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Patient, consumer and societal values, perceptions and preferences on high-cost gene therapies

Amanda Rush

amanda.rush@sydney.edu.au

The University of Sydney

Maria Gomez

University of Sydney

Kristine Pierce

University of New South Wales

Richard De Abreu Lourenco

University of Technology, Sydney

Kylie Mason

The University of Melbourne

Kirsten Howard

The University of Sydney

Gary Lynch

The University of Sydney

Pippy Walker

The University of Sydney

Rosalie Viney

The University of Technology, Sydney

Jo Watson

Australian Government

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Abstract

Novel cell and gene therapies hold great potential to alter the clinical course of a range of chronic diseases, yet significant uncertainties remain regarding their long-term efficacy and impact. These uncertainties pose challenges for Health Technology Assessment (HTA) committees, which systematically assess health interventions seeking public subsidy. Hematological conditions are a common target for gene therapies; however the perceptions of those both directly and indirectly impacted by funding decisions have not been investigated. To support HTA of gene therapies, this study explored the perspectives of individuals living with hematological conditions who may become eligible for such treatments, alongside their carers and members of the general population. We undertook interviews and focus groups with 55 participants with lived experience and 32 general population members to elicit responses on what might influence decision making on gene therapies (GTs); the potential benefits or harms of GTs; any perceived barriers to GT access; and/or uncertainties associated with the respective GT. Here, we compare and contrast health consumer and general population responses, providing valuable insights for HTA decision-making on gene therapy. Additionally, we elucidate barriers to access and associated uncertainties that will require resolution if acceptability and uptake of GT are to be optimised in future.

Introduction

Novel cell and gene therapies have the potential to alter the outcomes of a growing array of severe, lifelong genetic disorders (1), with recent progress in their commercialisation providing new treatment options for patients, healthcare professionals and society. However, the rapid expansion of these emerging therapies has brought ensuing challenges to the evaluations undertaken by health technology assessment (HTA) committees, which guide government decisions on which therapies to publicly subsidise. These multi-disciplinary committees systematically assess the safety, efficacy, and cost-effectiveness of health interventions seeking public subsidy (2), including novel and cell gene therapies.

Currently, there are substantial uncertainties surrounding the long-term efficacy and impact of gene therapies, which can challenge HTA committees' ability to assess the value and benefits of these interventions. Due to the mechanism of treatment, many available gene therapies have been developed to treat rare diseases caused by single faulty genes (3). Here, relevant clinical trials tend to be non-comparative, with small participant numbers and short duration of follow-up (4). Gene therapies are also often associated with high upfront costs for governments or other payers (5, 6) which presents a tension for patients in terms of holding reservations or uncertainties about the benefits of treatment, but also needing access to be supported within the health system (7). These factors can create potential challenges when considering the opportunity costs of supporting alternative interventions for other population groups.

Collectively, the uncertainties and high costs of novel gene therapies represent a unique set of circumstances for HTA committees. Consequently, there is a lack of consistency in HTA approaches

currently applied to this group of therapies (8). To inform a standardised approach to assessing gene therapies, multi-disciplinary data sources are required. Evidence should address social, ethical, legal and economic considerations, and should include consultation with groups who are directly and indirectly affected by the decision-making process.

Australia is one of a number of countries (8) where HTA decision makers are currently experiencing challenges associated with applications for funding of novel gene therapies. In Australia, three gene therapies have been considered (9, 10). Here, HTA of gene therapies has been undertaken by two Commonwealth committees: the Pharmaceutical Benefits Advisory Committee (PBAC) (9) and the Medical Services Advisory Committee (MSAC) (10). The fact that the assessment of potential therapies has occurred across both of these decision making bodies highlights the current complexity in assessing novel gene therapies at the Commonwealth level in Australia, with funding across two separate schemes – the PBS and the MBS.

One key priority for HTA committees assessing gene therapies is ensuring that the perspectives of those living with genetic conditions (and their carers), as well as the general population, are incorporated. There is a growing body of literature that seeks to understand the perceived impacts of gene therapies from the perspectives of various stakeholder groups (11–13). As haematological conditions are a common target for novel gene therapies, many publications focus on seeking perspectives on this disease area, including from those with lived experience (11), carers (12), and clinicians (13).

However, to our knowledge, there are no studies that describe the parallel perspectives of consumers and the general population, where the latter may indirectly support subsidization of GT via tax payments but hold no personal interest in the diseases or their treatments.

Our study is part of a larger project that explores the development of a generic model for HTA of high-cost gene therapies. In part, that project seeks to determine what is valued by Australian consumers living with three haematological diseases, their families and the general population, with respect to decision making about the uptake of high-cost gene therapy. As a first step, we describe herein the methods and results of a qualitative inquiry of the perspectives of the Australian general population and patients and their carers with inherited haematological conditions.

