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Assessing the economics of vaccination for *Neisseria meningitidis* in industrialized nations: A review and recommendations for further research

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Objectives: To review the existing health economic literature on meningococcal disease vaccination.
Methods: A Medline search for economic evaluations of vaccination programs for meningococcal disease in developed countries was conducted. All identified studies were reviewed.
Results: Nine published studies were identified examining either mass vaccination during outbreaks or routine vaccination. Although net expenses were estimated in almost all studies, the resulting cost-effectiveness ratios varied widely. Vaccination of college-age students was found to be potentially cost-effective in Australia but not in the United States. With one exception, routine vaccination of children and adolescents in Europe was predicted to be cost-effective. Many simplifying assumptions were made, and important elements were often left out, in particular the potential for reduced transmission of disease.
Conclusions: The methods used and the vaccination strategies vary widely, and results do not provide strong grounds for making conclusions as to whether vaccination is cost-effective. Furthermore, in all instances, transmission of disease, changes in population carriage rates, and outbreaks are either ignored, dealt with using very broad simplifying assumptions, or are not necessarily generalizable to other settings. The analyses provide some insight into the potential cost-effectiveness of vaccination, but more importantly, they highlight areas requiring further study. Economic evaluations based on observed outcomes from recently implemented strategies would be helpful, as would more sophisticated health economic models. The choice of vaccination strategies cannot be based on the results of existing economic analyses.

Keywords: Meningococcal disease, *Neisseria meningitidis*, Cost-effectiveness, Review, Vaccines

Neisseria meningitidis is the most common cause of meningitis and sepsis, and although its incidence is low in developed nations, the potentially serious consequences of invasive disease make it an important public health concern. In the United States, for example, the average incidence from 1992 to 1996 was only 1.1 per 100,000 population, or roughly 2,500 cases per year (42). The disease, however, is associated with a case fatality rate of approximately 10 percent (16;42). Furthermore, for those patients who survive, rates of permanent sequelae are also high at between 11 percent and 19 percent and can include neurological disabilities, amputations, hearing loss, renal problems, and scarring (16;28).

Of the thirteen serogroups of *Neisseria meningitidis* that have been identified, A, B, C, Y, and W-135 are most commonly implicated in disease, with B and C making up the majority of cases in most industrialized countries.Serogroup distributions have changed over time, however, at times dramatically. For example, from 1998 to 1991, serogroup Y accounted for only 2 percent of all cases in the United States, but from 1992 to 1996 this had increased to 26 percent (25;42).

Although the vast majority of cases in developed nations are due to endemic disease, there is growing concern about the increasing rate of outbreaks in several countries (2;23;34;43;53;54). In addition to periodic outbreak campaigns, several large-scale mass vaccination campaigns against meningococcal disease have been undertaken, including well-documented ones in Quebec and Spain (9;10; 39;45;46). In the United Kingdom, routine vaccination of all children against serogroup C disease was initiated in 1999 to combat both endemic and epidemic disease (34).

Although incidence is typically highest in infants, outbreaks and an increasing incidence in adolescents and young adults have also garnered greater attention (8). Incidence of disease in college and university students, in particular, has been the subject of numerous recent studies, although identification of this population as a "high-risk" group to be targeted for vaccination has been controversial (7;18–20;27;35;36).

Until recently, polysaccharide vaccines were the only type of meningococcal vaccine available (quadrivalent A, C, Y, W-135 in the United States). While these vaccines are effective, new conjugate vaccines are now available or in development. Conjugate vaccines are thought to be highly effective and to provide longer-lasting protection (41). Currently, only a single-target conjugate vaccine for serogroup C disease is available, although a quadrivalent conjugate vaccine (A, C, Y, W-135) is now in development. A vaccine for serogroup B disease, for which there is currently no effective vaccine, is also in development.

While the consequences of invasive infection can be devastating, the low incidence of disease and relatively high cost of vaccines calls into question the economic viability of routine vaccination against meningococcal disease. The availability of new, more effective vaccines may lead to renewed calls for expanding their role. Decisions on whether to implement routine or even one-time mass vaccination campaigns should consider economic efficiency. In this study, we review published health economic studies for meningococcal disease vaccination to determine the cost-effectiveness of possible vaccination strategies and whether existing research and data are sufficient.

