

Teaching mothers to provide home treatment of malaria in Tigray, Ethiopia: a randomised trial

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Summary

Background No satisfactory strategy for reducing high child mortality from malaria has yet been established in tropical Africa. We compared the effect on under-5 mortality of teaching mothers to promptly provide antimalarials to their sick children at home, with the present community health worker approach.

Methods Of 37 tabias (cluster of villages) in two districts with hyperendemic to holoendemic malaria, tabias reported to have the highest malaria morbidity were selected. A census was done which included a maternity history to determine under-5 mortality. Tabias (population 70 506) were paired according to under-5 mortality rates. One tabia from each pair was allocated by random number to an intervention group and the other was allocated to the control group. In the intervention tabias, mother coordinators were trained to teach other local mothers to recognise symptoms of malaria in their children and to promptly give chloroquine. In both intervention and control tabias, all births and deaths of under-5s were recorded monthly.

Findings From January to December 1997, 190 of 6383 (29.8 per 1000) children under-5 died in the intervention tabias compared with 366 of 7294 (50.2 per 1000) in the control tabias. Under-5 mortality was reduced by 40% in the intervention localities (95% CI from 29.2–50.6; paired *t* test, $p < 0.003$). For every third child who died, a structured verbal autopsy was undertaken to ascribe cause of mortality as consistent with malaria or possible malaria, or not consistent with malaria. Of the 190 verbal autopsies, 13 (19%) of 70 in the intervention tabias were consistent with possible malaria compared with 68 (57%) of 120 in the control tabias.

Interpretation A major reduction in under-5 mortality can be achieved in holoendemic malaria areas through training local mother coordinators to teach mothers to give under-5 children antimalarial drugs.

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Introduction

Falciparum malaria is a major cause of mortality in children less than 5 years of age in Africa. No satisfactory strategy for reducing the high child mortality has yet been established for most of tropical Africa. Although several studies have shown that insecticide-treated bednets can reduce parasitaemia,^{1,2} clinical attacks,³ and mortality,^{4,5} they have limited widespread use. There is as yet no vaccine.⁶

Treatment with antimalarial drugs has been the most widely used approach in efforts to reduce the effect of malaria in Africa.^{7,8} However, treatment provided through health centres and health posts has been of little help in reducing infant and deaths in young children because severe falciparum malaria in these children strikes so rapidly that mothers are not able to obtain treatment in time.^{9–11}

Because of Ethiopia's varied geography and ecology, transmission of malaria is highly variable—ranging from holoendemic in low-lying tropical-valley areas mainly in the south, to hypoendemic and mesoendemic transmission in the central and northern highland plateaux. Tigray, too, is characterised by great variability in altitude, ranging from more than 2400 m in the high plateau areas to less than 1200 m in the low-lying rifts and valleys that crisscross the plateau.¹²

Civil war raged in Tigray from 1974 until 1991 when the combined Tigrayan and Eritrean forces finally overthrew the Mengistu regime and peace was restored to the area. During the civil war the only health services available in the Tigray area were community-based primary health care initiated by the Tigray Peoples Liberation Front (TPLF).^{12–14} This programme was strengthened after the end of the civil war, becoming a community-based malaria control programme with volunteers mainly recruited from among former TPLF community health workers (CHW)¹² who received a 7 day malaria training course.

Being based on local community involvement, this programme was generally well accepted. However, limitations that were related to the sparse numbers of CHWs, who were generally located only in main villages and were virtually all men, became evident over time. An assessment of the programme in 1994–95 found that the main users were older children and adults and that very few of the young and most vulnerable children were actually being seen or treated for malaria. After careful review and extensive discussions with community leaders and local women, a completely new approach was designed to overcome these limitations and meet the needs of the under-served rural women and their families. The new approach was based on the selection and training of mother coordinators to teach all mothers to recognise possible malaria and give chloroquine to their young children. To assess its effectiveness, we decided to do a randomised trial of this new approach. The objective of the trial was to determine the effect on