Patients and Methods

A qualitative approach was utilised to ascertain the perspectives of those living with one of three conditions of interest (haemophilia B, sickle cell disease, and beta thalassemia), their carers and advocates, and a representative cross section of the general population. The three genetic diseases selected were all haematological in nature, and with associated gene therapies in various stages of the commercialization pipeline. Both focus groups and interviews were offered to participants in order to maximise participant uptake and provide a more private space for reflection if preferred. Focus group/interview material was co-designed with consumers to ensure audience relevance.

This study has been reported in accordance with the Consolidated criteria for reporting qualitative research (COREQ) guidelines (14).

Ethics Approval

Ethical approval

for the study was granted by the University of Sydney Human Research Ethics Committee (HREC) (ID: 2024/HE000224). All participants provided written informed consent.

Participant selection and recruitment

Two main groups of participants were recruited for the study: i) consumers, including those living with one of the conditions of interest, their immediate families, and disease advocates; and ii) members of the general population who do not live with any of the haematological conditions of interest. Participants were required to be adults (≥ 18 years of age) and have sufficient English language skills to participate in discussions.

Consumers were recruited via established member communication channels (newsletters, social media) of four Australian disease advocacy groups (Haemophilia Foundation of Australia; Thalassemia and Sickle Cell Australia; Australian Sickle Cell Advocacy Inc; and Rare Voices Australia). Recruitment material comprised a brief description of the study, and a link to an online expression of interest (EOI) form. A participant information sheet (PIS) was also included. Interested consumers were contacted by a member of the research team (MG) with further information on the study, including a consent form. Consented participants were asked to complete an anonymous online demographic survey prior to allocation to a focus group or interview timeslot, depending on participant availability. There were no participant withdrawals after consent was provided.

General population participants were recruited via the market research agency Taverner Research Group, which purposively selected a cross-section of the population according to age, gender, education level, and rurality. Potential participants were provided with a PIS and a link to an online screening consent form. Those selected on the basis of representativeness were emailed a second consent form to participate in the focus groups. Consented participants completed a similar demographic survey as the consumers, with disease-specific questions omitted. All participants were then allocated to a focus group/interview timeslot. There were six general population participant dropouts after consent was provided; all of these were able to be replaced with other consented participants prior to focus group commencement.

Pre- focus group/interview preparation

Prior to commencement of the focus groups and interviews, an interview guide was developed with input from all research team members. The guide included one discussion question to ascertain participant baseline knowledge of gene therapies, followed by indicative discussion questions across four key topic areas: i) what might influence decision making on gene therapies; ii) potential benefits and harms of gene therapies; iii) perceived barriers to access to gene therapies; and iv) uncertainties associated with the gene therapies (Table 1).

Table 1
Indicative topic areas and questions for focus groups and interviews

Topic area	**Indicative questions**
Determination of baseline knowledge: Experience with gene therapies	- Let's talk about any personal experience you might have had with gene therapy
Influences on decision making	- Thinking about the video and the sorts of funding decisions that are made, what kinds of information do you think would influence recommendations on whether to fund gene therapy or not?
Potential benefits and harms	- If you had a condition that a gene therapy was available for, would you have the gene therapy? Why or why not? - What do you think the positive changes would be for someone having gene therapy? - Would you have any concerns?
Perceived barriers to access	- Even though gene therapies exist for some conditions, not everybody chooses to use them. What do you think prevents people from using gene therapies? - Some people have accessed gene therapies in different ways, for example through clinical trials, going overseas, crowd sourcing, paying for it themselves, or when it is publicly funded. How would you access gene therapy for you or your family member?
Uncertainties	- Gene therapies are a new way of treating people. This means that there are some things that we still don't know about them. What more would you like to know about gene therapy before you made a decision?

A run sheet template was developed for use by focus group/interview facilitators, which included the indicative discussion questions and prompts (to probe for identified topics of interest if they had not arisen organically). A separate project background information sheet to be delivered to the groups on the day was also developed, along with a distress protocol to be activated if required.

Finally, a brief educational video was developed to ensure that all participants were exposed to the same baseline knowledge on gene therapies prior to the discussions. The video provided information on the three haematological conditions of interest, and how gene therapies are approved and funded in

Australia. The video content was developed with input from all members of the research team, including a clinical haematologist (KM), members of Australian HTA committees (JW, KM, KH, RV), and consumers (KP, GL). Advice was also sought from relevant consumer organisations, to ensure that the video content was appropriate for their respective memberships.

Data collection

Anonymous demographic data for consumers were collected via a survey in the Research Electronic Data Capture (REDCap) platform (15). Consumers were additionally requested to report on whether they were related to anyone else participating in the study, the disease group they represented, and the severity of their disease (mild, moderate, severe). The market research company were provided with a similar list of demographic survey questions to be asked of general population participants. Questions sought information on age, gender, ethnicity, postcode, regionality, and whether participants had heard of gene therapy prior to engagement.

Each focus group/interview comprised only one participant type ie. representing one haematological disease group and one stakeholder type (patient, immediate family member/carer, disease advocate). General population focus groups were held separately to consumer discussions. Participants were given the option of attending in person at a designated meeting facility or online.

