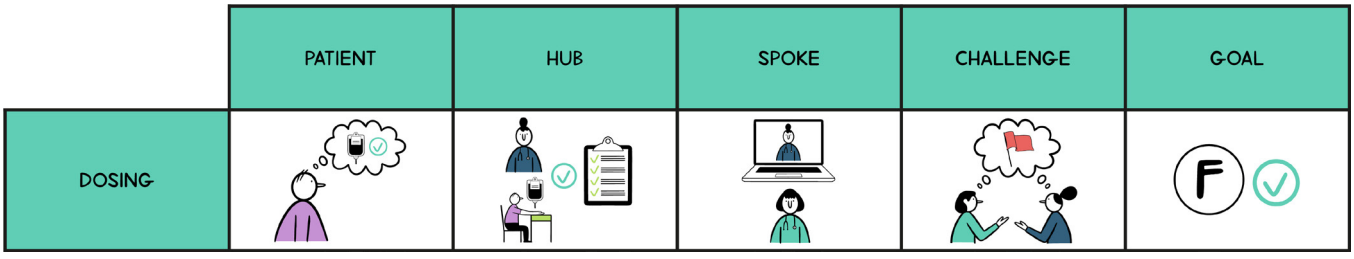
Dosing should take place at the hub, where the specialist expertise resides [2]. As the dosing centre, the hub must ensure eligibility and identify any red flags as early as possible. PwH should know what to expect in terms of how the therapy will be delivered and what monitoring equipment will be used. They should also understand that, at any point prior to dosing, they still have a choice not to have gene therapy. After dosing, the hub should inform the spoke how the treatment went, and there should be liaison between hub and spoke on plans for monitoring and follow-up.

The main challenge at the dosing stage rests ultimately with the hub. As gene therapy is still new, it is essential that all potential issues are taken into consideration and that dosing goes ahead in such a way that the treatment and response are optimised for each individual who chooses to have it (Figure 6). Awareness of signs to look out for in the event of a reaction or signals that could result in better outcomes will help ensure that PwH have their best opportunity with haemophilia gene therapy.

## FOLLOW-UP YEAR 1

For the patient, the follow-up in the first year after receiving gene therapy is intensive and necessitates well-coordinated links between hub and spoke (Figure 7). Regular visits to a treatment centre will be needed, particularly during the first 6-12 months. If this is the spoke, clear identification on who will liaise with the hub will be necessary. For patients who live at a distance to their hub and/or spoke centre, sampling could be performed by mobile or local hospital teams to enable fewer long-distance visits. The focus will be on the individual's response to gene therapy, with blood tests and general monitoring focused principally on the liver and factor levels (with a conversion factor for chromogenic to one-stage assays, and vice versa), all of which must be managed and recorded in a

Figure 6. Dosing
The patient must be sure of their choice to have gene therapy. Dosing will take place at the hub, with the ultimate goal being the instigation of factor expression. Communication between the hub and spoke centres on dosing and plans for monitoring and follow-up is essential.



consistent way [14,20]. Although the risk of third-party infection is limited, the shedding of vector DNA should be monitored and the patient advised to use double barrier contraception until indicated, as required by the licence [9,16,21].

Additional medications may be required in cases where the liver tries to reject the gene therapy (steroid medication/immunosuppressive therapy) so that factor levels are potentially not lost, or where there is a very high response of factor levels and a risk of clotting. Although medications may be prescribed by the spoke, this is most likely to be under the direction of the hub overseeing a larger population. In either case, consultation between the spoke and hub around prescribing will be essential. Any side effects, however minor, should be closely monitored by the spoke team and the information liaised with the hub team. Additional medications may be recommended by the hub to alleviate side effects. Recommendations on additional treatments will be an ongoing role for the hub as knowledge around gene therapy changes, in order to minimise the burden and any risk of other medications to PwH [22].

