Biomedical and Clinical Medicine

https://bcmjournal.org

Forecasting Readmission Risk in Older Heart Failure Patients with Frailty Assessment Tools

Dong-Hyun Lee*

Department of Anesthesiology and Pain Medicine, College of Medicine, Chonnam National University, Gwangju, Republic of Korea

Corresponding author: dong.h.lee@gmail.com

Abstract

The intersection of advanced age and chronic heart failure presents a profound challenge to modern healthcare systems, primarily driven by high rates of hospital readmission. Traditional risk stratification models often fail to account for the complex vulnerability associated with biological aging, specifically the syndrome of frailty. This paper presents a comprehensive cohort study designed to evaluate and predict readmission risk in older heart failure patients utilizing multiple validated frailty assessment tools. By integrating clinical, demographic, and geriatric assessment data from a prospective cohort, the study systematically compares the predictive utility of instruments such as the Fried Phenotype and the Clinical Frailty Scale. The primary objective is to determine how the incorporation of frailty metrics into standard clinical models enhances the precision of predicting thirty-day and ninety-day readmissions. Furthermore, the analysis explores the underlying trajectories of functional decline that precipitate acute decompensation. The findings aim to facilitate a transition from disease-centric risk assessment to a multidimensional, patient-centered paradigm, ultimately guiding targeted interventions to mitigate the escalating cycle of recurrent hospitalizations in this vulnerable demographic.

Keywords: Heart Failure; Frailty Assessment; Hospital Readmission; Cohort Studies; Readmission Risk

1. Introduction

1.1 The Clinical Challenge of Heart Failure in Older Adults

Heart failure remains one of the most prevalent and debilitating chronic conditions affecting the aging population globally. As medical advancements have successfully reduced mortality rates from acute cardiovascular events, the incidence of chronic heart failure has paradoxically increased, creating a massive clinical and economic burden. Older adults suffering from heart failure are uniquely vulnerable due to the progressive decline in cardiovascular reserve and the frequent presence of multiple interacting comorbidities. A defining characteristic of the clinical trajectory of heart failure in this demographic is the high frequency of acute decompensation, which necessitates emergency department visits and subsequent inpatient hospitalizations. Following discharge, these patients face an exceptionally high risk of recurrent decompensation, often leading to a vicious cycle of repeated hospital readmissions. This phenomenon is commonly referred to as post-hospital syndrome, an acquired condition of generalized vulnerability that occurs following an acute illness and hospitalization.

Traditional clinical models designed to predict hospital readmission have historically relied on disease-specific markers, such as left ventricular ejection fraction, brain natriuretic peptide levels, and renal function. While these parameters are integral to understanding the primary pathology of the failing heart, they frequently fall short in accurately identifying which older patients will require readmission [1]. The discrepancy between disease severity and clinical outcomes suggests that other, non-cardiac factors play a dominant role in determining the post-discharge trajectory of older adults. Consequently, healthcare providers and researchers have increasingly recognized the necessity of broadening the scope of risk assessment to include markers of global physiological reserve and vulnerability.

1.2 The Paradigm Shift Toward Frailty Assessment

Frailty is defined as a clinically recognizable state of increased vulnerability resulting from aging-associated decline in reserve and function across multiple physiologic systems such that the ability to cope with every day or acute stressors is compromised. In the context of heart failure, frailty acts as a critical effect modifier, transforming a manageable chronic condition into a highly unstable clinical state. The presence of frailty severely impairs a patient's capacity to tolerate standard heart failure medications, engage in necessary lifestyle modifications, and recover from the physiological stress of an acute exacerbation [2]. Recognizing the profound impact of this geriatric syndrome, major cardiovascular societies have advocated for the routine assessment of frailty in older patients presenting with cardiovascular disease.

