

# Immunisation against respiratory diseases

## Introduction



### Key points

- Although pertussis vaccination coverage is high across Europe, vaccination rates for influenza, pneumococcal disease and tuberculosis vary wildly.
- Vaccinating groups other than the most vulnerable can have a protective 'herd effect' on society as a whole by reducing disease transmission within the population.
- New vaccines against *Streptococcus pneumoniae* offer the possibility of striking reductions in invasive disease.
- The only available vaccine against tuberculosis dates to the early 20th century. Although it is generally safe, its efficacy is limited and it does not provide complete protection.

Population protection by vaccination against infections has been one of the major achievements of public health and is of considerable importance in controlling respiratory disease. This chapter will discuss vaccines for the prevention of seasonal and pandemic influenza, pertussis, pneumococcal infection and tuberculosis (TB).

## Influenza

After the second world war, vaccination became the main strategy for preventing and controlling seasonal and pandemic influenza worldwide. European Respiratory Society (ERS) and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines define influenza as an acute illness, usually with fever, with one or more of the following: headache, myalgia (muscle pain), cough or sore throat. Influenza is caused by influenza viruses. While most illnesses are brief and without consequence, regular seasonal epidemics of influenza include significant rates of severe illness and death, particularly among elderly people and those with underlying chronic medical conditions. Type A virus causes the most severe disease and is associated with epidemics and pandemics. Spontaneous mutations in the viral surface proteins, haemagglutinin and neuraminidase, are responsible for so-called 'antigenic drift'. If this results in changes in the viral

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amino acid structure, pre-existing antibodies might be unable to bind to viral particles to a sufficient extent to prevent disease. This phenomenon is responsible for the annual influenza waves observed worldwide.

Avian influenza infections are much more severe than the common seasonal influenza, and are associated with severe illness and a mortality rate exceeding 50%. Occasionally, a new strain develops to which many humans have little or no immunity and a worldwide pandemic occurs, as was seen in 2009. This pandemic, caused by the influenza A (H1N1) virus, spread in two waves, a modest spring/summer wave and a more sustained wave in the autumn and early winter with moderate intensity. Almost all influenza cases in 2009 were caused by the pandemic virus. Surveillance of hospitalised acute respiratory cases was implemented in various forms by 10 European Union (EU) countries during the pandemic, with 9469 laboratory-confirmed cases reported and 569 deaths. Severe disease was more frequent, and the death rate was higher in individuals under 65 years of age and in those with underlying disease, even though in 25% of the severe cases there were no underlying conditions.

Seasonal influenza vaccine has proved effective in preventing laboratory-confirmed influenza among healthy adults (16–65 years of age) and children (6 years of age or older). The evidence of vaccine effectiveness is much more limited in relation to the prevention of complications such as pneumonia, hospitalisation and influenza-specific and overall mortality. However, vaccinating children might have a protective effect for nonrecipients of the vaccine of all ages living in the same community as it prevents transmission. Scientific evidence suggests there would be advantages to vaccinating older people and those with chronic disease.

