

ALL-CAUSE MORTALITY AMONG YOUNG CHILDREN IN WESTERN KENYA. VI: THE ASEMBO BAY COHORT PROJECT

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Abstract. Although all-cause mortality has been used as an indicator of the health status of childhood populations, such data are sparse for most rural areas of sub-Saharan Africa, particularly community-based estimates of infant mortality rates. The longitudinal follow-up of more than 1,500 children enrolled at birth into the Asembo Bay Cohort Project (ABCP) in western Kenya between 1992 and 1996 has provided a fixed birth cohort for estimating all-cause mortality over the first 5 yr of life. We surveyed mothers and guardians of cohort children in early 1999 to determine survival status. A total of 1,260 households were surveyed to determine the survival status of 1,556 live births (99.2% of original cohort, $n = 1,570$). Most mothers (66%) still resided but 27.5% had migrated, and 5.5% had died. In early 1999, the overall cumulative incidence of all-cause mortality for the entire 1992–1996 birth cohort was 26.5% (95% confidence interval, 24.1–28.9%). Neonatal and infant mortality were 32 and 176 per 1,000 live births, respectively. These community-based estimates of mortality in the ABCP area are substantially higher than for Kenya overall (nationally, infant mortality is 75 per 1,000 live births). The results provide a baseline description of all-cause mortality among children in an area with intense *Plasmodium falciparum* transmission and will be useful in future efforts to monitor changes in death rates attributable to control programs for specific diseases (e.g., malaria and HIV/AIDS) in Africa.

INTRODUCTION

Descriptions of early childhood mortality rates are critical for planning public health strategies in sub-Saharan Africa. Studies of mortality and disease-specific case fatality rates in African children are most often conducted in hospitals. However, in many African settings, most children do not die in medical facilities and their deaths may not be represented by hospital-based studies or recorded in any manner.^{1,2} The scarcity of community-based childhood mortality rates often leads to assumptions that hospital-based estimates mirror mortality in the surrounding communities.³ These data deficiencies impede health ministries' abilities to direct resources to highest-risk communities and to evaluate the effectiveness of their prevention programs.

Evaluations of interventions to prevent mortality from malaria, such as permethrin-treated bed nets, have depended on measuring reductions in all-cause child mortality.^{4–6} Efforts are now under way via the Roll Back Malaria initiative to reduce the burden of malaria mortality in African children by 50% by the year 2010. Simultaneously, the increasing incidence of HIV/AIDS among the same population may hamper our ability to detect such a reduction. Thus, descriptive reviews of mortality in rural communities are needed as part of implementing programs and monitoring the impact of promising interventions.⁸

Disease-specific mortality rates are most sensitive for detecting the protective effect of a specific intervention. Unfortunately, in rural areas of developing countries reliable numerators for disease-specific deaths and at-risk denominator data are generally unavailable.² Furthermore, in malaria-endemic areas, *Plasmodium falciparum* contributes to different syndromes (e.g., respiratory distress and anemia) that often lead to death, even though the cause of death may be classified as nonmalarial.^{9,10}

This report presents a community-based evaluation of age-specific and temporal trends in all-cause child mortality in a

large, well-characterized cohort of children born in rural western Kenya between 1992 and 1996, before the implementation of a randomized controlled trial of insecticide-treated bed nets. These results are part of an ongoing longitudinal study of the epidemiologic and immunologic determinants of *P. falciparum* infection and malaria-associated morbidity and mortality known as the Asembo Bay Cohort Project (ABCP). The initial report in this series describes the overall study design and population¹¹ and is followed by a description of *P. falciparum* and anemia prevalence¹² and an analytic approach for repeated hemoglobin measures.¹³ Reports concerning the effect of parasitemia density on anemia¹⁴ and development of antibodies to a merozoite surface protein (MSP-1 19kD)¹⁵ have also recently been published.

METHODS

Asembo Bay Cohort Project. The ABCP has been recently described in detail.^{11,13} Between June 1992 and August 1996, pregnant women in the 15-village study area were enrolled and monitored at monthly intervals until the final month of gestation, when weekly visits were conducted. Pregnancy was determined by asking date of last menstrual period. Women with neither evidence of a miscarriage nor stillbirth were classified as having had a false pregnancy. Traditional birth attendants monitored each birth and completed a data collection form detailing each birth event. Presence/absence of a delivery complication, location of birth (home/hospital/clinic), number of infants born, birth status (alive or stillborn), and sex were recorded. Capillary blood films were obtained from the mother and from the maternal side of the placenta. Birth weight was obtained within 24 hr after delivery. Specially trained staff recorded gestational age within 48 hr after delivery using a modified Dubowitz scoring system.¹⁶ Intrauterine growth retardation was defined as having a sex-specific birth weight less than the 10th per-

centile of weight-for-gestational-age of an international reference group.¹⁷ Informed consent was obtained from all adult participants and from parents or legal guardians of minors. Institutional review boards from the Centers for Disease Control and Prevention and the Kenya Medical Research Institute approved the study protocol.

During the longitudinal follow-up between 1992 and 1996, each child was visited every 2 wk. If measured fever ($> 37.5^{\circ}\text{C}$) was present, a thick blood film was obtained. Sulphadoxine-pyrimethamine (SP), known to be highly effective against *P. falciparum* in this area (ter Kuile FO, unpublished data), was given when measured fever was accompanied by any detectable level of parasitemia. A mother/guardian could request a body temperature measurement by a study staff member from the community at any time. As this was principally a malaria investigation, malaria treatment was provided as noted for uncomplicated malaria, but children with severe malaria or other illnesses were referred to local health care facilities.

