Update on Pediatric Overuse

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As concerns over health care–related harms and costs continue to mount, efforts to identify and combat medical overuse are needed. Although much of the recent attention has focused on health care for adults, children are also harmed by overuse. Using a structured PubMed search and manual tables of contents review, we identified important articles on pediatric overuse published in 2015. These articles were evaluated according to the quality of the methods, the magnitude of clinical effect, and the number of patients potentially affected and were categorized into overdiagnosis, overtreatment, and overutilization. Overdiagnosis: Findings included evidence for overdiagnosis of hypoxemia in children with bronchiolitis and skull fractures in children suffering minor head injuries. Overtreatment: Findings included evidence that up to 85% of hospitalized children with radiographic pneumonia may not have a bacterial etiology; many children are receiving prolonged intravenous antibiotic therapy for osteomyelitis although oral therapy is equally effective; antidepressant medication for adolescents and nebulized hypertonic saline for bronchiolitis appear to be ineffective; and thresholds for treatment of hyperbilirubinemia may be too low. Overutilization: Findings suggested that the frequency of head circumference screening could be relaxed; large reductions in abdominal computed tomography testing for appendicitis appear to have been safe and effective; and overreliance on C-reactive protein levels in neonatal early onset sepsis appears to extend hospital length-of-stay.

Medical overuse is the provision of health care for which net benefits do not exceed net harms.[1] Often, discussions surrounding this topic center on the cost of care provided to adult patients, and low-end estimates suggest that at least $200 billion in annual domestic costs are attributable to overuse.[2] Reducing medical overuse is a means to mitigate the currently unsustainable outlay of health care resources for the American people.[3] Although determining to whom and how many medical resources should be supplied can be complex, ideological, and contentious, there is broad consensus that patients should experience more benefit than harm as a result of their interaction with the health care system. Nevertheless, modern medicine has repeatedly exposed large populations of patients to well-meaning, apparently rational medical interventions, only to learn later from large randomized trials that the tests and interventions actually caused more harm than good (eg, hormone replacement therapy[4,5] and prostate cancer screening[6]).

Viewed from the lens of potential patient harm, addressing medical overuse is just as critical for children as it is for adults. However, studies of pediatric overuse have been limited.[7] Randomized trials evaluating the efficacy of some of the most common aspects of pediatric care (eg, well-child exams and developmental screening) do not exist. Reasons for lack of interest in pediatric overuse may include that the most effective pediatric

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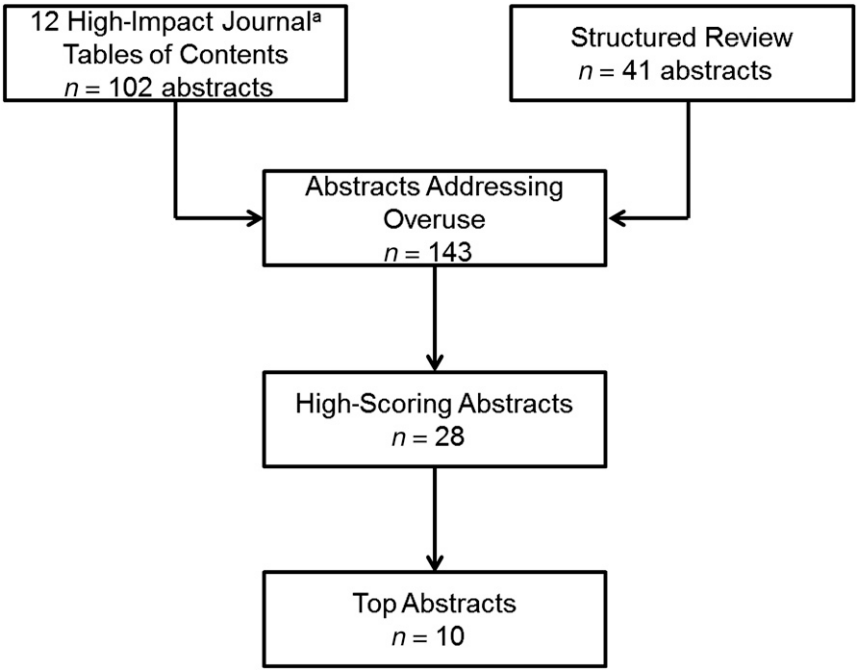

