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Impact of measles national vaccination coverage on burden of measles across 29 Member States of the European Union and European Economic Area, 2006–2011

E. Colzani[a,*], S.A. McDonald[b], P. Carrillo-Santisteve[a], M.C. Busana[c], P. Lopalco[a], A. Cassini[a]

[a] European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden
[b] National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands
[c] London School of Hygiene and Preventive Medicine, London, United Kingdom

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ABSTRACT

Background: Challenges in reaching good vaccination coverage against measles emerged in several European Union/European Economic Area Member States (EU/EEA MS) leading to progressive accumulation of susceptible individuals and outbreaks. The Burden of Communicable Diseases in Europe (BCoDE) project developed a methodology for measuring the burden of communicable diseases expressed in Disability-Adjusted Life Years (DALYs) in the EU/EEA MS. The aim of this study was to compare national vaccination coverage and burden of measles across EU/EEA MS.

Methods: Country-specific data on measles national vaccination coverage 2006–2011 from 29 EU/EEA MS (MCV1) were retrieved from Centralized Information System for Infectious Diseases (CISID). DALYs were calculated for each country separately using a disease progression model with a single input parameter (annual measles incidence, adjusted for under-estimation). A software application was used to compute estimated DALYs according to country-specific and year-specific population age-distributions (data retrieved from Eurostat). Log-linear mixed-effect regression modeling approach was used to investigate a linear relation between natural logarithm-transformed DALYs and coverage.

Results: The reported annual vaccination coverage ranged from 72.6% to 100%. The estimated national annual burden ranged from 0 to 30.6 DALYs/100,000. Adjusting for year, there was a significant negative relationship between coverage and burden. For a given country there was a decrease in log-transformed DALYs/100,000 of 0.025 (95% confidence interval: −0.047 to −0.003) for every percentage increase in vaccination coverage. The largest effect of calendar time on estimated burden of measles was observed for the year 2011, the smallest was for the year 2007.

Conclusions: This study shows that the degree of success of national measles vaccination programs, when measured by the coverage obtained, is significantly associated with overall impact of measles across EU/EEA MS. In EU/EEA MS each percentage point increase in national vaccination coverage seems to lead to early significant reduction of overall burden of measles.

1. Introduction

A comprehensive assessment of the overall impact of a disease requires information not only on its occurrence, but also on severity, disease-related mortality, and morbidity due to the sequelae of the disease. Several composite health measures, or summary measures of population health, have been developed for this purpose, and many projects and studies have been carried out globally in the last few decades to reach the goal of assessing the burden of disease by taking into account all of these aspects of disease impact [1–7].

In order to gain insight into the overall impact of communicable diseases on population health in Europe and to support health policy-making, in 2009 the European Centre for Disease Prevention and Control (ECDC) initiated the Burden of Communicable Diseases in Europe (BCoDE) project. The BCoDE project developed a methodology and a software application (BCoDE toolkit) for measuring the current and future burden of communicable diseases in the European Union and European Economic Area Member States (EU/EEA MS). The burden of communicable diseases was obtained through a pathogen-based and incidence-based approach, which allows for the calculation of Disability-Adjusted Life Years (DALYs)

* Corresponding author. Tel.: +46 858 60 1459; fax: +46 8 58601 296.
E-mail address: edoardo.colzani@ecdc.europa.eu (E. Colzani).

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for 32 infectious diseases under ECDC's remit, including measles [8,9].

Measles is a highly infectious disease and about 90% of individuals would be infected by the age of 10 in the absence of vaccination [10,11]. With the resolution of 16th September 2010, all countries in the European Region of the World Health Organization (WHO), which includes EU/EEA MS, have renewed their commitment to eliminate measles and rubella by 2015, and have identified essential criteria for elimination of measles and rubella in the WHO European region, including the demonstrated protection of at least 95% of the population against measles and rubella [12–14]. Challenges in reaching good vaccination coverage have emerged in several EU/EEA MS leading to progressive accumulation of susceptible individuals, loss of heard immunity and several outbreaks of measles across Europe in recent years [11,15–19]. These challenges are due, among other reasons, to the reluctance of specific subgroups of the population to undergo vaccination, and to the difficulty in reaching specific communities [20–24].

Previous studies have investigated the relationship between the incidence of measles, or the likelihood of new outbreaks, and the vaccination coverage of a population [25–28]; however, no studies to our knowledge have studied the relationship between vaccination coverage across EU/EEA MS and the burden of measles using DALYs. In this study we wanted to investigate the effect of vaccination programs on the burden of measles in Europe. In order to reach this goal we compared measles national vaccination coverage and burden of measles expressed in DALYs across EU/EEA MS and studied their correlation in the period 2006–2011.

