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Living with Uncertainty: Patients' Experiences of Off-Label Drug Use in Rare Disease Treatment

Nining Ade Ningsih
Universitas Tamalatea Makassar, Indonesia
niningadeningsihh03@gmail.com

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ABSTRACT

The field of pharmacological research increasingly recognizes the importance of patient centered approaches, especially in contexts involving rare diseases and off-label drug use. While off-label treatments are commonly prescribed when standard therapies are unavailable, little is known about how patients interpret and navigate these decisions emotionally and ethically. This study addresses that gap by asking: how do patients with rare diseases experience and assign meaning to their use of off-label medications? Using a descriptive phenomenological approach, this study explores the lived experiences o ten patients through in-depth, semi-structured interviews. Thematic analysis revealed four core themes: off-label use as a last resort of hope, emotional and ethical ambiguity the influence of family dynamics, and the reassertion of personal agency. These finding were derived through systematic coding, thematic clustering, and careful interpretation of patient narratives using NVivo software. The results highlight the complex, deeply human dimensions of off-label pharmacological choices, emphasizing that such decisions are not only clinical but also profoundly existential. This study contributes to a more nuanced understanding of therapeutic uncertainty and calls for the integration o experiential narratives into ethical frameworks and clinical practice.

INTRODUCTION

In the evolving field of pharmacological research, the treatment of rare diseases presents a unique set of challenges that transcend biomedical considerations and enter the deeply personal realm of patient experience. Rare diseases, by definition, affect a small percentage of the population, yet collectively impact millions of individuals globally. Due to limited research investment and commercial incentives, therapeutic options for such conditions remain scarce, and patients often encounter significant barriers in accessing appropriate treatment (Alnuaimi & Almalik, 2021). Within this context, the use of off-label medications—drugs prescribed for indications not officially approved—has emerged as a practical but complex alternative for patients and clinicians alike.

While much of the discourse around off-label drug use has focused on regulatory, clinical, and ethical aspects, less attention has been paid to the lived experiences of patients who pursue these treatments under conditions of medical uncertainty. The off-label context often lacks the assurance of established treatment protocols, leaving patients to navigate emotional and psychological landscapes marked by fear, hope, skepticism, and agency. This phenomenon is not only biomedical but also deeply human, reflecting how individuals construct meaning, assert autonomy, and respond to systemic gaps in care.

Exploring the subjective experiences of patients using off-label therapies is essential to gaining a holistic understanding of rare disease treatment (Aronsen dkk., 2019). Phenomenology, as a research approach, is uniquely suited to uncovering the nuanced ways in which individuals interpret their health journeys. Rather than relying solely on clinical outcomes, a phenomenological inquiry invites the voices of those directly affected, revealing the textures of their emotional, existential, and relational realities. In doing so, it addresses an important epistemological gap in pharmacological research—namely, the absence of patient-centered narratives in the development and evaluation of therapeutic interventions. By focusing on meaning-making, this approach enables a deeper appreciation of how off-label treatment decisions are experienced in real-world, culturally embedded contexts.

Within the growing body of literature addressing rare diseases and off-label drug use, there has been an increasing emphasis on understanding the subjective experiences of patients. This shift reflects a broader recognition that beyond biomedical outcomes, the personal narratives of patients offer critical insights into how medical decisions are made and lived through in real contexts. Particularly in cases involving experimental or non-standard therapies, such as off-label medications, patients are often left to navigate a therapeutic landscape marked by ambiguity, limited clinical guidance, and emotional strain(Belay & Yirdaw, 2022). As such, research into their lived experiences has become an important sub-area within health and pharmacological studies.

However, capturing the depth and nuance of such experiences poses considerable methodological challenges. Traditional quantitative research methods, while valuable for measuring clinical outcomes, often fall short in accessing the rich, complex, and sometimes contradictory meanings that individuals assign to their health journeys. Standardized surveys and metrics may obscure rather than reveal how patients experience hope, uncertainty, fear, and decision-making in the context of off-label treatment. Furthermore, much of the existing literature tends to prioritize objective efficacy over interpretive insight, leading to a critical gap in understanding how patients interpret and emotionally process the use of treatments outside conventional medical approval.