Despite the growing consensus regarding the importance of frailty, its integration into routine clinical practice and predictive modeling has been hindered by the lack of a universally accepted measurement tool. Numerous instruments have been developed to capture the multidimensional nature of frailty, ranging from performance-based measures of physical function to cumulative deficit indices based on electronic health records. The challenge lies in identifying which specific tools, or combinations thereof, provide the most robust and clinically actionable prognostic information regarding hospital readmission [3]. This study addresses this critical gap by conducting a rigorous cohort investigation to evaluate the predictive performance of different frailty assessment tools when added to conventional clinical risk models for older heart failure patients.

2. Background and Literature Review

2.1 The Intersection of Aging and Heart Failure Pathophysiology

The physiological changes associated with normal aging share significant mechanistic overlap with the pathophysiology of heart failure, making it difficult to disentangle the two in older patients. Aging is characterized by structural and functional alterations in the myocardium and vasculature, including increased arterial stiffness, myocardial hypertrophy, and impaired diastolic relaxation. These age-related changes lower the threshold for the development of heart failure, particularly heart failure with preserved ejection fraction, which is disproportionately prevalent among older adults. Furthermore, aging is associated with a chronic, low-grade inflammatory state, often termed inflammaging, which promotes endothelial dysfunction and systemic fibrosis.

When clinical heart failure supervenes upon an aging cardiovascular system, the resultant hemodynamic compromise exacerbates the decline of other end organs, notably the kidneys, skeletal muscle, and brain. The hypoperfusion and neurohormonal activation inherent to heart failure accelerate the loss of skeletal muscle mass and function, a condition known as sarcopenia, which is a core component of physical frailty [4]. This bidirectional relationship creates a negative feedback loop: heart failure accelerates the onset and progression of frailty, while frailty diminishes the body's resilience to the stress of heart failure, thereby predisposing the patient to recurrent acute decompensation and subsequent readmission.

2.2 Frailty Assessment Instruments in Clinical Practice

The operationalization of frailty in clinical research and practice has largely followed two distinct conceptual models: the phenotypic model and the cumulative deficit model. The phenotypic model, pioneered by Fried and colleagues, defines frailty as a distinct biological syndrome characterized by three or more of the following criteria: unintentional weight loss, self-reported exhaustion, weakness assessed by grip strength, slow walking speed, and low physical activity. While highly predictive of adverse outcomes, the phenotypic approach requires specialized equipment and space, limiting its feasibility in fast-paced acute care settings.

Conversely, the cumulative deficit model calculates a frailty index based on the proportion of health deficits a patient has accumulated, including diseases, symptoms, abnormal laboratory values, and functional impairments [5]. This approach provides a continuous measure of biological age and risk. In an effort to bridge the gap between comprehensive assessment and clinical utility, several rapid screening tools have been developed. The Clinical Frailty Scale is a judgment-based tool that allows clinicians to stratify patients into categories ranging from very fit to terminally ill based on their overall level of fitness and dependence. Other notable tools include the Edmonton Frail Scale and the FRAIL questionnaire, which balance multidimensionality with ease of administration. Previous investigations have demonstrated that these tools capture different domains of vulnerability, yet their comparative efficacy in predicting short-term readmission in heart failure remains a subject of ongoing debate [6].

2.3 Existing Predictive Models for Hospital Readmission

Predicting readmission has been a major priority for healthcare systems due to the immense financial penalties and quality metrics tied to this outcome. Numerous risk prediction models have been developed and validated for heart failure populations. The LACE index, which incorporates length of stay, acuity of admission, comorbidities, and emergency department visits in the previous six months, is among the most widely used generic models. Another prominent tool is the HOSPITAL score, which utilizes similar clinical parameters [7]. However, systematic reviews of these conventional models consistently reveal modest predictive accuracy, with C-statistics rarely exceeding the moderate threshold.

The primary limitation of these existing models is their reliance on administrative data and traditional clinical variables, which fail to capture the nuanced realities of an older patient's functional and cognitive status [8]. For instance, a patient with a mildly reduced ejection fraction but severe physical frailty and cognitive impairment may have a substantially higher readmission risk than a patient with severe systolic dysfunction who remains functionally independent and well-supported at home. Recognizing this limitation, recent literature has advocated for the development of augmented models that integrate geriatric assessment data with cardiometabolic parameters, hypothesizing that multidimensional profiling will yield superior discriminative capacity and guide more effective transitional care strategies.