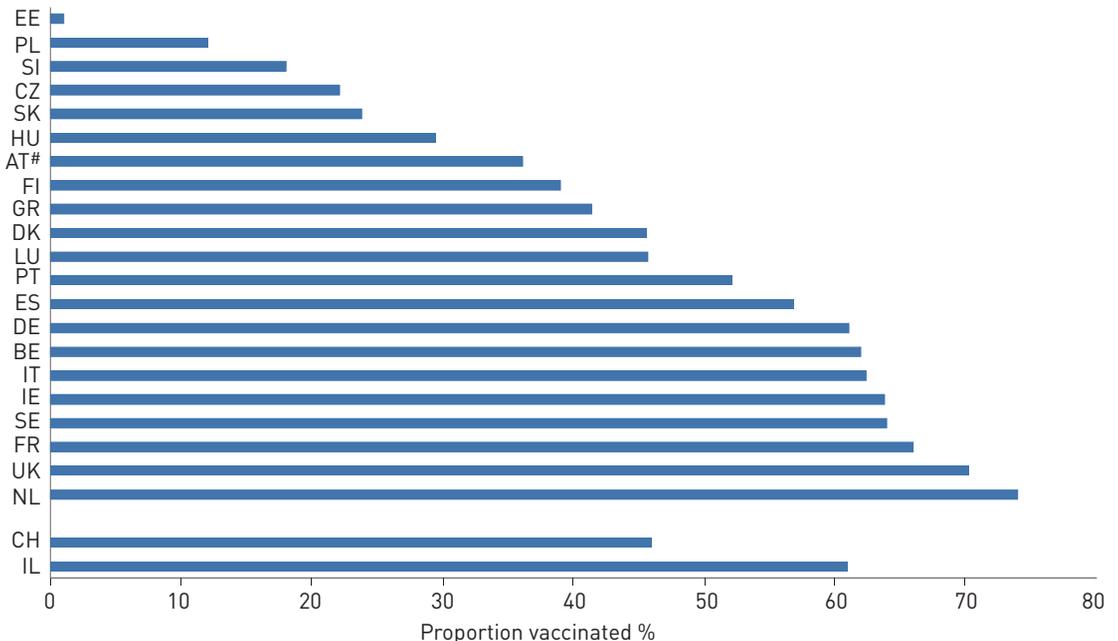
The ERS/ESCMID guidelines recommend that influenza vaccine should be given yearly to people at increased risk of complications due to influenza. Vaccination should be given to immunocompetent adults belonging to one or more of the following categories: over 65 years of age; resident in an institution (such as a nursing home); chronic cardiac disease; chronic lung disease; diabetes mellitus; chronic renal disease; haemoglobinopathies; and women who will be in the second or third trimester of pregnancy during the influenza season. In addition, the guidelines suggest yearly vaccination for healthcare personnel, especially in settings where elderly people or other high-risk groups are treated. Figure 1 shows the influenza

vaccination rates in Europe in people over 65 years of age in the 2008–2009 influenza seasons.

