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ACUTE RESPIRATORY INFECTIONS CONTROL PROGRAMME

CASE MANAGEMENT OF ACUTE RESPIRATORY INFECTIONS IN CHILDREN: INTERVENTION STUDIES

Report of a Meeting

CONTENTS

CASE MANAGEMENT OF ACUTE RESPIRATORY INFECTIONS IN CHILDREN: INTERVENTION STUDIES

Report of a Meeting
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1. INTRODUCTION

When the World Health Organization decided to establish the Acute Respiratory Infections (ARI) Control Programme, the importance of bacteria as the principal cause of death from pneumonia in children in developing countries was already known. There was also ample clinical evidence that antimicrobials reduce mortality from pneumonia in developed countries. However, there was doubt that mortality could be similarly reduced in developing countries because, in order to reach the many children dying of pneumonia, the assessment of cases, administration of antimicrobials and decisions on referral would in many areas have to be entrusted to primary health care workers with limited training. In addition, some experts suggested that antimicrobials would have only a limited efficacy because of the high rate of malnutrition and low birth weight.

2. DEVELOPMENT OF INTERVENTION STUDIES FOR THE CONTROL OF ACUTE RESPIRATORY INFECTIONS

Because of the above concerns, intervention studies were designed in 1982 to test both the effectiveness and the feasibility of reducing pneumonia mortality through a case management strategy in the context of an ARI control programme, which included immunization against the vaccine-preventable acute respiratory infections (ARI). The strategy emphasized the peripheral delivery of good case management of ARI in the context of primary health care, using community-based health workers to recognize the signs of pneumonia in children under 5 years of age and to provide antimicrobial treatment. Extending care also involved health education of the family to recognize the signs of pneumonia and, in most studies, active case-finding through home visits by community health workers. The studies were originally designed to be carried out in rural areas where the infant mortality rate is high and the delivery of health care dependent upon paramedical personnel and community health workers.

Earlier projects in Punjab State, India, and in Papua New Guinea suggested that such a simplified case management approach could be successfully used by community-based workers. In the Punjab, treatment protocols were simplified to allow paramedical health workers to deliver antimicrobials to avert death from bacterial pneumonia. Cough with fever or laboured respirations were used to identify cases that might benefit from injectable penicillin. The project also implemented simple methods to allow this disease control intervention to be delivered by health workers in the community during weekly home visits. Mothers were taught to recognize the signs indicating that an acute respiratory infection had become serious. The results suggested that there had been a reduction in pneumonia mortality (1).

In Papua New Guinea, in the mid-1970s, simplified classifications and management plans for ARI were devised to allow health workers to classify and treat or refer life-threatening infections. These were the first protocols which taught health workers to count the respiratory rate to help distinguish pneumonia requiring antimicrobials from colds and other mild respiratory infections. Work in Papua New Guinea also established the importance of Haemophilus influenzae and Streptococcus pneumoniae as causes of fatal pneumonia in children in developing countries (2).

Ten intervention studies were initiated with WHO support between 1983 and 1985. Six were implemented according to plan and all but two are continuing. Four proceeded to the collection of baseline information but were then discontinued, either because local constraints precluded the gathering of reliable information (Somalia) or because the infant mortality rate was too low to permit the measurement of an impact (Kenya, Sri Lanka and Tunisia). Most recently, a study of ARI case management as the sole intervention in the absence of any other disease control programme has been initiated with support from the US Agency for International Development in Jumla, Nepal, in an area with very high infant and child mortality rates and serious malnutrition. The methodology and results of the 6 fully implemented projects and preliminary results from Jumla are summarized below.

3. METHODS AND RESULTS OF THE INTERVENTION STUDIES

Annex 1 contains a description of each of these 7 ARI intervention studies. Preceding this information is a note on the methods used for evaluating the studies. The studies are summarized in this section in 4 tables. Table 1 describes the location, study design, population and interventions (other than case management) of each study. The elements of the case management intervention are summarized in Table 2. Tables 3 and 4 give the acute lower respiratory infection (ALRI) specific and total mortality rates that resulted in infants and children under 5 years of age. Results from chi-square comparisons of the mortality rates in the intervention and control areas (or periods) are included. (The limitations of this analysis are discussed in Annex 1, Section 1.6.)

As can be seen from Tables 1 and 2, the studies varied in several important ways: study design, the concurrent implementation of other disease control interventions, and the method of case detection and treatment. Five of the 7 studies had a concurrent control area. Because of local circumstances or financial constraints, the remaining 2 studies instead compared pneumonia mortality in children in one area before and after implementing the interventions (Kathmandu Valley and Kediri). In 3 studies, improved ARI case management was either the sole intervention (Jumla) or the only intervention applied in the intervention but not in the control area (Abbottabad and Bohol). The effect of improved case management alone can be assessed from these projects, whereas in the remaining 4 projects (Bagamoyo, Kathmandu, Haryana and Kediri) the mortality impact of ARI case management cannot be reliably separated from the effect of improved immunization coverage and other disease control interventions.

