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Research Report

Clinician Perspectives of Gene Therapy as a Treatment Option for Duchenne Muscular Dystrophy

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Abstract.
Background: Duchenne muscular dystrophy (DMD) is a progressive, life-limiting, neuromuscular disorder. Clinicians play an important role in informing families about therapy options, including approved gene therapies and clinical trials of unapproved therapies.
Objective: This study aimed to understand the perspectives of clinicians about gene therapy for DMD, which has not previously been studied.
Methods: We conducted interviews with specialist clinicians treating patients with DMD in the United States ($n = 8$) and United Kingdom ($n = 8$). Interviews were completed in 2022, before any approved gene therapies, to gain insight into barriers and facilitators to implementing gene therapy and educational needs of clinicians.
Results: Most respondents expressed cautious optimism about gene therapy. Responses varied regarding potential benefits with most expecting delayed progression and duration of benefit (1 year to lifelong). Concern about anticipated risks also varied; types of anticipated risks included immunological reactions, liver toxicity, and cardiac or renal dysfunction. Clinicians generally, but not uniformly, understood that gene therapy for DMD would not be curative. Most reported needing demonstrable clinical benefit to justify treatment-related risks.

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Conclusions: Our data demonstrate variability in knowledge and attitudes about gene therapy among clinicians who follow patients with DMD. As our knowledge base about DMD gene therapy grows, clinician education is vital to ensuring that accurate information is communicated to patients and families.

Keywords: Patient preference, duchene muscular dystrophy, gene therapy; clinical trials, clinician perspectives

INTRODUCTION

Duchenne muscular dystrophy (DMD, OMIM# 310200) is a progressive, life-limiting neuromuscular disorder affecting approximately 1 in 5000 live male births [1]. DMD is caused by hemizygous pathogenic variants in the largest known human gene, the *DMD* gene, which encodes for the protein dystrophin [2]. Current supportive treatments have prolonged the life expectancy to a median of 29 years [3]. However, no treatment prevents the loss of ambulation or other severe disease manifestations such as respiratory failure and cardiomyopathy [4]. Gene therapy is a potential disease-modifying treatment that has risks and unique challenges in the context of DMD due to the size of the *DMD* gene [5]. Due to vector size limitations, a micro-dystrophin must be inserted, instead of the entire gene [6]. Clinical trials reported some serious adverse reactions including acute serious liver injury, immune-mediated myositis, and myocarditis with one death [7].

At the time of data collection for this study, no gene therapy for DMD had been approved by the Food and Drug Administration (FDA) or the European Medicines Agency (EMA), although multiple clinical trials were ongoing. During manuscript preparation, the first gene therapy for DMD, ELEVIDYS, was approved by FDA for the treatment of ambulatory patients aged 4 through 5 years. Patient and caregiver enthusiasm for gene therapy is reportedly high in the DMD community [8]. Clinicians play an essential role in informing families about gene therapy and its potential use, yet clinician perspectives of gene therapy as a treatment for DMD have not been studied.

Across all indications, few studies exploring clinician perspectives of gene therapy have been reported in the literature. A survey done in 2021 to assess knowledge and attitudes of gene therapy that included 419 clinicians in Saudi Arabia found that most respondents (87.4%) knew what gene therapy was. However, less than half (45.3%) recognized that gene therapy could have serious health risks. Most clinicians in this cohort (77.5%) felt that gene therapy is or will soon be a useful treatment strategy, and 57.4% were concerned about the use of gene therapy [9]. Another study in 2022 explored patient and clinician perspectives of gene therapy for hemophilia in the United Kingdom (UK) through semi-structured interviews. Self-reported knowledge of gene therapy was good or very good for approximately half of the respondents. Still, patient and clinician data were reported together, limiting clinician-specific interpretation of the data. Respondents cited uncertainty about the effectiveness and side effects of gene therapy as reasons not to receive or recommend gene therapy. However, participants indicated a general willingness to receive or recommend gene therapy for hemophilia, with responses ranging from very willing (10%) or willing (45%) to neutral (20%) and not willing (25%) [10]. Two other studies found that clinicians generally had a positive attitude about gene therapy for inherited eye diseases [11, 12].

