

REVIEW

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A guideline for economic evaluations of vaccines and immunization programs in China

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ABSTRACT

This study aimed to develop a consensus framework for economic evaluations of vaccines as a national guideline in China. Some unique and important aspects were particularly emphasized. Nineteen Chinese experts in the field of health economics and immunization decision-making were nominated to select and discuss relevant aspects of vaccine economic evaluations in China. A workshop attended by external experts was held to summarize unique and important aspects and formulate consensus recommendations. There were ten unique and/or important aspects identified for economic evaluations of vaccines in China, including study perspectives, comparator strategies, analysis types, model choices, costing approaches, utility measures, discounting, uncertainty, equity, and evaluation purposes. Background information and expert recommendations were provided for each aspect. Economic evaluations of vaccines should play an important role in China's immunization policy-making. This guideline can help improve the quality of economic evaluations as a good practice consensus.

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Introduction

In the past four decades, mainland China (hereafter referred to as China) has achieved tremendous gains in preventing and controlling vaccine-preventable diseases and improving overall population health by promoting its immunization programs.^{1,2} China's National Immunization Program (NIP) currently provides 14 vaccines against 15 infectious diseases, which are completely sponsored by national and local governments.³ There are also some non-NIP vaccines (i.e. for Rotavirus, Hib, PCV, and HPV), available for the public to be voluntarily vaccinated and self-paid.⁴

Vaccines can prevent and control infectious diseases and are regarded as a special group of drugs with longer and broader benefits. Evaluation methods of vaccines and immunization programs are available in the literature. Particularly, we reviewed the most important vaccine economic guidelines from the World Health Organization (WHO), the European Community, the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), and the Advisory Committee on Immunization Practices (ACIP) in the USA, which have been widely applied.^{5–10} Economic evaluations of

vaccines and immunization programs help allocate scarce health resources in the context of budget constraints. When introducing new vaccines into immunization programs in high-income countries and international organizations, results of health economic evaluations are often considered by national immunization technical advisory groups (NITAGs) or equivalent national institutions. In China, the National Immunization Program Expert Advisory Committee founded in 2017 also requires health economic evidence.

The vaccine market and immunization programs in China are rather unique and different from other countries.¹¹ China has the largest private market of non-NIP vaccines in the world, which are paid for by individuals instead of public funders or health insurance programs. NIP vaccines (i.e. DTP and MMR) are provided at very low prices in China, with high coverage rates of more than 95% among the eligible population.¹² Non-NIP vaccines (i.e. PCV13 and HPV) cost much more in China, and some are even sold at higher prices than those in developed countries.¹³ Some non-NIP vaccines have been introduced to China's immunization market for a long time, but their coverage rates remain suboptimal and diverse among different population groups. Almost all these

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non-NIP vaccines were recommended by the WHO to be included in NIP. All these unique features in China lead to different study backgrounds, study perspective, analysis type, comparative vaccine strategies (private market of non-NIP vaccines and adding them into NIP), cost approaches, etc. The economic evaluation of vaccines has not been used in immunization policy-making in China, even if there are increasingly more relevant studies published in both Chinese and English. An urgent need for economic evaluations of vaccines in China is how to economically add non-NIP vaccines into NIP or provide free non-NIP vaccines by local governments.

A systematic review reported poor quality of vaccine economic evaluation studies in China and suggested local guidelines for good practice and reporting.¹⁴ Comprehensive guidelines or frameworks on conducting vaccine economic evaluations and implementing the findings in decision-making are needed in China. In addition, it is still worth making discussions on several important and/or unique aspects of vaccine economic evaluations. A guideline for economic evaluations of vaccines and immunization programs specially designed for China will help domestic policymakers understand the values of vaccines and immunization programs, know how to introduce the most cost-effective vaccines into NIP, adjust the present NIP vaccines, and improve equity of non-NIP vaccines.

A Joint Center for Vaccine Economics was founded by Peking University Health Science Center and Chinese Center for Diseases Control and Prevention in 2019, with the main tasks of promoting economic evaluations of vaccines and immunization programs in China and serving working groups of the National Immunization Expert Advisory Committee in China. Members of the vaccine economic community in China, mainly from universities and centers for disease control and prevention, jointly developed a guideline on how to deal with relevant aspects in the field of economic evaluation of vaccines in 2021–2022.