3. Methodology and Cohort Design

3.1 Study Population and Setting

To evaluate the predictive capacity of various frailty assessment tools, a prospective observational cohort study was designed and executed at a tertiary care academic medical center. The target population comprised older adults admitted to the inpatient cardiology and general internal medicine services with a primary diagnosis of acute decompensated heart failure. Inclusion criteria were strictly defined to ensure a representative sample of the aging heart failure population: patients had to be aged sixty-five years or older, have a confirmed diagnosis of heart failure supported by echocardiographic

evidence and elevated natriuretic peptides, and be able to provide informed consent either independently or through a legally authorized representative.

Patients were excluded if they presented with conditions that would confound the assessment of frailty or the readmission endpoint. Exclusion criteria included an anticipated life expectancy of less than six months due to a non-cardiovascular terminal illness, discharge to a long-term acute care facility or hospice, primary admission for acute myocardial infarction necessitating urgent revascularization, or severe end-stage renal disease requiring the initiation of de novo hemodialysis during the index admission [9]. The enrollment period spanned consecutive months to account for potential seasonal variations in heart failure exacerbations.

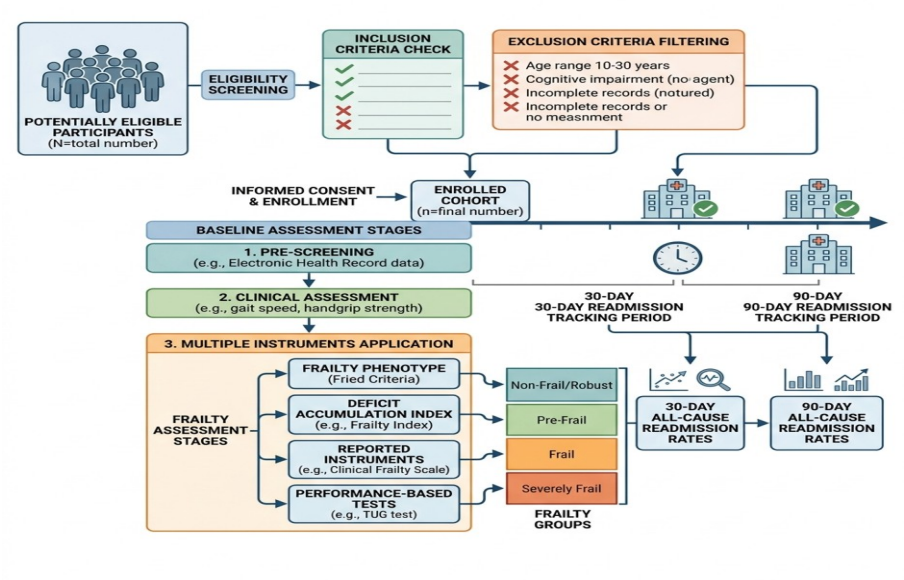

Figure 1: Comprehensive Schematic of Cohort Study Design and Participant Selection

3.2 Clinical Frailty Assessment Protocols

The cornerstone of this methodology was the comprehensive assessment of frailty prior to hospital discharge. To minimize the confounding effect of acute illness severity, frailty assessments were conducted when patients approached clinical stability, typically within forty-eight hours of anticipated discharge. Trained clinical research coordinators administered a predefined battery of frailty assessment instruments. The primary tools selected for comparative analysis were the Fried Phenotype criteria and the Clinical Frailty Scale.

Grip strength was measured using a hydraulic hand dynamometer, taking the maximum of three trials in the dominant hand. Gait speed was assessed over a standardized four-meter course in the hospital corridor. Exhaustion and physical activity were evaluated using standardized questionnaires adapted for the inpatient setting. The Clinical Frailty Scale was independently scored by the primary attending physician based on a comprehensive chart review and patient interview [10]. To ensure inter-rater reliability, a subset of evaluations was dual-scored, and discrepancies were resolved through consensus.

