Original Contribution

Dynamics of Pneumococcal Transmission in Vaccine-Naïve Children and Their HIV-infected or HIV-uninfected Mothers During the First 2 Years of Life

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Pneumococcal vaccine-naïve mother-child dyads in South Africa had nasopharyngeal swabs taken 9 times within the first 2 years of the children’s lives between January 2007 and May 2009. To quantify the strength of the association of serotype-specific carriage in mother-child dyads, a stochastic transmission model was fitted to the data. Children were more susceptible to individual serotypes included in the 7-valent pneumococcal conjugate vaccine (PCV7) transmitted by their mothers than vice versa; however, children infected their mothers with these serotypes more frequently than mothers infected children. The child-to-mother steady-state forces of pneumococcal acquisition were between 0.36 and 3.29 (per 1,000 days) compared with 0.06–0.51 for mother-to-child transmission. Although children of mothers infected with human immunodeficiency virus were more often exposed to PCV7 serotypes by their mothers, their risk of acquisition remained low compared with the risk of child-to-mother transmission. Mothers acquired pneumococci at lower rates (per 1,000 days) from unmeasured exposure within families and in the wider community (range, 0.12–1.69 per 1,000 days) than did children (range, 1.10–5.21 per 1,000 days). Pneumococcal immunization of young children is expected to have an indirect effect of reducing PCV7 serotype maternal colonization and possibly disease even in settings such as ours, in which there is a high prevalence of human immunodeficiency virus–infected mothers.

Streptococcus pneumoniae (the pneumococcus) is a bacterial pathogen commonly associated with asymptomatic nasopharyngeal carriage, and it comprises at least 93 capsular serotypes. Some of these serotypes have the propensity to cause mucosal and invasive disease, usually within 2 months of new colonization in the nasopharynx (1, 2). Reducing the transmission of disease-causing serotypes has the potential for reducing disease due to these serotypes (3).

The spread of pneumococci is a complex process that is influenced by the genetic, physiological, and behavioral characteristics of the susceptible host and the strain diversity of the pathogen (4, 5). The inherently dynamic nature of this process presents significant challenges in understanding transmission patterns and the possible effect of vaccination on nasopharyngeal pneumococcal carriage. Therefore, evaluations of serotype-specific transmission characteristics and interaction patterns are critical to the design and implementation of effective intervention strategies. In particular, there is a need to quantify the contribution of specific groups or subpopulations to pneumococcal carriage and transmission.

Mathematical models are useful in understanding the population dynamics of infectious diseases and may help us...
understand the burden of the disease and inform control efforts. They are also necessary for extracting critical parameters from empirical data. Baseline estimates of pneumococcal transmission parameters, such as the rates of acquiring and clearing carriage, have been derived in previous studies among households in the United Kingdom (6–9), Finnish and Danish day care centers (10), Kenyan children (11), and Bangladeshi families (12, 13). Previous studies have shown that there is a positive association between pneumococcal colonization of mothers and their infants (14) and that mothers acquire colonization less frequently than do infants (6, 15).

There are, however, limited data on the dynamics of serotype-specific transmission from mothers to their children and vice versa, particularly in settings with a high prevalence of both human immunodeficiency virus (HIV) and pneumococcal carriage. Nunes et al. (16) reported a higher prevalence of vaccine serotype acquisition in HIV-infected mothers compared with HIV-uninfected mothers and a positive association of vaccine serotype carriage in mothers and their children. Consequently, there is a concern that HIV-infected adults may serve as a reservoir of pneumococcal colonization and may consequently diminish the impact of childhood immunization with pneumococcal conjugate vaccine.

In the present article, we present a new analysis of the dynamics of pneumococcal carriage in mother-child dyads in South Africa based on a statistical transmission model. We quantify the association of serotype-specific exposures in mothers and their children with the rates of pneumococcal acquisition. We also elucidate the association of maternal HIV-infection status with mother-child pneumococcal transmission dynamics and discuss the prospect of obtaining herd immunity in settings with a high prevalence of HIV in the adult population.