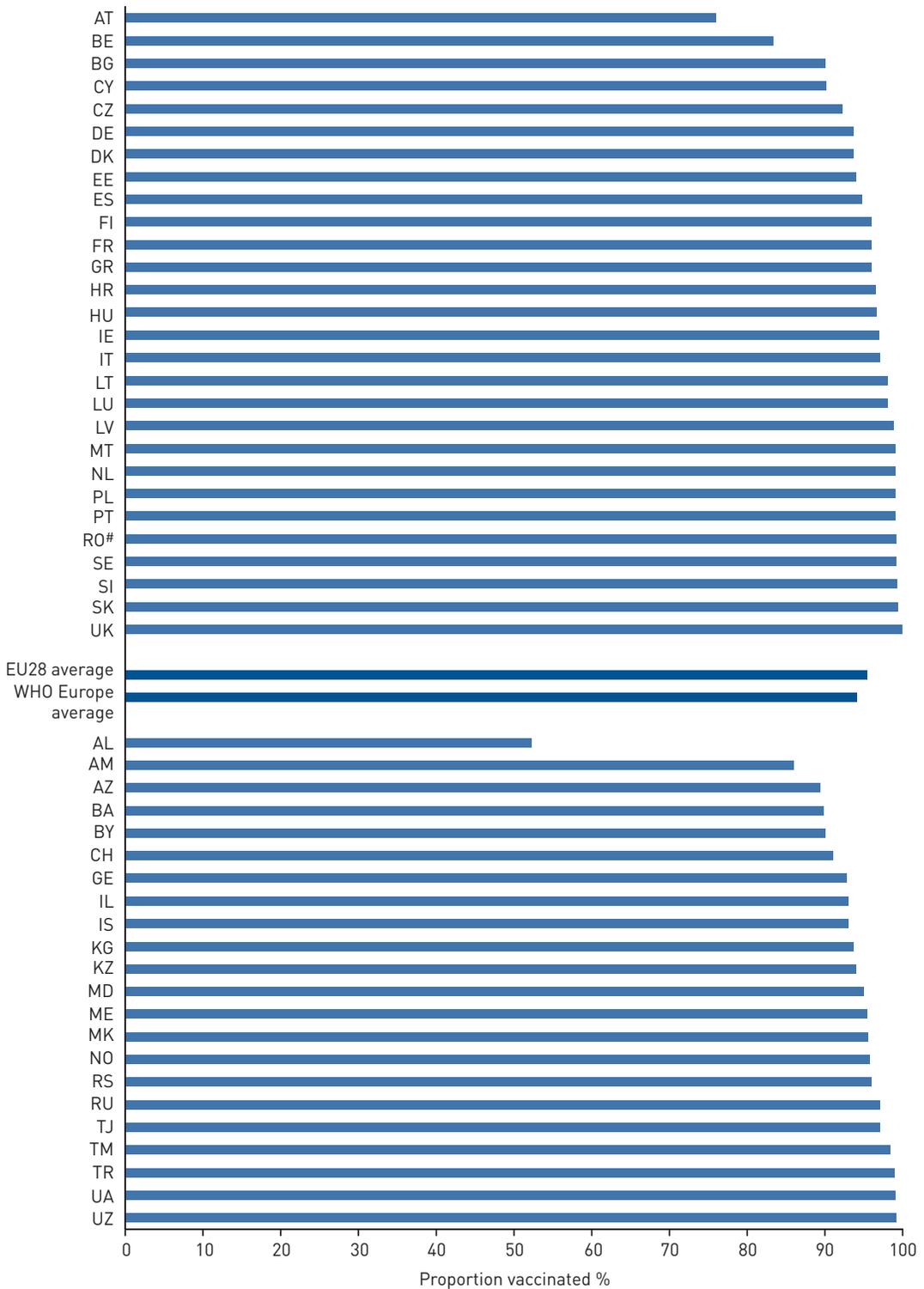
## Pertussis

*Bordetella pertussis* infection, known as pertussis or whooping cough, is one of the leading causes of vaccine-preventable deaths. Worldwide, an estimated 50 million cases of pertussis and 300 000 deaths occur every year, mainly in unvaccinated children younger than 12 months of age. *B. pertussis* infection in adults and adolescents usually causes mild or atypical symptoms. Pertussis should be considered in the differential diagnosis of illnesses with cough lasting more than 1–2 weeks. Pertussis may also cause infection in adults with comorbid conditions such as chronic obstructive pulmonary disease (COPD), and it is one of the less common causes of exacerbations of COPD. Pertussis shows a slight seasonality, with a usually modest increase in cases in the summer and autumn. The percentage of infants reaching their first birthday fully vaccinated against pertussis is shown in figure 2. Vaccination coverage is high throughout the EU28 countries.

Pertussis vaccination schedules vary between European countries, as do the indications for booster vaccination in



**Figure 1** – Influenza vaccinations: proportion of people aged >65 years vaccinated, 2008–2011. Data not available for other countries. #: Austrian data are for 2006. Data from the Organisation for Economic Cooperation and Development.



**Figure 2 – Pertussis vaccination: proportion of infants fully vaccinated by 1 year of age.** Data are for the latest available year (2005–2010). #: Romanian data are for 2004. Data from the World Health Organization European Health for All Database.

adolescents and adults. These differences in approach are, at least in part, related to the varying incidence of pertussis in adolescents and adults in Europe. Data from EUVAC-NET show an increase in the number of reported cases in the EU and in European Economic Area (EEA)/European Free Trade Association (EFTA) countries between 2006 and 2009, from 3.75 to 4.89 per 100 000; the most affected group was 5–14-year-olds with a confirmed case rate slightly above 17 per 100 000.

The main problem in epidemiological analysis of the disease is the heterogeneity of pertussis surveillance, particularly in terms of the surveillance systems, coverage, laboratory methods used and case definition applied.