FIGURE 1
Selection of articles for inclusion. [a] *Lancet, BMJ, JAMA, The New England Journal of Medicine, Pediatrics, JAMA Pediatrics, Journal of Pediatrics, Journal of Perinatology, Archives of Disease in Childhood, Archives of Disease in Childhood (Fetal), Journal of Developmental and Behavioral Pediatrics, Journal of Adolescent Health.*

intervention, childhood immunizations, has been troubled by underuse, and an implicit assumption that children are fragile might cultivate a belief that more care is better care.

Such well-intentioned perceptions of children's inherent vulnerability may lead to the delivery of diagnostic and treatment interventions of unknown net efficacy, which can result in harm to children. Beginning with descriptions of unwarranted variation in the frequency of tonsillectomies in England and Wales in the 1930s[8] and Vermont in 1969,[9] a burgeoning body of literature exploring overuse of medical care for children has developed. Two recent examples include the overprovision of steroids and surgical closure of the patent ductus arteriosus in premature infants, resulting in greater risk of neurodevelopmental impairment[10,11] in both cases and an additional risk of retinopathy of prematurity and bronchopulmonary dysplasia after surgical treatment of patent ductus arteriosus.[11] Our objective in the current study is to describe the most important research related to pediatric overuse published in 2015, provide generalizable lessons from currently overused medical practices, and raise awareness for this critical topic among all providers of pediatric health care.

LITERATURE SEARCH AND ARTICLE SELECTION PROCESS

Articles were selected through a structured review of studies published in 2015, mirroring the approach of 2 recent articles reviewing important adult medical overuse research.[12,13] We searched PubMed using the medical subject headings term "health services misuse" 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 words 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 2 authors (D.M., S.D.) for relevance to medical overuse. Additionally, 2 pediatric authors (E.C., R.Q., P.Y., or A.S.) reviewed all of the 2015 tables of contents for 12 major medical and pediatric journals (Fig 1) and read abstracts and full journal articles for those of potential relevance.

The structured review identified 1445 articles. Manual review of the titles characterized 821 articles as addressing medical overuse, 41 of which were pediatric. The tables of contents review uncovered an additional 102 articles suggesting the presence of overuse and/or the need to reduce it. These 143 abstracts were scored by all 4 pediatric authors according to 3 criteria: (1) quality of the methods, (2) magnitude of clinical effect, and (3) number of patients potentially affected (Table 1). Abstracts were given a score of 1 (highest) to 3 by each author; 28 abstracts received a score of 1 from at least 1 reviewer. These 28 articles were summarized and discussed, with group consensus ultimately deciding on the 10 most relevant to be highlighted in this article. The selected articles were organized into categories of overdiagnosis, overtreatment, and overutilization, according to a previously reported classification scheme.[14] The evidence quality of each article was scored by using the Oxford Centre for Evidence-Based Medicine's "Levels of Evidence."[15]

ARTICLES

Overdiagnosis

A Lower Oxygen Saturation Threshold Safely Decreases Length-of-Stay in Bronchiolitis Hospitalizations[19]

Background: Routine pulse oximetry use has been associated with increased hospitalizations and length

of stay in bronchiolitis. There are no evidence-based oxygen saturation thresholds to guide the use of supplemental oxygen.

Findings: A multicenter randomized, blinded trial comparing an oxygen saturation threshold of 90% (American Academy of Pediatrics recommendation[20]) with 94% (NHS Scotland Quality Improvement[19]) in infants hospitalized with bronchiolitis demonstrated that the time on supplemental oxygen was 22 hours shorter and the time to discharge was 10 hours shorter in the 90% threshold arm. The lower threshold did not result in any adverse outcomes.