Pneumonia case detection can be increased both by educating mothers to recognize the signs of pneumonia and by active case-finding through regular home visits by health workers. Five of the studies employed both of these methods and provided treatment through the health worker in the community. The Bohol and Bagamoyo projects treated most children in clinics, relying on maternal recognition of pneumonia and care-seeking, rather than active case-finding, although the Bagamoyo project used community health workers for maternal education and for some community-based treatment.

The verbal autopsy methods used in the studies identified respiratory deaths based on symptoms of serious acute lower respiratory infections. Most of these deaths were most likely due to pneumonia, although deaths from bronchiolitis, croup and pulmonary complications of other diseases would also be included. Acute upper respiratory infections (AURI) are rarely fatal and would not have been classified as an ARI death by the verbal autopsy methods. The mortality rates are therefore ALRI-specific mortality rates.

TABLE 1: STUDY DESIGN, BASELINE DATA AND INTERVENTIONS BESIDES CASE MANAGEMENT

LOCATION	STUDY DESIGN	STUDY POPULATION: BASELINE DATA				INTERVENTIONS BESIDES CASE MANAGEMENT***	
		IMR (DEATHS/ 1000 LIVEBIRTHS)	MEASLES IMM. COVERAGE (%)	MALNUTRITION (BY WEIGHT FOR AGE) (%)	LITERACY (%)	IMMUNIZATION	CDD PROGRAMME
Haryana, India Low birthwt. study (1982-84)*	Concurrent control group	All infants in control area: 106. Low birth weight: 210-275	0	Severe(at 12 months) 9-13	Male 43	DPT/BCG: intervention area-higher coverage	Started in intervention area
Jumla, Nepal (1986-87)	Concurrent control group plus phased intervention in control area	200	15-20	Severe 35 Mild,mod 32	Male 33 Female 5	Remained low	Absent
Abbottabad, Pakistan (1985-87)	Concurrent control group plus intervention in control area	90-100	5.4	NA	NA	Increased in both areas	Started in both areas
Bohol, Philippines (1984-87)	Concurrent control group	49 -63	58-60	Mild,mod,severe 70	80	Increased (C:89% I:95% in 1985)	Present
Bagamoyo, Tanzania (1983-87)	Concurrent control group plus intervention in control area**	137	53	Severe 7 Moderate 35	Female 67	Increased	Started
Kathmandu, Nepal (1984-1987)*	Before and after	162	11	Severe 7 Mild,mod 62	Male 57 Female 6	Increased	Started
Kediri, Indonesia (1986-87)	Before and after	154	1.5	NA	Male 45 Female 23	Increased	Present

C = control area
I = intervention
NA = not available
* Study completed. All other studies are continuing.
** Randomly selected areas.
*** Other interventions are listed by study in Annex 1.

TABLE 2: ARI CASE MANAGEMENT

LOCATION	CASE DETECTION:		PNEUMONIA TREATMENT:			
	CASE-FINDING	ARI-SPECIFIC MATERNAL ED.	LOCATION (SOURCE) OF PRIMARY TREATMENT:	FIRST LINE ANTIMICROBIAL	CRITERIA FOR IDENTIFYING PNEUMONIA (BESIDES COUGH)	REFERRAL CARE
Haryana, India Low birth weight study (1982-84)*	Active: every week	Yes	CHW	Penicillin (oral)	RR >50; retractions, inability to drink	None
Jumla, Nepal (1986-87)	Active: every 2 weeks	Yes	CHW	Cotrimoxazole	As above	None (chloramphenicol from supervisor for Rx failure)
Abbottabad, Pakistan (1985-87)	Active: every 10-14 days	Yes	CHW or supervising team (in community) or clinic	Cotrimoxazole	As above	Poor access to hospital. (Clinics: second line antibiotics)
Bohol, Philippines (1984-87)	Passive	No (planned)	Clinic only	Cotrimoxazole	As above	Yes
Bagamoyo, Tanzania (1983-87)	Passive	Yes	Clinic (predominantly) or CHW	Cotrimoxazole	As above although RR estimated	Yes
Kathmandu, Nepal (1984-87)	Active: every 2 weeks	Yes	CHW	Ampicillin	Difficulty breathing associated with rapid RR (estimated) and/or retractions	Limited utilization
Kediri, Indonesia (1986-87)	Active: every 2 weeks	Yes	CHW	Cotrimoxazole	RR >50; retractions, inability to drink	Poor access

CHW = community health worker
Rx = treatment
RR = respiratory rate
ed. = education
Cotrimoxazole = trimethoprim-sulfamethoxazole

TABLE 3: ALRI-SPECIFIC AND TOTAL INFANT MORTALITY RATES (IMR)
(deaths per 1000 livebirths)