While clinical monitoring is key, there must also be focus on the individual who has had gene therapy, with consideration given to how they feel in themselves. If their factor expression drops, what they understand about this or are unsure of should be taken into account. Being able to discuss their thoughts and how they feel is essential, and there may be a need for psychological support [9]. Peers and patient organisations can also be an important source of support – we know from PwH involved in haemophilia gene therapy clinical trials that they value the opportunity to be able to speak with others going through the same experience, and this should be facilitated if possible. These kinds of opportunities for discussion are helpful in bringing awareness and understanding of what could happen – having a sense of this can help in being able to cope, whether in relation to factor levels decreasing or a poor response to gene therapy, or managing side-effects of additional medications, which may ultimately increase ability to maintain the regimen in the medium to long term.

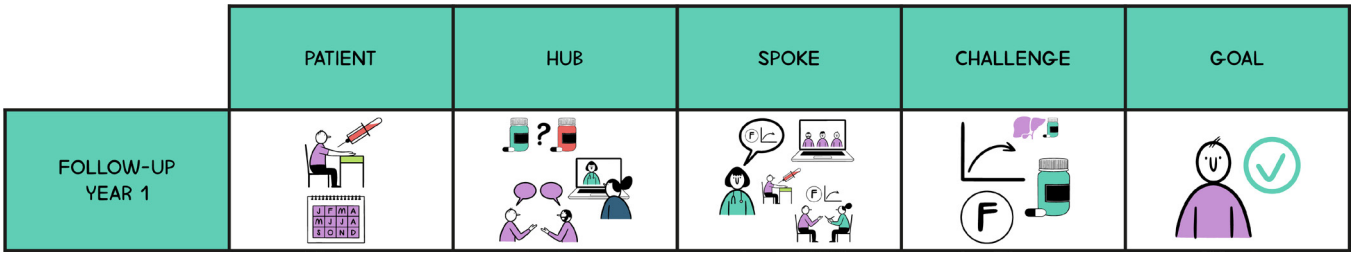
Ultimately, the aim of follow-up during the first year is to ensure that PwH who have had gene therapy achieve the best possible outcome. This requires work and commitment from both the patient and their care team. It is essential that PwH remain engaged and continue to ask questions about all aspects of their follow-up, and that monitoring by hub and spoke is effective, clearly communicated, and remains patient focused. The submission of standardised outcomes monitoring data to the WFH Gene Therapy Registry from this point onwards is also crucial in terms of building knowledge on safety and long-term efficacy [14].

## FOLLOW-UP YEAR 2

By Year 2, the intensity of follow-up visits to the treatment centre should reduce to between two and four per year, if all is going as it should (Figure 8). For the most part, monitoring will be undertaken by the spoke in liaison with the hub – the hub will continue to link with the spoke with regard to the monitoring of factor levels (blood tests) and liver health tests. For the majority of PwH needing additional medication, this will have stopped, although continuation may be indicated for a small number. Given the burden of immunosuppressive medications, the patient's right to decide whether or not to continue must be acknowledged. In such cases, it is important that the individual understands the risk of losing factor expression.

In the spoke, and depending on the response to gene therapy, conversations related to follow-up may begin to change. If factor expression remains high, it may be that PwH want to start to do more [23] – while there may be enough protection for more strenuous

Figure 7. Follow-up Year 1
Follow-up in the first year post-dosing is intensive and focused on the individual's response to gene therapy (factor expression, liver). Additional medications may be required to support factor expression (steroids/immunosuppressants). Coordination between hub and spoke is essential.



activities, it is important to discuss how to increase activity levels safely, and to consider any impact on joint health from living with haemophilia. If factor expression starts to drop, facilitating a conversation around expectations is incredibly important. PwH should have the opportunity to discuss thoughts and feelings around decreasing factor levels and supported in coping with feelings of loss. The psychological impact may be considerable and ensuring that this is recognised and that appropriate support is provided is as important as monitoring factor levels.

