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Review

How and why researchers use the number needed to vaccinate to inform decision making—A systematic review

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ABSTRACT

Background: The number needed to vaccinate (NNV) is a measure that has been widely used in the scientific literature to draw conclusions about the usefulness and cost-effectiveness of various immunization programmes. The main objective of this review is to examine how and why the NNV has been used and reported in the published literature.
Methods: Electronic databases were searched and records were screened against the eligibility criteria by two independent authors. We included papers that reported and interpreted NNV.
Results: We identified 27 studies, the designs including observational studies, economic analyses, systematic reviews, and commentaries. The NNV has been used in the literature to describe three main themes: potential benefits of vaccination programmes, cost-effectiveness, and economic analyses, and modelling studies to compare different vaccination strategies.
Conclusions: NNV has been used in a wide variety of ways in the literature, yet there are no defined thresholds for what is a favourable NNV. Furthermore, the generalizability of the NNV is usually limited. Further work is required to determine the most appropriate use of this measure.

1. Introduction

Vaccines have saved more lives than any other health intervention in the last century. The World Health Organization estimates that more than two million deaths annually are prevented due to immunization programmes worldwide [1]. Despite this measurable impact, the benefits of immunization are sometimes taken for granted, which can pose a significant challenge [2,3]. Sustaining the priority of vaccine-preventable diseases in the eyes of the public and policy makers is more difficult when these diseases are well-controlled because they are out of sight and therefore out of mind. The benefits of immunization need to be promoted using simple and intuitive measures that enable fair comparison with other competing priorities.

The number needed to vaccinate (NNV) is used as a simple summary calculation to evaluate the possible benefits of immunization programmes in preventing and controlling communicable diseases. It is defined as the number of persons needed to vaccinate in order to prevent one outcome, and it combines both vaccine effectiveness and incidence of disease [4]. Generally, the NNV is calculated as NNV = 1/(annual incidence of event in the unvaccinated × vaccine effectiveness (VE)). This is equivalent to the reciprocal of the annual absolute risk reduction, since the VE measures the relative risk reduction. [4]

In recent years there have been an increasing number of analyses that use NNV to evaluate the usefulness and cost-effectiveness of several vaccines. Although NNV is an intuitive measure of the benefit of a given vaccine, there remains no agreed threshold for interpreting this number, and questions have been raised as to whether it is an appropriate measure [31]. This systematic review aims to explore how and why NNV is used in the scientific literature in order to draw conclusions about the appropriate use of NNV for public health decision making.

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2. Methods

We searched the online databases MEDLINE, EMBASE, and CINAHL in February 2013 for all primary research studies that have reported, calculated, and interpreted NNV. We included all review articles, commentaries, and published letters that reported and interpreted NNV. Studies that did not interpret NNV were excluded. Search strategy was restricted to English-language publication on human subjects. Eligibility criteria were applied to examine all the records at the title, abstract, and full text stages. This was conducted systemically by two reviewers (AH and VD) using Microsoft® Office Excel® 2007 version 12 (Microsoft Corporation, Richmond, USA). Discrepancies between the two reviewers were resolved through consensus. If the title or abstract of a given study was not enough to determine inclusion or exclusion from our study, the full texts were assessed against the same criteria. In addition, the references of all articles were reviewed for other potentially eligible studies. The search strategy used the following terms: "number-needed-to-vaccinate" or "NNV" or "prevent case or illness or death or outcome or event or disease or hospitalisation or hospitalization" and "vaccination or immunisation or immunization". Data extracted from the eligible studies comprised of study objectives, study design, NNV definition, vaccine type, disease outcome, population characteristics, parameters used in calculating NNV, vaccine effectiveness, and interpretation.

Table 1
Number of studies by study design and vaccine type.