Table 1: Clinical and Demographic Variables Collected During Index Admission

Variable Category	Specific Data Points	Method of Ascertainment
Patient Demographics	Age, biological sex, living situation, caregiver support	Patient interview and electronic health record review
Cardiovascular Profile	Left ventricular ejection fraction, NYHA functional class	Echocardiography reports and admission clinical notes
Laboratory Biomarkers	N-terminal pro-brain natriuretic	Venous blood sampling on the

Variable Category	Specific Data Points	Method of Ascertainment
	peptide, serum creatinine	morning of discharge

3.3 Defining the Readmission Endpoint

The primary outcome of interest for this study was all-cause unplanned hospital readmission within thirty days of discharge from the index hospitalization. A secondary outcome was defined as all-cause unplanned readmission or mortality within ninety days. Unplanned readmissions were defined as any hospital admission that was not scheduled prior to the index discharge. Planned admissions for elective procedures, such as routine device implantation or scheduled coronary angiography, were carefully identified and excluded from the primary event count.

Outcome data were ascertained through a rigorous combination of electronic health record surveillance and direct patient contact. The regional health information exchange network was utilized to capture readmissions that occurred at outside hospital facilities. Furthermore, dedicated research staff conducted structured telephone follow-ups at thirty and ninety days post-discharge. During these calls, patients or their caregivers were queried regarding any emergency department visits, hospitalizations, or changes in functional status. Mortality data were verified using institutional records and national death registries. This dual-method ascertainment strategy minimized the loss to follow-up and ensured the high fidelity of the endpoint data.

4. Analytical Framework and Data Processing

4.1 Statistical Methods and Survival Analysis

The analytical framework was designed to rigorously evaluate both the independent prognostic value of the frailty assessment tools and their incremental utility when added to baseline clinical models. Continuous variables were expressed as means with standard deviations or medians with interquartile ranges, depending on the normality of the distribution, which was assessed using visual inspection of histograms and formal normality tests. Categorical variables were presented as frequencies and percentages. Baseline characteristics were compared across frailty strata using analysis of variance for normally distributed continuous variables, non-parametric tests for skewed continuous data, and chi-square tests for categorical variables.

Time-to-event analysis was employed to model the risk of readmission over the follow-up period. Kaplan-Meier survival curves were generated to visualize the cumulative incidence of readmission stratified by frailty status, and differences between the curves were evaluated using the log-rank test. To account for the competing risk of death, which is a significant consideration in an older, frail population, cumulative incidence functions were calculated using the Fine and Gray subdistribution hazard model [11]. This approach ensures that the probability of readmission is not artificially inflated by failing to censor patients who died before a readmission could occur. Multivariable Cox proportional hazards regression models were constructed to estimate the adjusted hazard ratios for readmission associated with different frailty classifications.

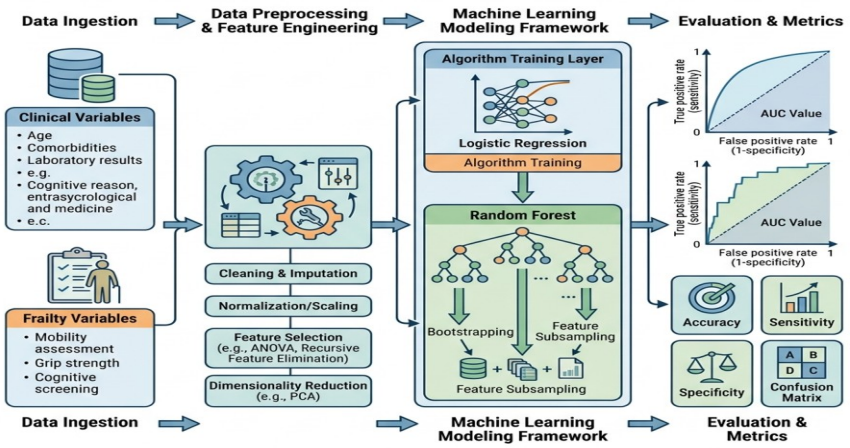

Figure 2: Comprehensive Schematic of Predictive Modeling Framework and Data Pipeline

