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Core pertussis transmission groups in England and Wales: A tale of two eras

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ABSTRACT

The recent resurgence of pertussis in England and Wales has been marked by infant deaths and rising cases in teens and adults. To understand which age cohorts are most responsible for these trends, we employed three separate statistical methods to analyze high-resolution pertussis reports from 1982 to 2012. The fine-grained nature of the time-series allowed us to describe the changes in age-specific incidence and contrast the transmission dynamics in the 1980s and during the resurgence era. Our results identified infants and school children younger than 10 years of age as a core group, prior to 2002: pertussis incidence in these populations was predictive of incidence in other age groups. After 2002, no core groups were identifiable. This conclusion is independent of methodology used. Because it is unlikely that the underlying contact patterns substantially changed over the study period, changes in predictability likely result from the introduction of more stringent diagnostics tests that may have inadvertently played a role in masking the relative contributions of core transmission groups.

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1. Introduction

Pertussis (whooping cough) is an extremely contagious vaccine-preventable respiratory disease [1–4]. In England and Wales, following the introduction of routine immunization in the 1950s, pertussis incidence decreased dramatically [5–7] and although not eradicated, steadily faded from the public consciousness [2,7]. However, a national pertussis outbreak was announced in April 2012, despite high vaccine coverage [4,8–11], characterized not only by increased incidence but also a spate of pertussis-related infant deaths [8,10,12].

An interesting feature of this resurgence has been the notable shift in the age-distribution of cases: what had historically been regarded as primarily a childhood disease, is now encompassing all age groups, with increasing incidence trends in adolescents and adults [2,4,11,13,14]. These events have reignited a debate regarding changes in those key age groups that may contribute disproportionately to transmission, with teenagers proposed as the

new “drivers” of recent epidemics [11,15–18]. The concern over the transmission contribution of teenagers was, in part, responsible for the roll out of the Tdap booster vaccine in the US and other countries [10,18,19].

A greater contribution to transmission by core groups, perhaps due to higher contact rates or lower immunity, may consequently translate into their over-representation in incidence reports as an epidemic takes off. Thus, identifying potential sentinel age cohorts that may be driving transmission could be central for a re-evaluation of control strategies. Hence, we attempted to harness this information from age-stratified incidence reports in order to quantify the relative transmission contribution of different age cohorts [20]. We analyzed pertussis case reports in England and Wales, collected through the Notifications of Infectious Diseases (NOIDs), for the period 1982–2012, during which a pre-school booster was introduced (late 2001) and the whole cell vaccine was replaced by an acellular vaccine (2004) [7]. We submit that systematic shifts in the transmission network of pertussis would translate into detectable changes in the age-stratified patterns of its incidence through time. In this regard, NOIDs data by virtue of their longitudinal span across changes in vaccine type used may be especially informative.

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We applied three independent statistical techniques, each aimed at identifying potential core groups driving outbreaks. These methods were: (I) Correlation analysis – which quantifies linear associations between reported incidence in different age groups [21]; (II) Transfer entropy – developed in the field of information theory [22], provides a measure of predictability in the incidence of each age group, given information regarding the kinetics of other age classes; and (III) Relative risk analysis – which calculates the ratio of the probability of an event occurring in one group to the probability of it occurring in another group [20,23].

Using all three methods, we contrast potential changes in age-specific drivers of pertussis transmission by exploring incidence records before and after the introduction of the acellular vaccine booster in October 2001, and the introduction of serological and PCR diagnostic methods in late 2001. This highly resolved, long-term epidemiological dataset allows us to determine transitions and patterns, that otherwise might have been overlooked. Key groups may vary in time due to many factors; from behavior changes that impact actual transmission patterns, to changes in reporting fidelity and statistical artifacts.

2. Methods

2.1. Data sets

We used the Notifications of Infectious Diseases (NOIDs), collected by Public Health England (PHE) – weekly incidence data stratified by age (in months if under 1 year old, in years otherwise) reported in England and Wales from 1982 to 2012. The weekly cases in each age group are plotted in Fig. 1, along with the total cases by week, and the mean cases in each age group and estimated vaccine coverage (available from Public Health England

[11]). During the time period (1982–2012) of our study, two vaccines were in use for routine immunization: the whole cell vaccine (1982–2004) and the acellular vaccine (2004 onwards) [7]. An accelerated primary schedule was introduced in England and Wales in June 1990, shifting from a 3, 5, 11 month schedule to a 2, 3, 4 month schedule [7]. In 2001, a pre-school booster was introduced for children between 3½ and 5 years of age [7].