These limitations highlight the inadequacy of conventional approaches in grasping the full essence of the phenomenon. By focusing on surface-level variables, prior methodologies often miss the existential and relational dimensions that define patients' experiences with off-label drug use. This underscores the need for a phenomenological approach—one that centers on individual meaning-making and allows researchers to engage deeply with how such pharmacological decisions are subjectively experienced in real-world contexts.

Despite the increasing clinical reliance on off-label medications for rare disease management, most research and decision-making frameworks continue to prioritize pragmatic solutions grounded in regulatory standards, pharmacological efficacy, and cost-effectiveness (Biggs & Doubrava, 2019). These approaches, while necessary for policy and clinical safety, are largely driven by quantitative data and biomedical models that inadequately address the experiential realities of patients. As a result, the emotional, psychological, and existential dimensions of navigating treatment decisions under uncertainty remain marginalized in the literature.

Conventional methods—such as randomized trials, case series, or retrospective analyses—offer limited insight into how patients interpret and live through the ambiguities surrounding off-label drug use. These methods often abstract the patient experience into data points, overlooking the complex and contextually embedded meanings that shape their choices, relationships, and sense of agency (Cole dkk., 2023). Particularly in rare disease contexts, where medical guidance may be minimal and patients must actively construct personal frameworks for decision-making, this oversight can obscure critical layers of understanding.

Addressing this gap requires a methodological shift from objective measurement to interpretive engagement. Phenomenology offers a powerful alternative by foregrounding the subjective experience and privileging the voices of patients themselves. Through this lens, the study aims to explore the essence of how individuals with rare diseases make sense of, cope with, and assign meaning to their experiences with off-label pharmacological treatment (Collier-Robinson dkk., 2019). Such an approach not only enriches the academic understanding of therapeutic journeys but also contributes to more empathetic and ethically responsive practices in clinical care.

Several studies have explored patient experiences in clinical decision-making, especially in areas involving chronic illness and experimental treatments. Research by Kearney et al. (2020) and

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Smith & Osborn (2017) has highlighted how patients interpret uncertain medical outcomes through personal, emotional, and relational frameworks. These studies demonstrate the importance of capturing lived experiences to inform ethical and patient-centered healthcare. However, few studies have specifically focused on how patients with rare diseases navigate the emotional and cognitive aspects of accessing off-label medications. This study builds on existing work by examining a less understood but increasingly common therapeutic scenario.

To address the limitations identified in previous research, this study adopts a descriptive phenomenological approach based on Husserl’s framework. This method emphasizes understanding how participants make sense of their experiences in their own words, without imposing external interpretations. It is chosen specifically to uncover the subjective meanings and existential realities that shape off-label treatment decisions (Collier-Robinson dkk., 2019). By engaging directly with patient narratives, the study offers a deeper understanding of how pharmacological uncertainty is experienced in practice. In doing so, it answers the central question: how do patients with rare diseases assign meaning to their use of off-label medications?

This article is structured as follows: The introduction outlines the general and specific background of the phenomenon and presents the knowledge gap. The method section details the phenomenological approach, sampling strategy, and data collection process (Cummins dkk., 2019). This is followed by the results section, which presents thematically organized narratives derived from participant interviews. The discussion interprets the findings in relation to existing literature and theoretical insights. Finally, the conclusion summarizes key contributions and suggests implications for practice and further research.

RESEARCH METHODS

Study Design

This study adopted a descriptive phenomenological design grounded in the philosophical tradition of Edmund Husserl, emphasizing the essence of lived experiences as conveyed by individuals confronting a specific phenomenon. The phenomenological approach was chosen to explore, in depth, the subjective experiences of patients with rare diseases who accessed off-label medications, a domain where quantitative measures often fail to capture emotional nuance and existential meaning (Jones dkk., 2023). By suspending preconceptions through epoché and engaging in phenomenological reduction, this design facilitated the emergence of pure experiential data, enabling a nuanced understanding of how individuals interpret and assign meaning to their pharmacological choices in the context of clinical uncertainty.