Considerations for Economic Evaluations of Vaccination Programs

Economic evaluations of vaccination for infectious disease are complex because of the potential for "herd immunity"—the protective benefits conferred upon the individuals who are not vaccinated due to changes in the transmission of disease (17).Vaccination of a significant proportion of the population reduces the opportunity for the infection to spread by decreasing the chance of others coming into contact with an infectious individual. In the extreme, a sufficiently effective, widely used vaccine may lead to eradication of the disease, eventually eliminating the need for further vaccination, as has been observed with smallpox and polio. It is also possible that herd immunity might have negative consequences. For example, herd immunity to varicella could delay infection in unvaccinated individuals to adulthood when it is more dangerous (6). In the case of meningococcal disease, infection is serious at any age, although case fatality rates are higher in adolescents than in infants. The impact of a shift in the age distribution of cases, however, has not been evaluated nor has the potential herd immunity benefit, given that the vast majority of cases are due to endemic disease. Mass campaigns in Spain and Canada, as well as the recent routine vaccination for serogroup C meningococcal disease in the United Kingdom, however, indicate that significant disease reductions in at least some parts of the unvaccinated population are attained as a result of vaccination (9;39;40;45;46).

Furthermore, the seriousness of meningitis and the intense public reaction during outbreaks routinely force health authorities into widespread and expensive outbreak control measures (9;30;38). Routine vaccination may reduce or even eliminate the need for such measures.

A full accounting of the health economic benefits of any vaccine policy for meningococcal disease needs to consider more than the costs of the vaccine itself. These include vaccine wastage, the cost of administering the vaccine (e.g., syringes, professional time, etc.), and the costs associated with any adverse reactions. Funding for the program in terms of education campaigns, as well as wages and capital costs associated with administering the program, may also be substantial and need to be accounted for. Savings associated with the reduced number of cases in the population need to be incorporated, making it necessary to estimate the full costs of the disease.These costs can include both the direct medical cost associated with managing the illness and its aftermath, as well as indirect costs due to lost productivity at work and other activities.While assigning value to these indirect costs is not straightforward, they should be accounted for if a societal perspective replaces that of a health-care payer (29;32).Another potentially important saving to consider is that of the reduced need for outbreak control measures.

Any changes in costs need to be examined in light of the health benefits attained, not just those conferred upon vaccinated individuals, but those that might result from herd immunity as well. In a cost-effectiveness analysis, benefits could be measured as cases avoided, but other outcomes such as deaths averted and life years gained should also be considered. These benefits may be assessed by using quality- or disability-adjusted life years gained, or by assigning a monetary value to the health outcomes using a technique such as willingness-to-pay (26).

METHODS

A Medline search for economic evaluations of vaccination programs for meningococcal disease in developed countries was conducted. The search covered from 1985 through 2002 and included English, French, and Spanish language articles. The following search criteria were used: "Meningococcal" or "Meningitis" and "Cost" and "Vaccine," "Meningococcal" or "Meningitis" and "Economic," "Meningococcal" or "Meningitis" and "Model" and "Vaccine." Articles that evaluated both economic and effectiveness outcomes in developed countries were selected for detailed review. Bibliographies of all selected articles were also reviewed to identify other potentially relevant studies.

Given the small number of analyses identified, all were included in the review. No formal quality assessment was used in determining which studies would be included, and adjustment was unnecessary as no meta-analyses were pursued. This approach was believed to be more informative, especially because no accepted standard exists for assessing the quality of economic evaluations, particularly given the very heterogeneous methods used.

RESULTS

Since 1995, nine economic evaluations of vaccination strategies for meningococcal disease in industrialized countries have been published—the majority in the past 4 years. Three have been set in North America, four in Europe, and two in Australia (Table 1) (4;11;24;37;44;47;48;49;51). Six analyzed polysaccharide vaccines, only one each a conjugate vaccine and a B outer-membrane vesicle vaccine, and one did not specify the vaccine type. With the exception of an analysis set in Quebec, Canada, all used models to assess the health economic consequences (11). Even the Canadian study incorporated some modeling elements.