To expand this limited literature, this research aimed to gain insight into clinician perspectives on gene therapy for DMD to inform future clinical implementation, educational needs, and research. Our aims were as follows:

- Assess self-reported understanding of, questions regarding, and experience with gene therapy.
- Explore perceived benefits, limitations, and implementation challenges associated with gene therapy.
- Explore experiences discussing gene therapy with patients and families.

PARTICIPANTS AND METHODS

This study was part of a larger international research study on patient, caregiver, and clinician attitudes and preferences regarding gene therapy for DMD. The project was sponsored by Duchenne UK and the DMD Hub at Newcastle University, in partnership with Parent Project Muscular Dystrophy (PPMD). The research lead was RTI International, and members of the research team included representatives from each organization. The interview guide, results interpretation, and results write up were informed by a project Advisory Board comprising representatives from six biopharmaceutical

companies (Audentes Therapeutics Inc, Pfizer Ltd, Regenxbio Inc., Sarepta Therapeutics, Solid Biosciences, and Vertex Pharmaceuticals); six clinical experts; two parents of children with DMD; two adults with DMD; and an ethicist.

A convenience sample of specialist clinicians who provide care to patients with DMD in the United States and the UK were recruited for interviews via direct email invitation by research staff at PPMD or the DMD Hub at Newcastle University. UK clinicians came from DMD Hub sites, a network of clinical sites in the UK involved in the delivery of DMD clinical trials, or the North Star Clinical Network of pediatric neurologist or neuromuscular specialists who provide regular care to patients with DMD. U.S. clinicians known to PPMD staff were invited. Clinicians who agreed to participate provided consent electronically and completed a short online survey prior to scheduling the interview. The online survey collected participant age, gender, country of residence, practice specialty, number of years in the specialty, number of patients with DMD seen per year, experience as part of a clinical trial team, and self-rated understanding of gene therapy (see Survey as a supplemental file).

This study used interpretive description [13], an applied qualitative approach designed for the study of applied health and clinical problems that lends well to a multi-expertise research team. The study team generated the draft instruments, and the advisory committee provided feedback that was integrated into the final instruments. The interview included questions grouped under the following domains (see Interview Guide as a supplemental file):

- Knowledge of, experience with, and questions about gene therapy.
- Attitudes about gene therapy as a treatment option for DMD and anticipated benefits, harms, and challenges.
- Perceptions of whether and when gene therapy would be approved for use in DMD.
- Communication about gene therapy with patients and families.

Several additional questions on clinical site readiness were part of the interview but are not included in this report. This research was approved by RTI's Committee for the Protection of Human Subjects (STUDY00021864) and Newcastle University Faculty of Medical Sciences Ethics Committee (2254/17024/2021).

One interviewer (HC), an experienced genetic counselor who is trained in qualitative research and who had no prior experience with the respondents, conducted all the semi-structured interviews using the interview guide. Interviews were conducted from April through July 2022. Interviews were recorded and transcribed. Quantitative data from the online survey were analyzed descriptively. During qualitative data immersion, investigators reviewed the transcribed interviews for emergent themes, which were cross-referenced with the interview guide to generate deductive categories to maintain alignment with the research questions, while allowing for categories that emerged inductively. This resulted in 31 domains used for coding. We conducted coding using a matrix approach in Excel [14]. The research team developed the matrix containing the 31 domains as columns and defined each domain to ensure consistent analysis. Three researchers trained to conduct the analysis were assigned five to six transcripts to conduct analysis. The reviewers used the matrix to summarize each clinician's responses according to the identified domains. In cases where a certain domain did not emerge in a particular transcript, researchers noted the absence in the matrix. Upon completion of the summaries, another researcher entered the pre-survey responses in the matrix and conducted a quality control review, which resulted in adjustments to the domain summaries to ensure alignment with the domain definitions. As a final step in the analysis, the research team used the matrix to complete synopses for each interview and domain. Emerging results were reviewed and discussed by the advisory committee before final refinement and reporting.