MATERIALS AND METHODS

Ethics statement

This study was approved by the Human Research Ethics Committee (HREC 050705) at the University of the Witwatersrand, South Africa. Signed informed consent was obtained from the mothers for themselves and on behalf of their children.

Experimental data

The data were derived from a longitudinal cohort of mother-child dyads, from whom pharyngeal swabs were taken to examine pneumococcal colonization, as previously described (16). Briefly, vaccine-naive mothers and their children who attended the well-baby immunization clinics in Soweto, South Africa, were asked to participate in the study with their infants. Mother-infant pairs were enrolled upon confirmation of the maternal HIV-infection status, which had been determined as part of the standard of care during pregnancy. The enrollment continued from January 2007 through May 2007, until 125 pairs were enrolled in the groups of both HIV-infected and HIV-uninfected mothers. The cohort included 126 children who were born to HIV-infected mothers but who tested negative for HIV using HIV-1 polymerase chain reaction testing (Roche Amplicor RNA polymerase chain reaction, version 1.5, Roche Molecular Systems, Inc., Branchburg, New Jersey) at study enrollment (HIV-exposed but uninfected; HEU) and 125 children born to mothers who were seronegative for HIV during pregnancy (HIV-unexposed and uninfected; HUU).

Mothers had 9 nasopharyngeal and oropharyngeal swabs and children had 9 nasopharyngeal swabs taken during visits scheduled when the children were 6–12, 9–18, 12–24, 15–30, 32–36, 38–42, and 44–52 weeks of age. The follow-up continued until May 2009. Swabs were cultured for pneumococci according to standard methods (17) and serotyped using the Quellung method (Statens Serum Institute, Copenhagen, Denmark) at the National Institute for Communicable Diseases, South Africa. Serotype 6C was distinguished from serotype 6A by polymerase chain reaction (18). Strains that did not react to the Quellung method were confirmed as being pneumococci by lytA polymerase chain reaction detection and categorized as nontypeable. Serotypes included in the 7-valent pneumococcal conjugate vaccine (4, 6B, 9V, 14, 18C, 19F, and 23F) were termed PCV7 serotypes. South Africa only introduced PCV7 into the national childhood immunization program in April 2009, with doses administered when children were 6 weeks, 14 weeks, and 9 months of age, with no catch-up for older children. The prevalence of pneumococcal carriage in the community/immediate contacts of the study participants was not known; however, a recent study from South Africa indicated prevalences before pneumococcal conjugate vaccine introduction of 83.0%, 80.2%, 60.0%, 22.8%, 10.7%, and 5.1% in persons 0–2, 3–5, 6–12, 13–18, 19–45, and older than 45 years of age, respectively (19).

Definitions

For each sampling point, previous maternal exposure to a specific serotype was defined as any isolation of that serotype from the child at the current or previous visits and vice versa. Because of the long interval between sampling times, we were unable to ascertain whether the mother or child had acquired the serotype first for serotypes identified concurrently at the same visit. Therefore, in the exploratory analysis, both the mother and child were regarded as having been exposed by each other in instances of concurrent colonization by the same serotype at the same visit. A new acquisition was defined as the first isolation of the serotype in the mother or child. In the analysis of pneumococcal acquisition and transmission, we only considered separately the most common serotypes in the data recovered from both mothers and children (19F, 23F, and 6B), as well as the combined serotypes (PCV7 serotypes and PCV7 plus the 6A (PCV7 + 6A) serotypes). These serotypes are referred to as the target serotypes, and for each analyzed set of target serotypes, the rest were defined as other serotypes.

Exploratory analysis

The $\chi^2$ test was used to compare the prevalences of pneumococcal carriage in HIV-infected and HEU children with those in HIV-uninfected mothers and HUU children. A generalized estimating equations model with an exchangeable correlation structure and the logit link function was used to explore the association of concurrent pneumococcal carriage in mothers and children. The ages of the mothers and children were
included in the model to adjust for possible confounding. As an exploratory analysis, serotype-specific risks of new acquisition were estimated in persons with previous exposure to pneumococci compared with those without exposure.

