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Divergent Mortality for Male and Female Recipients of Low-Titer and High-Titer Measles Vaccines in Rural Senegal

Peter Aaby,[1,2] Badara Samb,[1] Francois Simondon,[1] Kim Knudsen,[2,3] Awa Marie Coll Seck,[4] John Bennett,[5] and Hilton Whittle[6]

The female/male mortality ratio among unimmunized children and children vaccinated with standard or high-titer measles vaccines was examined for all children born in the period 1985–1991 in a rural area of Senegal. The female/male mortality ratio from 9 months to 5 years of age for unvaccinated children was 0.94 (95% confidence interval (CI) 0.75–1.19), significantly different from the ratio of 0.64 (95% CI 0.48–0.85) for recipients of the Schwarz standard measles vaccine ($p = 0.040$). In the 4-year period, where high-titer measles vaccines were used in the study area, the female/male mortality ratio was 1.33 (95% CI 1.00–1.78) for recipients of high-titer Edmonston-Zagreb or Schwarz vaccines compared with 0.67 (95% CI 0.42–1.07) for recipients of the Schwarz standard vaccine ($p = 0.013$). Hence, the Schwarz standard and high-titer measles vaccines have divergent sex-specific effects on mortality throughout childhood. Further studies of the underlying mechanisms are needed. *Am J Epidemiol* 1993;138:746–55.

measles; measles vaccine; mortality; sex

Studies from Guinea-Bissau and Senegal have found significantly higher mortality among girls who received a high-titer measles vaccine than among female controls who received the Schwarz standard measles vaccine at 9–10 months of age (1–3). In these studies, high-titer vaccines were given from the age of 4–5 months, whereas controls received placebo or inactivated polio vaccine (IPV) at a similar age. The observation of higher female mortality among recipients of high-titer vaccines has raised problems for immunization strategies in developing countries. The recommendation for use of high-titer measles vaccines at 6 months of age in areas with a high incidence of measles (4) has been rescinded (5). To investigate the reasons for these findings, we examined the sex differences in mortality among measles vaccinees and unvaccinated children during a 6-year period from 1985 to 1991 in a rural area of Senegal, Niakhar. Most children born in this area from February 1987 to January 1989 were recruited for a study of high-titer Edmonston-Zagreb and Schwarz measles vaccines. In addition, we included all children born during the 2 years before and the 2 years after the high-titer vaccine study.

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Abbreviations: CI, confidence interval; DPT, diphtheria-pertussis-tetanus vaccine; IPV, inactivated polio vaccine.

[1] ORSTOM, Dakar, Senegal.
[2] Epidemiology Research Unit, Statens Seruminstitut, Copenhagen, Denmark.
[3] Statistical Research Unit, University of Copenhagen, Copenhagen, Denmark.
[4] Université Cheikh Anta Diop, Dakar, Senegal.
[5] Task Force for Child Survival, Atlanta, GA.
[6] MRC Laboratories, Banjul, The Gambia.
Reprint requests to Dr. Peter Aaby, Artillerivej 5, 2300 Copenhagen S, Denmark.

MATERIALS AND METHODS

The Sereer population of Niakhar, the demographic surveillance system (6), and the epidemiology of measles (7, 8) have been described in detail elsewhere. From 1983 to 1987, the demographic monitoring system was based on annual censuses during which information was collected on migration, marriages, births, mortality, vaccinations, breast feeding, and infections. Since 1987, these annual censuses have been supplemented with weekly surveillance visits to all compounds in the study area.

Study cohorts

The present study includes all children born to a resident mother. Mortality has been examined from 9 months of age (>272 days), the recommended age for immunization with the Schwarz standard measles vaccine. Children were followed to death, migration, 5 years of age, or the annual census in February 1992. There were no children for whom information could not be obtained. Children who moved back to Niakhar reentered the study, but only from the date on which they were registered again.

Pretrial period. Of 2,417 children born between February 1, 1985, and January 31, 1987, 2,093 were still under surveillance from 9 months of age. In this period, there was little routine measles vaccination in the study area until late 1986 when the national Accelerated Immunization Program was initiated. Because vaccines were provided in a campaign rather than being part of a routine program, the mean age at immunization was higher (table 1), and more children were vaccinated after 12 months of age (60 percent, 599 of 992) than in later cohorts. There were similar numbers of male and female measles cases among unvaccinated (58 boys, 54 girls) and the Schwarz standard-vaccinated children (eight boys, 14 girls).