Implications: A threshold of 90% is safe and associated with a shorter duration of oxygen use and length-of-stay. Additional research is needed to determine whether an even lower threshold can be used and whether a specific threshold is always necessary.

Evidence quality: 1b (individual randomized controlled trial with narrow confidence intervals [CIs]).

Children With Skull Fractures Do Not Routinely Require Hospitalization or Re-imaging[17]

Background: Skull fractures are common in children with head injuries and often trigger hospitalization for a period of observation.

Findings: A secondary analysis of the Pediatric Emergency Care Applied Research Network multicenter prospective observational study of 350 patients with traumatic brain injury who had isolated linear skull fractures and a Glasgow Coma Scale of 14 to 15 demonstrated that over half (57%) of patients were hospitalized. Twenty-one percent of hospitalized patients and 13% of nonhospitalized patients had repeat head imaging. No patients had new findings requiring surgical intervention, and no patients suffered neurologic deterioration.

Implications: Children with an isolated linear skull fracture and a reassuring neurologic exam do not require reimaging or hospitalization. These findings also suggest that these types of skull fractures are overdiagnosed. That is, children may not benefit from the diagnosis and may in fact be harmed by being hospitalized and/or subjected to additional radiation.

Evidence quality: 2b (individual cohort study).

TABLE 1 Criteria Used To Evaluate the Importance of Overuse Articles

Criterion	Description	High-Scoring Examples
(1) Quality of methods	Were studies adequately powered and to what extent were selection bias and confounding mitigated?	Silver et al[16] randomized patients to an intervention and were powered to detect a difference in their primary outcome, length-of-stay, of 0.6 d.
(2) Magnitude of clinical effect	How substantial are the potential ramifications of overuse?	Powell et al[17] found that children diagnosed with skull fractures were unnecessarily hospitalized and exposed to repeated head CT scans.
(3) Number of Patients Potentially Effected	How large is the population being exposed to overuse?	Frequent HC screening is recommended for all US infants. Wright et al[18] found that 18% of their cohort had at least 1 extreme measurement in the first 2 years of life.

Overtreatment

Antidepressants for Adolescents Are Determined to Be Ineffective and Possibly Harmful in Reanalysis of a Pivotal Trial[21]

Background: A 2001 randomized trial ("Study 329") comparing paroxetine, imipramine, and placebo for adolescents with major depression concluded that both drugs were superior to placebo in reducing depression scores.[22] A 2013 initiative entitled "restoring invisible and abandoned trials" called for study funders of misreported or abandoned trials to disclose their data.[23]

Findings: A reanalysis of 275 participants in Study 329 demonstrated that neither paroxetine nor imipramine was superior to placebo in terms of the primary outcome, change in Hamilton depression score (–10.7, –9.0, and –9.1 in the paroxetine, imipramine, and placebo groups, respectively; $P = .20$), or secondary outcomes, contrary to the initial study's findings. The reanalysis also demonstrated previously non-eported harms associated with both antidepressants, including suicidal ideation and behavior.

Implications: The current widespread use of antidepressants in adolescents may have been driven in part by misleading results from the initial 2001 trial. This reanalysis demonstrating no benefits and new concerns about harms should encourage clinicians to use these medications cautiously. Better data transparency from clinical studies and unbiased reanalyses may help to provide a better understanding of risks and benefits of medications in general.

Evidence quality: 1b

Most Children Hospitalized With Pneumonia Do Not Have a Bacterial Pathogen Isolated[24]

Background: The introduction of *Streptococcus pneumoniae* and *Haemophilus influenzae* vaccines have reduced the burden of invasive

infections caused by these bacteria.[25,26] Reliable estimates of the etiology of childhood pneumonia since their introduction are not available. Improvements in molecular diagnostic testing provide an opportunity to better characterize the current epidemiology of childhood pneumonia.