RESULTS

Participants

Interviews were completed with 16 clinicians (Table 1); 41 were approached, yielding a response rate of 39%. Clinicians were mostly neurology/neuromuscular specialists ($n = 12$) and were split equally between males and females. They ranged from seeing 25 to 500 patients with DMD per year, with U.S. clinicians reporting higher numbers of patients than UK clinicians; five of eight U.S. clinicians reported seeing 100 or more patients with DMD per year. UK clinicians mostly saw pediatric patients only, whereas all U.S. clinicians saw both pediatric and adult patients. All but one clinician had been part of a DMD clinical trial team; five were part of a DMD gene therapy clinical trial at their site.

Table 1
Clinician self-reported characteristics

	Clinicians ($n = 8$)	
	US	UK
Age range	38–60	36–56
Gender		
Male	4	4
Female	4	4
Area of specialty		
Cardiology	2	0
Neurology/neuromuscular disorders	4	8
Rehabilitation medicine	1	0
Not specified	1	0
Number of years in specialty	6 to more than 20	4 to more than 20
Number of patients with DMD seen per year	40–500	25–80
Patient population		
Pediatric only	0	6
Pediatric and adult	8	2
Adult only	0	0
Clinical trial experience		
DMD gene therapy trial	4	1
DMD clinical trial (not gene therapy)	7	7
Gene therapy trial for other condition	2	2
Clinical trial (not gene therapy) for other condition	5	4
Understanding of gene therapy		
Has some understanding	0	1
Understands quite well	3	1
Understands and could explain to others	5	6

Table 2
Common clinician-reported questions about gene therapy for DMD

- How to select patient groups to use gene therapy (e.g., ages outside those included in clinical trials)?
- When is the best time, in terms of age and disease progression, to use gene therapy?
- How effective is gene therapy?
- How safe is gene therapy?
- How can we modulate the side effects of gene therapy?
- How long will the benefits last?
- Will re-dosing be possible/necessary?
- What are the long-term outcomes of gene therapy?
- What benefits could gene therapy have when used in combination with other therapies?
- Are there biomarkers to predict which patients are going to respond to gene therapy and which are not?
- How do we scale gene therapy from clinical trials to the entire DMD population?

Knowledge of gene therapy

Most clinicians reported being confident in their knowledge of gene therapy and were able to define gene therapy. However, when asked to explain the difference between gene therapy and gene editing, some clinicians acknowledged a lack of understanding of specific concepts:

> *I think with gene therapy, we are putting in and introducing a gene to replace the faulty gene or the absent gene. With gene editing, it's a bit like sort of chopping and cutting and pasting together. So that we can actually create a gene that can be read.*

> *Gene therapy for me is an overarching word that encompasses different ways of altering the way your genes work. So that even exon skipping would for me be a kind of gene therapy, whereas gene editing…I think about the CRISPR kind of stuff where you change a bit. I have to admit that maybe I'm not entirely clear about the names we give it and maybe I don't use them consistently enough.*

Clinicians were asked to delineate their biggest questions about gene therapy. Respondent questions were numerous and varied. The most common questions are listed in Table 2.

Clinician attitudes about gene therapy as a treatment for DMD

Clinicians reported mixed attitudes about gene therapy, which did not seem to be related to their degree of clinical experience or their country of residence. Although several clinicians were very optimistic and several others were skeptical, most expressed a cautious optimism about gene therapy in the context of DMD. They were hopeful about the potential, and most (but not all) were realistic about the limitations of gene therapy in DMD. Some noted that gene therapy has seemingly been "around the corner" for years and that their enthusiasm over time has decreased. All recognized that there were significant challenges to the development and approval of a gene therapy for DMD.

> *I think [gene therapy] is a revolution. I think it is science fiction made real, and I think that it will open the door to a lot of progress in terms of improvement for patients.*

> *I think for human diseases it is a very good option, and I'm happy that it is being investigated. I'm more hesitant, I don't think sadly that we're gonna see that same profound impact in Duchenne.*

> *I guess we need a treatment that improves the condition, improves quality of life, and gene therapy would seem to be a candidate. But the challenge is big, and there's still a lot of work to be done.*

Anticipated benefits from gene therapy

Clinician responses varied regarding potential degree of benefit (ranging from curative to time-limited stabilization) and duration of benefit (ranging from 1 year to lifelong), as shown in Table 3.