This study emphasizes the importance of economic evaluations of vaccines in China and strongly suggests that evaluation results should be used as one criterion for including vaccines in local, provincial, and national immunization programs in China. This study aimed to provide a consensus guideline for economic evaluations of vaccines in China, focusing on ten important aspects which could also provide a reference for other developing countries and/or middle-income countries still with many non-NIP vaccines.

Methods

The Joint Center for Vaccine Economics between Peking University Health Science Center and Chinese Center for Diseases Control and Prevention invited 19 experts (authors of this paper) in the field of health economics, pharmacoecomics, and immunization policy to develop a framework for the economic evaluations of vaccines and immunization programs in China in 2021. Two criteria were used to select Chinese experts from academia and national public health agencies: published important articles about health economic evaluations of vaccines; and/or a member of working groups of

China's National Immunization Expert Advisory Committee. Experts employed by pharmaceutical companies were not invited to avoid potential and perceived conflicts of interest.

A published systematic review of economic evaluations of vaccination programs in China provided a very clear background up to 2015.¹⁴ We also did a literature review about the unique or most important aspects of economic evaluations of vaccines published after 2015. Pertinent aspects were identified from the published literature and expert discussions on the most important opinions and issues. In the opening workshop conducted on February 6, 2021, 19 experts in the field of health economics, pharmacoecomics, and immunization policy-making in China selected the most important aspects for discussion and participated in two rounds of online workshops. Three experts work in one group to provide professional opinions on one aspect (a total of 10 aspects finally identified in the opening workshop) for the China guideline. One senior expert worked as the lead expert, and two experts assisted in reviewing the relevant guidelines, previous literatures, and unique background in China. Consistent opinions were reached in each group, and the senior expert made the final decisions. If some opinions were not consistent within the specific group, those would be evaluated by all the experts in the second workshop.

Four guidelines for economic evaluations of vaccines and immunization programs from the WHO, ISPOR, Europe, and the USA were carefully referred to.^{7–10} The Guideline for Economic Evaluations of Vaccines in China was drafted by experts for further revisions and discussions. On September 12, 2021, an online consultation was attended by 74 external experts from China with very diverse backgrounds in health economics, health service research, epidemiology, disease prevention and control, child and adolescent health, vaccine and immunization, etc. External experts, who are acknowledged at the end of this paper, provided their comments and suggestions on the draft version of the Guideline for Economic Evaluations of Vaccines in China. Later on, the guideline was reviewed and revised by all 19 experts.

Results

International, regional, and national guidelines for economic evaluations of vaccines have provided a comprehensive framework on most technical and non-technical aspects of vaccine economic analyses. The Guideline for Economic Evaluations of Vaccines in China also covered all of the above aspects. In the present study, ten aspects were listed concerning unique and/or important features of vaccines and immunization programs in China. For each aspect, background information in China is provided in [Table 1](#), and expert recommendations are formulated in [Table 2](#).

Study perspectives

In China, NIP vaccines are financed by governments' fiscal funds^{13,15} while most non-NIP vaccines are totally paid for by individuals at the national level.¹⁶ Provincial governments in China have the authority to include non-NIP vaccines in local vaccination programs,¹⁵ and increasingly more local

Table 1. Ten Items for economic evaluations of vaccines and background in China.