Trial period. The study cohort included children born between February 1, 1987, and January 31, 1989. At 5 months of age, children were randomized to receive a placebo or a high-titer dose of Edmonston-Zagreb or Schwarz standard measles vaccine (>10^5 plaque-forming units). Children in the placebo group as well as children who did not appear at the 5-month vaccination were offered a Schwarz standard vaccination when they were 10 months old (mean age, 10.1 months). In the present analysis, we have included all 2,467 children born in the period irrespective of whether they entered the trial. Of these children, 2,118 lived in the study area after the age of 9 months. Of the Schwarz standard-vaccinated children, 11 percent received their vaccination after 12 months of age (92 of 810). After 9 months of age, there were 29 boys and 26 girls who had measles among unvaccinated (22 boys, 21 girls), Schwarz standard-vaccinated (one boy, two girls), and high-titer-vaccinated (six boys, three girls) children.

Posttrial period. After completion of the high-titer vaccine study, we used the Edmonston-Zagreb high-titer vaccine routinely for the children in the area who took part in a subsequent pertussis vaccine study and received a vaccine at 6

TABLE 1. Vaccine coverage by sex, vaccine type, and period: Niakhar, Senegal, 1985–1991*

	Females			Males		
	Coverage (%)	Vaccinated/ all	Mean age (days)†	Coverage (%)	Vaccinated/ all	Mean age (days)
Schwarz standard vaccine						
1985–1986	19	186/992	489	20	207/1,038	472
1987–1988	60	353/585	348	61	352/574	356
1989–1990	65	341/530	315	63	359/565	310
High-titer vaccines						
1987–1988	73	500/689	157	70	450/641	157
1989–1990	70	489/694	196	71	502/710	196

* Vaccination coverage is measured at 12 months of age in the Schwarz standard group and at the time of convening the children for vaccination in the high-titer group. Hence, numbers do not correspond exactly with the number of children under observation at 9 months of age.
† Age (days) at time of immunization.

or 7 months of age. Children who had not been vaccinated with the Edmonston-Zagreb high-titer vaccine were subsequently offered the Schwarz standard vaccine at 9–10 months of age. We have included the 2,404 children born between February 1, 1989, and January 31, 1991, of whom 2,104 lived in the area after the age of 9 months. The Edmonston-Zagreb high-titer vaccine had been offered to the children born until April 1990 and was suspended in November 1990. Of the Schwarz standard-vaccinated children, 6 percent received their vaccination after 12 months of age (46 of 759). After 9 months of age, there were only four unvaccinated children (one boy, three girls) who had measles in this cohort.

Measles immunizations, surveillance, and vaccine efficacy

Since 1987, when the high-titer vaccine study started, most measles vaccinations were provided directly by the project. Prior to 1987, information on vaccinations was collected from vaccination cards during home visits in connection with the annual census. It is likely that some children may have been immunized in campaigns or outside the study area without this being registered by the field assistants.

Measles surveillance in the study area has been described elsewhere (7, 8). Prior to 1987, the study was based on parental diagnoses of measles that have been found to be very reliable (7). After the beginning of the vaccine trial, we conducted weekly surveillance and active follow-up of all identified cases; most cases with a typical rash or typical desquamation were seen by a physician (8).

Vaccine efficacy was calculated as 1 – relative risk (incidence of vaccinated children/incidence of unvaccinated children). The analysis of vaccine efficacy was adjusted for the same age groups and study periods as the analysis of mortality.

Cause of death

Information on the cause of death was obtained through parental postmortem interviews (9) reviewed by two physicians who were blind to the vaccine group of the dead children. Though the specificity of such diagnoses is debatable (10), postmortem interviews should be able to detect major differences in causes of death between different groups.

Statistics

Children were randomized to different groups only during the trial, and even then no children were assigned to receive placebo only. Differences in mortality between the vaccinated and unvaccinated children are therefore likely to be affected by selection bias. However, it seems unlikely that any selection bias for vaccination operates differently for the sexes in different groups.

