MAJOR ARTICLE

New Malaria-Control Policies and Child Mortality in Senegal: Reaching Millennium Development Goal 4

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Background. The Demographic Surveillance System established in 1962 in Niakhar, Senegal, is the oldest in Africa. Here, we analyze trends in overall child mortality, malaria, and other causes of death in Niakhar from the beginning of data collection to 2010.

Methods. After an initial census, demographic data were updated yearly from 1963 through 2010. From 1984, causes of death were determined by the verbal autopsy technique.

Results. During 1963–2010, infant and under-5 mortality rates decreased from 223‰ to 18‰ and from 485‰ to 41‰, respectively. The decrease was progressive during the entire observation period, except during 1990–2000, when a plateau and then an increase was observed. Malaria-attributable mortality in under-5 children decreased from 13.5‰ deaths per 1000 children per year during 1992–1999 to 2.2‰ deaths per 1000 children per year in 2010. During this period, all-cause mortality among children aged <5 years decreased by 80%.

Conclusions. Inadequate treatment for chloroquine-resistant malaria and an epidemic of meningitis during the 1990s were the 2 factors that interrupted a continuous decrease in child mortality. Direct and indirect effects of new malaria-control policies, introduced in 2003 and completed during 2006–2008, are likely to have been the key cause of the recent dramatic decrease in child mortality.

Child mortality in tropical Africa has decreased dramatically since the 1960s [1]. However, it remains the highest in the world for several reasons, including the fragility of the health system in many countries of the continent [2, 3]. Overall, under-5 mortality in West Africa decreased by only 18% from 1990 through 2007 [4]. This has led some commentators to suggest that, in such countries, achieving the Millenium Development Goals may prove to be very difficult, especially the fourth Millenium Development Goal (MDG4) of decreasing under-5 mortality by two-thirds between 1990 and 2015 [3, 5–7]. One of the leading causes of death in African children is malaria, and mortality attributable to this disease increased at least 2-fold during the 1990s, associated with the spread of chloroquine resistance [8, 9]. The replacement of chloroquine by more-effective drugs was initiated in some African countries during 2000–2003, but it was not until 2006 that artemisinin-based combination therapy was used on a large scale in Africa [10, 11].

The oldest Demographic Surveillance System (DSS) in Africa, started in 1962, is in Niakhar, Senegal, a rural area in the Sahel [12–14]. After an initial census, data on births, deaths, and migrations were collected prospectively at least yearly from 1963 through the present. In 1984, the study area was extended and systematic recording of causes of deaths through verbal autopsy was introduced. In this article, we describe trends in overall child mortality since the origin of the DSS and analyze the trends in causes of deaths since 1984. After a decade of stagnation during the 1990s, a new, dramatic decrease in child mortality has been observed during the past few years. This decrease was temporally related to the

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deployment of new malaria control policies, suggesting that malaria has both a direct and an indirect effect on overall mortality and that MDG4 can be achieved primarily through malaria control and vaccination in poor rural areas of Africa.

METHODS

Study Area and Population

The Niakhar study area is located in the district of Fatick, Senegal, 120 km southeast of the capital city of Dakar. The population covered by the DSS lives in 30 villages composed of several different hamlets and comprising 43 000 inhabitants as of 1 July 2010. Most of the population (96.4%) belong to the Sereer ethnic group, live traditionally on 1 food crop (millet), and raise 1 cash crop (groundnuts) and a few cattle. The climate is typical of the sub-Sahel. Rains are concentrated during a 4-month period (July–October), and the mean annual rainfall was 506 mm during 1962–2010 (457 mm during 1984–2010). A detailed description of the Niakhar DSS is given elsewhere [14].

Healthcare System

There are 3 health posts in the study area (the first opened in 1953 and the last in 1983) and 2 outside the area that provide first-line healthcare services, including curative care for common illnesses, vaccination, prenatal care, delivery, and management of malnutrition. These health posts are staffed by nurses and midwives. The closest health center is located at Fatick, 20–30 km from the study area. Surgery, cesarean sections, and blood transfusions are available only in the regional hospitals of Kaolack and Diourbel, 60–70 km from the study area.

