

Strategies for improving health of residents in rural Nigeria: cost-effectiveness of a women's health cooperative versus ministry workers in ivermectin (Mectizan) distribution.

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Summary

Ivermectin (Mectizan, MSD), a new broad-spectrum endo and ecto-parasiticide is a highly effective microfilaricide which has recently become the primary focus of control and treatment of onchocerciasis or river blindness in endemic regions of the world. In spite of the free donation of the drug by its manufacturers to the governments of countries with endemic onchocerciasis, the logistics of distribution including costs of transportation and personnel continue to hamper its distribution to the millions of persons infected or at risk of river blindness in the many remote areas of the world where the disease is endemic. In order therefore, to extend the pharmaceutical use of ivermectin in mass chemotherapy programs in endemic regions of the world, we compared costs and cost-effectiveness of distribution of this drug through literate and semi-literate rural mothers and care-givers trained in the ivermectin distribution process and formed into health cooperatives in an area of high endemicity in eastern Nigeria, to distribution by female village health workers from the ministry of health office in the same district. The study was granted ethical approval by the University of Nigeria Teaching Hospital Ethical Committee and the local administrative authority. Close supervision was provided by our project team from the Onchocerciasis Research Unit of the College of Medicine, Enugu.

Our studies were initiated through community mobilization which sensitized residents to issues relating to onchocerciasis and to other diseases in the community and created a favorable climate for two-way communication, information and education between the project team and the community residents and their local authority. Through a KAP survey carried out in early 1992, the knowledge, attitude and perceptions of the residents regarding onchocerciasis were studied and health education messages designed, based on the results and used for the distribution of 1993. In order to determine what adverse effects may arise and to assess the extent of surveillance necessary following ivermectin distribution in this community, adverse drug reactions were monitored by trained resident nurses following both yearly treatment rounds.

Out of an ivermectin-eligible population of 2358 persons, 2184 were treated by the women in health cooperatives, while 2054 out of an eligible population 2763 persons were treated by female village health workers, thereby achieving coverages of 92.7% and 75% respectively. The average cost per patient treated in the HC villages was N3.10 compares to N5.8 in the OW village. Both differences were statistically significantly different, (Student's t $p < 0.005$, $p < 0.05$). Women formed into health cooperatives therefore achieved higher coverages of the ivermectin-eligible population at approximately half (52.8%) of OW's cost.

Results of the Kap survey showed an abysmal lack of knowledge of onchocerciasis as a disease entity by itself. Though residents were conversant with "filaria" and "eye-filaria", they did not associate this disease to the bites of the blackfly vector of onchocerciasis, *Simulium damnosum*, neither did they associate any of the other

manifestations of the disease, such as the hanging groin and other anatomical disfigurements of onchocerciasis to the disease.

Nodulectomy was widely practiced with local nodulectomy teams existing side by side with orthodox physicians operating from private clinics or the nearby general hospital.

In order to determine what adverse effects would arise and the extent of surveillance necessary following ivermectin distribution, adverse reactions were monitored by trained resident nurses following ivermectin administration. Out of a total of 5098 recipients of ivermectin in this study, 806 persons suffered adverse drug reactions attributable to ivermectin, giving an adverse reaction rate of 16%. Most adverse reactions were mild and transient, occurring within the first 72 hours following drug administration, did not interfere with the daily routines of community residents of this traditional farming villages and subsided promptly following treatment with simple analgesics, anti-inflammatory and anti-pyretic agents. No severe adverse effects requiring hospitalization were encountered. Shedding of worms, mostly *Ascaris lumbricoides*, by residents (35%) was a positive event which enhanced and maintained communal interest and high coverages in this program.

Comparisons of period prevalence of family fevers in each of 100 randomly-selected households covered by both groups of women showed the number of reported cases of fevers in HC villages to be less than those of OW villages (1,825 cases versus 2340 cases respectively). These differences were statistically significant, (Student's t $p < 0.005$). Results of parasitological responses to the first treatment, based on the community mean microfilarial load (COMFY) of the same randomly-selected adults in these randomly-selected households, showed no differences. CMMFL results ranged from 5.5-22.3mf/mg skin snip and 7.2-18.6mf/mg skin snip respectively from the HC and OW villages. The mean values were not statistically significantly different ($p > 0.05$). Feedback through the questionnaire survey showed higher rates of acceptability among villages treated by women and care-givers in the health cooperative.

Our findings in this study suggest that:

1. literate and semi-literate rural women can be mobilized, trained and used in a cost-effective manner to distribute ivermectin and perhaps similar simple health intervention programs in remote communities with little or no access to modern healthcare facilities such as those principally at risk of diseases such as onchocerciasis.
2. All villagers should be exposed to knowledge regarding issues of vector biology and disease causation especially with regards to the diseases of endemicity in their various communities. This can be done through inclusion of such knowledge into the curriculum of the primary level of education or in the absence of formal

education through community health action through grassroots organizations which are the usual channels of communication in such areas.