Transmission model

We constructed an epidemiologic model of pneumococcal transmission within mother-child dyads. This is a basic mechanistic population-dynamic susceptible-infected-susceptible type model with 3 compartments keeping track of the colonization state of each individual (Web Appendix 1 and Web Figure 1, available at http://aje.oxfordjournals.org/). Mothers and their children could carry either a specific target serotype or one of the other serotypes pooled together or they could be uncolonized and thus remained susceptible to colonization. The model assumed that there was no natural immunity to subsequent infection, as has been proposed by others (7, 12). The rate of pneumococcal acquisition in the child was conditioned on concurrent carriage in the mother and vice versa, separately for the target serotypes and the nontarget serotypes. The community rates of acquisition in the children and maternal participants represented unmeasured exposure within family and in the wider community. In the model, there was no need to define a priori who in the mother-child dyad began carrying a specific serotype first, and exposure was always concurrent and considered in continuous time.

The model was formalized using a transition matrix (Web Appendix 1 and Table 1). Because of the nonstandard likelihood for a large number of model parameters (Web Appendix 1 and Table 2), Bayesian inference was used to derive their posterior means and 95% credible intervals. We were interested in the transmission rates, so the clearance rates and competition parameters were fixed in the estimation scheme. Alternative values were used in a sensitivity analysis. Because the rates of mother-to-child and child-to-mother exposure depend on how often the mother or child is colonized, we derived the average rate at which the mother exposed the child and vice versa (i.e., the steady-state force of infection) by weighing the conditional transmission rates by the estimated steady-state prevalence of carriage in the mothers/children. For more details, see Web Appendix 2.

RESULTS

Pneumococcal prevalence in children and mothers

Overall, 1,851 and 1,846 samples were obtained to evaluate pneumococcal colonization in the children and women, respectively, including 1,843 samples that were undertaken concurrently in the mother-child dyads. Collectively, 74.1% (186 of 251) of the mother-child dyads had at least 7 visits. There were no differences between the HEU and HUU children in PCV7-serotype colonization (Table 1). Among children, pneumococcus was identified in 59.3% (1,097 of 1,851) of all swabs sampled over the 2-year period, including 575 (31.1%) PCV7 serotypes and 649 (35.1%) PCV7 + 6A serotypes (Table 1).

The overall prevalences of pneumococcal colonization were similar between HIV-infected women (18.2%) and HIV-uninfected women (19.3%; P = 0.53; Table 1). The overall prevalence of PCV7 serotypes was, however, 2-fold greater in HIV-infected women (8.1%) than in HIV-uninfected women (4.3%; P = 0.0008), as was the prevalence of PCV7 + 6A serotypes (8.8% vs. 4.9%; P = 0.0009). Because of differences in PCV7-serotype colonization between HIV-infected and HIV-uninfected mothers, pneumococcal acquisition was modelled separately for the HEU and HUU mother-child pairs for the pooled PCV7 serotype and PCV7 + 6A serotype analyses. Because of the small numbers of observations, the HEU and HUU groups were pooled in the analysis of individual serotypes to enhance statistical power.

Figure 1A and 1B present the distributions of pneumococcal serotypes among all colonized samples in children and women over the 2-year period, respectively. In children, 1,140 pneumococcal isolates were detected, and the most common serotypes were 19F (n = 170; 14.9%), 23F (n = 160; 14.0%), 6B (n = 123; 10.8%), 6A (n = 76; 6.7%), and 14 (n = 65; 5.7%), which collectively accounted for 52.1% of all isolates detected. Of the 533 pneumococcal isolates detected in women,

### Table 1. Overall Prevalence of Pneumococcal Colonization and the Impact of Maternal Human Immunodeficiency Virus Status on Colonization Over a 2-year Follow-up Period, South Africa, January 2007–May 2009*