Several clinicians mentioned the variability in anticipated benefits based on the age or disease stage during which the patient receives gene therapy; they expected more benefits for patients who were treated early. If gene therapy is introduced early enough, many clinicians expected a slowing of disease progression and possibly minimal need for other interventions or treatments. Specific anticipated benefits that respondents described included the postponement of loss of ambulation and cardiac and respiratory dysfunction. A common theme among clinicians was the desire for clinically relevant benefits that will translate to improvement for the daily life of patients, not only benefits to biomarkers such as dystrophin. Many clinicians expressed uncertainty about the duration of benefits, as shown in Table 3.

> *Hopefully, we will stop the process and will make these kids look more like a Becker muscular dystrophy phenotype than a Duchenne.*

> *From my standpoint, I would love to get dystrophin expression in the heart enough that nobody has cardiomyopathy.*

> *I think it would depend upon how early we've infused them. But if... you could have newborn screening, and it detects Duchenne really early, then potentially, and this is all theoretical, in maybe 50 years' time, and you could completely correct the genetic defect, then potentially there's a cure there.*

Potential risks from gene therapy

Most risks mentioned were associated with administering gene therapy via a viral vector. The degree of concern for the potential risks of gene therapy varied among participants. Anticipated risks included immunological reactions, liver toxicity, and cardiac and renal dysfunction. Most clinicians stated that they felt the risks would mostly be mild and treatable in a clinical setting. However, respondents acknowledged a small chance for severe adverse reactions such as death. A few clinicians stated the risk of death is never acceptable, whereas others cited the severity of the disease as justification for an acceptable gene therapy-related risk of death. Some clinicians stated a numerical risk of death that would seem acceptable to them, responses ranged from zero to as high as 10%.

> *I don't think personally that the risk is extremely high. And I think personally it's an acceptable risk given the devastating nature of this disease and what we've learned so far. So, I am not extremely concerned about risk at this point... I think that each individual is going to have to decide for themselves how much risk they want to take.*

> *I'm concerned. I mean, some of the risks could be quite severe, and you're giving this usually to children and this is not a fatal disease, or at least not immediately fatal.*

> *These severe side effects that have either death or prolonged hospitalization, irreversible kidney, or liver damage; to me it's not acceptable.*

Table 3
Clinician-reported anticipated benefits and duration of benefit

Participant	Benefits anticipated	Duration
UK1	Slow disease progression, stabilization, potentially even improvement	Unsure
UK2	Improve, then stabilize, disease progression, which will ultimately continue	More than 1 year, less than 5 years
UK3	Stop disease progression	Forever
UK4	Reduce DMD-related decline	Unsure, "a number of years"
UK5	Improve ambulation, stabilize decline	5–10 years
UK6	Slow disease progression	5–10 years
UK7	Potential cure	Lifelong
UK8	Stop disease progression	Unsure
US1	Improve symptoms, delay other complications, decrease the rate of decline	Unsure, "it looks like they're durable"
US2	Change DMD to milder Becker muscular dystrophy phenotype, stabilize progression	10 years
US3	Slow disease progression, keep the disease more static	5 years
US4	Stabilize disease progression	Unsure
US5	Improve symptoms, delay disease progression	7–8 years
US6	Slow down disease progression or completely prevent progression	10–15 years
US7	Stabilization, improvement over the natural history, slow disease progression	Several years
US8	Prevent cardiomyopathy, not able to reverse existing damage	Lifelong

Talking with patients and families about gene therapy

Most clinicians have talked with their patients about gene therapy, but three had not. Some reported that they bring up the topic routinely during clinic visits, and others only discuss it when patients ask about it. Many noted that parents commonly ask about gene therapy and when it will be available. Those who do not routinely talk with their patients about gene therapy expressed the desire to focus on what they can do now to make patients' lives better. About half of clinicians in both the United States and the UK stated they have enough time to talk with families and explain gene therapy, whereas the other half stated they do not have enough time (with variation seen in both countries).

