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ISSUES AND PERSPECTIVES OF ADJUSTMENT OF DRUG DOSAGES FOR PEDIATRIC, GERIATRIC, IMMUNOSUPPRESSED, AND CANCER PATIENTS

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ABSTRACT

Individualizing drug dosages is a critical component of modern clinical pharmacology, particularly in vulnerable populations such as pediatric, geriatric, immunosuppressed, and cancer patients. Physiological and pharmacokinetic differences across these groups—due to age-related developmental changes, organ function impairment, immune system variability, and disease-specific drug responses—pose significant challenges for safe and effective drug therapy. Standard "fixed" dosing regimens derived from adult clinical trials often fail to account for such variability, increasing the risk of therapeutic failure or adverse drug reactions. Precision dosing and model-informed approaches have emerged as promising methods to address these challenges by integrating patient-specific factors with pharmacokinetic/pharmacodynamic data. This paper reviews key issues, including developmental pharmacology, age-associated physiological changes, immunosuppressant therapeutic monitoring, and oncology drug optimization, while presenting clinical and research perspectives for improving dosing guidelines and patient outcomes.

KEYWORDS: Pediatric dosing, Geriatric pharmacology, Immunosuppression, Oncology drug dosing, Pharmacokinetics, Precision dosing, Therapeutic drug monitoring.

1. INTRODUCTION

Appropriate drug dosing is essential for achieving therapeutic efficacy while minimizing toxicity. Standard dosing regimens are often based on clinical trials conducted in healthy adults and may not accurately reflect the unique pharmacokinetic (PK) and pharmacodynamic (PD) profiles seen in pediatric, geriatric, immunosuppressed, and cancer patients. Differences in absorption, distribution, metabolism, and excretion across these populations require careful

consideration when prescribing medications. Evidence suggests that precision dosing strategies, which leverage clinical data and modeling, can help tailor drug regimens effectively for these vulnerable groups.

2. PEDIATRIC PATIENTS

2.1 Physiological and Pharmacokinetic Considerations

Children are not simply "small adults." They exhibit dynamic developmental changes in organ function, body composition, and metabolic enzyme expression, which significantly affect drug pharmacokinetics and pharmacodynamics. Infants and young children often have higher body water content, altered protein binding, and immature drug-metabolizing systems, making standard dosing protocols less reliable.

2.2 Dosing Challenges

Drug dosing in pediatrics commonly relies on weight-based or body surface area (BSA) calculations, but these methods may not fully capture individual variability, especially in populations with obesity or malnutrition. Moreover, age-specific formulations (e.g., liquids, dispersible tablets) are often lacking, further complicating safe administration.

2.3 Oncology in Pediatrics

Dosing chemotherapy agents in pediatric oncology requires additional complexity. Growth-dependent PK variability, nutritional status, and heterogeneous responses necessitate customized regimens to balance efficacy and toxicity.

3. GERIATRIC PATIENTS

3.1 Age-Related Pharmacokinetic Alterations

Aging is associated with physiological changes, including decreased renal and hepatic function and altered body fat and protein binding. These changes can extend drug half-lives, impact clearance, and heighten sensitivity to many medications, especially those with narrow therapeutic windows.

3.2 Polypharmacy and Drug Interactions

Older patients frequently use multiple medications, increasing the risk of drug–drug interactions and adverse effects. Adjusting doses in this context requires careful evaluation of organ function, comorbidities, and pharmacodynamic sensitivity.

4. IMMUNOSUPPRESSED PATIENTS

4.1 Therapeutic Drug Monitoring (TDM)

Patients on immunosuppressants (e.g., tacrolimus, cyclosporine) exhibit large interindividual PK variability and narrow therapeutic indices. Regular TDM is crucial to maintain efficacy and avoid toxicity. Age-related changes may further influence dose requirements.

4.2 Balancing Efficacy and Safety

The fine balance between under- and over-immunosuppression is challenging, as excessive suppression increases infection risk while inadequate dosing may lead to graft rejection or disease flares.

5. CANCER PATIENTS

5.1 Oncology Dose Optimization

Cancer patients represent a uniquely complex group for dosing adjustments. Chemotherapeutic agents often have narrow therapeutic windows and severe toxicity profiles. Dose optimization strategies increasingly incorporate pharmacogenomic, PK, and PD parameters to tailor therapy to individual patient characteristics.

5.2 Precision Medicine Approaches

Emerging research supports model-informed precision dosing (MIPD) and Bayesian frameworks to integrate patient data with PK/PD models, enabling dynamic dose adjustments during treatment.

