MALNUTRITION AND INFECTIOUS DISEASE MORBIDITY AMONG CHILDREN MISSED BY THE CHILDHOOD IMMUNIZATION PROGRAM IN INDONESIA

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Abstract. Although it has been thought that child immunization programs may miss the children who are in greatest need, there are little published quantitative data to support this idea. We sought to characterize malnutrition and morbidity among children who are missed by the childhood immunization program in Indonesia. Vaccination and morbidity histories, anthropometry, and other data were collected for 286,500 children, aged 12-59 months, in rural Indonesia. Seventy-three point nine percent of children received complete immunizations (3 doses of diphtheria-pertussis-tetanus, 3 doses of oral poliovirus, and measles), 16.8% had partial coverage (1-6 of 7 vaccine doses), and 9.3% received no vaccines. Of children with complete, partial, and no immunization coverage, respectively, the prevalence of severe underweight (weight-for-age Z score <-3) was 5.4, 9.9, and 12.6%, severe stunting (height-for-age Z score <-3) was 10.2, 16.2, and 21.5%, and current diarrhea was 3.8, 7.3, and 8.6% (all p <0.0001), respectively. In families where the child had complete, partial, and no immunizations, the history of infant mortality was 6.4, 11.4, and 16.5%, and under-five child mortality was 7.3, 13.4, and 19.2% (both p <0.0001). Expanded programmatic coverage is needed to reach children who are missed by childhood immunizations in rural Indonesia, as missed children are at higher risk of morbidity and mortality.

INTRODUCTION

Each year, more than 10 million children die, and the vast majority of child deaths are in developing countries (Black *et al*, 2003). Although childhood immunization programs have led to substantial reductions in measles, poliomyelitis, diphtheria, tetanus, and whooping cough, worldwide about 2.5 million children under five years of age still die every year as a result of vaccine-preventable diseases (WHO/UNICEF, 2005). More child deaths could be prevented through optimal use and wider coverage of currently existing vaccines (Jones *et al,* 2003; WHO/UNICEF, 2005; CDC, 2006). In many developing countries, immunization coverage has increased only marginally since the early 1990s, and an estimated 27 million infants were not immunized in 2003 (WHO/UNICEF, 2005). Child survival interventions, such as basic childhood immunizations, may not be reaching the children who need them the most (Bryce *et al* 2003).

In 2005, the Global Immunization Vision and Strategy (GIVS) was jointly developed by the WHO, the United Nations Children's Fund (UNICEF), and global partners in order to establish goals for 2006-2015 that included protecting more people against disease by sus-

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taining current levels of vaccine coverage and by extending immunization services to those who are currently unreached (WHO/UNICEF, 2005). The GIVS recommends that strengthened surveillance, monitoring, and evaluation will be needed in order to reach these goals (WHO/UNICEF, 2005). The GIVS will be critical to achieving the Millennium Development Goals of reducing child mortality by two-thirds between 1990 and 2015 (WHO/UNICEF, 2005).

The Expanded Program on Immunization (EPI) of the WHO was launched in 1974 and included an immunization schedule in which infants receive diphtheria-pertussis-tetanus vaccine (DPT) and oral poliovirus vaccine (OPV) at 6, 10, and 14 weeks, and measles vaccine at 9 months of age (Kim-Farley *et al,* 1987). The overall coverage rates for the EPI in Indonesia in 2003 were 70% for OPV and DPT and 72% for measles (WHO, 2004), and these rates of immunization coverage are consistent with overall rates of coverage for three doses of DTP of 69% reported in the Southeast Asian region in 2004 (CDC, 2006).

The effectiveness of a vaccine program depends in part upon the proportion of individuals who are covered by the immunization schedule, and the characteristics of children who are missed by immunizations and their families in developing countries are not well known. We hypothesized that children who are missed by childhood immunizations are more likely to be malnourished, anemic, with higher infectious morbidity, and to come from families with higher infant and under five child mortality. In order to address these hypotheses, we investigated childhood immunization coverage in a large nutritional surveillance program in Indonesia from 2000 through 2003.