Mortality survey of the 1992–1996 birth cohort. Follow-up of the cohort during the original enrollment period (1992–1996) included recording the deaths of children who remained in the study through 1996. However, the completeness of the recording procedures used during this period was never verified, and deaths among children of mothers who declined to continue participation in the study were missed. In early 1999, we conducted a retrospective mortality survey of children born into the 1992–1996 ABCP birth cohort. A pre-coded structured questionnaire was designed to interview the child's mother or other surviving family member (usually the father or another of his wives) regarding the current survival status of the cohort child.

The questionnaire first established whether the mother was alive, and if so, whether she still resided at the original household or had relocated. If the study mother had died or relocated, date of death or relocation was elicited from the family member. In instances of relocation, the name of the geopolitical district and location was obtained. After the interviewer stated the full name of the enrolled child, the respondent was asked to recall the child's exact date of birth. If the respondent was unable to recall the child's birth date within 30 d of the date in the ABCP records, the interviewer asked to see the child's birth record or vaccination card. This helped establish mutual understanding between the interviewer and respondent regarding which child the survey was inquiring about. These steps were particularly critical for situations where the respondent was someone other than the mother and in cases of multiple births. For purposes of determining validity of the survey, each interview established whether or not the respondent successfully confirmed the child's date of birth (based upon study records).

Definitions of mortality rates. Neonatal mortality rate is defined as the number of deaths before the 28th day of life per 1,000 live births. Post-neonatal mortality includes the number of deaths between Day 28 and Day 365 of life per 1,000 live births, after subtraction of the neonatal deaths from the denominator. Infant mortality rate is the number of deaths on or before Day 365 of life per 1,000 live births. Postinfant mortality rate is the number of deaths per 1,000 survivors of infancy. Except where indicated, all 3 rates use

the standard convention of including both singleton and multiple live births in the denominator.¹⁸

Analysis. To maintain statistical independence, all mortality rates were calculated using the first live birth enrolled into the cohort by each mother (N.B., first birth enrolled is *not* necessarily a primigravidae woman). Year of birth was categorized according to 12-mo intervals beginning in June 1992 (initial delivery) and ending May 1996 (final delivery). Later in the study, because we followed only the pregnancies of previously enrolled women, the number of live births in the 4th study year (June 1995–May 1996) were markedly lower than the previous 3 yr.

Calculation of 95% confidence intervals (CI) was based on a Poisson distribution for rates < 50 per 1,000 live births and on a normal distribution for rates > 50 per 1,000.¹⁹ To control for the possibility of either a harmful effect of moving away from the study site (e.g., no regular SP therapy available) or a beneficial effect (e.g., moving to an area of less intense *P. falciparum* exposure), we also calculated death rates among study participants who had not migrated from the study area between 1992 and 1999.

Validity of the survey results was evaluated by stratifying the data according to which family member was interviewed for the survey (e.g., mother versus other family member). Because of sample size restrictions, this evaluation was performed for infant mortality rates only.

Geographic information system. The mapping of the study area using a differential global positioning system (GPS) has been described.²⁰ Briefly, all family compounds (including households within the compounds), market areas, schools, health facilities, roads, streams, the shore of Lake Victoria, and potential mosquito breeding sites (dams and burrow pits) were mapped with Trimble Pro XRS GPS Units (Trimble Navigation Limited, Sunnyvale, CA). Estimated area mortality rates were computed using the Spatial Analyst Extension version 1.1 for ArcView. The methodology uses the mortality experiences for households within a distance of the user's choice (half a mile in this case) to produce an estimate for that particular area. The resulting smoothed estimates are then used to produce shaded or contoured maps that are easier to interpret than the maps showing the mortality experience of the individual households or villages.

RESULTS

Enrollment period (1992–1996) and birth outcomes. A total of 1,847 pregnancies were recorded during the 4-yr enrollment period (Figure 1). After accounting for women who either relocated before delivery, declined to continue participating in the study, were not actually pregnant, or were lost to follow-up before delivery, the cohort included 1,600 pregnancy events among 1,332 enrolled women. During the 4-yr enrollment, 2 and 3 pregnancies were recorded for 255 (19%) and 12 (1%) women, respectively. Among all pregnancies, 70 (4%) miscarriages or stillbirths were recorded. The remaining birth cohort included 1,570 live births contributed by 1,274 pregnant women, and included 1,497 singleton and 73 twin live births. Descriptive data for these live births are presented in Table 1. Most (85%) births occurred at home. Birth weight was recorded for 94% of the live births, with low-birth-weight ($< 2,500$ g) and very-low-