Participants

Participants included individuals diagnosed with rare diseases who had undergone off-label pharmacological treatment within the past two years. Selection was based on purposive sampling to ensure participants had firsthand, meaningful engagement with the phenomenon under investigation. Inclusion criteria required participants to be adults (aged 18 years or older), possess the cognitive ability to articulate their experiences, and provide written informed consent. Exclusion criteria included individuals currently experiencing acute psychological distress or those who lacked direct involvement in decision-making regarding their off-label treatment (Joo dkk., 2024). A total of ten participants (six females and four males), aged between 22 and 58 years, were recruited. This sample size aligns with established phenomenological research standards, which prioritize depth over breadth, enabling detailed exploration of subjective experiences. Additionally, the size was deemed sufficient based on data saturation, as no new themes emerged after the tenth interview, indicating adequate informational redundancy for capturing the essence of the phenomenon (Guest, Bunce, & Johnson, 2006). Participants represented diverse educational and socio-economic backgrounds, enhancing the depth and variability of experiential data.

Data Collection

Data were collected through in-depth, semi-structured interviews guided by a flexible interview protocol designed to elicit detailed narratives around decision-making, emotional responses, and personal meanings associated with off-label drug use. Interviews were conducted face-to-face in private clinical or home settings, depending on participant preference, to ensure a safe and comfortable environment. Each session lasted between 45 to 90 minutes and was audio-recorded with participant consent. Interview questions were open-ended, allowing participants to describe their experiences freely, and follow-up probes were used to explore emerging themes (Klingemann & Wieczorek, 2022). The interview guide was informed by existing literature and pre-tested with two individuals for clarity and relevance. All interviews were transcribed verbatim for analysis.

Data Analysis

Data were analyzed using a thematic approach consistent with descriptive phenomenology, aimed at uncovering essential structures of experience. The analysis followed a systematic process: initial reading of transcripts for holistic understanding, identification of meaning units, coding of significant expressions, and clustering into thematic categories (Liu dkk., 2020). Thematic reduction was employed to distill core meanings while maintaining fidelity to participant narratives. NVivo software was used to organize and manage the data, facilitating transparency and coherence in theme development. Throughout the process, themes were validated against raw data to ensure alignment with participants' original expressions, enabling the emergence of essential meanings related to the phenomenon of accessing off-label medications.

Ethical Considerations

Ethical approval for the study was obtained from the appropriate institutional ethics review board. Written informed consent was secured from all participants prior to data collection, following a thorough explanation of the study’s purpose, procedures, and potential risks. Participants were assured of the voluntary nature of their involvement and their right to withdraw at any time without consequence. All data were anonymized, and confidentiality was strictly maintained through secure data storage and pseudonymization during transcription (Martinez-Lopez dkk., 2021). The research adhered to international ethical standards for studies involving human subjects, including the Declaration of Helsinki and relevant national guidelines.

RESULTS

Off-Label as a Last Resort—A Path of Desperation and Hope

Participants consistently expressed that the use of off-label medications was not a proactive choice but a consequence of exhausting standard therapeutic options. The decision to use such treatments was often made in moments of desperation, driven by the progressive nature of their illnesses and the absence of viable alternatives.

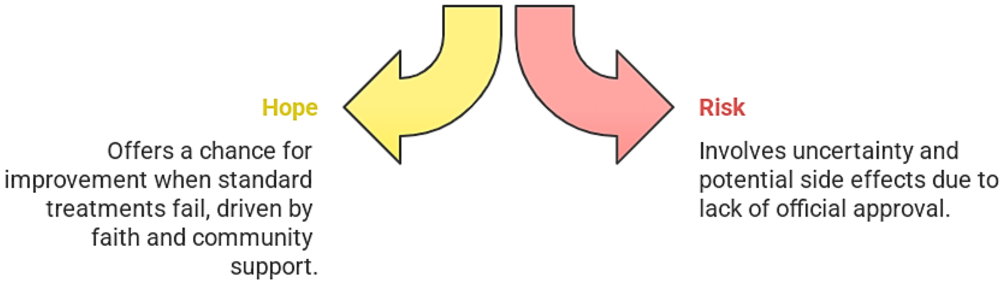
“I knew it wasn't an officially approved treatment, but at that point, it was the only hope I had left. Everything else had failed.” (P3)

This hope was frequently coupled with anxiety and fear of the unknown. Patients described feeling caught between scientific uncertainty and the instinct for survival. The off-label treatment symbolized both risk and salvation.