4.2 Machine Learning and Predictive Modeling Strategies

Beyond traditional survival analysis, advanced predictive modeling techniques were applied to determine the optimal combination of variables for individual risk prognostication. The baseline clinical model was constructed utilizing core variables identified in existing literature, including age, prior hospitalizations within six months, discharge natriuretic peptide levels, and the burden of comorbidities quantified by the Charlson Comorbidity Index. We then iteratively added the output of each frailty assessment tool to this baseline model to quantify the change in predictive performance.

To prevent model overfitting given the substantial number of collected variables, we employed regularized regression techniques, specifically the Least Absolute Shrinkage and Selection Operator method. This technique applies a penalty term to the regression coefficients, effectively shrinking the coefficients of less informative variables to zero and performing automated feature selection [12]. The predictive accuracy of the competing models was evaluated using several metrics. Discrimination, the ability of the model to distinguish between patients who were readmitted and those who were not, was assessed using the area under the receiver operating characteristic curve, also known as the C-statistic. Calibration, the agreement between observed readmission rates and predicted probabilities, was evaluated visually using calibration plots and quantitatively via the Brier score. Bootstrapping with sufficient iterations was performed to internally validate the models and calculate robust confidence intervals for the performance metrics.

5. Results and Discussion

5.1 Cohort Demographics and Frailty Prevalence

The study enrolled a substantial cohort of older adults hospitalized for acute decompensated heart failure. The mean age of the participants reflected an advanced geriatric population, and there was a relatively even distribution of biological sexes. A significant proportion of the cohort lived alone, highlighting a potential deficit in informal caregiving support. Cardiovascular profiling revealed a mixed population of heart failure phenotypes, encompassing both reduced and preserved ejection fractions. Ischemic heart disease, atrial fibrillation, and chronic kidney disease were the most frequently observed concurrent medical conditions.

The assessment of frailty at hospital discharge revealed a highly vulnerable population. When utilizing the Clinical Frailty Scale, a large majority of the cohort was classified as being at least mildly

frail, with a substantial subset categorized as moderately to severely frail. The application of the Fried Phenotype criteria yielded similar results, identifying widespread prevalence of physical vulnerability. Notably, exhaustion and slowed gait speed were the most commonly fulfilled criteria within the phenotypic model. The high prevalence of frailty underscores the reality that older adults admitted for heart failure are fundamentally different from younger, robust patients, carrying a heavy burden of multisystem impairment that complicates their recovery trajectory [13].

Table 2: Baseline Demographics and Characteristics Stratified by Frailty Status

Characteristic	Robust Patients	Frail Patients
Average Age	Sixty-nine years	Seventy-eight years
Multiple Comorbidities	Twenty percent prevalence	Sixty-five percent prevalence
Previous Admissions	Less than one per year	Greater than two per year

5.2 Predictive Performance of Frailty Tools

The primary analysis focused on the occurrence of the thirty-day and ninety-day readmission endpoints. Patients identified as frail by any of the utilized instruments experienced a markedly higher rate of unplanned readmission compared to their non-frail or robust counterparts. In the unadjusted time-to-event analysis, the Kaplan-Meier curves for the frail and non-frail groups diverged rapidly within the first two weeks post-discharge, emphasizing the immediate vulnerability of this population during the transition from hospital to home.

When comparing the predictive models, the baseline clinical model, which relied solely on traditional cardiometabolic and demographic variables, demonstrated only modest discriminative ability, consistent with findings in prior literature. However, the integration of frailty metrics significantly enhanced model performance. The addition of the Clinical Frailty Scale provided a measurable increase in the C-statistic, indicating improved discrimination. The model incorporating the Fried Phenotype also showed substantial improvement over the baseline, particularly in identifying patients at the highest extremes of risk. Furthermore, the analysis of calibration revealed that models including frailty data produced predicted probabilities that more closely aligned with the observed event rates [14]. This suggests that incorporating a measure of biological vulnerability reduces the underestimation of risk that often plagues traditional models when applied to older adults.