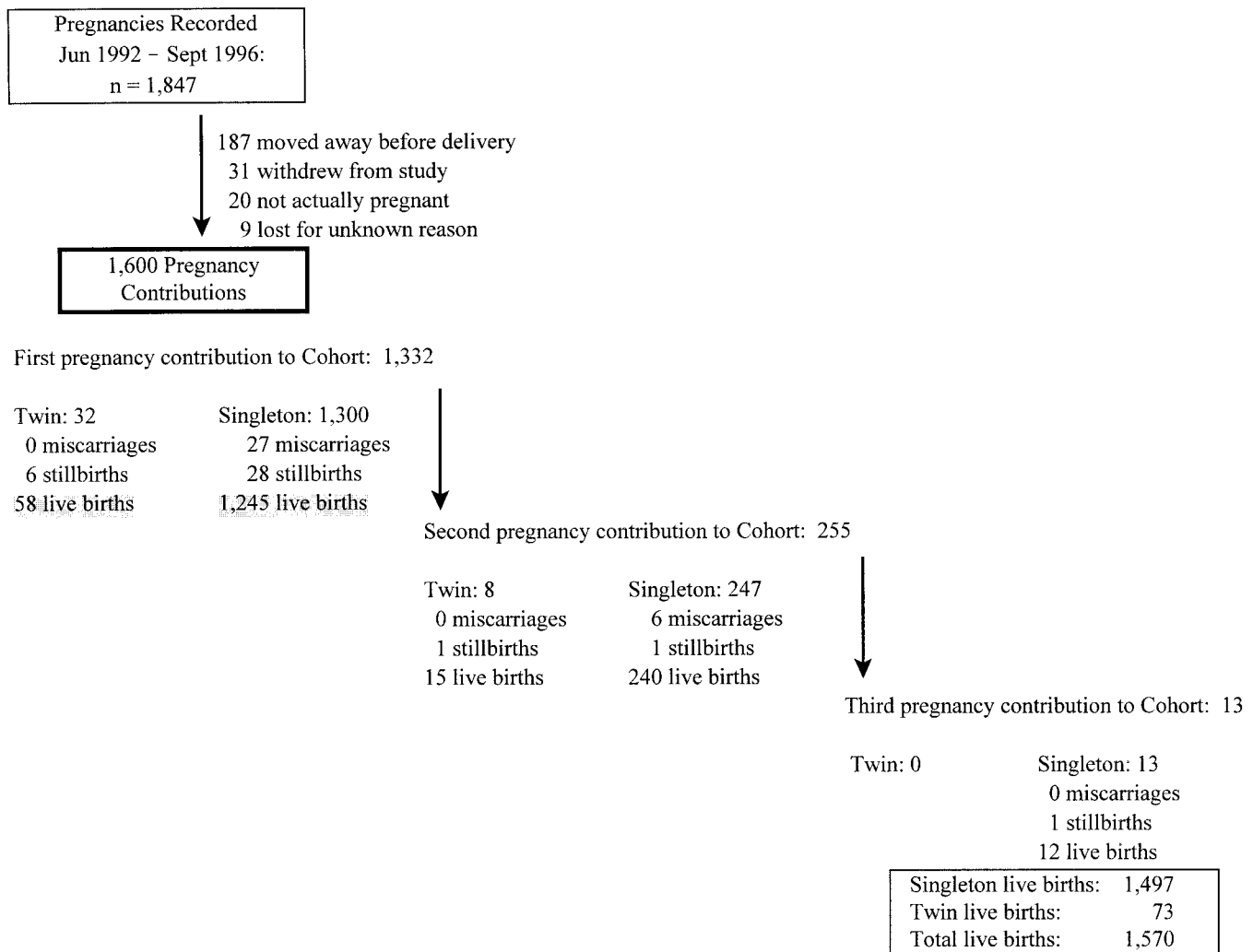


FIGURE 1. Pregnancy events included in the Asembo Bay Cohort Project and outcome of these pregnancy contributions during the 4-yr (1992–1996) enrollment period.

birth-weight (< 1,500 g) children accounting for 11.5% (95% CI, 9.9–13.1%) and 0.3% (95% CI, 0.0–0.6%) of all births, respectively. Gestational age was measured for 92% of the live births, with preterm delivery (gestational age < 37 wk) occurring in 4.1% (95% CI, 0.0–9.0%) of the births.

Maternal status in 1999. In early 1999, the mortality survey was successfully conducted for 1,260 (98.9%) of the 1,274 mothers who originally contributed a live birth to the cohort between 1992 and 1996. Most (66.0%) of the mothers were alive and still living in the ABCP study area, but 350 (27.5%) had moved away from the study site and were reported by a family member to be currently alive. Most (78%) of this migration took place after January 1996, a time after most infant mortality had already occurred. Seventy (5.5%) of the mothers were reported to be deceased, and status was not determined for 14 (1.0%) women.

Characteristics of these mothers at time of enrollment in 1992–1996 and their subsequent status at time of the 1999 survey are presented in Table 2. No significant differences were observed according to year of enrollment in the study. Women who were older at time of enrollment or had less education were significantly more likely to still reside in the

ABCP study area in 1999 ($P < 0.001$). However, these 2 sociodemographic factors were not associated with survival status of the mothers.

Overall status of children in 1999. The survey was successfully conducted for 1,556 (99.2%) of the 1,570 live births in the ABCP birth registry. Interviews regarding the remaining 14 children were not conducted. The respondent providing information (71.0% of whom were mothers) regarding the study child was able to verify the child's date of birth in 1,292 (83.0%) of the 1,556 interviews. Among the 1,556 interviews conducted, 922 (59.3%) children were present and accounted for, 403 (25.9%) were deceased, and 225 (14.5%) were currently alive but were not residing within the ABCP study area. Two of the 14 children not successfully surveyed in early 1999 were known to have died during the 1992–1996 follow-up period. Among these 405 total deaths, the number of deaths in the neonatal period (< 28 d), postneonatal period (28–365 d), second year, and post-second year of life was 47, 217, 71, and 57, respectively (age of death missing for 13 children).

