Vaccine xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

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

Review

Inclusion of the value of herd immunity in economic evaluations of vaccines. A systematic review of methods used

Liv S. Nymark [a,b,c,*], Tarang Sharma [d,e], Alexander Miller [f], Ulrika Enemark [a,b], Ulla Kou Griffiths [g,h]

[a] Department of Public Health, Aarhus University, Bartholins Allé 2, DK-8000 Aarhus C, Denmark
[b] Research Center for Vitamins and Vaccines, Bandim Health Project, Statens Serums Institut, Artillerivej 5, DK-2300 Copenhagen S, Denmark
[c] Department of Health Services Research & Policy, London School of Hygiene & Tropical Medicine, 15-17 Tavistock Place, London WC1H 9SH, UK
[d] Nordic Cochrane Centre, Rigshospitalet, Blegdamsvej 9, DK- 2100 Copenhagen Ø, Denmark
[e] Faculty of Health and Medical Sciences, University of Copenhagen, Blegdamsvej 3, 2200 København N, Denmark
[f] Independent Researcher, London, UK
[g] Department of Global Health and Development, London School of Hygiene & Tropical Medicine, 15-17 Tavistock Place, London WC1H 9SH, UK
[h] UNICEF, 3 UN Plaza, New York, NY 10007, USA

ARTICLE INFO

Article history:
Received 14 December 2016
Received in revised form 4 October 2017
Accepted 12 October 2017
Available online xxxx

Keywords:
Vaccine
Cost-effectiveness
Modelling
Herd immunity

ABSTRACT

Objective: The objectives of this review were to identify vaccine economic evaluations that include herd immunity and describe the methodological approaches used.
Methods: We used Kim and Goldie's search strategy from a systematic review (1976–2007) of modelling approaches used in vaccine economic evaluations and additionally searched PubMed/MEDLINE and Embase for 2007–2015. Studies were classified according to modelling approach used. Methods for estimating herd immunity effects were described, in particular for the static models.
Results: We identified 625 economic evaluations of vaccines against human-transmissible diseases from 1976 to 2015. Of these, 172 (28%) included herd immunity. While 4% of studies included herd immunity in 2001, 53% of those published in 2015 did this. Pneumococcal, human papilloma and rotavirus vaccines represented the majority of studies (63%) considering herd immunity. Ninety-five of the 172 studies utilised a static model, 59 applied a dynamic model, eight a hybrid model and ten did not clearly state which method was used. Relatively crude methods and assumptions were used in the majority of the static model studies.
Conclusion: The proportion of economic evaluations using a dynamic model has increased in recent years. However, 55% of the included studies used a static model for estimating herd immunity. Values from a static model can only be considered reliable if high quality surveillance data are incorporated into the analysis. Without this, the results are questionable and they should only be included in sensitivity analysis.

Contents

* Corresponding author at: Department of Public Health, University of Aarhus, Bartholins Allé 2, DK-8000 Aarhus C, Denmark.
E-mail address: lsny@protonmail.com (L.S. Nymark).

https://doi.org/10.1016/j.vaccine.2017.10.024
0264-410X/

1. Introduction

Vaccination confers both direct and indirect effects. The direct effect implies protection against disease in vaccinated individuals [1]. Indirect protection is when susceptible individuals avoid infection because the people who surround them are immunized [2]. The magnitude of indirect effects is a function of transmissibility of the infectious agent, population mixing patterns, distribution of vaccine, and distribution of immunity in the population [3]. 'Herd immunity' refers to population-scale immunity. The herd immunity threshold is defined as the proportion of a population that need to be immune in order to halt the spread of a communicable disease. The key parameter defining the herd immunity threshold is R_0, which is the number of new infections generated by the first infectious individual in a completely susceptible population [2]. R_0 is affected by duration of infectivity of infected patients, infectiousness of the organism, and the number of susceptible people the infectious carrier is in contact with [3]. Measles is known to have a relatively high R_0 while diseases like Haemophilus influenza type b and polio spread less easily from person to person [4].