> *I will be honest that I don't directly talk about it because I want to talk about day-to-day life, getting on with things, and all the things that I feel are important.*

> *We absolutely will not have enough time. Because it takes a lot of time, and we like to take time to do it properly.*

> *Actually, a third of our Duchenne patients are... lower socioeconomic, not well educated. So, they're not running around like, 'What's the latest therapy for Duchenne?'*

Anticipated implementation of gene therapy

Clinicians reported variable estimates of when they anticipated that gene therapy for DMD will be approved and available to patients in their country. Some said as little as a year or two, whereas others thought clinical availability will take longer (up to 10 years). U.S. clinicians were more likely to say 1 to 2 years, and UK clinicians were more likely to say 3 to 5 years. If more than one gene therapy were approved for the treatment of DMD, clinicians said they would consider several factors when selecting which to pursue, primarily the demonstrated short- and long-term benefits and reported adverse events.

The following were most reported resource gaps for sites to administer gene therapy:

- Adequate staff
- Cost
- Physical space to administer the transfusions and monitor patients

Related to cost, U.S. clinicians were concerned about access and insurance approvals for the use of DMD gene therapy, whereas UK clinicians expressed the need for adequate cost-benefit analysis for the government to approve its use.

> *What the worry is, the numbers of patients with DMD is so much higher [than SMA] and how will it be delivered... So, the same model of delivering*

gene therapy in a small number of centers. I don't look forward to that.

We don't know the cost of the drug and what is going to be approved, what is not going to be approved.

I think there are families who might have cultural or social barriers to accessing a treatment like this, that I look after. I think that there are families who are quite risk averse who'd be really scared about putting their sons through this sort of treatment.

Comparisons to Spinal Muscular Atrophy (SMA)

Most clinicians reported experience administering gene therapy for SMA or caring for patients who had received SMA gene therapy. Many referenced their experience with SMA gene therapy when they were asked about the potential risks/benefits of gene therapy for DMD.

I keep coming back to SMA because that's where I have some more experience with the gene therapy. You'd hope that the government would say, 'Well, it works for SMA and should work for Duchenne. Let's start funding it.'

I guess it's easy to be distracted by the relative ease in which gene therapy for SMA has arrived, and superficially, that's wonderful and babies are surviving, but it's a different condition, a different patient group. [Gene therapy for DMD] may not be curative in the way that it is for SMA.

It was generally felt that bringing DMD gene therapy to clinics would be more straightforward than it was for SMA, now that the hospital infrastructure has been established.

DISCUSSION

To our knowledge, this is the first study exploring clinician perspectives of gene therapy as a treatment for DMD. The clinicians interviewed are DMD experts who are likely to be involved in administering gene therapy and follow-up of patients who receive gene therapy. Understandably, respondents made comparisons to gene therapy for SMA [15], as most of these clinicians have experience with both patient groups. However, gene therapy for DMD has challenges beyond those faced by SMA due in part to the size of the *DMD* gene, which cannot fit into an adeno-associated viral vector. For DMD, a microdystrophin must be inserted into the vector, which may result in ameliorating the DMD phenotype to a milder phenotype [6]. In addition, the target cells are muscle cells, which are a much larger target than motor neurons [6] and which degenerate, which is expected to result in limited duration of benefit [5]. There are insufficient data currently to make conclusions about duration of benefit.

Clinicians generally agreed that, although gene therapy has potential benefits for DMD, these benefits need to be demonstrated, and the risks and safety must be better understood. Clinicians desired clinically significant benefits (e.g., improvements in body function and quality of life). However, recognizing that these benefits will take years to measure, FDA may grant accelerated approval on the basis of a surrogate endpoint that is reasonably likely to predict clinical benefit, with a requirement to confirm clinical benefit in the post-approval setting. Clinician findings clearly indicate the importance of continuing to follow patients and collect longer-term outcome data to more fully understand benefits over time.