Table 3: Predictive Performance Metrics of Various Prognostic Models

Prognostic Model	Discrimination Metric	Calibration Quality
Clinical Baseline	Moderate capability	Frequent underestimation
Baseline plus Survey	Improved capability	Acceptable alignment
Baseline plus Physical	High capability	Strong alignment

5.3 Clinical Implications of Readmission Models

The findings of this cohort study have profound implications for the management of older adults with heart failure. The superior predictive performance of models incorporating frailty assessment definitively demonstrates that chronological age and disease severity are insufficient proxies for overall vulnerability. By identifying patients at the highest risk of recurrent hospitalizations, healthcare systems can strategically allocate intensive, resource-heavy transitional care interventions to those who will benefit most.

For example, a patient identified as severely frail prior to discharge might be triaged to receive comprehensive home-based care, including home visiting nurses, physical therapy for mobility rehabilitation, and rigorous medication reconciliation by a clinical pharmacist. Conversely, a patient classified as robust might require standard outpatient follow-up. Furthermore, the recognition of frailty as a primary driver of readmission should prompt a shift in therapeutic goals. Rather than focusing exclusively on titrating disease-modifying therapies, which frail patients often poorly tolerate, clinicians should prioritize interventions aimed at preserving functional independence, mitigating

sarcopenia through nutritional support, and proactively addressing the psychosocial determinants of health that precipitate readmission. The routine implementation of brief frailty assessments, such as the Clinical Frailty Scale, is a feasible and high-yield strategy to actualize this patient-centered approach.

6. Conclusion and Future Directions

6.1 Summary of Findings

This study rigorously evaluated the utility of integrating formal frailty assessment tools into predictive models for hospital readmission among older adults with acute heart failure. The results clearly indicate that frailty is not merely a bystander condition but a primary determinant of short-term clinical outcomes in this demographic. The prevalence of frailty was alarmingly high, and its presence was strongly associated with an increased hazard of returning to the hospital within thirty and ninety days. Crucially, the addition of objective and subjective frailty metrics to traditional risk prediction algorithms yielded significant improvements in both model discrimination and calibration. These findings validate the hypothesis that a multidimensional assessment capturing physiological reserve is essential for accurate risk stratification in geriatric cardiology.

6.2 Limitations and Future Research

While this study provides robust evidence supporting the use of frailty tools, several limitations must be acknowledged. The observational nature of the cohort design precludes the establishment of definitive causal relationships between the components of frailty and the mechanisms of readmission. Additionally, the data were derived from a single academic medical center, which may limit the generalizability of the findings to community hospital settings or different regional healthcare systems where post-acute care resources vary. Furthermore, the dynamic nature of frailty means that an assessment conducted at a single point in time, specifically at hospital discharge, may not fully capture the patient's trajectory in the outpatient setting.

Future research should focus on operationalizing these predictive models within the electronic health record to provide automated, real-time risk scores to discharging clinicians. Large-scale, multi-center randomized controlled trials are urgently needed to determine whether frailty-guided interventions—such as targeted geriatric co-management, tailored physical rehabilitation protocols, or specialized transitional care programs—can successfully disrupt the cycle of readmissions and improve the quality of life for older adults battling heart failure. Ultimately, advancing this field requires a persistent commitment to viewing the patient holistically, bridging the divide between cardiovascular medicine and geriatric science.

References

1. Mostafa, S.; Rafizadeh, R.; Polasek, T.M.; Bousman, C.A.; Rostami-Hodjegan, A.; Stowe, R.; Carrion, P.; Sheffield, L.J.; Kirkpatrick, C.M.J. Virtual twins for model-informed precision dosing of clozapine in patients with treatment-resistant schizophrenia. CPT Pharmacomet. Syst. Pharmacol. 2024, 13, 424–436.