Findings: Among a prospective cohort of 2222 children admitted to 1 of 3 children's hospitals with symptoms of an acute respiratory illness and a chest radiograph consistent with pneumonia, extensive testing for respiratory pathogens revealed a virus in 73% of patients and a bacterium in 15% (only 7% if mycoplasma is excluded). For bacteria, testing included cultures of blood, endotracheal aspirate, bronchoalveolar-lavage, or pleural fluid (specimens obtained at the discretion of the medical team); polymerase chain reaction (PCR) of blood or pleural fluid; and PCR of nasopharyngeal or oropharyngeal swab for *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*. Viruses could be detected by nasopharyngeal and oropharyngeal PCR swabs, as well as from acute and convalescent serum titers.

Implications: A bacterial pathogen could be isolated from only a small portion of hospitalized children with respiratory illness and radiographic evidence of pneumonia. Widespread antibiotic use for possible pneumonia or indistinct respiratory syndromes is not supported. Future studies should examine how antibiotics can be more precisely targeted for bacterial pneumonia.

Evidence quality: 2b.

Oral Antibiotics Are Just as Effective and Safer Than Intravenous Antibiotics for Postdischarge Treatment of Acute Osteomyelitis[27]

Background: The treatment of acute osteomyelitis requires a prolonged course of antibiotics, delivered either orally or intravenously through a peripherally inserted central catheter (PICC). There are no large scale clinical trials comparing the 2 approaches in children, but significant unwarranted variability in the choice of treatment route exists.[28]

Findings: A multicenter retrospective cohort study of 2060 children hospitalized for acute osteomyelitis from the Pediatric Health Information System database found that 51% received antibiotic therapy via a PICC at discharge. There was no difference in treatment failure between children receiving antibiotics via a PICC and those receiving oral antibiotic therapy (absolute risk difference, 0.3%; 95% CI, –0.1%–2.5%). Children receiving PICC therapy had higher rates of adverse drug reactions (absolute risk difference, 1.7%; 95% CI, 0.1%–3.3%) and higher rates of return emergency department visits or rehospitalization for PICC complications (absolute risk difference, 14.6%; 95% CI, 11.3%–17.9%).

Implications: Prolonged intravenous antibiotic therapy is commonly prescribed for acute osteomyelitis, but oral antibiotic therapy appears equally effective and has fewer treatment-related harms.

Evidence quality: 2b.

Current Thresholds for Treating Hyperbilirubinemia Are Probably Too Low[29]

Background: Because of an association between infant hyperbilirubinemia and neurodevelopmental abnormalities, the American Academy of Pediatrics recommends treatment of hyperbilirubinemia, including exchange transfusion, when serum levels reach certain thresholds in the context of patient risk factors.[30]

Findings: A multicenter study evaluating 525 409 infants born within an integrated health care system in Northern California between 1995 and 2011 found small increases in the absolute risk of cerebral palsy for hyperbilirubinemia in excess of recommended exchange transfusion thresholds. Compared with infants whose total serum bilirubin levels were never above the exchange transfusion threshold (ETT), infants with peak bilirubin values of 0 to 4.9 mg/dL above the ETT had a slightly increased risk of cerebral palsy (absolute risk difference, 0.2%; 95% CI, 0%–0.5%). Of the 3/525 409 patients who developed kernicterus, all had ≥2 neurotoxicity risk factors and peak bilirubin levels >5 mg/dL higher than the currently recommended ETT.

Implications: Risk of cerebral palsy and kernicterus is extremely low among infants with modest elevations in peak serum bilirubin values beyond the current ETT. Current treatment thresholds for hyperbilirubinemia can likely be raised without putting infants at greater risk of brain injury.

Evidence quality: 2b.

