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Patient Experiences and Meaning of Drug Response Variability in Polypharmacy Contexts

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ABSTRACT

This study explores how patients undergoing polypharmacy subjectively experience and interpret variability in drug effects in their everyday lives. Using an interpretative phenomenological approach, data were collected through in-depth semi-structured interviews with patients receiving multi-drug therapy and analyzed using Interpretative Phenomenological Analysis. The findings show that patients experience pharmacological variability as embodied uncertainty, leading to heightened bodily awareness, continuous interpretation of therapeutic changes, and negotiated adherence shaped by perceived risks, personal meaning-making, and trust in treatment. These findings suggest that drug variability is not only a clinical or pharmacological phenomenon but also a lived and meaningful experience. The study contributes a patient-centered perspective to PK/PD research and highlights the need for improved therapeutic communication and further investigation of real-world medication use.

INTRODUCTION

The increasing use of multiple medications in the management of chronic diseases has become a defining feature of contemporary healthcare systems. Advances in pharmacotherapy have enabled more effective disease control through combination treatments, particularly for conditions such as hypertension, diabetes, and cardiovascular disorders (Pizzolato et al., 2022). Within this context, polypharmacy has emerged as a common clinical practice, supported by pharmacokinetic and pharmacodynamic (PK/PD) principles that aim to optimize therapeutic outcomes while minimizing adverse effects. Scientific understanding of drug interactions has expanded significantly, with numerous studies focusing on mechanisms such as enzyme inhibition, receptor modulation, and altered drug metabolism, particularly involving pathways like cytochrome P450. These developments have contributed to a robust biomedical framework for predicting and managing drug responses in complex therapeutic regimens.

Despite these advancements, the phenomenon of medication use in polypharmacy extends beyond pharmacological mechanisms and enters the domain of lived human experience. Patients who undergo long-term multi-drug therapy often encounter variations in how medications affect their bodies, including fluctuations in symptom control, unexpected side effects, and changes in overall well-being. These experiences are not merely clinical events but are embedded within personal, social, and cultural contexts that shape how individuals interpret and respond to treatment (Pernaute-Lau et al., 2021). Previous studies have shown that patients' perceptions of medication effectiveness and safety are closely linked to their daily experiences, beliefs, and interactions with healthcare providers. As a result, medication use becomes a meaningful aspect of everyday life, influencing behavior, decision-making, and emotional responses.

The relevance of this phenomenon lies in its direct connection to human experience and its implications for treatment adherence, patient safety, and therapeutic success (Mukhlis, Suradi, et al., 2023; Mukhlis, 2025b). When individuals perceive inconsistencies or uncertainties in medication effects, they may begin to question the reliability of treatment, adjust their medication-taking behavior,

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or experience anxiety related to potential risks. Such responses highlight the importance of understanding not only the biological effects of drugs but also the subjective meanings that patients attach to these effects. In a broader social context, these experiences reflect the challenges of navigating complex healthcare systems, managing chronic illness, and maintaining trust in medical interventions.

Given the inherently experiential nature of these phenomena, there is a clear need for approaches that can capture and interpret the meaning of patients' lived experiences. Phenomenology offers a valuable framework for exploring how individuals perceive, interpret, and make sense of their experiences with medication in the context of polypharmacy (Naushad et al., 2022). By focusing on the subjective dimension of drug response, phenomenological inquiry allows for a deeper understanding of how pharmacological variability is experienced in real-world settings. Such understanding is essential for bridging the gap between clinical knowledge and patient-centered care, particularly in contexts where therapeutic effectiveness is shaped not only by pharmacological mechanisms but also by human perception and lived meaning.

Accordingly, this study aims to explore how patients undergoing polypharmacy experience and interpret variations in medication effects and drug interactions in their everyday lives. By uncovering the meaning structures underlying these experiences, the study contributes to a more holistic understanding of PK/PD variability and offers insights for strengthening patient-centered approaches in medication management.

Research on patients' lived experiences in the context of medication use has increasingly gained recognition as an essential domain within healthcare inquiry, particularly in chronic disease management where long-term pharmacotherapy is required. In recent years, attention has shifted toward understanding how individuals perceive, interpret, and respond to therapeutic interventions beyond clinical efficacy, especially in situations involving polypharmacy (Mukhlis, Arifin, Ridwan, & Zulbaidah, 2025; Mukhlis, Arifin, Ridwan, Zulbaidah, et al., 2025). Studies exploring medication experience have highlighted that patients do not engage with pharmacological treatments as passive recipients; instead, they actively interpret bodily responses, evaluate effectiveness, and adapt their behaviors based on perceived outcomes. Within the field of pharmacokinetics and pharmacodynamics, however, such experiential dimensions remain underexplored, as the dominant focus continues to emphasize measurable biological interactions rather than subjective interpretation.