<table>
<thead>
<tr>
<th>Serotype</th>
<th>Children</th>
<th></th>
<th>Mothers</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td>HEU</td>
<td>HUU</td>
<td>HIV-positive</td>
</tr>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>All pneumocci</td>
<td>1,097</td>
<td>59.3</td>
<td>561</td>
<td>56.7</td>
</tr>
<tr>
<td>PCV7 + 6A</td>
<td>649</td>
<td>35.1</td>
<td>355</td>
<td>35.9</td>
</tr>
<tr>
<td>PCV7</td>
<td>575</td>
<td>31.1</td>
<td>320</td>
<td>32.3</td>
</tr>
<tr>
<td>Noncolonized</td>
<td>754</td>
<td>40.7</td>
<td>429</td>
<td>43.3</td>
</tr>
</tbody>
</table>

Abbreviations: HEU, HIV-exposed but uninfected; HIV, human immunodeficiency virus; HUU, HIV-unexposed and uninfected; PCV7, serotypes included in the 7-valent pneumococcal conjugate vaccine; PCV7 + 6A, serotypes included in the 7-valent pneumococcal conjugate vaccine plus serotype 6A.

* P = 0.53; ** P = 0.0009; *** P = 0.0008.

*P-values represent comparisons of pneumococcal prevalence in HIV-positive versus HIV-negative mothers.

The most common serotypes were 19F (n = 36; 10.2%), 23F (n = 26; 7.4%), and 3 (n = 23; 6.5%). Carriage in both children and mothers increased over time (Figure 1C). In particular, the level of carriage in the mothers early after delivery was lower than carriage later on (i.e., several months after delivery). Mother-child dyads concurrently carried pneumococcus at 251 visits, and 55.4% (139 of 251) of the time, the serotype was the same. Considering the PCV7 + 6A serotypes, the rate of concordance was 78.7% (59 of 75).

**Exploratory analysis**

Table 2 summarizes the associations of concurrent pneumococcal colonization in the children and their mothers. The child’s
colonization with any pneumococcal serotype, PCV7 serotypes, or PCV7 + 6A serotypes was associated with increased odds of colonization with 1 of the respective serotypes by the mother (for any serotype, adjusted odds ratio (AOR) = 1.87, 95% confidence interval (95% CI): 1.43, 2.47; for PCV7 serotypes, AOR = 2.87, 95% CI: 1.91, 4.32; and for PCV7 + 6A serotypes, AOR = 2.53, 95% CI: 1.71, 3.74). Similarly, colonization of the mother by any pneumococcal serotype, PCV7 serotypes, or PCV7 + 6A serotypes was positively associated with colonization with these serotypes in the child (for any serotype, AOR = 1.68, 95% CI: 1.25, 2.25; for PCV7 serotypes, AOR = 2.28, 95% CI: 1.53, 3.41; and for PCV7 + 6A serotypes, AOR = 2.02, 95% CI: 1.37, 2.98).

Based on the 1,843 mother-child dyads with pneumococcal carriage data at all measured time points, the probabilities of acquiring a new serotype were compared between children who had been exposed to a specific serotype (19F, 23F, 6B, 6A, 14, or 19A) and children who had not been exposed to that serotype, and the same analysis was undertaken among the mothers (Table 3). New acquisitions were more frequent in the children and women if they were exposed to a particular serotype by the other member of the dyad than if they had not been exposed by that person. Specifically, serotype-specific exposure was associated with a 1.8-fold to 5.3-fold increase in the risk of acquisition among children, and the risk ratio was even higher in the mothers (3.3-fold to 9.9-fold increase). Nevertheless, women had a much lower baseline risk of colonization, and the serotype-specific rates of new acquisition were higher in children who were not exposed to pneumococcus by the mother as compared with mothers exposed to pneumococcus by the child.

**Mother-child and community transmission rates**

Mothers carrying one of the target serotypes (19F, 23F, 6B, PCV7, and PCV7 + 6A) had mother-to-child transmission rates that were higher than the reverse. The mother-to-child transmission rates varied between 10.7 and 20.0 per 1,000 days for individual serotypes, compared with child-to-mother rates that were between 6.9 and 13.6 per 1,000 days (Web Appendix 2 and Web Table 3). There was wide a posteriori uncertainty around the mother-to-child transmission rates.