“It felt like a gamble… but when you're told there’s nothing more they can do, you either accept it or fight back with whatever is available.” (P7)

The theme illustrates how patients reframe medical uncertainty into personal agency, often grounding their decisions in faith, anecdotal evidence, or peer testimonies from online communities.

Should I pursue off-label medication as a last resort?



Navigating Uncertainty and Medical Ambiguity

Patients highlighted the psychological toll of ambiguity surrounding off-label drug efficacy and safety. Many felt that medical professionals could offer little assurance, creating a vacuum where patients had to make decisions in a grey zone of information.

“The doctors themselves seemed unsure. They couldn’t say for certain if it would help, or even what the side effects might be. I had to decide with incomplete information.” (P1)

This uncertainty extended beyond clinical data to ethical and financial concerns. Some patients reported having to negotiate with healthcare providers or pharmaceutical companies directly, which further alienated them from the typical patient-care model.

“It was like entering a private deal, not part of regular treatment. I had to find the supplier, convince the doctor, and pay from my own pocket. It felt underground.” (P6)

This theme underscores the fragmented and emotionally burdensome experience of seeking unstandardized treatment in a structured health system.

Moral Ambivalence and Family Dilemmas

The use of off-label medications generated moral tension not only for the patients but also within their families. Participants often discussed the emotional labor of involving loved ones in decision-making, especially when outcomes were uncertain and financial costs high.

“My husband didn’t agree at first. He thought it was reckless. But when you’re the one in pain every day, you see things differently.” (P2)

Patients frequently carried a dual burden: the physical impact of their illness and the psychological weight of influencing the emotional well-being of family members.

“I could see the fear in my daughter’s eyes every time I took a dose. She didn’t say it, but I knew she was terrified I might not survive.” (P5)

This theme emphasizes the broader socio-emotional context of off-label medication use, revealing how these decisions reverberate through intimate relationships.

Asserting Control in Medical Vulnerability

Despite their vulnerability, patients described the off-label journey as a means to reclaim a sense of control over their health narrative. Engaging with non-conventional pharmacological pathways allowed them to resist passive patienthood and engage more actively with their treatment.

“Even though it was risky, I finally felt like I was doing something—not just waiting to die.” (P4)

Many expressed that making informed decisions, even under uncertainty, restored a measure of personal dignity and autonomy often lost during prolonged illness.

“I researched for weeks, joined forums, read medical journals. It was empowering. For once, I wasn’t just being told what to do—I was deciding.” (P8)

This assertion of agency became a central feature of how patients constructed meaning around their experiences and justified their choices.

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The findings reveal a complex, emotionally charged landscape in which patients with rare diseases engage with off-label pharmacological options. These decisions are marked by hope, desperation, ethical tension, and a deep desire for control in the face of medical uncertainty. Far from being passive recipients of care, these individuals emerge as active agents navigating a path filled with ambiguity and risk, striving to reclaim their lives through choices outside conventional medical paradigms.

DISCUSSION

The present study revealed that patients with rare diseases who undergo off-label treatment experience a journey marked by hope, uncertainty, moral tension, and a drive to reclaim agency over their health. These themes collectively answer the central research question by illustrating how off-label pharmacological decisions are not merely clinical choices but deeply personal acts shaped by emotional, ethical, and existential factors.

The findings directly address the research question by illuminating how patients assign meaning to their use of off-label medications amidst medical ambiguity. Rather than passively following medical advice, participants actively engaged in decision-making processes driven by a need for survival, emotional resilience, and personal dignity. This study contributes uniquely by foregrounding the patient’s voice in an area often dominated by regulatory and efficacy-based discourse. It shifts the lens from the pharmacological substance to the experiential substance—how treatment is lived, interpreted, and narrated in real-world, high-stakes situations.

