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Living Through the Unknown: Exploring Hope, Uncertainty, and Identity in First-Time Gene Therapy for Rare Diseases

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ABSTRACT

Gene therapy represents a major breakthrough in molecular medicine, offering hope t individuals with rare genetic disorders who previously had limited treatment options While the clinical efficacy of gene therapy continues to evolve, little is known about ho patients experience this novel intervention, particularly when receiving it for the firs time. Despite its promise, current research lacks insight into how patients make sense o the emotional and existential dimensions of undergoing gene therapy.

This study employs a descriptive phenomenological approach to explore how individual with rare diseases interpret the experience of hope and uncertainty during their initia exposure to gene therapy. Data were collected through in-depth, semi-structure interviews with eight participants and analyzed using Colaizzi's method to uncove essential thematic meanings. Four major themes emerged: hope as a negotiated lifeline uncertainty as a psychological terrain, the body as a site of transformation, and th ethical burden of being among the first to receive experimental treatment. These finding illuminate how patients navigate emotional complexity and reconfigure identity throug their encounters with advanced biomedical innovation.

The study contributes to a deeper understanding of patient experience in the context o gene therapy and highlights the value of phenomenology in capturing subjectiv meaning. These insights may inform more ethically responsive and emotionall supportive models of care, as well as raise important implications for how hope can b effectively managed and supported throughout the gene therapy process. Future researc should continue to examine strategies for facilitating emotional resilience in patient undergoing highly novel and uncertain treatments.

INTRODUCTION

Gene therapy has emerged as a transformative advancement in molecular medicine, offering new possibilities for the treatment of previously incurable genetic disorders. As biomedical technologies continue to evolve, therapies that alter the human genome are transitioning from experimental concepts to clinical realities (Springer dkk., 2023). These developments are particularly significant for individuals diagnosed with rare genetic diseases, many of whom face limited treatment options and a progressive decline in quality of life. Within this context, gene therapy represents not only a biomedical intervention but also a convergence of science, hope, and existential uncertainty—especially for first-time recipients.

However, this promise also brings a range of psychosocial and ethical complexities. Patients undergoing gene therapy often find themselves navigating uncharted emotional terrain—balancing optimism with fear and autonomy with vulnerability—particularly in early-phase clinical trials where outcomes are uncertain. These lived experiences carry deeply personal and cultural meanings that cannot be captured by biomedical metrics alone.

Despite growing interest in patient-centered care, research continues to underrepresent the subjective dimensions of such transformative therapies. Quantitative approaches dominate the field, focusing on efficacy, safety, and outcome indicators (Watson dkk., 2019), but often fail to reflect the emotional, existential, and identity-related aspects of the experience (Vandekerckhove dkk., 2019). Even qualitative studies may lack depth when using overly structured designs that constrain narrative agency.

Consequently, there remains a significant gap in understanding how patients interpret and give meaning to gene therapy. A phenomenological approach—particularly within the descriptive tradition—offers a robust and philosophically grounded framework for exploring these rich and layered experiences. It prioritizes the lived meanings articulated by patients themselves, illuminating what it means to undergo gene therapy under conditions of radical uncertainty (Tian dkk., 2021).

This study adopts a descriptive phenomenological methodology to address this gap. Focusing on individuals with rare diseases, it investigates how they experience and make sense of hope, uncertainty, and identity during their first exposure to gene therapy. Using Colaizzi’s method of analysis and in-depth, semi-structured interviews, the study captures essential themes grounded in participants’ own words and reflections.

By emphasizing subjective insight, this research contributes to ethical, humanistic, and psychological discourses in biomedical innovation. It highlights the limitations of prevailing objectivist paradigms and advocates for integrative frameworks that recognize the complexity of human experience in clinical advancement.

The article is structured as follows. The introduction outlines the background, knowledge gap, and rationale for the study. The methods section describes the phenomenological framework, data collection through in-depth interviews, and thematic data analysis. Results are presented through major themes supported by direct participant quotes (Al-Massri dkk., 2020). The discussion connects findings with existing literature and highlights implications for ethical care and policy. Finally, the conclusion summarizes key insights and suggests directions for future phenomenological research in biomedical contexts.