United States

Two economic models with a U.S. setting have been published, both evaluations of routine administration of a quadrivalent polysaccharide vaccine to students entering college (24;47). The earliest of these followed a hypothetical cohort of 2.3 million freshmen over a period of 4 years (24). The evaluation considered only benefits to vaccinated individuals but included both direct and indirect costs, using the human capital approach to value lost earnings from premature death. The value of benefits to individuals and society was not included. Ratios of savings from reduced number of cases divided by costs of vaccination were calculated assuming a cost per vaccine dose of $15 (1992 U.S. dollars). Based on the reported effectiveness of the vaccine in the literature, efficacy was set at 85 percent. Cost of meningococcal disease was estimated at $8,145 per case, but heavily based on assumption. Results, calculated over a range of incidence to address uncertainty in this parameter, varied from net costs of almost $47 million (savings to vaccine cost ratio of 0.16) if incidence in college students was the same as in the general population of similar age, to savings of $7.6 million (ratio of 1.1) if incidence were 15 times higher. The authors estimated that incidence in college students was no higher than 1.3 per 100,000, a rate that results in estimated net costs of roughly $45 million. Savings came primarily from reductions in work productivity losses, with direct costs making up only around 5 percent of total savings. While the results of this study were negative, key elements were missing in the analysis, which, if included, may have led to more favorable outcomes. For one, the long-term costs of caring for individuals with serious disability were not included. These costs can be substantial and are almost certainly greater than the initial acute-care costs. The analysis also failed to look at the indirect benefits of vaccination to unvaccinated individuals resulting from herd immunity, or the possibility that routine vaccination of college students could potentially avert the need for costly emergency vaccination measures in the event of an outbreak.

Results of the more recent U.S. analysis were also not very favorable (47).That analysis followed a hypothetical cohort of first-year college students for four years.Only students living in dormitories were targeted for vaccination, as updated incidence data for meningococcal disease indicated that these individuals are at a higher risk of infection (incidence set at 3.04 per 100,000 in the model, based on 4 years of surveillance data from the U.S.). Both direct and indirect costs were included, with lost productivity due to premature death and long-term disability valued using the human capital approach.Cost estimates were from diverse sources and included values used in the earlier U.S. study (24). Neither long-term medical costs of disability nor benefits resulting from herd immunity were considered. Vaccine efficacy of 85 percent, based on results reported in the literature, was assumed, and costs for the vaccine ranged from $36 (wholesale price of a 10-dose vial) to $68 (wholesale price for a single-dose vial) per vial (1999 U.S. dollars). In all cases, despite the relatively high incidence of disease in this group, vaccination led to increased costs; and the best estimate of cost per case averted was $0.6 million. Net costs per life

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Table 1. Characteristics and Conclusions of Economic Analyses of Meningococcal Vaccination Programs

Study	Country & Currency Year	Target Population	Vaccine Investigated	Summary Outcome Measures	Analysis Result	
Jackson 1995	U.S.A., 1992	College students	A, C, Y, W-135 polysaccharide	Ratio of savings from reduced disease to vaccine costs varying incidence	1 per 100,000 3 per 100,000 7.5 per 100,000	0.16 0.46 1.1
Round 1999	U.K., not provided	School children	C polysaccharide	Cost-effectiveness	Per case prevented Per death avoided	£220,939 >£2 million
Skull 2001 (#1)	Australia, 1999	Adolescents	A, C, Y, W-135 polysaccharide	Cost-effectiveness[a]	Per case averted Per life saved Per DALY averted	$4,470 to $146,781 $2,042 to $66,917 $1,823 to $58,812
Skull 2001 (#2)	Australia, 1999	Adolescents	A, C, Y, W-135 polysaccharide	Cost-effectiveness[a]	Per case averted Per life saved Per DALY averted	$2,420 to $101,546 $1,109 to $46,532 $990 to $41,541
Scott II 2002	U.S.A., 1999	First-year college students living in dormitories	A, C, Y, W-135 polysaccharide	Cost-effectiveness	Per case prevented Per death avoided Per life year saved	$0.6 to $1.9 million $7 to $20 million $62,042 to $489,185
Bos 2002	The Netherlands, 1998 Euros	Infants	B outer-membrane vesicle	Cost-effectiveness	Per life year saved Per QALY gained	£21,415 £15,721
Oostenbrink 2002	The Netherlands, 1996 Euros	Individuals 0.1 to 15 years	Not specified	Cost-effectiveness	Per QALY gained	£22,635
Trotter 2002	U.K., 2000	Individuals under 18 years	C conjugate	Cost-effectiveness	Per case averted Per life year saved	£18,112 £6,259
De Wals P 2002	Canada, 1993	Individuals 0.5 to 20 years	A, C, Y, W-135 polysaccharide and A, C polysaccharide	Cost-effectiveness[b]	Per death averted Per life year saved Per QALY gained	$1.7 to $3.0 million $58,000 to $105,000 $49,000 to $87,000