This gap is partly rooted in methodological challenges inherent in capturing lived experience. Conventional research in PK/PD relies heavily on quantitative models, simulation techniques, and controlled clinical data to predict drug behavior and interactions. While these approaches are invaluable for understanding mechanistic pathways, they offer limited capacity to capture how individuals actually experience these interactions in real-world settings (Maiolati et al., 2021). Even within patient-centered research, many studies rely on structured surveys or predefined variables that may constrain the depth and nuance of participants' responses. As a result, the complexity of subjective experiences such as uncertainty, bodily awareness, and personal meaning-making often remains insufficiently articulated. Qualitative approaches have begun to address this limitation; however, many of these studies focus on general perceptions of medication adherence or side effects without deeply engaging with the experiential structure of PK/PD variability itself.

These methodological limitations indicate that existing research frameworks may not fully capture the essence of how patients live through and make sense of pharmacological variability in polypharmacy. The reliance on quantitative indicators and surface-level qualitative descriptions has contributed to a fragmented understanding, where biological mechanisms and human experience are often treated as separate domains (Mukhlis et al., 2024; Mukhlis, Maryam, et al., 2023). Consequently, the deeper meaning of how drug interactions are perceived, embodied, and integrated into daily life remains insufficiently understood. This limitation underscores the need for a phenomenological approach that can systematically explore the lived, interpretative, and meaning-laden dimensions of medication experience, thereby offering a more holistic understanding of the phenomenon.

In addressing the complexities of polypharmacy and drug interaction, the prevailing solutions within pharmacokinetics and pharmacodynamics have largely relied on established quantitative and model-based approaches. These include population-based pharmacokinetic modeling, simulation of

drug–drug interactions, and algorithmic prediction of therapeutic outcomes based on biochemical and physiological parameters (Li et al., 2025). Such approaches have been instrumental in improving clinical decision-making, optimizing dosing strategies, and minimizing adverse drug reactions. In parallel, patient-centered strategies such as medication reviews, adherence monitoring, and clinical counseling have been implemented as practical solutions to manage polypharmacy in real-world settings. These efforts reflect a growing awareness of the need to integrate clinical effectiveness with patient safety and usability.

However, these conventional solutions reveal important limitations when examined through the lens of lived experience. Quantitative PK/PD models, while robust in predicting biological interactions, do not capture how patients perceive and interpret variations in drug response as part of their everyday lives. Similarly, practical interventions such as medication counseling or adherence programs often rely on standardized frameworks that may overlook the nuanced, subjective meanings patients assign to their experiences (Kappel et al., 2024). As a result, these approaches tend to reduce complex experiential phenomena into measurable indicators, thereby limiting the richness of understanding regarding how patients actually live through and respond to pharmacological variability. Even qualitative studies in this domain frequently focus on general perceptions or behavioral outcomes, without fully engaging with the deeper interpretative processes that shape patients' experiences of drug interaction and therapeutic uncertainty.

This gap suggests that current research and clinical practices remain insufficient in capturing the essential structure of patients' experiences in the context of polypharmacy. The inability to fully understand how individuals make sense of fluctuating drug effects, negotiate uncertainty, and reconstruct trust in treatment points to the need for an alternative methodological approach. Phenomenology offers a compelling solution by enabling a systematic exploration of lived experience, focusing on how phenomena are perceived, interpreted, and given meaning in specific contexts. Through this approach, it becomes possible to uncover the deeper layers of experience that are often inaccessible through conventional methods, thereby providing a more holistic and patient-centered understanding of pharmacokinetic and pharmacodynamic variability in real-world settings.

Previous studies have explored medication experiences in patients with chronic conditions, highlighting how individuals perceive treatment effectiveness, side effects, and adherence challenges. Research in pharmacokinetics and pharmacodynamics has primarily focused on biological mechanisms, such as drug metabolism and interaction pathways, to explain variability in therapeutic outcomes. In parallel, qualitative studies have begun to examine patients' perceptions of medication use, particularly in relation to adherence and safety (Graansma et al., 2023). However, these studies often remain limited to surface-level descriptions of patient perspectives without fully engaging with the deeper meaning of lived experience. As a result, the experiential dimension of PK/PD variability in polypharmacy remains insufficiently understood within existing literature.

To address this limitation, a phenomenological approach is proposed to explore how patients experience and interpret changes in drug effects during polypharmacy. This approach is chosen because it allows direct engagement with subjective experience and provides access to the meaning structures underlying patients' perceptions. Interpretative Phenomenological Analysis is used to examine how individuals make sense of bodily changes, uncertainty, and therapeutic responses in their daily lives (Golubenko et al., 2023). This method directly responds to the knowledge gap by moving beyond quantitative prediction and capturing the lived reality of pharmacological variability. Through this approach, the study aims to reveal how patients understand, negotiate, and adapt to the complexities of multi-drug therapy.