RESEARCH METHODS

Study Design

A descriptive phenomenological approach, rooted in the philosophical tradition of Edmund Husserl, was employed to explore the lived experiences of individuals with rare diseases undergoing gene therapy for the first time. This design was selected for its capacity to uncover the essential structure of subjective experiences as they are perceived and interpreted by individuals in their natural contexts (Anand dkk., 2019). Phenomenology focuses on understanding phenomena through the lens of those who have directly encountered them, allowing for deep insights into emotional, psychological, and existential dimensions. In this study, the descriptive approach enabled the elucidation of participants’ conscious experiences of hope and uncertainty without the imposition of prior theoretical assumptions or interpretive frameworks.

Participants

Participants consisted of individuals aged between 18 and 50 who had been diagnosed with a rare genetic disorder and had undergone gene therapy for the first time within the past six months. Selection was conducted using purposive sampling to ensure that participants had rich, first-hand experiences relevant to the phenomenon under investigation. Inclusion criteria required that participants be mentally and physically capable of engaging in in-depth interviews, have completed at least one round of gene therapy, and be willing to share their experiences openly. Individuals with comorbid psychiatric conditions or who were unable to communicate effectively in the language of data collection were excluded (Dzobo dkk., 2021). The sample included eight participants (5 males, 3 females), with an average age of 34.6 years, representing diverse cultural and socio-economic backgrounds to enrich contextual understanding.

Data Collection

Data were collected through in-depth, semi-structured interviews conducted face-to-face in a private clinical consultation room or the participant’s home, depending on their preference. An interview guide was used to facilitate open-ended dialogue, focusing on participants' experiences of hope, uncertainty, bodily perception, and ethical reflections during gene therapy. Each interview lasted between 45 and 75 minutes and was audio-recorded with the participants' consent. Interviews were transcribed verbatim to preserve the authenticity of responses (Gholizadeh-Ghaleh Aziz dkk., 2019). A safe and supportive environment was ensured to promote honest and reflective communication. Field notes were also recorded to capture non-verbal cues and contextual observations. The interview protocol was adapted from validated instruments used in phenomenological health research, with modifications made to suit the specific context of gene therapy.

Data Analysis

Data were analyzed using Colaizzi’s method for descriptive phenomenological analysis, which involves a rigorous, step-by-step process to derive essential meanings from participants’ narratives (Hartheimer dkk., 2019). The process began with reading each transcript multiple times to achieve immersion, followed by the identification of significant statements related to the phenomenon. Meaning units were then extracted and organized into clusters of themes through thematic reduction. These themes were synthesized into exhaustive descriptions that reflected the essence of the lived experience. Software such as NVivo 14 was used to manage and organize qualitative data but did not dictate thematic development. The final themes were validated by returning them to participants for verification, ensuring fidelity to their intended meanings and reducing interpretive bias.

Ethical Considerations

Ethical approval was obtained from the appropriate institutional review board prior to data collection. Participants provided written informed consent after being thoroughly briefed on the aims, procedures, and potential risks of the study. Anonymity and confidentiality were maintained by using coded identifiers and securing all data in encrypted files accessible only to the research team. All procedures adhered to the ethical guidelines outlined in the Declaration of Helsinki and followed local ethical standards for research involving human subjects.

RESULTS

Hope as a Negotiated Lifeline

Participants described hope not as a static belief but as a dynamic construct that evolved in response to their deteriorating conditions and exposure to gene therapy. Hope was experienced as an internal strategy to sustain meaning in the face of biomedical uncertainty.