At this stage, the challenge for both PwH and the care teams supporting them is to learn to live well with their new situation. For many, this will represent a completely new way of life and it may take some getting used to. Regardless of factor expression levels, PwH must remain engaged with their care team, and it is important that they are able to access support through peers and patient organisation. The aim is to ensure that the individual's situation is well managed and that there is a clear, defined treatment plan in place. If factor levels are falling, this may include plans for the use of other medications. Plans must also be put in place for treatment in the event of an accident or surgery – this will be similar and familiar to that needed prior to gene therapy but is likely to be somewhat different due to the new factor level.

## FOLLOW-UP BEYOND YEAR 2

By this time, PwH who have had gene therapy should be back to regular six-monthly visits to their treatment centre (Figure 9). The hub will be broadly involved in the monitoring of factor levels and liver health through liaison with the spoke, which will be responsible for blood testing to ensure factor levels continue to provide enough protection, and liver tests or fibro scans. As long-term liver health post-gene therapy remains an unknown, the hub should also have a more in-depth role here and may request that PwH who have had gene therapy have a liver biopsy [20,24] – however, while helpful in advancing the science, PwH should know that they are under no obligation to do this.

The long-term goal, of course, involves learning more about gene therapy for haemophilia and how best to manage it going forward. Every individual who receives gene therapy has a part to play in this and can help those considering or who have themselves received gene therapy, with the possibility that more options may become available in the future. Gaining greater insights around gene therapies will help to improve them and to increase the benefits achieved by individuals as a result of having gene therapy in the future. The submission of long-term outcomes data to registries such as the World Federation of Hemophilia Gene Therapy Registry is key [14].

**Figure 8. Follow-up Year 2**
The intensity of follow-up reduces. Liaison between hub and spoke continues, and the individual will be adapting to post-gene therapy life. A clear and defined treatment plan should be in place for the patient to cover any decrease in factor expression, accidents or surgery.

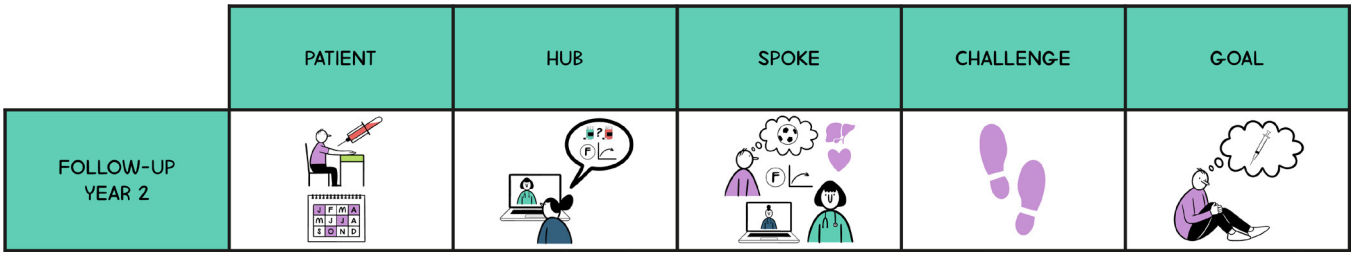
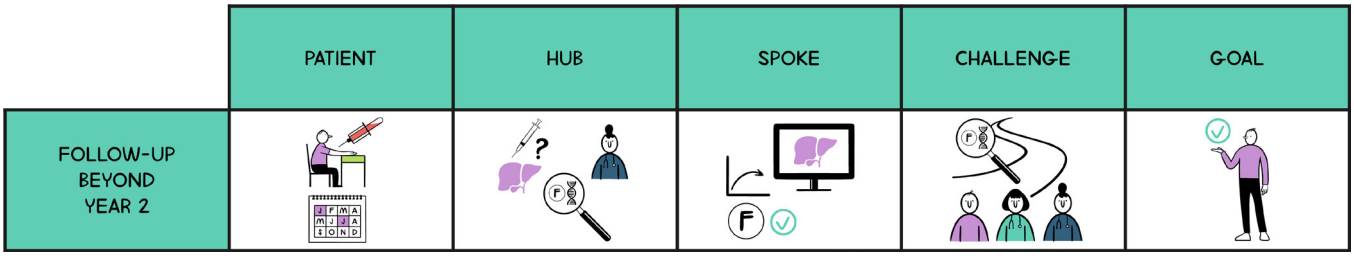