The natural disease mechanisms associated with communicable diseases require a dynamic model structure to simulate pathogen transmission among individuals. A dynamic approach captures both direct and indirect effects by modelling mixing patterns and risks of infection between vaccinated and unvaccinated individuals. Conversely, static models assume constant risk of infection and are therefore unable to account for disease transmission in populations. Hence, these are less likely to accurately estimate the full value of vaccination [5]. Compared to static models, dynamic models tend to show more favorable incremental cost-effectiveness ratios [6]. The exception to this is for vaccines where herd immunity can have a negative impact. This can be due to an upward shift in the age of the susceptible population or due to serotype replacement. Rubella has for instance substantially more severe consequences in the first trimester of pregnancy than in infants and the currently used pneumococcal vaccines lead to serotype replacement, which decreases the overall health impact of vaccinations. In such situations, a dynamic model would lead to a less favorable cost-effectiveness ratio than a static model.

In best practice guidelines on economic evaluation of vaccines, a dynamic model is recommended when the rate at which susceptible individuals acquire infection is reduced due to vaccination or when it is not possible to obtain a conservative estimate with a static model [7,8]. To our knowledge, a systematic review has not yet assessed to what extent economic evaluations of vaccines consider herd immunity and if so, which model approach is employed for this. The objectives of this review were to identify economic evaluations of vaccines that include herd immunity and assess which model properties were used.

2. Methods

2.1. Search strategy and data extraction

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed [9]. We searched PubMed/MEDLINE and Embase. Kim and Goldie conducted a systematic review detailing the modelling approaches used in cost-effectiveness analyses (CEAs) of vaccines from 1 st January 1976 to 31 st May 2007 [10]. We adopted their search to identify CEAs of vaccines from 1 st June 2007 to 31 st July 2015, and we searched for the same monovalent and multivalent vaccines (Table S1 in the supplement). Kim and Goldie used free text and MeSH terms, such as vaccin*, economic evaluat*, humans, and they limited the search to English language. A detailed description of the search process using rotavirus vaccine as an example is presented in Table S2. English-language, human vaccine CEAs were eligible for inclusion if the analysis had an explicit comparator, included both costs and health effects and presented a decision-analytic model. Two reviewers independently screened titles and abstracts and reviewed full-texts to determine inclusion of herd immunity in either the main analysis (base case) or sensitivity analysis. Kim & Goldie included 275 CEAs of vaccines in their review and we also screened these for inclusion of herd immunity. Vaccination will not induce herd immunity where human transmission (including via a vector) is non-existent. Humans are the end of the transmission cycle for rabies, Q Fever, Japanese Encephalitis and Lyme disease and tetanus does not have a transmission cycle. We therefore excluded CEAs of these vaccines.

2.2. Data analysis

Four main categories were used to classify CEA models: Static (type 1), dynamic (type 2), hybrid (type 3) and 'model not clearly stated' (type 4) (Table 1). Types 1 and 2 were based on Kim and Goldie's framework for modelling approaches while type 3 was defined based on literature, which describes the hybrid model as combining characteristics of both dynamic and static models [11,12]. The number of type 1–4 models and associated subtypes were counted. For each vaccine type, the methods used to estimate herd immunity were described. We focused this description on the static models as it is especially for these that the methods are debatable and not well established. Dynamic models are in contrast primarily developed to account for herd immunity. For vaccine types with only few studies that included herd immunity, we also described the methods used in the dynamic models. We counted the number of CEAs that included herd immunity in their main analysis versus how many did so in the sensitivity analysis only (including scenario analyses). We extracted data on time horizon used and compared this between static and dynamic models. Main health outcomes measures were identified and counted.

Table 1
Classification of model types.

Model types
Type 1: Static (e.g. flow tree, cohort, Markov)
Type 2: Dynamic (e.g. transmission dynamic, SIR, SEIR)
Type 3: Hybrid (e.g. Markov and transmission dynamic)
Type 4: Not clearly stated (classification of model was not possible due to incomplete description)

Abbreviations: SIR = Susceptible-Infected-Recovered, SEIR = Susceptible-Exposed-Infectious-Recovered.

Please cite this article in press as: Nymark LS et al. Inclusion of the value of herd immunity in economic evaluations of vaccines. A systematic review of methods used. Vaccine (2017), https://doi.org/10.1016/j.vaccine.2017.10.024