After exclusion of the second and third children born into the cohort by the same mother (for statistical independence),

TABLE 1

Distribution of birth weight, gestational age, and intrauterine growth retardation among all 1,570 live births contributed by 1,274 women enrolled in the Asembo Bay Cohort Project, 1992–1996, according to birth order into the Cohort

	Delivery by a particular cohort mother			All live births (n = 1,569)
	First (n = 1,303)	Second (n = 254)	Third (n = 12)	
Singleton births	1,245	239	12	1,497
Birth weight (g)				
≥ 2,500	1,039	221	12	1,273
1,500–2,500	108	14	0	122
< 1,500	4	0	0	4
Missing	94	4	0	98
Gestational age (wks)				
≥ 37	1,104	223	12	1,340
< 37	45	1	0	46
Missing	96	15	0	111
IUGR*				
Yes	220	44	2	267
No	885	180	10	1,075
Missing	140	15	0	155
Twin births	58	15	0	73
Birth weight (g)				
≥ 2,500	22	5	0	27
1,500–2,500	34	8	0	42
< 1,500	0	1	0	1
Missing	2	1	0	3
Gestational age (wk)				
≥ 37	40	14	0	54
< 37	13	1	0	14
Missing	5	0	0	5
IUGR*				
Yes	38	12	0	50
No	15	2	0	17
Missing	5	1	0	6

* Small-for-gestational age.

our analysis included 1,303 live births, with 345 deaths through early 1999 (time of mortality survey), a mortality rate of 26.5% (95% CI, 24.1–28.9%). Age at death was unknown for 10 (3%) of these deceased children. As only 14 children died after they had migrated away from the study site, no attempt was made to calculate mortality rates for this group.

Neonatal mortality. Among the 42 neonatal deaths, nearly 55% occurred within the first week of life, with the proportion declining to 10% through the fourth week of life (Figure 2). The overall neonatal mortality rate was 32 per 1,000 live births (95% CI, 22–42). Rates of death within the first 28 d of life were similar across all 4 yr of the enrollment period (Table 3). Birth weight and gestational age were strongly associated with neonatal mortality. The crude risk of neonatal death among low-birth-weight (< 2500 g) children was over 9 times higher (risk ratio [RR] = 9.1, 95% CI, 4.3–19.0) than normal-birth-weight children. The crude risk associated with preterm delivery was nearly 18 times higher than for term delivery (RR = 17.8, 95% CI, 7.5–42.0). Village-specific rates of neonatal mortality were not calculated (inadequate power). However, geographic differences in neonatal mortality were present within the study site, with the probability of neonatal mortality highest near the Lake Victoria shore (Figure 3).

TABLE 2

Status of the 1,274 mothers at the 1999 mortality survey who were originally enrolled into the Asembo Bay Cohort Project and contributed a live birth, 1992–1996

Maternal characteristic	No.	Maternal Status in Early 1999			
		Surveyed (%)	Moved (%)	Deceased (%)	Unknown (%)
Year of 1 st birth to cohort					
6/92–5/93	426	67.1	26.3	5.6	0.9
6/93–5/94	428	66.6	25.9	6.1	1.4
6/94–5/95	287	63.8	30.3	4.9	1.0
6/95–5/96	133	65.4	30.1	4.5	0.0
Age at enrollment (yrs)					
15–19	290	43.4	49.3	6.6	0.7
20–29	611	65.3	28.0	5.2	1.5
≥ 30	373	84.7	9.7	5.1	0.5
Education (yr)					
≤ 3	155	81.3	12.3	5.2	1.3
4–7	676	68.2	24.9	5.8	1.2
≥ 8	442	57.2	36.9	5.2	0.7
Delivery < 2,500 g					
Yes	128	46.1	47.7	4.7	1.6
No	1,051	69.8	24.0	5.2	1.0
Missing	95	50.5	38.9	9.5	1.1
Delivery < 37 wks					
Yes	52	53.8	40.4	5.8	0.0
No	1,124	67.8	25.9	5.2	1.2
Missing	98	52.6	38.1	9.3	1.0

Postneonatal and infant mortality. Rates of postneonatal and infant mortality were strikingly similar during the first 3 yr of enrollment but increased substantially in the fourth enrollment year (June 1995 to May 1996; Table 4). Compared with children born in all 3 previous years, children born in the fourth enrollment year had a 70% (RR = 1.7, 95% CI, 1.2–2.4) and 60% (RR = 1.6, 95% CI, 1.2–2.2) higher risk of death during the postneonatal and infant periods, respectively.

Low birth weight was also associated with substantially increased mortality risk during the postneonatal (RR = 1.5, 95% CI, 1.1–2.2) and infant (RR = 2.0, 95% CI, 1.5–2.7) periods as compared with normal-birth-weight children (Table 4). Among all postneonatal deaths (n = 187), the smallest proportion (5%) occurred in the second month of life

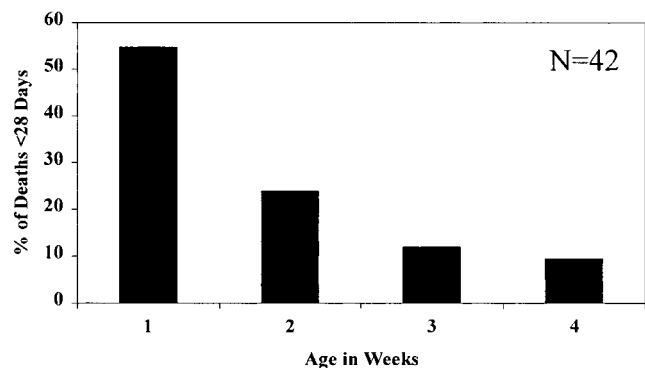


FIGURE 2. Percentage of neonatal deaths occurring during the first 4 wk of life, Asembo Bay Cohort Project, 1992–1999.