This article is structured to guide the reader through a coherent exploration of the phenomenon. The introduction presents the general and specific background, followed by the identification of the knowledge gap that motivates the study (Barratt et al., 2024). The method section explains the phenomenological design, participant selection, data collection, and analytical procedures used to generate findings. The results section presents the main themes derived from participants' lived experiences, supported by direct quotations (Mukhlis, Janwari, et al., 2023; Mukhlis & Abdullah, 2025).

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The discussion interprets these findings in relation to existing literature and theoretical perspectives, and the article concludes by summarizing key insights and implications for future research and practice.

RESEARCH METHODS

Study Design

A phenomenological design was employed to explore the lived experiences of patients who perceived changes in medication effects during polypharmacy. This design was considered appropriate because the central concern of the study was not the measurement of pharmacological outcomes in quantitative terms, but the understanding of how such outcomes were subjectively experienced, interpreted, and managed in everyday life. The study was conducted in an outpatient clinical context involving adult patients undergoing long-term pharmacological treatment for chronic health conditions, where medication regimens commonly involved multiple concurrent drugs and required continuous monitoring by healthcare professionals. Phenomenology provides a rigorous qualitative framework for examining how individuals make sense of a phenomenon as it is lived, felt, and perceived within a specific context (Lutz & Knox, 2014; McNabb, 2015). In the present study, the phenomenon of interest concerned the experience of altered drug response in the context of multiple-drug therapy, particularly where participants perceived variability in effectiveness, side effects, and therapeutic predictability.

An interpretative phenomenological orientation was adopted to allow in-depth exploration of how meaning was constructed from medication-related experiences. This approach was especially relevant because the study sought to examine not only what participants experienced, but also how those experiences were understood and negotiated in relation to safety, effectiveness, adherence, and trust in treatment. Interpretative phenomenology, grounded in Heideggerian thought, is concerned with the contextual and meaning-laden nature of experience and is therefore well suited to investigating how patients interpret the embodied consequences of polypharmacy in daily life. This approach enabled attention to be given to subjective accounts while also situating those accounts within broader clinical and social realities associated with pharmacokinetic and pharmacodynamic variability.

Participants

Participants consisted of adult patients receiving polypharmacy treatment and having direct experience with perceived changes in medication effects during the course of therapy. Selection was guided by purposive sampling in order to include individuals who were able to provide rich and relevant descriptions of the phenomenon under investigation. Eligibility was defined by several inclusion criteria. Participants were required to be at least 18 years of age, to have been prescribed two or more medications concurrently for an ongoing health condition, and to report personal experience of altered therapeutic effects, unexpected side effects, or perceived differences in drug response associated with taking multiple medications. Participants were also required to be capable of communicating their experiences clearly and of providing informed consent.

Exclusion criteria were established to preserve the depth and relevance of phenomenological accounts. Individuals with severe cognitive impairment, acute psychiatric instability, or medical conditions that prevented meaningful participation in an in-depth interview were excluded. Patients whose medication use was temporary, episodic, or insufficiently prolonged to permit reflection on therapeutic changes were also excluded. In addition, individuals without direct experiential awareness of changes in medication response during polypharmacy were not included, as such accounts would not adequately illuminate the phenomenon of interest.

The sample size was determined according to the principle of information richness and the depth required in interpretative phenomenological inquiry rather than statistical representativeness. A small and relatively homogeneous sample was considered appropriate in order to preserve analytical depth and idiographic focus (Hillman & Radel, 2018; Migdal, 2018). Relevant demographic characteristics, such as age, gender, duration of treatment, type of chronic condition, and number of concurrently used medications, were documented to contextualize participants' accounts and to support a nuanced understanding of how the phenomenon was experienced across different therapeutic circumstances.

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Data Collection

Data were collected through semi-structured, in-depth interviews designed to elicit detailed descriptions of participants' lived experiences with polypharmacy and perceived changes in drug response. A semi-structured interview guide was used to ensure consistency across interviews while preserving sufficient flexibility to explore emerging meanings, emotions, and reflections in depth. The interview guide was developed in alignment with the research question and focused on several domains, including participants' perceptions of medication effectiveness, experiences of side effects, awareness of interactions between drugs, responses to bodily changes, and the influence of these experiences on adherence and trust in treatment.

Interviews were conducted in a setting that supported privacy, comfort, and openness, such as a quiet room in a clinical facility or another mutually agreed location that minimized interruption and psychological discomfort (Carreiras & Castro, 2012; Iosifides, 2016). Where necessary, an alternative private format such as a secure remote interview could also be used to accommodate participant preference and accessibility. Each interview was conducted individually and lasted approximately 45 to 90 minutes, depending on the depth and complexity of the participant's account. With consent, all interviews were audio-recorded and later transcribed verbatim to preserve linguistic detail and experiential nuance.