SR of pairs	Tabia code Number	Name of tabias paired	Under-5 mortality rate per 1000
1	03 vs 17	Bala vs Maru Hadiskegn	121.2 vs 158.3
2	06 vs 14	Abebagnet vs Haerehiwot	107.5 vs 120.00
3	15 vs 20	Selenwoha vs Hadiskegn (Adiwogenat)	72.2 vs 88.2
4	05 vs 12	Wodefit Abeba vs Harele	61.0 vs 69.4
5	07 vs 19	Bagedelbo vs Genete	58.8 vs 49.2
6	04 vs 11	Adis Berhan vs Mendefera	39.2 vs 40.5
7	09 vs 22	Adis Alem vs Tsega	34.0 vs 38.8
8	16 vs 18	Hadealga vs Boyegerersa	33.8 vs 28.2
9	13 vs 24	Amsalegenet vs Ebohawolt	27.6 vs 14.5
10	02 vs 08	Hadiskegne (Chercher) vs Delate	13.0 vs 13.8
11	01 vs 10	Tao vs Erba Hadiskgne	12.3 vs 11.1
12	21 vs 23	Mechare vs Worabayee	10.8 vs 8.4

Bold tabias were selected from each pair randomly for intervention. When one is selected for intervention, the other serves as a control. The under-5 mortality rate was based on the maternal history taken at the time of the census in June, 1996. The average under-5 mortality in the tabias randomised for intervention was 60.8 per 1000 whereas the rate for the control tabias was 47.6 per 1000.

Table 1: Pairing of the tabias by their under-5 mortality rates

under-5 mortality of teaching mothers to promptly provide antimalarials to their sick children at home compared with the present CHW facility-based approach.

Patients and methods

Study population

The study was done in the Alamata and Raya Azebo districts of the Tigray region in northern Ethiopia (figure 1) in 1996–98. Most of Tigray is high plateau, and has little if any malaria transmission. However, in these two districts in the southern part of Tigray much of the population lives in lower-lying land at 1000–1250 m in which there is seasonal hyperendemic malaria. The rainfall in 1997, the year the intervention was in place, was unusual because it was untimely and irregular, with rain nearly every month rather than the heavy seasonal rains in January to February and June to July. Normally most malaria cases occur between September and November. Chloroquine resistance has not been reported from this area of Ethiopia.

The two districts consisted of 37 tabias (a cluster of villages), each with a population of between 1000 and 3000. Within each tabia are three to five kushets (villages). The 24 tabias with the highest morbidity rates were selected based on the 1994 annual malaria morbidity reports from the zonal office of the Tigray Community-Based Malaria Control Programme (TCBMCP). Mapping was done in the 24 tabias in June, 1996, as well as a household census including a maternity history to calculate under-5 mortality. The population was registered with a unique identification number by name, locality, household number, age, sex, and relation to head of household.

The 24 tabias were paired according to their under-5 childhood mortality rates estimated from the maternal histories obtained in the June 1996 census. One tabia from each of the 12 pairs was allocated by random number to the intervention group and the other to the control. Table 1 presents the pairing of the tabias; figure 1 shows the geographical location of the pairs.

Procedure

Mother coordinators were selected in all tabias. By means of the registration book, neighbour groups were formed from every 20 neighbouring houses with children less