[a] Two options are considered: vaccinating all students in years 10–12 and first year university in high-incidence region, vaccinating all students in year 12 in low-incidence region. Results are presented excluding the costs of lost earnings, as cost-effectiveness ratios including these costs were not reported. When lost earnings are included, the first option is expected to lead to savings, while the second is expected to lead to incremental costs.
[b] Outcomes are presented for direct immunity only and for direct and herd immunity combined.
DALY, Disability adjusted life year; QALY, Quality adjusted life year.

year gained were quite unfavorable, ranging from $62,042 to $489,185. Despite the higher incidence from the earlier study, results were largely consistent between the two U.S. analyses. However, as with the earlier study, the long-term medical costs of disability, herd immunity, and the impact on outbreak measures were not taken into consideration.

Canada

The Canadian study was an analysis of an actual one-time mass vaccination of all residents 0.5 to 20 years of age with bivalent or quadrivalent polysaccharide vaccines in the province of Quebec between 1992 and 1993 after an outbreak of serogroup C disease (11). Effectiveness was estimated by comparing actual incidence after the campaign with expected incidence given prior experience in Quebec (48 cases were averted due to direct immunity and a further 26 due to herd immunity) and the costs from a survey and government statistics. Both health-care and productivity costs were included, as was long-term management of sequelae. A scenario incorporating herd immunity was also analyzed. The actual data were supplemented by projecting the long-term consequences of infection, both in terms of costs and health (life years lost and quality-adjusted life years lost). The net societal costs ranged from $18 to $21 million (1993 Canadian dollars) with cost-effectiveness ratios of $105,000 per life year gained and $87,000 per quality-adjusted life year gained when only direct benefits were included. These dropped to somewhat more modest levels in the scenario with herd immunity ($58,000 and $49,000). These cost-effectiveness results, however, rest on the assumption that changes in incidence were due entirely to the vaccination campaign and not other factors. Given variations in year-to-year incidence, and considering that mass vaccination in Quebec took place after a fairly sharp increase in incidence, the possibility that at least some of the decrease in incidence may have occurred in the absence of vaccination cannot be entirely discounted.

United Kingdom

The earliest of the two UK studies focused on prevention of serogroup C disease in schoolchildren, comparing

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several strategies, including attempting to eradicate carriage in households where the strain is circulating, prophylaxis or vaccination of all pupils in a school where one case appears, and routine vaccination of all school age children every 3 years. Vaccination in all cases was with a polysaccharide serogroup C vaccine (£7.25 per dose with efficacy of 85 percent) (44). Only acute medical-care costs were included (neither long-term sequelae nor indirect costs were explicitly considered). The analysis includes both the direct impact of vaccination, as well as the benefits of reduced disease transmission. The latter were calculated based on estimates of the number of contacts of the index case of disease, the relative risk of infection given contact with the index case, and changes to that risk given the effectiveness of vaccination and/or chemoprophylaxis. The time horizon of the analysis was not specified. The analysis found that vaccination strategies were not as cost-effective as other strategies in dealing with the appearances of serogroup C disease, although they did prevent the most cases. Routine vaccination every three years was the most effective option, preventing almost 20 times more cases than household and close contact tracing, but had particularly poor results with the cost per case prevented relative to the next most effective option estimated at £220,939 (or roughly £2 million per death avoided). Whereas epidemiologic inputs derived from the literature and used in the model seem reasonable, reporting of methods for this model is sparse, making it difficult to establish whether these methods were appropriate. The cost per case of meningococcal disease is also not clearly reported, but as it excludes all long-term costs associated with premature death or disability, it likely seriously underestimates the economic consequences of cases.

