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National Advisory Groups and their role in immunization policy-making processes in European countries

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Abstract

During the twenty-first century, the development of national immunization programmes (NIP) has matured into robust processes where evidence-based methodologies and frameworks have increasingly been adopted. A key role in the decision-making and recommending processes is played by National Immunization Technical Advisory Groups (NITAGs). In a survey performed among European Union member states, Norway and Iceland, in February 2013, 85% of the 27 responding countries reported having established a NITAG, and of these, 45% have formal frameworks in place for the systematic development of vaccination recommendations. Independent of whether a formal framework is in place, common key factors are addressed by all NITAGs and also in countries without NITAGs. The four main factors addressed by all were: disease burden in the country, severity of the disease, vaccine effectiveness or efficacy, and vaccine safety at population level. Mathematical modelling and cost-effectiveness analyses are still not common tools. Differences in the relative weighting of these key factors, differences in data or assumptions on country-specific key factors, and differences in existing vaccination systems and financing, are likely to be reasons for differences in NITAG recommendations, and eventually NIPs, across Europe. Even if harmonization of NIPs is presently not a reasonable aim, systematic reviews and the development of mathematical/economic models could be performed at supranational level, thus sharing resources and easing the present work-load of NITAGs. Nevertheless, it has been argued that harmonization would ease central purchase of vaccines, thus reducing the price and increasing access to new vaccines.

Keywords: Decision-making, Europe, evidence, immunization programme, recommendations, vaccination

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Introduction

In Europe, licensure of vaccines and indications for their clinical use are regulated by the European Medicines Agency and national regulatory authorities. Before licensure, a candidate vaccine undergoes extensive immunogenicity and safety evaluations, and usually also evaluation of efficacy under ideal conditions in the intended main indication target group(s). Once a vaccine is licensed and available on the market, qualified medical personnel can prescribe and administer the vaccine to individual subjects. Off-label use is discouraged, but at times indications or schedules may be altered from those on the label, based on an individual benefit–risk assessment or on population risk–benefit or cost-effectiveness assessments.

How widely the commercially available vaccines are eventually used in a population depends largely on the delivery and

financing system of the national immunization programme (NIP). The adoption of a vaccine in a NIP is usually linked to its funding through public sources. In contrast to the treatment of sick patients, vaccines as a preventive measure do not only confer a benefit on the vaccinated individual, but often also on the total population in which the vaccine has been introduced. The public health benefits of large-scale vaccination in a population can include overall disease burden reduction; for several diseases, the protection of vulnerable (potentially unvaccinated) individuals by reducing disease transmission (herd protection); the complete elimination of a disease in a geographic region; and/or cost-savings in the healthcare system. To make the most efficient use of a vaccine and to maximize its benefits, specific strategies can be implemented within a NIP, e.g. by targeting either the total population or only specific age cohorts or other population subgroups with an increased risk of acquiring the disease or of developing more severe disease once infected.

Since the birth of the Expanded Programme on Immunization after successful eradication of smallpox in the 1970s, there has been a steady drift away from thinking that one programme can fit all countries. Therefore, the WHO has recommended and the Global Vaccine Action Plan has recently endorsed as a strategic goal, that countries should establish or strengthen formal and, if possible, independent technical expert committees to guide country immunization policies and aid national decision-making for NIPs [1,2]. The underlying thinking is that national decision-making and recommendation on the use of vaccines at population level should be based as much as possible not only on universally applicable best-available scientific evidence, but also on local disease burden, and country-specific cost-effectiveness [2]. Taking these into account would then be the core tasks of a National Immunization Technical Advisory Group (NITAG), together with ensuring that the process of adopting a vaccine in a NIP is less likely to depend on commercial or other vested interests.

Frameworks and Key Factors Considered by NITAGs

A NITAG is a technical resource providing evidence-based guidance to national authorities and policy-makers [1]. Such a resource is particularly important in view of the complex and vast bodies of evidence, as well as a dynamic vaccine market, with new products targeting a variety of age groups and specific at-risk populations [1].

To systematically assess and weigh the available evidence, to minimize bias, to improve transparency, and to enable a structured evaluation, different evidence-grading systems have been developed and applied, especially for clinical practices [3]. However, the public health domain has been slow in adopting such approaches [4]. Nevertheless, in recent years, the approach of the Grading of Recommendations' Assessment, Development and Evaluation (GRADE) Working Group has increasingly been proposed and used as a tool for the development of evidence-based recommendations, also in the field of immunization [5,6]. The GRADE system has the advantage that it does not only grade the quality of evidence related to the efficacy and safety of an intervention; it also takes into account that other factors beyond the quality of evidence (e.g. preferences, values and resource implications) influence our confidence that adherence to a recommendation causes more benefit than harm [7]. Another advantage of GRADE is that the quality of evidence derived from observational studies, which in most evidence-grading systems are considered *a priori* to provide lower quality of evidence, can be up-rated under specific conditions. This is of particular importance in the field of immunization, because some aspects (e.g. very rare adverse events or population-level effects such as herd protection) are difficult to assess in randomized controlled vaccine trials [8].

Even without a methodologically rigorous system like GRADE, most NITAGs have a framework in place to consider various key factors when developing a recommendation [9]. These key factors are evaluated either informally or formally. Often, decision-making tools are used, such as health technology assessment, in combination with epidemiological, ethical and behavioural analyses; such analyses can include mathematical modelling to predict population level and long-term impacts in a given population, depending on different vaccination strategies, and health-economic evaluations of strategies. In the Netherlands, for example, the factors that determine a vaccine's suitability for inclusion in the NIP have been translated into seven selection criteria, grouped under five thematic headings: seriousness and extent of the disease burden, effectiveness and safety of the vaccination, acceptability of the vaccination, efficiency of the vaccination, and priority of the vaccination [10]. In Canada, the analytical framework proposed included 58 criteria classified into 13 categories [11]. As in other systems, the National Advisory Committee on Immunization in Canada has three broad stages in the preparation of a recommendation statement: (i) knowledge synthesis (based on individual studies); (ii) synthesis of the body of evidence on benefits and harms, considering the quality of the evidence and the magnitude of effects observed; and (iii) translation of evidence into a recommendation [12]. Other frameworks have been established elsewhere; we describe these briefly for Finland, Germany and Italy in the Supplementary material, Appendix S1 [13,14].