Because the prevalence of carriage was much lower in mothers than in children, the steady-state forces of infection were derived by weighing the transmission rates with the steady-state probability of carriage to investigate whether mothers exposed their children more to pneumococcus than vice versa. Based on the estimated model parameters, the steady-state prevalence of PCV7-serotype colonization was 34.3% among the children (39.0% for PCV7 + 6A serotypes) and 7.2% among the mothers (8.0% for PCV7 + 6A serotypes) (Web Appendix 2 and Web Table 4). Table 4 shows the estimates of the steady-state forces of infection within the mother-child pair. Children exposed their mothers more often than mothers exposed their children: The child-to-mother steady-state forces of infection were between 0.36 and 2.70 per 1,000 days compared with mother-to-child forces of infection that were between 0.06 and 0.44 per 1,000 days.

The community steady-state forces of infection were generally higher than the within-pair rates (Table 4). The serotype-specific community forces of infection in children were between 1.10 and 5.10 per 1,000 days, whereas in mothers they were between 0.12 and 1.30 per 1,000 days. The community steady-state forces of infection in children were always greater than the steady-state forces of infection from carrying mothers, whereas the community forces of infection in women were much lower than the steady-state forces of infection from carrying children. These findings remained qualitatively the same (i.e., children still acquired infection more often from the community than from their mothers) in the sensitivity analysis in which we used alternative values of the fixed parameters (mean duration of carriage in children (Web Appendix 2 and Web Figures 2 and 3) and the competition parameters (Web Appendix 2 and Web Figures 4 and 5)).

**Impact of HIV on transmission rates of vaccine serotypes**

For the pooled serotypes, transmission rates were estimated separately for the HUU and HEU child-mother pairs. In both groups, the average child-to-mother forces of infection were again higher than the mother-to-child forces (Table 4). The average force of infection from HEU children to mothers for both the PCV7 and PCV7 + 6A serotypes was 3.2 per 1,000 days, and that for HUU children to mothers was 2.6 per
1,000 days. The average mother-to-child forces of infection were between 0.4 and 0.5 per 1,000 days in HEU children compared with 0.15 and 0.17 per 1,000 days in HUU children. Both HEU and HUU children acquired PCV7 serotype from the community at similar rates. The derived steady-state prevalence of PCV7-serotype colonization was 9.2% in HIV-infected mothers (10.0% for PCV7 + 6A) and 5.1% in HIV-uninfected mothers (5.7% for PCV7 + 6A) (Web Appendix 2 and Web Table 4).

**DISCUSSION**

In the present study, we analyzed longitudinal data on pneumococcal carriage in children and their mothers to study the impact of pneumococcal exposure on acquisition in mother-child pairs. The data set was derived from a setting with high prevalences of HIV infection and pneumococcal colonization. The data showed a positive association of concurrent or previous serotype-specific colonization in children and their mothers. A transmission model capturing the mother-child interactions was used to quantify the association of concurrent exposure with pneumococcal acquisition rates. The rate of pneumococcal acquisition in children from colonized mothers was larger than was the reverse. Children, however, had a higher prevalence of pneumococcal colonization and transmitted pneumococci more often to their mothers than vice versa.

We found that there was a positive association between pneumococcal colonization in mothers and their children, that is, that colonization in children was positively associated with carriage in mothers and vice versa. We also found that the serotype-specific risk of carriage in the child depended on previous or concurrent colonization of that serotype in the mother. The same result applied in the reverse direction from children to mothers, suggesting that both mothers and children have an important role in within-family transmission. Moreover, the effect of exposure was most likely on acquisition because of the temporal sequence of events in the analysis.

To gain more insight into the intensity and direction of transmission within mother-child pairs, we estimated serotype-specific transmission rates between the mothers and children. Mother-to-child transmission rates were always found to be greater than child-to-mother rates, suggesting a higher level of susceptibility in children and/or a higher level of infectiousness among mothers (6). The much lower prevalence of pneumococcal colonization in the mothers, however, means that the child-to-mother steady-state forces of infection were higher than the corresponding mother-to-child steady-state forces of infection. Lower rates of pneumococcal acquisition from the community were observed in mothers than in children.