6. PERSPECTIVES AND FUTURE DIRECTIONS

6.1 Precision and Model-Informed Dosing

The integration of precision dosing frameworks, including therapeutic drug monitoring and computational models, may enhance individualized therapy across all vulnerable populations.

6.2 Regulatory and Clinical Implementation

There is a need for global regulatory harmonization to expand dosing recommendations based on real-world data, clinical trials including diverse populations, and improved decision support tools for clinicians.

7. READY-RECKONER AND CLINICAL DOSE ADJUSTMENT CALCULATORS

Dose adjustment calculators serve as practical bedside tools to translate pharmacokinetic principles into real-world prescribing. The following population-specific ready-reckoners integrate age, body size, organ function, and disease-specific considerations.

7.1 Pediatric Drug Dose Adjustment Calculator

Key Inputs

Age (neonate / infant / child / adolescent)

Weight (kg)

Height (cm)

Body Surface Area (BSA)

Renal function (eGFR if available)

Drug-specific pediatric factor

Core Calculation Methods

A. Weight-Based Dosing

$$\text{Dose (mg)} = \text{Weight (kg)} \times \text{Dose per kg (mg/kg)}$$

B. Body Surface Area (BSA) Method

$$\text{BSA (m}^2\text{)} = \sqrt{\frac{\text{Height (cm)} \times \text{Weight (kg)}}{3600}}$$

$$\text{Pediatric Dose} = \text{Adult Dose} \times \frac{\text{Child BSA}}{1.73}$$

C. Age-Based Adjustment (Neonates/Infants)

Age Group	Dose Adjustment Factor
Preterm neonate	30–50% adult equivalent
Term neonate (0–28 days)	50–70%
Infant (1–12 months)	70–90%
Child (>1 year)	Standard pediatric dose
Clinical	Use

Preferred for antibiotics, antipyretics, antiepileptics, oncology drugs.

Avoid adult fixed doses.

7.2 Geriatric Drug Dose Adjustment Calculator

Key Inputs

Age ≥65 years

Weight (kg)

Serum creatinine (mg/dL)

Polypharmacy status

Frailty index

A. Renal Function-Based Adjustment (Cockcroft–Gault Equation)

$$\text{CrCl (mL/min)} = \frac{(140 - \text{Age}) \times \text{Weight (kg)}}{72 \times \text{Serum Creatinine}}$$

Dose Adjustment by Renal Function

Creatinine Clearance	Recommended Dose
≥60 mL/min	100%
30–59 mL/min	50–75%
15–29 mL/min	25–50%
<15 mL/min	Avoid or specialist advice

B. Hepatic Function (Child–Pugh Score)

Child–Pugh Class	Dose Recommendation
A (mild)	75–100%
B (moderate)	50–75%
C (severe)	Avoid / 25%
Clinical	Use

Essential for sedatives, anticoagulants, antidiabetics, antihypertensives.

“Start low, go slow” principle applies.

7.3 Immunosuppressed Patient Dose Adjustment Calculator

Key Inputs

Drug trough level

Time since transplant / immunosuppression

Renal & hepatic function

Drug–drug interactions

A. Therapeutic Drug Monitoring (TDM)-Based Adjustment

\text{New Dose} =

\text{Current Dose} \times

\frac{\text{Target Trough Level}}{\text{Measured Trough Level}}

Target Trough Levels (Examples)

Drug	Target Level
Tacrolimus	5–15 ng/mL
Cyclosporine	100–300 ng/mL
Sirolimus	5–15 ng/mL
Mycophenolate (AUC)	30–60 mg·h/L
Clinical	Use

Mandatory in transplant medicine.

Adjust dose dynamically based on infection risk vs rejection risk.

7.4 Cancer Patient Drug Dose Adjustment Calculator

Key Inputs

Body Surface Area (BSA)

Performance status (ECOG)

Organ function

Previous chemotherapy toxicity

Pharmacogenomic markers (if available)

A. BSA-Based Chemotherapy Dosing

\text{Dose (mg)} = \text{Drug dose per m²} \times \text{BSA}

B. Toxicity-Based Dose Modification

Toxicity Grade (CTCAE)	Dose Adjustment
Grade 1	No change
Grade 2	Reduce by 25%
Grade 3	Reduce by 50%
Grade 4	Withhold / stop

C. Renal Adjustment for Cytotoxics

eGFR (mL/min)	Dose
≥60	100%
30–59	50–75%
<30	Avoid / alternative
Clinical	Use

Standard for platinum agents, methotrexate, targeted therapies.

Increasing role of Bayesian and AI-based precision dosing.