More recently, an analysis was undertaken on the potential cost-effectiveness of establishing routine meningococcal group C disease vaccination in individuals under 18 years in the United Kingdom using a conjugate vaccine (£12 per dose, at efficacy of between 92 and 97 percent) (51). Unlike the other UK analysis, vaccination for group C disease was found to have a good chance of being cost-effective, with the cost per case averted in the base case estimated at £18,112 (2000 UK pounds), and the cost per life year gained at £6,259. Although both studies included only health-care costs, several differences help explain the variance in outcomes. The more recent study included the lifetime costs of treating patients with permanent sequelae, ranging from £500 to £21,500 per year over a lifetime and more than doubling the annual cost of disease. These long-term cost estimates, however, were based almost entirely on assumption. The effectiveness of the conjugate vaccine was estimated to be higher than that for the polysaccharide vaccine. A major difference is how benefits to non-vaccinees were modeled. In the earlier UK study, rates of secondary disease were explicitly modeled while the second study assumed that vaccination would eliminate all 11 outbreaks of serogroup C disease estimated to occur each year, and costing £245,500 per outbreak. This accords vaccination an annual savings of over £2.5 million—with no evidence to base it on.

The Netherlands

Two studies have also been published for The Netherlands. One study only briefly examined the potential cost-effectiveness of vaccination (type of vaccine unspecified), as the main focus was to assess the cost-utility of various strategies for diagnosis of children presenting with meningeal signs (37). The analysis included only acute health-care costs. Routine vaccination of 195,749 children with a four-dose regimen was estimated to prevent 111 cases in the vaccinated children each year, resulting in a cost-effectiveness estimate of €22,635 per quality-adjusted life year gained (1996 euros).These positive results, compared to outcomes in other studies, are heavily dependent on the surprisingly high incidence of *Neisseria meningitidis* used in the study: approximately 173 cases annually in a population of 195,749 children, or almost 90 cases per 100,000 children.

A more detailed analysis was published on the cost-effectiveness of routine vaccination of Dutch children with a hexavalent serogroup B outer-membrane vesicle vaccine (assumed €10 per dose, 90 percent efficacy for 3 years after 4 doses) (4).This study followed a cohort of Dutch children over 76 years and included both direct and indirect costs, although lost productivity costs were limited to those costs associated with parents missing work because of illness in their child. The long-term care costs for those with serious sequelae were included. Only cases avoided in vaccinated children were considered (no herd immunity). Cost-effectiveness was estimated at €15,721 per quality-adjusted life year gained (1998 euros).These by-in-large positive results can also be attributed, in part, to a relatively high incidence of disease in the target group in the absence of vaccination: ∼15 to 20 cases per 100,000 children 0 to 5 years of age, and 2 to 4 cases per 100,000 in the general population.The inclusion of long-term care costs for those with permanent disability also leads to an attractive cost-effectiveness ratio.

Australian Analyses

Two publications for Australia have used the same economic model and inputs, although reporting somewhat different results (48;49). These analyses addressed a similar question to that posed in the U.S. studies: what is the cost-effectiveness of vaccinating Australian adolescents 15 to 19 years of age with a quadrivalent polysaccharide vaccine ($30 per dose in 1999 Australian dollars, assumed 90 percent efficacy for 5 years).Two scenarios were modeled: vaccination of all students in grades 10 to 12 and first-year university students in a 'high' incidence region (at least 20 cases per 100,000 for those 15 to 19 years old), and vaccination only of grade 12 students in a region with lower (general population) incidence (6 per 100,000). Both direct and indirect costs were included, although cost-effectiveness ratios were calculated

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only with direct costs. Herd immunity impact on cases avoided was not factored in but the costs associated with decreased need for outbreak control were. Discrepancies in results between the two studies, despite using what appear to be identical methods, makes interpretation difficult, and raises the possibility of methodological errors in one or both of the analyses. Generally, though, vaccination was found likely to be cost-effective or even to lead to savings in high-incidence regions. It also was found to have the potential to be cost-effective in general-incidence regions when both direct and indirect costs were considered.