3. Health education messages which are both gender and culture-sensitive should be developed and targeted to the different participants in this community mass chemotherapy program and information regarding the positive effects of treatment already perceived by residents such as the emerging decrease in family fever indices of households and the worm-shedding properties of the drug, should be fed back to residents in order to enhance their compliance and so increase the chances of sustaining the program for the long period of time needed for the disease to cease to be a factor of concern in such areas.
4. Considering the cluster of adverse reactions within the first 72 hours following ivermectin administration, our results suggest that selective use of clinical monitoring beyond 72 hours of treatment with ivermectin may increase the cost-effectiveness of community distribution programs in Nigeria.
5. In view of the present pandemic of HIV in many parts of Africa, the government should as a matter of urgency, establish local nodulectomy programs, similar to what obtains in Guatemala and other countries of Latin America with endemic onchocerciasis so that the risk of spreading HIV posed to residents by this rampant, uncontrolled nodulectomy practice in the hands of untrained rural workers with little or no formal education, would be minimized and with time, abolished.

CHAPTER ONE

1. INTRODUCTION AND STATEMENT OF THE PROBLEM

Onchocerciasis or river blindness is caused by the parasitic filarial worm *Onchocerca volvulus*, transmitted in West Africa by the blackfly vector, *Simulium damnosum*. It is endemic in large parts of Africa and in isolated foci in Latin America and the Yemen. It is often described as a disease that occurs "au bout de la piste"- at the end of the road and beyond. This disease affects primarily the economically disadvantaged and the politically unenfranchised. It is prominent among the great neglected diseases of mankind as having been more neglected than most.

It is estimated that approximately 85million people are at risk of infection and about 20 million people are infected with *O. volvulus* which is considered the fourth leading cause of blindness globally. The other clinical manifestations of the disease include dermatitis, dermal nodules, lymphatic and systemic complications. It has been described as a leading cause of disfiguring and disabling dermatitis and is second only to polio as a cause of long-term disability in endemic areas.

Blindness due to onchocerciasis affects 40,000 new victims each year. In areas such as the West African Savannah where the parasite strain is the most pathogenic to the eye, onchocerciasis blindness rates for persons 50 and above may be as high as 40% with a four-fold increase in mortality among such blind adults. In these areas, able-bodied men are "reduced to human scarecrows, led to the fields by sighted young boys" (Bruce M. Greene, 1992). Onchocerciasis is therefore considered one of the most socio-economically devastating diseases known to mankind (River Blindness Foundation 1994).

1.1 Burden of Onchocerciasis Disease in Nigeria

With a population estimated between 80-110 million people, Nigeria is the most populous nation in Africa south of the Sahara. Correspondingly, Nigeria's burden of onchocerciasis is such that 17 million people are at risk of the disease, 7 million are currently affected, hence Nigeria has been estimated to account for nearly 40% of the world's prevalence of onchocerciasis (Abiose et al., 1991, Edungbola, 1992).

1.2 Ivermectin in Onchocerciasis Treatment and Control

Nearly a decade after the original reports of the efficacy of the new drug ivermectin against *Onchocerca volvulus* in humans were published, this agent has become the primary focus for the treatment and control of this disease in man (Whitworth et al., 1991).

In the use of such newly developed chemotherapeutic agents as ivermectin among the target population of a disease endemic region, the accompanying costs of transportation, administration and the economic consequences of successful disease treatment are all influenced by the chemical and pharmacological characteristics of the pharmaceuticals (Weinstein 1981).

In an effort to reduce the functional and operational costs involved in distributing ivermectin and by so doing reach effectively, the target population, some of these new chemotherapeutic agents are donated free of charge by the pharmaceutical manufacturers to the health ministries of the countries in which the disease is endemic (Mectizan Donation Program). In spite of this free donation to the poorer nations, the projected cost of getting the drug to this population of afflicted individuals not only remains astronomical (Drummond et al., 1984) but the cost of drug delivery including transportation and distribution often far outweighs the actual costs of the medicaments (Bundy 1990).

Community-based studies on the use of ivermectin in over 100,000 people in 14 countries in Africa and Latin America, by 1990, showed that ivermectin is an effective and safe microfilaricidal agent when given as a single oral dose (WHO 1989). In spite of the efficacy and tolerability of ivermectin established in these studies, (Aziz et al., 1982, Awadzi et al., 1985, Pacque et al., 1990, Remme et al., 1990, Taylor et al., 1990, Whitworth et al., 1991), logistical costs of ivermectin distribution including costs of transportation remain astronomical and unaffordable by most governments of countries with endemic onchocerciasis. Optimization of drug delivery strategies to provide cost-effective methods for identifying and treating communities infected with onchocerciasis therefore continues to be among the operational research priorities for ivermectin use in onchocerciasis, both for WHO's TDR and the governments of endemic countries.

1.3 Objectives of the Study

Our Onchocerciasis Research Unit (College of Medicine Enugu) has been in the forefront of the research for elucidating the population pharmacokinetics of ivermectin since 1987 (Okonkwo et al., 1991) and in operational research for its optimal community distribution through the Free Mectizan Donation program since 1992 (Ogbuokiri et al., 1992). This work is an extension of the latter whose primary objective is to extend the pharmaceutical use of ivermectin by investigating the feasibility of using rural women organized into health cooperatives in endemic communities to distribute ivermectin.