<table>
<thead>
<tr>
<th>Serotype</th>
<th>New Acquisition Events in Children and Mothers*</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Children</td>
<td>Mothers</td>
</tr>
<tr>
<td></td>
<td>No. With Events</td>
<td>No. Without Events</td>
</tr>
<tr>
<td>19F</td>
<td>Yes</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>84</td>
</tr>
<tr>
<td>23F</td>
<td>Yes</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>66</td>
</tr>
<tr>
<td>6B</td>
<td>Yes</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>54</td>
</tr>
<tr>
<td>6A</td>
<td>Yes</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>48</td>
</tr>
<tr>
<td>14</td>
<td>Yes</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>46</td>
</tr>
<tr>
<td>19A</td>
<td>Yes</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>29</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; RR, relative risk.

*Numbers of new acquisition events for 6 serotypes (19F, 23F, 6B, 6A, 14, and 19A) in children and mothers, stratified by exposure to that serotype from the mother and child, respectively, during any of the previous visits. The table presents the relative risks in those exposed versus not exposed.
These results support the assertion that children transmit pneumococci more frequently to their mothers than vice versa and that mothers acquire pneumococci more frequently from their children than from the community. The observation that the maternal prevalence of pneumococcal carriage was initially (i.e., at first visits) low and increased as the children became older further supports the notion that young children were the main drivers of pneumococcal transmission to mothers.

Despite HIV-infected mothers transmitting pneumococci to their children more often than HIV-uninfected mothers, the risk of transmission to HEU children was still lower compared with the risk of children transmitting pneumococci to their mothers. There were no major differences between HEU and HUU children in acquiring PCV7 serotypes from the community, although the HEU children tended to transmit more PCV7 serotypes to their mothers. HIV-infected mothers were more susceptible to community acquisition of pneumococci than were HIV-uninfected mothers.

Our estimated pneumococcal acquisition rates (Web Appendix 2 and Web Table 3) are comparable to previous estimates derived in other settings with the same overall level of pneumococcal carriage among young children (6, 7). In children, the community acquisition rates were between 2 and 13 per 1,000 days whereas in studies in the United Kingdom, rates ranged from 8 to 16 per 1,000 days (6) and from 1 to 3 per 1,000 days (7). Mother-to-child acquisition rates in our study (10–20 per 1,000 days) were lower than those in Bangladeshi families (12, 13), in which they ranged from 21 to 37 per 1,000 days. The child-to-mother acquisition rates per 1,000 days in our study ranged from 6 to 16, which was also consistent with the rates observed in studies by Melegaro et al. (0–18 per 1,000 days (6) and 2–41 per 1,000 days (7)). Also, the steady proportion of children who were colonized by PCV7 serotypes (34.3%) was comparable to the observed prevalence (31.1%), whereas the predicted prevalence of pneumococcal colonization among mothers was 7.2% and the actual observed prevalence was 6.3%. Similar observations were evident for PCV7 + 6A serotypes in children and mothers.

Although both the exploratory and model-based analyses yielded concordant results, our study had some limitations, as all analyses were based on model assumptions on the underlying dynamics of infection. First, the lack of colonization data among the other family members means that part of transmission assigned as child-to-mother by the model may have been due to a third party, most likely a sibling carrying the same serotype as the youngest child. The estimated child-to-mother transmission rates then have a broader interpretation as within-family transmission to mothers. It is not as likely that the same applies to mother-to-child transmission rates because of the much lower susceptibility to colonization in mothers. The community rates in children may reflect transmission paths from the community via an older sibling. Second, we managed to evaluate serotype-specific parameters for only a few serotypes because of the sample size. Modeling transmission of pooled

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### Table 4. Estimates of Steady-State Forces of Infection From the Community and Within Mother-Child Pairs With 95% Credible Intervals Obtained From the Fitted Model Using Longitudinal Mother and Child Data, South Africa, January 2007–May 2009