PROJECT	TOTAL ARLI-SPECIFIC IMR (no. deaths)			NON-MEASLES ASSOCIATED ALRI-SPECIFIC IMR (no. deaths)			TOTAL IMR (no. deaths)			Study population: Number livebirths
HARYANA, INDIA										
C: LBW only	71.0	(15)	p=0.06				275		p=0.13	211 LBW
I: LBW only	30.0	(6)					210			199 LBW
C: all BW	28.8	(19)								659
JUMLA, NEPAL										
C:	48.4	(62)					200.9	(192)		1098
I:	34.6	(41)					162.3	(175)		1009
ABBOTTABAD, PAKISTAN										
Control										
C:1985	36.8	(12)	p<0.001				95.1	(31)	p=0.11	326
C:1986	28.5	(10)					91.2	(32)		351
I:1987	15.0	(6)					54.9	(22)		401
Intervention										
I:1985	21.9	(29)					81.5	(108)		1325
I:1986	9.4	(13)					66.4	(92)		1386
I:1987	9.7	(14)					52.7	(76)		1443
BOHOL, PHILIPPINES										
Control:										
PreC:	13.8	(31)		11.1	(25)		48.8	(110)		2252
C:85-86	14.2	(30)		12.3	(26)		51.2	(108)		2108
C:86-87	14.4	(32)		11.3	(25)		48.3	(107)		2217
PreI:84-85	21.8	(45)	p=0.19	20.3	(42)	p=0.11	63.3	(131)	p=0.28	2068
I:85-86	16.7	(32)		15.1	(29)		62.6	(120)		1916
I:86-87	17.3	(34)		14.3	(28)		50.4	(99)		1964
KATHMANDU V., NEPAL										
C:1984	52.6	(12)	p<0.01				162.3	(37)	p<0.05	228
I:1985	20.0	(4)					110.0	(22)		200
I:1986	5.2	(1)					98.4	(19)		194
KEDIRI, INDONESIA										
C:7-12/86				43.5	(36)	p<0.01	171.8	(139)	p<0.001	809
I:7-12/86				19.7	(16)		95.5	(81)		848

C Control area
I Intervention area
LBW Low birth weight
PreI Baseline year in intervention area
PreC Baseline year in control area

TABLE 4: ALRI-SPECIFIC AND TOTAL UNDER-5 MORTALITY RATES (MR)
(deaths per 1000 children)

PROJECT	TOTAL ALRI-SPECIFIC UNDER 5 MR (no. deaths)	NON-MEASLES ASSOCIATED ALRI-SPECIFIC UNDER 5 MR (no. deaths)	TOTAL UNDER 5 MR (no. deaths)	STUDY POPULATION: NO. CHILDREN <5 YEARS
JUMLA, NEPAL				
C:	18.0 (53)		100.2 (301)	3313
I:	15.0 (52)		82.5 (274)	3259
ANBOTTABAD, PAKISTAN				
Control				
C:1985	14.2 (17)		39.4 (47)	1194
C:1986	14.5 (18)		39.4 (49)	1245
I:1987	6.5 (8)		27.8 (34)	1224
	p<0.001		p<0.01	
Intervention				
I:1985	8.8 (40)		31.9 (149)	4665
I:1986	4.0 (19)		26.2 (124)	4741
I:1987	3.8 (19)		21.0 (105)	5000
BOHOL, PHILIPPINES:				
Control:				
PreC:	6.7 (73)	4.9 (53)	16.6 (181)	10912
C:85-86	5.0 (53)	4.0 (42)	15.0 (159)	10604
C:86-87	6.6 (70)	4.4 (46)	15.4 (162)	10545
PreI:84-85	7.2 (73)	6.7 (68)	18.5 (189)	10209
I:85-86	5.9 (59) p=0.55	5.2 (52) p=0.07	16.6 (166) p=0.11	10028
I:86-87	7.2 (72)	4.8 (48)	15.5 (154)	9938
BAGAMOYO, U.R. OF TANZANIA				
Control				
C:1983	14.4 (117)	9.6 (78)	40.1 (325)	8098
I:1984 p<0.001	12.2 (121) p=0.11	9.4 (93)	35.0 (347)	9915
I:1985	8.6 (86)	7.0 (70) p<0.05	38.7 (389)	10054
I:1986	8.7 (89) p<0.05	7.3 (75)	32.9 (338) p<0.001	10274
		p=0.25		
Intervention				
I:1983	11.4 (92)	8.0 (64)	32.4 (260)	8028
I:1984	10.4 (85)	8.7 (79)	29.2 (266)	9099
I:1985	8.1 (85)	6.7 (71)	30.8 (325)	10542
I:1986	8.0 (76)	6.5 (62)	29.5 (281)	9533
KATHMANDU VALLEY, NEPAL				
C:1984	20.3 (20)	17.2 (17)	64.8 (64)	987
I:1985	8.4 (8) p<0.01	8.4 (8) p<0.01	38.1 (37) p<0.01	947
I:1986	6.3 (6)	4.2 (4)	38.7 (37)	956
KEDIRI, INDONESIA				
C:7-12/86		8.7 (81)	26.7 (241)	9039
I:7-12/87		2.3 (22) p<0.001	12.0 (113) p<0.001	9431

C Control area PreC= baseline year in control area
I Intervention PreI= baseline year in intervention area

As shown in Table 3, the studies in Haryana, Jumla, Abbottabad, Kathmandu Valley, and Kediri showed a reduction in ALRI-specific infant mortality rate in the intervention area although the results in Haryana were of borderline significance (p=0.06) and a statistical analysis of the Jumla project is pending. In Jumla, the reduction was seen only in infants less than 6 months of age although total mortality fell in all age groups. In Bohol, only the reduction in ALRI deaths not associated with measles approached statistical significance.