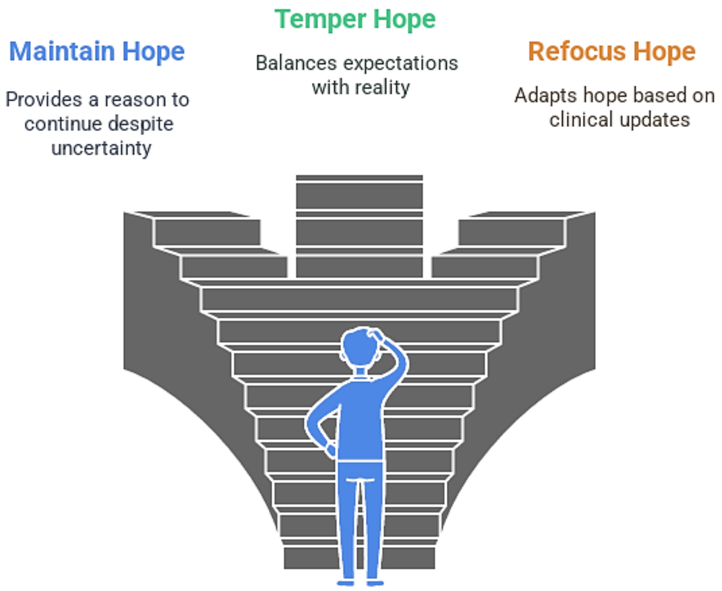
“Every morning I wake up and remind myself that this therapy might not cure me, but it gives me a reason to keep going. It’s like holding onto a rope in a storm.” (P4)

This sense of hope was not naïve or overly optimistic but was consciously tempered with caution. Participants negotiated their hope in parallel with clinical updates, often reframing it to maintain emotional balance.

“I don’t expect miracles. I just want one more year with my kids, maybe less pain. That’s what this treatment means to me.” (P2)

Hope, therefore, served as both a coping mechanism and a framework through which participants interpreted the value of the therapy.

How to manage hope during gene therapy?



Uncertainty as a Daily Psychological Terrain

Participants unanimously conveyed that uncertainty dominated their cognitive and emotional landscape throughout the therapy process. It manifested not only in fear of adverse effects but also in existential ambiguity about identity, bodily changes, and future prospects.

"What terrifies me isn't the treatment, it's not knowing what's next. Am I still me if my genes change?" (P7)

The uncertainty extended beyond scientific unknowns into deeply personal domains. The unpredictability of gene therapy outcomes caused emotional vacillation between hope and despair, stability and fragility.

"Some days I feel like a medical experiment. Other days I believe I'm a pioneer. It's mentally exhausting." (P1)

Uncertainty, thus, became an ever-present psychological terrain that participants had to navigate, often without clear guidance or emotional support.

The Body as a Locus of Transformation and Ambivalence

For many, the body was not merely a site of disease but became the subject of profound transformation through therapy. This transformation was accompanied by ambivalence—both a sense of renewal and alienation.

"After the second infusion, I started feeling... different. My body doesn't hurt like before, but I don't recognize myself fully." (P6)

Some participants expressed a spiritual reconnection with their physical selves, while others reported a distancing effect, as if their identity was shifting with the biological changes induced by the therapy.

"This new body feels like it doesn't belong to the old me. It's like I'm sharing my skin with someone else." (P3)

These narratives reveal that the body, post-therapy, becomes both a source of hope and a complex terrain of estrangement.

Ethical Tensions and the Burden of Being a 'First'

Participants conveyed a heavy ethical weight associated with being among the first to receive experimental gene therapy. While some embraced the label of "pioneer," others perceived themselves as reluctant subjects in an unpredictable biomedical journey.

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“I want to help science, but sometimes I wonder if I’m just part of a trial. A data point.” (P5)

This sense of burden was often coupled with gratitude but complicated by feelings of being “medicalized” or “used.” Participants highlighted a lack of psychosocial infrastructure to support their ethical and emotional concerns.

“No one asks how we feel about being first. They just want to know if the therapy works.” (P8)

Such reflections point to an unmet need for ethical dialogue and psychosocial care alongside clinical treatment.

The findings illuminate the intricate interplay between hope, uncertainty, bodily transformation, and ethical reflection in the lived experiences of individuals undergoing gene therapy for rare diseases. These themes do not exist in isolation but interact to form a complex emotional and existential reality that extends beyond clinical metrics. The essence of the phenomenon lies in the continuous negotiation of meaning amidst scientific innovation and personal vulnerability.