An enhanced surveillance scheme for pertussis infection (based on laboratory-confirmed cases with epidemiological follow-up) was established in 1994. Since 2001, serology and PCR have been used routinely to diagnose pertussis, especially in adults and adolescents [7,34]. Prior to this date, cases were conventionally confirmed by culture only, a method not as sensitive as the newer ones, but more specific [34].

2.1.1. Wavelet analysis

In order to investigate the periodicity of pertussis epidemics over this period, we used wavelet analysis [24,25] to decompose time series and to detect the dominant frequencies through time. Wavelets are especially powerful when time series data are inherently non-stationary [26–28]. For this analysis, we used the Morlet wavelet of log-transformed total weekly cases. Further details provided in the [supplementary material](#).

2.2. Statistical analysis

We used three independent statistical approaches, each subject to assumptions and limitations (for details refer to [21,22,29]). The purpose of these methods was to identify the existence of key age groups driving outbreak waves, as well as, how incidence in specific age groups may provide information regarding changes in other age groups.

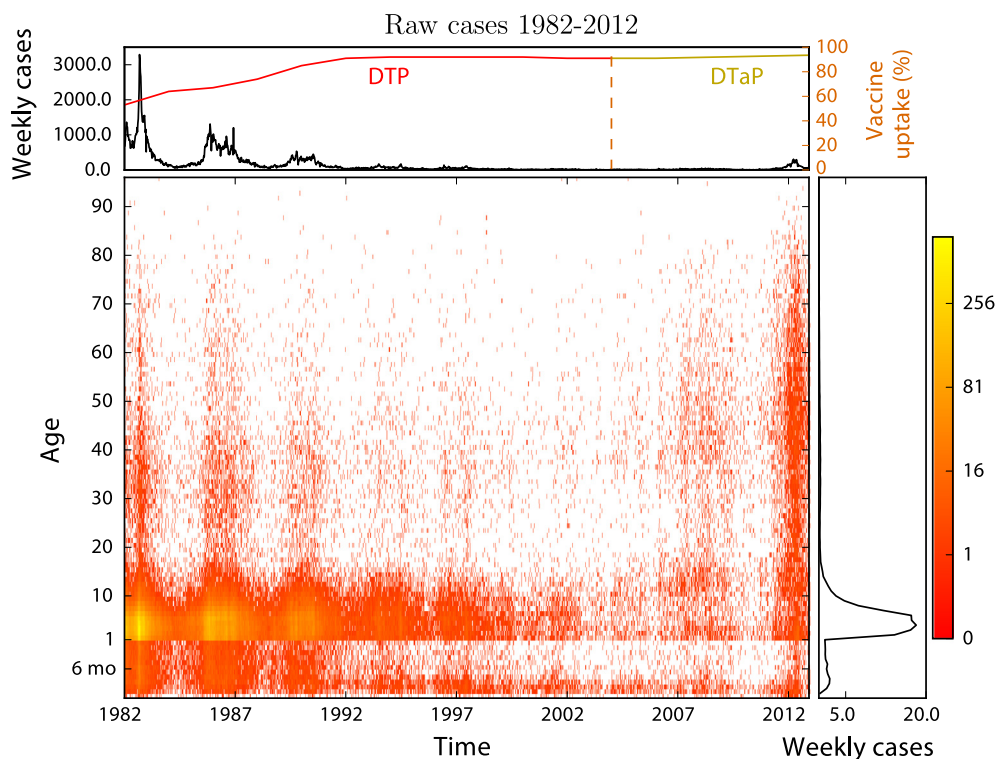


Fig. 1. Weekly cases of pertussis by age in England and Wales. The total cases each week and vaccine coverage for both DTP and DTaP are plotted in the top panel. The heat map in the bottom left panel depicts the cases reported each week and age group, with white indicating zeros, and the colors from red to yellow with increasing cases. The mean weekly cases in each age group are plotted in the bottom right panel. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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