

2017 Update on Pediatric Medical Overuse

A Review

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IMPORTANCE Medical overuse has historically focused on adult health care, but interest in how children are affected by medical overuse is increasing. This review examines important research articles published in 2016 that address pediatric overuse.

OBSERVATIONS A structured search of PubMed and a manual review of the tables of contents of 10 journals identified 169 articles related to pediatric overuse published in 2016, from which 8 were selected based on the quality of methods and potential harm to patients in terms of prevalence and magnitude. Articles were categorized by overtreatment, overmedicalization, and overdiagnosis. Findings included evidence of overtreatment with commercial rehydration solution, antidepressants, and parenteral nutrition; overmedicalization with planned early deliveries, immobilization of ankle injuries, and use of hydrolyzed infant formula; and evidence of overdiagnosis of hypoxemia among children recovering from bronchiolitis.

CONCLUSIONS AND RELEVANCE The articles were of high quality, with most based on randomized clinical trials. The potential harms associated with pediatric overuse were significant, including increased risk of infection, developmental disability, and suicidality.

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Attention is growing for the fact that some medical care routinely provided to children is at best ineffective and at worst harmful. In the 5 years since the American Board of Internal Medicine Foundation launched the Choosing Wisely campaign, the original list of 5 pediatric tests and treatments that clinicians and patients should question has matured into 140 such pediatric recommendations.¹ In collaboration with the American College of Physicians, a group of pediatrician educators recently released a National Pediatric High Value Care Curriculum.² Following the "Less is More" and "Too Much Medicine" series at *JAMA Internal Medicine* and *BMJ*, respectively, another pediatric journal has started a similar series titled "Bending the Value Curve."³

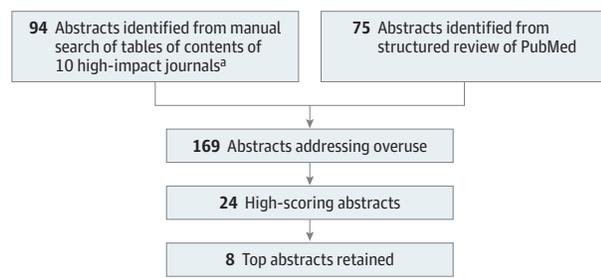
Rigorous science must provide the foundation for these efforts to raise awareness of *pediatric overuse*, defined as the provision of health care for which net benefits do not exceed net harms.⁴ We followed the model of a series of annual articles in *JAMA Internal Medicine*⁵⁻⁷ and an inaugural pediatric review of 2015 articles⁸ to describe the most important studies related to pediatric overuse published in 2016. The need for these annual updates continues. A recent systematic review⁹ found that clinicians overestimate the benefits and underestimate the harms of medical interventions that they provide. These biases are exacerbated by the fact that quality metrics tend to focus on underuse of health care interventions.^{10,11} Despite the neglected focus on medical harms and overuse, physicians still believe that 20% of all the medical care that they provide is unnecessary.¹² Although the outsized financial

burden of adult overuse makes it challenging to focus attention on pediatric overuse, this effort is particularly paramount because children have more years of life ahead of them in which to realize harm from exposure to medical overuse.¹³ The purpose of this review is to raise awareness of pediatric overuse and to highlight the articles that can serve as the basis for future improvement and education efforts that lead to higher-value care.