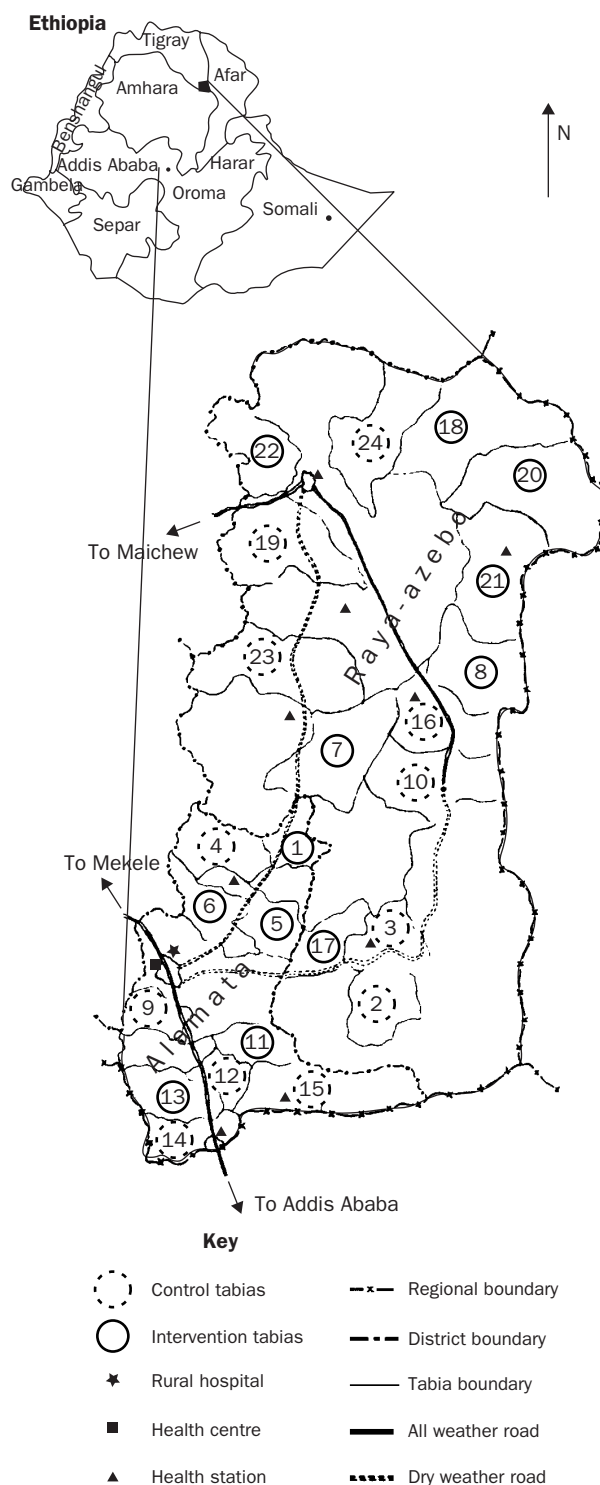


Figure 1: Map of Ethiopia and sketch map of study area. The numbers are the geographical location of the pairs shown in table 1.

than 5 years in the intervention tabias, and similarly from every 33 households in the control tabias. Originally, the intention was to select from each of 20 households in the control tabias as well, but when it became evident that there was much less for mothers to do, the community leaders recommended fewer mother coordinators in these tabias and the investigators felt no compelling reason to insist. In collaboration with the local community leaders, women's associations, and neighbouring mothers, neighbour groups were formed by consensus generally

from contiguous households. Each group selected a mother coordinator, which resulted in one per 10–22 households in the intervention tabias and one per 15–44 in the control area.

In all tabias a list of children for every mother coordinator was prepared in a monthly report format. Mother coordinators were taught to keep track of and record, in this monthly format, all births and deaths, and were taught where to refer sick children. The supervisor could then readily check this report. The supervisors along with mother coordinators and neighbourhood mothers verified births and deaths. Supplies of essential drugs were guaranteed at the health station and tracking of these drugs was the responsibility of the mother coordinators.

In each tabia one mother coordinator was chosen to coordinate all other mother coordinators in the tabia. In three tabias men were chosen as the tabia coordinator: one was a CHW, the second was a youth-association leader, and the third was a CHW and executive for social affairs of the local community. These coordinators collected the monthly reports on births, deaths, migration in and out of the community, and referrals, and checked whether drugs were short and reported any problems.

Seven field supervisors from the TCBMCP were appointed to supervise the tabia coordinators through four to six visits per supervisor each month, and to directly supervise a sample of the mothers by visiting at least five of them per day. Opportunities such as market days were used to meet with the coordinators of the mothers, often in groups; comments or suggestions were welcomed.

In the intervention tabias mother coordinators had additional responsibilities related to malaria. The TCBMCP provided 20 trainers to train the mothers. These trainers were taught to train mother coordinators to teach neighbour-group mothers to recognise symptoms in their under-5 children that might be a result of malaria, to give the appropriate course of chloroquine for their age, to share chloroquine properly, and to recognise possible adverse reactions from the drug. The mother coordinators were supplied with chloroquine for distribution to all households and were responsible for reporting the use to the tabia coordinator and replenishing the drugs used. Special pictorial treatment charts were designed and produced for use and reference by mother coordinators giving standard chloroquine doses by age. The only contraindication to giving chloroquine was if the child had received it within the past 2 weeks. All presumed malaria cases and doses of