Hypertonic Is Not Superior to Normal Nebulized Saline in Inpatient Bronchiolitis[16]

Background: Previous trials assessing the efficacy of nebulized 3% hypertonic saline for infants with bronchiolitis demonstrated conflicting results, and important study design and population differences limit generalizability to US children. The current study was performed at a US children's hospital, did not exclude children with a history of previous wheezing, and did not use bronchodilators in either treatment arm.

Findings: This randomized, double-blind, controlled trial of 227 infants <12 months of age hospitalized for bronchiolitis compared nebulized 3% hypertonic saline with 0.9% normal saline and found no difference in the primary outcome, length-of-stay (2.1 days in both treatment arms). There

was also no difference in clinical worsening (transfer to the pediatric ICU or bronchospasm) or 7-day readmissions.

Implications: Hypertonic 3% saline is one in a long line of therapies attempted in children with bronchiolitis where early studies suggested some promise, but follow-up studies ultimately demonstrated no benefit. This study should give us pause when interpreting early results of therapeutic interventions in bronchiolitis.

Evidence quality: 1b.

Overutilization

Head Circumference Screening Is Neither Sensitive nor Specific for Neurocognitive Disorders[18]

Background: The American Academy of Pediatrics recommends head circumference (HC) screening 8 times in a child's first 2 years of life and the World Health Organization recommends HC screening twice, after birth and at 8 weeks of age.[18]

The value of routine HC measurements at any interval has not been demonstrated.

Findings: A population-based cohort study tracking 14 701 children since 1991 found that although extreme head size (≥2 *z* scores above or below the mean) was commonly detected (18% of children had at least 1 extreme measurement in the first 2 years of life), it was neither sensitive nor specific for identifying neurocognitive disorders (NCD), defined as receipt of a neurodevelopmental diagnosis, classroom special education needs by age 11 years, or low Wechsler Intelligence Scale for Children IQ at age 8 years. More than 20% of infants experienced a >1 *z*-score shift in HC between 6 to 8 weeks and 9 months of age. However, only 15% of children with small average HC *z* scores and 9% of those with large average HC *z* scores developed an NCD, whereas 93% of children who did develop a NCD had normal HC *z* scores.

Implications: Current HC screening recommendations should be reconsidered. Routine measurement of HC may precipitate unnecessary investigations and parental anxiety.

Evidence quality: 2b.

Additional C-reactive Protein Testing in Newborns Associated With Longer Duration of Hospitalization and More Lumbar Punctures Without Change in Outcome[31]

Background: Because newborn babies are at heightened risk of infection, laboratory testing and empirical antibiotic therapy are frequently prescribed. A new National Institutes of Health and Care Excellence guideline for management of neonatal early onset sepsis was introduced in the United Kingdom in 2012, recommending additional C-reactive protein (CRP) testing.

Findings: In a single center retrospective comparison of outcomes before and after implementation of the early onset sepsis guidelines, the rate of repeat CRPs doubled (45% before guidelines, 97% after). The number of babies hospitalized for ≤72 hours decreased from 38% to 18% and the number of lumbar punctures performed increased from 14% to 23%. Demographic characteristics were similar before and after guideline introduction and there were no positive blood or cerebrospinal fluid cultures.

Implications: Recommendations to increase CRP testing among newborn babies appear to precipitate more invasive testing and prolong duration of hospitalization without improving outcomes for these newborns.

Evidence quality: 2c (outcomes research).

Decreasing Use of Computed Tomography for Appendicitis Associated With Equivalent or Better Outcomes[32]

Background: Compared with ultrasound, computed tomography (CT) is superior in the evaluation of children with suspected appendicitis.[33] However, concerns for an increased risk of malignancy associated with radiation exposure have led to the replacement of CT with ultrasound.[34] The consequences of this substitution have been incompletely evaluated.

Findings: Among a retrospective cohort of patients receiving care for appendicitis at 35 children's hospitals between 2010 and 2013, a 48% reduction in CT accompanied by a 46% increase in ultrasound was not associated with a change in the proportions of children with either appendiceal perforations or 3-day emergency revisits. The proportion of children with a negative appendectomy declined slightly (absolute risk difference, 1.1%).