Malaria in Niakhar is endemic, with a seasonal peak of transmission from August through November [15]. Until November 2003, chloroquine was the first-line treatment of malaria in Niakhar and elsewhere in Senegal. The first cases of chloroquine resistance were detected in 1992, and subsequently, the proportion of RII and RIII strains increased rapidly, reaching 10% in 1993, 15% in 1994, and 29% in 1996 [8]. A study conducted in a random sample of the population of the 30 villages of the study area in 1995 indicated that the prevalence of malaria among asymptomatic children aged <5 years was 36% in February, 33% in June, and 79% in November, with 95% of the infections being due to *Plasmodium falciparum* [16]. In November 2003, the Senegalese Ministry of Health introduced the combination amodiaquine plus sulfadoxine-pyrimethamine (AQ+SP) as a replacement for chloroquine for the first-line treatment of malaria in all healthcare facilities in Senegal. In May 2006, artemisinin-based combination therapy with artesunate plus amodiaquine (AS+AQ) was deployed in Senegal as a replacement for AQ+SP [17]. In June 2008, long-lasting insecticide-treated nets (ITNs) were distributed to all children, and universal coverage with ITNs was achieved in the area in 2009 [17, 18].

Although there was still no resident physician, midwife, laboratory facilities, or emergency transportation, the healthcare available to the study population improved considerably from 1962 through 2010, in most part because of the activities of national programs, such as Primary Health Care, the Expanded Programme on Immunization, and the Maternal and Infant Protection program. Specific interventions have been short term and have generally involved only a subsample of children in the study population. These included clinical trials of new vaccines against measles and whooping cough [19, 20], conducted during 1989–1996, and trials of seasonal intermittent preventive treatment of malaria in children, conducted during 2002, 2004, and 2006 [21].

Demographic Surveillance System

In December 1962, a demographic survey of the 65 villages forming the administrative area of Niakhar (population, ~33 000 persons) was undertaken [12, 13]. Annual surveys were performed up to 1969, when surveillance was restricted to 8 villages (population, ~4300 persons). In 1983, surveillance was extended to 30 villages (population, 23,391 persons in 1984 and 43 576 persons in 2010), 19 of which were part of the initial study [14].

Demographic events collected included pregnancies, births, deaths, marriages, and migrations. From 1963 through 1987, the population census was updated on a yearly basis. From 1987 through February 1997, each compound was visited once per week as part of the follow-up of vaccine trials; demographic information was collected during these weekly visits, and its accuracy was checked during the annual census. Since March 1997, demographic data have been collected every quarter or twice per year. Infant and child mortality rates during 1963–1999 are published elsewhere [14]. During 1963–1983, mortality rates were based on data from only the 8 villages under continuous surveillance and are presented for 5-year periods, resulting in a smoothing of the mortality trend. During 1984–2010, annual probabilities of death, based on the 30 villages of the Niakhar area, were computed. The death rate ($_nM_x$) between age x and age x + n was computed as the ratio of deaths to the person-time accrued over the same period. Death rates were transformed into probabilities of death ($_nq_x$) from age x through x + n using the standard equation:

$$_nq_x = (n \times {}_nM_x)/[1 + (n - {}_na_x) \times {}_nM_x],$$

where $_na_x$ is the mean number of person-years lived in the interval (x, x + n) by those who died during the interval.

Since 1984, all deaths that occurred in the study population have been investigated using the verbal autopsy technique. The same postmortem questionnaire was used during 1984–2010, and the causes of deaths were determined from the responses to these questionnaires and from any additional medical information available. Each questionnaire was reviewed by at

least 2 physicians, and the most likely cause of death was defined by consensus between at least 2 reviewers. Every death for which the cause was classified as undetermined and a sample of deaths of each determined cause were reexamined by 2 or 3 physicians in 2009, to check that similar criteria for attributing causes of deaths had been used during the whole study period. When there was a discrepancy, the cause of death was reattributed by consensus between at least 2 reviewers. Malaria-related deaths during 1984–1995 [8] and the main causes of deaths during 1989–2000 [22] have been published elsewhere. The main criteria used for attributing causes of deaths are given elsewhere [22].