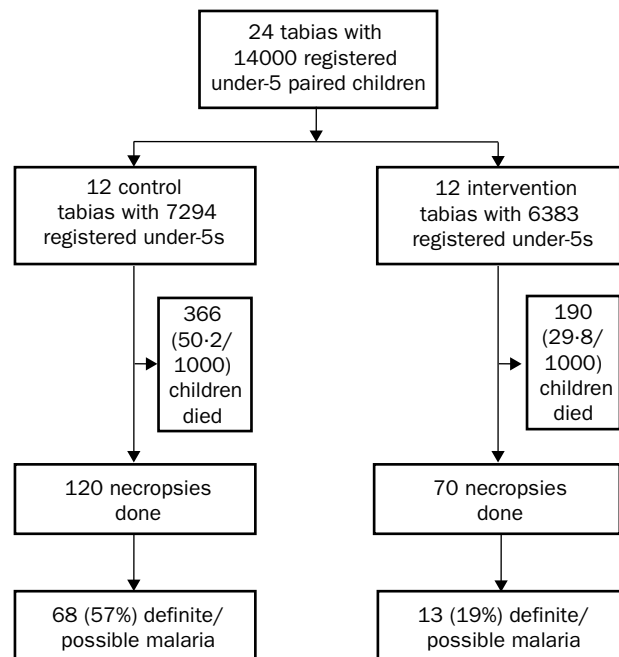


Figure 2: Trial profile

drug given were recorded and reported monthly. The mother coordinators were also taught to refer a child if no improvement occurred within 48 h.

Structured verbal autopsies were carried out by our investigator (GK) on mothers for every third child that died, which were later reviewed independently and by a second masked assessor. Deaths were categorised as either consistent with or possible malaria, or unlikely to be caused by malaria.

Details of the quality design methods used to assess the situation that led to mother coordinator approach, the development of the training cascade, the approach to selection of mothers and their continued involvement, the doses of chloroquine given to each child, assessment of costs and problems that arose, and details of the verbal autopsies will be published elsewhere.

The training of the mother coordinators in the intervention tabias took place in November and December 1996 and mothers began treating children at the end of December. The field-trial study period was from Jan 1, to Dec 31, 1997. The census taken in June, 1996, was updated on Jan 1, 1997, and subsequently each month for the study period, by subtracting all deaths and those who reached age 5 years during the period. We

Pair group	Intervention tabias				Control tabias			
	Tabia code	Under-5 children (n=6383)			Tabia code	Under-5 children (n=7294)		
		n	Number who died (n=190)	Mortality rate		n	Number who died (n=366)	Mortality rate
1	1	482	10	20.7	10	476	17	35.7
2	5	644	25	38.8	12	577	36	62.4
3	6	513	17	33.1	14	528	32	60.6
4	7	812	21	25.9	19	1027	43	41.9
5	8	449	12	26.7	2	376	25	66.5
6	11	400	11	27.5	4	703	29	41.3
7	13	654	28	42.8	24	731	26	35.6
8	17	361	14	38.8	3	451	24	53.2
9	18	632	10	18.9	16	386	31	80.3
10	20	528	10	18.9	15	627	42	67.0
11	21	491	16	32.6	23	852	41	48.1
12	22	417	16	38.4	9	560	20	35.7
Total	6383	190	29.8	7294	366	50.2

Table 2: Under-5 mortality rate per 1000 child-years according to intervention and control tabias from Jan 1, to Dec 31, 1997

also adjusted for migration in and out of the community and new births.

Analysis

The unit of intervention and for randomisation was the tabia. The sample size of 12 tabias for each group was determined by the following equation:¹⁵

$$C=1+(Z_1+Z_2)^2[(r_1+r_2)/n+K^2(r_1^2+r_2^2)]/(r_1-r_2)^2$$

Where C is the number of communities (tabias); Z_1 is $\alpha=5\%$; Z_2 is $\beta=80\%$, r_1 and r_2 are the average rates assumed for the intervention and control groups; n is the person-time units of observation in each community; and $K=0.25$ and is the intrinsic variation between communities or the coefficient of variation of the incidence rates.

The minimum expected under-5 mortality for the area was 55 per 1000 under-5 per year.¹⁶ We used this rate for r_1 . Estimated malaria specific mortality in under-5s in hyperendemic to holoendemic areas in Africa¹⁷ is from 20 to 36 per 1000. Other studies in holoendemic areas have attributed at least a third of under-5 deaths to malaria.¹⁸ Prompt treatment with chloroquine is expected to reduce mortality from chloroquine-sensitive malaria in under-5s by at least 66%. For r_2 therefore we used 43 per 1000 (0.055 times one-third=0.0183 malaria-specific times 0.66=0.012 as reduction in rate; 0.055-0.012=0.043). The study was planned for n to be 570 child-years of observation in each tabia.

