Effect of Target Age of Supplemental Immunization Campaigns on Poliomyelitis Occurrence in China


Chinese Academy of Preventive Medicine, and Disease Control Department, Expanded Programme on Immunization Division, Ministry of Public Health, Beijing, People's Republic of China; National Immunization Program, Centers for Disease Control and Prevention, Atlanta, Georgia

The World Health Organization recommends conducting supplemental immunization activities to eradicate poliomyelitis by the year 2000. Although effective in eliminating poliomyelitis from the Americas, supplemental campaigns require substantial resources. To assess differential campaign effectiveness in eliminating this disease, poliomyelitis occurrence was compared in counties in China that targeted children <3 versus <4 years of age. Counties that targeted children <3 years of age reported poliomyelitis more frequently after the campaigns. This association was observed even after accounting for the effects of previous poliomyelitis occurrence, urban versus rural setting, and population density. While several limitations emphasize the preliminary nature of these findings, these data support targeting the widest possible age group of susceptible children to ensure maximum effectiveness in eliminating poliomyelitis. Thus, while reducing the target age of these activities may result in considerable resource savings, such campaigns may not be as effective in eliminating poliomyelitis.

Supplemental immunization campaigns against poliomyelitis, particularly national immunization days (NIDs), were an essential element in the Pan American Health Organization's successful strategy to eliminate poliomyelitis from the Americas [1]. Based on this success, the World Health Organization currently recommends supplemental campaigns as an integral part of global eradication activities [2]. These campaigns involve administering a dose of oral poliovirus vaccine (OPV) over a short period of time (usually in the low-risk season of poliovirus transmission) to all children in a target age group, followed by an additional OPV dose 4–6 weeks later. In 1995, 62 countries conducted NIDs; 92 countries are expected to conduct NIDs in 1996. With strong support from the highest levels of government, China conducted three NIDs during the 1993–1994, 1994–1995, and 1995–1996 winter seasons. More than 70 million children <4 years of age were immunized with two doses of OPV in the 1993–1994 and 1994–1995 campaigns [4, 5], and more than 60 million children in this target age group were immunized during the 1995–1996 NID (Wang K, unpublished data). Despite strengthened surveillance, the reported number of poliomyelitis cases fell to 307 in 1994 and to 154 in 1995 (Zhang J, unpublished data).

While proven effective in reducing poliomyelitis cases, supplemental immunization activities require substantial indirect and direct costs. Restricting the target age of these campaigns from <4 to <3 years of age could result in substantially reduced resource requirements in China and other countries conducting supplemental immunization campaigns. However, if “age-restricted” supplemental activities are not as effective in halting the occurrence of poliomyelitis, limiting the age range of the target group may not be cost-effective in the long run and may prolong the number of years in which supplemental immunization campaigns are necessary.

To evaluate the effect of reducing the target age of supplemental immunization activities on eliminating poliomyelitis, poliomyelitis occurrence after two-round, subnational immunization campaigns conducted in China in the winters of 1991–1992 and 1992–1993 was compared in all counties with avail-
Figure 1. Age distribution of cases confirmed by wild poliovirus isolation, China, 1993 (n = 61).

Methods

Data collection. County-specific immunization data on the supplemental campaigns were reported by provincial health bureaus to the Chinese Academy of Preventive Medicine (1992–1993 supplemental immunization data were available from only 14 provinces) and included information on the number of OPV doses administered in each immunization round, the target age group of each round, the expected number of target children in each round, and the start and end dates of each round.

Information on reported poliomyelitis cases by year and county was obtained from the acute flaccid paralysis (AFP) surveillance system, established by the Chinese Ministry of Health in 1991. This system collects case information for all reports of AFP, which are then confirmed as poliomyelitis on the basis of standard criteria. During the study period, cases of poliomyelitis were confirmed that met at least one of the following criteria: isolation of poliovirus from stool specimens, residual paralysis at a follow-up examination at least 60 days after onset of paralysis, positive poliovirus-specific IgM test, 4-fold rise in poliovirus-specific IgG antibodies, death, or loss to follow-up. Counties were assessed for the occurrence of polio in the period beginning 15 days after the second (last) round of each supplemental campaign and ending on the first day of the first round of the following winter campaign.

Several additional variables were assessed for their potential confounding effects on the association between target age of the supplemental campaigns and polio occurrence. The occurrence of polio was assessed in each county during the previous calendar year of the second round of each supplemental campaign. Population density was defined as the county population per square kilometer in 1990. Urban versus rural status was based on codes assigned by the Administrative Unit of the State Standard Bureau, People’s Republic of China.

Although data were available on the number of OPV doses administered during the supplemental immunization campaigns and on the size of the target population, the potential confounding effect of vaccine coverage achieved in each immunization round could not be assessed, as subsequent reviews indicated that campaign target populations were nonuniformly underestimated (Zhang J, unpublished data).