<table>
<thead>
<tr>
<th>Strata and Change by Serotype</th>
<th>Steady-State Forces of Infection From the Communitya</th>
<th>Within-Pair Steady-State Forces of Infectiona</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean 95% CI</td>
<td>Mean 95% CI</td>
</tr>
<tr>
<td>Children</td>
<td></td>
<td>Parent-Child Probabilityb</td>
</tr>
<tr>
<td>19F</td>
<td>1.90 1.60,2.30</td>
<td>0.22 0.06,0.41</td>
</tr>
<tr>
<td>23F</td>
<td>1.40 1.10,1.70</td>
<td>0.12 0.002,0.31</td>
</tr>
<tr>
<td>6B</td>
<td>1.10 0.82,1.40</td>
<td>0.14 0.04,0.29</td>
</tr>
<tr>
<td>PCV7</td>
<td>4.70 4.10,5.20</td>
<td>1.10 0.66,1.70</td>
</tr>
<tr>
<td>HEU/HIV positive</td>
<td>4.93 4.19,5.62</td>
<td>1.47 0.83,2.27</td>
</tr>
<tr>
<td>HUU/HIV negative</td>
<td>4.65 3.91,5.32</td>
<td>0.50 0.03,1.25</td>
</tr>
<tr>
<td>Fold increasec</td>
<td>1.06 0.79,1.44</td>
<td>2.94 0.66,7.57</td>
</tr>
<tr>
<td>PCV7 + 6A</td>
<td>5.10 4.40,5.60</td>
<td>1.30 0.79,1.90</td>
</tr>
<tr>
<td>HEU/HIV positive</td>
<td>5.21 4.39,5.99</td>
<td>1.69 0.94,2.60</td>
</tr>
<tr>
<td>HUU/HIV negative</td>
<td>5.04 4.30,5.77</td>
<td>0.77 0.15,1.40</td>
</tr>
<tr>
<td>Fold increasec</td>
<td>1.03 0.76,1.39</td>
<td>2.35 0.67,17.3</td>
</tr>
</tbody>
</table>

Abbreviations: CI, credible interval; HEU, HIV-exposed but uninfected; HIV, human immunodeficiency virus; HUU, HIV-unexposed and uninfected; PCV7, serotypes included in the 7-valent pneumococcal conjugate vaccine; PCV7 + 6A, serotypes included in the 7-valent pneumococcal conjugate vaccine plus serotype 6A.

a The community and within-family forces of infection (per 1,000 days) are those pertaining to the steady-state prevalence of exposure (carriage) in mothers and children.

b Posterior probability that the force of infection in the child (or from the child to the mother) is greater than force of infection in the mother (or from the mother to the child).

c Compares the rates in HEU/HIV positive and HUU/HIV negative groups.
types (PCV7 and PCV7 + 6A) provided a partial remedy to this but might have led to biased estimates. However, the high concordance of concurrently carried serotypes by the child and its mother implies that the results based on pooled types could still be interpreted as vaccine type–specific transmission rates.

The clearance rates and between-serotype competition were taken to be the same for all serotypes and assigned previously published values (6, 7, 13, 14, 20). The main findings remained essentially the same under alternative values for these fixed parameters. Finally, our sampling methods were also not designed to detect colonization by multiple serotypes but rather only by the dominant serotype. Nevertheless, we identified an association between serotype-specific carriage among the mother-child dyads, suggesting that the dominant serotype was transmitted between the mother and child and in the families, despite the possibility of multiple serotype colonization.

In summary, these results indicate that in South Africa, the transmission dynamics of pneumococci appears to be similar to that in industrialized countries. Despite HIV-infected women being more likely to be colonized by PCV7 serotypes and being at increased risk of disease from these serotypes, they are still unlikely to be a significant source of transmission of PCV7 serotypes in the community, including to their children. Consequently, targeted vaccination of children using the pneumococcal conjugate vaccine is likely to induce an indirect effect even in settings with a high prevalence of adult HIV-infection positivity.

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