RESULTS

All-Cause Mortality

During 1963–1972, infant and child mortality rates were very high, and almost half of all children died by the age of 5 years (Table 1). During the 1970s and the 1980s, both infant and child mortality decreased markedly, and the probability of dying before the age 5 years decreased to 179‰ in 1990 (a 62% reduction within 2 decades) (Figure 1). In contrast, infant and child mortality remained almost unchanged during most of the 1990s and increased dramatically during 1998 and 1999, with a probability of dying before age 5 years reaching a maximum of 295‰ in 1998. Under-5 mortality was still high in 2000 (probability of dying before age 1 year, 83‰; probability of dying before age 5 years, 198‰), but it decreased rapidly in the following years. In 2010, the probability of dying before the age of 5 years was only 41‰ (ie an 80% reduction, compared with the mean value for the period 1992–1999). Figure 2 shows that the characteristic seasonal peak in deaths among children aged <5 years that occurred each year from September through November was no longer evident during 2008–2010.

Cause-Specific Mortality Rates

From 1984 through 2010, a total of 1521 deaths were attributed to malaria among children 0–9 years of age. Figure 3 shows the evolution of malaria-associated mortality among these children. From 1984 through 1987, the mean annual malaria-associated mortality rate was 7.1 deaths per 1000 children <5 years of age and 1.1 deaths per 1000 children 5–9 years of age. From 1988 through 1991, the mean annual malaria-associated mortality rate was 5.4 deaths per 1000 children per year among children <5 years and 1.2 deaths per 1000 children per year among children 5–9 years. From 1992 through 1999, a large increase in the number of malaria-associated deaths was observed, reaching 19.7 deaths per 1000 children per year among children <5 years in 1998 and a mean of 13.5 deaths per 1000 children per year among children <5 years during the entire period (12.1 deaths per 1000 children per year among children <5 years and 2.7 deaths per 1000 children per year among children aged 5–9 years during 1992–1997). Malaria-associated mortality has decreased markedly from 2000 onward. It was 10.5, 7.6, 6.6, and 2.0 deaths per 1000 children per year among children <5 years during 2000–2003, 2004–2005, 2006–2007, and 2008–2010, respectively. In 2010, it was only 2.2 deaths per 1000 children among children <5 years and 0.3 deaths per 1000 children among children aged 5–9 years.

Figure 4 shows the evolution of mortality attributable to meningitis. From 1984 through 2010, a total of 292 deaths were attributed to this disease among children aged 0–9 years. Most of these deaths (96 in children <5 years and 80 in children aged 5–9 years) occurred during an outbreak during 1998–2000. During 1998 and 1999, at the peak of the epidemic, the mean mortality associated with meningitis was 8.2 deaths per 1000 children per year among children <5 years

Table 1. Trends in Overall Mortality, Niakhar, Senegal (1963–2010)

Year	Neonatal	1q0	4q1	5q0	5q5
1963–67	…	223	340	485	60
1968–72	…	214	342	480	53
1973–77	…	182	291	421	53
1978–82	…	167	242	369	52
1984	58	129	197	301	29
1985	46	128	259	354	36
1986	50	106	154	244	24
1987	56	121	173	273	30
1988	73	125	131	239	15
1989	45	84	111	186	16
1990	46	96	92	179	15
1991	30	76	132	198	17
1992	29	85	130	204	27
1993	39	86	139	214	27
1994	39	69	102	164	32
1995	36	79	123	193	30
1996	37	81	118	190	34
1997	23	62	93	150	25
1998	22	103	214	295	66
1999	25	88	203	273	51
2000	25	83	125	198	39
2001	27	67	91	151	20
2002	24	66	84	145	18
2003	25	65	71	132	11
2004	17	36	53	88	10
2005	16	45	79	121	22
2006	16	36	62	96	13
2007	7	31	47	76	8
2008	9	22	34	55	8
2009	7	13	17	30	2
2010	9	18	23	41	4

Neonatal mortality (deaths between 0 and 28 days per 1000 living births) and probability of dying (deaths per 1000 children per year) before age 1 year (1q0), between ages 1 and 5 years (4q1), between birth and age 5 years (5q0), and between ages 5 and 10 years (5q5).