In Kathmandu Valley and Kediri there were large decreases in the total infant mortality rate (IMR). There were also reductions in the total IMR in the Haryana, Abbottabad, and Bohol studies, but these did not reach statistical significance. The IMR fell 19% in Jumla (statistical analysis is pending). Infant mortality rates cannot be calculated from the Bagamoyo data.

As shown in Table 4, the ALRI-specific under-5 mortality rate and the total under-5 mortality rate fell significantly in Abbottabad, Bagamoyo, Kathmandu Valley, and Kediri. An 18% reduction in the latter occurred in Jumla (statistical analysis is pending).

Table 5 presents the significant reduction in ALRI case-fatality rate achieved by case management in low-birth-weight infants in Haryana.

Overall, the greatest mortality reduction resulting from ARI case management was seen in infancy. The Jumla project showed the greatest absolute reduction in mortality rate in the neonatal period and the greatest percent mortality reduction in the 3-5 month age group. Despite this reduction, the highest ALRI mortality rates continue to occur in the first 3 months of life (Figure 1). In contrast, no change in the total neonatal mortality rate was reported by the Kathmandu Valley study, although some decline occurred in the ALRI-specific neonatal mortality rate.

4. DISCUSSION

4.1 Impact on mortality

4.1.1 General comments

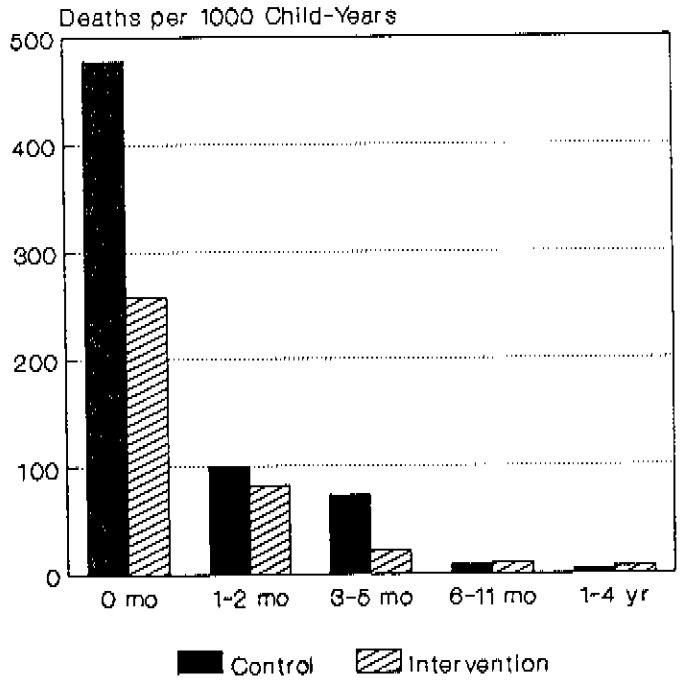
The results of the studies in Abbottabad and Jumla demonstrate the effectiveness of community-based case management with active case-finding in reducing ALRI and total mortality. In Jumla, ARI case management was the only health intervention. In Abbottabad, although immunization coverage and access to oral rehydration therapy were also improved during the project, these interventions were of the same intensity in both the intervention and the control area.

Subject to statistical review, the Jumla study provides strong evidence of mortality reduction through community-based ARI case management even when it is applied as the sole intervention in a setting of unusually high mortality and adverse conditions. The Abbottabad study illustrated the effectiveness of adding community-based case management to a pre-existing health clinic system in a setting with an infant mortality rate of approximately 100 per 1000 livebirths.

Table 5: ALRI CASE-FATALITY RATES AMONG INFANTS IN HARYANA, INDIA

Population Group	Number of deaths/cases		Case-fatality rate (%)
Low-birth-weight infants:			
Intervention area	6/69	p<0.05	8.7
Control area	15/61		24.6
Normal-birth-weight infants:			
Control area	4/125		3.2

Figure 1
ALRI-Specific Mortality Rates
Jumla: By Age



The Bagamoyo, Haryana, Kediri and Kathmandu Valley studies combined ARI case management with other interventions in such a way that their individual impacts on mortality cannot be easily separated. All 4 studies showed a fall in both ALRI-specific and total mortality in children below age 5. The Bagamoyo study and the 2 studies without concurrent control areas, Kathmandu Valley and Kediri, as a group demonstrate the effectiveness of projects combining ARI case management with immunization (especially against measles). In both the Kathmandu Valley and the Kediri project these reductions were large (and statistically significant) despite the small sample size in Kathmandu and the fact that the Kediri results are based on only the first 6 months of intervention. In the Bagamoyo study, a randomized controlled trial which has collected mortality data over 4 years, this fall was less dramatic but still significant. In the Haryana low-birth-weight study, ARI case management combined with improved access to oral rehydration therapy and immunization against diphtheria, tetanus, pertussis and BCG resulted in reduced ALRI-specific and total mortality in a group at particularly high risk of death. The significant fall in the ALRI case-fatality rate in low-birth-weight infants gives some indication of the impact of ARI case management alone.