At the commencement of each focus group or interview, facilitators provided a summary of the study, including the rationale for conducting the research. Participants then viewed a brief educational video, which provided background information required for the ensuing discussions. Experienced facilitators (KP, RDAL, JW) provided context to participants on their own role within the research study. Facilitators then led discussions, based on the interview guide. Each discussion was audio recorded, then transcribed verbatim with participant identifiers removed. All participants were reimbursed for their time with a gift card.

Data analysis

Transcripts were imported into NVivo (Version 14)(16) and analysed using content and inductive thematic analysis (17, 18). Consumer group (patients, carers, disease advocates) responses were deemed sufficiently similar to combine for analysis. Two coding frameworks were therefore developed (patient/family/disease advocate and general population) by the primary analyst (AR). The frameworks were circulated to the facilitators (KP, RDAL, JW) for their input and refinement. Facilitator characteristics are described in **Supplementary Data 1**. All interviews were coded in NVivo by another member of the research team (MG). Coding hierarchies were initially developed by the primary analyst (AR), and a thematic analysis workshop was held with members of the research team (AR, JW, KP, GL, MG) to refine the themes. Thematic saturation was achieved for consumer and general population discussions.

Results

Participant demographics

During the recruitment period, a total of 92 EOI to participate in the consumer focus groups were received, comprising 19 people living with Haemophilia B, 29 family members or carers of people living with Haemophilia B, 8 people living with beta thalassemia, 8 family members or carers of people living with beta thalassemia, 11 people living with sickle cell disease, and 17 family members or carers of people living with sickle cell disease.

Twenty-three focus groups and interviews ranging in size from 1–10 participants were conducted between June and September 2024 (Table 2). Focus groups/interviews ranged in length from 44–82 minutes. Participants comprised 23 people living with one of the three haematological diseases of interest, 30 family members/carers of people living with one of the three haematological diseases of interest, 2 disease advocate representatives, and 32 members of the general population.

Table 2
Focus group/interview characteristics

Focus group/interview type	Focus group (FG) Interview (I)	Setting	Facilitator*	No. of participants
Haemophilia B Patient	FG	Online	KP	6
Haemophilia B Patient	FG	Online	JW	6
Haemophilia B Patient	FG	Online	KP	2
Haemophilia B Family/Carer	FG	Online	KP	5
Haemophilia B Family/Carer	FG	Online	JW	6
Haemophilia B family/carer	I	Online	KP	1
Haemophilia B Family/carer	FG	Online	KP	3
Haemophilia B family/carer	I	Online	KP	1
SCD Patient	I	Online	KP	1
SCD Patient	I	Online	KP	1
SCD Patient	I	Online	KP	2
SCD Patient	FG	Online	KP	3
SCD Patient	I	Online	KP	1
SCD Family/Carer	FG	Online	KP	5
SCD Family/Carer	FG	Online	KP	6
SCD Family/carer	FG	Online	KP	2
Beta Thalassemia Patient	I	Online	KP	1
Beta Thalassemia family/carer	I	Online	KP	1
Disease advocate	FG	Online	JW	2
General Population	FG	In-person	RDAL	10
General Population	FG	Online	RDAL	6
General Population	FG	In-person	RDAL	10

SCD: Sickle Cell Disease

*KP (Kristine Pierce), JW (Jo Watson), RDAL (Richard De Abreu Lourenco)

Focus group/interview type	Focus group (FG) Interview (I)	Setting	Facilitator*	No. of participants
General Population	FG	Online	RDAL	6
				TOTAL = 87
SCD: Sickle Cell Disease				
*KP (Kristine Pierce), JW (Jo Watson), RDAL (Richard De Abreu Lourenco)				

Five participants did not complete the demographic survey. Of the remaining 82 participants (consumers and general population combined), there were 42 males, 39 females and 1 non-binary participant, ranging in age from 18 to 75 years (Fig. 1). The majority of participants identified as Australian (n = 46/82, 56%), with other ethnicities represented including English, Chinese, Greek, Irish, Scottish, Indian, Dutch and Aboriginal Australian. Participants resided across metropolitan (52/82, 63%), regional (24/82, 29%), and rural/remote (6/82, 7%) areas.

Prior knowledge of gene therapies

The majority of those living with haematological disease and their carers/disease advocates (n = 44/50, 88%) had heard of gene therapy prior to attending the focus groups. Some participants specifically mentioned being aware of Australian gene therapy clinical trials for their disease type. Disease advocates were particularly informed on gene therapy treatment options for Australians and internationally, and the progress being made in approving new treatments.