Since 9 months of age has been the official age for receiving the Schwarz standard vaccine, we compared mortality from 9 months to 5 years of age. Only Schwarz standard vaccinations given from 6 months of age were considered valid, since seroconversion before 6 months of age was assumed to be too low. However, including the 30 children (14 boys, 16 girls) vaccinated with standard vaccine before 6 months of age (of whom two died, one boy and one girl) would not change the mortality ratios. Children changed from "unvaccinated" to "vaccinated" on the day of immunization. Children vaccinated after having had measles infection were considered unvaccinated; however, the risk ratios would be the same if censoring was done at the time of measles vaccination. A few children who received high-titer vaccines after a Schwarz standard vaccination were censored at the day of revaccination.

Crude death rates based on person-years at risk were used for comparing the sex ratios. Pooled estimates have been calculated using the method of maximum likelihood (11). The variation in sex mortality ratios has been tested by a likelihood ratio test. The comparison of unvaccinated and Schwarz standard-vaccinated children covers the whole cohort of children born between February 1985 and January 1991. In the comparisons involving high-titer vaccines, analyses have been limited to the children born from February 1987 to April 1990, the cohort which was offered high-titer vaccines.

In the comparisons between the sexes in the different vaccine groups, a Cox regression model (12) was used to adjust for background factors such as age, season (rainy, July to October, vs. dry, November to June), year of birth, and measles infection. Migration patterns before 5 years of age were different for boys and girls. Because this could be associated with different patterns of separation when the mother died, the death of the mother was included as a time-dependent background factor.

RESULTS

Vaccine coverage, vaccine efficacy, and patterns of migration by sex

Though vaccine coverage and the ages at vaccination differed in the study cohorts, they were similar for male and female recipients of standard and high-titer vaccines within all periods (table 1). A similar number of boys and girls had measles among unvaccinated (81 boys, 78 girls) and vaccinated (15 boys, 19 girls) children. Hence, the vaccine efficacy for Schwarz-standard vaccine was similar for male (0.85, 95 percent confidence interval (CI) 0.72–0.92) and female (0.75, 95 percent CI 0.60–0.85) children. Because of the small number of cases, we have not computed the sex-specific vaccine efficacy for recipients of high-titer vaccines.

Between 9 months and 5 years of age, girls tended to migrate more than boys (relative risk = 1.15, 95 percent CI 0.98–1.34).

TABLE 2. Deaths, person-years at risk, and mortality ratio by sex, vaccine type, and period: Niakhar, Senegal, 1985–1991

Age (months) by period	Unvaccinated				Schwarz standard vaccinated			
	Females		Males		Females		Males	
	Deaths (no.)	Person-years at risk	Deaths (no.)	Person-years at risk	Deaths (no.)	Person-years at risk	Deaths (no.)	Person-years at risk
1985–1986								
9–23	62	847.5	62	866.3	18	355.2	35	381.9
24–60	37	1,211.3	38	1,274.1	24	1,204.2	35	1,226.0
Female/male mortality ratio		1.02 (0.77–1.35)*				0.63 (0.43–0.92)		
1987–1988								
9–23	18	309.6	16	296.4	12	406.2	19	409.4
24–60	7	245.8	5	241.6	12	698.6	19	695.9
Female/male mortality ratio		1.15 (0.64–2.05)				0.63 (0.38–1.05)		
1989–1990								
9–23	10	209.6	25	213.0	7	238.7	13	255.7
24–60	3	50.3	2	44.5	4	48.1	4	60.4
Female/male mortality ratio		0.48 (0.25–0.93)				0.73 (0.34–1.54)		
Total ratio		0.94 (0.75–1.19)				0.64 (0.48–0.85)		

* Numbers in parentheses, 95% confidence interval.

Female/male mortality ratios for Schwarz standard-vaccinated and unvaccinated children

The overall female/male mortality ratios after 9 months of age for the three time periods combined (table 2) were 0.94 (95 percent CI 0.75–1.19) for unvaccinated children and 0.64 (95 percent CI 0.48–0.85) for recipients of the Schwarz standard vaccine, a significant difference ($p = 0.040$). When survival was compared (figure 1), there was no difference for the Schwarz standard-vaccinated and unimmunized boys (mortality ratio = 0.96, 95 percent CI 0.75–1.23; $p = 0.351$), whereas the difference was marked for girls (mortality ratio = 0.65, 95 percent CI 0.49–0.87; $p = 0.0005$).