Methods

We adhered to a previously published search method and selection process for reviews of articles about medical overuse.⁵⁻⁸ Our search was limited to articles published in 2016 and occurred in 2 stages (Figure) as (1) a structured PubMed review and (2) a manual review of journal tables of contents. For stage 1, we searched PubMed using the Medical Subject Headings term *health services misuse* alone or with any of the following words in the title: *overuse*, *overtreatment*, *overdiagnosis*, *inappropriate*, and *unnecessary*. In EMBASE, a search was performed with the Emtree term *unnecessary procedure* in addition to the search terms used for PubMed. Articles with *overuse injury* or *overuse injuries* in the title were excluded. Searches were limited to human studies in the English language. All titles from the search were reviewed by 1 of us (including E.R.C., D.J.M., or S.S.D.) for relevance to medical overuse. For the second stage, 2 of us (including E.R.C., P.C.Y., R.A.Q.,

Figure. Selection of Articles for Inclusion



^a Journals include *Lancet*, *BMJ*, *JAMA*, *The New England Journal of Medicine*, *Pediatrics*, *JAMA Pediatrics*, *Journal of Pediatrics*, *Journal of Perinatology*, *Archives of Disease in Childhood*, and *Archives of Disease in Childhood (Fetal)*.

or A.R.S.) reviewed all the 2016 tables of contents for 10 major medical and pediatric journals (Figure) and selected abstracts related to overuse.

We manually reviewed the titles of 2252 articles identified by the structured review and determined that 1224 addressed medical overuse. Seventy-five of the articles focused specifically on children. The review of the tables of contents classified an additional 94 articles as related to pediatric overuse. We scored the 169 abstracts according to the following 3 criteria: (1) quality of methods, (2) magnitude of potential harm, and (3) number of patients potentially harmed (Table).¹⁴⁻¹⁶ The quality of methods for each article was assessed using the Oxford Centre for Evidence-based Medicine's levels of evidence.¹⁷ Scoring for the magnitude of potential harm was modeled on the Joint Commission on Accreditation of Healthcare Organizations patient safety event taxonomy, for which injury severity and permanence are foundational.¹⁸ The number of patients harmed was approximated as a combination of how common the clinical scenario and the resulting harm might be and was applied to the population for which the study would reasonably generalize. The 24 highest-scoring articles were summarized and discussed by the authors, with group consensus ultimately deciding on the 8 most relevant studies to be highlighted in this article. The selected articles are organized into categories of overtreatment, overmedicalization, and overdiagnosis according to a previously reported classification scheme.¹⁹

Results

Overtreatment

Let Children With Acute Gastroenteritis Have Their Preferred Drink

Background | Treatment with a commercially available oral rehydration solution is recommended at the onset of diarrhea for children with acute gastroenteritis.²⁰ Commercially available oral rehydration solutions are less palatable and more expensive than are children's preferred drinks, and the superiority of oral rehydration solutions has not been established in developed countries where significant dehydration is uncommon.

Findings | Freedman et al²¹ performed a randomized single-blind clinical trial (evidence quality, 1b) comparing the effects of diluted

Table. Criteria Used to Evaluate the Importance of Overuse Articles

Criterion	Scoring Rubric	High-Scoring Examples
Quality of methods	High indicates an RCT (single or systematic review); moderate, a cohort study (single or systematic review) or a poor-quality RCT (unblinded, marked loss to follow-up); and low, a case-control study, a case series, a cross-sectional study, an expert opinion, or a poor-quality cohort study.	Boyle et al ¹⁴ performed a systematic review and meta-analysis of RCTs using a prespecified, registered protocol and included an assessment of risk of bias.
Magnitude of potential harm	High indicates severe harm (profound impairment or life-threatening); moderate, prolonged, nonsevere harm; and low, transient, nonsevere harm or costly.	The potential harm evaluated by Sharma et al ¹⁵ was suicidality.
Number harmed	High indicates a common clinical scenario and common harm; moderate, a common clinical scenario and uncommon harm or an uncommon clinical scenario and common harm; and low, an uncommon clinical scenario and uncommon harm.	Bentley et al ¹⁶ reported that planned births account for nearly half of births before 39 weeks of gestation and found that 11% of children born in this manner became developmentally high risk.

