



Contents lists available at ScienceDirect

Vaccine

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

Core values for vaccine evaluation

James Kenneth Timmis^a, Fabio Rigat^b, Rino Rappuoli^{c,*}^a University of Freiburg, Fahnbergplatz, D-79085 Freiburg i. Br., Germany^b GSK, Gunnels Wood Road, Stevenage, Herts SG1 2NY, UK^c GSK Vaccines, Via Fiorentina, 1, 53100 SI, Italy

ARTICLE INFO

Article history:

Available online xxx

Keywords:

Vaccine evaluation

Vaccine policy

Core values

Health policy

Health Technology Assessment (HTA)

Decision-making

MCDA

GH2035

ABSTRACT

Currently, most health economic modelling approaches tend to inadequately incorporate crucial disease-specific criteria and other attributes of benefit resulting from vaccination, which limits their utility for evaluating vaccines and, in consequence, for optimally guiding vaccine decision-making. Additionally, vaccine evaluation methods are frequently poorly standardised and non-transparent, leading to a potentially low level of accountability that can hinder acceptance of resulting decisions. To address these issues, we have considered whether it is possible to identify a set of universal vaccine-disease considerations, which we have called *Core Values*. To begin to identify such a set of criteria, and to establish whether strong agreement around such core values exists, we conducted two studies based on the Delphi technique. Both studies surveyed a cohort consisting of expert members of the global vaccine community with diverse professional backgrounds. Formal statistical analysis of both studies identified four attributes with strong agreement: 1. *Incidence disease cases prevented per year*, 2. *Cost-effectiveness (including cost-benefit and cost-utility analysis)*, 3. *High mortality disease (case-fatality-rate)*, and 4. *Severity of target disease (risk of morbidity and mortality)*. These results suggest the feasibility of identifying a clear consensus on a specific set of *Core Values for Vaccine Evaluation*.

© 2016 Published by Elsevier Ltd.

1. Introduction

Vaccination is considered the most effective and cost-effective health intervention [1]. Vaccines not only prevent serious health conditions and death caused by vaccine preventable diseases (VPDs), they also prevent their long-term sequelae, disabilities and impairments that may result from some infectious diseases that may seriously impact on individuals, their families and ultimately society at large [2].

Historically, vaccine development and adoption was predicated on the morbidity and mortality rates of infectious diseases, and the potential for preventing them, leading to the development of vaccines for diphtheria, pertussis, tetanus and later polio, measles, mumps and rubella [3]. More recently, vaccine evaluation has focused on economic feasibility, but often simple health economic analyses (HEA) used in isolation may not adequately capture the full spectrum and magnitude of benefits offered by vaccination. Nevertheless, the results of HEA and assessments of the cost saving potential of vaccines have, in many cases, become a gating criterion for introducing a vaccine into national healthcare plans/systems

[3]. However, recent research has clearly demonstrated that vaccination holds a substantially higher value than has been traditionally appreciated, extending well beyond individual and aggregate health gains, and has identified highly beneficial and diversified, sustainable, broad societal and economical benefits of vaccination [4–7]. For instance, Bloom et al. demonstrated that vaccinated children had significantly higher scores in cognitive ability tests [8], translating into “a 21% rate of return on the vaccine spending”. A further study by Bloom et al. (2005) investigated the return of investment (ROI) for a GAVI proposal for expanding the variety of vaccines employed until 2020. The ROI was estimated to reach 18% by 2020 [9]. This 18–21% ROI is similar to the social (11–25%) and private (17–24%) rates of return for primary, secondary and high/school education [7,10,11] - often held up as the “gold standard” for ROI. Preventing disease and sequelae due to infectious diseases facilitates *inter alia* a considerable increase in time spent in education, higher income, financial stability and attraction of foreign direct investment and, in consequence, economic development and increased individual and national welfare [7].

If these substantial broad benefits of vaccination are not included in vaccine evaluation to complement the standard economic assessments of health gains and costs, there is a significant risk of inappropriate vaccine decisions being taken and novel or

* Corresponding author.

E-mail address: rino.rappuoli@gsk.com (R. Rappuoli).

improved, safe and efficacious vaccines excluded from national vaccination schedules. The recent challenges of adequately evaluating the meningitis B vaccine *Bexsero*[™] with traditional HEA, particularly the considerable spectrum of economic assumptions and their values feeding into the health economic modelling approaches, resulted in a one-year delay (from 2013 to 2014) in the introduction of the vaccine in the UK [12–17]. During this period, circa 410 lab confirmed cases of meningococcal group B disease were reported in England [18], many of which could have been prevented by timely introduction of the vaccine. This example, and others [6,7], illustrates the significance of evaluating vaccines with adequate methods and a broad set of relevant evaluation criteria.

Fortunately, Multi-Criteria-Decision-Analysis (MCDA) tools are well suited to comprehensively structure and compound the diverse attributes of broad benefits of vaccination and render them readily available for integration in health economic analyses and, more importantly, deliver more useful results to guide decision-makers [19–21]. However, one significant challenge for contemporary vaccine evaluation and MCDA is a lack of standardisation by guiding principles that ensure a baseline degree of alignment for achieving equity and accountability for vaccine decision-making outcomes [21–25].