**Figure 9. Follow-up Beyond Year 2**
Follow-up should usually be regular six-monthly clinic visits. Monitoring of factor expression and liver health will continue, and the hub may request a liver biopsy. Data collected will enable greater understanding and support development of gene therapies going forward. The goal is for the patient to live well post-gene therapy, whatever their individual outcome.



## VISUALISING THE PATIENT GENE THERAPY JOURNEY

As an evolving treatment, considerations around gene therapy on the part of the patient are complex. The patient gene therapy journey comprises a multifaceted sequence of stages, all of which present challenges for the hub and spoke model of care. Understanding these from the patient point of view will help to ensure that the individual people with haemophilia (PwH) treading this path receive the information, guidance and support they need from hub and spoke clinicians throughout their journey, and that they, as the patient, remain the focus of care. As we move forward, it is essential that we identify potential barriers at all stages and mitigate these accordingly.

The 'map' shown in Figure 10 visualises all the key stages of the haemophilia gene therapy journey, focusing on the needs of the patient. Similar to the Patient Journey maps developed by ERN GENTURIS [25], it takes into account the questions and answers for shared decision-making in gene therapy for haemophilia outlined by Wang et al. [8], identifying common elements in the considerations, processes and challenges for PwH, hubs and spokes – including patient needs, screening, foreseen medical interventions and follow-up – across the haemophilia gene therapy journey.

A visualisation of this kind has potential for use in explaining the gene therapy clinical pathway to PwH and could provide a useful tool for HCPs in spoke centres. It is a complex journey and there is a need for materials that enable information to be presented in an accessible way – for both PwH and HCPS – and in a way that can facilitate discussion, not only in terms of initial discussions and education, but throughout the various stages.

The visual map also serves as a useful reminder that the gene therapy journey is ultimately made by individuals. Understanding the various parts of that journey and recognising the challenges at each stage can ensure that each patient is a full partner in their own care and enabling them to achieve the greatest benefit from having gene therapy.