Abbreviation: RCT, randomized clinical trial.

preferred fluids and electrolyte maintenance solution in 647 children presenting to the emergency department with acute gastroenteritis but minimal dehydration. The trial found that children randomized to oral hydration with half-strength apple juice and preferred fluids were less likely to experience treatment failure compared with children randomized to oral hydration with an electrolyte maintenance solution (16.7% vs 25.0%; $P < .001$). Treatment failure included several components, but the difference in failure rates was predominantly attributable to a nearly 4-fold reduction in the need for subsequent intravenous hydration among children randomized to oral hydration with half-strength apple juice (2.5% vs 9.0%; $P = .001$).

Implications | Care of children with mild dehydration secondary to acute gastroenteritis can be simplified. Families can be spared the trouble and the expense of obtaining commercially available rehydration solutions, and children can be hydrated with their preferred fluids, including drinks previously considered to be contraindicated owing to high glucose loads.

Meta-analysis Finds Questionable Efficacy of Antidepressant Medications for Children and Adolescents With Depression

Background | Depression is a serious and common condition that can result in substantial impairment in children and adolescents. Antidepressants are often used to treat severe cases of depression.

Findings | Cipriani et al²² performed a network systematic review and meta-analysis (evidence quality, 1a) of 34 published and unpublished randomized clinical trials (including 4 from trial registers and pharmaceutical company websites) that included 5260 study children and adolescents and concluded that methods used in individual studies were poor. Despite the weaknesses of individual studies, all antidepressants except fluoxetine had no clinical benefit. Data for fluoxetine suggest a medium effect at reducing depressive symptoms compared with placebo but with a large credible interval close to no difference (standardized mean difference, -0.51 ; 95% credible interval, -0.99 to -0.03).

Implications | This comprehensive network meta-analysis²² suggests that better evidence for efficacy of medication treatment of major depression for children and adolescents is needed. Nonpharmacologic treatments such as psychotherapy should remain first-line options. If medications are deemed to be necessary for treatment of depression, fluoxetine may be considered.

Antidepressant Medications Increase Suicidality and Aggression in Children and Adolescents

Background | Although the association between antidepressant use and suicide has been recognized for decades, these medications continue to be prescribed widely. Published trials of antidepressants may have less comprehensive data on harms than clinical study reports, which Sharma et al^{15(p2)} describe as “detailed summaries of trial results prepared by the drug industry for submission to regulatory authorities to obtain authorisation for marketing.”

Findings | Sharma et al¹⁵ performed a meta-analysis of 68 clinical study reports from 70 randomized, double-blind trials of serotonin and serotonin norepinephrine–reuptake inhibitors (evidence quality, 1a), including 11 trials that enrolled children and adolescents. Among children and adolescents taking antidepressants, the odds ratio for suicidality was 2.39 (95% CI, 1.31-4.33); for aggression, 2.79 (95% CI, 1.62-4.81); and for akathisia, 2.15 (95% CI, 0.48-9.65). Because of limitations in study design and reporting, the actual magnitude of harm may have been underestimated.

Implications | Given the concerning adverse effects found in this study,¹⁵ antidepressants should be used with caution in children. Published trial data are insufficient to adequately quantify the risk-benefit profile of these medications.

Worse Outcomes for Critically Ill Children Who Receive Early vs Late Parenteral Nutrition

Background | Critically ill children are often malnourished, and adequate nutrition is crucial to facilitate clinical recovery. Parenteral nutrition (PN) can be administered to children who cannot receive enteral feeding. However, PN has associated risks and costs, and the ideal timing of PN initiation is controversial.

Findings | Fizez et al²³ performed a multicenter, randomized clinical trial of 1440 children (evidence quality, 1b) that demonstrated no difference in mortality between early (within 24 hours of intensive care unit admission) vs late (withheld through the first 7 days of intensive care unit admission) PN. However, new infection rates were lower in the late PN group (10.7% vs 18.5%; adjusted odds ratio, 0.48; 95% CI, 0.35-0.66). In addition, late PN was associated with a shorter duration of mechanical ventilation, lower rates of renal replacement therapy, a shorter hospital stay, and less laboratory evidence of cholestasis. Of note, enteral nutrition was not completely withheld from study participants. For example, patients in both groups were receiving approximately 200 to 300 kcal/d of enteral nutrition by day 4.