Essentially similar results were obtained in a multivariate analysis where a Cox model was used to adjust for the effects of age, year of birth, season, death of mother, and measles infection, all significant background factors. Mortality was at least two times higher in the rainy than in the dry season in the different groups. In the Cox model, unvaccinated children had a female/male mortality ratio of 0.93 (95 percent CI 0.74–1.18) over the 6-year period versus 0.64 (95 percent CI 0.48–0.84) for Schwarz standard-vaccinated children.

Though there were fewer female deaths among the Schwarz standard-vaccinated children, there was no difference in the distribution of causes between vaccinated and unvaccinated children nor between boys and girls. The main causes of death according to the parental postmortem interview were diarrhea (28 percent, 137 of 487), malaria (16 percent, 80 of 487), malnutrition (16 percent, 77 of 487), and undefined (21 percent, 103 of 487) (data available on request). None of the vaccinated children died of measles, whereas seven unvaccinated children (four boys, three girls) died in the acute phase of infection, giving a case fatality ratio of 4.3 percent. Only 2.5 percent (seven of 284) of all deaths among unvaccinated children occurred in the acute phase of measles.

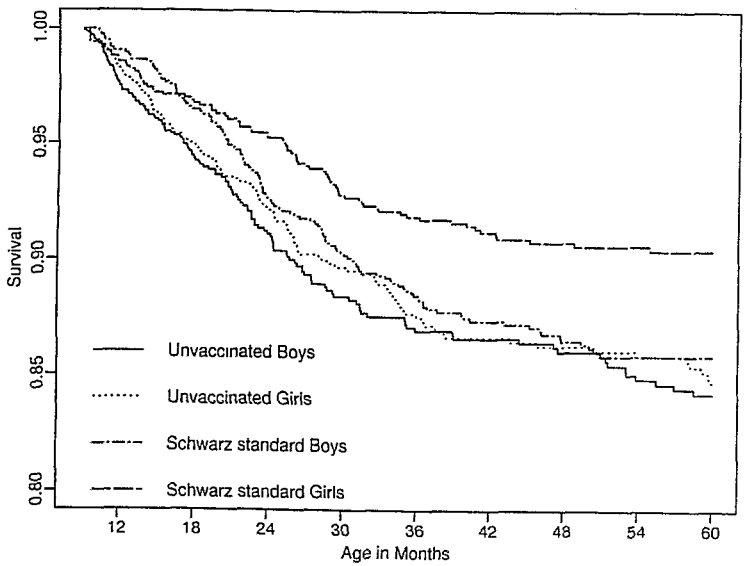

FIGURE 1. Survival curves from 9 months of age by sex for unvaccinated and Schwarz standard measles-vaccinated children born between February 1985 and January 1991 in Niakhar, Senegal.

TABLE 3. Deaths, person-years at risk, and mortality ratio by sex, vaccine type, and periods: Niakhar, Senegal, 1987–1990

Age (months) by period	Unvaccinated				Schwarz standard vaccinated				High-titer vaccinated			
	Females		Males		Females		Males		Females		Males	
	Deaths (no.)	Person-years at risk	Deaths (no.)	Person-years at risk	Deaths (no.)	Person-years at risk	Deaths (no.)	Person-years at risk	Deaths (no.)	Person-years at risk	Deaths (no.)	Person-years at risk
1987–1989*												
9–23	18	309.6	16	296.4	12	406.2	19	409.4	39	568.8	22	522.4
24–60	7	245.8	5	241.6	12	698.6	19	695.9	30	829.0	25	772.7
Female/male mortality ratio		1.15 (0.64–2.05)†				0.63 (0.38–1.05)				1.36 (0.94–1.97)		
1989–1990‡												
9–23	8	148.0	13	138.7	1	73.9	3	89.0	30	561.6	24	576.5
24–60	3	50.3	2	44.5	4	48.1	4	60.4	10	151.3	8	160.0
Female/male mortality ratio		0.68 (0.31–1.48)				0.89 (0.28–2.79)				1.29 (0.81–2.06)		
Total ratio		0.95 (0.60–1.51)				0.67 (0.42–1.07)				1.33 (1.00–1.78)		

* From February 1987 to January 1989.
† Numbers in parentheses, 95% confidence interval.
‡ From February 1989 to April 1990.