Characteristics	Number of studies
Study design	
Observational studies	9
Economic evaluation	7
Systematic reviews +/− Meta-analysis	6
Commentary	3
Modelling	2
Vaccine type	
Influenza	8
Tuberculosis	4
Herpes Zoster (HZ)	3
Human Papilloma Virus (HPV)	3
Pertussis	3
Hepatitis A	2
Pneumococcal	2
Meningococcal B (MenB)	1
Respiratory Syncytial Virus (RSV)	1
Rabies	1
Outcome	
Case	20
Death	7
Hospitalization	6
Outpatient visit	1
Quality-adjusted life year (QALY)	1
Disability-adjusted life year (DALY)	1
Life-years lost	1

3. Results

3.1. Study selection and characteristics

The initial search resulted in 432 entries, of which 11 were duplicates; 393 were excluded on the basis of our screening criteria at the title and abstract stage. At the full-text screening stage, five records were excluded for not meeting the inclusion criteria. Reference and citation tracking identified an additional four eligible papers, providing a total of 27 papers for review. Fig. 1 illustrates a flow diagram of the study selection process.

The disease outcomes reported were influenza in eight studies [4–11], tuberculosis in four studies [12–15], as well as three studies each of herpes zoster (HZ) [16–18], human papilloma virus (HPV) [19–21], and pertussis [22–24]. Two studies each focused on Hepatitis A [25,26] and pneumococcal disease [4,27]. Other disease outcomes included serogroup B meningococcal disease [28], respiratory syncytial virus (RSV) [29], and rabies [30]. Outcomes for which NNVs were measured included being a case of a specific disease, death, hospitalization, outpatient visit, quality-adjusted life year (QALY), disability-adjusted life year (DALY), and life-years lost. One third of the included studies ($n = 9$) used data from observational studies, which were primarily cohort studies [8–10,12,17,23,27,28,30]. In addition, seven studies were cost-effectiveness and economic analyses [4,5,13,15,16,21,22], six studies were systematic reviews [6,7,11,14,26,29]; three were commentaries [18,20,25], and two studies utilized mathematical modelling [19,24]. Study characteristics of the included studies are summarized in Table 1.

3.2. How is NNV being used in the literature?

3.2.1. Potential health-related benefits of vaccination programmes

Fourteen studies (52%) used NNV as a measure of potential benefits of vaccination programmes.

Of these, five articles in the literature utilized NNV to measure the potential benefit of influenza vaccination using different health outcomes. Kelly and colleagues [10] quantified the benefits of an influenza vaccination programme by calculating the number of persons required to be vaccinated to avoid one hospital admission due to influenza. They reported that 1852 children would have to be vaccinated to avoid one hospitalization due to any strain of circulating influenza in 2009. Lewis and colleagues also quantified the numbers of children who needed to be vaccinated to prevent one hospitalization and outpatient visit [7]. This was found to range from 1031 to 3050 for children 6–23 months of age and from 4255 to 6897 for children 24–59 months of age. They estimated that 12–42 children 6–59 months of age need to be vaccinated to prevent one outpatient visit, and that vaccination was therefore an important means of reducing influenza associated outpatient visits in this age group. Similarly, two other studies used NNV to measure the benefits of influenza vaccination in preventing influenza and cases of influenza-like illness in pregnancy and postpartum women, and HIV-infected individuals, respectively [8,11]. Voordouw and colleagues investigated the benefit of influenza vaccination for preventing all-cause mortality. The authors stated that in order to prevent one death due to influenza, it is required to vaccinate 302 individuals or one for every 195 repeated vaccinations at a vaccination coverage up to 74%. They concluded that the annual influenza immunization of the elderly population has the potential to reduce all-cause mortality [9].

Two studies used NNV to evaluate the potential benefits against HZ. Skootsky described the NNV as an alternate measure of efficacy against HZ [18]. It was reported that one case of HZ was avoided for every 175 adults over 60 years of age who were vaccinated, and one prevented for every 231 adults 70 years of age or older. A similar analysis for patients 70 years and older showed that 231 people needed to be vaccinated to prevent one episode of HZ. Skootsky concluded that these numbers are greater than what many physicians and most patients might expect (although what would be expected was not defined precisely) and therefore a less attractive HZ vaccination programme. In another HZ study, Brisson [17] estimated the NNV for various HZ related health outcomes for patients who are 65 years. Brisson estimated that the NNV to prevent a case of HZ is 11, to prevent a case of post herpetic neuralgia (PHN) is 43, to prevent an HZ death is 23,319, to prevent a life-year lost is 3762, and to prevent a lost QALY is 165. The study stated that,