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Vaccines and Outpatient Antibiotic Stewardship

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Antibiotics pose a great public health irony. Their existence and use have made possible the treatment of previously untreatable infections. But simultaneously, rampant antibiotic overuse has promoted the development of antibiotic resistance and new untreatable, highly resistant infections. To address this growing threat, The National Action Plan for Combating Antibiotic-Resistant Bacteria established a goal to reduce inappropriate outpatient antibiotic use by 50% by 2020.¹ Antibiotic stewardship, the effort to measure and improve antibiotic use, is a central component to achieving this goal and aims to promote and facilitate judicious antibiotic use.

In addition to the problems of resistance, antibiotic overuse also poses other significant health threats including adverse drug events and *Clostridium difficile* infections, consequences that can also be mitigated by antibiotic stewardship. Additionally, young children and especially infants, who receive more antibiotics per capita than any other age group, are particularly vulnerable to other problems associated with antibiotic use due to disruption of the normal microbiome which may include increased risks for chronic diseases such as inflammatory bowel disease, allergy and asthma.² As a result, minimizing unnecessary early life antibiotic exposure is crucial to protect the health of children.

In the study by Kinlaw, et al., “Birth cohort effects on antibiotic prescribing during infancy”,³ the authors used Danish national antibiotic dispensing data matched with a birth registry to conduct surveillance for changes in antibiotic exposure during infancy among annual birth cohorts from 2004–2012. During this time, two pneumococcal conjugate vaccines (PCV7 in 2007 and PCV13 in 2010) were introduced along with national antibiotic prescribing guidelines in 2007. Overall the authors found that antibiotic prescribing to infants decreased, from 40.7% of infants born in 2004 receiving at least one antibiotic prescription in their first

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year of life to 34.6% of infants born in 2012 receiving at least one antibiotic. During the same time frame, Denmark had low levels of penicillin-resistance among *Streptococcus pneumoniae* (pneumococcal) isolates from invasive disease.⁴

This story is similar to what happened in the United States. In 2000, PCV7 was introduced, which was replaced by PCV13 in 2010,⁵ and several national treatment guidelines aimed at common pediatric infections were released during this time.⁶ While there is still need for improvement,⁷ rates of antibiotic prescribing to children in the United States have declined since the 1990s.^{8,9} PCV has directly led to decreases in the incidence of pneumococcal disease, both invasive and non-invasive including acute otitis media (the major driver of antibiotic use in children), and in penicillin-resistance among pneumococcus.^{5,10} PCV has also had significant indirect effects in preventing pneumococcal disease among unvaccinated persons.⁵ Decreasing inappropriate antibiotic use for young children may also be another indirect effect of PCV and other vaccines like *Haemophilus influenzae* b (Hib) vaccine, introduced decades earlier. The fear of serious infectious complications, like meningitis, leads clinicians to prescribe antibiotics inappropriately.¹¹ Widespread PCV and Hib vaccination have led to the near elimination of two of the most feared invasive bacterial infections in children, with substantial implications for the care of febrile infants and toddlers.¹² In the PCV and Hib vaccine era, observation, rather than antibiotic treatment, may be more likely to be perceived as the appropriate and safer management strategy for many febrile infants and toddlers as most of these children have viral etiologies of fever.

Vaccines, guidelines, and other factors likely synergized to lead to the reductions observed in antibiotic prescribing for children. Education of the public and clinicians and interventions targeted at clinicians to promote more judicious antibiotic prescribing are recommended stewardship interventions.¹³ There is growing evidence of greater awareness of the harms caused by antibiotic overuse, and parental demand for antibiotics for non-specific respiratory illnesses may be diminishing.¹⁴

The Danish and American experiences demonstrate that vaccines combat antibiotic resistance through the direct effect of preventing disease from antibiotic resistant pathogens and likely also through the “indirect” effect of changing the way pediatric clinicians practice medicine. Vaccines have long been hailed as one of the greatest public health achievements of the 20th century. Combined with other measures to reduce unnecessary antibiotic use, vaccines remain at the forefront of our tools for antibiotic stewardship and combating antibiotic resistance in the 21st century.

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