Aspect	Background in China
Study perspectives	<ul style="list-style-type: none"> Both NIP vaccines and non-NIP vaccines exist in China. NIP vaccines are completely financed by governments fiscal fund, and non-NIP vaccines are self-paid. Public health insurance does not cover vaccines or immunizations.
Comparator strategies	<ul style="list-style-type: none"> More new vaccines have been introduced into China. Coverage rates of NIP vaccines in China are fairly high, but those of non-NIP vaccines are diverse. Comparator vaccination strategies for NIP and non-NIP vaccines may be different.
Analysis types	<ul style="list-style-type: none"> Very few economic evaluations of vaccines in China justified the analysis types used. Vaccination in China was not compared with non-vaccine intervention. More funds and resources are needed in China to expand NIP.
Model choices	<ul style="list-style-type: none"> Static models are often used in China, even if dynamic models are more appropriate. No justification of model choices was made. A few economic evaluations of vaccines in China have used dynamic models.
Costing approaches	<ul style="list-style-type: none"> The micro costing has more advantages than the macro costing Macro costing approach are commonly used in economic evaluations of vaccines in China. Major components of vaccination programs were often not included.
Utility measures	<ul style="list-style-type: none"> Utility measures, such as QALY and DALY, were often not reported in economic evaluations of vaccines in China. Utility measures of vaccine-preventable diseases are often from other countries instead of China. Very few economic evaluations of vaccines in China used DALY.
Discounting	<ul style="list-style-type: none"> Both uniform and differential discounting are mythologically sound in international guidelines. Health outcomes may or may not be discounted. China has higher interest rates and economic growth rates than other countries, which may affect discounting rates.
Uncertainty	<ul style="list-style-type: none"> Uncertainty is related to methodological choices, model structure, and values of parameters. Economic evaluations of vaccines in China used sensitivity analyses to account for uncertainty. Univariate sensitivity analyses of parameter values were often used.
Equity	<ul style="list-style-type: none"> Coverage rates of vaccines are diverse in terms of urban-rural, provincial, and different socioeconomic population groups in China The coverage rates of non-NIP vaccines are relatively low. Burdens of infectious diseases are higher in western and less-developed provinces, where vaccination could be more cost-effective. Very few economic evaluations of vaccines in China consider equity.
Evaluation purposes	<ul style="list-style-type: none"> NIP and non-NIP vaccines are related to budget and funding, so immunization policy-making in China is also an economic issue. Very few economic evaluations of vaccines were carried out to inform NIP policies in China. Some provinces and cities made policies of free non-NIP vaccines to eligible people without economic evidence.

governments have considered providing free non-NIP vaccines like flu shots and PPSV23 for eligible population.^{17,18} Public health insurance does not finance vaccines in China with one exception of the COVID-19 vaccines.¹⁹ Very few individuals have private or supplementary health insurance, which may cover some vaccines. A systematic review found that 10 of 23 economic evaluations of vaccines in China did not adopt a societal perspective.¹⁴ The financing mechanism for vaccines

and NIP in China determines the study perspective of vaccine economic evaluations.

Recommendation:

Study perspectives should be reported as early as possible. The societal perspective should always be taken to ensure that indirect costs are well measured. Government perspective may be considered if governments need to make budgets and allocate funding to introduce new NIP vaccines. Economic evaluations of vaccines may be conducted at the national or provincial levels, as individual provinces are empowered to make their immunization policies by the Vaccine Administrative Law in China. Perspectives of provincial and local governments in China may be taken as they start to finance non-NIP vaccines. Results from other relevant perspectives, such as government, health-care system, employers, and individuals, can be obtained from the societal perspective, and will help design a joint financing mechanism for non-NIP vaccines.²⁰

Comparator strategies

In recent years, several new vaccines have been introduced into China as non-NIP vaccines, such as HPV and Shingles vaccine. It is necessary to estimate their economic values by conducting economic evaluations which compare at least two alternative vaccination strategies.⁷ On average, coverage rates of NIP vaccines in China are fairly high (often exceeding 95%),¹² so the comparator strategy for NIP vaccines could be no vaccination and NIP vaccination. By contrast, non-NIP vaccines are not widely vaccinated in China²¹ except for only a few vaccines with comparatively higher coverage rates such as Hib vaccine^{22,23} so another comparator strategy for non-NIP vaccines could be status quo vaccination in the private market and NIP vaccination, as adopted by a few previous studies.^{22,24}

When a new vaccine is licensed in China, the above two sets of comparators are the same since nobody has been vaccinated at the very beginning. However, for non-NIP vaccines already used in the private market for a long time, the choice of comparator strategies may really matter, especially when the status quo coverage rates are fairly high. For non-NIP vaccines with very low coverage rates, such as PCV 13 and Rotavirus vaccines, the choice of two comparator strategies will turn into similar results.^{23,24}

Recommendation

For NIP vaccines in China, the recommended comparator strategy is no vaccination and NIP vaccination. For non-NIP vaccines, NIP vaccination can be compared with both no vaccination and status quo vaccination, and the two choices will provide different policy implications. A zero-coverage rate can be assumed in the no vaccination strategy. Real coverage rates of non-NIP vaccines at the national and/or local levels should be used, when status quo vaccination strategy in the private market is examined. The coverage rate for NIP vaccination can reasonably be assumed to be 95% in China.