The 2 studies which implemented case management in a less intensive manner, without active case-finding in the home and with all (Bohol) or most (Bagamoyo) antimicrobial treatment delivered in health clinics (rather than in the community), showed smaller reductions in mortality. In Bohol, a reduction of borderline statistical significance was seen in ALRI mortality not associated with measles in an area with a moderate infant mortality rate (50-60), well established health services and previous availability of antimicrobials for serious respiratory infections through doctors at health centres. Improved ARI case management protocols and health worker training were instituted in clinics, though the coverage of this intervention is uncertain. In addition, maternal health education on ARI was planned but not implemented, and the project did not include active case-finding. These factors partially explain the limited mortality impact in Bohol.

The Bagamoyo project initiated ARI case management within a primary health care programme and delivered health education to mothers in the community but did not implement regular, active case-finding through home visits. Village-based health workers were supplied with antimicrobials, though irregularly, and most cases were sent to the dispensary for treatment. ARI case management was accompanied by improved immunization coverage, nutrition education and malaria and diarrheal disease control activities, progressively implemented as elements of primary health care. The project resulted in reductions in ALRI-specific and total mortality.

A separate analysis of mortality rates from pneumonia with and without preceding measles allows a better estimate of the effectiveness of case management alone in reducing pneumonia mortality (see Bagamoyo, Bohol and Kathmandu Valley data in Table 4). Measles-associated pneumonia mortality rates can fall as a result of both improved case management and a reduction in the number of measles cases. In the Bagamoyo project, observations from the field suggest that the observed reduction in measles mortality was partially attributable to improved ARI case management. The benefits of better case management and improved immunization coverage can be difficult to interpret without measles morbidity rates and case-fatality data, since increasing immunization coverage does not always mean fewer measles cases.

The potential reduction in ARI mortality that can be achieved by the introduction of case management cannot be quantified from the 7 studies both because of difficulties in separating the effects of several interventions in the Bagamoyo, Kediri, Haryana and Kathmandu Valley studies, and, in all the studies, because of incomplete or unknown coverage of project interventions within the community. For example, despite a large mortality reduction in infants, substantial mortality from pneumonia continued to occur in all age groups in Jumla and most pneumonia cases were found during the scheduled home visit. Active case-finding through home visits will detect only a proportion of pneumonia cases (because of the time lapse between visits and the failure to reach children who develop pneumonia in the interval). More effective maternal education to recognize pneumonia and to promote behavioural change in seeking care would probably result in an even greater reduction in mortality.

4.1.2 **Specific comments**

(a) The case management intervention

Although the projects reported mortality from ARI in general, antimicrobials were provided only for children with clinical signs of serious ALRI, predominantly pneumonia. The projects did not recommend the use of antimicrobials for treatment of upper respiratory infections, except in Abbottabad where antimicrobials were recommended for purulent pharyngitis and otitis media.

The mortality reduction resulting from ARI case management is primarily attributable to ARI case management through community health workers and basic health units, since adequate referral care to better equipped health care facilities was not available in most projects (Table 2). Greater mortality reductions might have been achieved if effective referral care had been more widely accessible.

(b) Cause of death ascertainment by verbal autopsy

The ascertainment of cause of death by verbal autopsy is a method of limited accuracy. Verbal autopsy results are influenced by factors affecting both maternal reporting (the original collection of data) and the assignment of cause based on those data.

Maternal reporting can be influenced by cultural beliefs, by the time between the autopsy and the child's death, and by health education on ARI or other interventions. For example, teaching mothers to recognize the signs of pneumonia may result in increased reporting of such signs and hence an increase in the number of deaths classified as being due to pneumonia.

Potential inaccuracies in the method can be reduced by blinding the assessment, having it carried out by professional staff who are independent of the project, using improved protocols and case definitions, and cross-validating the results to assure adequate replicability. The reliability of the assignment of cause must be monitored, especially when new staff are recruited. Inherent inaccuracies will remain as disease control projects tend to exclude other causes before concluding that a death was due to "their" disease.

These limitations in the accuracy of verbal autopsies (see also section 5.2.4 [a]) emphasize the importance of demonstrating a reduction in overall mortality in a successful ARI intervention study, rather than a reduction in ALRI-specific mortality alone which might in part result from inaccuracies in the assignment of cause of death. In Jumla, the fact that ARI case management as a sole intervention resulted in a reduction in total mortality in 6-11 month and 1-4 year old children without a reduction in ALRI-specific mortality suggests inaccuracies in the verbal autopsies, as well as possible effects of cotrimoxazole on other causes of death.

(c) Impact on total mortality

It is important to note that most of the studies did show a reduction in total mortality and that the absolute mortality reduction was larger than that due to ALRI alone. This is in contrast to some disease control intervention studies which have noted significant "replacement mortality" limiting the reduction in overall mortality.