TABLE 3
Neonatal mortality according to birth weight, gestational age, and small-for-gestational age (intrauterine growth retardation [IUGR])

Birth outcome	Live births	Neonatal deaths	Neonatal mortality rate (95% CI)
Birth weight (g)			
≥ 2,500	1,061	12	11 (5–18)
< 2,500	146	15	103 (53–152)
Missing	96	15	156 (84–229)
Gestational age (wk)			
≥ 37	1,144	10	9 (3–14)
< 37	58	9	155 (62–248)
Missing	101	23	228 (146–310)
IUGR*			
Normal	900	8	9 (3–15)
Present	258	11	43 (18–67)
Missing	145	23	160 (100–220)
Year of birth			
6/92–5/93	435	13	30 (14–46)
6/93–5/94	439	14	32 (15–49)
6/94–5/95	292	10	34 (13–55)
6/95–5/96	137	5	36 (5–68)
Overall	1,303	42	32 (22–42)

* Defined as birth weight less than 10th percentile weight-for-gestational age by sex, based on an international reference group.

(Figure 4A), and the highest proportion (16%) in the fourth month, followed by a continued significant ($P < 0.001$) downward trend through the end of the first year of life. When all deaths within the first 365 d of life are considered together ($n = 229$), the highest proportion (18.8%) of infant deaths occurred in the first month and the lowest proportion (4.4%) in the second month ($P < 0.001$; Figure 4B).

Village-specific estimates of infant mortality reflect

marked differences in the force of mortality within the relatively small geographic area of the ABCP study site (Table 5). After controlling for low birth weight, village-specific infant mortality rates ranged from 58 per 1,000 live births (95% CI, 0–121 per 1,000 live births) to 253 per 1,000 live births (95% CI, 157–349). The variation in village-specific infant mortality rates was not explained by intervillage differences in maternal age, education, maternal survival, or number of living children (data not shown).

In contrast to postneonatal and infant mortality, postinfant mortality was not significantly associated with year of birth (RR = 1.4, 95% CI, 0.8–2.3) or birth weight (RR = 1.3, 95% CI, 0.8–2.3). The highest proportion (37%) of deaths in the postinfant period ($n = 106$) occurred in the 6-mo period following infancy (13–18 mo), with less than 10% of postinfant deaths occurring after 42 mo of age (Figure 4C).

Figure 5 shows geographic variation in risk of postneonatal mortality. In general, risk of postneonatal mortality was highest among children residing closer to the shore of Lake Victoria. Areas with postneonatal mortality risk exceeding 0.4 were frequently close (< 1 mile) to other areas with risk of 0.1 or lower.

Finally, we examined death rates exclusively among study participants who had not migrated away from the study area between 1992 and 1999. These neonatal (30 per 1,000, 95% CI, 19–41), postneonatal (150 per 1,000, 95% CI, 127–173), infant (175 per 1,000, 95% CI, 151–199), and postinfant (82 per 1,000, 95% CI, 63–101) mortality rates were not significantly different from the rates for the cohort overall, regardless of migratory status. Only 1 mother had moved away from the study site during the neonatal period, and only 14 deaths occurred in the postmigration period of the mother-

Neonatal mortality, Asembo Bay

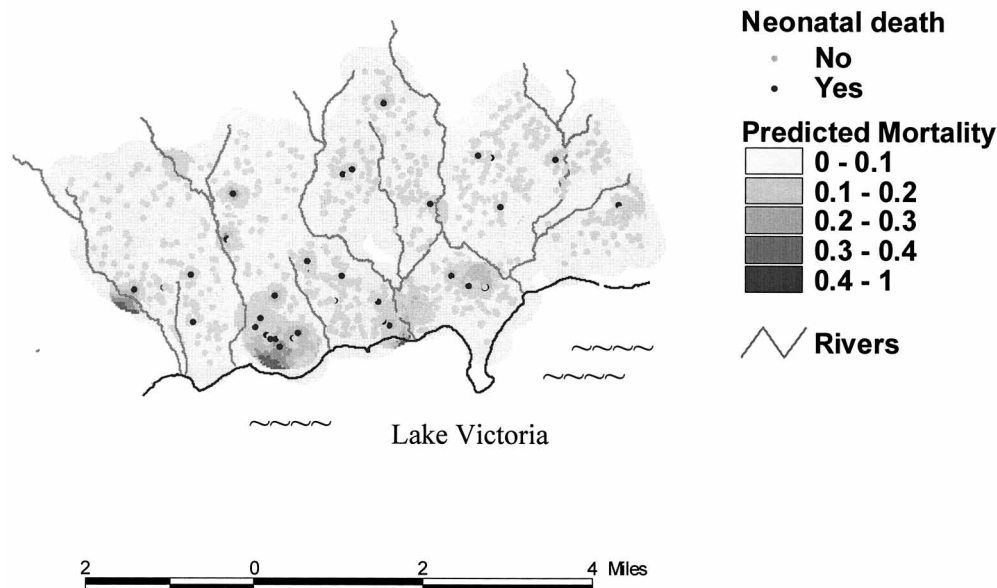


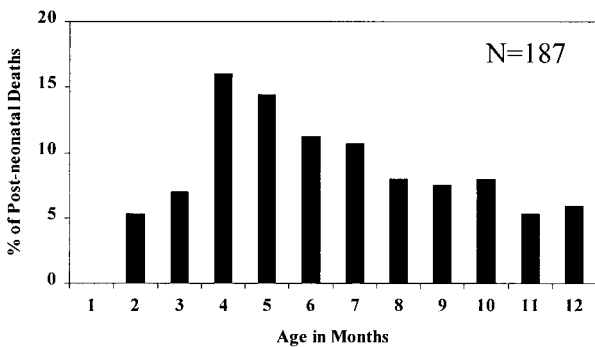
FIGURE 3. Geographic locations of neonatal deaths within the 15-village study area, 1992–1999.