2. Methods

We obtained measles incidence and vaccination coverage data for 29 EU/EEA MS, from 1998 through 2011 inclusive. Age-group specific incidence data were available from The European Surveillance System (TESSy), an European database held by ECDC [29]. The incidence data reported to TESSy were corrected for underestimation by applying a multiplication factor of 2.5 as suggested by Stein et al., under the assumption that EU/EEA MS have good measles control [6]. Vaccination coverage (MCV1; measles containing vaccine, first dose) was obtained from WHO's Centralized Information System for Infectious Diseases (CISID) [30]. Country names were anonymised before analysis.

Because of extensive missing coverage data and the sparse availability of incidence data before 2006, the dataset was reduced by restricting to the period 2006–2011. For 14 countries, vaccination coverage for one or more years in the period 2006–2011 was missing; these missing values were imputed using the previous year's value (or the value from two or more years previous, if the previous year's value was also missing); 13.8% (24/174) of vaccination coverage values were consequently imputed.

2.1. DALY calculation

The DALY is a standard summary measure of population health obtained by adding two independent quantities: years of life lost due to premature mortality (YLL), which reflect the mortality contribution of a certain disease or condition, and years of life lived with a disability (YLD), which account for the morbidity of the disease or condition under study. DALYs were calculated for each country separately using a disease natural history model with a single input parameter (annual measles incidence, adjusted for under-estimation) and the "BCoDE toolkit" software application was used to compute estimated DALYs according to country-specific and year-specific population age-distributions (data retrieved from Eurostat) [31].

The measles disease model was created from the information collected through an extensive literature review and via consultation with measles experts, by linking the incidence of measles to all possible sequelae (health outcomes) through a disease progression model, or outcome tree. Health outcomes were considered part of the outcome tree if there was evidence of a causal relationship between measles and the health outcome (Fig. 1). In the disease burden calculations, years of life lost (YLL) were estimated using the Standard Expected Years of Life Lost (SEYLL) based on the highest observed life expectancy, which is that of the Japanese population. The Japanase population has been commonly used as a standard population in DALYs calculations since it has the longest life expectancy, so that in principle every human being can be expected to live at least as long [32–36]. Data on mortality were embedded into the model and were taken from both national sources and Eurostat [31]. Severity weights (i.e., disability weights) for non-fatal health outcomes were obtained from the Global Burden of Disease (GBD) study [2,5]. In conditions for which no weights existed, weights were adapted from existing GBD severity weights for similar conditions. Transition probabilities and mean duration of each health outcome were derived from the literature review. Time discounting and age-weighting were not applied in the base case analysis. The modeling approach applied assumed a steady-state and is therefore not suitable for forecasting of burden.

Information on gender was not provided, so cases were distributed evenly between males and females in each age group. Cases (<1%) for which information on age was missing were not included in the analysis.

2.2. Statistical modeling

Our dataset consists of time-series cross-sectional data [28], and therefore appropriate methods are required given the non-independence of observations. We used log-linear mixed-effect regression modeling approach to investigate a linear relation between natural logarithm-transformed outcome and predictor variables. The outcome variable was *burden* (in DALYs per 100,000 persons, transformed using log(DALYs + 1)), and the primary predictor variable was *vaccination coverage* (coded as a percentage). We assumed all cases in a given year, *t*, relate to the ability of the vaccination program to immunize the target population, estimated by using vaccination coverage with MCV1 in the same year. A Hausman test was conducted to assess the appropriateness of specifying *country* as a random instead of a fixed effect, and the need to include *year* as an additional fixed effect was assessed using a Lagrange multiplier test. Based on the tests, *year* was fitted as dummy-coded fixed effect, and *country* was fitted as a random effect. By specifying a random intercept for *country*, unexplained heterogeneity between countries is taken into consideration (i.e., *burden* values for a given country across years are more similar to each other than compared with other countries). As the single coefficient for *coverage* aggregates both between-country and within-country effects (i.e., time-invariant and time-varying components), a test for equality of these parameters was conducted before final model specification [37,38].

Thus, we fitted a linear mixed-effects regression model with two fixed effects (*coverage* and *year*) and one random effect (*country*). Model fitting and inference were carried out using the plm package [39] for the R statistical computing environment [40].

3. Results

MCV1 was recommended by all national vaccination calendars to occur during the second year of life [41]. The reported annual MCV1 vaccination coverage ranged from 72.6% to 100%. The country