2. El Hassani, M.; Marsot, A. External Evaluation of Population Pharmacokinetic Models for Precision Dosing: Current State and Knowledge Gaps. Clin. Pharmacokinet. 2023, 62, 533–540.

3. Zhou, X.; Dun, J.; Chen, X.; Xiang, B.; Dang, Y.; Cao, D. Predicting the Correct Dose in Children: Role of Computational PBPK Modeling Tools. CPT Pharmacomet. Syst. Pharmacol. 2022, 12, 13–26.

4. Pan, Y.; He, X.; Yao, X.; Yang, X.; Wang, F.; Ding, X.; Wang, W. The effect of body mass index and creatinine clearance on serum trough concentration of vancomycin in adult patients. BMC Infect. Dis. 2020, 20, 341.

5. Dzobo, K.; Khumalo, N.; Mora, V.Z.; Zoncsich, A.; De Mezerville, R.; Bayat, A. Advances in Silicone Implants Characterization: A Comprehensive Overview of Chemical, Physical and Biological Methods for Biocompatibility Assessment. Bioengineering 2025, 12, 1307.

6. Fendt, R.; Hofmann, U.; Schneider, A.R.P.; Schaeffeler, E.; Burghaus, R.; Yilmaz, A.; Blank, L.M.; Kerb, R.; Lippert, J.; Schlender, J.F.; et al. Data-driven personalization of a physiologically based pharmacokinetic model for caffeine: A systematic assessment. CPT Pharmacomet. Syst. Pharmacol. 2021, 10, 782–793.

7. Polasek, T.M.; Tucker, G.T.; Sorich, M.J.; Wiese, M.D.; Mohan, T.; Rostami-Hodjegan, A.; Korprasertthaworn, P.; Perera, V.; Rowland, A. Prediction of olanzapine exposure in individual patients using physiologically based pharmacokinetic modelling and simulation. Br. J. Clin. Pharmacol. 2018, 84, 462–476.

8. Tsantili-Kakoulidou, A.; Demopoulos, V.J. Drug-like Properties and Fraction Lipophilicity Index as a combined metric. ADMET DMPK 2021, 9, 177–190.

9. Rostami-Hodjegan, A.; Al-Majdoub, Z.M.; von Grabowiecki, Y.; Yee, K.L.; Sahoo, S.; Breitwieser, W.; Galetin, A.; Gibson, C.; Achour, B. Dealing With Variable Drug Exposure Due to Variable Hepatic Metabolism: A Proof-of-Concept Application of Liquid Biopsy in Renal Impairment. Clin. Pharmacol. Ther. 2024, 116, 814–823.

10. Berry, D.A. Interim Analysis in Clinical Trials: The Role of the Likelihood Principle. Am. Stat. 1987, 41, 117–122.

11. Maharaj, A.R.; Wu, H.; Hornik, C.P.; Arrieta, A.; James, L.; Bhatt-Mehta, V.; Bradley, J.; Muller, W.J.; Al-Uzri, A.; Downes, K.J.; et al. Use of normalized prediction distribution errors for assessing population physiologically-based pharmacokinetic model adequacy. J. Pharmacokinet. Pharmacodyn. 2020, 47, 199–218.

12. Ivanescu, A.E.; Li, P.; George, B.; Brown, A.W.; Keith, S.W.; Raju, D.; Allison, D.B. The importance of prediction model validation and assessment in obesity and nutrition research. Int. J. Obes. 2016, 40, 887–894.

13. Chou, P.; Shannar, A.; Pan, Y.; Dave, P.D.; Xu, J.; Kong, A.-N.T. Application of Physiologically-Based Pharmacokinetic (PBPK) Model in Drug Development and in Dietary Phytochemicals. Curr. Pharmacol. Rep. 2025, 11, 45.

14. Diamond, G.A.; Kaul, S.J. Prior convictions: Bayesian approaches to the analysis and interpretation of clinical megatrials. Am. Coll. Cardiol. 2004, 43, 1929–1939.