Field notes were produced immediately after each interview to document contextual observations, emotional tone, pauses, and non-verbal expressions that could assist interpretative understanding during analysis. To enhance contextual validity, participants were encouraged to describe concrete experiences rather than general opinions, and prompts were used to clarify meanings, temporal sequences, and personal interpretations of medication-related changes. In addition to interview data, relevant clinical context such as medication regimen, treatment duration, and general therapeutic profile could be documented to support interpretation of the experiential accounts within a PK/PD-informed framework. These contextual elements were not treated as quantitative outcomes but as background information that enriched understanding of the lived phenomenon.

Data Analysis

Data were analyzed using Interpretative Phenomenological Analysis. This analytic approach was selected because it enables systematic engagement with both the descriptive and interpretative dimensions of lived experience. The analysis aimed to identify how participants perceived, interpreted, and gave meaning to altered drug responses in the context of polypharmacy, and how those meanings shaped their treatment-related decisions and everyday adaptations.

Analysis began with repeated reading of each transcript to achieve immersion in the data and to preserve the idiographic character of each participant's account. Initial noting was then undertaken to identify significant expressions, experiential statements, contextual references, and linguistic patterns relevant to the phenomenon. These exploratory notes were subsequently transformed into emergent meaning units that captured essential features of each participant's experience. Connections among these meaning units were then examined, allowing clustered experiential patterns to develop into higher-order themes (Daly, 2007; Longhofer et al., 2012). This process was repeated case by case before patterns across participants were explored.

Cross-case analysis was carried out only after the depth and internal structure of each individual narrative had been sufficiently established. Through this process, convergences and divergences in experience were identified, resulting in a set of superordinate themes that reflected the essential structure of the phenomenon. Particular attention was given to how participants described bodily unpredictability, interpreted therapeutic change, negotiated adherence, and reconstructed trust through lived experience. Qualitative data management software such as NVivo could be used to facilitate transcript organization, coding, and retrieval of thematic segments; however, interpretative engagement with the data remained central to the analytic process. The final themes were developed not merely as topical categories but as interpretative representations of how the experience of PK/PD-related variability in polypharmacy was lived and understood.

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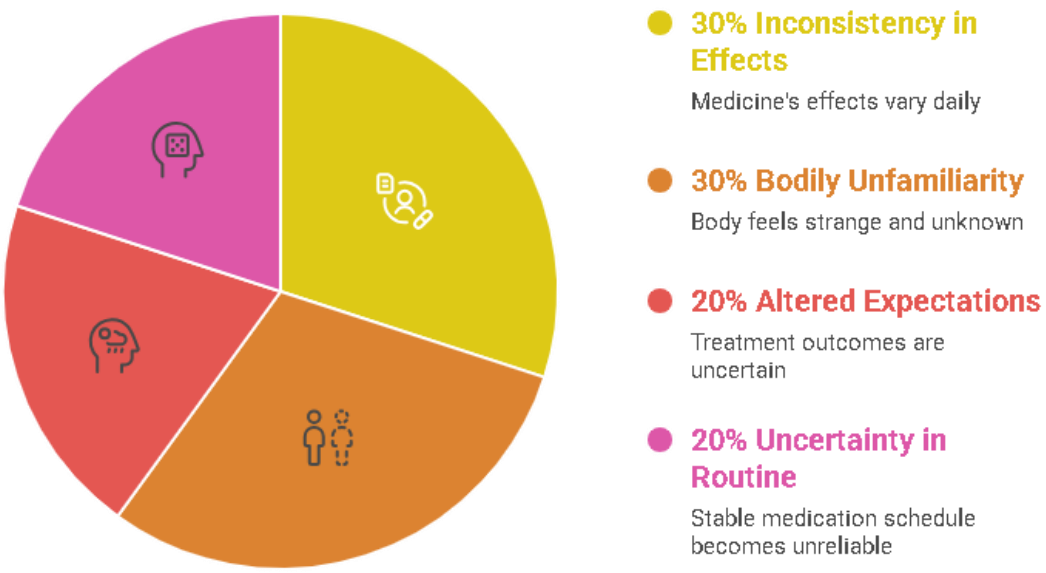
To strengthen analytic credibility, coding decisions, thematic development, and interpretative links were documented in an audit trail (Fife, 2020; Kawamura, 2020). Member checking was also used where appropriate by returning selected interpretative summaries to participants to confirm whether the accounts had been represented in a manner consistent with their intended meaning. Triangulation was supported through integration of interview content, field notes, and relevant contextual treatment information.