Adequacy of Existing Economic Analyses

Economic analyses published to date differ greatly in methods, data sources, assumptions and results. Given the large discrepancies and absence of a comprehensive analysis, neither trends nor definitive conclusions can be drawn in any country. Table 2 outlines some of the differences and assumptions in economic evaluations to date.

Results are inconsistent across studies. Whereas one UK study found routine vaccination of schoolchildren with a polysaccharide to be highly cost-ineffective, another found that vaccination with a conjugate vaccine of all individuals under the age of 18 was likely to be cost-effective (44;51). It is unclear to what extent these differences can be attributed to the different approaches and inputs used in each study. Differences in the potential impact of vaccination on outbreaks and costs per case of meningitis all likely play some role, as do differences in efficacy between the polysaccharide and conjugate vaccines. The largely negative results regarding vaccination of college students found in two U.S. studies contrast with the much more positive results presented in analyses for Australia (24;47;48;49). Some of these differences result from dissimilar inputs: the incidence used in the Australian studies, for instance, was much higher than those used in the U.S. studies, suggesting that, even at relatively low levels of disease, differences in incidence in groups targeted for vaccination can be a strong determinant of vaccination's cost-effectiveness.

Differences in costs and outcomes considered (e.g., long-term disability) in the various analyses also are important. The potentially high costs of permanent sequelae, for example, have often not been considered, thereby seriously underestimating cost savings from avoided cases of meningococcal disease. Similarly, the exclusion of indirect costs, especially as they pertain to lost work productivity due to premature death or disability, will grossly underestimate the societal benefits associated with vaccination. Compounding this problem, economic analyses to date have made important simplifying assumptions about the epidemiology of meningococcal disease. Of note, only two studies have made some attempt at calculating the impact of herd immunity (11;44) and two at assessing the reduced need for outbreak control measures (48;49;51). As the study in Quebec demonstrated (11), the indirect benefits resulting from herd immunity can change cost-effectiveness results significantly, indicating that failing to take these into consideration may compromise the validity of estimates. Outbreak control measures can also be costly, and avoiding the need for these measures has not been adequately addressed. No published economic evaluation to date has attempted to assess the health economic implications resulting from long-term changes in disease incidence (e.g., eradication, shifting age of infection, changes in population carriage rates, etc.) resulting from large vaccination campaigns, which could all have major effects on the cost-effectiveness of vaccination.

Despite these shortcomings, these studies do provide some insight into the potential cost-effectiveness of vaccination. Clearly, incidence of disease is an important determinant of potential cost-effectiveness, with relatively small changes having a major impact on results. This finding is especially

Table 2. Aspects Considered in Economic Evaluations of Vaccination for Meningococcal Disease

Study	Direct and Indirect Costs Included?	Long-Term Disability Considered?	Herd Immunity Considered?	Costs of Outbreak Control Considered?	Long-Term Changes in Epidemiology Considered?
Jackson 1993	Yes	No	No	No	No
Round 1999	Direct only	No	Yes	Yes	No
Skull 2001 (#1,#2)	Yes	DALYs & indirect costs	No	Partially	No
Scott II 2002	Yes	Indirect costs only	No	No	No
Bos 2002	Yes[b]	Yes	No	No	No
Oosterbrink 2002	Direct only	Yes	No	No	No
Trotter 2002	Direct only	Yes	Partially[a]	Yes[a]	No
De Wals 2002	Yes	Yes	Yes	Mass campaign for outbreak control	No

[a] Herd immunity was included only insofar as it was assumed that, after vaccination, outbreaks would be eliminated. The costs of cases avoided due to herd immunity were not included.
[b] Only lost work productivity for parents of infected children were included.
DALY, Disability adjusted life year.

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true when, in addition to acute-care costs, the long-term cost and quality-of-life implications of disease-related sequelae are considered. The economic evaluation of the mass vaccination campaign in Quebec (11), also highlighted the importance of herd immunity as a potential determinant of any vaccine strategy's cost-effectiveness.