The findings align with and extend previous work in the domain of experiential medicine. (Pang dkk., 2023) emphasized the symbolic significance of orphan drugs, a perspective reinforced here through patients' portrayal of off-label medications as sources of last hope. Similarly, (Pronk dkk., 2023) highlighted the emotional burden and moral dilemmas faced by patients engaging with experimental treatments. The current study complements these insights by situating them within the underexplored context of rare diseases and pharmacological uncertainty. Moreover, the results support phenomenological understandings of patient agency, illustrating how decision-making in extreme clinical contexts reflects a search for meaning and control rather than mere treatment compliance.

The implications of these findings extend beyond the individual patient experience to inform clinical ethics, health policy, and patient-provider communication in the treatment of rare diseases. The narratives captured in this study highlight the need for more empathetic and participatory healthcare models that recognize the emotional and existential dimensions of pharmacological decision-making. Clinicians may benefit from understanding the profound moral and psychological labor that patients undertake when faced with off-label options, prompting more supportive conversations around uncertainty and hope. Furthermore, policy frameworks governing off-label drug use should consider integrating patient narratives as part of the ethical justification for access, particularly in underserved and rare disease contexts. This phenomenological insight contributes to a more holistic appreciation of therapeutic journeys in modern medicine.

This study, however, is not without limitations. The use of purposive sampling and the relatively small number of participants, while appropriate for phenomenological inquiry, limits the transferability of findings to broader populations. The cultural and healthcare setting in which the study was conducted may also influence the way patients articulate and interpret their experiences, making the findings context-dependent. Additionally, the reliance on retrospective narratives may be shaped by recall bias or emotional distance from the actual events. These limitations do not detract from the depth of insight gained but suggest caution in generalizing the themes beyond similar socio-medical environments.

Future research could expand on these findings by exploring cross-cultural comparisons of off-label treatment experiences or by examining how healthcare professionals perceive and respond to patient narratives of uncertainty. Longitudinal studies may also provide deeper insight into how these experiences evolve over time and influence ongoing treatment choices. Importantly, integrating phenomenological perspectives with participatory or narrative-based research designs could further enrich our understanding of patient agency in complex therapeutic contexts. This study lays the groundwork for continued exploration into how meaning-making processes shape clinical engagement in scenarios of pharmacological ambiguity.

CONCLUSION

This study explored how patients with rare diseases experience and assign meaning to the use of off-label medications under conditions of medical uncertainty. Using a descriptive phenomenological approach, the study revealed key themes of hope, moral conflict, psychological resilience, and a desire for personal agency in the face of ambiguous treatment options. These findings offer valuable insights into the emotional and existential dimensions of pharmacological decision-making that are often overlooked in conventional clinical research. By centering patient narratives, the study addresses a critical gap in understanding how therapeutic choices are lived and understood beyond clinical efficacy. The research contributes to more empathetic, patient-centered care models and highlights the importance of integrating subjective experiences into ethical and policy frameworks. Future studies may build upon this work by examining diverse cultural contexts or expanding the method into longitudinal designs to track evolving patient perspectives.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article. All stages of the research, including design, data collection, analysis, and interpretation, were conducted independently of any commercial or financial relationships that could be construed as a potential conflict.

REFERENCES

Alnuaimi, K., & Almalik, M. (2021). Sexual educational needs of Jordanian women after giving birth. *Birth*, *48*(1), 52–60. Scopus. https://doi.org/10.1111/birt.12509

Aronsen, G. P., Fehren-Schmitz, L., Krigbaum, J., Kamenov, G. D., Conlogue, G. J., Warinner, C., Ozga, A. T., Sankaranarayanan, K., Griego, A., DeLuca, D. W., Eckels, H. T., Byczkiewicz, R. K., Grgurich, T., Pelletier, N. A., Brownlee, S. A., Marichal, A., Williamson, K., Tonoike, Y., & Bellantoni, N. F. (2019). "The dead shall be raised": Multidisciplinary analysis of human skeletons reveals complexity in 19th century immigrant socioeconomic history and identity in New Haven, Connecticut. *PLoS ONE*, *14*(9). Scopus. https://doi.org/10.1371/journal.pone.0219279