The data were analysed on the basis that all mothers in the intervention tabias intended to treat their sick children with antimalarials. Data analysis and comparison of data were done with a t-test paired and non-parametric Wilcoxon's test. SPSS/PC+ (version 7.5), Epiinfo (version 6.046), and Excel software were used for data processing.

Results

The registered population of the 24 tabias was 70 506, with 14 001 children less than 5 years of age (figure 2).

Table 2 gives the under-5 mortality rates per 1000 under-5s by tabia and lists them by tabia pair group, one of which had been randomised to the intervention group and the other to the control group. The overall under-5 mortality in the intervention tabias was 29.8 per 1000 child-years compared with 50.2 per 1000 in the control tabias; a 40.6% reduction in the under-5 mortality rate. The ratio of rates is 29.8/50.2=0.5936. Thus, the mortality rate reduction is (1-0.5936) or 40.6% [95% CI 29.2-50.6]. The difference in rates is 20.4 per 1000 (95% CI from 13.9-26.9 per 1000). The difference is highly significant; a paired *t* test gave a test statistic of 3.43 with 11 degrees of freedom ($p<0.003$). In ten of 12 tabia pairs, mortality was less in those whose mothers were taught to give chloroquine to their children. Tabia 13, which had the highest under-5 mortality in the intervention group (42.8 per 1000) was hit by drought, had a severe dysentery outbreak, and had a measles outbreak (that also involved 18 other tabias, but not its paired control, tabia 24). Under-5 mortality in tabia 24 was among the lowest (35.6 per 1000) in the control tabias.

The differences in mortality between the intervention and the control tabias held true in each age and sex grouping (table 3).

	Age (months)			Total
	<12	12-35	36-59	
Intervention tabias				
Male				
Number of deaths	61	26	12	99
Under-5 population	632	1189	1476	3297
Mortality rate (per 1000 child-years)	96.5	21.9	8.1	30.0
Female				
Number of deaths	38	39	14	91
Under-5 population	563	1145	1378	3086
Mortality rate (per 1000 child-years)	67.5	34.1	10.2	29.5
Total intervention tabias				
Number of deaths	99	65	26	190
Under-5 population	1195	2334	2854	6383
Mortality rate (per 1000 child-years)	82.8	27.8	9.1	29.8
Control tabias				
Male				
Number of deaths	124	44	30	198
Under-5 population	844	1297	1625	3766
Mortality rate (per 1000 child-years)	146.9	33.9	18.5	52.6
Female				
Number of deaths	85	56	27	168
Under-5 population	705	1235	1588	3528
Mortality rate (per 1000 child-years)	120.6	45.3	17.0	47.6
Total control tabias				
Number of deaths	209	100	57	366
Under-5 population	1549	2532	3213	7294
Mortality rate (per 1000 child-years)	134.9	39.5	17.7	50.2
Total				
Number of deaths	308	165	83	556
Under-5 population	2744	4866	6067	13677
Mortality rate (per 1000 child-years)	112.2	33.9	13.7	40.6

Table 3: Under-5 mortality per 1000 child-years in intervention and control tabias by age and sex

There were no important seasonal differences in mortality between the intervention and control tabias. The rainfall pattern in 1997 was unusual with rain occurring in most months; the measles outbreak that involved 19 of the tabias also may have partly obscured the expected seasonal increase in malaria deaths in the control tabias. The measles outbreak continued throughout most of the year for both the intervention and control tabias.

The results of the verbal autopsies are given in table 4. Of the 190 necropsies, only 13 (19%) of 70 in the intervention tabias were classified as consistent with or

Study group	Possible malaria (%)	Numbers without malaria (%)	Total (%)
Intervention tabias			
Female	5 (18)	23 (82)	28 (100)
Male	8 (19)	34 (81)	42 (100)
Total	13 (19)	57 (81)	70 (100)
Control tabias			
Female	35 (56)	28 (44)	63 (100)
Male	33 (58)	24 (42)	57 (100)
Total	68 (57)	52 (43)	120 (100)
Total	81 (42)	109 (57)	190 (100)

Difference of possible malaria between intervention and control area=38.1% (95% CI: 25.3-50.8); $\chi^2=26.3$ (degrees of freedom 1); $p<0.001$. No difference by sex in the intervention. $\chi^2=0.016$ (1); $p=0.579$. No difference by sex in the control $\chi^2=0.67$ (1); $p=0.471$.