Specifically to:

1. investigate the costs, efficacy and cost-effectiveness of a women's health cooperative versus ministry of health workers in ivermectin distribution;
2. determine by sentinel surveillance, the safety, tolerability and side effect profile of ivermectin when distributed by village health workers supervised by our project team;

3. to determine the magnitude of the effect of this intervention and to identify the social determinants of program acceptability and sustainability in these communities.

2. MATERIALS AND METHODS

2.1 Description of the project area

The study area, Nachi Inland Town, Oji River is located 15 miles from Achi in Oji River focus, the project site of the on-going multi-disciplinary UNDP/WHO/TDR sponsored onchocerciasis research and control program (Grant No 880218) based at Enugu since 1988. The area is 25 kilometers south of Enugu, the capital of the former eastern Nigeria. Nachi Inland Town, estimated total population. midyear 1992, 24,000 inhabitants, falls within the rain forest savannah mosaic climatic zone, and agriculture provides employment for over 95% of the population. Four villages of an ethnically homogeneous population of Igbo farmers and petty traders make up Nachi Inland Town, 4 of these villages, were studied after random stratification to distribution by community health workers from Udi district or ivermectin distribution by women formed into health cooperatives. Based on data from the records of the population registry, the population growth rate of Nachi between 1991 and 1992 was 3.5%. Literacy rates were low, with only 12% of the villagers completing the equivalent of primary school education. The population was young, with 45% of the residents being less than 20 years. There was a preponderance of females, the male to female ratio being 1.3 by January 1992.

2.2 Level of endemnicity in the area

This area harbors some of the most serious and most severe forms of onchocerciasis in Nigeria. In a study on onchocerciasis in this area in 1988-1989, (Okonkwo et al., 1991), microfilaria was found in 76% of the population and the CMFL was 3.1mf/mg skin, the overall nodule carrier rate was 62% and increased with age, being 80% in the third decade of life and 100% in the seventh. Skin and ocular lesions including "SOWDA" were common.

2.3 Community mobilization and enlightenment campaigns

The purpose of the project and the methods to be used were explained to the traditional authorities and the supervisory councilors for health from the wards representing the 2 study villages. Following their approval and with their support and direct participation, the community was mobilized through rallies in their community halls during which the aims and objectives as well as the logistics, procedures and expectations of the program were similarly explained to all adult residents.

2.4 Recruitment and training of women in health cooperatives and community health extension workers

By January 1993, prior to the beginning of the farming season, following community mobilization and familiarization campaigns, a village health cooperative comprising of 20 women, aged 35-50 years, randomly selected from the registry of Nachi Christian Mothers' League, was formed in Okpobeze with the primary objective of mobilizing literate and semi-literate mothers and care-givers to participate actively and directly in the yearly distribution of ivermectin. Criteria for selection of these women included status within the community, reputation, interpersonal skills, desire to help others and an eagerness to participate in community health action programs.

In the adjacent village, Amagu, a group of 20 women extension workers, aged 30-50 years, randomly selected from the office of the district health office in Udi, by the principal investigator, were deployed to our team from the area headquarters with the mandate to distribute ivermectin to these rural dwellers under the supervision of the project team. Both groups of women were given training in a pool, on the rudimentary aspects of river blindness treatment and control especially with regard to the causes, clinical manifestations, skin and eye involvement, complications as well as the economic and social impact of the diseases. The role of the new drug ivermectin, its method of dosing, relationship of dosages to body weights as well as the reasons for the exclusions were explained. Each study participant was taught to weigh residents on a bathroom scale and to record and relate those weights to dosages, based on a simplified dosage chart prepared and distributed to them by the project team. This iterative teaching and learning process called the "Oncho School" was carried out over a period of 4 weeks in a competency -based process whereby the curriculum was tailored to the demands of the tasks that needed to be accomplished. An attempt was made to cover all the knowledge and skills needed to perform correctly the ivermectin community distribution exercise as well as adverse drug reaction monitoring in a satisfactory manner. No extraneous or theoretical material was offered.

2.5 Eligibility for ivermectin treatment

All persons in endemic areas from the age of 6 years onwards are eligible for ivermectin treatment in mass chemotherapy programs. Persons to exclude in treatment are those who are severely ill or with concurrent central nervous system diseases such as epilepsy, pregnant and breastfeeding mothers up to the age of three months post-partum.

2.6 Adverse drug reaction monitoring and treatment following ivermectin distribution

Monitoring for and treatment of adverse reactions to ivermectin were provided for through the use of 2 licensed nurses armed with diagnostic equipment and drugs, resident in each of the 2 villages. Ivermectin distribution was carried out by both groups based on the central location method which has been shown in recent studies (WHO 1993) to be more cost-effective.

2.7 Effectiveness

In this study effectiveness was defined as the level of compliance with the ivermectin community distribution achieved by each of the 2 groups of workers. Given the short-term programmatic purposes of this analysis, a process measure of effectiveness which is the level of compliance as determined by the number of eligible persons who actually received ivermectin within a dosing round, was used rather than an outcome measure such as the number of cases of blindness or onchocerciasis prevented.

