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The Measels-Mumps-Rubella Vaccination from a health political and economical point of view

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Introduction

The present Health Technology Assessment report (report on technological consequences, HTA report) addresses various aspects of the MMR vaccination, the key question being how the MMR-immunisation coverage rate can be increased in Germany.

Health policy background

MMR are highly contagious infectious diseases which may, despite a generally good prognosis, lead to severe complications and thus represent an avoidable burden on the health care system. Vaccination is the most important and most effective preventive measure. The German Standing Vaccination Committee (STIKO) recommends two MMR doses for all children (up to the age of 17) as well as for persons at risk. However, probably because of the decreasing awareness of the danger of these diseases, it seems that the German population's willingness to be vaccinated, at least in certain regions, cannot be sufficiently increased any more. The same holds true for the acceptance of the vaccination due to the increasing number of sceptics or persons opposing vaccinations altogether.

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Scientific background

A measels infection causes lowered immunity for about six weeks. Complications (e. g. ear infection, pneumonia, bronchitis) which occur in about 30 % of cases, may arise especially during this time period. An especially dangerous complication is post-infectious encephalitis (inflammation of the brain). Another possible, though rare, long-term consequence of measles is subacute sclerosing panencephalitis (SSPE). SSPE is always fatal.
The most common complications of mumps infections are meningitis (inflammation of the cerebral membranes), orchitis (testicular inflammation), and pancreatitis (inflammation of the pancreas). In rare cases, mumps infections can lead to one-sided deafness. Orchitis occurs in about 25 % of men infected after puberty. It develops during the first days of illness and causes swelling of the testis and fever attacks. If both testes are affected orchitis causes sterility.
Complications of post-natal rubella infections are rare, however, they become more common with age. A rubella infection of the foetus through the placenta is considerably more critical. The danger of birth defects is greatest during the first trimester. Anomalies of the heart, eyes (cataract) and ears (inner ear deafness) are the most common defects. Additional possible complications are foetal mental development disorders, disorders of the musculo-sceletal system, encephalitis and low birth weight. The probability that complications and sequelae occur after masern, mumps, or rubella infections increases with age.
For MMR immunisation, live virus vaccines are used; they contain attenuated wild-type viruses, which can no longer cause disease. The vaccine is

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available as a combined trivalent MMR vaccine and as fourvalent vaccine against measles, mumps, rubella and varicella (MMRV). As is the case with all vaccines, the immunogenicity of the MMR vaccine is < 100 %. About five to ten vaccines do not develop immunity. Therefore, a second MMR vaccination is recommended in many countries.
Severe adverse events and complications after MMR vaccinations are very rare. They may occur in persons who are hypersensitive to some components of the vaccine. Technical problems or incorrect vaccination technique may also cause vaccine damage and complications. Regarding the discussion about vaccine damage and complications, various sources point out that the risk of adverse events and complications of the three infectious diseases considered are by far greater than the risk of complications caused by vaccinations.
The priority objective is to achieve stage III ('Approaching measles elimination and prevention of congenital rubella syndrome') of the WHO surveillance guidelines by 2010. In order to meet this goal, a coverage with two doses of measles vaccine of at least 95 % and a coverage with at least one dose of rubella vaccine among women of childbearing potential of 90 % needs to be achieved. According to the WHO, the basic requirement for achieving this coverage is adequate surveillance (80 % of measles and rubella cases confirmed by seroprevalence testing in the laboratory). The WHO target of a 95 % coverage with one dose of measles vaccine and of an incidence of < 1 in 100,000 residents should be achieved by 2007.

Objectives

The present HTA report commissioned by DIMDI by authority of the Federal Ministry of Health intends to address the benefits of the MMR vaccination for Germany (also the economic benefit) and to analyse how the desired MMR immunization rate of > 95 % can be achieved.
The general research questions were clearly defined and divided into subquestions.
Epidemiological aspects of vaccination coverage and incidence in Germany are analysed and compared to international data.
From an economical point of view this report intends to clarify whether economical analyses concerning the economic benefit of the MMR vaccination and / or the benefit for the health care system in Germany have been published so far. In addition, results of such analyses and the question if international analyses of the economic benefit of the MMR vaccination exist are of interest.
Furthermore, this HTA report deals with programs / interventions and their efficiency in increasing the willingness of people to get vaccinated.

Search strategy

In a first step, a systematic literature search was performed in 29 literature data bases. The systematic literature search yielded a total of 2766 abstracts. Unfortunately, important information particularly regarding the organisation of and data on the immunisation systems in Germany and other countries were either not published in international journals or the publications were not sufficiently precise. This made additional extensive (internet) searches and enquiries at relevant institutions and organisations, as well as expert interviews necessary.