Potential confounding variables were identified by comparing the population density, urban versus rural status, and history of previous polio cases in counties that targeted children <3 and <4 years of age. Fisher’s (two-tailed) exact test was used to identify statistically significant differences.

The presence or absence of polio following the campaigns was compared between campaign strategies using odds ratios to estimate risk ratios. Pre- and postcampaign polio rates could not be calculated because population denominators were unknown for as many as 68% of counties (information availability varied according to year and campaign target age group).

Multivariate logistic regression models were developed to evaluate the independent effect of campaign strategy on the occurrence of polio. For each model, a stepped-down model-building approach was used. Variables in the initial models included the primary
Table 1. Comparison of characteristics of counties by supplemental immunization campaign strategy.

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<tbody>
<tr>
<td></td>
<td>&lt;3 years</td>
<td>&lt;4 years</td>
</tr>
<tr>
<td></td>
<td>(n = 280)</td>
<td>(n = 529)</td>
</tr>
<tr>
<td>Density*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–499</td>
<td>195 (70)</td>
<td>441 (84)</td>
</tr>
<tr>
<td>&gt;=500</td>
<td>85 (30)</td>
<td>87 (16)</td>
</tr>
<tr>
<td>Missing</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Geography</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>37 (13)</td>
<td>112 (21)</td>
</tr>
<tr>
<td>Rural</td>
<td>243 (87)</td>
<td>417 (79)</td>
</tr>
<tr>
<td>Polio in the previous year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3 (1)</td>
<td>35 (7)</td>
</tr>
<tr>
<td>No</td>
<td>277 (99)</td>
<td>494 (93)</td>
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* Population per km². Data are no. (%).

Results

Table 1 presents characteristics of counties in 1991–1992 and 1992–1993 that conducted two-round campaigns targeted at children <3 or <4 years of age. In 1991–1992, a larger percentage of counties that targeted children <3 years of age had population densities ≥500/km². However, in 1992–1993, such counties had lower population densities. In both 1991–1992 and 1992–1993, counties that conducted campaigns targeted at children <3 years of age were more likely to be rural and previously polio-free.

Table 2 presents the percentage of counties with postcampaign polio that targeted children <3 and <4 years of age, as well as odds ratios summarizing the odds of subsequent polio in counties that targeted children <3 years of age compared with the odds of polio in counties that targeted children <4 years of age.

In 1991–1992, 17 (6%) of the 263 counties that conducted campaigns targeted at children <3 years of age reported polio after the campaigns, compared with 7 (1%) of the 522 counties that conducted campaigns targeted at children <4 years of age. Compared with the odds of polio in counties that conducted campaigns targeted at children <4 years of age, counties that targeted children <3 years old had nearly 5-fold increased odds of polio after the campaigns (P < .05).

A similar association was observed after the 1992–1993 campaigns. Of the 82 counties that conducted campaigns targeted at children <3 years of age, 16 (20%) reported polio after the campaigns. Only 31 (10%) of the 315 counties that targeted children <4 years of age reported postcampaign polio. This 2-fold increase associated with a <3-year target age remained after simultaneously adjusting for previous polio occurrence and urban versus rural status (P < .05).

Discussion

About 40 million doses of OPV per year could have been conserved if China’s National Immunization Days had been...
restricted to children <3 years of age instead of targeting children <4 years of age. This age restriction would have saved between $680,000 (i.e., 40,000,000 × $0.017/dose of domestic vaccine) and $3,600,000 (i.e., 40,000,000 × $0.09/dose of imported vaccine) per year in vaccine costs alone. However, these data suggest that counties that conducted campaigns targeted at children <3 years of age were at least 2-fold more likely to have polio cases after the campaigns than counties that conducted campaigns targeted at children <4 years of age. An increased risk for polio still existed after adjusting for the possible effects of previous polio occurrence, urban versus rural setting, and population density.

Several limitations may have affected these findings. One limitation is different probabilities of exposure to vaccine delivered in the supplemental campaigns: While county-specific vaccine coverage figures were available for the 1991–1992 and 1992–1993 supplemental campaigns, population denominators were underestimated. Estimated coverage levels achieved were generally >95%. Another limitation is different probabilities of poliomyelitis case reporting in the surveillance system: No county-specific information is available on the completeness of case reporting in counties in 1992 and 1993. It is unclear whether under- or overreporting of polio cases varied by campaign strategy. A third limitation is different probabilities of poliomyelitis case misclassification: No information is currently available on county-specific rates of polio misclassification or on the proportion of cases confirmed by wild poliovirus isolation. While misclassification estimates of 0.3–0.4/100,000 have been proposed based on data from provinces where polio cases were clinically confirmed but where no wild poliovirus was isolated, it is unknown whether misclassification varied in counties that conducted different campaign strategies. Another limitation is different probabilities of exposure to vaccine before the campaigns: County-specific routine coverage data are not available for 1992 and 1993. Finally, there are different probabilities of exposure to immunogenic vaccine administered before or during the campaigns: While 30–50% of cold-chain equipment in China is reported to be in poor condition (Zhang J, unpublished data), information is lacking to compare the quality of the cold chain in counties that conducted different supplemental immunization strategies.