4.2 Impact on morbidity

No reduction in the total incidence of ARI was expected from the interventions. However, morbidity results were obtained in the course of active case-finding and home treatment in most studies. Several studies confirmed the high incidence of ARI in children and the substantial proportion of clinic visits due to ARI in this age group. Other studies showed the seasonality of ARI, which is of potential use for planning programme activities. One study (Abbottabad) reported a decrease in the incidence of moderate and severe ARI; this was not expected and could not be fully explained since no data exist at present to show that supportive care provided to mild ARI cases can be expected to reduce the rate of progression to moderate or severe disease. The impact on severity of pneumonia, complications or sequelae other than death was not monitored by the projects.

5. IMPLICATIONS OF THE RESULTS OF THE INTERVENTION STUDIES FOR THE WHO ARI PROGRAMME

5.1 Implications for the services component

5.1.1 General comments

Review of the intervention studies has shown that it is feasible to convey to health workers the knowledge and skill required to assess and manage ARI, particularly pneumonia, in children in inaccessible and underprivileged areas of the world.

The simple case management protocol using oral antimicrobials has been shown to be appropriate for implementation by peripheral health workers, even in settings with a high prevalence of important risk factors such as malnutrition and low birth weight and where management must rely on home treatment because referral is impossible. The studies have provided epidemiological and clinical evidence to show that a properly implemented case management approach to ARI will reduce overall mortality and specifically mortality due to pneumonia. Although the efficacy of the case management approach could not be precisely quantified by these studies, a clear mortality impact was observed when the strategy was implemented in a community-based fashion.

An impressive aspect of these projects was the credibility which ARI case management gives to the individual health worker. It answers a strongly felt need of the community, perhaps more so than other elements of child survival packages. As such, its inclusion among other child survival interventions may enhance their acceptability. There is no technical justification for delaying any longer the expansion of ARI control programmes as an essential component of child survival efforts, with the same priority as that attached to Expanded Programmes on Immunization (EPI) and diarrhoeal disease control (CDD) programmes.

5.1.2 ARI case management by paramedical health workers

Community health workers and other paramedical staff, even with little formal education, were able to:

- understand and apply correctly a simple protocol for the recognition of pneumonia based on a few objective signs, mainly cough, fast breathing and chest indrawing;
- administer the correct doses of an oral antimicrobial to cases of moderate disease under project supervision;
- refer the severe cases to a higher level of health care; and
- instruct mothers on the essential supportive measures for the care of a child with ARI.

The experience in the studies indicates that community health workers can be trained to responsibly dispense antimicrobials for pneumonia according to a simple classification of ARI. The feasibility of putting antimicrobials in the hands of the most peripheral level of health worker has been demonstrated, although it was noted that this made considerable demands on programme management (including a need for regular supervision). Several studies summarized their experience in this area and found that there was no abuse by the community health workers, i.e., they did not use the antimicrobials as a panacea or for other conditions. It is appreciated that in less controlled situations this could be a difficulty, particularly if there is little other access to antimicrobials.

While serious side effects from drug use were rare, some minor side effects were observed and methods of managing them should be added to training materials. No problems were observed in Jumla with the use of cotrimoxazole in neonates. Several projects successfully used tablets rather than syrups, but the feasibility of their use must be determined locally, paying special attention to their administration to very young children.

5.1.3 Early pneumonia case detection and treatment

The projects have demonstrated the importance of early case detection and prompt treatment of pneumonia. The average duration from the appearance of signs of moderate/severe ARI to death was found to be 3.5 days in Jumla; in Bagamoyo, 50% of deaths occurred within 3 days of the onset of symptoms. Programme emphasis should therefore be put on rapid access to good case management.

In many settings, such access will be achieved only by allowing health workers to bring antimicrobials to mothers at home.

Good parental education is essential for early case detection. Effective communication with the mother should enable her to recognize the signs of pneumonia and the need to seek care rapidly. For this purpose, it is important to understand current ARI treatment practices and motivations for behaviour. Several of the projects developed health education materials that were effective in increasing the mother's ability to recognize pneumonia.

Adaptation of health education materials to the local cultural setting is essential. Materials need to be developed that overcome the intrinsic limitations of using still materials to illustrate key clinical signs involving movement like chest indrawing.

5.1.4 Case detection and treatment in the very young infant

The current management classification using cough, respiratory rate and chest indrawing signs to recognize pneumonia has been shown to be functional. Reliance on these clinical signs is inadequate in young infants, however, where the clinical picture of pneumonia may differ (such as no cough, normal respiratory rate of 40-50). Because of the large number of deaths in this age group in many settings, programme training materials should be enhanced to provide better guidance on dealing with pneumonia in the first 2 months of life. Methods of increasing coverage, e.g., assuring access through traditional birth attendants and other health workers who have more contact with neonates, should be explored.

5.1.5 Reducing the inappropriate use of antimicrobials in mild respiratory infections

The Programme should not only promote prompt antimicrobial treatment of pneumonia but also discourage the inappropriate use of antimicrobials and other drugs for mild ARI. The mortality reductions in the projects were achieved by using antimicrobials for pneumonia only (except in Pakistan).