Table 2. Recommendations for economic evaluations of vaccines in China.

Aspect	Recommendation in China
Study perspectives	<ul style="list-style-type: none"> • Study perspectives are reported as early as possible. • Societal perspective should be taken. • Results from other perspectives, such as governments, employers, and individuals, may also be reported.
Comparator strategies	<ul style="list-style-type: none"> • For NIP vaccines, no vaccination and vaccination in NIP can be compared. • For non-NIP vaccines, both no vaccination and keeping as non-NIP vaccines are comparators to introducing them into NIP. • Coverage rates of NIP vaccines in China are more than 95% • Coverage rates of non-NIP vaccines at the national level are very diverse.
Analysis types	<ul style="list-style-type: none"> • Cost-utility analyses are recommended. • Incremental cost-utility ratios (ICUR) should be reported. • The threshold prices of cost-utility vaccines should be provided.
Model choices	<ul style="list-style-type: none"> • Model choices should be justified. • More dynamic models are recommended to be used appropriately.
Costing approaches	<ul style="list-style-type: none"> • Micro costing approach is more preferable to macro costing approach. • Full costing instead of only incremental costing should be measured. • The component of indirect costs for patients and care givers should be included. • Costs by different bearers and sources should be disaggregated. • Human capital method is recommended for cost of productivity and life losses. • Unit prices and costs should be reported.
Utility measures	<ul style="list-style-type: none"> • QALY is preferred for economic evaluation of vaccines in China. • DALY may be used only if QALY is not available. • A country-specific threshold value of 1 QALY can be 1 GDP per capita in the study year. • China should try to make own QALY and/or HR-QOL of vaccine-preventable diseases for Chinese populations.
Discounting	<ul style="list-style-type: none"> • Health outcomes should be discounted. • Uniform discounting instead of differential discounting is recommended. • A discounting rate of 5% is suggested as the base case, which reflects higher real interest rates and/or economic growth rates in China. • Sensitivity analyses many employ discounting rates of 3% and 8%.
Uncertainty	<ul style="list-style-type: none"> • Potential types and sources of uncertainty should be well justified. • Scenario analyses are recommended for methodological uncertainty. • Probabilistic sensitivity analyses are recommended to account for uncertainty of model structure and/or parameter values. • Uncertainty of vaccine prices, indirect costs, and morbidity/mortality of infectious diseases prevented are particularly assessed.
Equity	<ul style="list-style-type: none"> • Equity should carefully be taken account for in economic evaluations of non-NIP vaccines in China. • Economic evaluations of vaccines at the national level are suggested to estimate provincial burdens of vaccine-preventable diseases and provincial economic impacts of vaccinations. • Economic evaluations of vaccines can also be carried by rural-urban and income levels, which significantly affects coverage rates of non-NIP vaccines.
Evaluation purposes	<ul style="list-style-type: none"> • Economic evaluations of vaccines should be applied to sort non-NIP vaccines to be included into NIP in China. • It is recommended that health economists are involved in an economic-related vaccine or immunization programs from the inception in China. • Adjusting the NIP vaccine types and/or vaccine procedures also needs health economic evaluations.

Analysis types

Cost-effectiveness analysis, cost-utility analysis, and cost-benefit analysis are commonly used in economic evaluations of vaccines. It is often difficult to turn the effectiveness and utility of vaccines into benefits as a monetary measure,⁷ and very few studies in China employed willingness to pay (WTP) to estimate the benefits of vaccines.^{16,25} A flow diagram provided by the WHO revealed how to choose appropriate types of economic analysis, while very few vaccine economic evaluation studies in China have justified their analysis types. Recent economic evaluations of vaccines in China often adopted the cost-utility analysis.^{22,24}

Recommendation

Cost-utility analysis (CUA) is recommended, which sometimes is also called cost-effective analysis (CEA) with QALYs as the outcome measure. In cost-utility analysis, the incremental cost-utility ratios (ICUR) should be reported, and the threshold prices should be provided. CUA is particularly recommended to economically compare different vaccines, but CEA is also appropriate to conduct economic evaluations of one specific vaccine. Cost-benefit analysis may be employed, if results of vaccine economic evaluations are compared with non-health interventions to achieve the most efficient allocation of social resources.