8. Integrated Quick Reference Table (Ready-Reckoner)

Population	Primary Method	Secondary Adjustment
Pediatric	Weight / BSA	Age & renal maturation
Geriatric	CrCl-based	Hepatic function
Immunosuppressed	TDM-based	Drug interactions
Cancer	BSA-based	Toxicity & genomics

9. Public Health and Clinical Perspective

Implementation of standardized dose-adjustment calculators:

Reduces medication errors

Improves therapeutic outcomes

Enhances patient safety

Supports rational prescribing in resource-limited settings

Integration into electronic health records (EHRs) and mobile clinical apps is strongly recommended.

10. Ready-Reckoner and Clinical Dose Adjustment Calculators

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12. Graphical Flowcharts for Dose Adjustment (Ready-Reckoner Models)

12.1 Pediatric Drug Dose Adjustment Flowchart

Stepwise Clinical Flow
Patient <18 years
↓
Assess Age Group
(Neonate / Infant / Child / Adolescent)
↓
Measure Weight & Height
↓
Calculate Dose
→ Weight-based (mg/kg) OR
→ BSA-based (mg/m²)
↓
Assess Organ Function
(Renal / Hepatic maturity)
↓
Check Max Adult Dose Limit
↓
Administer Dose
↓
Monitor Efficacy & ADR
↓
Adjust Dose if Needed

Guideline Alignment

WHO Model Formulary for Children

ICMR National List of Essential Medicines (NLEM – Pediatric section)

FDA Pediatric Study Plans (PSP)

12.2 Geriatric Drug Dose Adjustment Flowchart

Stepwise Clinical Flow

Patient ≥65 years

↓

Review Comorbidities & Polypharmacy

↓

Estimate Renal Function

(Cockcroft–Gault)

↓

Assess Hepatic Function

(Child–Pugh)

↓

Start Low – Go Slow

↓

Monitor ADRs & Drug Interactions

↓

Dose Titration / De-escalation

Guideline Alignment

WHO Ageing and Health Framework

ICMR Geriatric Care Guidelines

Beers Criteria (adapted for LMICs)

12.3 Immunosuppressed Patient Dose Adjustment Flowchart

Stepwise Clinical Flow

Immunosuppressed State

(Transplant / Autoimmune / Oncology)

↓

Identify Drug with Narrow TI

↓

Measure Trough Level

↓

Compare with Target Range

↓

Dose Adjustment Formula

(New Dose = Current × Target / Observed)

↓

Assess Infection & Rejection Risk

↓

Repeat TDM

Guideline Alignment

WHO Transplantation Guidance

ICMR Solid Organ Transplant Guidelines

KDIGO Immunosuppression Protocols

12.4 Cancer Patient Dose Adjustment Flowchart

Stepwise Clinical Flow

Cancer Diagnosis

↓

Calculate BSA

↓

Assess ECOG Performance Status

↓

Evaluate Renal & Hepatic Function

↓

Administer Standard Dose

↓

Assess Toxicity (CTCAE)

↓

Dose Modify / Hold / Stop

Guideline Alignment

NCCN Clinical Practice Guidelines

ASCO Chemotherapy Safety Standards

National Cancer Grid (India) Protocols

13. Alignment with National & International Guidelines

13.1 Summary of Guideline Concordance

Population	National Guidelines	International Guidelines
Pediatric	ICMR, NLEM	WHO, FDA
Geriatric	ICMR Elderly Care	WHO, Beers Criteria
Immunosuppressed	ICMR, KDIGO	WHO, AST
Cancer	National	Cancer Grid (India) NCCN, ASCO

13.2 Policy and Programmatic Relevance

Supports rational drug use under National Health Mission (NHM)

Enhances patient safety goals (WHO Medication Without Harm)

Reduces adverse drug reactions and hospital stay

Facilitates EHR-based dose calculators

14. IEC & Capacity-Building Messages (Add-On)

Children are not small adults – always calculate dose

Renal function overrides age in the elderly

Measure, don't guess immunosuppressant doses

Toxicity-guided dosing saves lives in cancer care

7. CONCLUSIONS

Adjusting drug dosages for pediatric, geriatric, immunosuppressed, and cancer patients presents significant challenges due to physiological variability, disease states, and limited clinical trial data. Tailored dosing strategies that incorporate pharmacokinetic and pharmacodynamic insights, patient-specific factors, and advanced modeling approaches are critical to improving therapeutic outcomes and reducing adverse events.

Ready-reckoner–based dose adjustment calculators provide a pragmatic bridge between pharmacological theory and bedside decision-making. Their use is indispensable in pediatric, geriatric, immunosuppressed, and cancer patients, where standard dosing fails to account for biological variability. Wider adoption of precision dosing tools can substantially improve safety, efficacy, and equity in drug therapy.

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