Implications | Parenteral nutrition may be harmful if initiated early in the intensive care unit hospitalization. However, because patients in both groups received some amount of enteral nutrition in the first 7 days, these findings may not apply to patients in whom enteral nutrition is expected to be withheld completely for a prolonged period.

Overmedicalization

Association of Planned Birth Before 39 Weeks of Gestation With Increased Risk of Poor School Age Development

Background | Rates of early, planned births (labor induction or prelabor cesarean delivery) are increasing.²⁴ Although complications and worsened neurodevelopmental outcomes for preterm births are well documented, pregnant women generally believe that planned births after 37 weeks of gestation carry minimal risk for harm.²⁵

Findings | In a population-based cohort of 153 730 live births in New South Wales, Australia (evidence quality, 2b), Bentley et al¹⁶ found that planned birth before 39 weeks of gestation was associated with children being developmentally high risk by school age. Risk increased for each additional week of early gestational age to 38 weeks of gestation, for which the adjusted relative risk was 1.13 (95% CI, 1.08-1.19). Findings were similar when analysis was limited to a subgroup of 54 848 women with low-risk pregnancies.

Implications | Medical overuse with an adverse effect on long-term childhood outcomes begins before birth. Pediatricians can advocate that pregnant women and their clinicians strive to delay delivery until the natural onset of labor.

Radiograph-Negative Lateral Ankle Injuries in Children: Almost Never an Occult Growth Plate Fracture

Background | As a result of the seminal 1963 study on physeal injuries by Salter and Harris,²⁶ growing children are believed to be more likely to sustain a fracture through the physis than to rupture ligaments.²⁷ Therefore, injuries associated with tenderness overlying the physis of the distal fibula that show no radiographic evidence of a fracture have traditionally been labeled as nondisplaced Salter-Harris type I physeal fractures of the distal fibula (SH1DF), for which children may be prescribed weeks of immobilization, repeated radiographs, and follow-up in an orthopedic clinic.

Findings | A prospective cohort study by Boutis et al²⁷ examined 135 children with negative radiographic findings for ankle injuries and used magnetic resonance imaging to determine the true frequency of fractures (evidence quality, 2b). Although ligament injuries were identified in 108 patients, only 4 were found to have an SH1DF. Thirty-eight distal fibular avulsion fractures were identified only by magnetic resonance imaging. No differences in measures of functional recovery were identified among children with SH1DF, ligament injuries, and fibular fractures.

Implications | Children with negative radiographic findings for lateral ankle injuries rarely have SH1DF. Even when these fractures are present, outcomes are excellent.

Hydrolyzed Formula Does Not Reduce the Risk of Allergic or Autoimmune Disease

Background | Compared with breastfeeding, infant formula feeding is associated with increased future risk of allergic disease, perhaps owing to large, intact proteins present in formula. If formula feeding is used, national guidelines in North America and Europe^{28,29} recommend hydrolyzed formula for infants who have a high baseline risk of allergic disease.

Findings | Thirty-seven trials met inclusion for a systematic review of the literature regarding the use of partially or extensively hydrolyzed formula for preventing eczema, recurrent wheeze, allergic rhinitis, food allergy, allergic sensitization, or type 1 diabetes mellitus (evidence quality, 1a).¹⁴ Most studies demonstrated high or unclear risk of bias and conflict of interest. Of 27 subgroup analyses by age and allergen, only 2 demonstrated a decreased pooled risk of allergy. Boyle et al¹⁴ indicated that studies in the review that were of lower quality (quasirandomized or nonrandomized trials) were more likely to report positive findings.