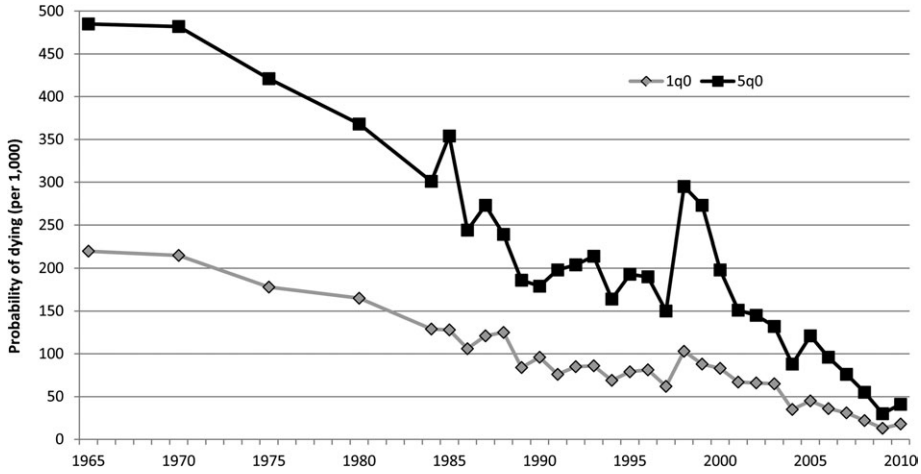

Figure 1. Changes in infant (1q0) and under-5 (5q0) mortality in Niakhar area, Senegal.

and 6.6 deaths per 1000 children per year among children aged 5–9 years.

Mortality rates associated with diarrheal diseases and acute respiratory infection are shown in Table 2. Deaths from diarrheal disease among children <5 years decreased considerably during the study, from 14.8 deaths per 1000 children per year during 1984–1991 to only 2.3 deaths per 1000 per year during 2009–2010. The decrease was also marked for deaths from acute respiratory infection, which decreased from 5.4 deaths per 1000 children per year during 1984–1991 to 0.2 deaths per 1000 children per year during 2009–2010.

DISCUSSION

In most rural areas of West Africa, very high child mortality was still common during the 1960s, with approximately one-half of all children dying before the age of 5 years [1]. Most of these deaths were attributable to infectious diseases, especially neonatal tetanus, diarrhea, whooping cough, malaria, measles, pneumonia, and meningitis [1, 23]. The decrease in child mortality that we observed in Niakhar during the 1970s and the 1980s was also observed in other parts of Africa and was generally attributed to the implementation of immunization programs and better access to chloroquine for treatment of malaria [24, 25]. In the Niakhar area, a major immunization campaign against measles from 1978 through 1982, the introduction of the Expanded Programme on Immunization during the early to mid-1980s, and campaigns for promoting malaria chemoprophylaxis and presumptive treatment of fever with chloroquine are likely to be the main reasons for the initial decrease in mortality observed from the mid-1970s through the early 1990s. The rapid progress made during these 2 decades contrasts with the setback observed during the 1990s.