Model choices

Both static and dynamic models are available for economic evaluations of vaccines in the literature. WHO provided a flow chart to help determine when static or dynamic models were appropriate and to understand the limitations of potentially justifiable static models when epidemiologically influential subgroups were directly affected.⁷ Choices of static versus dynamic models depended on pathogens, target groups, and vaccine effectiveness. Basic static models included decision-tree models and cohort models, and basic dynamic models included stochastic versus deterministic models and compartmental versus individual-based models. Stochastic models should be applied if chance significantly affected the transmission process of pathogens. Economic evaluations of vaccines in China often used static models, but did not justify model choices.¹⁴ Only a few studies used dynamic or stochastic models.²⁶

Recommendation

WHO flow charts of static versus dynamic models should be used to choose appropriate models for economic evaluations of vaccines in China. Dynamic models might be more appropriate than static models for vaccine-preventable infectious diseases. If a static epidemiological cohort model is used instead of a dynamic model, it should be justified.

Costing approaches

Two costing approaches are commonly used in economic evaluations of vaccines: micro (bottom-up) and macro (top-down). Micro costing has more advantages than macro costing, as the former measures detailed costs of vaccination programs throughout the entire procedure, including vaccine purchase, administration, surveillance, adverse events, waste, travel time, transportation, personnel training, campaign, etc. Major cost components of vaccination programs were not included in 10 of 23 studies published before 2015.¹⁴ The most important cost components in economic evaluations of vaccines include productivity loss of caregivers and premature death as the indirect costs. Both the human capital method and friction cost method can be used for costs of productivity and life losses.

Recommendation

The micro costing approach is recommended, while macro costing can be used only if micro costing is not feasible. All costs that happened in the vaccination process instead of only incremental costs should be measured, and the indirect costs for patients and caregivers should not be ignored. Indirect costs include productivity loss of time for adults (who receive vaccination) or parents of children (who receive vaccination), as they have to miss their work time for vaccination. Vaccine prices are available from governmental purchasing agreements and should be weighted by volumes and manufacturers. The administrative and vaccinating costs of non-NIP vaccines could be considered the same as NIP vaccines.²⁷ Detailed cost ingredients are suggested to be reported, and costs of different parties should be disaggregated. Hidden costs are difficult to be measured and are often omitted, even if they are important. Unit prices and costs should also be provided and reported in both Chinese Yuan and US Dollars (also converted to international dollars). The human capital method is recommended to measure the costs of productivity and life losses.

Utility measures

Utility measures like Quality Adjusted Life Year (QALY) and Disability Adjusted Life Year (DALY) can be used as output measures for vaccines, while previous economic evaluations of vaccines in China often failed to report them.¹⁴ It is fairly difficult to measure QALYs among young children who account for the largest share of vaccine-preventable disease burden, and health-related quality of life (HR-QOL) of adult caregivers is often obtained. The adoption of HR-QOL is also subject to biases regarding anticipated protection and/or fear of adverse events. In addition, few QALY results are available among the Chinese population in terms of vaccine-preventable diseases. Most published articles in economic evaluations of vaccines in China directly used QALY measures from other countries or international literature.^{22,24}

Recommendation

When conducting vaccine economic evaluations in China, QALY is preferred, while DALY can be applied only if QALY measure is not available. It is recommended to use a country-specific threshold value of 1 GDP per capita per QALY gained,

and 3 times GDP per capita can be considered in sensitivity analyses. HR-QOL of children's caregivers is a potential alternative when the QALY of young patients is not available. It would be valuable if domestic QALY and/or HR-QOL of vaccine-preventable diseases can be accessed in China. EQ-5D-Y, Pediatric Quality of Life Inventory (PeDsQL), and Child Health Utility 9D Instrument Application (CHU9D) are recommended to measure children's life quality. The time frame and analytic horizon for health utility depend on specific vaccines of interest and their protection durations and should carefully be specified.