In this communication, we report an approach towards addressing the challenges inherent in current vaccine evaluation and decision-making practices by tethering them to universal priorities (attributes), - *Core Values for Vaccine Evaluation* - with the goal of rendering (a) vaccine evaluation more efficient, transparent, equitable and comparable, and thereby (b) decision-making outcomes more accountable.

2. Study design

We predicated our research on the following question: is it feasible, by surveying leading experts of the global vaccine community, to identify for vaccine evaluation a general set of universally applicable priority attributes which we have called *Core Values*?

The survey study design we chose to address this question was based on the Delphi technique, a systematic methodology originally developed at RAND in the 1950s for interviewing experts in a field with the endpoint of forecasting future developments or/and assessing expert consensus on a specific topic or a set of decision-making criteria. For this purpose, multiple consecutive rounds of interviews are performed, each subsequent round meant to further consolidate/refine the issue/criteria under consideration [26,27].

The first step of our study (*status quo assessment round*) was designed to familiarise the participants with the broad spectrum of vaccine evaluation attributes used in this study (a list of 33 attributes including the 29 SMART Vaccines attributes [28] and 4 additional attributes), and to establish a broad baseline for potential agreement, for different vaccine evaluation scenarios (8 sets of 5 chosen and ranked attributes). To place the proposed attributes in context, we selected target diseases to be considered in the survey. In this first round, participants were asked to select and rank 5 vaccine evaluation attributes (*potential priority attributes*) for each of 8 different target infections – Cholera, Dengue, Ebola, Influenza, Meningococcal disease, Rotavirus, Schistosomiasis and Varicella disease - selected to cover a spectrum of disease severity and frequency, and be familiar to the participants. In a second step (*refinement round*), we asked participants to select and rank a set of 5 *universal* priority attributes for general overall vaccine evaluation, which required them to reflect on and prioritise their former choices and allow establishment of a *refined scope of potential*

priority attributes. This procedure is shown in Fig. 1 and, in detail, in Fig. S2 in the supplementary materials.

Employing this design, we conducted two survey studies: an *exploratory* and later a consecutive *focus study*.

3. Methods

The two surveys were analysed sequentially using the same statistical methods. This analysis consisted of three steps: dimensionality reduction, selection of attributes attracting strong agreement and calculation of prediction intervals. Dimensionality reduction proceeded by calculating one survey score for each combination of disease and vaccine attribute. Each score was calculated by aggregating the survey responses across participants and ranks. All participants who completed the survey contributed equally to this calculation and attributes selected with higher ranks had higher weights compared to attributes selected with lower ranks. Attributes attracting strong agreement were identified as those scoring above the 99.5% percentile of the probability distribution of survey scores under random attribute choice. The spread of this distribution directly reflected the survey sample size. Likewise, attributes with scores below the 0.5% percentile of the same distribution were identified as strongly irrelevant for vaccine evaluation in general. This conservative decision rule ensured that any attribute identified as attracting exceptionally strong agreement or as strongly irrelevant had each a false positive rate of 0.5%. Prediction intervals of the survey scores were derived from the observed survey responses using the non-parametric bootstrap [29].

The results of the *exploratory study* identified a set of attributes felt to be less relevant by the survey participants, and which were subsequently eliminated from the consecutive *focus study*, leaving a total of 24 selectable attributes. Additionally, we sharpened the formulation of some of the remaining attributes to render them more precise and distinct. Both lists of attributes and an overview and comparison of modifications (Table S1) can be found in supplementary materials. The design and analysis of the *focus study* were otherwise identical to those of the *exploratory study*. As the goal of both studies was to identify universal priority attributes for vaccine evaluation, *candidate priority attributes* had to fulfil the following condition to be taken into consideration: their score had to attract exceptionally strong agreement for at least two disease cases simultaneously. Further details on study design and analysis are available in the supplementary materials.

4. Results

4.1. Cohorts/samples

In February 2015, we invited 115 experts of the global vaccine community with diverse professional backgrounds and affiliations, as shown in Fig. 2, to participate in the *exploratory study*, an online questionnaire: *Parameters for vaccine priority setting*. In total, 46% (N = 53), as indicated by the dark blue columns in Fig. 2, of the invited experts completed the questionnaire (participants). A statistical comparison of the composition of professional backgrounds of those experts invited and those participating using the Kruskal-Wallis test produced a p-value of 0.4, demonstrating that the sample compositions of the invitee and the participant groups were not statistically different.

The subsequent *focus study* involved the participants of the *Global Health 2035: Mission Grand Convergence* meeting (N = 65) in June 2015 and was undertaken in advance of the meeting. In total, 66% (N = 43) of the invited experts completed the questionnaire, as indicated by the dark orange columns in Fig. 2. Also in this study, the compositions of invitees versus participants were not statistically

Download English Version:

<https://daneshyari.com/en/article/5537241>

Download Persian Version:

<https://daneshyari.com/article/5537241>

[Daneshyari.com](https://daneshyari.com)