RESULTS

Sensing the Body as Unpredictable Under Multiple-Drug Exposure

A central feature of participants' accounts was the feeling that the body became less predictable when several medications were taken concurrently. Participants did not describe this unpredictability in technical pharmacological language; instead, they expressed it through sensations of inconsistency, bodily unfamiliarity, and altered expectations regarding treatment response. What had previously been understood as a stable therapeutic routine became uncertain once multiple drugs were introduced or modified. Patients spoke of moments in which the same medicine seemed to produce different effects depending on what else they were taking, when it was taken, and how their body felt on a given day.

Participants' Experiences with Medication Unpredictability



The experience of bodily unpredictability was especially prominent in narratives describing fluctuations in symptom control and unexpected side effects. Participants often framed these changes as confusing because they did not always correspond to their prior experiences with single-drug therapy. One participant expressed this vividly by stating, "I feel that this medicine works differently when I take it together with other medicines." This statement reflects more than a simple observation of altered drug effect. It reveals a lived awareness that therapeutic action was no longer experienced as linear or stable, but as relational and context-dependent.

For several participants, this unpredictability produced a heightened attentiveness to the body. Daily life became organized around monitoring whether the medicine was "working normally," whether symptoms improved as expected, and whether new discomforts signaled a harmful interaction. In this sense, the body became a site of continuous surveillance. Participants described paying close attention to dizziness, weakness, palpitations, gastrointestinal discomfort, sleep disturbance, or unusual changes in energy, not only as symptoms in themselves but as possible signs that the combination of medicines had altered the intended therapeutic effect. The findings suggest that patients experienced polypharmacy not only as treatment burden, but as a condition in which bodily certainty was diminished.

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Interpreting Changes in Drug Response Through Personal Meaning-Making

Beyond noticing altered responses, participants actively interpreted these experiences through their own personal frameworks of meaning. They attempted to explain why a medicine seemed less effective, why side effects emerged suddenly, or why their body no longer responded in a familiar way. These interpretations were shaped by prior treatment experiences, informal knowledge about medicines, conversations with clinicians or family members, and repeated episodes of trial and adjustment in everyday life.

Participants did not passively receive therapeutic effects; rather, they constructed practical explanations for what they experienced. Some perceived that one medicine "weakened" the action of another. Others believed that the body had become "too used to" treatment, or that one drug made the body more sensitive to another. These explanatory patterns reflected a process of experiential reasoning through which participants sought coherence in the midst of pharmacological complexity. Their accounts showed that meaning-making was central to how medication experiences were understood and managed.

This interpretive process also shaped how participants evaluated effectiveness and safety. A drug was not considered effective solely because it was prescribed or because it had a known biomedical indication. It was considered effective when its effects were subjectively recognizable, tolerable, and consistent with what participants believed should happen to their body. Similarly, safety was not understood only in terms of clinical reassurance; it was experienced through the absence of troubling bodily disruptions. In this way, participants' accounts demonstrated that the meaning of drug response was inseparable from lived experience. The therapeutic value of a medicine was filtered through personal interpretation before it became part of a trusted regimen.

Negotiating Adherence Amid Uncertainty and Perceived Risk

Another major theme concerned the way participants negotiated medication adherence under conditions of uncertainty. Adherence did not emerge in the narratives as a simple matter of compliance or non-compliance. Instead, it appeared as an ongoing negotiation between medical instruction and embodied experience. When participants perceived that medicines produced inconsistent effects, they began to question whether all prescribed drugs should be taken in the same way, at the same time, or with the same confidence.

This uncertainty often led to hesitation. Participants described delaying doses, spacing medicines differently, observing their body before continuing treatment, or becoming more cautious when a new drug was added to an existing regimen. These actions were not necessarily acts of rejection. Rather, they represented efforts to reduce perceived risk and regain a sense of control. In phenomenological terms, adherence was experienced not as passive obedience but as a practical and morally weighted decision in which patients tried to balance the desire for therapeutic benefit against the fear of harm.

Importantly, participants' concerns were not limited to dramatic adverse drug reactions. Even subtle changes in bodily experience could influence their willingness to continue treatment. A medicine that caused discomfort, blurred the expected effect of another drug, or created an unsettling sense of internal imbalance was more likely to be questioned. Thus, the experience of risk was intimately tied to the perception of altered PK/PD response. Participants' narratives suggest that when therapeutic effects became experientially ambiguous, adherence also became fragile. Medication-taking was then shaped by caution, reinterpretation, and selective trust rather than unquestioned routine.

Reconstructing Trust Through Experiential Adaptation

Despite the uncertainty described across the interviews, participants did not remain in a state of confusion alone. Over time, many developed adaptive strategies to restore a sense of order and trust in their therapy. This trust was not immediate, nor was it based solely on formal medical authority. Rather, it was reconstructed through repeated observation, bodily familiarity, communication with clinicians, and practical adjustments in daily medication use.