Discounting

Discounting reflects time preferences and depreciation. Most experts agreed that discounting for costs and/or effects should be considered in vaccine economic evaluations, and our panel discussion focused on uniform discounting versus differential discounting for costs and effects. The WHO Guide provided a comprehensive review of uniform discounting versus differential discounting.⁷ A European consensus framework on methods for economic evaluations of vaccines and immunization decisions recommended the discount rate of health effects to be half of that for costs.⁹ The WHO Guide for Standardization of Economic Evaluations of Immunization Programs recommended a differential discounting of 3% and 0% for costs and health effects in the base case and a uniform of 3% for both costs and health effects as a sensitivity analysis.⁷ The ISPOR guideline of economic evaluations of vaccines recommended uniform discounting as the base case,⁸ but the US ACIP Guide did not explicitly distinguish them.¹⁰

China Guidelines for Pharmacoeconomic Evaluations suggested that both costs and health effects be discounted with a uniform discounting rate of 5%,²⁸ which has been widely adopted by vaccine economic evaluation studies in China.¹⁴ The discounting rate used in China could be higher than in other developed countries given its higher interest rates and economic development rates.²⁹

Recommendation

Both costs and health effects should be discounted in vaccine economic analysis, and a uniform discounting approach is recommended. A discounting rate of 5% is preferable in the base case, allowing vaccine economic evaluation results to be comparable to economic results of other health interventions, such as pharmacoeconomic analyses. As a reflection of real interest rates and economic growth rates, the discounting rate could be higher in China than in other countries. Sensitivity analyses may employ discounting rates of 3% and 8%. Both discounted and undiscounted results should be reported.

Uncertainty

Uncertainties commonly exist in economic evaluations of vaccines and are almost not avoidable.³⁰ Sources of uncertainty include methodological choices, model structure, and parameter values, which need different analysis methods to account for.⁷ Previous literature on vaccine economic evaluations in China did not well distinguish sources of uncertainty, and only

univariate sensitivity analyses of parameter values were often used by researchers.¹⁴ In recent years, more studies in China applied probabilistic sensitivity analyses to account for uncertainties.^{22,24}

Recommendation

Uncertainty should be carefully accounted for, and potential sources of uncertainty should be well justified. Scenario analyses and deterministic sensitivity analysis (i.e., Tornado Diagram) are recommended for methodological and parametric uncertainty, and the probability of cost-effective results should be reported in a probabilistic sensitivity analysis. Vaccine prices, indirect costs, and morbidity/mortality of infectious diseases are particularly important in the sensitivity analyses for the uncertainty of model structure and parameter values.

Equity

Coverage rates of vaccines are diverse in terms of urban-rural/provincial residence and socioeconomic conditions in China,^{31–33} especially for non-NIP vaccines. The burden of infectious diseases is higher in western and less-developed provinces, where vaccination could be more cost-effective.^{22,23} Methods to incorporate equity into economic evaluations include equity-based weighting (EBW) methods, extended cost-effectiveness analysis (ECEA), distributional cost-effectiveness analysis (DCEA), multi-criteria decision analysis (MCDA), and mathematical programming (MP).³⁴ EBW and MP methods adjust incremental cost-effectiveness ratios related to equity, and financial risk protection (FRP) outcomes in ECEA, social welfare functions (SWFs) in DCEA, and scoring/ranking systems in MCDA reflect equity. Very few vaccine economic evaluations in China considered equity, although an ECEA of HPV vaccine in China found a larger reduction in treatment costs and higher improvement in health benefits among those with inferior socioeconomic status.³⁵ Economic evaluations of vaccines at a national level have not drawn a clear picture of the distributional benefits of vaccination in China.

Recommendation

Equity should be considered in economic evaluations of non-NIP vaccines in China. Provincial burden of vaccine-preventable diseases and provincial economic impacts of vaccinations are recommended to be estimated in vaccine economic evaluations at the national level. Additionally, economic evaluations of vaccines can also be conducted by rural-urban, parental education, and income level, which significantly affect coverage rates of non-NIP vaccines in China.

Evaluation purposes

Budget and funding are essential to NIP and non-NIP vaccination, so immunization policy-making in China is also an economic issue of much importance.⁴ China's NIP was expanded from five vaccines to 14 vaccines in 2007, but no economic evaluations of vaccines have been done before this expansion. Since then, no vaccine has been added to NIP yet, while more

non-NIP vaccines have been introduced into China's private market. Lots of non-NIP vaccines, such as HPV vaccine, Hib vaccine, Varicella vaccine, PCV, PPSV23, Rotavirus vaccine, and EV71 vaccine, have been used for a long time in China. Some of them have fairly high coverage rates like Varicella and EV71 vaccines. Several provinces and cities in China provide free non-NIP vaccines to eligible people, for example, flu vaccine in Beijing, PPSV vaccine in Shanghai, and PCV13 vaccine in Weifang, but no studies were found to estimate the cost-effectiveness of these local immunization policies. It is urgent to identify the most cost-effective non-NIP vaccines and add them to China's NIP and adjust the current vaccination strategies for NIP vaccines under the guidance of vaccine economic evaluation results.^{7,10}