Reported sources of information on gene therapy for those living with haematological disease and their families included disease advocacy groups, news articles, social media, conducting their own research into treatment options, clinicians including general practitioners and haematologists, and relevant conferences. Due to the perceived benefits of widespread gene therapy availability in the future, some consumers reported keeping abreast of progress on commercializing gene therapy in Australia:

'As a family we've been following it quite closely because it can have obviously a very significant impact on how my brother's condition is managed' [Carer]

Across the general population focus groups, almost two thirds of participants (n = 20/32, 63%) had heard of gene therapy via the media and/or their own vocation (nurse, biomedical scientist, medical receptionist). However, their knowledge of what gene therapy involved, and the implications for patients, was less informed than for the consumer groups:

'…it was just mainly from what I've seen in news and documentaries. Particularly American documentaries and just about the significant cost…' [General population]

Focus group/interview discussion themes

Five overarching themes were derived from analysis of the focus groups and interview transcripts: patient, disease and treatment considerations; accessing gene therapy; impacts of gene therapy (benefits and harms); impacts of gene therapy (costs); and uncertainties related to gene therapy (Table 3). Within each overarching theme, a number of sub-themes were identified (Table 3).

Table 3
Themes and sub-themes arising from focus groups and interviews

***Theme*/sub-theme**	**Participant group***	**Indicative question/s**	**Example quote**
Patient, disease and treatment considerations			
Disease prevalence	C, GP	Influences on decision making	'it depends on the number of people affected by this, the number of families who have someone with this condition … and also the impact it has' [C]
Disease severity	C, GP	Influences on decision making	'Because those with … less severe symptoms might be more reluctant to engage in gene therapy' [C]
Patient life stage	C	Influences on decision making	'Glad to be an advocate for it, but my time's come and gone for having a crack at the trial. As I said, 20s, 30s, even 40s, I would've gone' [C]
Evidence of prior success	C, GP	Influences on decision making	'I'd actually like to hear from someone who's gone through the treatment. Just get their thoughts and feelings on what they've gone through and how the process is so you can make an informed decision' [GP]
Availability and type of alternative treatments	GP	Influences on decision making	'how many different treatments are available? If I have a particular condition, do I only have one line of treatment or are there a couple of choices that I can make?' [GP]
Accessing gene therapy			
Patient/clinician awareness of gene therapy options	C, GP	Perceived barriers to access	'my GP … didn't really know the side effects. Since it's a new development, he doesn't really understand how it's important, he doesn't understand how it could affect the human body when used' [C]
Availability of person-centred care	C	Influences on decision making	'I think person-centred care is so important just in general, in making patients feel comfortable and building their knowledge and making them feel like they can make executive decisions about their care' [C]
Trust in healthcare professionals	C, GP	Influences on decision making	'So I think if my nursing team and my haematologist had the risks and benefits outlaid for me and were able to sit down in depth with me and discuss … that would influence me quite a lot because I trust their opinion' [C]

*C = consumers, GP = general population

Theme/sub-theme	Participant group*	Indicative question/s	Example quote
Wait time to receive gene therapy	GP	Perceived barriers to access	'I remember during COVID surgeries and people waiting on the waiting list for years. So is there a backlog for this treatment?' [GP]
Distance from gene therapy centre	C, GP	Perceived barriers to access	'where can you go to, to access these services? How would they make it easily accessible for even people living in rural areas to access? That's a concern for me' [C]
Impacts of gene therapy: benefits and harms			
Minimising symptoms or cure	C	Potential benefits and harms	'you'd be able to do more of the normal stuff without the damage, because every bleed causes – it all adds up, it's detriment to joints. So that'd be brilliant' [C]
Quality of life improvements	C, GP	Influences on decision making Potential benefits and harms	'the quality-of-life issue is one of importance as well … So [for example], travel, you don't have to take your Factor [VIII] with you. It opens up opportunities for employment' [C]
Societal benefits	C, GP	Influences on decision making Potential benefits and harms	'Because a patient is not having an illness in a vacuum. I said there's a domino effect. So, if you can improve one thing, those positives can spillover other areas as well and everyone can benefit' [C]
Adverse effects	C, GP	Influences on decision making Perceived barriers to access	'But long term as well, what does [it do] to me? Does it fix me? … does this also cause another disease that no one ever thought of?' [GP]
Impacts of gene therapy: costs			
Individual out of pocket costs	C	Perceived barriers to access	'If you've got multiple children with sickle cell that would be I think, quite a large contributing factor.' [C]
Health system costs	GP	Influences on decision making	' these are incredibly expensive technologies … when the government's going to spend money, [does] the net benefits outweigh the costs? Could that money be better spent elsewhere to cure things that are perhaps easier to cure?' [GP]
Cost savings to the health system	C	Influences on decision making	'If this reduces our rates of haemorrhaging and bleeding, then it's

*C = consumers, GP = general population

Theme/sub-theme	Participant group*	Indicative question/s	Example quote
			actually a better thing, because you don't have the issues of cost' [C]
Uncertainties related to gene therapy			
Details on the process	C	Uncertainties	'Understanding the full treatment option. How it's been taken. How would the treatment be? How long the whole process is involved?' [C]
Effectiveness	C, GP	Uncertainties	'Successful rate and how long does it take to actually cure the disease? Is it going to be done within one shot, or multiple shots a month or lifelong treatment?' [GP]
Alternative treatments becoming available in the future	C, GP	Uncertainties	'the changes to medicine and the changes in healthcare seem to be pretty exponential at the moment... Like, are people holding out because they think, well, I can just keep on going for the next five years and it might be even better then? And if I have this gene therapy, does that then close the doors on future possible better [treatments]?' [C]
*C = consumers, GP = general population			