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Of 200 full texts and other sources used in the preparation of the present report, 84 were yielded trough hand search and written enquiries. Using inclusion and exclusion criteria, 21 texts (studies and / or information from data bases) remained which were assessed and subjected to a detailed analysis.

Epidemiology

Methods

For this section of the report, few data were available in the published literature. Therefore, necessary information on prevalence of MMR and vaccination coverage was supplemented through hand search in various sources (RKI - Robert-Koch-Institute, WHO - World Health Organization, OECD - Organisation for Economic Co-Operation and Development).

Results

At 92.5 % (as of 2004), the current immunisation coverage rate for measles in children based on the whole of Germany is above the weighted EC-15-average of 90.67 %.
In the new Laender, the WHO target of herd immunity (~ 95 % vaccination coverage) is already achieved with a coverage of 96.7 % the need for interventions to increase the vaccination coverage is greatest in the old Laender with a coverage of only 92.2 % (as of 2004).
Statements on incidences can only be made for measles as no data are available for mumps and rubella. With 2.8 infections (per 100,000 residents) in 2006, Germany has not achieved the WHO target of less than one new case per 100,000 annually. In addition, large discrepancies exist between the Laender; e. g., the prevalence was 0.02 to 0.35 per 100,000 residents in the new Laender, whereas it ranged between 0.00 and 9.55 in the old Laender (as of 2006).
Of cases submitted to the laboratory in 2005, only 32 % were validated by diagnostic laboratory findings and 45% confirmed clinical-epidemiologically. According to the WHO, adequate surveillance is the basic requirement to achieve laboratory confirmation in 80 % of cases (‘Approaching measles elimination’) which corresponds to stage III of the WHO criteria.
Information on the social status of vaccinated vs. unvaccinated persons would make it possible to more efficiently select target groups that need the highest attention. However, detailed data thereon is hardly available. Particularly, there is a shortage of longitudinal studies on vaccination coverage and disease prevalence which take socioeconomic parameters into account.
Measels outbreaks in Germany show a clear correlation between low vaccination coverage and a higher probability of illness.
The comparison of vaccination coverage and incidence of measles between the different EU member states confirms this correlation; countries with higher coverage have a lower incidence than countries with a lower coverage, especially when viewed over a long time period.

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Discussion

From the authors´ point of view, deficits remain despite the efforts made during the past years to achieve herd immunity in Germany: i. e. there are still ample regional differences between and within German federal states. This increases the probability that infectious diseases spread in individual areas, as was shown during the recent outbreaks of measles.

The surveillance of measles in Germany is also problematic. Germany is far from achieving laboratory confirmation (by virus detection) in 80 % of cases, which is the WHO criterion indicating a reliable “surveillance”. Currently, Germany is at stage II (‘Measles control’) according to the WHO criteria. During interviews, experts pointed out that no directives exist on how to monitor progress and what measures should be taken in case WHO targets are missed.
Regarding regional differences, a practical implementation or operationalisation of WHO targets at regional level is of great importance for Germany: the lack of vaccination targets in Germany represents a major deficit.

Economic evaluation

Methods

A systematic literature search, supplemented by hand search, was performed in international literature data bases. For the selection of literature assessed, studies calculating the cost per measles case (disease cost analysis) or including a cost effectiveness, cost benefit or cost utility analysis were used. Studies selected mainly focused on Germany and other European countries, as well as the USA, Canada and Australia. Economic analyses comparing different vaccination strategies were also considered. References with publication date between 1999 and 2004 were included.

Results

Analysis of the literature showed that no comprehensive economic analysis (cost effectiveness, cost benefit or cost utility analysis) of the MMR vaccination program in Germany is available. However, an international analysis exists which estimates the annual societal disease costs per case of measles for ten Western European countries, among them Germany. This study describes the average disease costs per case of measles to range between 165 Euro (Spain) and 373 Euro (Denmark); with 263 Euro, Germany is placed at midrange. These are the costs (direct and indirect) which could be saved for every prevented measles case. Other analyses of disease costs, e. g. for Belgium, estimated average costs per measels case to range between 320 Euro (for children < 4 years of age) and 625 Euro (for adults > 20 years of age) for society as a whole. For Austria, the ÖBIG (Austrian Health Institute) estimated a net benefit of 593 Euro for every measles case prevented.
There was only one economic study, which evaluated not only measles vaccinations but a total MMR vaccination program. This study evaluated a cost-benefit ratio in favour of the MMR vaccination program of 1 : 14.2 (health care system) or 1 : 26 (society as a whole) compared to the alternative of ‘no vaccination program’. This means that the monetary benefit of the MMR vaccination program is 14.2 times higher than its costs from the point of view of the health care system and 26 times higher from the point of view of society as a whole. Even though vaccination coverage of the population with the second MMR dose causes high economic costs per additional prevented measles case, it is crucial for the elimination of measels.
Results of the international analyses cannot easily be transferred to Germany (different settings, medical practise, cost structures etc.). To make detailed economic predictions for Germany, the development of a complex economic model calculation is essential. One of the main problems is that relevant data are not or only incompletely available (particularly valid epidemiological data) and therefore need to be estimated.

