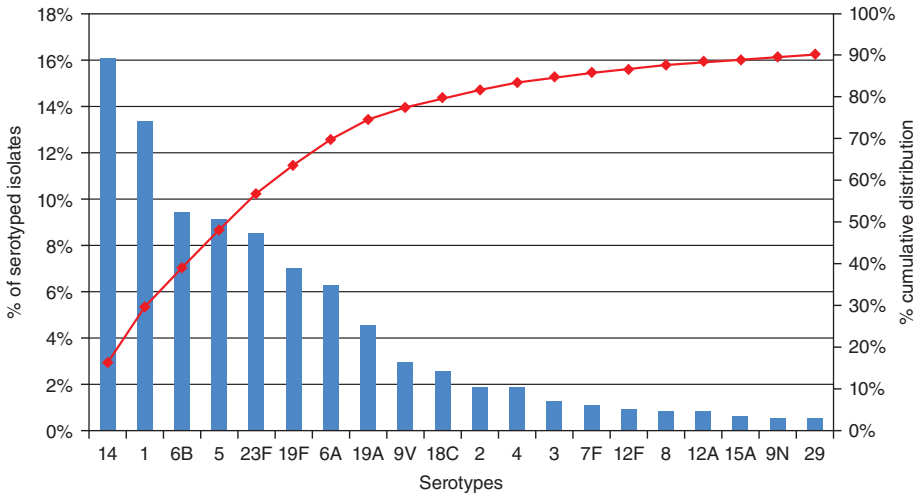

FIGURE 171-3 Meta-analysis of available global pneumococcal serotype data, adjusted for regional disease incidence. The red line shows cumulative incidence, as indicated on the right-hand Y axis. *(Source: Global Serotype Project Report for the Pneumococcal Advance Market Commitment Target Product Profile; available at http://www.gavi.org/library/gavi-documents/amc/tpp-codebook/.)*

seven serotypes may not all rank as the most common disease strains (Fig. 171-3). Some serotypes (e.g., types 1 and 5) not only tend to cause disease in areas with a high disease burden but also cause waves of disease in lower-burden areas (e.g., Europe) or outbreaks (e.g., in military barracks; meningitis in sub-Saharan Africa). The broader range of serotypes causing disease among adults than among children is apparent from a comparison of the coverage of existing multiserotype vaccines in different age groups. For example, data from the United States for 2006–2007 on the serotypes causing IPD indicated that a polysaccharide vaccine containing 23 serotypes (PPSV23) would cover 84% of cases among children <5 years of age and 76% of those among persons 18–64 years of age but only 65% of those among persons ≥65 years of age.

Nasopharyngeal Carriage Pneumococci are intermittent inhabitants of the healthy human nasopharynx and are transmitted by respiratory droplets. In children, pneumococcal nasopharyngeal ecology varies by geographic region, socioeconomic status, climate, degree of crowding, and particularly intensity of exposure to other children, with children in day-care settings having higher rates of colonization. In developed-world settings, children serve as the major vectors of pneumococcal transmission. By 1 year of age, ~50% of children have had at least one episode of pneumococcal colonization. Cross-sectional prevalence data show rates of pneumococcal carriage ranging from 20% to 50% among children <5 years of age and from 5% to 15% among young and middle-aged adults; Fig. 171-4 shows relevant data from the United Kingdom. Data on colonization rates among healthy elderly individuals are limited. In developing-world settings, pneumococcal acquisition occurs much earlier, sometimes within the first few days after birth, and nearly all infants have had at least one episode of colonization by 2 months of age. Cross-sectional studies show that up to the age of 5 years, 70–90% of children carry *S. pneumoniae* in the nasopharynx, and a significant proportion of adults (sometimes >40%) also are colonized. Their high rates of colonization make adults an important source of transmission and may affect community transmission dynamics.