2.8 Monitoring for effects of distribution methods on health indices of residents: Period Prevalence of family fevers.

This is simply referred to as the family fever index (FFI). It is a standard index of household health status used in malaria studies to indicate the degree of general health of individual rural households. In this study, it is recorded as the number of persons in a household within any 2 week period who have suffered from febrile illness which has been certified by the resident nurse, multiplied by the number of times they experienced this fever within the period in question. Three specific criteria have to be met, namely: the fever had to have been higher than 98 F; it shall have lasted for a period of more than 2 hours and lastly, it shall have responded to the use of antimalarials. This is an objective measure which both recipients of programs as well as planners can appreciate and has been used to illustrate the effectiveness of interventions or lack of it in various programs (Ruebush et al. 1991).

2.9 Surveillance of body weights

Based on our experience with Oncho mothers of 1991, we hypothesized that villages with mothers in health cooperatives, will, with time, record improvements in indices of household and individual health status as shown by a decrease in period prevalence of family fevers and an increase in body weights of children aged 6-15years. As part of our efforts to sustain the interest of the community in this yearly program, we have an on-going monitoring of body weights of all ivermectin- eligible residents since 1991-1994.

2.10 Comparison of parasitological responses

With the prevalence in this community established as 85% in the survey by the Federal Ministry of Health and a sample population 2,000 each in each of the 2 villages, skin snipping of 100 randomly selected adults of both sexes in the 2 villages was carried out in order to assess the nature of the parasitological response among the villages of study.

Skin snips were collected from the iliac crest of 100 randomly-selected adult residents in each of the two groups of villages. These snips were weighed on a torsion balance and incubated overnight in 100 ul of normal saline. The microfilariae that emerged over the 24 hours were counted and expressed as a number per mg/skin snip as is the standard procedure used in most studies of the disease (Greene et al., 1991).

2.11 Assessment of communal acceptability and sustainability of programs

A post-intervention semi-structured open and close-ended questionnaire survey of 200 program recipients each from the 2 groups of villages were studied to determine acceptability and sustainability of this program in these rural communities.

3. RESULTS OF THE STUDY

3.1 Results of Kap survey

In order to facilitate development of health education messages that would have an impact on onchocerciasis among local residents in an area of high disease endemicity selected for river blindness treatment and control through the Free Mectizan Donation Program, it was necessary to investigate what was known, perceived and practiced with regard to the disease in this area. This survey will serve as baseline information against which the success of future health education strategies will be compared. Though knowledge of the three established illness terms in the area was common with all respondents (100%) being familiar with all 3 terms as well as the dermal and ocular manifestations of the disease, knowledge of causation of onchocerciasis was almost non-

existent. None of the 436 respondents, except for 3 itinerant laborers in the group, had knowledge of any association between bites of blackflies and the disease. Nodules were widely practiced among residents of all age groups with local nodules teams existing side by side with physicians from a district hospital performing clinic-based nodules in their private practice or throughout the clinics of Udi General Hospital located 20 kilometers away. Treatment-seeking for the dermal manifestations of the disease consisted mostly of the use of diethylcarbamazine (DEC) as oral tablets in regimens that varied from person to person depending on the level of literacy of the individual, their previous experience with adverse drug reactions due to the drug as well as their socio-economic circumstances. Given the high level of pharmaceutical use, use of herbal remedies was hardly significant with regard to onchocerciasis in this community. Onchodermatitis and other skin manifestations appeared to exert a greater toll socially on young unmarried females than all other members of the community. The presence of a strongly-knit social network with respect for age, knowledge and community service constituted a favorable environment which facilitated positive program outcomes. Though knowledge and appreciation of the vector biology and relationship to disease was weak and hardly existent for river blindness, the existence of such knowledge in relation to malaria among residents as well as the favorable pharmaceutical experience with antimalarials were positive aspects on which community health education could be instituted. A detailed report of this study is included as annexe 1.

3.2 A comparison of the coverages of the eligible population achieved in OW and HC villages

Table 1 shows the results of ivermectin distribution in the 2 sets of villages. Of the total number of persons counted, 3340, in the HC villages, 2358 were eligible and 2184 were treated, thereby achieving a coverage of 92.75% by the end of the 1993 dosing program. In the OW villages, out of a total of 3948 persons censused, 2763 were eligible while 2054 were treated, thereby achieving a community coverage of 75% within the same study period.

3.3 A comparison of the costs and cost-effectiveness of a women's health cooperative in HC villages versus female MOH workers in OW villages in ivermectin (Mectizan) distribution

Table II shows a breakdown of the costs incurred in ivermectin distribution in all four villages. Honoraria paid to women in health cooperatives were calculated based on what the women considered a "fair" wage in relation to what they earned as a daily wage at the time of the study. The amount reached by general consensus among the women was doubled by the principal investigator in order to bridge to some extent the disparity that existed in their wages compared to those of the female MOH workers. MOH workers on the hand were paid based on their standard rates but in addition they received an amount of daily per-diem which was 50% higher than what the ministry paid at the time.

None of the groups knew the data they were generating was part of an on-going study but each group was encouraged to participate to the best of their ability in order that they would be called upon to take part in future community programs.