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Discussion

In international publications, mainly measles have been validated economically. The wide range of results described in the available disease cost analyses for measles has various reasons: the accuracy of the results mainly depends on incidences during the study period and the level of vaccination coverage; however, documentation of these data is often fragmentary. Furthermore, the disease cost analyses do not always include the same cost types (e. g. if costs for persons in need of care or loss of production are considered). In addition, the different cost structures (e. g. cost of the vaccine, distribution costs, costs of hospital stays etc.) in health care systems of the countries compared are mirrored in the economic results. As the peculiarities of each country's health care system lead to different cost structures, uncritical transfers of results between other countries is not feasible. Despite these restrictions, economical studies can show the potential financial benefit which may be achieved trough the eradication of measles.

Immunisation concepts and programs

Methods

The systematic literature search was done using the key words 'mumps and measles and rubella' and 'MMR', each in combination with 'programs' and 'vaccination coverage'. Assessed were studies relating to Germany (focus on children and adolescents), studies relating to measures for achieving or maintaining high coverage levels and low incidences particularly for industrialised countries (such as the USA, The Netherlands, Finland), as well as studies analysing different intervention strategies. The information gained through the literature search on 'best-practice' countries was supplemented by information yielded through an internet search and provided by telephone or in written form. For international comparison, data on The Netherlands and Finland (e. g. on the organisation of the immunisation system) were supplemented by hand search and telephone interviews conducted with experts from these countries.

Results

Interventions to increase the immunization coverage were categorized in three main groups according to their goals:

- interventions increasing the demand for vaccinations,
- interventions improving access to vaccination services,
- interventions aiming at the providers (e. g. physicians) of vaccinations.

By means of ‚best-practice' models, vaccination strategies of other countries (Finland, the USA, The Netherlands) which lead to a high vaccination coverage and a low incidence, were described. The USA focus their immunisation policy on compulsory vaccinations in schools / day care facilities, whereas the Netherlands have developed a strongly centralised governmental immunisation system. This system features a central vaccination register listing vaccination data for all children, reminders, and free and easy access to vaccinations. Finland has a central immunisation strategy and national immunisation targets as well as guidelines which are evaluated on a regular basis. In addition, high importance is ascribed to informing residents on the pros and cons of vaccinations.

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Discussion

Interventions suitable to increase vaccination coverage are reminders to clients (provided in written, electronic or oral form) as well as provider based interventions.
Regarding the 'best-practice' countries, a central 'immunisation reminder system' as it is used in the Netherlands is of interest to Germany. The Finnish strategy, particularly concrete national immunisation targets would also be a useful choice for Germany, as the lack of specific regional targets represent a large deficit. Compulsory vaccinations such as in the USA are not compatible with the German constitution and are therefore not an option.

Conclusions

Despite efforts to increase the vaccination coverage rate, the WHO target of a vaccination coverage for measles of 95 % until 2007 and an elimination of measles and rubella until 2010 has not (yet) been achieved. From the authors' point of view, the following measures are necessary in order to achieve stage III A ('Approaching measles elimination') or III B ('Approaching measles elimination and prevention of congential rubella syndrome'):

1. **National Immunisation Targets:** A basic starting point is the development of a binding vaccination program in Germany.
2. **Plan for Implementation:** Clear structures and the assignment of responsibilities (between federal government, Laender, and health insurance funds) are necessary for implementing a national vaccination program.
3. **‚Surveillance'-System':** To achieve stage III ('Approaching measles elimination') according to the WHO surveillance guidelines, continuous observation and documentation of the development of the vaccination coverage, measles and rubella cases, possible complications and the origins of virus clades (endemically transmitted or introduced) are required. A total of 80 % of measles cases need to be laboratory confirmed by means of seroprevalence testing to fulfil the WHO criterion indicating a reliable "surveillance".
4. **Communication and Convincing:** Communication and convincing, e. g. through communication strategies and education programs for physicians and parents, are important for the implementation of a nationwide vaccination program.
5. **Evaluation:** It is necessary to regularly evaluate measures implemented to achieve immunisation targets. Currently, there are no directives on how to monitor progress and what measures should be taken in case targets are not met.
6. **Economic Issues:** To increase vaccination coverage a differentiated approach is suggested. First of all, the first dose coverage in regions with a coverage < 95 % needs to be increased. This measure involves the largest economic cost-saving. In regions with a coverage > 95 % (of the first dose) the coverage of the second dose is to be increased.

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