Invasive Disease and Pneumonia IPD develops when *S. pneumoniae* invades the bloodstream and seeds other organs or directly reaches the cerebrospinal fluid (CSF) by local extension. Pneumonia may follow aspiration of pneumococci, although only 10–30% of such cases are associated with a positive blood culture (and thus contribute to the measured burden of IPD). The dramatic variation of IPD rates with age is illustrated by data from the United States for 1998–1999, a period prior to PCV introduction. Rates of IPD were highest among children <2 years of age and among adults ≥65 years of age (188 and 60 cases/100,000, respectively; Fig. 171-5). Since the introduction of PCV, IPD rates among infants and children in the United States have fallen by >75%, a decrease driven by the near elimination of vaccine-serotype IPD. A similar impact of PCV on vaccine-serotype IPD rates has been consistently observed in countries where PCV has been introduced into the routine pediatric vaccination schedule. However, changes in the non-vaccine-serotype IPD rate in various countries have been heterogeneous; the interpretation of this heterogeneity is a complex issue. In the United States, Canada, and Australia, rates of non-vaccine-serotype IPD have increased but the magnitude of the increase is generally small relative to the substantial reductions in vaccine-serotype IPD. In contrast, in other settings (e.g., Alaska Native communities and the United Kingdom), the reduction in vaccine-serotype IPD has been offset by notable increases in rates of disease caused by non-vaccine serotypes. Explanations for the heterogeneity of findings include replacement disease resulting from vaccine pressure, changes in clinical case investigation, secular trends unrelated to PCV use, antibiotic pressure selecting for resistant organisms, changes in surveillance or reporting systems, rapidity of introduction, and inclusion of a catch-up campaign. A recent systematic review concludes that serotype replacement in IPD follows the use of PCV7 but that the magnitude of this phenomenon is small relative to the reduction in disease from vaccine serotypes. The net effect of PCV is to reduce the rate of pneumococcal disease both in the age group targeted for vaccination and in unvaccinated age groups.

Pneumonia is the most common of the serious pneumococcal disease syndromes and poses special challenges from a clinical and public health perspective. Most cases of pneumococcal pneumonia are not associated with bacteremia, and in these cases a definitive etiologic diagnosis is difficult. As a result, estimates of disease burden focus primarily on IPD rates and fail to include the major portion of the burden of serious pneumococcal disease. Among children, PCV trials designed to collect efficacy data on syndrome-based outcomes (e.g., radiographically confirmed pneumonia, clinically diagnosed pneumonia) have revealed the burden of culture-negative pneumococcal pneumonia.

The case-fatality ratios (CFRs) for pneumococcal pneumonia and IPD vary by age, underlying medical condition, and access to care. In addition, the CFR for pneumococcal pneumonia varies with the

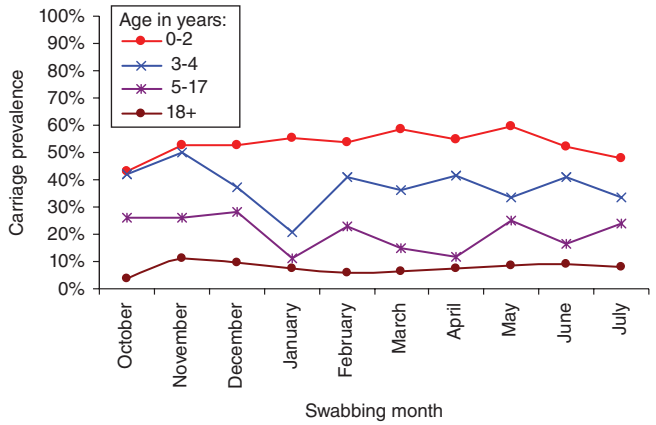

FIGURE 171-4 Prevalence of pneumococcal carriage in adults and children resident in the United Kingdom who had nasopharyngeal swabs collected monthly for 10 months (no seasonal trend; *t* test trend, >.05). *(Data adapted from D Goldblatt et al: J Infect Dis 192:387, 2005.)*