The average cost per patient treated in the HC villages was N3.10 as against N5.8 in the OW villages. Both differences were statistically significantly different, Student's t $p < 0.05$. Women in health cooperatives therefore achieved higher coverages of the ivermectin-eligible population at approximately half (52.8%) of OW's cost; even when the women were paid twice what they considered a fair wage.

3.4 Adverse drug reaction treatment and surveillance

In order to determine what adverse effects may arise and to assess the extent of surveillance necessary following ivermectin distribution, adverse drug reactions were monitored in a rural farming community by trained resident nurses following the first treatment round. The drug was well tolerated with most of the reactions being mild and transient, occurring within the first 72 hours following ivermectin administration.

Out of the eligible population of 6,218 residents (75% of the censused population) of the 2 study villages, 5098 were treated for onchocerciasis by mid February 1992, representing an 80.2% coverage of the eligible population at the first contact; this number increased to 95% by the end of February 1992. 815 persons (16%) reported adverse effects that were assessed to be related to ivermectin administration. Table III gives a breakdown of the adverse drug reaction profile of the 4 villages. 16% of ivermectin recipients ($n = 804$) developed adverse drug reactions that were attributable to ivermectin administration. Commonest among these were edema (51%), fever, (49%), pruritus (47%) and musculo-skeletal pains (27%). Ivermectin administration exacerbated both pruritus and rashes in 47.3 and 24%, as well as fever in 37.5% of recipients, respectively. Two male subjects reported scrotal swelling. This was particularly disturbing in the younger of them who was in the process of espousal at the period of the study, but subsided with treatment within 48 hours. Shedding of worms, mostly *Ascaris lumbricoides*, was reported by 38% of residents who had taken ivermectin and was a positive effect which helped to sustain compliance with ivermectin among rural dwellers. Selective use of clinical monitoring beyond 72 hours of treatment with ivermectin may increase the cost-effectiveness of community distribution programs in Nigeria.

A detailed report of this aspect of our work is given in annexe 11.

3.5 Surveillance of body weights of children in 100 households each of OW and HC villages, 1991 to 1993

Table IV shows a breakdown of the values of weights for children aged 6-15 years in both sets of villages. An analysis of trends of these recorded weights show that when confounding variables such as age and literary status of mothers as well as estimated household incomes were controlled for, children in HC villages seem to be improving in their gain weight gains relative to their age- and weight-matched mates in OW villages. A few of these values have begun to show statistical significance, Student's t $p < 0.05$ level.

3.6 Results of monitoring of period prevalence of family fevers (PFFIs) in OW and HC households over the period , 1991-1993.

A comparison of fever ratios in households based on 76 households (which completed monitoring by June 1993) showed that in the 3 years of monitoring, FFIs were lower in HC than OW villages but only reached statistical significance in 1991 and 1992. Table V gives the highlights of this surveillance program.

3.7 Results of survey on parasitological response to treatment in OW and HC villages based on 100 households

Of the 100 households each in OW and HC villages, randomly chosen and registered for post-treatment parasitological response, only 63 households in the OW villages and 56 households in the HC villages completed this surveillance. The high rate of non-compliance was caused by out-migration among the adult population of all 4 villages. Of the compliers, 76% of subjects in OW villages had received ivermectin in the 1992 treatment dosing round, whereas 82% had received same treatment in the HC villages. Community mean microfilarial loads ranged from 7.2-18.6 mf/mg skin snip in OW villages and 5.2-22.3 mf/mg skin snip in HC villages. These differences were not statistically significant (Table VI).

Table 1
Ivermectin distribution through health cooperatives (HCs) and onchocerciasis workers (OWs) in Nachi, 1993.

	HCs (n=2)	Ows (n=2)
Total # persons censused	3340	3948
Total # persons eligible	2358	2763
Total # persons treated	2184	2054
Total # persons refusing treatment	174	709
Percentage refusals *	7.3%	25%
Percentage coverages *	92.7%	75%

*Differences statistically significant, Student' t, $p < 0.0005$.
 McNemar's test for significance of changes between values obtained in 1992 and 1993 for HC villages showed no statistically significant difference.

TABLE 11
Cost of ivermectin distribution in HC and OW villages

	HC (n=2)	OW (n=2)
Total fixed costs (includes salaries and per diems paid to project team)	N38,450.00	N84,706.00
Total variable costs (includes cost of IVM tablets and ADR monitoring, drugs and supplies)	N23,606.00	N28,552.00
Total semi-fixed costs	N5,680.00	N7,236.00
Average cost per patient treated *	N31.00	N58.66

CEA ratio*: Sum off all program costs associated with intervention divided by the number of cases treated by the intervention.

HC villages achieved higher coverages at approximately half (52.8%) of OWs cost.