Most respondents described the risks associated with administering gene therapy via a viral vector. For many, the severity of the disease justifies a risk for serious adverse events, including death, due to gene therapy; some respondents noted that the risk tolerance of patients and families is most important in decision-making. In a prior study evaluating patients' and caregivers' maximum acceptable risk (MAR) of mortality for gene therapy to treat DMD, the average MAR of death was 3.5% for therapy used at the time [16]. The true risk of death due to any specific gene therapy will not be known until thousands of individuals undergo treatment.

Respondents identified several challenges to administering gene therapy as a clinical treatment. First, the population of patients with DMD is estimated at 5.1 per 100,000 people in the United States [17]. Scaling up gene therapy from clinical trials to an approved treatment would require sufficient staff, time, and clinic space—all of which were cited as current limitations. It will be important to build from experiences with SMA to support clinicians and health care systems in overcoming these challenges. The potential cost of the drug was also cited as a concern to both U.S. and UK clinicians, but the specific concerns varied due to the different health care systems in these countries.

Interviewed clinicians were largely confident in their knowledge about gene therapy, which is con-

sistent with prior studies [9, 10]. Interview data suggest that most understand critical concepts, but some had knowledge gaps, and clinicians had many questions about DMD gene therapy that remain to be answered. Although most clinicians voiced an understanding of the differences between expected gene therapy outcomes for SMA and DMD, a few respondents expected a similar benefit profile. Misconceptions among clinical experts may exacerbate over-expectation of benefit in patients and families. A prior systematic review of patient perspective of gene and cell therapies found that patients tend to express minimal consideration for the potential side effects and have unrealistic expectations of potential benefits [18]. Patients perceive physicians as the most reliable source of information [18]. Clinicians have an ethical obligation to practice evidence-based medicine and a professional obligation to stay abreast of new information in their practice areas; thus, clinician education is vital not only for instrumental purposes (ensuring accurate information is communicated, facilitating optimal clinical and psychosocial outcomes), but also so that clinicians are fulfilling the duties of their role and their fiduciary responsibilities to their patients and families.

Limitations

There are limitations to this study. Interviewed clinicians were a convenience sample of DMD experts in the UK or United States, and several were involved in DMD clinical trials. Knowledge of DMD gene therapy is expected to be higher among this group of experts and not representative of all clinicians. Clinicians with different specialties and expertise may have less knowledge of DMD gene therapy and more misconceptions. The viewpoints of interviewed clinicians may not reflect those of clinicians from other countries or those with different specialties. A broader study of clinician knowledge and beliefs about gene therapy for DMD is warranted, particularly as new therapies for DMD and other neuromuscular conditions become available to patients and families.

CONCLUSION

Clinicians' viewpoints on gene therapy for DMD vary, but most are cautiously optimistic and look for additional evidence of safety and effectiveness. Given the non-curative and still uncertain durability of long-term benefits expected from the first generation of DMD gene therapies, clinicians play an essential role in setting realistic expectations and supporting informed decision-making. This facilitates optimal clinical and psychosocial outcomes in patients and families facing a life-limiting condition with unmet treatment needs. As our knowledge base about DMD gene therapy grows, clinician education is vital to ensuring that accurate information is communicated to patients and families.

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CONFLICT OF INTEREST

KB is an employee of Pfizer Inc. IOCW is an employee of Pfizer Ltd. KB and IOCW were representatives of Pfizer on the Study Advisory Board and provided input into the design of the study, development of study materials and review of the manuscript. DP and VF are employees of Regenxbio Ltd. DP and VF were representatives of Regenxbio on the Study Advisory Board and provided input into the design of the study, development of study materials and review of the manuscript. AG and RDD are employees of Solid Biosciences Inc. AG and RDD were representatives of Solid Biosciences Inc. on the Study Advisory Board and provided input into the design of the study, development of study materials and review of the manuscript. There are no other conflicts of interest reported by authors.

SUPPLEMENTARY MATERIAL

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REFERENCES

[1] Crisafulli S, Sultana J, Fontana A, Salvo F, Messina S, Trifiro G. Global epidemiology of Duchenne muscular dystrophy: An updated systematic review and meta-analysis. Orphanet J Rare Dis. 2020;15(1):141.

