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Chapter 17

Pediatric and Geriatric Therapeutics

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Abstract: Age represents one of the most critical determinants of pharmacological response, as both pediatric and geriatric populations exhibit unique physiological characteristics that significantly influence drug pharmacokinetics and pharmacodynamics. Pediatric pharmacotherapy is challenged by developmental changes in organ maturation, body composition, enzyme activity, and renal clearance, necessitating weight-based or surface area-based dosing strategies and innovations in formulations tailored for children. Conversely, geriatric therapeutics must contend with age-related declines in organ function, receptor sensitivity alterations, polypharmacy, multimorbidity, and frailty, all of which heighten the risk of drug interactions and adverse drug events. This chapter provides a comprehensive analysis of developmental pharmacokinetics in children, major pediatric drug classes, and disease-specific therapies. It further addresses geriatric pharmacotherapy, emphasizing polypharmacy, de-prescribing strategies, and cognitive impairment management. The pharmacology of immunization across the lifespan is also discussed, alongside clinical trial gaps, individualized dosing strategies, and smart device-assisted adherence approaches. Ethical considerations, underrepresentation in trials, and the need for age-appropriate data remain persistent challenges. By integrating contemporary research, clinical guidelines, and translational perspectives, this chapter highlights the importance of age-tailored pharmacology in enhancing therapeutic safety, efficacy, and quality of life for both pediatric and geriatric populations.

Keywords: Pediatric pharmacology, Geriatric therapeutics, Polypharmacy, Developmental pharmacokinetics, Immunization strategies.

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17.0 INTRODUCTION

Age plays a pivotal role in determining the pharmacological response to drugs. Both the pediatric and geriatric populations are considered therapeutic outliers, with unique physiological and clinical characteristics that distinguish them from the general adult population. Unlike middle-aged adults, neonates, infants, children, and adolescents undergo rapid developmental changes in organ maturation and metabolism, which directly influence the absorption, distribution, metabolism, and excretion of drugs [1]. Similarly, aging is associated with progressive decline in organ function, altered receptor sensitivity, and increased vulnerability to adverse drug reactions, especially when coupled with comorbidities and polypharmacy [2].

Physiological changes across the lifespan account for much of the variability in drug response. For example, neonates exhibit elevated gastric pH, immature hepatic enzyme activity, and reduced renal clearance, whereas older adults experience decreased hepatic blood flow, reduced glomerular filtration, and impaired homeostatic mechanisms [3]. These alterations often require modifications in drug choice, dosing, formulation, and monitoring, yet clinical trial data to guide such decisions are often limited due to underrepresentation of these vulnerable populations in drug development programs [4].

In pediatrics, clinical pharmacology is further complicated by challenges such as appropriate dosing strategies, development of age-appropriate formulations, and ethical considerations in conducting trials in children [5]. Similarly, geriatric therapeutics must address issues such as inappropriate prescribing, drug–drug interactions, medication adherence, and optimizing therapy to balance efficacy and safety in the presence of multimorbidity [6]. Both populations highlight the ethical imperative of ensuring that vulnerable patients receive safe and effective drug therapy tailored to their physiological and psychosocial needs.

The significance of this chapter lies in exploring the intersection of pediatric and geriatric pharmacology, which although vastly different in biological context, share common challenges such as underrepresentation in clinical trials, limited evidence-based dosing data, and ethical dilemmas. The focus is to integrate modern pharmacological principles with real-world practices to optimize outcomes for both children and the elderly. Through systematic exploration of developmental pharmacokinetics, therapeutic classes, disease-specific management, polypharmacy, de-prescribing, immunization, and technological innovations in dosing and adherence, this chapter offers a comprehensive framework for clinicians, researchers, and policymakers.

17.1 Developmental Pharmacokinetics in Pediatrics

Drug disposition in children is influenced by the dynamic process of growth and maturation, which alters pharmacokinetic parameters in ways that are distinctly different from adults. Absorption, for instance, is impacted by the higher gastric pH in neonates, which reduces the solubility of weakly acidic drugs while enhancing the bioavailability of weak bases [7]. Gastric emptying and intestinal motility are slower in neonates but accelerate during infancy, leading to variability in oral drug absorption [8]. Furthermore, immature bile salt secretion in early infancy affects lipid-soluble drug absorption, such as fat-soluble vitamins and certain antimicrobials [9].