5.1.6 Training requirements for good case management

Although the health worker required only limited knowledge and skills to perform the ARI duties, the experience of the projects points to the need for effective training of adequate length (at least a week for the ARI case management skills, longer if the health worker has a very limited educational background, as in Jumla). Health workers should be trained to count the respiratory rate using a timing device. This reduced the rate of antimicrobial use in the Jumla study. The training should be practical, followed by frequent supervision and refresher training.

Mild disease, however, must receive adequate attention in the Programme because of its importance to the mother who has to deal with many episodes of mild ARI in her child.

5.1.7 Programme monitoring and evaluation

Programmes must be continuously monitored and evaluated. Programme indicators need to be developed that have a documented relationship to mortality reduction, e.g., the proportion of pneumonia cases receiving adequate case management. These can then be used in programme evaluation and implementation research when it is not feasible or appropriate to measure mortality effects. The indicators could be applied at a health care facility or at community level. To measure indicators of programme effectiveness in the community, better survey methods are needed to assess the occurrence and severity of ARI episodes.

Case-fatality rates determined by prospectively following children identified during home or clinic visits and consistently classified by clinical signs can be valuable for the evaluation of case management at small and large hospitals. To be reliable, the numerators and denominators in case-fatality calculations must come from the same population. Comparisons over time or involving different locations must incorporate the same mix of cases categorized by severity within the denominator.

Because the behaviour of individuals, families and health professionals is so important for ARI case management, better and simpler methods are needed to document relevant behaviour. Are the caretakers of ill children willing and able to recognize signs of pneumonia, seek care, and follow management or referral recommendations? Do the health professionals at all levels follow established standards of case management? What are the optimal training or motivation methods to assure health system compliance?

5.2 Implications for the research component

The clinical efficacy of selected antimicrobials in the treatment of specific types of bacterial pneumonia, e.g., penicillin for the treatment of pneumococcal pneumonia, has been well established. The intervention studies have demonstrated that empirical antimicrobial therapy delivered by health workers can reduce mortality from pneumonia and total mortality. Further documentation is needed, however, of the clinical efficacy of specific elements of ARI case management and of ARI programme effectiveness when delivered in the context of a national health system. (See Annex 1, Section 1.3, for definitions of efficacy and effectiveness.)

5.2.1 **Case management**

(a) Effectiveness of various methods of case detection and treatment

Important questions remain about the optimal programme approaches to the early detection and treatment of pneumonia. The respective roles in effective parental education of mass communication versus health education delivered by a health worker during a home visit or in the clinic need to be determined. The effectiveness of case management delivered only through clinic visits compared with its availability through community-based health workers needs further assessment.

(b) Clinical diagnosis

More information is needed to be able to advise the health worker properly on what the child's state should be during the respiratory rate measurement (awake, breast-feeding), and to further assess the sensitivity, specificity and predictive value of the clinical signs as they are combined in a decision chart or algorithm. Further work is also needed to define the clinical signs of pneumonia in the neonate that can be used by primary health care workers.

(c) Clinical efficacy

The clinical efficacy of the commonly used antimicrobials, delivered according to current protocols and with shortened or less frequent dosage regimens, should be determined in hospital or clinic-based studies. Such studies should document the rates of treatment success or failure, the need for an additional diagnostic or therapeutic intervention (after treatment failure), the duration of illness and the case-fatality rate. Studies are needed in various population groups, such as neonates, infants and 1 to 4-year-old children, and should consider underlying risk factors such as protein-energy malnutrition. The reasons for treatment failure should be documented when possible.

(d) Risk group management

Certain children are at particularly high risk both of developing pneumonia and dying from it. Factors which put them at high risk include low birth weight, very young age, malnutrition and antecedent illness with measles and other infections. Research is needed to develop strategies to manage these special high-risk groups. Research could also attempt to identify other high-risk subpopulations for whom specific programmatic approaches would be appropriate.

(e) Cultural beliefs and ARI-management practices

Clearly, traditional beliefs and superimposed scientific medicine (i.e., use of antimicrobials) jointly determine the practices of child caretakers in regard to ARI recognition, classification and management. An understanding of these beliefs could be useful in the design of a culturally acceptable educational strategy and management approach. Ultimately this applied research should attempt to identify the minimum information needed to design effective communication components or management strategies for a given country programme.

5.2.4 Programme evaluation research

(a) Programme effectiveness

Studies conducted to date have varied in the degree to which they have implemented an "ideal" or practical intervention. Thus, they represent a spectrum ranging from studies of programme efficacy (can it work in very controlled conditions?) to studies of programme effectiveness (does it work in the real world?). In addition, ARI case management has been introduced as either a package of services together with EPI, CDD and other interventions or as a single intervention. Finally, since results from one setting cannot always be generalized to other settings, there remain a number of questions about the optimal programme structure for a particular national or local situation.

Of particular interest to health service planners is information about the marginal effectiveness of case management in reducing total and ALRI-specific childhood mortality when added to existing health interventions. This marginal effectiveness could be more, the same as or less than the effectiveness of ARI case management when performed alone.