### *Streptococcus pneumoniae*

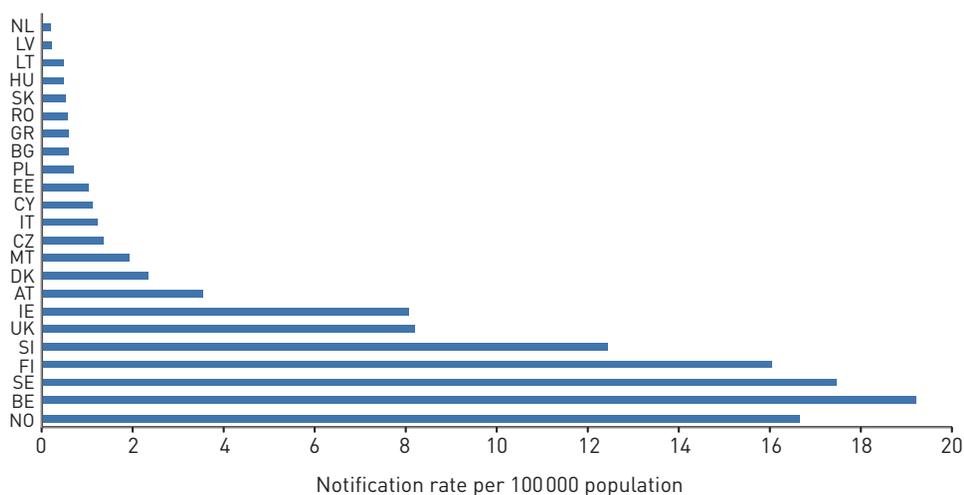
Despite good access to antibiotics, *Streptococcus pneumoniae* is still a significant cause of illness and death worldwide. *S. pneumoniae* causes several acute, invasive and noninvasive clinical infections; it is one of the leading causative agents in COPD exacerbations; and it is the most frequently detected pathogen responsible for community-acquired pneumonia (CAP). Pneumococcal pneumonia is accompanied by bacteraemia (bacteria in the blood) in 10–30% of cases.

*S. pneumoniae* is gaining resistance to the *in vitro* activity of several antimicrobial agents and, even if questions remain regarding the clinical impact of this phenomenon, increasing numbers of reports indicate that antibiotic resistance can lead to more treatment failures, if not higher mortality.

Reported incidence rates of invasive pneumococcal disease in European and US studies indicate an overall incidence of 11–23.2 per 100 000 people, rising to 16.2–59.7 per 100 000 in adults over 65 years of age. The studies in question were conducted between 1995 and 2003, before widespread use of pneumococcal conjugate vaccine in children, which has been associated with a 'herd immunity' effect, reducing the incidence of invasive pneumococcal disease in unvaccinated adults.

Figures reported by the European Centre for Disease Prevention and Control (ECDC) in EEA countries indicate a slight decrease in the rate of confirmed and notified cases of invasive pneumococcal disease between 2006 to 2009, from 5.92 per 100 000 to 4.32 per 100 000 (figure

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*Pertussis  
vaccination  
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the EU*  
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**Figure 3** – Rates of invasive pneumococcal disease, 2009. No data were reported for some countries. Data from the European Centre for Disease Control and Prevention and Control Annual Epidemiological Report 2011.

3). It should be noted, however, that there is a wide heterogeneity of the type of surveillance systems in place in different countries, as well as in their coverage and the case definition used, while in some countries there are no surveillance systems at all.

The development of effective pneumococcal vaccines was hampered by the poor immunogenicity of bacterial cell-surface polysaccharides. In the early 1980s, a vaccine containing purified capsular polysaccharides from 23 of the known pneumococcal serotypes (PPV-23) was marketed in the USA, and later in Europe. These 23 serotypes are involved in about 85–90% of invasive pneumococcal disease cases among adults. This polysaccharide vaccine stimulates short-lived B-cell immune responses by causing B-cells to differentiate into plasma cells, producing antibodies without producing memory B-cells. The immunological antibody response is age- and serotype-dependent, and is generally lower in elderly people than in younger adults. There is no memory response to a booster vaccination.

ERS/ESCMID guidelines indicate that the PPV-23 polysaccharide pneumococcal vaccine prevents invasive pneumococcal disease in older people and in other high-risk groups, and should be given to all adults at risk of pneumococcal disease including those over 65 years of age, those resident in institutions and those with dementia, seizure disorders, congestive heart failure, cerebrovascular disease, COPD, history of previous pneumonia, chronic liver disease, diabetes mellitus, functional or anatomical absence of the spleen or chronic cerebrospinal fluid leakage.