Distribution parameters also differ significantly. Neonates have a higher total body water-to-fat ratio, leading to larger volumes of distribution for hydrophilic drugs such as aminoglycosides, which may require higher loading doses [10]. Conversely, reduced plasma protein concentrations and lower binding affinity increase the free fraction of drugs such as phenytoin and bilirubin-displacing agents, raising the risk of toxicity [11]. Additionally, the immaturity of the blood–brain barrier in early life

facilitates higher central nervous system penetration of certain medications, which may be beneficial for drugs like antibiotics but raises concerns regarding neurotoxicity [12].

Metabolic capacity undergoes profound ontogeny. Cytochrome P450 (CYP) enzymes mature at different rates, with CYP3A7 dominating in the fetus and transitioning to CYP3A4 after birth, affecting metabolism of drugs such as midazolam [13]. Phase II reactions, such as glucuronidation and sulfation, also develop gradually, explaining phenomena such as the “gray baby syndrome” observed with chloramphenicol use due to deficient UDP-glucuronosyltransferase activity [14]. These maturational changes necessitate careful age-specific dosing regimens and continuous therapeutic monitoring.

Renal excretion is another critical determinant. Glomerular filtration rate (GFR) is significantly reduced at birth, reaching adult levels only after the first year of life [15]. Tubular secretion and reabsorption also mature progressively, altering clearance of drugs such as aminoglycosides, vancomycin, and digoxin. Failure to account for renal immaturity may lead to drug accumulation and toxicity [16].

To address these complexities, pediatric pharmacokinetic modeling and allometric scaling have been increasingly applied in drug development and dosing. These approaches incorporate weight, age, and developmental physiology to predict pharmacokinetics more accurately across pediatric age groups [17]. For example, allometric scaling allows extrapolation of adult dosing to children based on body surface area or weight, although refinements are needed to incorporate enzyme ontogeny and organ function [18]. Pharmacometric tools and physiologically based pharmacokinetic (PBPK) modeling are now integral to regulatory submissions for pediatric drug approvals, offering a more scientific framework than empirical dose adjustments [19]. In summary, pediatric pharmacokinetics is characterized by rapid developmental changes that require tailored therapeutic strategies. Understanding these ontogenic variations is critical not only for clinical practice but also for the design of safe and effective pediatric drug formulations and clinical trials.

17.2 Common Pediatric Drug Classes

Pharmacotherapy in pediatric populations often necessitates modifications in drug selection, dosing, and formulations compared with adults. Antibiotics remain among the most commonly prescribed medications for children, particularly in the treatment of respiratory and ear infections. Dosing is usually calculated on a milligram-per-kilogram basis to account for developmental differences in pharmacokinetics [20]. However, inappropriate dosing or overuse poses a significant risk of antimicrobial resistance, highlighting the importance of stewardship programs tailored for pediatric settings [21]. Narrow-spectrum antibiotics are often preferred where possible, and therapeutic drug monitoring is vital for agents with narrow therapeutic indices such as aminoglycosides.

Antipyretics and analgesics are another major class of drugs widely used in children. Paracetamol (acetaminophen) remains the first-line antipyretic, but risks of hepatotoxicity due to dosing errors or parental misinterpretation of instructions remain a concern [22]. Ibuprofen serves as an alternative, with evidence supporting its safety in children above six months, although renal complications may arise in cases of dehydration [23]. Guidelines emphasize precise weight-based dosing and avoidance of aspirin due to the risk of Reye’s syndrome [24].

Antiepileptic drugs (AEDs) play a crucial role in pediatric neurology. Agents such as valproate, levetiracetam, and carbamazepine are widely used, though their developmental effects on cognition and growth remain areas of ongoing research [25]. Therapeutic drug monitoring is often required, as

pharmacokinetic variability is pronounced during growth. Newer AEDs, including brivaracetam, offer favorable safety profiles but require validation in younger populations [26].

Psychotropic medications in pediatrics remain controversial, especially in the treatment of attention-deficit/hyperactivity disorder (ADHD), anxiety, and depression. Stimulants such as methylphenidate are first-line agents for ADHD, though concerns persist regarding appetite suppression, sleep disturbances, and long-term neurodevelopmental outcomes [27]. Selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine, are increasingly used in adolescent depression, but require close monitoring for behavioral changes and suicidality [28].