Patient, disease and treatment considerations

Five sub-themes pertained to patient, disease and treatment considerations. Firstly, disease prevalence was seen to be a major influence on HTA decision making for both consumers and the general population. Individual health and social circumstances (disease severity and patient life stage) were also discussed as influences on individual decision making, with consumers stating that they would be less inclined to select gene therapy as an option if their symptoms were mild:

I think the severity of the symptoms of the patient would also be a big factor in decision making about whether to engage in the gene therapy or not. Because those with maybe less severe symptoms might be more reluctant to engage in gene therapy. [Carer]

Both consumers and the general population expressed a preference to be able to communicate with patient/s who had already received the therapy, to be assured of their ongoing health and wellbeing. In particular, general population participants discussed the number of people who had had the therapy already, in the context of the treatment data that would be available to review:

Are you the first group of people to receive this treatment? Or is it being offered half a dozen times, and you've got a whole lot of history and stats to look back on? [General population]

Lastly, the availability and type of treatments other than gene therapy were raised by the general population as influences for HTA decision making.

Accessing gene therapy

Within the ‘accessing gene therapy’ theme, five sub-themes were identified. Firstly, both consumers and the general population discussed that there was a need for patients and their treating clinicians to be aware of gene therapy options, and what these would entail. Here, consumer participants referred to the need for self-advocacy:

It's [gene therapy] never been mentioned as a viable treatment. My research has purely been personal and yeah, my own interest in sickle cell and the ongoing treatments that are available for it. [Patient]

Availability of person-centred care was highly valued by consumers, to ensure that they maintained autonomy over treatment decision making. Trust in healthcare professionals was also raised as a consideration for accessing gene therapy by both consumers and the general population. Here, the reliance on healthcare professionals’ understanding of gene therapy data was apparent:

Because that's the person that you're going to seek the information from. So it's making sure that they are very well informed of all the data and they're able to guide you in your treatment decision with the best available data. [Carer]

Wait-time to receive therapy was identified as an accessibility concern by the general population, and geographical distance from the centre where gene therapy would be administered was identified as a potential access barrier by both consumers and the general population. In particular, consumers raised concerns about personal travel and accommodation costs for gene therapy recipients who do not live proximally to a gene therapy centre:

So, for people that live remote, or are a long way from the centres that are going to offer the treatments, there's going to be a significant financial burden in regards to travel, accommodation, those sorts of expenses. [Patient]

Impacts of gene therapy: benefits and harms

There were three main benefits of gene therapy identified by focus group/interview participants. Firstly, consumers recognised the potential that gene therapy has to minimise their symptoms or cure their disease. Consumers and the general population also discussed improvements in quality of life as a benefit of gene therapy, along with broader societal benefits that could ensue. For consumers, improved quality of life included specific examples such as altruism, less discrimination and improved family life. Consumers raised the potential contribution that citizens could make to society if gene therapy was administered early in life, in the context of worsening effects of disease as individuals age:

...if you give gene therapy now to a child who's three or four, or whatever the age is that they can start, it's a wonderful prophylaxis to stop joint damage for that person, which means they will truck on through life, go

to uni, get a job, become a citizen rather than a potential burden. [Patient]

Focus group/interview participants also discussed the potential harm of patients experiencing adverse effects from gene therapy. A hypothetical question was raised as to whether any adverse effects would be worse than disease symptoms currently experienced, with consumers introducing a number of adverse scenarios that could arise following the provision of therapy:

If it was ongoing and it is not just a one hit thing, I think you would have to look at the risk factors once it wore off, like if it was going to be worse than having haemophilia itself or, yeah, what are the risk factors for when you need it again, or if you couldn't get it again would there be any risk, or would the Haemophilia go back to normal to the way it was before? [Carer]

Impacts of gene therapy: costs

Discussions on the potential cost impact of gene therapy addressed both costs incurred and potential cost savings. Firstly, consumers raised concerns about out-of-pocket costs, which could be compounded in instances where multiple members of a family may be eligible for treatment. Consumers and the general population also considered costs and potential savings to the health system in their discussions on gene therapy costs. Here, the general population recognised the concept of 'opportunity costs' for the government, whereas consumers focused on the potential cost savings that could be made through avoidance of future treatment and care:

But if you are looking at that patient over however many years, it's going to be cheaper to reimburse that single dose of the gene therapy drug rather than keep on paying for the Factor IX replacement prophylaxis… And also if it's a more effective treatment for Haemophilia, it's also going to reduce healthcare costs further because he's going to have less admissions to hospital and require less treatment from that perspective. [Carer]

Uncertainties related to gene therapy

For uncertainties regarding gene therapies, consumers raised their need to better understand the actual details of the therapy process. Both consumers and the general population discussed two other sub-themes pertaining to uncertainty: the effectiveness of gene therapy, and the potential ongoing nature of the treatment. Consumers also raised their concerns that the therapy may not work at all:

And I'll want to understand, is there a possibility that it just doesn't work on me? Am I investing my time in this for potentially no positive result? [Patient]

Finally, consumers and the general population discussed the possibility of other treatments becoming available in the future, and the quandary of needing to elect for gene therapy at the time at the expense of possibility receiving a more beneficial therapy in the future.