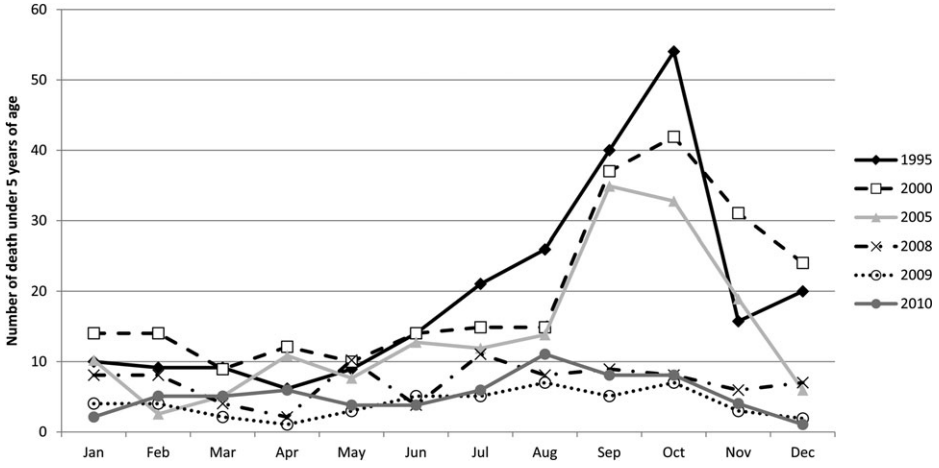

Figure 2. Seasonal pattern of deaths among children <5 years of age in 1995, 2000, 2005, and each year since 2008 (note the disappearance of the seasonal peak during 2008–2010).

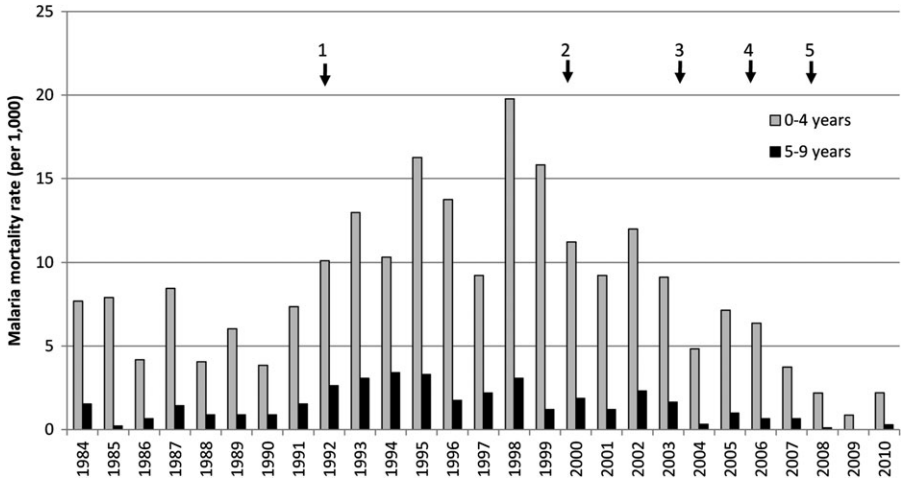

Figure 3. Trends in mortality rates attributable to malaria and their relationship to the malaria-control interventions. 1, Emergence of chloroquine resistance. 2, Sulfadoxine-pyrimethamine made available for second-line treatment. 3, Amodiaquine plus sulfadoxine-pyrimethamine introduced for first-line treatment. 4, Artesunate plus amodiaquine introduced for first-line treatment. 5, Widespread deployment of impregnated bednets.

Analysis of causes of deaths by the verbal autopsy method suggest that an increase in malaria-associated deaths and an epidemic of meningitis were successively responsible for the plateau in mortality and then the peak of deaths that occurred during 1992–1999. Both the sensitivity and the specificity of verbal autopsy technique vary considerably according to causes of deaths and epidemiological context [26]. Although severe malaria and meningitis have some symptoms in common, such as fever and impairment of consciousness, we believe that correct estimates of deaths attributable to these 2 diseases were obtained in Niakhar using this method. In the Sahel and sub-Sahel, rains occur only during a short period of the year, and the seasonal peak of deaths among children, with a presentation of high fever, seizure, and/or coma occurring a few weeks after the malaria vectors increase massively in numbers, allows a diagnosis of malaria to be made with a much better sensitivity and specificity than in areas where rains occur year-round. Malaria-associated mortality increased almost 3-fold during the 1990s, and this was temporally related to the emergence of chloroquine resistance in *P. falciparum* [8]. Meningitis caused by *Neisseria meningitis* is well known for causing devastating epidemics in the meningitis belt of Africa [27, 28]. The dramatic outbreak that occurred in Niakhar during 1998–1999 was responsible for the return to mortality rates among children <5 years of age of approximately 300‰ during the late 1990s. As usual for epidemic meningitis, cases occurred primarily during the last part