Respiratory drugs represent another cornerstone, particularly in asthma and cystic fibrosis (CF). Inhaled corticosteroids are effective in controlling airway inflammation in asthma, but require training in inhaler use to ensure adherence and efficacy [29]. For CF, CFTR modulators such as ivacaftor and lumacaftor have transformed care, though access and long-term safety remain challenges [30]. Formulation innovations, including suspensions, orally disintegrating tablets, and taste-masked syrups, have improved adherence in children, who often reject bitter-tasting formulations [31]. Furthermore, advances in vaccine delivery systems, including microneedle patches and dissolvable oral strips, promise greater acceptability and coverage among children [32].

17.3 Pediatric-Specific Diseases and Therapies

Certain conditions are unique or particularly prevalent in children, necessitating age-specific therapeutic approaches. ADHD is one such condition where pharmacological management plays a central role. Stimulants such as methylphenidate and amphetamines remain the gold standard, while non-stimulants like atomoxetine or guanfacine are considered in cases of intolerance or contraindications [33]. Long-term studies suggest improved academic and behavioral outcomes, though the potential impact on growth trajectories and cardiovascular risk necessitates ongoing monitoring [34].

Asthma is one of the most common chronic diseases in children, and management focuses on inhaled corticosteroids combined with short- or long-acting β2-agonists depending on severity [35]. Device choice is particularly important; nebulizers are commonly used in younger children, while dry powder inhalers and metered-dose inhalers with spacers are preferred in older children [36]. Education on inhaler technique remains a cornerstone of effective therapy. Cystic fibrosis exemplifies the progress of precision medicine in pediatrics. CFTR modulators such as ivacaftor and the triple combination elexacaftor/tezacaftor/ivacaftor have shown remarkable improvements in pulmonary function and survival [37]. Antibiotic cycles targeting Pseudomonas aeruginosa, together with mucolytic agents like dornase alfa, remain vital supportive therapies [38].

Pediatric oncology presents additional complexity. Chemotherapy protocols are adapted to account for the unique physiology of children, but treatment-related toxicities such as growth impairment and secondary malignancies remain significant long-term risks [39]. Ethical issues in pediatric cancer trials such as consent, assent, and balancing innovation with safety continue to be debated [40]. Supportive care with antiemetics, growth factors, and infection prophylaxis is integral to maintaining treatment intensity while minimizing morbidity.

Other therapeutic challenges include developmental disorders and autism spectrum disorders, where pharmacotherapy is largely supportive, focusing on symptom control such as irritability with atypical antipsychotics [41]. Pediatric palliative care, though less discussed, is an essential field involving multimodal pain management, sedation, and psychosocial support [42].

Opioids may be required in severe cases, but careful titration is essential to avoid respiratory depression.

Table 1: Comparative Pharmacokinetic Alterations in Pediatrics and Geriatrics

Parameter	Pediatrics	Geriatrics
Gastric pH	Higher in neonates (↓ weak acid absorption)	Increased due to atrophy (↓ weak acid absorption)
Gastric Emptying	Delayed in neonates, accelerates in infants	Delayed due to reduced motility
Body Composition	Higher water/fat ratio, ↓ plasma proteins	↓ lean body mass, ↑ fat, ↓ albumin
Hepatic Metabolism	CYP maturation ongoing	↓ hepatic blood flow and enzyme activity
Renal Function	GFR immature, matures by ~1 year	Progressive decline in GFR and tubular function
BBB Permeability	Immature (↑ CNS drug penetration)	Relatively intact but ↑ sensitivity to CNS drugs

17.4 Polypharmacy and Frailty in Geriatrics

In contrast to pediatrics, geriatric pharmacotherapy is dominated by the challenges of multimorbidity, polypharmacy, and frailty. Pharmacokinetic changes in aging include reduced gastric acidity, delayed gastric emptying, and decreased hepatic first-pass metabolism, which alter oral drug bioavailability [43]. Hepatic metabolism declines due to reduced hepatic blood flow and enzyme activity, while renal clearance decreases with age-related decline in glomerular filtration and tubular function [44]. These changes prolong half-life and enhance drug accumulation, particularly for renally cleared drugs such as aminoglycosides and digoxin.