Table 111*Adverse reactions following ivermectin treatment during the first treatment round***Number of IVM recipients N=5098****Number of complainants n= 816**

Rate of attributable adverse drug reactions =16%

Adverse Effects	% Sufferers	% Never Experienced	% Previously experienced/ worsened	% Previously experienced/ not worsened
Edema (facial, limb or peripheral)	51.6(n=2630)	36.5(n=1860)	15.1 (n=76)	
Fever	65 (n=3314)		49 (n=2498)	
Pruritus	47.3 (n=2412)		46.3 (n=2360)	1.0 (n=51)
Headache	36 (n=1836)		36 (n=1836)	
MSP	26 (n=1327)			
Joint Pain (arthralgia)	7.4 (n=377)		7.4 (n=377)	
Rashes	25.9 (n=1322)		24 (n=122)	1.9 (n=97)
Lymph node enlargement	8.3 (n=426)		5.9 (n=301)	2.4 (n=122)
Anorexia	8.2 (n=416)		4.5 (n=230)	3.7 (n=188)
Malaise	8.1 (n=413)		4.3 (n=218)	3.8 (n=194)
Dizziness	6.5 (n=330)		2.1 (n=101)	4.4 (n=224)
Diarrhea	6.2 (n=318)			
Pain (of specific muscle groups)	3.2 (n=163)		3.2 (n=163)	
Eye irritation	3.6 (n=184)		1.2 (n=61)	2.4 (n=123)
Eye pain	3.1 (n=152)		3.1 (n=152)	
Chest pain	2.9 (n=151)		0.1 (n=50)	2.8 (n=142)

NE =Never experienced

PEW= Previously experienced , worsened

PENW = Previously experienced not worsened.

Table IV

Body Weight Surveillance of 356 children in 100 households each of income and aged matched households in OW and HC villages in Nachi Oji River Focus in eastern Nigeria from 1991-1993

MEAN BODY WEIGHTS (KG) + SD

AGE (Yrs)	1991		1992		1993	
	A	B	A	B	A	B
6	17.5 +2.9	18.2 +1.8	16.5 +0.5	17.3 +1.2	18.2 +.2	17.6 +.7
7	19.4 +.4	20.2 +0.8	18.3 +0.6	19.1 +0.4	19.4 +0.7	21.2 +0.3
8	20.2 +1.2	21.5 +1.3	19.6 +0.3	19.3 +1.2	20.3 +0.4	21.2 +1.1
9	24.6 +.7	25.2 +0.4	25.7 +1.1	28.2 +0.3	25.3 +1.8	25.3 +0.4
10-12	25.7 +.6	27.3+0.3	26.6 +1.4	27.3 +0.7	28.3 +0.6	29.6 +0.6
13	35.3 +1.1	37.1 +1.8	36.0 +0.5	34.4 +0.2	35.4 +1.2	36.2 +0.7
14	39.2 +0.2	39.4 +1.2	37.9 +0.7	37.7 +0.8	38.0 +1.3	39.3 +1.2
15	43.2 +1.1	44.7 +0.9	41.2 +1.3	43.6 +1.2	43.2 +0.5	44.7 +1.4

A refers to the 2 OW villages

B refers to the 2 HC villages.

When confounding factors such as age and literacy level of mothers as well as estimated household incomes were controlled for, these values were not significant within each year except for those asterisked*. Students t was applied at the level of significance $p < 0.05$.

(Detailed discussion of the implications of loss in body weights due to onchocerciasis is included in the paper of Annex 5).

Table V

Period Prevalence of Family fevers (PFI) in 200 households in the OW and HC villages in Nachi Oji River Focus in eastern Nigeria, 1991-1993

	1991	1992	1993
OW (N=76 hhlds)	2666	2764	2340
HC (N=76 hhlds)	2485	2613	2248
Ratio of fever per child in household	5.1 in OW versus 4.7 in HC villages*	4.9 in OW versus 4.2 in HC villages*	4.0 versus 3.9 in HC villages

PFFIs were recorded over a period of 6 months for children aged 6-10 years in 200 households matched for mothers' age, literacy status and estimated family income, 100 each from both sets of villages. Data presented here only for 76 homesteads who completed monitoring by June of 1993.

Average number of children aged 6-10 years in OW villages =3.2 and in HC villages =3.4.

* Differences in PFFIs were statistically significant Student's t p <0.05.

PFFIs were defined as the number of children aged 6-10 years in a household with fever that responded to antimalarial treatment within a 2 week period, monitored over a period of 6 months. Surveys were done simultaneously in all 4 villages at the same period from January to June 1991, 1992 and 1993.

Table VI

Table of results of parasitological surveillance in OW and HC villages in Nachi, Oji River, 1993

	<u>OW villages (n=2)</u>	<u>HC villages (n=2)</u>
CMMFL*	7.2- 18.6 mf/mg skin snip	5.5-22.3 mf/mg skin snip
CMMFL* =	Community mean microfilarial load in # microfilaria /mg skin snip.	

TABLE VII

Kap survey of mothers and care-givers in both communities

Community	Total # families	Number of mothers interviewed	% coverages *
Okpobeze (HC)	62	64	96.8%
Amagu (HC)	49	53	92.1%
Ameke (OW)	63	58	92%
Umubo (OW)	56	50	89.3%
Total	230	225	

*Coverages refers to the number of mothers and care-givers in the study who participated in the KAP survey methods, namely the orally-administered post-intervention questionnaire, the FGDs for women and the in-depth interview if applicable. In polygamous households, more than one mother or care-giver may participate accounting for the greater number of participants than families.