A more rigorous analysis of the epidemiological impact of vaccination for meningococcal disease is essential for proper health economic estimates. The Quebec study goes the furthest in terms of exploring the overall consequences of vaccination, but the results presented in that study are for a specific strategy and primarily observed outcomes—a framework for analysis of other programs under consideration is not provided (11).

Possible Directions for Future Research

Existing economic assessments of vaccination strategies against meningococcal disease do not allow for definitive conclusions on the desirability of new strategies but can serve as an important first step in understanding the health and economic consequences of meningococcal disease and the aspects of the disease and vaccination that are strong determinants of economic outcomes. They are also helpful in identifying areas where further research or data are required.

The greatest limitation of existing studies has been the relatively simple approach taken in dealing with the epidemiological consequences of vaccination given the complexity of this question (3;6;14). A more sophisticated approach to the modeling of the epidemiology of meningococcal disease, consistent with its actual complexity of this impact, should provide more definitive estimates. Complex, age-structured dynamic transition models, have been used to evaluate both the short- and long-term consequences of large-scale vaccination programs for other infectious diseases (12;13;21;22;31). These models compartmentalize populations into various susceptibility categories (e.g., completely susceptible to infection, immune, partially immune, infectious, etc.), and by incorporating assumptions on mixing patterns in the population, information on the duration of protection from infection (either due to vaccination or prior infection), and data on the strength of transmission, can estimate the number of cases in a population over time. While powerful, these models have extremely intensive data requirements; thus, the accuracy of estimates is often hampered by important data gaps. Given the availability of adequate data, these types of models should allow for a better understanding of both the direct and indirect benefits, and consequently on the cost-effectiveness, of vaccination.

Another, more flexible approach may be discrete event simulation (15). While these simulations have not been widely used in health economic evaluations, studies using the technique are beginning to appear; with the most prominent case being a recently published study comparing various smallpox management strategies (5). Discrete event simulations allow for modeling to occur at the level of the individual, with individuals in a population passing through the model based on events occurring at discrete time periods. Individual characteristics, prior events and environmental factors (including events in the rest of the population) can all be used to determine the risk any given individual is exposed to over time. The timing of future events resulting from these risks can then be calculated, and a stochastic element can be introduced by sampling from appropriate probability distributions. Although potentially just as data intensive as transmission dynamic models, the greater flexibility may allow the analyst to overcome some data gaps.

Regardless of the modeling approach adopted, however, lack of data in certain areas will limit the precision of economic estimates for meningococcal disease vaccination, and estimated outcomes should be reported along with sensitivity analyses on key model inputs. For example, only limited data exist on the long-term protection of the conjugate C vaccine, and none on the newer quadrivalent vaccines in development. Furthermore, whether or not mass vaccination will lead to capsular switching of meningococcal strains will clearly have an impact on the long-term cost-effectiveness of any immunization campaign. Data from mass vaccination campaigns are filling some of these needs (1;9;33;45;50;52) and may prove useful for validation of new health economic models.

CONCLUSIONS

Given budget constraints facing decision-makers, health economic evaluations are necessary to gauge the appropriateness and feasibility of implementing an intervention. Increased opportunities to prevent infection from *Neisseria meningitidis* are arising with the availability of newer meningococcal vaccines. The expected high unit cost of these vaccines, however, as well as the large investment required for any mass campaign or routine vaccination program mandate further health economic studies. Although existing studies have provided a solid foundation, further research and the development of models with greater sophistication and scope will provide decision-makers with the tools and information necessary to evaluate vaccination strategies more precisely.

Policy Implications

Existing cost-effectiveness studies of vaccination for meningitis yield conflicting estimates of the economic efficiency of implementing widespread vaccination programs. It appears that very high efficacy for prolonged periods plus a substantial increase in herd immunity and reduction in outbreaks are required for vaccination to be in a cost-effective range. This finding is particularly true if the incidence is in the range reported in most industrialized countries. In addition, a wide perspective that encompasses both long-term sequelae and indirect costs must be taken. While other considerations, such as calming public anxiety—especially in times of outbreaks—may move policy makers to implement either routine or mass vaccination programs, these decisions cannot be based on existing health economic analyses. Funding the development of adequately sophisticated epidemiologic and economic models, and the collection of data required to populate them, must be considered.

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