Discussion

In this study, we describe the findings of focus group discussions and interviews with 87 stakeholders on patient, disease and treatment considerations; access, benefits and harms; costs; and uncertainties associated with high-cost gene therapies. Many of the study findings on consumer perspectives align with previously published literature. As the first study comparing the perspectives of consumers and general population members, our work builds upon previous and new consumer findings, enabling an in-depth understanding of the views of those with lived experience of disease as well as members of society who are not directly affected. Our data highlight concrete informational priorities (real world effectiveness, long term safety and geographic access) that current Australian HTA templates do not systematically capture.

Perhaps unsurprisingly, the outcomes of focus groups and interviews with patients and carers reflected a more nuanced understanding of the range of potential benefits, uncertainties and harms associated with receiving high-cost gene therapy. This is likely to reflect the greater interest in gene therapy for this cohort, including a deeper awareness of the range of advantages and disadvantages of currently available treatments. Consumer awareness of the implications of gene therapy is supported by reports from some consumer participants of following the progress of gene therapy availability in Australia in order to keep abreast of evolving treatment options for their particular condition.

While strong consumer knowledge of gene therapy was apparent across all three haematological disease experiences studied, it was particularly evident in responses on potential health and social benefits from patients and carers living with severe disease symptoms. This may reflect the more significant post-therapy improvements anticipated to occur within this cohort, and the aspirations associated with these.

Discussions on influences on decision making gave rise to five considerations (disease prevalence, disease severity, patient life stage, evidence of prior success, and availability and type of alternative treatments). Disease prevalence was raised by both participant groups, with the general population discussing this influence on decision making in the context of the opportunity cost of funding high-cost gene therapies for rare diseases versus other condition/s with a higher prevalence. This suggests a greater sense of objectivity for general population participants. General population and consumer participants discussed disease severity as a decision-making influence, however only consumers discussed their current life stage in the context of whether they may have been amenable to receiving gene therapy at an earlier age but not at their current age and level of health and wellbeing. The impact of disease severity and its associated treatment burden on decision making has also been previously raised as part of a study of ten adult men with haemophilia, where most participants judged that their current low level of treatment burden did not justify consideration of gene therapy (19).

Despite an initial lower level of understanding of gene therapy in general population participants, evidence of prior success of therapy featured as a decision-making influence for both participant groups. This suggests that current uncertainties associated with gene therapy play a role in individual decision making, a finding that is consistent with a previous study on sickle cell disease patients (11), who

reported a preference to review data from previous clinical trials before making a decision on gene therapy. Similarly, an earlier study by Vasquez-Loarte et al (20) reported on the influence that previous efficacy, emotional health and quality of life information had on 21 patients with haemophilia and family members considering gene therapy.

Both consumers and the general population raised the issue of awareness of gene therapy and its suitability for their individual health needs as a current barrier. Discussions focused on a lack of understanding of the process and outcomes for gene therapy for potential recipients and their healthcare providers. This finding suggests a future need for gene therapy education campaigns targeted at relevant patient groups and their clinicians, as gene therapy becomes more broadly available.

In locations where gene therapy administration becomes available, those with lived experience valued the availability of person-centred care, a preference also reported in a summary of round table discussions held by the Council of the Haemophilia Community (21). Trust in clinicians with knowledge on the potential benefits and risks of gene therapy was also raised as an influence on decision making by both general population and consumer participants, despite general population representatives having no direct experience of the diseases studied. The importance of patient trust in clinicians has been widely reported (22), with specific studies in haemophilia highlighting the value of clinician-patient relationships in medical information provision (23) and shared decision making (24).

While the general population raised wait time as a barrier to accessing gene therapy, this was not considered a barrier by consumers. This may be due to the general population drawing parallels with other treatments where backlogs exist, and consumers having a more nuanced understanding of the lead time likely to be present as part of the gene therapy process. Finally, consumers and the general population both raised geographical distance as a barrier, in the context of the complexity and duration of the process, and the need for ongoing monitoring. This is particularly relevant in Australia where there are vast distances between metropolitan centres, a relatively small population, and a high cost associated with establishing treatment centres (25).

In the context of their lived experience of disease, consumers discussed the anticipated benefits to their health that gene therapy may bring about. This is consistent with a study of 26 people with haemophilia and their family members, who anticipated that gene therapy treatment would be life changing (26). Similar improvements were not raised by the general population, which may reflect their lack of lived experience of disease symptoms. However, both consumers and the general population were able to envisage the quality of life benefits that gene therapy could potentially generate. This aligns with findings in a study by Quarmyne et al, where 25 adults and parents of children with transfusion dependent thalassemia identified quality of life improvements as a major factor in decision making on gene therapy (27). Specifically, consumer participants in our study were able to articulate that less discrimination and improved family life would improve their quality of life, likely reflecting their more intimate understanding of the challenges currently faced by those living with haematological disease. Here, consumers were able to identify the deleterious effects of their disease, and the compounding of these effects over time,

and how gene therapy could potentially benefit them if introduced early enough to avoid severe and irreversible changes.