TABLE 4
Birth-weight specific postneonatal, infant, and postinfant mortality rates, Asembo Bay Cohort Project

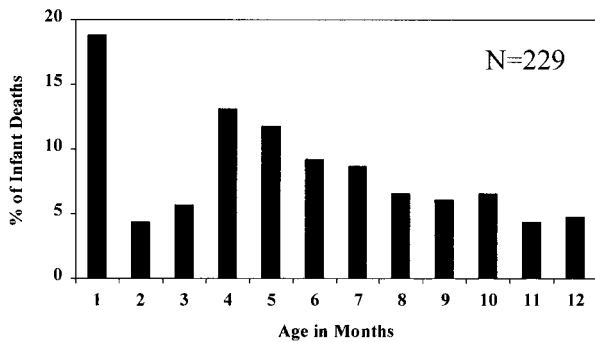
Birth weight (g)	Live Births	Postneonatal†		Infant		Postinfant	
		Deaths	Rate* (95% CI)	Deaths	Rate (95% CI)	Deaths	Rate (95% CI)
≥ 2,500	1,061	142	135 (115–156)	154	145 (124–167)	86	95 (76–114)
< 2,500	146	27	206 (137–275)	42	288 (214–361)	13	125 (61–189)
Missing	96	18	222 (132–313)	33	344 (249–439)	7	111 (34–189)
Year of birth							
6/92–5/93	435	59	140 (107–173)	72	166 (131–200)	34	94 (64–124)
6/93–5/94	439	58	136 (104–169)	72	164 (129–199)	35	95 (65–125)
6/94–5/95	292	39	138 (98–179)	49	168 (125–211)	24	99 (61–136)
6/95–5/96	137	31	235 (163–307)	36	263 (189–336)	13	129 (63–194)
Overall	1,303	187	148 (129–168)	229	176 (155–196)	106	99 (81–117)

* To preserve statistical independence, data exclude outcomes from the second (n = 254) and third (n = 12) live births contributed by the same mother. Date of death (and thus age) was unknown for 10 deceased children.

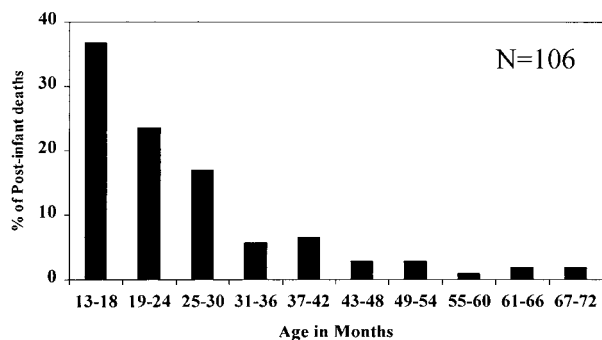
† Postneonatal mortality rates exclude neonatal deaths from denominator.



A



B



C

FIGURE 4. Percentage of postneonatal, infant, and postinfant deaths according to age, Asembo Bay Cohort Project, 1992–1999.

child pairs, precluding the calculation of rates for these observations.

DISCUSSION

In this longitudinal study of mortality in rural western Kenya during the mid- and late 1990s, we observed high neonatal mortality (32 per 1,000 live births), high postneonatal mortality (148 per 1,000 neonatal survivors), high infant mortality (176 per 1,000 live births), high postinfant mortality for children under 5 yr of age (99 per 1,000 infant survivors), high mortality for children under 5 yr of age (257 per 1,000), and high maternal mortality (10 per 1,000 person-years). These high mortality rates were variable by year, birth weight, gestational age, and geographic location, and there is evidence that mortality is increasing in this setting.

The overall neonatal mortality rate observed in the ABCP (32.0 per 1,000 live births) is 2–3 times higher than estimates from several other districts within Kenya. Neonatal

TABLE 5

Infant deaths and mortality rates according to village of residence and birth weight, Asembo Bay Cohort Project

Village	≥ 2,500 g		≥ 2,500 g Infant mortality rate† (95% CI)	All births		All births Infant mortality rate† (95% CI)
	Births	Died		Births	Died	
1	88	12	136 (65–208)	102	19	186 (111–262)
2	67	6	90 (21–158)	85	14	165 (86–244)
3	77	8	104 (36–172)	94	18	191 (112–271)
4	104	11	106 (47–165)	130	21	162 (98–225)
5	78	13	167 (84–249)	97	18	186 (108–263)
6	52	3	58 (0–121)	61	3	49 (0–103)
7	67	6	90 (21–158)	94	13	138 (69–208)
8	77	19	247 (150–343)	97	24	247 (162–333)
9	37	7	189 (63–315)	47	10	213 (96–330)
10	62	5	81 (13–148)	74	8	108 (37–179)
11	85	13	153 (76–229)	95	14	147 (76–219)
12	79	20	253 (157–349)	102	31	304 (215–393)
13	75	17	227 (132–321)	95	19	200 (120–280)
14	43	4	93 (6–180)	48	5	104 (18–191)
15	70	10	143 (61–225)	82	12	146 (70–223)
Total	1,061	154	145 (124–166)	1,303	229	176 (155–196)

* Insufficient data to calculate rates among children with missing birth weight or birth weight <2,500 g.

† Rates based on fewer than 10 deaths are unstable and should be interpreted with caution. B = births and D = deaths.