Female/male mortality ratios for recipients of high-titer and Schwarz standard measles vaccines

In the cohort born between February 1987 and April 1990 (table 3), the female/male mortality ratios were 0.67 (95 percent CI 0.42–1.07) for recipients of the Schwarz standard vaccine and 1.33 (95 percent CI 1.00–1.78) for recipients of the high-titer vaccine, a significant difference ($p = 0.013$) (figure 2). Ratios were similar for the Schwarz high-titer vaccine (1.38, 95 percent CI 0.72–2.66) and Edmonston-Zagreb high-titer vaccine (1.50, 95 percent CI 0.84–2.66) during the part of the trial when both vaccines were used. When the mortality rates of high-titer-vaccinated and unvaccinated children were compared (table 3), there were no significant differences (boys: mortality ratio (high titer/unvaccinated) = 0.78, 95 percent CI 0.52–1.16; $p = 0.260$; girls: mortality ratio = 1.15, 95 percent CI 0.78–1.67; $p = 0.544$). There was no difference in the distribution of causes of deaths for unvaccinated children and children vaccinated with standard vaccine and high-titer measles vaccine (authors' unpublished observations).

Estimates of the female/male mortality ratios remained unchanged when controlling for background factors in a Cox model (Schwarz standard vaccine: 0.65, 95 percent CI 0.41–1.04; high-titer vaccine: 1.32, 95 percent CI 0.99–1.77).

Female/male mortality ratio after the administration of other vaccines

Measles vaccine is usually administered at 9–10 months of age together with other vaccines (diphtheria-pertussis-tetanus (DPT)-inactivated polio vaccine (IPV) and yellow fever). Because other vaccines could have had an effect on the sex ratio, we examined whether the administration of DPT-IPV and yellow fever had an effect on the female/male mortality ratio during the high-titer vaccine trial. The female/male mortality ratio was 1.56 (95 percent CI 0.98–2.48) among children who received DPT-IPV and yellow fever at 10 months after high-titer vaccine at 5 months, whereas it was only

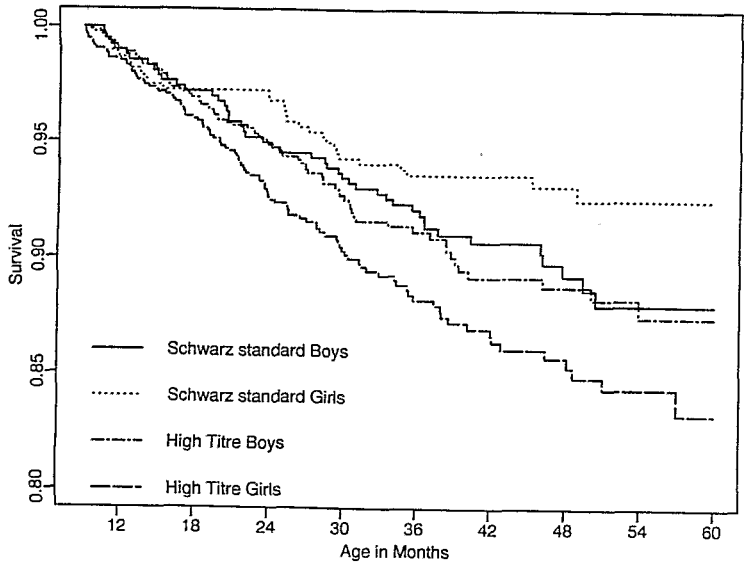

FIGURE 2. Survival curves from 9 months of age by sex for recipients of the Schwarz standard and high-titer measles vaccines. Children were born between February 1987 and April 1990 in Niakhar, Senegal.

0.55 (95 percent CI 0.29–1.04) among children who received DPT-IPV and yellow fever at 10 months together with the Schwarz standard vaccine ($p = 0.008$). The impact of DPT-IPV alone without simultaneous administration of yellow fever could be examined only between 5 and 10 months of age. In the placebo group, the female/male mortality ratio was 1.39 (95 percent CI 0.53–3.64), whereas it was 1.27 (95 percent CI 0.56–2.85) among recipients of high-titer vaccines.