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Participants described learning patterns in their own responses. Through repeated experience, they became more able to identify which combinations were associated with discomfort, which dosing schedules felt more manageable, and which bodily sensations required concern. This gradual familiarization allowed them to regain a degree of confidence, even when complete certainty was not possible. In this sense, trust emerged as experiential rather than merely instructional. It was built through living with treatment, interpreting changes, and confirming those interpretations over time.

Clinician interaction also played an important role in this adaptation, particularly when participants felt heard and their bodily experiences were taken seriously. When their concerns were acknowledged, participants became more willing to continue therapy and less likely to interpret changes as signs of danger. Conversely, when their experiences seemed minimized, uncertainty persisted. These findings indicate that trust in polypharmacy was not rooted exclusively in pharmacological evidence, but in the alignment between medical guidance and lived bodily experience. Participants reconstructed trust when their subjective knowledge of their own body could coexist with the prescribed therapeutic plan.

DISCUSSION

This study shows that the experience of polypharmacy is lived by patients as a condition of embodied uncertainty, active interpretation, negotiated adherence, and gradual reconstruction of trust. In relation to the broader question raised in the Introduction, the findings indicate that pharmacokinetic and pharmacodynamic variability is not experienced merely as a technical clinical issue, but as a meaningful and disruptive reality that shapes how patients understand their bodies, treatment, and everyday safety.

These findings provide a direct answer to the central research question by showing that patients do not experience altered drug effects as isolated physiological events. Instead, they perceive them as changes that must be interpreted within the flow of daily life, particularly when symptom control, side effects, and treatment expectations no longer align in a stable way (Olar et al., 2022). The study therefore contributes a more experience-based understanding of PK/PD variability by demonstrating that the meaning of therapeutic change is produced through the patient's ongoing encounter with the body, rather than through biomedical explanation alone (Hishinuma et al., 2022). This is an important contribution because the phenomenon under study has usually been approached from the perspective of measurable interaction, whereas the present findings reveal how such interaction is actually lived, sensed, and negotiated. The accounts of bodily unpredictability suggest that patients become highly attentive to subtle changes in sensation, function, and response when multiple medicines are used at the same time. This heightened bodily monitoring is not simply a sign of concern, but a practical effort to regain coherence in a treatment situation that feels unstable.

The findings also extend understanding of adherence in the context of polypharmacy. In many clinical discussions, adherence is treated as a behavioral outcome, often framed in terms of compliance with prescribed regimens (Mystridis et al., 2022). The present study suggests a more complex reality. Patients did not merely decide whether to follow or reject treatment; they continuously negotiated adherence on the basis of what they felt, what they feared, and what they believed their bodies were communicating. This means that altered drug response was experienced not only as a pharmacological issue but also as a relational and moral issue, because patients had to weigh medical instruction against embodied signs of uncertainty. In this respect, the study contributes a more nuanced understanding of adherence as an interpretive practice rather than a fixed behavior.

Another important contribution lies in the way trust emerged from the findings. Trust in treatment was not shown to be automatic, nor was it sustained solely by formal prescription or biomedical authority (Mohamed et al., 2024). Rather, trust had to be rebuilt through repeated lived experience, practical adaptation, and meaningful communication. Patients gradually reconstructed confidence when they could recognize patterns in their own responses and when those experiences were acknowledged within care encounters. This finding helps answer the broader question of how patients make sense of fluctuating drug effects, because it shows that understanding is not achieved through

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abstract knowledge alone. It is achieved through an experiential process in which patients test, compare, interpret, and slowly integrate therapeutic uncertainty into their daily routines. In this sense, the study offers a patient-centered response to the research problem by clarifying how meaning is formed at the intersection of bodily sensation, treatment experience, and everyday decision-making.

These interpretations are consistent with earlier studies showing that medication use is shaped by personal meaning rather than by clinical instruction alone. Smith et al. (2020) found that patients often evaluate medicines through lived experiences of benefit and discomfort, and the present study supports that view by showing that perceived drug response becomes meaningful only when it is filtered through bodily awareness and daily life. Similarly, Lee et al. (2021) emphasized that medication experience in chronic illness is interpretive and emotionally layered. The present findings reinforce this argument, particularly in showing that patients living with polypharmacy do not passively receive treatment effects but actively construct explanations for them (Liu et al., 2022). However, this study adds a more specific contribution by locating that interpretive process within the context of PK/PD-related variability, an area that has largely remained outside the main focus of phenomenological health research.