To enhance the immunogenicity of pneumococcal vaccines, conjugate vaccines have been developed. Polysaccharide antigens are chemically joined to a highly immunogenic protein carrier (such as tetanus or diphtheria toxoid). This process leads to the



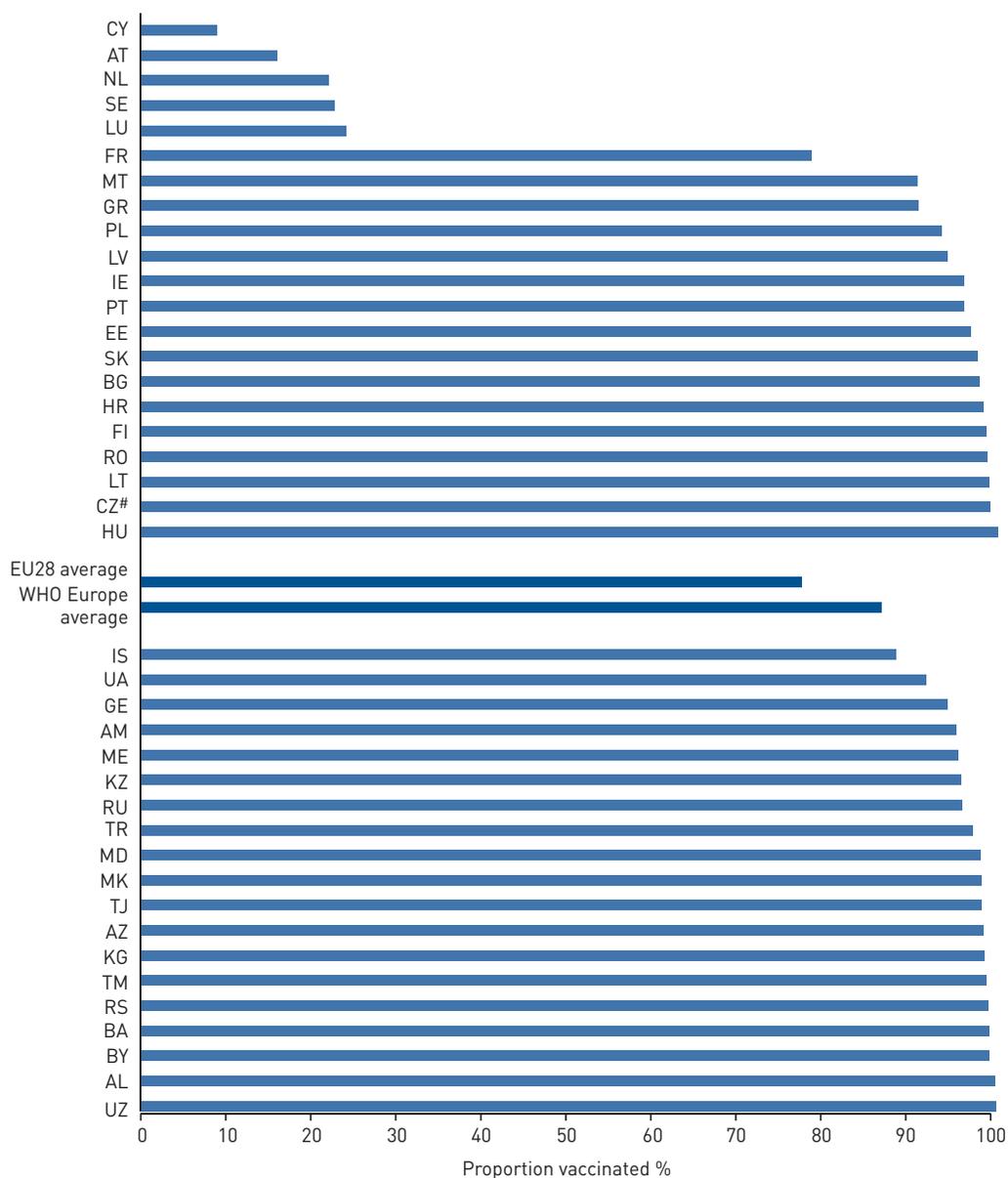
induction of both a B- and a T-cell-dependent response and a memory response to a booster dose of the vaccine.