Pharmacodynamic changes are equally important. Older adults often demonstrate heightened sensitivity to central nervous system depressants, such as benzodiazepines and opioids, due to altered receptor density and impaired compensatory mechanisms [45]. Likewise, diminished β-adrenergic receptor sensitivity reduces the efficacy of β-blockers, whereas increased anticoagulant sensitivity elevates bleeding risks [46]. Homeostatic decline in blood pressure regulation, thermoregulation, and glucose control further increases susceptibility to adverse outcomes.

Polypharmacy commonly defined as the concurrent use of five or more medications is prevalent among the elderly and strongly associated with adverse drug reactions, hospitalizations, falls, and frailty progression [47]. Drug–drug and drug–disease interactions are frequent, particularly when medications for one condition exacerbate another, as in the case of β-blockers worsening chronic obstructive pulmonary disease [48]. The presence of multimorbidity compounds the complexity of prescribing, making individualized care essential.

Medication-related falls and fractures remain a serious concern. Sedatives, antipsychotics, and antihypertensives are leading contributors to fall risk, with substantial morbidity and mortality in frail populations [49]. Hospitalizations due to drug-related adverse events are disproportionately higher in older adults compared to younger populations [50]. These risks underscore the necessity of frequent medication reviews, de-prescribing when appropriate, and close collaboration between geriatricians, pharmacists, and primary care physicians to optimize therapeutic outcomes.

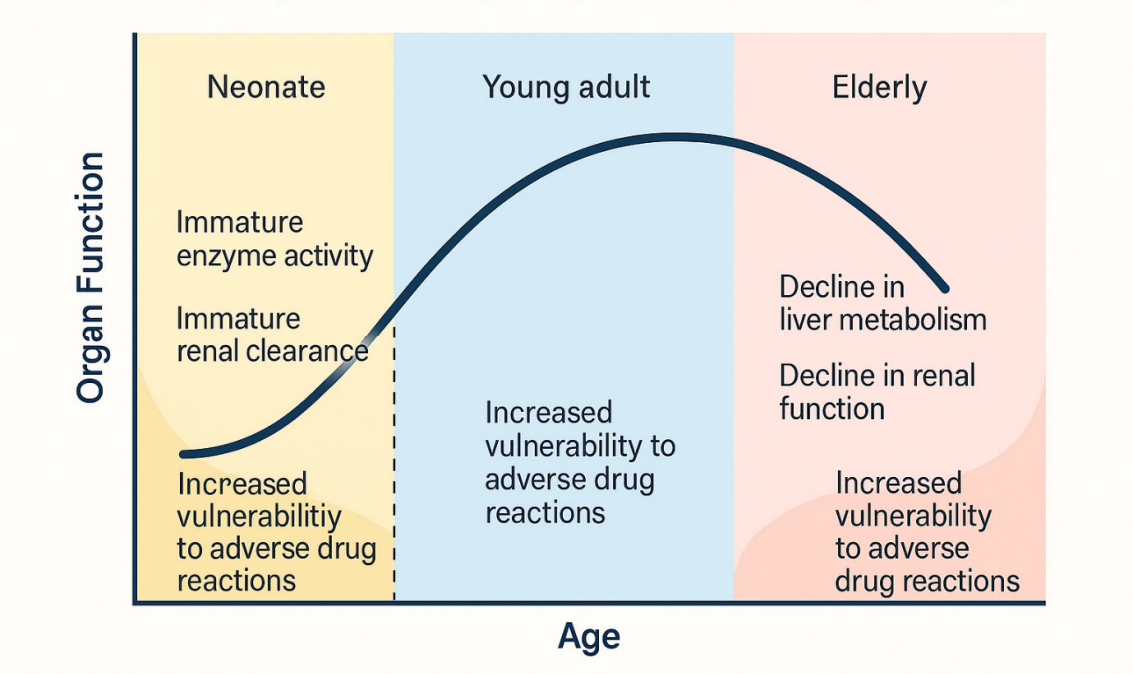

Figure 1: The Lifecycle of Drug Response Across Age Groups

17.5 De-prescribing and Risk Minimization

In geriatric pharmacotherapy, polypharmacy often leads to inappropriate prescribing, with substantial consequences on morbidity, mortality, and healthcare costs. De-prescribing, defined as the systematic process of tapering or discontinuing drugs that may no longer be beneficial or may be causing harm, has emerged as a central strategy to optimize therapy in older adults [51]. Tools such as the STOPP (Screening Tool of Older People's Prescriptions) and START (Screening Tool to Alert to Right Treatment) criteria provide structured approaches to identifying potentially inappropriate medications and omissions in care [52]. These tools are supported by evidence showing reductions in drug-related hospitalizations and improvements in quality of life [53].