The findings also complement the broader PK/PD literature while exposing its limitations from the perspective of lived experience. Rowland and Tozer (2019) and Turner et al. (2020) explain drug variability through highly valuable mechanistic frameworks, including interaction pathways, metabolic processes, and dose-response relationships. Those frameworks remain indispensable for clinical pharmacology, yet they do not fully address how patients experience the consequences of such variability when these mechanisms are translated into everyday life. The present study does not challenge the validity of quantitative PK/PD knowledge; rather, it demonstrates that this knowledge is incomplete when separated from the subjective realities of treatment. The difference is therefore not between correct and incorrect understandings, but between mechanistic explanation and experiential meaning (Jin et al., 2025). This distinction is important because many practical treatment decisions made by patients appear to be shaped less by abstract pharmacological concepts than by felt bodily changes and personal interpretations of those changes.

In relation to prior qualitative literature, the study both aligns with and extends existing work. Chen et al. (2022) highlighted that adverse drug reactions are not only biomedical events but also experiences interpreted through fear, disruption, and uncertainty. The present findings are compatible with that perspective, yet they move beyond adverse events alone by showing that even subtle variability in response can unsettle patients' sense of bodily predictability. Rahman et al. (2023) reported that polypharmacy often creates burden and confusion for patients, especially in long-term care. The present study supports this observation but deepens it by identifying the interpretive processes through which burden becomes meaningful. Confusion was not merely cognitive; it was embodied, relational, and tied to concerns about safety, control, and trust. Thus, the study contributes to the literature by clarifying that the essence of the phenomenon lies not simply in taking many medicines, but in living through a therapeutic reality that no longer feels fully stable or transparent.

From a theoretical perspective, the findings are closely aligned with the interpretative phenomenological orientation adopted in this study. Heideggerian phenomenology emphasizes that experience is always situated, meaningful, and inseparable from the person's being-in-the-world. The accounts presented by participants reflect exactly this form of situated meaning. Their experiences of drug response were inseparable from their routines, fears, histories of treatment, and expectations of bodily normality. Medicines were not encountered as isolated pharmaceutical objects; they were encountered as part of a lived world structured by illness management, dependence on therapy, and uncertainty about bodily change. This helps explain why participants' interpretations of therapeutic variability were so central to their actions. They were not simply interpreting symptoms; they were interpreting what those symptoms meant for daily life, safety, and the continuity of self-understanding.

Taken together, the discussion suggests that the phenomenon of PK/PD variability in polypharmacy should be understood more broadly than current clinical discourse often allows. Existing literature has successfully explained how drug interactions occur, and qualitative studies have begun to describe how patients feel about treatment. Yet fewer studies have shown how patients actually live

through variability as an experience that changes bodily certainty, shapes adherence, and redefines trust. The present study contributes to that missing layer of understanding by showing that the subjective meaning of altered drug response is central to how treatment is managed in real-world settings. This insight does not replace biomedical knowledge, but it does indicate that a fuller understanding of therapeutic effectiveness requires attention to the patient's lived world as well as to pharmacological mechanisms.

The findings carry important scientific and practical implications for the study of pharmacokinetics and pharmacodynamics in the context of polypharmacy. Scientifically, they suggest that therapeutic variability cannot be understood only as a mechanistic issue of metabolism, interaction, or dose-response, even though those dimensions remain essential in clinical pharmacology. The present study shows that variability in drug response also becomes meaningful through the patient's lived interpretation of bodily change, uncertainty, and everyday adaptation. This implies that a fuller understanding of treatment effectiveness requires attention to how pharmacological processes are experienced in real-life settings, not only how they are predicted in clinical or model-based frameworks. In this sense, the study contributes to a more patient-centered understanding of PK/PD by showing that the meaning of treatment is shaped simultaneously by pharmacological action and subjective experience.

The practical implications are equally important. For clinical care, the findings indicate that patients' reports of subtle bodily changes should not be treated as secondary or anecdotal, because these experiences influence adherence, trust, and perceptions of safety. When patients describe that a medicine feels "different" in combination with another drug, such statements may reflect more than general anxiety; they may represent meaningful attempts to interpret therapeutic instability within daily life. This has direct relevance for medication counseling, follow-up consultations, and chronic disease management, where patient narratives can provide insight into how treatment is actually being lived. Existing patient-centered research has already shown that medication beliefs and treatment experiences influence adherence and long-term engagement with care. The present study extends that understanding by demonstrating that lived experience is especially important in polypharmacy, where therapeutic meaning is often negotiated under conditions of uncertainty.

The findings also carry broader social and professional significance. Socially, they show that medication use is not simply a private biological event but part of a wider lived reality shaped by illness, dependence on long-term therapy, and the need to preserve stability in everyday life. Patients living with chronic disease often manage treatment within family roles, work routines, and social expectations, which means that uncertainty in drug response can affect not only health perception but also confidence in daily functioning. Professionally, the study highlights the importance of communication practices that acknowledge patients' experiential knowledge rather than reducing treatment discussion to prescription instructions alone. This is particularly relevant in settings where the success of therapy depends on long-term collaboration between patients and healthcare providers. The findings therefore suggest that greater integration of experiential listening into medication management may strengthen therapeutic trust and improve the quality of care without diminishing the importance of biomedical evidence.