DISCUSSION

Prior to the general introduction of measles vaccination, the mortality between 9 months and 5 years of age was the same for females and males, the mortality ratio being 1.01 (95 percent CI 0.82–1.26) for the cohort born during 1983–1985 (unpublished observations). This tendency continued for the unvaccinated children in the following two periods. However, in the posttrial period, the mortality increased, particularly for boys, and the female/male mortality ratio was low among the unvaccinated children. For recipients of the Schwarz standard vaccine, the female/male mortality ratio was consistently low and, for recipients of high-titer vaccine, it was high, the difference being significant. Apparently, other vaccines (DPT-IPV and yellow fever) were associated with neither low nor high female/male mortality ratios. Adjustment for age, season, migration, measles infection, and the death of a mother did not alter the female/male mortality ratios.

Since the study was not planned, behavioral factors of importance for immunization and mortality may not have been controlled. However, as the two measles vaccines were associated with markedly divergent female/male mortality ratios, a simple cultural preference for one sex, if it exists, is unlikely to explain the observed pattern of childhood mortality. There is no obvious indication of sex differences in the care or access to health services in the study area. The duration of breast feeding is the same for boys and girls. The vaccine coverage for boys and girls was exactly the same (table 1). In records from health centers from 1987, there were the same numbers of consultations, 481 boys and 470 girls under 5 years of age.

Because the children were not randomized to the different groups, it is not possible to determine definitely the relative impact of these vaccines on mortality. Because the measles incidence and case mortality ratio were low in the study cohorts, only a limited impact should be expected from vaccination. However, we found that girls receiving the Schwarz standard vaccine benefited from measles vaccination compared with vaccinated boys and unvaccinated boys and girls (figure 1). The mortality of female recipients of high-titer vaccines was not significantly different from the mortality of unvaccinated girls (table 3).

An impact of the Schwarz standard measles vaccine on survival beyond the expected benefits from control of measles infection has been noted before (13, 14), but sex-specific effects have not been emphasized. However, one study from Bangladesh of a large number of Schwarz standard-vaccinated children reported that the reduction in mortality for girls (37 of 1,000) was larger than that for boys (17 of 1,000) (15). Sex-specific effects of the vaccine could be due to protection conferred against measles if there were different case mortality ratios for girls and boys, as found in some areas of West Africa (16–18). Though previous studies from Niakhar have found higher female case mortality (16, 17), there was little measles in the present study cohorts, and there was no difference in vaccine efficacy or the case mortality ratio. Hence, as suggested by the regression analysis controlling for measles infection, the low mortality among female recipients of the Schwarz standard vaccine cannot be explained by control of measles infection. Since the pattern observed in Niakhar could be a chance observation, further studies are needed to verify the finding of a lower female/male

mortality ratio for recipients of the Schwarz standard vaccine in West Africa and elsewhere.

Differences in female mortality between recipients of high-titer vaccines and standard titer vaccines have been found in several studies in Guinea-Bissau (1, 2), Senegal (3), and Haiti (5). An increased female/male mortality ratio was also observed in the post-trial period (table 3), when the Edmonston-Zagreb high-titer vaccine was given routinely.

Given the consistency of findings on increased mortality among female recipients of high-titer vaccine, an international expert panel has recommended that routine use of high-titer measles vaccination be discontinued (5), although it has not been documented that high-titer vaccines are harmful compared with unvaccinated controls. The present study suggests that a large part of the observed differences in mortality is due to the improved survival of girls after the Schwarz standard vaccine compared with that of all other groups.

There is no known biologic explanation for these findings, because the possibility that vaccines have effects beyond the protection against specific diseases has rarely been studied. The dose of vaccine virus may be important in producing divergent sex ratios, since differences in female mortality were not found in the previous trials in Guinea-Bissau and The Gambia using medium-titer Edmonston-Zagreb vaccine (<50,000 plaque-forming units) (19, 20). It is possible that the interaction between dose and maternal antibody levels at the time of vaccination is important for the unexpected ratios, because girls were found to have lower antibody levels at 10 months of age than boys (authors' unpublished observations). During the trial period during which systematic anthropometric data were collected, height, weight, and arm-circumference measurements indicated that girls were generally better nourished when vaccinated at 10 months of age than were boys, and this may have conferred a survival advantage for them. In addition, it is also possible that the Schwarz standard vaccine had a selectively beneficial impact on girls.

Further studies are needed to define the biologic basis of these observations. Sex differences will have to be taken into consideration in future studies of measles vaccination (5).