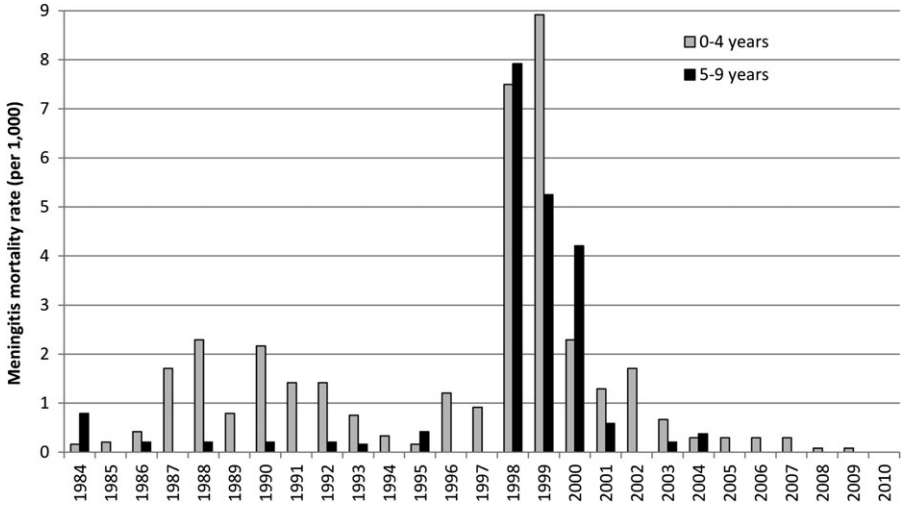

Figure 4. Trend in mortality rates attributable to meningitis.

Table 2. Mortality Rates (per 1000 Person-Years) Associated With Diarrheal Diseases and Acute Respiratory Infection, Niakhar, 1984–2010

Age	Period	Diarrhea	Acute Respiratory Infection
0–4 y	1984–91	14.8	5.4
	1992–99	12.4	3.8
	2000–03	8.5	3.3
	2004–08	3.0	0.6
	2009–10	2.3	0.2
5–9 y	1984–91	0.9	0.2
	1992–99	0.9	0.3
	2000–03	0.2	0.1
	2004–08	0.4	0.0
	2009–10	0.1	0.0

of the dry season, thus facilitating the differential diagnosis from malaria. An immunization campaign launched by the regional health authorities in 1999 contributed to the control of the outbreak.

The decrease in child mortality that occurred during 2000–2010 is striking. There has been no change in the functioning of the DSS or in the structure of the study populations during this period. Rains were either similar or higher during this period than during the 1990s. Vaccine coverage was very high during the early 1990s; approximately 80% of children were fully vaccinated and figures during the 2000s were either similar or lower. No additional health post has been opened, and only limited improvements in facilities and services have occurred. Sociologic changes have been limited, with most villagers maintaining a traditional way of life. Fertility remains high; the mean number of births per woman was 8.0 during 1984–1986, 7.0 during 1999–2000, and 6.4 during 2006–2008. The only major change in healthcare delivery that has occurred during the 2000s has been the launching of improved malaria-control policies. AQ+SP replaced chloroquine in all health facilities in Senegal in November–December 2003, and this combination proved to be very effective both for curing malaria attacks and for preventing new infections for at least 3 weeks after treatment [21]. Artemisin-based combination therapy with AS+AQ was deployed in May 2006 and has also been very effective [17]. Its introduction was accompanied by the implementation of guidelines for the diagnosis and treatment of children presenting with a febrile illness that requires a positive rapid diagnostic test before treatment with artemisinin combination therapy. In addition, long-lasting ITN coverage increased dramatically in June 2008 in the Niakhar area, as in most other rural areas of Senegal, because they were distributed free to children and mothers and became available at low cost to others in 2008 before becoming free to everyone in 2009 [17, 18]. Forty percent of the population of the study area reported using ITNs in 2008 during the rainy season, compared with <5% in preceding years. In December 2008, the prevalence of malaria among Niakhar children <5 years of age was only 2%, compared with 79% in November 1995 and 31% in December 2003. These data from Niakhar support other reports from Africa. During recent years, there have been substantial changes in malaria control throughout Africa [11, 29]. From 2006 through 2010, artemisinin-based combination therapy was deployed in all African countries, and this was often accompanied by the mass distribution of ITNs [30–32]. Recent dramatic decreases in malaria prevalence and mortality have also been reported from The Gambia, Kenya, Zanzibar, and São Tomé and have been attributed, in large measure, to changes in malaria-control policies, although other biological and environmental factors may have contributed [29, 33–35].