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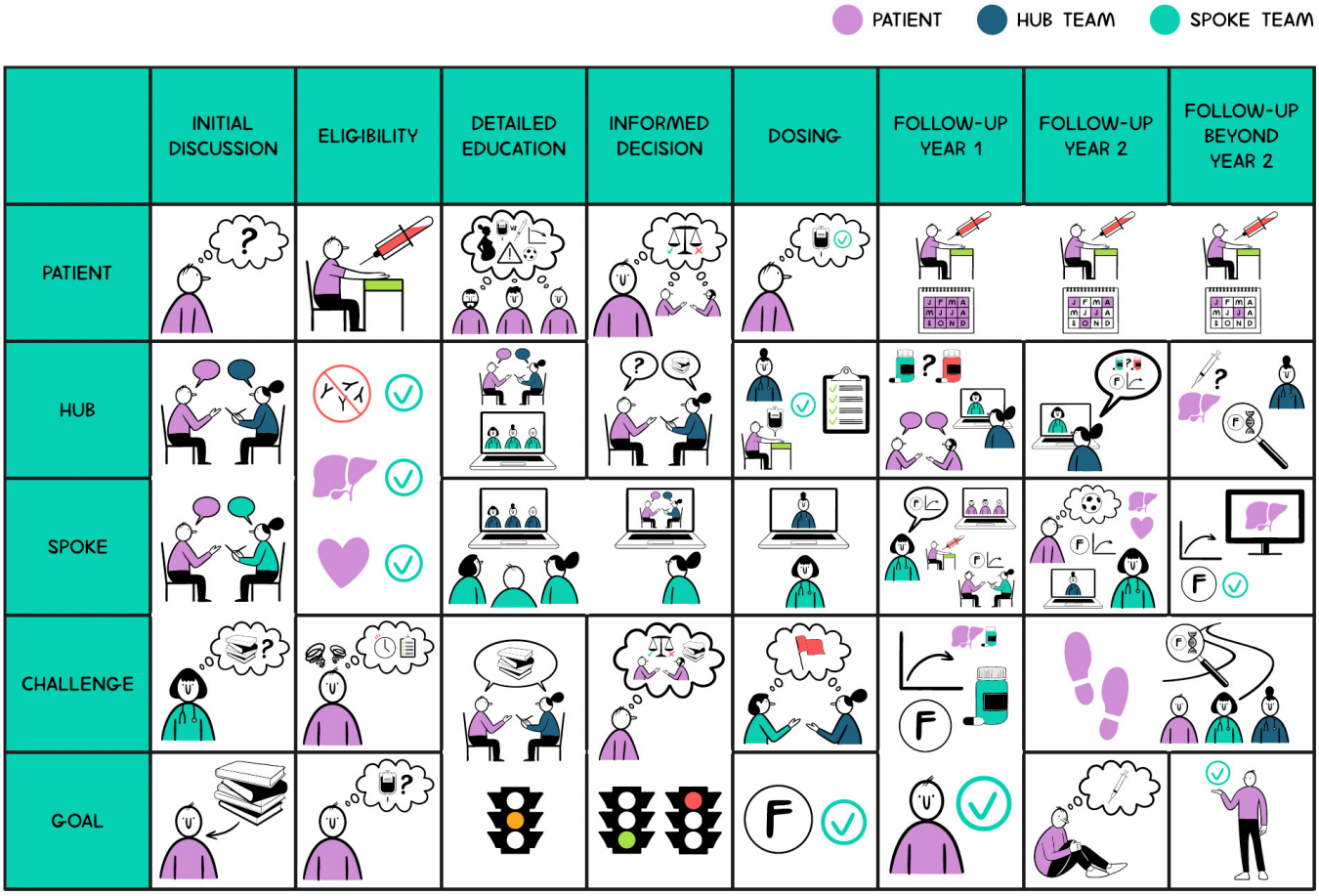
Figure 10. Map of the patient haemophilia gene therapy journey

Visualisation of the key stages of the haemophilia gene therapy journey, focused on the needs of the patient. The journey is complex and the map identifies common elements in the considerations, processes and challenges for PwH and the hub and spoke centres involved in delivering gene therapy and follow-up.




Key

| | | | | | |
|---|---|---|---|---|---|
| | Patient | | Potential stress to patient while waiting for confirmation of eligibility | | Red flags (i.e., problems or issues that may occur during or after dosing) |
| | Hub team | | Gene therapy | | Factor expression post gene therapy |
| | Spoke team | | Communication/sharing of information between hub and spoke teams | | Frequency of follow-up clinic visits (by month) |
| | Patient-HCP discussions and education (e.g., with clinician, nurse, psychologist) | | Weighing up information to make an informed decision | | Additional medications (e.g., steroids, immunosuppressive, cardiovascular) |
| | Patient peer-to-peer discussions | | Readiness to make an informed decision | | Adjusting to post gene therapy life |
| | Information/education on gene therapy and alternative options | | Informed decision – yes | | Post gene therapy treatment plans (e.g., for injury or surgery) |
| | Blood test | | Informed decision – no or not yet/wait for now | | Learning more about haemophilia gene therapy for the future |
| | Cardiac health | | Gene therapy dosing | | Patient acceptance of their individual gene therapy outcome |
| | Liver health | | Pre-gene therapy checklist | | |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