MATERIALS AND METHODS

The study subjects consisted of children from families that participated in a major nutritional surveillance system (NSS) in Indonesia that was established by the Ministry of Health, Government of Indonesia and Helen Keller International (HKI) in 1995 (de Pee *et al,* 2002). The NSS was conducted in the provinces of Lampung, Banten, West Java, Central Java, East Java, Lombok, and South Sulawesi. The subjects included in this analysis were surveyed between January 1, 2000 through September 27, 2003. The NSS was based upon UNICEF's conceptual framework on the causes of malnutrition (de Pee and Bloem, 2001) with the underlying principle to monitor public health problems and guide policy decisions (Mason *et al,* 1984). The NSS was based upon multistage cluster sampling of households in rural villages and in slum areas of large cities (de Pee *et al,* 2002).

The NSS in Indonesia involved the collection of data from approximately 40,000 randomly selected rural households every quarter. New households were selected every round. Data were collected by two to four-person field teams. A structured coded questionnaire was used to record data on children aged 0-59 months, including anthropometric measurements, date of birth, and sex. The mother of the child or other adult member of the household was asked to provide information on the household's composition, parental education, and weekly household expenditures, along with other socioeconomic, environmental sanitation, health indicators, and attendance at the local integrated health post (*posyandu*) where childhood immunizations are administered. For each child, the mother, father, or guardian was asked whether the child received diphtheria-pertussis-tetanus (DPT) vaccine (DPT-1, DPT-2, DPT-3), oral poliovirus vaccine (OPV) (OPV-1, OPV-2, OPV-3), and measles vaccine. The questionnaire did not include OPV-0 (at birth). The interviewer asked to review the child immunization card in order to verify the responses. A child was considered to have received a vaccine if the response was "yes" in the absence of an immunization card or "yes" as verified as recorded on the immunization card. A child was considered to have missed a vaccine if the response was "no" in the absence of an immunization card or verified as not recorded on the immunization card. The NSS included questions regarding vaccination status beginning in 2000. Axillary temperature was recorded. Hemoglobin was measured using a HemoCue© instrument (HemoCue AB, Angelholm, Sweden). Morbidity histories were obtained for each child, including history of diarrhea in the previous week and current diarrhea. Data was collected on the history of any infant dying in the family before one month of age, any infant dying before 12 months of age, and any child deaths in the family before 5 years of age.

The field teams measured and recorded the weight of each child age 0-59 months to the nearest 0.1 kg and the length/height to the nearest 0.1 cm. Birth dates of the children were obtained from the birth certificate or other records. When not available, the birth dates were estimated using a calendar of local and national events and converted to the Gregorian calendar. Z-scores of weight-for-height (wasting), weight-for-age (underweight), and height-for-age (stunting) were calculated using EpiInfo software (Centers for Disease Control and Prevention, Atlanta, GA), which uses the reference population of the US National Center for Health Statistics. Children with Z-scores < -2 standard deviations (SD) for weight-for-height, weight-for-age, or height-for-age were considered wasted, underweight, or stunted (de Onis, 2001). Severe wasting, underweight, and stunting were defined by respective Z scores < -3 SD. Children who had a mid-upper arm circumference <125 mm were considered at high risk of malnutrition (Dramaix *et al,* 1993). HKI provided training to new field teams, field supervisors, and assistant field officers, and refresher training prior to each new round of data collection. During each round, a monitoring team from HKI visited all field sites to check and calibrate the equipment and supervise data collection. A quality control team from HKI revisited 10% of households without prior warning within two days of data collection by the field teams and recollected data on selected indicators, including anthropometric measurements. Data collected by these quality control teams were later compared with the data collected by the field teams to check the accuracy of the data collection.

The study protocol complied with the principles set out in the Helsinki Declaration (World Medical Association, 2001). The field teams were instructed to explain the purpose of the NSS and data collection to each child's mother or caretaker, and, if present, the father and/or household head; data collection and phlebotomy proceeded only after written informed consent. Participation was voluntary and all subjects were free to withdraw at any stage of the interview. The protocol for the NSS was approved by the Medical Ethical Committee of the Ministry of Health, Government of Indonesia. The plan for secondary data analysis by Johns Hopkins investigators was reviewed by the Johns Hopkins School of Medicine Institutional Review Board and granted an exemption on July 14, 2006 under Department of Health and Human Services 45, Code of Federal Regulations 46.404.