CHAPTER FOUR

4. DISCUSSION

The findings of our study confirm the relative safety of ivermectin as well as the simplicity of its once yearly dosing regimen, allowing for broad distribution of the drug in programs by ancillary personnel such as our village health workers without continuous physician monitoring , as long as close supervision is provided by a project team.

It was not surprising that higher coverages were reached by resident mothers in health cooperatives at lower costs than the community health extension workers. We ascribe this achievement of higher coverages to the abolition of the usual social distance that exists between providers and recipients of healthcare services as well as the greater quantum stimulus provided by continuous interaction among local recipients and program providers in all other spheres of community life.

Adverse drug reaction surveillance and treatment in both groups of study villages are shown in Table 111. Similar to reports by previous workers, the drug was well - tolerated with most of the reactions being mild and transient, occurring within the first 72

hours following ivermectin administration. 16% of ivermectin recipients (n= 804) developed adverse drug reactions that were attributable to ivermectin administration.

Commonest among these were edema (51%), fever, (49%), pruritus (47%) and musculo-skeletal pains (27%). Ivermectin administration exacerbated both pruritus and rashes in 47.3 and 24%, as well as fever in 37.5% of recipients, respectively.

Two male subjects reported scrotal swelling. This was particularly disturbing in the younger of them who was in the process of espousal at the period of the study, but subsided with treatment within 48 hours. Shedding of worms, mostly *Ascaris lumbricoides*, was reported by 38% of residents who had taken ivermectin and was a positive effect which helped to sustain compliance with ivermectin among rural dwellers. Selective use of clinical monitoring beyond 72 hours of treatment with ivermectin may increase the cost-effectiveness of community distribution programs in Nigeria.

An on-going surveillance of body weights of all ivermectin-eligible residents in this community over the past 3 years has shown moderate to severe states of poor and under-nutrition as exemplified by less than optimal body weights for upto 82% (1993) of all residents and especially of children aged 6-15 years (table IV). As we pointed out in our previous publications, this state of malnutrition needs to be taken into account when translating data on the adverse effect profile of this relatively safe drug in such poor indigenous African communities especially since this situation is presently being aggravated by the general economic depression in this region as well as other regions of the world.

The implications of weight and fever monitoring by community residents in rural Nigeria on the other hand, may be quite important. Numerous reports in the medical literature have confirmed that when patients or communities participate actively in their own treatment regimens or in this instance health monitoring activities, positive behavioral attitudes conveyed through health education messages are reinforced. In our distribution program for the past four years, residents are forced to come to terms with the reality of their own indicators of personal and communal health using the body weights and PFFIs. This is probably one of the strongest attributes of the Nachi Mectizan Donation Program. Men, women and children in Nachi now enjoy jumping onto weighing scales and comparing who among husband and wife, brother and sister etc. is heavier and therefore (by their own interpretation) healthier than the other. This awareness has far-reaching implications for both the initial acceptance and sustainability of health action programs in such rural farming communities.

In order to facilitate development of health education materials which would have an impact on onchocerciasis among local residents in an area of high disease endemicity selected for river blindness treatment and control through the Free Mectizan Distribution Program, it was necessary to investigate what was known, perceived and practiced with regard to this disease in the area.

Though a report of this survey which will serve as baseline information against which the success of future health education strategies will be compared, is outside the scope of the present report, table VI provides a summary of the highlights of this post-intervention study. Ninety-eight percent of all respondents accepted that given the inefficiency of traditional medicines in the treatment of "filaria" as the disease was locally

called, they were willing not only to take yearly ivermectin themselves but to administer the drug to their families for as long it was recommended by the project team.

Given the present state of male-out migration in most of these households whereby 85% of their husbands had migrated into urban towns in search of paid employment, 92% of respondents said they could only participate in such CBD program if they were fully remunerated. Figure 1 shows the effect of male-out migration on Nachi households between 1991-1992 using the distribution of field staff by sex.

The presence of a strongly-knit social network with respect for age, wisdom and participation in community services constituted a favorable environment which facilitated positive program outcomes.

CHAPTER FIVE

5. STUDY CONCLUSIONS AND RECOMMENDATIONS

5.1 Framework for optimal community participation

The present study, like our previous studies in onchocerciasis in this geographical area over the past several years (Ogbuokiri et al. 1993, Klotz et al.; 1990, Okonkwo et al.; 1991) have provided us with an unparalleled opportunity to develop a framework for optimal community participation where individual households and communities must be recognized as being at the heart of the health system not merely as recipients of health intervention strategies but as participants in the design, funding and management of a wide range of interventions cutting across many sectors. The impact of such improved healthcare services on health outcomes of households and communities will of course, either be greatly facilitated or constrained, depending on conditions in the socio-economic and cultural enabling environment.

5.2 Cost-effectiveness analysis (CEA): the ivermectin model

All ivermectin distribution costs money. The money buys program activities which are designed to produce health outcomes of effects. In most distribution programs, it is possible to identify two or more distribution methodologies which are intended to produce the same effects, i.e. treatment of individuals or households with onchocerciasis. A logical question for health administrators is “Which is the least costly?” Cost-effectiveness analysis is intended to answer this question. Essentially CEA is a tool for decision-making. It has meaning only when it is possible to make a comparison between two or more different approaches, or a comparison of a single approach over time. It is a procedure that analyzes alternative means to reach the same end objective in terms of cost.