Table 3. Comparison of provincial performance indicators by immunization campaign strategies.

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<tbody>
<tr>
<td></td>
<td>&lt;3 years</td>
<td>&lt;4 years</td>
</tr>
<tr>
<td>No. of provinces</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>% of acute flaccid paralysis (AFP) cases with 2 stools collected within 1–14 days in children &lt;15 years old*</td>
<td>Not available</td>
<td>Not available</td>
</tr>
<tr>
<td>AFP rate per 100,000 population &lt;15 years old (1993 data)*</td>
<td>0.76</td>
<td>0.92</td>
</tr>
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* Calculated by averaging province rates, weighted by no. of counties within each province.

While these potential methodologic biases emphasize the preliminary nature of these findings, several attempts were made to minimize their potential effects. Precampaign differences in the levels of susceptibility to wild poliovirus were taken into account in multivariate risk equations by adjusting for possible differences in previous polio occurrence. Increased risk of polio remained in counties that did not conduct campaigns targeted at children <4 years of age. Furthermore, though age data were limited on polio cases, no differences were seen in the ages of previous polio cases in counties that targeted children <3 or <4 years of age (P > .05), suggesting similar age-specific immunity induced by wild virus. Limited age data on postcampaign polio cases suggest that 24% (12/51) of polio cases that occurred in counties that targeted children <3 years of age were in children older than the target age group. Only 14% (4/29) of counties that targeted children <4 years of age reported cases in children ≥3 years of age (P > .05).

Though it is likely that case detection, reporting, and confirmation are similar within provinces, as county immunization programs are administered at the provincial level, two provinces were identified that contained counties that conducted more than one supplemental campaign strategy in 1991–1992 or 1992–1993. In Hebei Province in 1991–1992, 1 (8%) of 12 counties that conducted campaigns targeted at children <3 years of age reported subsequent polio in the routine system, compared with 1 (5%) of 20 counties that targeted children <4 years of age (odds ratio = 1.73, P > .05). In Hubei Province in 1992–1993, 2 (33%) of 6 counties that targeted children <3 years old reported subsequent polio in the AFP system compared with 5 (17%) of 30 counties that targeted children <4 years old (odds ratio = 2.5, P > .05). While not statistically significant, these results support a real increase in subsequent risk of polio cases associated with campaigns targeted at <3-year-old children compared with campaigns targeted at <4-year-old children.

Although county-specific stool collection and AFP reporting rates are not known, weighted averages of these rates were calculated from provinces composed of counties that conducted supplemental immunization activities in 1991–1992 and 1992–1993 (table 3). In 1993, the percentage of AFP cases that had
2 stools collected within 1–14 days of onset was lower in provinces whose counties targeted <3-year-old children (14%) compared with provinces whose counties targeted <4-year-old children (25%).

While these differential stool collection rates support the possibility that counties that targeted <3-year-old children had poorer immunization programs and may have consequently conducted poorer supplemental campaigns, this suggestion is not supported by AFP reporting rates. In 1992, provinces comprising counties that targeted children <4 years of age had higher AFP reporting rates (0.92/100,000 population) than provinces comprising counties that conducted campaigns targeted at <3-year-old children (0.76/100,000 population). In contrast, 1993 reporting rates were higher in provinces comprising counties that targeted <3-year-old children (0.87/100,000 population) compared with provinces comprising counties that targeted <4-year-old children (0.76/100,000 population). In spite of these differences, increased odds of subsequent polio were seen in both 1991–1992 and 1992–1993 in counties that conducted campaigns targeted at children <3 years of age.

Although supplemental immunization activities have been highly successful in helping to eliminate wild poliovirus from the Americas, the specific mechanism for the effectiveness of these efforts has not been defined. Possible mechanisms include a reduction in the number of unimmunized children because of more aggressive approaches in vaccine delivery, higher immunogenicity of OPV given during mass campaigns [6, 7], repeated boosting of secretory antibody (IgA) levels in the gastrointestinal tract following multiple exposures to vaccine virus, higher levels of humoral and secretory immunity in the overall population due to more intensive spread of vaccine virus to susceptible persons in all age groups, and displacement of wild poliovirus and nonpolio enteroviruses following massive and widespread use of OPV [8, 9].

Whatever the mechanism, it seems likely that increasing the number of susceptible children vaccinated will decrease occurrence of poliomyelitis. However, in addition to this efficacy consideration, choice of the appropriate target age group rests on taking into consideration the increased direct and indirect costs of vaccinating additional children.

Acknowledgments

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References