The decrease in mortality in the Niakhar study area observed during the 2000s has involved decreases in all the main causes of child deaths, including neonatal mortality, and not only malaria. In particular, deaths due to diarrheal diseases and acute respiratory infection among children <5 years decreased by 5- and 7-fold, respectively, during the period 2004–2010, compared with the period 1992–1999, in the absence of any specific interventions directed at these conditions. Deaths due to acute respiratory infection are often difficult to distinguish from those due to malaria through verbal autopsy [26], but this is not the case for deaths due to diarrheal diseases. Sulfadoxine-pyrimethamine given for the presumptive treatment of malaria attacks could have had some impact on diarrheal diseases and acute respiratory infection, but it was used widely only during 2004 and 2005 and, thus, seems to be an unlikely cause for the dramatic changes that have been observed. Because there was no clear change in the treatment of these diseases, we suggest that the decrease in the incidence of these conditions has been attributable, at least in part, to the indirect consequence of improved malaria control.

There are both historical and recent examples of a reduction in overall mortality after implementation of effective malaria-control programs that was much higher than expected [36, 37]. During the 1950s, almost complete elimination of malaria in Sri Lanka and Guyana was accompanied by dramatic reductions in overall mortality that were greater than could be attributed to a direct reduction in deaths from malaria. In Guyana, deaths from respiratory infection decreased in parallel with those from malaria. During the 1980s, successful control of malaria with either seasonal chemoprophylaxis or ITNs in The Gambia reduced overall mortality among children by almost 50%, a much greater reduction than was anticipated, and reduced deaths attributed to pneumonia, diarrhea, and malaria [38]. More recently, an effective malaria-control program on the island of Bioko that used both ITNs and indoor residual spraying reduced under-5 mortality from 152 deaths per 1000 children to 55 deaths per 1000 children over a 4-year period [39]. How a reduction in the incidence of malaria could have

such a marked effect on overall mortality is uncertain, but there is evidence that malaria impairs the immune response, increasing susceptibility to other infections [40], and that continuous exposure to malaria impairs weight gain during the malaria transmission season [41].

To what extent are the results from Niakhar described in this article representative of the rest of Senegal? International funding for malaria control in Senegal increased from $1 million in 2004 to $30 million in 2010 [17]. Six million ITNs were distributed during 2006–2010, almost reaching universal coverage in rural areas [17, 18]. National estimates of malaria-associated mortality decreased 6-fold during 2003 and 2009 [42]. Overall under-5 mortality was reduced by 30% from 2005 through 2008–2009 [17]. In all regions of Senegal, these dramatic changes corresponded to the deployment of combination therapy and ITNs [17]. Although pyrethroid resistance in *Anopheles gambiae* emerged dramatically in Senegal in 2010 [43], our data suggest that it had, to date, only a limited impact on child mortality in Niakhar.

Experience from this study and a similar one undertaken in The Gambia [44] indicate that provision of simple healthcare measures and, in particular, effective control of malaria can be sufficient to allow poor rural areas of Africa to meet MDG4.

Notes

Author contributions. J.-F. T. supervised data analysis. C. S., L. D., and J.-F. M. conducted data analysis, with which all other authors assisted. All authors contributed to data collection and management. J.-F. T., C. S., and B. G. wrote the paper.

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Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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