In 2000, a pneumococcal conjugate vaccine containing capsular polysaccharides from seven pneumococcal serotypes (PCV-7), designed for children under 2 years of age, was approved in the USA. As a result of implementation of this vaccine, there was a striking decrease in invasive pneumococcal disease caused by the vaccine serotypes. Since children are the main reservoir of *S. pneumoniae* (about 60% of children are carriers), a reduction in the carrier rate in this population had beneficial effects on pneumococcal circulation, with a protective herd effect in adults. An additional observed benefit following the introduction of PCV-7 was a reduction in the rates of antimicrobial-resistant *S. pneumoniae* invasive pneumococcal disease. New conjugate vaccines are now being evaluated for children and adults: a 10-valent (PCV-10) version, which has been licensed in over 30 countries, and a 13-valent (PCV-13) vaccine. The increased serotype coverage of these vaccines, particularly PCV-13, may expand the clinical benefits of conjugate vaccines in adult populations at risk of pneumococcal disease. Vaccination strategies based on the use of more effective vaccines, in particular the PCV-13 vaccine, are expected to have a substantial public health impact on infectious disease and health service costs, reducing the burden of pneumococcal infection. However, there are concerns that, after introduction of the PCV-7 conjugate vaccine, serotypes covered by the vaccine could be replaced by serotypes not covered by it. Consequently, the introduction of the new conjugate vaccines in 2010 (PCV-10 and PCV-13) requires close monitoring.

## Tuberculosis

Vaccination against TB is also addressed in chapter 17.

In practice, the only available vaccine is the bacille Calmette-Guérin (BCG), which dates back to the early 20th century. Millions of doses of BCG have been used worldwide with a reported good safety profile and efficacy in preventing invasive TB in children. However, the protection induced against pulmonary TB, both in children and adults, is incomplete and the results of epidemiological studies on the duration of protection are inconsistent. In immunocompromised (HIV-infected) subjects, BCG vaccination seems to be associated with a higher risk of complications and even dissemination of BCG infection.



**Figure 4** – Bacille Calmette-Guérin vaccination rates, by 1 year of age. Data are for the latest available year (2007–2010). #: Czech Republic data are for 2006. No data were reported for some countries. Data from the World Health Organization European Health for All Database.

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*BCG has a good safety profile and efficacy in preventing invasive TB in children*  
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The rate of BCG vaccination in children in the EU is variable. Policies range from no use of BCG at all to vaccination of all children at birth, in infancy, at school entry and in later school years. Rates of infant vaccination in different EU and non-EU countries are presented in figure 4.

The World Health Organization (WHO) in Europe recommends that BCG vaccination should not be administered to HIV-positive children in areas with low TB incidence; in areas with high TB incidence, BCG vaccination should be restricted to HIV-positive children who do not have symptoms. WHO does not recommend BCG vaccination for adolescents and adults, including those with HIV infection, due to little or no evidence of protection from pulmonary TB.

New vaccines have been developed, including both therapeutic vaccines for immune therapy as an adjunct to chemotherapy, and potential preventive vaccines. Clinical trials are ongoing to test their efficacy.

### *Developments and research needs*

- There is a need for collection of better epidemiological data and surveillance across Europe.
- Active intervention should be used to enhance influenza and pneumococcal vaccination.
- There is a need for a better vaccine against TB.
- A uniform European policy for vaccination against TB in children, adolescents, adults, healthcare workers and immigrants is needed.

### *Further reading*



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vaccination programmes using bacille Calmette-Guérin (BCG) in countries with a low prevalence of tuberculosis. A statement of the International Union Against Tuberculosis and Lung Disease. *Tuber Lung Dis* 1994; 75: 179–180.

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