DISCUSSION

The findings of this study illuminate a complex interplay between hope, uncertainty, bodily transformation, and ethical responsibility among individuals undergoing gene therapy for rare diseases (Hu & Pan, 2020). These themes reflect how patients actively construct meaning within an unfamiliar therapeutic landscape—negotiating identity, moral agency, and emotional resilience. Rather than reiterating each result, this discussion interprets the findings in light of broader conceptual and clinical implications.

This study challenges the passive framing of patients as mere recipients of experimental treatments. Instead, participants demonstrated agency through conscious calibration of expectations and moral reflection on their roles as "firsts" in biomedical innovation (Lightner dkk., 2023). The emergence of ethical tension and altered body perception underscores the need for clinical approaches that go beyond efficacy and safety to encompass existential and psychological care.

In contrast to prior research—such as Mammana dkk. (2019), which addressed decision-making without deeper engagement with identity, or Mishra dkk. (2020), which touched on anxiety without thematizing bodily ambivalence—this study offers a phenomenologically grounded framework that integrates patients' words, meanings, and embodied realities. Consistent with Nasb dkk. (2020), it affirms that illness and therapy reshape one's being-in-the-world, not merely clinical status. Here, hope becomes an existential stance rather than a sentiment, and uncertainty a space for ontological reflection.

Clinically, the study suggests that practitioners must attune to the existential dimensions of therapy. Hope and uncertainty are not merely affective responses but shape how patients interpret and engage with biomedical change. Dialogical and empathetic communication models may therefore be more appropriate in managing these experiences. Culturally, the study highlights how identity transformation through gene therapy is influenced by moral and societal narratives—calling for ethically responsive and context-sensitive patient support.

At a systems level, these findings invite reconsideration of how experimental therapies are framed in discourse—not simply as scientific milestones but as deeply human experiences. Ethical dialogue, emotional validation, and participatory care models should accompany such innovations.

Nonetheless, this study has limitations. The purposive sample was small and context-specific, limiting generalizability. Moreover, while the phenomenological lens offered depth, it may have excluded other interpretive frameworks that could yield complementary insights. These boundaries do not diminish the findings but highlight the importance of contextualization.

Future research may explore these lived experiences across cultures, time points, and clinical conditions. Longitudinal phenomenological studies could trace how meaning evolves post-therapy, while interdisciplinary designs might bridge bioethics, narrative medicine, and science and technology studies. Such efforts can deepen ethical discourse and inform more human-centered innovations in experimental medicine.

CONCLUSION

This study explored how individuals with rare genetic disorders make sense of hope and uncertainty when undergoing gene therapy for the first time. Using a descriptive phenomenological approach, the findings revealed four central themes: negotiated hope, psychological uncertainty, bodily transformation, and ethical tension. These insights offer a deeper understanding of the lived experiences that conventional clinical research often overlooks.

The novelty of this study lies in its focus on first-time recipients of gene therapy—an emerging population whose subjective experiences remain largely undocumented in existing literature. While previous studies have examined psychological outcomes or ethical concerns in abstract terms, this research offers a thematically coherent, phenomenology-based account grounded in participants’ own words.

Methodologically, the study contributes by applying Colaizzi’s descriptive phenomenological method within a cutting-edge biomedical context. This approach enabled the articulation of essential meanings often missed by structured qualitative tools or outcome-based frameworks. It demonstrates how phenomenology can serve as a rigorous yet flexible lens for capturing emotional, ethical, and existential complexities in experimental therapies.

By highlighting these dimensions, the study addresses a critical gap in current literature and contributes to more patient-centered and ethically informed care practices. The findings also underscore the importance of integrating subjective experiences into the development of supportive clinical frameworks. Future research could expand this work across diverse cultural settings or explore longitudinal experiences to understand how meanings evolve as gene therapy becomes more widespread.

CONFLICT OF INTEREST

The authors declare no conflict of interest. This research was conducted independently, and the funder had no role in the design, execution, interpretation, or writing of the study. All views expressed are solely those of the authors.

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