The Beers Criteria, first published in 1991 and regularly updated by the American Geriatrics Society, remain one of the most widely used resources for identifying high-risk drug classes in older adults, including benzodiazepines, anticholinergics, and certain antihypertensives [54]. However, their application requires clinical judgment, as rigid adherence may inadvertently lead to under-treatment of symptoms.

Clinical practice now increasingly incorporates shared decision-making models, where patients and caregivers are engaged in discussions about the risks and benefits of continued pharmacotherapy [55]. This approach not only enhances adherence but also aligns therapeutic choices with patients' preferences and goals of care. Economic implications of de-prescribing are equally important, as reducing unnecessary medications can significantly lower healthcare expenditures [56]. Ethical considerations include balancing non-maleficence with the risk of undertreatment, particularly in populations with advanced frailty [57].

17.6 Cognitive Impairment and Drug Safety

Cognitive impairment, including dementia, poses significant challenges for medication safety in older adults. Polypharmacy, particularly drugs with anticholinergic properties, has been strongly

linked to accelerated cognitive decline and increased dementia risk [58]. The concept of anticholinergic burden quantifying cumulative exposure to such agents has become an important clinical metric, with higher scores correlating with worse cognitive outcomes [59].

Managing pharmacotherapy in dementia patients requires simplification of regimens to improve adherence and minimize adverse effects. Strategies include reducing pill burden through fixed-dose combinations, timing simplification (once-daily regimens), and using long-acting formulations [60]. Caregiver training and adherence aids such as pill organizers, blister packs, and smart pillboxes have shown significant benefit in reducing medication errors [61].

Neuropsychiatric symptoms such as agitation, sleep disturbance, and depression are common in dementia and often lead to psychotropic prescribing. However, drugs such as antipsychotics and benzodiazepines increase the risk of falls, stroke, and mortality, necessitating careful risk–benefit assessment [62]. Non-pharmacological approaches, including behavioral therapy and environmental modification, are recommended as first-line strategies [63]. Pharmacological options, when necessary, should be employed at the lowest effective dose with regular re-evaluation.

Ultimately, cognitive impairment not only complicates pharmacokinetics and pharmacodynamics but also demands innovations in medication delivery and caregiver support to ensure safety and therapeutic success.

17.7 Immunization Pharmacology Across the Lifespan

Vaccination remains one of the most effective pharmacological interventions for both pediatric and geriatric populations, though immunogenicity differs across the lifespan. Pediatric immunization schedules are designed to provide early protection against infectious diseases, with vaccines such as measles–mumps–rubella (MMR), diphtheria–tetanus–pertussis (DTaP), and pneumococcal conjugates forming the cornerstone of childhood preventive medicine [64]. Catch-up schedules are critical for children who miss doses, ensuring adequate immunity without restarting entire vaccine series [65].

In geriatric populations, immune senescence reduces vaccine responsiveness, necessitating booster strategies and adjuvanted formulations. Annual influenza vaccination, pneumococcal polysaccharide and conjugate vaccines, and shingles vaccination are strongly recommended for adults over 65 years [66]. High-dose influenza vaccines and novel adjuvant systems have demonstrated improved immunogenicity in older adults [67].

Vaccine hesitancy remains a shared challenge across age groups, often driven by misinformation, cultural beliefs, or fear of side effects [68]. Effective communication strategies, including community outreach and provider-patient counseling, are essential for maintaining public trust in vaccination programs.

The future of immunization pharmacology includes individualized approaches such as genetic profiling to predict vaccine responsiveness, and novel delivery methods including microneedle patches, intranasal sprays, and oral vaccines that improve accessibility and adherence [69].

17.8 Clinical Trial Gaps in Vulnerable Populations

Despite advances in pharmacology, both pediatric and geriatric populations remain consistently underrepresented in clinical trials. Most pivotal trials focus on adult participants aged 18–65, leading to a significant evidence gap for patients at the extremes of age [70]. For pediatrics, ethical challenges such as informed consent, assent, and concerns regarding potential harm hinder enrollment [71]. Parents and guardians often hesitate to involve children in trials, and researchers face difficulties in balancing the need for innovation with safeguarding vulnerable populations [72].