The anticipated societal benefits of gene therapy were recognised by both participant groups, illustrating an awareness of the societal burden of current treatments. This finding is supported by a previous study with haemophilia patients, where the societal burden of current haemophilia treatments was a concern for some participants (23). Concerns on the long-term side effects of gene therapy were also consistent with barriers in previous studies, including a study by Fletcher et al that identified possible side effects and associated consequences as a major barrier for haemophilia patients to receiving gene therapy (28).

Out-of-pocket costs such as travel, accommodation and time away from work were not considered as impacts of gene therapy by general population participants, however these were a consideration for consumer participants. For patients living in rural and remote areas, out of pocket costs are likely to be exacerbated by the geographical distance to their nearest treatment centre. Here, consumers discussed the impact that out-of-pocket costs may have on their ability to access therapy. In particular, they raised the genetic nature of diseases to be treated using gene therapy, as this feature could give rise to more than one relative being eligible for therapy within a single family thereby compounding any out-of-pocket costs. In such cases, governments may consider offsetting out-of-pocket costs for isolated patients, as already occurs in other instances (29).

Two other cost impacts of gene therapy were discussed by general population and consumer participants. The general population raised the costs to the health system that the widespread introduction of gene therapy would incur, aligning with their perspectives on opportunity costs according to the prevalence of those in need within the population. Conversely, consumers focused on cost savings to the health system as an influence on decision making. Both perspectives have veracity, with the differing focuses likely reflecting consumers' deeper understanding of the current ramifications of living with disease, and the economic benefits that a potentially curative therapy may bring.

Consumers' reported lack of certainty on the details of the gene therapy process is consistent with a previous study where participants reported wanting to know more about the process and logistics of the administration of the gene therapy product, including whether additional medication or hospital visits were needed (20). However, details of the gene therapy process were not raised as an uncertainty in general population discussions, which may be due to a lack of direct implications for this group.

Both participant groups raised uncertainties around gene therapy effectiveness, a factor that is likely to heavily influence a patient's consideration of the associated risks and benefits of the therapy. This finding is consistent with a previous study, where men with severe haemophilia discussed the need for transparent information on gene therapy risks and benefits, and the influence that this would have on decision making (30). Current uncertainties on the effectiveness of gene therapy underpins the need for a better understanding of both the benefits gene therapy are likely to bring, and the severity and likelihood of the risks associated with it. At present, while some evidence is available on the effectiveness of gene therapy, long term data in specific disease cohorts is not available, rendering any

predictions of long-term effectiveness speculative. A lack of evidence on gene therapy effectiveness is also linked to a separate challenge raised by both consumer and general population participants, whereby more favourable treatments for a particular condition may become available in the future. Participants were concerned that in this instance, previous administration of gene therapy may preclude them from accessing alternative treatments. This suggests that, despite anticipated improvements to quality of life, reservations on receiving gene therapy currently remain.

This study has a number of limitations. Firstly, the consumer participants may reflect a greater motivation to seek new treatments for themselves, their families or their representatives than others with lived experience who did not volunteer to participate in the study. There is also likely to have been variation in the extent of knowledge of gene therapies and the health system between consumer participants. General population representatives may also have been more interested and knowledgeable on gene therapies. There is also the possibility that focus group/interview facilitators subconsciously introduced their own lived experience into discussions on the topics introduced, although our structured question prompts are likely to have mitigated this risk.

This study contributes to the body of literature on perceptions of gene therapy by those living with haematological disease, those closely affected by disease, and the general population. Some findings are likely to be generalizable to any chronic disease with the potential to be treated by gene therapy in future. In addition to economic considerations, we put forward a clear set of decision-making considerations, barriers to access and uncertainties that will require resolution prior to the widespread adoption of gene therapies in Australia. The study also highlights unresolved concerns that potential recipients of gene therapy still hold, particularly in relation to the effectiveness of gene therapy and other types of treatments for their condition that may become available in the future.

Our study provides HTA committees with valuable insights into decision-making on gene therapies to be funded, with findings likely to be applicable to other nations with similar health systems and HTA processes. It provides the basis for broader work that must be undertaken to enable HTA committees to develop a generalizable model for assessing emerging gene therapies. Further work should encompass a larger study on consumer and societal preferences as well as deeper consideration of the ethico-legal factors at play, to enable a fair and equitable assessment of a class of potentially life-changing therapies for patients with a range of chronic diseases.

Declarations

Data Availability Statement:

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Ethical Approval:

This study was approved by The University of Sydney Human Research Ethics Committee (approval number 2024/HE000224). All participants provided informed consent.

