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EXPLORING THE CLINICAL ASPECTS OF VACCINE-PREVENTABLE INVASIVE AND NON-INVASIVE BACTERIAL DISEASE WITHIN EUROPE

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Bacterial infections remain the most common cause of mortality and morbidity in children worldwide. Implementation of vaccination programmes has decreased the incidence of bacterial disease caused by *Haemophilus influenzae* type b¹ and group C meningococci;² however, invasive disease and mucosal respiratory tract infections due to Gram-positive bacteria, primarily *Streptococcus pneumoniae*, remain prevalent.³ Pneumonia remains a leading cause of morbidity and mortality in Europe, causing an estimated 300,000 hospitalisations and 31,500 child deaths annually.⁴

S. pneumoniae causes invasive pneumococcal disease (IPD), characterised by bacteraemia, septicaemia and bacterial meningitis. The consequences can be severe, resulting in hospitalisation, complications and death. Whilst non-invasive diseases are generally less severe than IPD, their higher incidence poses a significant healthcare and social burden, including promotion of antibiotic resistance.⁵ The introduction of pneumococcal conjugate vaccines has led to important decreases in the incidence of IPD,⁶ and to a lesser extent on pneumonia hospitalisations⁷ and on acute otitis media (AOM) visits.⁸

Although non-typeable *H. influenzae* (NTHi) has been increasingly recognised as a pathogen in invasive diseases,⁹ it is also a causative agent of mucosal disease, predominantly in association with *S. pneumoniae*. The role of NTHi is well established in AOM,¹⁰ still controversial in lobar pneumonia, and increasingly implicated in chronic bronchial inflammation in young children with persistent wheezing.¹¹

In Europe, the spectrum of invasive and non-invasive disease that could be prevented by vaccination remains significant, with potential immediate effects on morbidity and mortality, and long-term impact on indirect disease burden.

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SYNFLORIX™: WHAT HAVE WE LEARNED FROM IMMUNOGENICITY STUDIES?

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Synflorix™ (10-valent pneumococcal conjugate vaccine; GlaxoSmithKline Biologicals, Belgium) has been investigated globally to evaluate immunogenicity, safety and reactogenicity with different vaccination schedules and routine co-administered vaccines.¹ As expected, population variability in immune responses following priming was observed between continents.^{2,3} In European studies, Synflorix™ was proven to be immunogenic post-primary and post-booster vaccination in terms of

-amount of antibody (ELISA) for the 10 serotypes and protein D (carrier for 8/10 serotypes) and

-functional antibodies (opsonophagocytic activity; OPA) for the 10 serotypes.¹ Furthermore, Synflorix™ induced similar immunological memory following the licensed 3+1 schedule or the investigational 2+1 schedule in Europe, with robust immune responses after a challenge dose 2 years post-booster.⁴

Although not indicated for non-vaccine-serotypes, in clinical trials, Synflorix™ has induced cross-reactive immune responses (ELISA and OPA) and immunological memory against serotypes 6A and 19A post-primary⁴ and post-booster vaccination.⁵ An 11-valent prototype vaccine included serotype 3; however, no efficacy or immune memory was observed⁶ and it was removed from the final formulation.¹ Synflorix™ decreased nasopharyngeal carriage of vaccine-serotypes in the second year of life by 23-35%.⁷ Whilst a trend towards increased carriage of non-vaccine-serotypes was observed,⁷