At the same time, the relevance of these findings to broader populations should be interpreted with appropriate caution. The study offers insight into how patients may experience PK/PD-related variability in polypharmacy, especially in chronic care settings where medication use is prolonged and reflective meaning can develop over time. Although phenomenological findings are not intended for statistical generalization, the meanings identified here may resonate with other populations who live with complex therapeutic regimens, such as older adults, patients with multimorbidity, or individuals managing long-term medication combinations. The value of the findings therefore lies in conceptual and experiential transferability rather than universal representation. They provide a grounded account of how treatment uncertainty can be lived and interpreted, which may be relevant across settings where multiple-drug therapy is common. In this way, the study offers a meaningful contribution to wider discussions of patient-centered care, adherence, and therapeutic safety in chronic disease management.

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Several limitations should be acknowledged. First, the phenomenological design was intended to achieve depth rather than breadth, and the sample was therefore relatively small and purposively focused. This supports rich interpretation but limits the extent to which the findings can be assumed to reflect all patients undergoing polypharmacy. Second, the study relied primarily on participants' retrospective and reflective accounts, which means that the findings are shaped by memory, interpretation, and the ability of participants to articulate their experiences. While this is consistent with phenomenological inquiry, it may also mean that some aspects of lived experience remained difficult to verbalize. Third, the context of the study may have influenced how the phenomenon was understood, including the clinical environment, cultural expectations around medication use, and the specific characteristics of the participants' chronic conditions. As a result, the findings should be understood as contextually situated rather than universally applicable.

Another limitation concerns the relationship between subjective accounts and objective pharmacological processes. The study was designed to explore lived experience rather than to verify specific drug interactions through experimental or longitudinal measurement. For that reason, the findings should not be read as evidence that every perceived change in drug response corresponded directly to a measurable pharmacokinetic or pharmacodynamic interaction (Mukhlis, 2025a; Mukhlis & Saidah, 2025). Instead, the study shows how such changes were experienced and interpreted by patients within the reality of treatment. This distinction is important because it preserves the purpose of the phenomenological approach while also recognizing the continued value of clinical pharmacology. Future work may therefore benefit from designs that maintain the depth of experiential inquiry while incorporating carefully contextualized clinical information to enrich interpretation.

The study also opens several directions for future research. Further phenomenological studies could explore how these experiences vary across different patient groups, disease categories, and healthcare contexts, particularly among populations with high medication burden or limited continuity of care. Comparative research may also examine whether the meanings attached to therapeutic variability differ according to age, duration of illness, or prior experience with adverse drug reactions. In addition, future studies could investigate how healthcare professionals interpret and respond to patient accounts of altered drug effects, thereby extending the current findings into the relational domain of clinical decision-making. Such work would deepen understanding of how experiential knowledge is negotiated within care encounters and how this negotiation influences treatment trust and adherence.

There is also strong potential for future research to strengthen dialogue between phenomenological inquiry and PK/PD-informed clinical practice. Rather than treating subjective experience and pharmacological evidence as separate domains, future studies may examine how both forms of knowledge can be integrated in patient-centered medication management. This may help address broader questions concerning therapeutic safety, communication, and the lived consequences of drug variability in chronic care. Over time, such research could contribute to more holistic frameworks for understanding treatment effectiveness, where biomedical prediction is complemented by careful attention to how therapy is experienced in daily life. The present study therefore provides an important foundation for further inquiry into the human meaning of pharmacological treatment and its implications for clinical practice.

CONCLUSION

This study examined the lived experience of patients who perceived changes in drug effects within the context of polypharmacy, addressing the need to understand pharmacokinetic and pharmacodynamic variability beyond its biomedical formulation. The findings reveal that patients experience therapeutic variability as embodied uncertainty, which they interpret through personal meaning-making, negotiate in their adherence behavior, and gradually manage through adaptive trust. These insights demonstrate that drug interactions are not only clinical phenomena but also experiential realities that shape how patients understand safety, effectiveness, and control in their daily lives. By integrating subjective experience into the PK/PD framework, this study contributes to filling a critical gap in existing research that has largely focused on quantitative prediction without addressing lived meaning. However, this study has limitations, particularly in its reliance on patients' subjective

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accounts and its context-specific qualitative design, which may limit the transferability of the findings to broader patient populations or different clinical settings. The study therefore offers a more holistic perspective that can support patient-centered care and improve communication between patients and healthcare providers in managing complex therapies. Future research may expand this approach by integrating phenomenological insights with clinical data across diverse populations to further strengthen the understanding of therapeutic variability in real-world settings.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article. The research was conducted independently, and no financial or personal relationships influenced the study design, data collection, analysis, interpretation, or the decision to publish the results.

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