Table 4: Cause of death according to verbal autopsy in under-5s

possible malaria, compared with 68 (57%) of 120 in the control tabias.

Discussion

The much lower under-5 mortality in the intervention group shows that although malaria is a major killer in this population mothers can ably take care of their sick children when taught and supplied with appropriate guidance and drugs for home medication. The approach taken in this study was based on quality design principles.¹⁹ After analysis of the then current TCBMCP and extensive discussions with mothers and community leaders in 1996, it was agreed that the TCBMCP would train mother coordinators selected in neighbouring households to recognise possible malaria in their children and promptly give chloroquine. Although this approach seems straightforward—and has been considered and even tried in one form or another^{20–22}—the method has been dismissed because of concerns about the use of drugs by illiterate, untrained householders. There have also been concerns about increasing drug resistance from indiscriminant use, and concerns about logistics and accountability.

The studies at Saradidi in western Kenya²¹ were among the first to examine community-based malaria control, but the investigators concluded that there was no evidence that the programme had any effect on overall mortality rates or on malaria-specific mortality rates. However, there were major differences in the nature of the interventions, in the study designs, and in the study outcome measures compared with our study. For example, village health workers rather than mothers were responsible for providing the antimalarials, no randomisation of interventions was done, and mortality outcomes were based on clinical reports of measles, malaria, or other diseases, but criteria for diagnosis and source of the reports were not given. There were also no baseline data for the population in the control area. A measles epidemic occurred during the preintervention studies in the two intervention areas; the drop in the postneonatal, under-5 mortality rate (from 0·0359 to 0·0288) that occurred in these two areas was attributed to the fall of reported measles cases. The mortality rate of 0·0305 in the control area during this period was judged to be equivalent to the intervention areas.

The report from Burkino Fasa²² confirmed that community-based programmes for training mothers to make presumptive diagnosis and provide treatment of their children was both feasible and affordable. However, the effect on mortality was not assessed.

Studies in the Gambia²³ have shown that antimalarial prophylaxis given by mothers in the under-5 compared with antimalarial treatment at nearby primary health care stations with diagnosis and treatment given by workers provided a more than 30% reduction in overall under-5 mortality and a 73% reduction in attacks of clinical malaria. The relative success of the prophylaxis was attributed to such rapid progression of disease that children without prophylaxis died before they could receive treatment, even though the treatment stations were nearby. However, despite this substantial reduction, it was thought that the potential harm that might result from prophylaxis (potential induction of drug resistance) outweighed its evident benefit. Consideration also was given to trying maternal administration of antimalarials to their sick children,²⁴ but the efforts under their

circumstances were not effective and the investigators focused their attention on studies of the promising insecticide-treated bednet approach.

The limitations of verbal autopsies in diagnosing malaria are well known,²⁵ but it was judged that they could be used to distinguish between deaths consistent with or possibly due to malaria from those almost certainly not malaria, such as deaths from measles (well known locally) or from chronic wasting with protein-energy malnutrition.²⁰ The finding that 19% of deaths in the intervention tabias compared with 57% of those in the control tabias were from malaria strongly supports the notion that the differences in under-5 mortality were due to a reduction in malaria-specific mortality. Quantitatively, with these proportions, mortality rates from deaths not consistent with malaria were quite similar in the control area—22 per 1000 ([1·0–0·57] times 50·2 per 1000) and the intervention area—24·1 per 1000 ([1·0–0·19] times 29·8 per 1000).

With the reinvigorated global efforts to rollback malaria, it is vital that increased attention be given to what family and community-based efforts can achieve when properly designed and applied in a receptive setting. With suitable modifications to fit each locale the approach reported here must be tried in other settings. However, it is important to recognise the special biological and sociopolitical factors of the Tigray study that may limit applicability in other parts of Africa such as the presence of chloroquine-sensitive falciparum malaria, a disciplined population accustomed to coping for themselves, strong community solidarity, and no alternative income opportunities for the mother coordinators.

Contributors

G Kidane was responsible for all field work including organisation, training, data entry, and carrying out of verbal autopsies. G Kidane and R H Morrow were involved in study design, analysis, and writing of the paper.

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