Data analyses were restricted to children who were 12-59 months of age because children are expected to have completed the DPT, OPV, and measles vaccine series by 12 months of age. The youngest child 12-59 months of age was selected to represent each family for families with more than one child in the 12-59 month age range. Children were classified as having received complete immunizations if they reportedly received all seven immunizations (three DPT immunizations, three OPV immunizations, and measles), or partial immunizations if they reportedly received one to six of the seven immunizations, and no immunizations if they reportedly received none of the seven immunizations. Continuous variables were compared using Student's *t*-test or ANOVA. Distance to the health post (*posyandu*) and time needed to walk to the health post were transformed using $\log_e$ in order to normalize the data. Categorical variables were compared using chi-square tests. Anemia was defined as a hemoglobin <11 g/dl, according to World Health Organization criteria (WHO, 1968). Multivariate logistic regression models were used to examine the relationship between not receiving any vaccines and different risk factors. Population-based weighting was used to account for differences in population size in the various provinces.

RESULTS

During the period of the study from 2000 through 2003, of 336,724 families with at least one child age 12-59 months immunization histories were obtained for 290,422 (86.2%) children. The proportion of children who received a DPT, OPV, and measles vaccines is shown in Table 1. The proportion of children who did not receive a DPT vaccine increased from 12.9% with the first immunization to 19.5% for the third immunization, and the proportion of children who did not receive an OPV vaccine increased from 11.3% for the first immunization to 17.5% for the third immunization. The proportion of children who missed the measles vaccine was 20.2%.

Demographic, nutritional, and morbidity characteristics of 286,500 children who received complete immunizations, partial immunizations, or no immunizations are shown in Table 2. There were 3,922 children (1.4%) for whom the parent or guardian answered "don't know" in response to receipt of all seven vaccinations, and these children are excluded from Table 2. Children who received partial or

Table 1
Immunization coverage among children (N = 290,422), 12-59 months of age, in rural Indonesia, 2000-2003.

Vaccine	No.	%
DPT vaccine dose 1		
Not received	37,425	12.9
Received, with record	147,283	50.7
Received, no record	99,692	34.3
Doesn't know	6,023	2.1
DPT vaccine dose 2		
Not received	48,173	16.6
Received, with record	141,605	48.8
Received, no record	94,339	32.5
Doesn't know	6,308	2.2
DPT vaccine dose 3		
Not received	56,742	19.5
Received, with record	136,483	47.0
Received, no record	90,425	31.1
Doesn't know	6,677	2.3
DPT vaccine series – total		
No vaccines received	36,556	12.6
Partial (received 1 or 2 vaccines)	21,824	7.5
Complete (received all 3 vaccines)	226,029	77.9
Doesn't know	5,920	2.0
OPV vaccine dose 1		
Not received	32,768	11.3
Received, with record	149,652	51.5
Received, no record	102,098	35.2
Doesn't know	7,914	2.0
OPV vaccine dose 2		
Not received	41,419	14.3
Received, with record	145,430	50.1
Received, no record	97,394	33.5
Doesn't know	6,182	2.2
OPV vaccine dose 3		
Not received	50,750	17.5
Received, with record	140,804	48.5
Received, no record	92,300	31.8
Doesn't know	6,518	2.2
OPV vaccine series – total		
No vaccines received	31,954	11.0
Partial (received 1 or 2 vaccines)	20,131	6.9
Complete (received all 3 vaccines)	232,392	80.0
Doesn't know	5,843	2.0
Measles		
Not received	58,775	20.2
Received, with record	132,647	45.7
Received, no record	93,771	32.0
Doesn't know	6,143	2.1

Table 2
Demographic and morbidity characteristics of children (N = 286,500) by vaccine receipt status in rural Indonesia.