Post-neonatal mortality, Asembo Bay

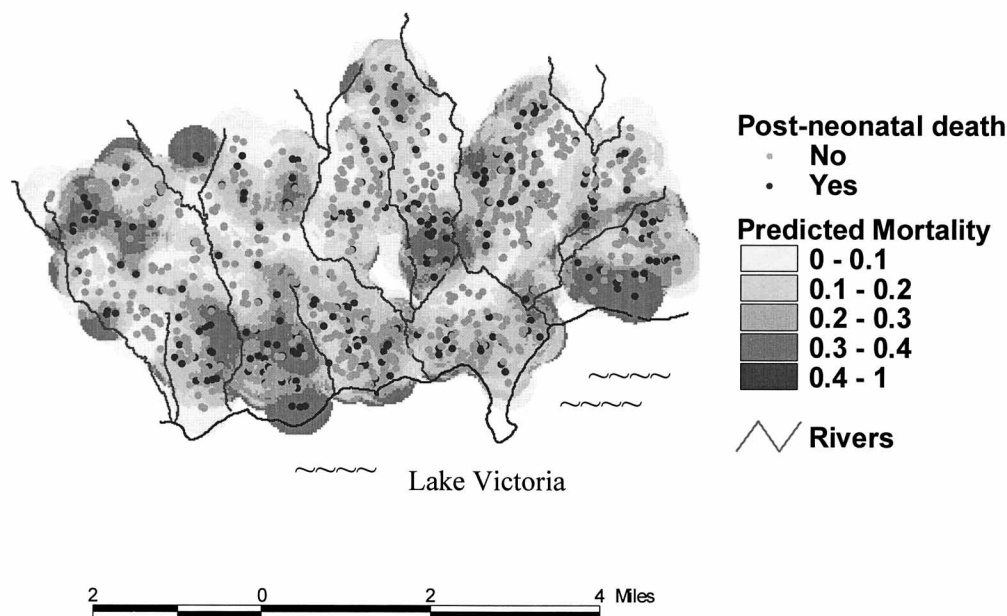


FIGURE 5. Geographic locations of postneonatal deaths within the 15-village area, 1992–1999.

mortality rates in Kisii (10 per 1,000), Meru (16 per 1,000), Kilifi (21 per 1,000), and Tana River (23 per 1,000) Districts are all less than the rate in Asembo Bay.^{21–23} However, only the point estimate of neonatal mortality in Kisii (10 per 1,000, 95% CI, 5–15) included 95% confidence limits that did not overlap with the ABCP estimate. The neonatal mortality rate in the ABCP population is significantly lower than the rate reported from a similarly designed study in rural Malawi (49 per 1,000, 95% CI, 42–57).²⁴ The higher prevalence of low-birth-weight delivery in Mangochi (17%) relative to Asembo Bay (12%) likely contributes to this difference.

The infant and under-5 mortality rates observed among ABCP children (176 and 257 per 1,000, respectively) are substantially higher than the most recent estimates in Kenya

TABLE 6

Infant and under age 5 mortality rates (per 1,000) for selected African countries in 1978 and 1998 as compared with Kenya and Asembo Bay Cohort Project (ABCP) populations

Country	Infant mortality rate		< 5 yr mortality rate 1998
	1978	1998	
Angola	161	125	208
Burundi	127	119	179
The Gambia	167	122	203
Guinea	167	124	208
Guinea-Bissau	176	130	203
Liberia	167	116	174
Malawi	177	138	220
Mali	180	118	236
Rwanda	133	124	202
Sierra Leone	192	170	263
Kenya	88	66	104
ABCP	—	176	257

(75 and 104 per 1,000 live births, respectively).²⁵ Similarly, our observed infant and under-5 mortality rates are considerably higher than current World Health Organization (WHO) estimates (1998 data) for the 10 African countries with the highest estimated infant mortality, but they are consistent with the infant mortality estimates in these countries 2 decades earlier²⁶ (Table 6). However, WHO mortality estimates are based on data from entire countries, and child mortality rates in smaller jurisdictions are often substantially different.²⁷

In this area of western Kenya, there has been no apparent substantial improvement in neonatal or infant mortality despite increases in vaccination coverage for early childhood illnesses. Spencer and colleagues²⁸ reported a pre-intervention neonatal mortality rate in the early 1980s of 37 per 1,000 live births among children in Saradidi, Kenya (< 5 km from the ABCP study site), a community-based estimate almost exactly the same as the current neonatal mortality rate in the ABCP (Table 3). Further, based on data from the same report by Spencer and others,²⁸ postneonatal mortality in the early 1980s (pre-intervention) was estimated at 72.8 per 1,000 live births; our estimate of postneonatal mortality for Asembo Bay was more than twice as high (148 per 1,000).

The infant mortality rate in the ABCP area is higher than published rates from several other malaria-endemic sites in east Africa. In the late 1980s, infant mortality in Kilifi district on the Kenya coast was estimated at 50 per 1,000 live births,²¹ a rate more consistent with the national rate reported by WHO. In the early 1990s, infant mortality for 5 villages in northeast Tanzania was 133 per 1,000 live births (95% CI, 98–168).²⁹ One of the few published infant mortality estimates to approach the rate of Asembo Bay comes from data collected in Mangochi District in Malawi in the late

1980s, where infant mortality was 157 per 1,000 live births, a rate more consistent with the national rate in Malawi.²⁴

The high rate of maternal mortality in the ABCP (10 per 1,000 person-years) was comparable to other estimates in east Africa.^{30,31} In both settings, high maternal human immunodeficiency virus (HIV) infection rates may contribute to the high maternal mortality. Since maternal death is often a risk factor for subsequent infant and child death,³² and because mother-to-infant transmission of HIV can be substantial in the absence of prevention efforts,³³ HIV-associated mortality among children can be expected to increase in parts of sub-Saharan Africa.