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REFERENCES

1. Expanded Programme on Immunization. Safety and efficacy of high titre measles vaccine at 6 months of age. Wkly Epidemiol Rec 1991; 66:249–51.
2. Aaby P, Knudsen K, Whittle H, et al. Long-term survival after Edmonston-Zagreb measles vaccination in Guinea-Bissau: increased female mortality rate. J Pediatr 1993;122:904–8.
3. Aaby P, Samb B, Simondon F, et al. Child mortality after high-titre measles vaccines in Senegal: the complete data set. (Letter). Lancet 1991;338:1518.
4. Expanded Programme on Immunization. Global Advisory Group. Part I. Wkly Epidemiol Rec 1990;65:5–11.
5. Expanded Programme on Immunization. Safety of high titre measles vaccines. Wkly Epidemiol Rec 1992;67:357–61.
6. Garenne M, Maire B, Fontaine O, et al. Risques de décés associés à différents états nutritionnels chez l'enfant d'âge préscolaire. (In French). Dakar: ORSTOM, 1987.
7. Garenne M, Aaby P. Pattern of exposure and measles mortality in Senegal. J Infect Dis 1990;161:1088–94.
8. Samb B, Aaby P, Whittle H, et al. Protective efficacy of high-titre measles vaccines administered from the age of five months in rural Senegal. Trans R Soc Trop Med Hyg (in press).
9. Garenne M, Fontaine O. Assessing probable causes of deaths using a standardized questionnaire. A study in rural Senegal. In: Proceedings of the IUSSP seminar on morbidity and mortality, Sienna, 7–10 July, 1986.
10. Snow RW, Armstrong JRM, Forster D, et al. Childhood deaths in Africa: uses and limitations of verbal autopsies. Lancet 1992;340:351–5.
11. Rothman KJ. Modern epidemiology. Boston: Little, Brown and Company, 1986.
12. Cox DR. Regression models and life tables (with discussion). J R Stat Soc (B) 1972;34:187–220.
13. Aaby P. Determinants of measles mortality: host or transmission factors? In: de la Maza LM, Peterson EM, eds. Medical virology. Vol 10. New York: Plenum Press, 1991:83–116.
14. Clemens JD, Stanton BF, Chakraborty J, et al. Measles vaccination and childhood mortality in rural Bangladesh. Am J Epidemiol 1988;128: 1330–9.
15. Koenig MA. Mortality reductions from measles and tetanus immunization: a review of the evidence. In: Hill K, ed. Child health priorities for the 1990s. Baltimore: Johns Hopkins Institute for International Programs, 1992.
16. Garenne M. Variations in the age pattern of infant and child mortality with special reference to a case study in Ngayokheme (rural Senegal). (PhD dissertation). Philadelphia: University of Pennsylvania, 1982.
17. Aaby P. The impact of cross-sex transmission on measles mortality in rural Senegal. Lancet 1992;340:388–91.
18. Fargues P, Nassour O. Douze ans de mortalité urbaine au Sahel. (In French). Paris: Presses Universitaires de France, 1988.
19. Aaby P, Jensen TG, Hansen HL, et al. Trial of high-dose Edmonston-Zagreb measles vaccine in Guinea-Bissau: protective efficacy. Lancet 1988;2:809–11.
20. Whittle HC, Campbell H, Rahman S, et al. Antibody persistence in Gambian children after high-dose Edmonston-Zagreb measles vaccine. Lancet 1990;336:1046–8.

APPENDIX

APPENDIX TABLE 1. Causes of death between 9 months and 5 years of age among unvaccinated and Schwarz standard-vaccinated children (Schwarz) according to sex, for children born between 1985 and 1991: Niakhar, Senegal, February 1992 follow-up

Cause of death	Females				Males			
	Unvaccinated		Schwarz		Unvaccinated		Schwarz	
	No.	%	No.	%	No.	%	No.	%
Diarrhea	34	25	21	27	41	28	41	33
Whooping cough	4	3	1	1				
Meningitis, sequelae	2	1	3	4	3	2	6	5
Measles	3	2			4	3		
Malaria	24	18	13	17	22	15	21	17
Malnutrition	19	14	18	23	22	15	18	14
Pneumonia	17	12	4	5	15	10	9	7
Congenital					3	2	1	1
Other specific	3	2	2	3	2	1	4	3
Accidents	1	1	1	1	1	1	1	1
Undefined, no information	30	22	14	18	34	23	25	20
Total	137		77		147		126	