CEA involves calculating a ratio with program cost as the numerator and program effects as the denominator. Whereas most calculations of CEA for different healthcare programs are riddled with difficulties in determining exact costs of a program activity since most programs are usually integrated into others, the case of ivermectin distribution in rural endemic communities, by virtue of its annual periodicity, clear-cut objectives, and target-specific approach (above 80% coverage) appears easily amenable to CEA. By comparing specific, time-limited experimental interventions, detailed and distinct program costs as well as clearly defined outcome measures, application of CEA to community-originated ivermectin distribution programs using different methodologies offers a powerful tool for program assessment in river blindness treatment and control. This has been the target of our operational research in this area for the past 4 years.

5.3 Issues of cost-effectiveness using selective sentinel surveillance:

A breakdown of costs of monitoring and treatment with number of persons treated up to day 7 in a community shows that upto 96% of all adverse events occurred and were reported and treated within the first 72 hours following treatment in each area.

This therefore suggests that selective surveillance rather than full surveillance may be needed especially for treatments after the first dosing round. This is the subject of another report in Annex III.

5.4 Cost- Benefit and Cost-effectiveness studies of onchocerciasis control programs

- Two types of CEA and cost-benefit studies have been done with onchocerciasis.
- a) Studies of OCP which looked at # persons treated through the vector control and chemotherapy programs
 - b) Studies that looked at the coverages- kilometers of agricultural land reclaimed through larviciding activities of OCP.

Some of these studies such as those done by our colleagues here at Harvard (Evans et al.; 1987, 1990), have shown that the cost of OCP is actually higher per patient treated than per patient cost through chemotherapy. The argument here of course is whether those 2 costs were actually comparable. The difficulty is understood because whereas the studies on chemotherapy were looking at persons treated for onchocerciasis, for whom blindness was prevented, who then live a normal lifespan and die; as opposed to land which is reclaimed for farming and remains there for agricultural use perpetually for generations of lives, so to speak.

The question here is , are these two measures truly comparable? This discussion illustrates some of the problems inherent in cost- effectiveness and cost-benefit analysis of various health interventions. Still a third type of CEA is presently done in studies of onchocerciasis where ivermectin has been used. This is the type illustrated by our studies.

Cost-effectiveness analysis: the ivermectin distribution model

5.5 Empowerment of rural women for health action programs : effect on community health

Use of rural health cooperatives for mothers and care-givers , when all other factors were controlled for, led to a significant decrease in point prevalence of fevers in individual households in Nachi over the study period. This is not unexpected and it is in keeping with results from all over the world and especially from the West African sub-region where household surveys in Ghana, Nigeria and the Sudan show that the single most important influence on the survival of children is the level of a mother's education. The effect of a mother having attained secondary level education in Africa may contribute to lowering the infant mortality in a given family by as much as 50% (World Bank 1993). Infact, studies have shown that having an educated female population can significantly increase the effectiveness of government expenditures in health; without an educated female population, the impact of government expenditures on health appears to fall dramatically (Better Health for Africa 1994, document of the World Bank, Africa Technical Development Program).

5.6 Effect of SAP and male-out migration on rural households in eastern Nigeria

Figure 1 illustrates the attrition we encountered with regard to our male field workers I Nachi between 1991 and 1992. The dramatic change in the sexual distribution of our village field workers, clearly illustrates the effect of migration in search of paid labor in

rural villages in eastern Nigeria. Out of a male population of 26 when we started in 1990, only 3 remained with the program by June of 1992. This left us with only females to work with. Program managers and planners should take into account this new trend in many parts of the country when health and other programs are to be executed.

5.7 Ivermectin distribution by ancillary non-medical workers

Our findings suggests that literate and semi-literate rural women can be used in a cost-effective manner to distribute ivermectin and perhaps similar health programs in remote communities with little or no access to modern healthcare facilities such as those principally at risk of diseases like onchocerciasis and malaria.

In an article published in the Lancet (Pond 1990), the issue of distribution of ivermectin by health workers was once more discussed in detail. The central question was “Is ivermectin safe enough to be distributed by village health workers?” The answer is yes.

Based on community trials of the drug in West Africa in which well over 150,000 persons have been treated, by 1989, experts from the World Health Organization and various research institutes monitoring these trials concluded : “ There are few if any drugs at present in use for the treatment of tropical diseases that have undergone the scrutiny that ivermectin has had. The drug is extremely safe and is without known pharmacological side effects in humans”.

Studies such as ours are an effort to increase the pharmaceutical use of ivermectin so that impoverished rural communities who remain in need of a drug which is donated free by its manufacturers can participate in the Free Donation Program through direct participation in community-based distribution of the drug. Our intention is to convince planners and administrators among country governments and other agencies who still hold the perception that tight controls are necessary and is a pre-requisite for receipt of the drug from Merck that health for all depends upon community participation and that community participation comes at the expense of tight central control.

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