Characteristic	Complete[1]		Partial[1]		No. receipt[1]		p-value
	No.	%	No.	%	No.	%	
Child age in months (%)							
12-23.9	79,368	37.5	23,470	48.8	10,943	40.9	0.0001
24-35.9	61,638	29.1	12,610	26.2	7,556	28.3	
36-47.9	43,740	20.8	7,763	16.2	5,134	19.2	
48-59.9	26,947	12.7	4,224	8.8	3,107	11.6	
Gender (% Male)	107,241	50.7	24,809	51.6	13,471	50.8	0.0001
Maternal age in years (%)							
≤24	57,823	27.3	15,608	32.5	8,782	32.9	0.0001
25-28.9	53,972	25.5	11,550	24.0	6,545	24.5	
29-32.9	49,341	23.3	9,538	19.9	5,015	18.8	
33+	50,392	23.8	11,331	23.6	6,380	9.4	
Maternal education in years (%)							
0-6.9	116,097	55.1	34,621	73.1	22,663	88.8	0.0001
7-9.9	46,739	22.2	7,760	16.4	1,968	7.7	
≥10	57,949	22.7	4,960	10.5	877	3.4	
Paternal education in years (%)							
0-6.9	99,891	48.8	28,261	63.7	18,582	80.6	0.0001
7-9.9	40,591	19.8	7,881	17.8	2,593	11.2	
≥10	64,237	31.4	8,242	18.6	1,888	8.2	
Number of children <5 years in family							
1	167,335	79.2	35,850	74.7	18,390	68.8	0.0001
2	40,449	19.1	10,927	22.8	7,238	27.1	
3	3,253	1.5	1,061	2.2	977	3.7	
4+	350	0.2	138	0.3	109	0.4	
Year in which interview was conducted							
2000	55,445	26.2	11,371	23.7	6,707	25.1	0.0001
2001	52,054	24.6	11,202	23.3	6,466	24.2	
2002	62,384	29.5	14,744	30.7	8,571	32.1	
2003	41,811	19.8	10,750	22.4	4,995	18.7	
Weight-for-age Z (WAZ) score (%)							
WAZ < -2	74,452	35.3	21,879	45.7	13,286	49.8	0.0001
WAZ < -3	11,349	5.4	4,721	9.9	3,373	12.6	0.0001
Height-for-age Z (HAZ) score (%)							
HAZ < -2	78,448	37.3	22,420	47.3	14,200	53.8	0.0001
HAZ < -3	21,457	10.2	7,668	16.2	5,662	21.5	0.0001
Weight-for-height Z (WHZ) score (%)							
WHZ < -2	13,629	6.5	3,945	8.3	2,295	8.6	0.0001
WHZ < -3	1,082	0.5	316	0.7	219	0.8	0.0001
MUAC <125 mm (%)	4,661	2.2	1,861	3.9	1,065	4.0	0.0001
Diarrhea today (%)	7,946	3.8	3,525	7.3	2,301	8.6	0.0001
Fever today (%)	2,535	1.3	857	1.9	430	1.7	0.0001
Diarrhea last week (%)	12,443	5.9	4,757	9.9	2,649	9.3	0.0001
Anemic (%)	21,610	47.9	5,772	57.5	3,247	58.4	0.0001
Weekly per capita household expenditure (US$)[2]	162,588	1.81 (1.80-1.81)	37,228	1.71 (1.69-1.73)	20,425	1.46 (1.44-1.48)	0.0001
Distance to health post (*posyandu*)							
In meters[2]	203,130	103.8 (103.1-104.6)	44,437	111.2 (109.6-113.0)	19,546	198.3 (193.2-203.5)	0.0001
In minutes[2]	202,292	5.11 (5.09-5.14)	44,269	5.55 (5.49-5.60)	18,516	7.26 (7.15-7.38)	0.0001

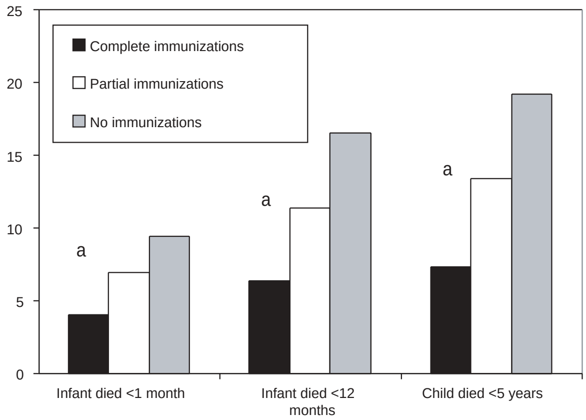
[1]Complete defined as receiving OPV-1, OPV-2, OPV-3, DPT-1, DPT-2, DPT-3, and measles vaccines; partial defined as receiving at least one of the seven vaccine doses, and no receipt as receiving none of the seven vaccine doses.
[2]Geometric mean (95% CI).

no immunizations were younger, had younger mothers, had lower levels of maternal and paternal education, and had more children in the family. There were slightly more males among children who received partial or no immunizations.