Recommendation

Economic evaluations of vaccines should be applied to help sort out non-NIP vaccines with greater cost-effectiveness and adjust NIP vaccine arrangements in China. Results of vaccine economic evaluations may help the government expand vaccination coverage rates, negotiate with manufacturers for vaccine purchases, and compare vaccines with other preventative and treatment alternatives. It is recommended that health economists are involved in economic-related vaccine or immunization programs from their inception in China. Budget impact analyses may also be useful for immunization policy-making.

Discussion

Economic evaluation of vaccines in policy decision-making has not been widely used in China. National Immunization Expert Consultation Committee has recognized the importance of vaccine economic evaluations, but no formal procedures exist to facilitate the use of health economic evidence in policy decision-making. In practice, economic evaluations were not applied in pilot immunization policy-making, such as local-free vaccination programs of flu vaccine, HPV vaccine, and PCV13. Economics is a major issue in China's immunization policies, especially the economic evaluations of non-NIP vaccines.

Economic evaluations of vaccines or immunization are not officially required in China's NIP, but the design of NIP is still an economic issue. At the national level, China needs to establish a formal process on how the guideline for economic evaluations of vaccines and immunization programs should be incorporated, and what economic evidence should be routinely prepared in immunization policy-making. Ideally, economic evaluations of vaccines and immunization programs in China should be carried out independently.

China's Guideline for Economic Evaluation of Vaccines does not try to alter the general guidelines for economic evaluations or the Guide for Standardization of Economic Evaluations of Immunization Programs proposed by the WHO. Instead, it serves as a supplement to existing knowledge that emphasizes unique and/or important aspects and adds new aspects of economic evaluations of vaccines from China.³⁶

A systematic review of economic evaluations of vaccination programs in 2015 concluded that "Major methodological flaws and reporting problems exist in current economic evaluations

of vaccination programs in China. Local guidelines for good practice and reporting, institutional mechanisms and education may help to improve the overall quality of these evaluations.” After 2015, more economic evaluations of vaccines and/or immunization programs were published for non-NIP vaccines, such as HPV, Hib, EV71, PCV17 and PPSV 23,^{37–47} which have carefully been reviewed in the present study. The 10 items in the present guidelines are recommended to be followed for future studies.

Nineteen experts for China’s Guideline have rich experiences in economic evaluations of vaccines and immunization programs, which is a crucial factor for the guideline quality. Some members are from Chinese CDC and serve in various working groups of China’s National Immunization Expert Advisory Committee. Knowledge in vaccine economics and working experiences in related areas are critical factors influencing the quality of the guideline. The most important and unique 10 items in the present study were selected by participated experts based on well-known international and national guidelines of vaccine economics, previous literatures, and background features in China. Two rounds of consultations and discussions were held to obtain the consensus. A group of 74 external experts were invited to participate in a web conference for the draft guideline, and all external experts provide oral or written comments and/or suggestions. All of them have been carefully applied to the final version of guideline. Specially, four top and senior external experts in China as cochairmen for above 74 external experts were invited to review and finalize the final version. All above procedures tried to ensure the guideline quality very well in the present study.

Economic evidence has been regarded as a necessary element for making immunization policies. Although China has recognized the importance of economic evaluations of vaccines, such evidence has not been widely and formally taken. Guidelines for Economic Evaluations of Vaccines in China will help improve research quality and provide more sufficient evidence to inform decision-making.¹⁴

This guideline will guide health economists to conduct economic evaluations of vaccines and immunization programs at the national, provincial, and local levels in China. The proposed 10 aspects of economic evaluations of vaccines and immunization programs in China will help improve the quality of economic evaluation publications in China. It is also conducive to program staff who use economic evaluation results to assist immunization policymakers in China, such as local and provincial departments of health, National Immunization Expert Advisory Committee and its working committee, Bureau of National Health Insurance, and Ministry of Finance. In the long run, economic evaluations would increase the efficiency of health system spending, which is essential to Universal Health Coverage and the campaign of “Healthy China 2030.”

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