Belay, M. Z., & Yirdaw, L. T. (2022). Management of postoperative pain among health professionals working in governmental hospitals in South Wollo Zone, Northeast Ethiopia. Prospective cross sectional study. *Annals of Medicine and Surgery*, *80*. Scopus. https://doi.org/10.1016/j.amsu.2022.104148

Biggs, A., & Doubrava, M. (2019). Superficial ballistic trauma and subjective pain experienced during force-on-force training and the observed recovery pattern. *Military Medicine*, *184*(11–12), e611–e615. Scopus. https://doi.org/10.1093/milmed/usz061

Cole, T., Jamwal, R., & Hirth, M. J. (2023). Photovoice to explore the patient experience of a relative motion orthosis following a hand injury. *Journal of Hand Therapy*, *36*(2), 433–447. Scopus. https://doi.org/10.1016/j.jht.2023.02.001

Collier-Robinson, L., Rayne, A., Rupene, M., Thoms, C., & Steeves, T. (2019). Embedding indigenous principles in genomic research of culturally significant species: A conservation genomics case study. *New Zealand Journal of Ecology*, *43*(3). Scopus. https://doi.org/10.20417/nzjecol.43.36

Cummins, D. P., Connor, J. R., Heller, K. A., Hubert, J. S., Kates, M. J., Wisniewski, K. R., Berliner, J. C., O'Dell, D. R., Elliott, J. M., Weber, K. A., & Smith, A. C. (2019). Establishing the inter-rater reliability of spinal cord damage manual measurement using magnetic resonance imaging. *Spinal Cord Series and Cases*, *5*(1). Scopus. https://doi.org/10.1038/s41394-019-0164-1

Jones, P. D., Schooley, R. C., Hon, S., Castañeda, S. M., McCauley, J. L., & Lee, D. L. (2023). Patients' views on HCC biospecimen research: Understanding the role of race and culture through interviews. *Hepatology Communications*, *7*(6). Scopus. https://doi.org/10.1097/HC9.0000000000000162

Joo, H. Y., Park, C. R., Ahn, S., & Choi, C. I. (2024). Development and evaluation of RFID-integrated endoscopic clips for laparoscopic surgery marking. *PLoS ONE*, *19*(5 May). Scopus. https://doi.org/10.1371/journal.pone.0302737

Klingemann, J., & Wieczorek, Ł. (2022). Mobile application recovery support for patients with an alcohol use disorder. Acceptance, usability, and perceived helpfulness. *Journal of Addictive Diseases*, *40*(4), 559–567. Scopus. https://doi.org/10.1080/10550887.2022.2049177

Liu, Y.-M., Wen, Y.-C., Weng, P.-Y., Jaing, T.-H., & Chen, S.-H. (2020). Exploring the concerns and experiences of parents of children scheduled to receive haematopoietic stem cell transplant. *Journal of Advanced Nursing*, *76*(7), 1737–1745. Scopus. https://doi.org/10.1111/jan.14386

Martinez-Lopez, M. V., Coll, E., Cruz-Quintana, F., Dominguez-Gil, B., Hannikainen, I. R., Rosales, R. L., Pérez-Blanco, A., Perez-Marfil, M. N., Pérez-Villares, J. M., Uruñuela, D., & Rodríguez-Arias, D. (2021). Family bereavement and organ donation in Spain: A mixed method, prospective cohort study protocol. *BMJ Open*, *13*(1). Scopus. https://doi.org/10.1136/bmjopen-2022-066286

Pang, X., Xu, Y., Xie, S., Zhang, T., Cong, L., Qi, Y., Liu, L., Li, Q., Mo, M., Wang, G., Du, X., Shen, H., & Li, Y. (2023). Gallic Acid Ameliorates Cognitive Impairment Caused by Sleep Deprivation through Antioxidant Effect. *Experimental Neurobiology*, *32*(4), 285–301. Scopus. https://doi.org/10.5607/en23015

Pronk, M. C., Zuidema, W. C., Weimar, W., Van De Wetering, J., Ismail, S. Y., & Massey, E. K. (2023). Twenty Years of Unspecified Kidney Donation: Unspecified Donors Looking Back on Their Donation Experiences. *Transplant International*, *36*. Scopus. https://doi.org/10.3389/ti.2023.10959