The proportion of children who were underweight or had stunting, wasting, or MUAC <125 mm was significantly higher among children who had partial or no immunizations compared with children who had complete immunizations. The proportion of children with severe underweight, stunting, or wasting (WAZ < -3, HAZ <-3, or WHZ <-3, respectively) was significantly higher among children who had partial or no immunizations compared with children who had complete immunizations. Children who had partial or no immunizations were more likely to have current diarrhea or fever or diarrhea in the previous week, and they were also more likely to be anemic compared with children who received complete immunizations. The distance to the health post (*posyandu*), whether reported in meters or in minutes walking, was significantly higher for children with partial or no immunizations compared with children who received complete immunizations.

The history of infant deaths and deaths of children under five years of age was compared between families where the child had complete, partial, or no immunizations (Fig 1). In families where the child had complete, partial, or no immunizations, a history of infant mortality was 6.4, 11.4, and 16.5%, and under-five child mortality was 7.3, 13.4, and 19.2%, respectively (both p <0.0001). The proportion of families in which there was at least one infant death under one month of age was also significantly higher for children who received no immunizations and was lowest among those who had complete immunizations.

Multivariate logistic regression models were used to characterize risk factors for not receiving any immunizations (Table 3). In a model adjusting for child age, gender, maternal age, and per capita weekly household expenditure, low maternal education of 0 through 6 years was a strong risk factor for the child receiving no immunizations (OR 8.39, 95% CI 8.08-9.11). In a second model adjusting for the above factors and distance to the local health post (*posyandu*), low maternal education of 0 through 6 years remained a strong risk factor for the child receiving no immunizations (OR 7.29, 95% CI 6.61-8.04). Lower maternal age was also significantly related to the child receiving no immunizations in the second model.



[a]p<0.0001 by Mantel-Haenszel chi-square.

Fig 1–History of infant and child under five deaths in the family by immunization status.

The general reasons given for not visiting the local health post (*posyandu*) are shown in Table 4. The five leading specific reasons that were given for not attending the *posyandu* were that the health post was not active, the child was already old, immunizations were complete, the child was usually brought to other health services, and the health post was too far.

DISCUSSION

This study shows that over 9% of children did not receive any of the seven immuni-

Table 3
Multivariate logistic regression models of risk factors for child receiving no immunizations.

Variable	OR	95% CI	p-value
Model 1			
Child age (per month)	0.998	0.996-0.999	0.001
Child gender (boy)	1.003	0.97-1.03	0.87
Maternal age (years)			
<24	1.30	1.24-1.35	0.0001
24-28.9	1.10	1.05-1.14	0.0001
29-32.9	0.94	0.89-0.99	0.013
33+	1.00	-	-
Maternal education (years)			
0-6.9	8.39	8.08-9.11	0.0001
7-9.9	2.00	1.81-2.21	0.0001
10+	1.00	-	-
Weekly household per capita expenditure (per US$)	0.949	0.942-0.957	0.0001
Model 2			
Child age (per month)	1.00	0.998-1.001	0.89
Child gender (boy)	0.99	0.96-1.03	0.77
Maternal age (years)			
<24	1.26	1.20-1.33	0.0001
24-28.9	1.07	1.02-1.13	0.01
29-32.9	0.92	0.87-0.97	0.003
33+	1.00	-	-
Maternal education (years)			
0-6.9	7.29	6.61-8.04	0.0001
7-9.9	1.95	1.73-2.19	0.0001
10+	1.00	-	-
Weekly household per capita expenditure (per US$)	0.98	0.97-0.99	0.0001
Log_e distance to health post (*posyandu*) (per minute walking)	1.36	1.33-1.38	0.0001

Table 4
Reasons for not taking child to health post (*posyandu*) in children who had partial or no immunizations.

Reason	N	%
Health post not active	11,285	26.7
Child is already old	4,890	11.6
Immunizations are complete	4,052	9.6
Usually bring child to other health services	3,148	7.4
Health post too far	2,949	7.0
Mother is too busy	2,713	6.4
Child afraid of weighing	2,018	4.8
Doesn't know schedule	1,444	3.4
Just moved to survey area	994	2.3
There is no food supplementation program	165	0.4
Need to pay	157	0.4
Other reasons	8,491	20.1

zations, and over 20% of children missed measles immunization in rural Indonesia. Children who missed their childhood immunizations were more likely to be malnourished and anemic, have higher infectious disease morbidity, and were more likely to come from a family in which there was already a higher rate of infant and under-five child mortality. In addition, children missed by childhood immunizations had higher rates of severe malnutrition, as indicated by weight-for-height, height-for-age, and weight-for-age Z scores <-3. These findings suggest that children who miss DPT, OPV, and measles immunizations are at a much higher risk of mortality, not only from missing the vaccines and having less protection against vaccine-preventable diseases, but from having a higher prevalence of malnutrition and morbidity. These findings support the idea that child survival interventions are not reaching the children who may need them the most (Bryce *et al,* 2003).