Competing Interests:

A/Professor Kylie Mason is a member of the Pharmaceutical Benefits Advisory Committee and a member of the Economics Sub Committee of the Pharmaceutical Benefits Advisory Committee. Professor Kirsten Howard is a member of the Pharmaceutical Benefits Advisory Committee and Chair of the Economics Sub Committee of the Pharmaceutical Benefits Advisory Committee. Professor Rosalie Viney is a member of the Life Saving Drugs Program Expert Panel. Adjunct Associate Professor Jo Watson is Deputy Chair of the Pharmaceutical Benefits Advisory Committee and a member of the Economics Sub Committee of the Pharmaceutical Benefits Advisory Committee.

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Author Contributions:

KH, RDAL and JW conceptualised the project and methodology, and acquired funding to conduct the project. MG, PW and AR conducted the project administration and investigations. RDAL, JW and KP facilitated interviews and focus groups. All team members contributed to formal analyses. AR wrote the original draft of the manuscript. All team members contributed to manuscript review and editing.

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Figures

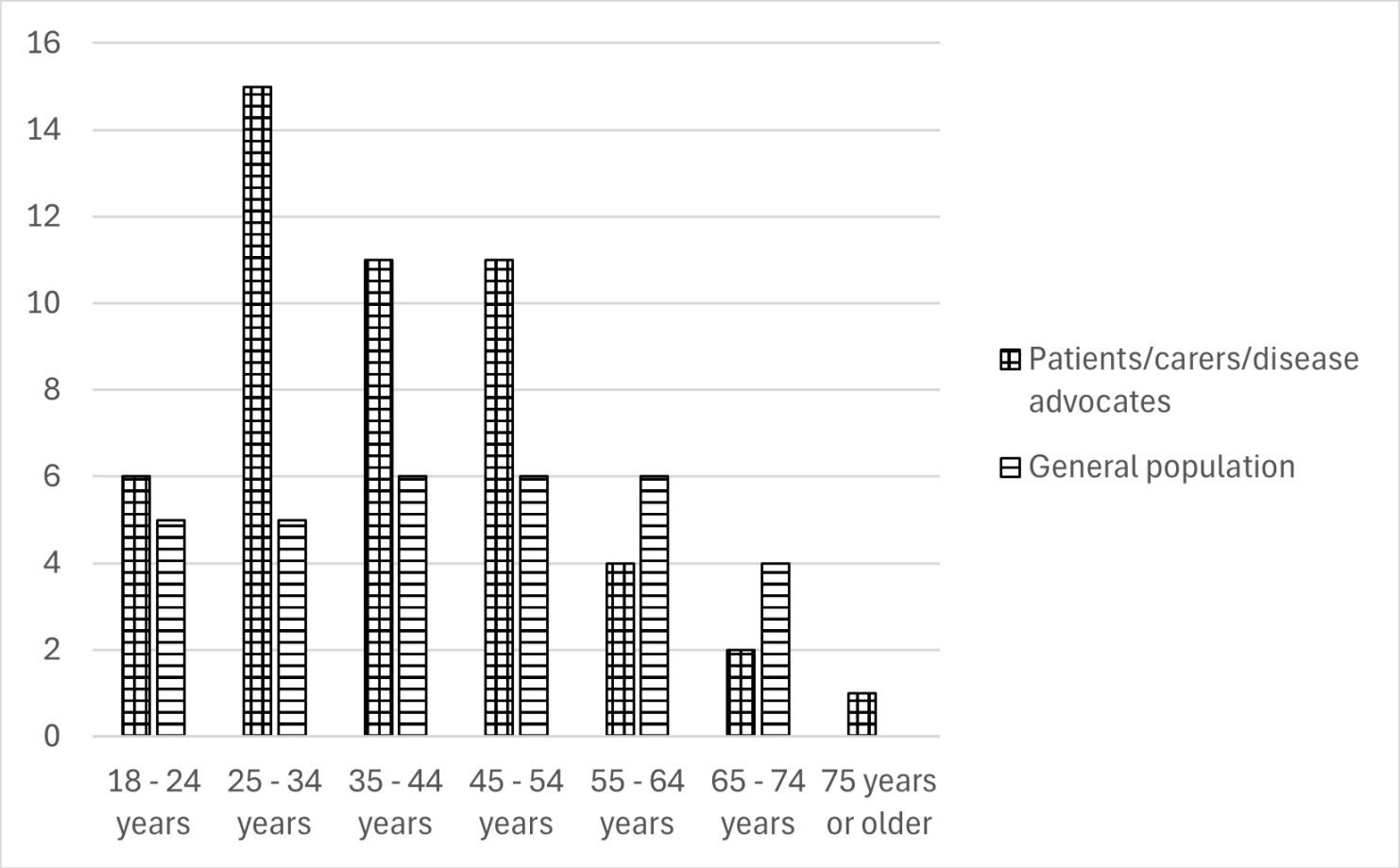


Figure 1

Age ranges of consumer focus group and interview (n=50) participants and general population focus group (n=32) participants

Supplementary Files

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