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Counterfactual Estimates of Pneumococcal Disease Incidence in England after Vaccine Introduction

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INTRODUCTION

Streptococcus pneumoniae is a leading cause of serious bacterial infections worldwide, including pneumonia, meningitis, and sepsis, especially in young children. The World Health Organization estimates that it is responsible for approximately 5% of global infant deaths [1]. Pneumococcal conjugate vaccines (PCVs) have been developed to protect against the most clinically relevant serotypes and introduced into infant immunization programs across multiple countries. PCV7, targeting seven serotypes, was followed by PCV13, extending protection to thirteen. These vaccines have substantially reduced vaccine-type invasive pneumococcal disease (VT-IPD). Nevertheless, over 80 additional serotypes remain uncovered [2; 3]. In recent years, several settings have reported increases in non-vaccine-type (NVT) IPD, suggesting possible serotype replacement. In England, this phenomenon has been particularly marked, raising concerns about whether the population-level benefits of PCVs might be offset. However, interpreting post-vaccination trends in IPD is challenging. Observed changes in disease incidence may reflect not only biological responses to vaccination but also coincident changes in surveillance systems, healthcare-seeking behaviour, diagnostic practices, or case definitions. Traditional before–after comparisons may misattribute such secular trends to vaccine effects, especially in ecological designs where randomized controls are absent.

OBJECTIVES

We aim to estimate the causal impact of PCV7 and PCV13 introduction on IPD incidence in England, focusing on both direct reductions in VT-IPD and potential increases in NVT-IPD. A key goal is to disentangle true serotype replacement from surveillance-driven artifacts by constructing a data-driven counterfactual using unaffected pathogens as controls.

METHODS

We analysed monthly national IPD surveillance data in England from 2000 to 2018, covering the introduction of PCV7 in 2006 and PCV13 in 2010. To estimate the impact of vaccination, we employed a Bayesian structural time series (BSTS) model [4], a causal inference framework designed for population-level interventions without randomized control groups. The model accounts for seasonality, underlying trends, and time-varying confounders. To adjust for secular changes unrelated to PCVs, we used time series of other bacterial infections (H. influenzae, E. coli, S. aureus, P. aeruginosa, and others) as control outcomes. These pathogens share similar diagnostic pathways and reporting mechanisms but are unaffected by pneumococcal vaccination. The model included a spike-and-slab prior for Bayesian variable selection, allowing only those control series with high predictive value in the pre-intervention period to inform post-intervention counterfactuals. This synthetic control design improves robustness over simple before–after approaches and helps isolate vaccine effects from unrelated system-level changes.

RESULTS

We estimate a 60% overall reduction in IPD incidence following the introduction of PCV7 and PCV13, comparing the pre-vaccine (2000–2006) and post-PCV13 (2011–2018) periods. The greatest reductions occurred among children under five (−73%). Specifically, PCV7-type IPD fell by 92% across age groups, and PCV13-type IPD declined by 42% following its introduction in 2010. These effects were consistent across subpopulations and robust to alternative model specifications. In contrast, NVT-IPD incidence increased by 36.5% after PCV7 and by 31.8% after PCV13 in raw surveillance data. However, when adjusted for confounding trends using control pathogens, the estimated increase in NVT-IPD was attenuated to +16% overall, with wide credible intervals

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and non-significant effects in most age groups. This suggests that previous unadjusted analyses may have overestimated the magnitude of serotype replacement by not accounting for coincident improvements in detection and reporting.

CONCLUSIONS

Our findings demonstrate that PCVs have had a substantial and sustained public health impact, dramatically reducing IPD caused by vaccine-covered serotypes. While serotype replacement is evident, much of the apparent increase in NVT-IPD can be explained by concurrent changes in surveillance and diagnostic practices rather than biological displacement alone. By leveraging control pathogens and a Bayesian synthetic control approach, we provide more credible causal estimates than conventional time series analyses. These results are important for public health planning and support continued investment in pneumococcal immunization, particularly as higher-valency PCVs are developed. Future evaluations of vaccine impact should incorporate similar causal modelling strategies to avoid misinterpretation of surveillance-based trends.

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