The high rates of all-cause mortality raise the question of disease-specific causes of mortality, particularly malaria-specific mortality. *Plasmodium falciparum* transmission in this area is known to be intense and perennial, with entomologic inoculation rates of approximately 200 infective bites per person annually.³⁴ Seventy-five percent of children are infected with malaria by their fourth month of life, and more than 90% are infected by 6 mo of age.^{12,14} The maternal HIV seroprevalence among pregnant women in the ABCP study area was 24% in 1999, a 78% increase in overall HIV seroprevalence since 1994 (ter Kuile F, unpublished data). Data on HIV infection among infants and children in the ABCP is not available. However, because as many as one-third of HIV-infected pregnant women in this population will transmit HIV to their infants,^{35,36} it is possible that up to 7–8% of the children born in the ABCP study area were infected with HIV and would have experienced a substantially higher rate of mortality than their non-HIV-infected counterparts.

As part of this study, children were seen on a twice-monthly basis, and early detection of clinical malaria episodes resulted in treatment with sulfadoxine-pyrimethamine. This access to effective antimalarial treatment likely resulted in subsequent periods of aparasitemia with hematologic recovery leading to increases in hemoglobin concentration.^{13,37} Thus, this cohort of children may have had some advantage compared to similar populations with more limited access to antimalarial treatment and lack of early referral for severe illness. Although this specific malaria care may have had some effect on reducing mortality, it was applied universally to the cohort population, thus precluding any assessment of its impact.

Striking differences in infant mortality existed within the 15-village study area and also within small geographic foci after the removal of artificial boundaries. The differences in infant mortality among villages remained even after controlling for low birth weight. Whether children closer to the lakeshore are at increased risk for infectious diseases compared with children farther inland has not been evaluated in the study area. The added benefit of more food and water nearer the lake may have been undermined by higher, more continuous exposure to pathogens among the lakeside residents. This variation in village-specific infant mortality rates may be related to overall variations in a variety of infectious diseases, particularly maternal HIV infection. In 1994, Nicoll and colleagues predicted a substantial increase in child mortality as HIV seroprevalence increased among adults.³⁸ In 1998, a review of several African studies by Boerma and colleagues showed a 2–5 times greater infant mortality rate among children born to HIV-infected mothers.³⁹ In a recent

meta-analysis of 31 studies, maternal HIV infection was not associated with neonatal mortality but was significantly associated with an increase in infant mortality (odds ratio = 3.7, 95% CI, 3.1–4.5).³³ For our study, stratification of the HIV data according to village resulted in unstable estimates of HIV seroprevalence (data not presented), precluding an evaluation of the effect on infant mortality.

The final months of this cohort study were conducted as permethrin-treated bed nets were distributed to half of the villages in the ABCP area as part of a randomized controlled efficacy trial (Phillips-Howard PA, unpublished data). We investigated the “randomization” status of births and deaths to ascertain if they were potentially altered by their inclusion in the bed-net study. Live births were equally distributed among villages randomized into intervention or control village clusters. We evaluated dates of death among the 229 infant deaths recorded in the ABCP and found that none occurred in children after December 31, 1996, because enrollment of pregnant mothers into the cohort was discontinued in December 1995. Among 25 deaths in older children registered as deceased since January 1, 1997, deaths were divided equally between bed-net intervention and control villages. Thus, we feel confident that bed-net implementation at the tail end of the ABCP study did not adversely affect the validity of these mortality estimates.

The data collection methods used in this study were unique, and numerous limitations to the interpretation of these mortality rates must be considered. First, mothers in this study were enrolled and closely followed during their pregnancies. Treatment with antimalarials during pregnancy may have reduced the prevalence of placental parasitemia, thereby reducing the likelihood of preterm delivery and low birth weight, 2 major risk factors for neonatal and infant mortality.^{40,41} Such a treatment effect is unlikely, because at the time of the study only chloroquine was available at the community level, and chloroquine would have had low efficacy based on the high level of chloroquine resistance in this area. Most malaria in pregnant women in this area is asymptomatic and therefore does not result in treatment.⁴² Likewise, because 15% of pregnant women within the study area did not consent to participate, there is the possibility that these results may not represent all pregnancy outcomes in Asembo Bay, particularly high-risk pregnancies. Women who were more mobile (and therefore not at home during enrollment procedures) on a regular basis may have had access to better antenatal and infant health services. However, where complete follow-up of all enrolled study participants was not possible, and where information on infant survival status was dependent upon reports from family members other than the study mother, analysis of the mortality rates did not reveal differences according to whether the mother was present in early 1999 or had moved away. The manageable size of the cohort permitted extended follow-up over an average of 5 yr. Although this likely resulted in estimation of more valid mortality estimates than other methods, the precision around these mortality estimates (width of confidence intervals) is reduced by the relatively smaller sample size than would be available through analysis of a large death registry or a hospital-based study.

These results can provide a backdrop for future intervention work, including efforts such as Roll Back Malaria. If

malaria accounts for 10–25% of infant/childhood mortality, as several studies suggest,^{43–45} there are many deaths (in absolute numbers) in this malarious area of western Kenya that are available for prevention. Whether a large-scale intervention against malaria, such as use of permethrin-treated bed nets, can achieve substantial reductions in early childhood mortality in this area with intense, perennial *P. falciparum* transmission will soon be known.

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