Implications: The substantial replacement of CT by ultrasound, a safer but less accurate imaging modality, was associated with the same or better outcomes for pediatric appendicitis. CT should rarely be used in the evaluation of children with suspected appendicitis.

Evidence quality: 2b.

DISCUSSION

We highlighted 10 rigorously conducted studies published in 2015 that demonstrate medical overuse for common childhood conditions. There was evidence for overdiagnosis of infant hypoxemia and isolated linear skull fractures. Adolescent depression, pneumonia, osteomyelitis, hyperbilirubinemia, and bronchiolitis appear to be overtreated. CT scans for appendicitis, CRP testing for newborns, and HC screening are

likely overused. This collection of articles provides several generalizable and actionable lessons for individuals and organizations committed to providing children with high quality health care.

Greater caution for providing more medical care should be exercised in the face of limited evidence. Even before publication of these 10 articles, high-quality evidence supporting the overused practices was lacking. With the exception of using paroxetine or imipramine for adolescent depression, none of the interventions were supported by a randomized trial. Observational studies directly supporting the efficacy of these interventions were likewise in short supply, with expert opinion forming the foundation for these overused practices. For example, the hyperbilirubinemia thresholds evaluated by Wu et al[29] come from guidelines published by the American Academy of Pediatrics,[30] despite unclear evidence that measuring and treating high bilirubin levels improves newborn outcomes, namely reducing risk of chronic bilirubin encephalopathy.[35] In addition to being more careful before advocating for poorly proven interventions, experts and medical societies might be well served to develop a mechanism to promptly revise recommended practices when more rigorous evidence emerges that undermines a recommendation. Guidelines tend to focus on practices that should be done; suggestions of practices to avoid in guidelines could be equally helpful.

The danger of disseminating a medical practice for which the benefit is largely unproven is that the net effect of the intervention may be detrimental. Each of the practices explored in the selected 10 overuse articles has the potential to harm children. As an example, exposing children diagnosed with skull fractures to repeated head CT imaging likely increases their risk for future malignancy.[36,37] Infants exposed to phototherapy as a result of hyperbilirubinemia thresholds that are too low may also have an increased risk of malignancy.[38,39] Pertinent to children who receive unnecessary antibiotic therapy for pneumonia are associations between antibiotic exposure and future chronic disease, including obesity,[40] asthma,[41] juvenile idiopathic arthritis,[42] and celiac disease.[43] Although HC screening may appear to have less direct medical harm, downstream implications include unnecessary follow-up testing and parental anxiety about neurocognitive status. Overused medical care is not just wasteful, it is potentially harmful.

Finally, this selection of overuse articles highlights the need to promote the publication of null findings and independent research that explores the potential harms of medical interventions. Compared with null findings, positive findings are much more likely to find their way to publication.[44] Similarly, the harms of medical practices are understudied, underreported, and misrepresented in comparison with the benefits.[45,46] Unfortunately, these discrepancies drive the adoption of practices that may later be found ineffective, harmful, and overused.

This article has limitations. The methods were adapted from a similar annual series targeting adult medical care.[12,13] Although these reviews are structured, the intent was not to perform a formal systematic review. Therefore, this article does not represent a comprehensive compilation of overdiagnosis, overtreatment, and overutilization research in pediatrics. Undoubtedly, arguments to include alternative, equally deserving publications could be made.

CONCLUSIONS

The importance of medical overuse research and facilitating the next generation of studies cannot be understated. Continuous reevaluation of existing practice is critical to ensuring children are benefitting from medical care.

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ABBREVIATIONS

CI: confidence interval
CRP: C-reactive protein
CT: computed tomography
ETT: exchange transfusion threshold
HC: head circumference
NCD: neurocognitive disorder
PCR: polymerase chain reaction
PICC: peripherally inserted central catheter

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