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## Health Policy

journal homepage: www.elsevier.com/locate/healthpol



### Effectiveness and cost-effectiveness of different immunization strategies against whooping cough to reduce child morbidity and mortality



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#### ARTICLE INFO

Article history: Received 3 July 2013 Received in revised form 30 October 2013 Accepted 19 December 2013

Keywords: Adolescent Adult Diphtheria-tetanus-pertussis vaccine Health personnel Immunization Whooping cough

#### ABSTRACT

*Introduction:* In the last years there has been a significant increase in reported cases of pertussis in developed countries, in spite of high rates of childhood immunization. Health institutions have recommended different vaccination strategies to reduce child morbidity and mortality: vaccination of adolescents and adults, pregnant women, people in contact with the newborn (cocoon strategy) and health care workers. The aim of this paper is to review the scientific evidence supporting these recommendations.

*Methods:* Systematic review on the effectiveness and cost-effectiveness of the above strategies for the reduction of morbidity and mortality from pertussis in infants under 12 months. The electronic databases Medline, PreMedline, Embase, CRD, Cochrane Central, and Trip Database were consulted from 1990 to October 2012. The evidence was assessed using the GRADE system.

*Results:* There were eight studies on the efficacy or safety of the strategies analyzed, and 18 economic evaluations. Direct evidence on the efficacy of these strategies is scarce. Economic evaluations suggest that vaccination of adolescents and adults would be cost-effective, although there is major uncertainty over the parameters used.

*Conclusions:* From the perspective of health technology assessment, there is insufficient evidence to recommend the vaccination strategies evaluated.

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#### 1. Introduction

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<sup>0168-8510/\$ –</sup> see front matter © 2013 Elsevier Ireland Ltd. All rights reserved. http://dx.doi.org/10.1016/j.healthpol.2013.12.007

adults may present a mild form of the disease with persistent cough, but neonates and small children may suffer from potentially fatal forms, which often require hospitalization. Whooping cough is highly contagious; teenagers and adults are the main source of infection for neonates and children [1–4].

In spite of the high rate of immunization coverage attained in developed countries whooping cough remains a public health problem; its incidence had increased in the 1990s [5,6]. In 2010, an average rate of declared cases in Europe of 3.7/100,000 inhabitants, with a broad variation between countries, was observed [7]. In Spain several peak incidences have been verified; the rate of 2/100,000 was exceeded in 1997 and 2000 [8], whilst from 2010 to 2011 declared cases multiplied threefold, from 1.94 to 6.73/100,000 [9].

Several factors could account for this epidemiologic situation: the identification of a genetic variant in the bacteria that would cause a response rate different from marketed vaccines [10], the lower immunogenetic capacity of acellular vaccines (tetanus–diphtheria–acellular pertussis, Tdap) marketed for approximately 10 years because of its lower reactogenicity against the full cell vaccine [11], or a weakening in natural immunity and that caused by the vaccine over time [12–14].

In light of this epidemiologic situation, during the last decade different health institutions such as the Centers for Disease Control and Prevention (CDC), of the USA, the Joint Committee on Vaccination and Immunization of the United Kingdom, or the European Center for Disease Prevention and Control, have recommended universal immunization of teenagers and adults or alternatively, specific risk groups: pregnant women, post-delivery immunization and people in contact with the infant (cocoon strategy), or health personnel [15-20]. However, in its latest report on immunization against whooping cough (2010), the World Health Organization (WHO) considered that there was no evidence to recommend these strategies. The WHO only recommended immunization of health personnel in those countries with demonstrated nosocomial transmission and warned that this strategy would only be cost-effective in case of attaining high rates of coverage [21].

In Spain, the Advisory Committee for Vaccines of the Spanish Pediatrics Association has recommended, in addition to the five doses set out currently (2, 4, 6, 18 months and 4–6 years), a sixth dose of Tdap during adolescence [22].

The aim of this paper is to review the scientific literature on the efficacy, safety and cost-effectiveness of different immunization strategies against whooping cough to reduce child morbidity and mortality. This work was developed to inform health policy decision making by the Spanish Ministry of Health.

#### 2. Materials and methods

A systematic literature review on the following electronic databases: Medline, PreMedline, Embase, CRD, Cochrane Central, and Trip Database was performed from 1990 to October 2012, using the keywords whooping cough, pertussis, vaccine, immunization, pregnant, adolescent, adult,

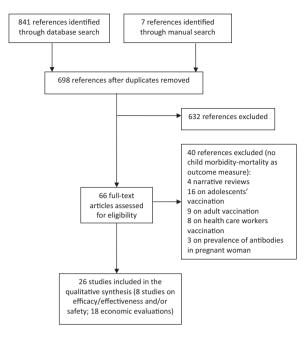


Fig. 1. Flow chart of the bibliographic search.

cocooning, health care providers and health care workers. A manual search from the papers' references included was also performed. Randomized controlled trials (RCT), observational studies (OS) or economic evaluations (EE) in which the Tdap vaccine was administered to teenagers, adults, pregnant women, family members/carers of the child or health personnel was also performed. Outcomes were the rates of incidence of the disease, number of cases of hospitalization, complications or death in infants under 12 months.

The risk of bias in the studies was assessed with the criteria of the Scottish Intercollegiate Guidelines Network (SIGN) [23], and the Cochrane Effective Practice and Organization of Care Review Group (EPOC) [24] for the designs of interrupted time series. The quality of the evidence was assessed by means of the GRADE system [25,26], which initially gives four points to the RCT and two to the OS. Subsequently, this score can be reduced according to the methodologic limitations of the studies included, the use of indirect results outcomes, the inconsistency and imprecision of the estimates or presence of publication bias. It can also be increased in case of observing intense effects, a dose-response gradient, or using a design that enables control of possible confounding factors. The evidence was assessed independently by two reviewers and discrepancies were resolved by means of a third party's opinion. The quality of EE was evaluated by means of the instrument proposed by López-Bastida et al. [27].

#### 3. Results

Of a total of 698 references identified without duplicates (including 7 articles identified by manual search), 66 were selected by title and abstract for a full text review (Fig. 1). Finally, 26 studies were included: eight on efficacy Download English Version:

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