Implications | Despite widespread marketing and promotion of hydrolyzed formula for the prevention of allergic diseases, this carefully conducted review found almost no evidence of benefit. Until industry-independent studies are conducted and show benefit of hydrolyzed formula, pediatricians should not recommend its use.

Overdiagnosis

Oxygen Desaturation in Outpatients With Bronchiolitis Is Not Associated With Worse Outcomes

Background | Increased use of pulse oximetry has been associated with an increasing rate of hospitalizations for bronchiolitis, and even minor changes in pulse oximetry have been shown to be a primary determinant for decisions to admit to the hospital. Although small deviations in hypoxemia alter care for infants with bronchiolitis, whether these infants benefit from such detection is less clear.

Findings | In a prospective cohort study of 118 children with bronchiolitis who were discharged from a tertiary care children's hospital emergency department with a pulse oximeter (display and alarm disabled) (evidence quality, 2b),³⁰ unscheduled medical visits were compared between infants who experienced outpatient desaturation with those who did not. Seventy-five children (63.6%) experienced a desaturation (<90% for ≥ 1 minute), of whom 59 (78.7%) experienced desaturations of 80% or less and 29 (38.7%) experienced desaturations of 70% or less. Infants with desaturations were no more likely to have unscheduled medical visits than those without desaturations (difference, -1.6%; 95% CI, -0.15 to ∞ ; $P = .66$).

Implications | Children with bronchiolitis undergoing outpatient treatment frequently experience desaturations that are self-limited and not indicative of worsening disease. These findings support reduced reliance on pulse oximetry among well-appearing children with bronchiolitis.

Discussion

The top articles on pediatric overuse from 2016 demonstrate the importance of questioning long-standing dogmas and maintaining an openness to challenging, even straightforward interventions that

may have strong intuitive appeal. That children do not have ankle sprains and that birth after 37 gestational weeks is as safe as at term are commonly accepted beliefs that appear to be inaccurate. Although commercial oral rehydration solutions should logically be most effective for mild acute gastroenteritis and prescription of hydrolyzed formula to infants at high risk of allergic disease is tempting, the new evidence presented herein suggests otherwise. No matter how basic or obvious a tenet in medicine may seem, it should be held accountable to sound experimentation.

Although the high cost of US health care is often the chief motivator behind interest in medical overuse, a more important reason to address medical overuse is to protect patients from harm. The potential harms to children uncovered by articles on overuse highlighted in this review are significant. The most convincing evidence to date has emerged that planned delivery from 37 to 39 weeks is associated with worse school-age child development, including physical health and well-being, language and cognitive skills, social competence, emotional maturity, communication skills, and general knowledge.¹⁶ Perhaps most concerning is the increased risk of suicidality and aggressive behavior among adolescents and children prescribed antidepressant therapy,¹⁵ a class of medications for which efficacy has been recently questioned.²² Despite a steadfast commitment to obtaining complete data, Sharma and colleagues¹⁵ were limited by pharmaceutical companies' incomplete reporting of harms and tactics to impede full analysis. Their findings therefore likely underestimate harm and cast broad concerns for unreported harms of pharmaceutical drugs in general.

Limitations

Limitations of our review should be considered. This article adheres to a previously used method and style for annual review of medical overuse literature,⁵⁻⁷ including 1 we performed last year.⁸ Therefore, we considered only articles published in 2016 and limited our summaries to the top original research articles. This work was not intended to be a formal systematic review of the literature, and not all high-quality research demonstrating overuse in pediatrics could be included. Although the included articles scored highly for evidence quality, they are not without limitations themselves, challenging the immediacy with which practice changes might be made. In many cases, gaps in knowledge remain, and further research is needed to definitively change care.

Conclusions

High-quality research addressing pediatric overuse is uncovering significant potential harms of commonly used medical interventions for children. Reducing the use of these interventions and supporting medical overuse research are critically important to protect children from unnecessary medical harm.

ARTICLE INFORMATION

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