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Pediatric Polypharmacy:

Time to Lock the Medicine Cabinet?

Nancy E. Morden, MD, MPH and **David Goodman, MD, MS**
Department of Community and Family Medicine (Dr Morden), Center for Health Policy and Research, Dartmouth Institute for Health Policy and Clinical Practice (Drs Morden and Goodman), and Dartmouth Atlas of Health Care (Dr Goodman), Dartmouth Medical School, Lebanon, New Hampshire.

The use of therapeutic agents represents a trade-off between the benefits of symptom relief or disease modification that increase quality or length of life and the risk of short- and long-term adverse effects. While evidence suggests that complex medication combinations greatly increase the odds of incurring an adverse drug event,[1-3] US Food and Drug Administration approval generally only requires testing of agents in isolation. As a consequence, we often do not know the net health outcomes associated with diverse and intense medication combinations. This uncertainty is magnified in the care of children for whom efficacy and safety studies are often lacking. Despite this therapeutic uncertainty, pediatric drug use is growing.[4] A study in this issue of the *Archives*[5] provides a critical examination of the drug exposure of pediatric inpatients. Polypharmacy is the norm for hospitalized infants and children. Should we be concerned?

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Using 2 large detailed inpatient administrative data sets to quantify drug exposure among pediatric patients hospitalized in the United States, Feudtner and colleagues[5] found a relatively high level of medication use. Median first-day exposure ranged from 3 to 5 unique product types. The median exposure on subsequent days ranged from 3 to 9 products. In fully adjusted models, hospital type (children's or general) was not associated with the number of drugs used; overall exposure generally increased with patient age and with additional inpatient days. For 3 highlighted, common Diagnosis Related Groups (DRGs) (asthma, appendectomy, and seizure), cumulative medication exposure varied substantially across hospitals.

Correspondence: Dr Goodman, Dartmouth Institute for Health Policy and Clinical Practice, Dartmouth Medical School, 35 Centerra Pkwy, Lebanon, NH 03766 (David.C.Goodman@Dartmouth.edu)..

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We share the authors' unease with the level of polypharmacy in pediatric inpatient settings, but our biggest concern is the lack of information that would tell us if these prescribing patterns are problematic for patients. Inpatient pediatric care is complex, and it is not clear which medications and medication combinations are best for a hospitalized child. Certainly, relief of symptoms should be a priority. While medications aimed at alleviating symptoms can be overused, patients should not suffer in the name of parsimonious prescribing or unfounded fear for adverse effects. In particular, the tragic undertreatment of pain in children has been extensively documented.[6,7] In addition, the use of anesthetics and sedatives may not be optional when surgery, procedures, or advanced imaging are required. After these general categories of drugs (symptom relief, sedatives, and anesthetics) children's next most common exposures, as detailed in Table 2 of the article by Feudtner et al,[5] are to antimicrobial and respiratory agents, broad categories in which appropriateness of some prescribing patterns is doubtful.[8-10] Are pediatric patients receiving too much or too little?

The variation in DRG-specific drug exposures seen across hospitals suggests a lack of consensus among pediatric clinicians about medication prescribing for children. Unnecessary and potentially hazardous drug exposure likely occurs in some facilities, while in other hospitals, pediatric patients may be undertreated. Studying the variation in further detail will help to identify concerning patterns of prescribing and guide further research and clinical care improvement.

In an effort to advance safe and effective inpatient pharmacotherapy for children, an important next step is to use administrative data (eg, medical claims) to determine the common medications that represent marginal exposure in hospitals with high drug use and the medications most commonly "lacking" in low-use hospitals. These large data sets could also be used to measure outcomes associated with distinct exposure patterns. Observational studies such as these could add valuable information to randomized clinical trials and improve our understanding of the health impact of pediatric polypharmacy. Better use of medications should improve outcomes, reduce adverse effects, and save money.

Surveillance and research on the effects of pediatric polypharmacy should be prioritized and funded in proportion to the prevalence and likely patient impact of this issue. Such research should be funded by noncommercial sources. While pediatric polypharmacy is likely most common in the inpatient setting where acute illness or procedures drive medication use, outpatient polypharmacy is increasingly prevalent in children and also deserves attention.[4] In nonhospitalized children, adverse effects related to short-term overlapping drug use similar to that in the inpatient setting, undoubtedly occur, but long-term effects of cumulative exposure may be equally important. Therapy with medications started in childhood for management of chronic conditions often continues for decades—well beyond the duration of any drug approval trials and thus well outside our understanding of potential drug effects.[11,12] As we advance the research agenda of pediatric polypharmacy, it is important to consider this broad trend and to move forward with studies on the effects of long-term polypharmacy in children. Outcomes studies will depend on high-quality administrative data. It is sobering to realize that the availability and completeness of medical claims data for children still falls far short of Medicare data used to study the elderly population. Feudtner et al[5] and other investigators could accelerate improvement in the care of children if permitted access to data that include all medical care events (eg, discharges, outpatient visits, pharmacy claims) for a large pediatric population whose care can be linked over time and to specific providers.

Clinicians, policy makers, researchers, and patient advocates should collaborate on efforts aimed at promoting the development of evidence to inform pediatric pharmacotherapy.

Moving toward an understanding of the balance of risks and benefits will require better data, a sustained research program, and a commitment to translating new knowledge into better practice.

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