Risk factors that have been associated with lack of childhood immunizations in developing countries include low socioeconomic status and low level of maternal education (Streatfield *et al,* 1990; Perry *et al,* 1998; Waters *et al,* 2004). In the present study, low maternal education was a strong risk factor for lack of child immunizations in multivariate models that adjusted for distance to the health post and other factors. The level of formal education of women is strongly associated with child mortality and other determinants, such as health care utilization (Basu and Stephenson, 2005). It is not completely clear why women who have a higher level of formal education have lower morbidity and mortality among their children, and it does not appear to be correlated with income or heightened knowledge of disease etiology (Basu and Stephenson, 2005). Factors that have been implicated include a better ability to understand decontextualized information from mass media and health workers, greater autonomy and empowerment of women, respect for authority, and ability to follow a time table of routine (Basu and Stephenson, 2005). For immunization programs, the implications of higher maternal education may be an enhanced capability of women to understand health messages regarding immunizations, to follow the recommendations of health care workers from the local health post, and to adhere to the timing of the immunization schedule.

The present study also shows that families with lower incomes and families living at a greater distance from the health post are at higher risk of having low immunization coverage among their children. There is an apparent inequity in coverage by the childhood immunization program, and potential solutions may include encouraging health workers to go the extra kilometer, literally, to reach the poorest of the poor and the families most remote from the health post.

Children who received no immunizations came from families in which the risk of underfive child mortality was about 2.6 times higher than that for families in which children received complete immunizations. Likewise, the risk of infant mortality was about 2.6 times higher for families in which children received no immunizations compared to families in which children received complete immunizations. The causes for the increased infant and under five child mortality in families in which the child received no immunizations cannot be determined from this study, but there are several possibilities, including previous siblings not receiving vaccines and higher rates of malnutrition and infectious disease morbidity clustered in the same families. Further studies will be needed to examine these issues.

Despite the successes of childhood immunization programs in many regions worldwide, existing vaccines are not being used to their fullest potential (CDC, 2006). For example, of the 2.5 million child deaths due to vaccine-preventable diseases in 2002, 4,000 children died from diphtheria, 198,000 children died from tetanus, and 540,000 died from measles (CDC, 2006). Rates of diphtheria-pertussis-tetanus immunization coverage have actually declined in both sub-Saharan Africa and South Asia since 1995 (Bryce *et al*, 2003).

In the present study, the main reasons cited by the mother, father, or guardian for not taking their child to the health post (*posyandu*) were that the health post was no longer active, or that they thought the child was too old, or that the child already had received immunizations. A limitation of the present study was the surveillance teams did not determine whether the closest health post was no longer active, thus, it was not possible to verify whether the health post was actually closed. The study suggests that in these rural communities there may be insufficient knowledge of the schedule of childhood immunizations.

The strategies of the GIVS for increasing immunization coverage include regular analysis to document success and failure of immunization activities and monitoring of coverage at local levels (WHO/UNICEF, 2005). The present study shows that large nutritional surveillance systems, as used in Indonesia and Bangladesh, can be used to provide ongoing surveillance of immunization coverage and other activities aimed at child survival. The nutritional surveillance system in Indonesia was discontinued in 2003, but the nutritional surveillance system in Bangladesh has been ongoing since 1990 (de Pee *et al,* 2002).

Whether the findings from the present study in Indonesia can be generalized to other countries in Southeast Asia or elsewhere in developing countries will need further investigation. The strength of the present study was that it was a population-based sample of over a quarter of a million children in rural Indonesia. There are important implications, since Indonesia is the largest country in Southeast Asia with a total population over 220 million and over 21 million children under age five years (UNICEF, 2006).

Achieving the Millenium Development Goals of increasing child survival will depend upon delivering effective and sustainable interventions for children who would benefit the most. The Expanded Program on Immunization is one of the strongest interventions to improve child survival, and higher and more equitable coverage will be needed. As recently emphasized, “we must do better” to expand coverage with existing interventions, as the goal for reducing child survival will only be achieved if public health can deliver (Bryce *et al,* 2003).

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