The result is that many drugs prescribed for children are used off-label, relying on extrapolated adult data rather than evidence-based pediatric trials. This increases the risk of dosing errors, therapeutic failure, and adverse drug events [73]. To address this, regulatory bodies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have introduced pediatric-only approvals and mandated Pediatric Investigation Plans (PIPs) as part of the drug approval process [74]. Similarly, for geriatric populations, there are no formal requirements for age-specific studies, even though pharmacokinetic and pharmacodynamic changes in the elderly are substantial [75].

Another gap lies in trial design. Traditional randomized controlled trials (RCTs) often exclude frail elderly patients with multimorbidity, who represent the majority of real-world cases [76]. Adaptive trial designs and pragmatic trials have been proposed as alternatives, allowing incorporation of flexible dosing schedules, smaller subgroups, and real-world conditions [77]. The use of real-world evidence, derived from electronic health records, registries, and post-marketing surveillance, is increasingly recognized by regulators as complementary to RCT data [78].

Bridging these gaps requires coordinated strategies that include regulatory incentives, ethical frameworks tailored for vulnerable populations, and innovative methodologies such as Bayesian adaptive designs and physiologically based pharmacokinetic (PBPK) modeling. Without such measures, both pediatric and geriatric patients will remain marginalized in drug development pipelines.

17.9 Individualized Dosing Tools and Devices

Dosing precision is central to optimizing therapeutic outcomes in both children and older adults. Weight-based dosing is commonly employed in pediatrics, while age-based dosing is sometimes used for convenience. However, age-based methods are prone to error because developmental physiology does not align strictly with chronological age [79]. For example, two children of the same age can differ significantly in weight, body composition, and metabolic capacity. Allometric scaling and pharmacometric modeling offer more accurate alternatives, yet these tools are not always available in everyday clinical practice [80].

Smart dosing devices have emerged as a solution to improve safety and adherence. Infusion pumps with programmable dose limits are now widely used in pediatric intensive care units to prevent overdosing or underdosing of critical drugs such as opioids and antibiotics [81]. Similarly, smart inhalers equipped with sensors track usage patterns, providing reminders and adherence data to clinicians and caregivers [82]. These innovations are particularly beneficial for children with asthma and older adults with chronic obstructive pulmonary disease (COPD).

Adherence aids are equally crucial, especially in the context of polypharmacy in geriatrics and complex regimens in pediatrics. Pill organizers, blister packs, and digital applications offer structured reminders, while wearable monitors and connected devices transmit adherence data to healthcare providers [83]. These technologies improve patient engagement and reduce the risk of missed doses or duplication.

Pharmacokinetic software and therapeutic drug monitoring (TDM) play vital roles in optimizing therapy in vulnerable groups. For drugs with narrow therapeutic indices, such as aminoglycosides, vancomycin, or antiepileptics, individualized monitoring ensures safe plasma concentrations [84]. Emerging AI-driven dosing calculators now integrate patient demographics, laboratory values, and genetic information to recommend personalized regimens, a trend that aligns with the broader move toward precision medicine [85].

Incorporating these tools into routine practice requires training, infrastructure investment, and regulatory guidance. Nonetheless, their potential to minimize medication errors, enhance adherence, and improve outcomes across both pediatric and geriatric populations is undeniable.

CONCLUSION

Pediatric and geriatric therapeutics represent two ends of the age spectrum where pharmacotherapy is most complex and vulnerable to error. In children, the challenges arise from developmental pharmacokinetics, immature organ systems, and the need for age-appropriate formulations. In the elderly, the issues revolve around polypharmacy, frailty, pharmacokinetic decline, and drug–disease interactions. Despite these differences, both groups face a common problem: underrepresentation in clinical trials and limited evidence-based dosing data.

Innovations in pharmacokinetic modeling, individualized dosing tools, and adherence technologies are bridging some of these gaps. Immunization strategies tailored to age-specific immunological responses further underscore the importance of lifespan pharmacology. Ethical frameworks and regulatory incentives are needed to ensure that vulnerable populations are adequately represented in drug development.

Ultimately, a patient-centered approach that integrates pharmacological science with clinical judgment, caregiver support, and technological innovation will be essential to improve safety, efficacy, and quality of life in both pediatric and geriatric populations.

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