[2] Aartsma-Rus A, Ginjaar IB, Bushby K. The importance of genetic diagnosis for Duchenne muscular dystrophy. J Med Genet. 2016;53(3):145-51.
[3] Landfeldt E, Thompson R, Sejersen T, McMillan HJ, Kirschner J, Lochmuller H. Life expectancy at birth in Duchenne muscular dystrophy: A systematic review and meta-analysis. Eur J Epidemiol. 2020;35(7):643-53.
[4] Broomfield J, Hill M, Guglieri M, Crowther M, Abrams K. Life expectancy in duchenne muscular dystrophy: Reproduced individual patient data meta-analysis. Neurology. 2021;97(23):e2304-e14.
[5] Elangkovan N, Dickson G. Gene therapy for duchenne muscular dystrophy. J Neuromuscul Dis. 2021;8(s2):S303-S16.
[6] Patterson G, Conner H, Groneman M, Blavo C, Parmar MS. Duchenne muscular dystrophy: Current treatment and emerging exon skipping and gene therapy approach. Eur J Pharmacol. 2023;947:175675.
[7] Lek A, Wong B, Keeler A, Blackwood M, Ma K, Huang S, et al. Death after high-dose rAAV9 gene therapy in a patient with duchenne's muscular dystrophy. N Engl J Med. 2023;389(13):1203-10.
[8] Heslop E, Turner C, Irvin A, Muntoni F, Straub V, Guglieri M, et al. Gene therapy in Duchenne muscular dystrophy: Identifying and preparing for the challenges ahead. Neuromuscul Disord. 2021;31(1):69-78.
[9] AlRasheed MM, AlAli H, Alsuwaid AF, Khalaf S, Ata SI, BinDhim NF, et al. Gene therapy knowledge and attitude among healthcare professionals: A cross-sectional study. Front Public Health. 2021;9:773175.
[10] Woollacott I, Morgan G, Chowdary P, O'Hara J, Franks B, van Overbeeke E, et al. Examining patient and professional perspectives in the UK for gene therapy in haemophilia. Haemophilia. 2022;28(4):588-609.
[11] Ganne P, Damagatla M, Naidu NK. Knowledge of genetic eye diseases and genetic services and attitudes toward genetic testing and gene therapy. Taiwan J Ophthalmol. 2021;11(4):372-9.
[12] Ganne P, Garrioch R, Votruba M. Perceptions and understanding of genetics and genetic eye disease and attitudes to genetic testing and gene therapy in a primary eye care setting. Ophthalmic Genet. 2015;36(1):50-7.
[13] Thorne S, Kirkham SR, O'Flynn-Magee K. The analytic challenge in interpretive description. Int J of Qual Methods. 2004;3(1):1-11.
[14] Nevedal AL, Reardon CM, Opra Widerquist MA, Jackson GL, Cutrona SL, White BS, et al. Rapid versus traditional qualitative analysis using the Consolidated Framework for Implementation Research (CFIR). Implement Sci. 2021;16(1):67.
[15] Claborn MK, Stevens DL, Walker CK, Gildon BL. Nusinersen: A treatment for spinal muscular atrophy. Ann Pharmacother. 2019;53(1):61-9.
[16] Peay HL, Fischer R, Mange B, Paquin RS, Smith EC, Sadosky A, et al. Patients' and caregivers' maximum acceptable risk of death for non-curative gene therapy to treat Duchenne muscular dystrophy. Mol Genet Genomic Med. 2021;9(5):e1664.
[17] Salari N, Fatahi B, Valipour E, Kazeminia M, Fatahian R, Kiaei A, et al. Global prevalence of Duchenne and Becker muscular dystrophy: A systematic review and meta-analysis. J Orthop Surg Res. 2022;17(1):96.
[18] Aiyegbusi OL, Macpherson K, Elston L, Myles S, Washington J, Sungum N, Briggs M, Newsome PN, Calvert MJ. Patient and public perspectives on cell and gene therapies: A systematic review. Not Commun. 2020; 11(1):6265.