Evaluation of programme effectiveness must include an assessment of programme coverage and quality as well as the usual outcomes of mortality and morbidity. The challenge is to develop relatively simple means of measuring outcomes of the programme.

The development of adequate programme indicators and evaluation methods requires improved methods for the measurement of ARI morbidity and mortality.

(i) Techniques to assess mortality levels and trends commonly used in demography need to be modified to make them more practical for evaluating programmes and assessing short-term mortality changes; alternatively, new techniques should be developed.

(ii) The verbal autopsy is commonly used to aseertain the illness(es) present at the time of death. This is a crude tool but it could perhaps be improved through research on techniques of data collection, interpretation and disease classification. Research is needed on the reliability, replicability and validity of "causes" identified by this tool. External validation against an objective measure, such as autopsy or hospital diagnostic information, although not usually available, should be used when feasible. Studies should attempt to develop better classifications of cause of death and underlying risk factors that will improve the comparability of studies.

The verbal autopsy method would be strengthened by the collection of information on relevant risk factors such as malnutrition and measles (both current and in the months prior to death) to permit mortality analysis stratified by important underlying contributors to ALRI mortality and to improve the ability to differentiate the effect of improved case management from that of other health interventions.

Particular difficulties have been identified in using the verbal autopsy to assign the cause of death in malarious areas, since cough, fever and breathlessness are commonly reported by mothers of children suffering both from malaria and from pneumonia. More work is needed to solve this problem.

Given the frequent co-existence of 2 or more possible causes of death, methods of classifying these deaths need to be standardized and this aspect must be considered in assessing programme effectiveness. For example, the possible effect of the case management (antimicrobial) intervention on diseases such as dysentery or persistent diarrhoea needs to be further evaluated in current and future studies.

(iii) Methods to determine pneumonia morbidity and to collect risk factor information by survey are also needed. An attempt should be made to determine the accuracy of a set of questions in classifying ARI and the optimal recall period, as well as the adequacy of recalled treatment information.

(b) Determining programme structure

For planning programmes, it is essential to have a better understanding of the number of cases that (i) can be managed adequately by community health workers or staff at a first-level facility with first-line antimicrobials, (ii) will require referral to a small hospital for more expert clinical assessment or for other treatment such as second-line antimicrobials, oxygen or bronchodilators, and (iii) require referral for diagnostic procedures (such as chest X-ray or microbiology) or more sophisticated clinical management. The effectiveness of various methods of communicating with parents and promoting early case detection and treatment also need to be compared. This will permit a better estimation of the resources needed for the programme. Ultimately, it may be possible to gain some understanding of the importance of these various components through an analysis of various effectiveness studies.

5.2.5 Economic analysis

It is important to begin to document the cost of adequate ARI case management and to evaluate the cost (to the health system and to the patient) of existing ARI practices, including the unnecessary provision of antimicrobials and other drugs. In collecting data on resource needs, it would be useful to keep in mind the type of information needed for cost analysis so that this can be collected simultaneously. In selected situations it may be possible to estimate the cost-effectiveness of ARI case management, but this is not simple to perform, nor is its interpretation a straightforward matter.

REFERENCES

1. McCord, C. & Kielmann, A.A. A successful programme for medical auxiliaries treating childhood diarrhoea and pneumonia. Tropical doctor, 8: 220-225 (1978).

2. Shann, F.A. et al. The aetiology of pneumonia in children in Goroka Hospital, Papua New Guinea. Lancet, ii: 537-541 (1984).

ANNEX 1

METHODS FOR THE EVALUATION OF A THERAPEUTIC OR PREVENTIVE INTERVENTION AND DESCRIPTIONS OF THE ARI INTERVENTION STUDIES

1. INTRODUCTION: METHODOLOGY

In reviewing the 7 ARI intervention studies which form the basis of this report, certain methodological issues arose which deserve comment for two reasons: (1) they affect interpretation of the results of the studies, and (2) they have implications for future ARI research. It should be added that these studies were conducted using guidelines set out in earlier WHO documents[1,2].

The following section summarizes the principles according to which the 7 studies were assessed.

1.1 Study design

The gold standard for the evaluation of a therapeutic or preventive intervention is the clinical trial, preferably according to double-blind technique with random allocation of subjects to the intervention and control groups, followed by measurement of an appropriate outcome using a valid and reliable technique.

Where, for reasons of ethics, feasibility or cost, a formal clinical trial cannot be carried out, it is important that as many of the features of such trials as possible be incorporated in the design. For instance, it is important to have a concurrent control group to ascertain changes in outcome that are not related to the intervention being tested. The use of a study population as its own control, as in a before-and-after study, has certain advantages in cost and feasibility, but uncertainty will always remain as to whether the changes detected might have occurred during the period of the study irrespective of the intervention, a so-called secular trend.

While it may not be feasible to randomly allocate the intervention to individuals, it may be possible to randomly select intervention and control areas, as was done in the Bagamoyo study. Although random selection does not guarantee comparability of the intervention and control areas, it reduces the likelihood of a systematic difference.

1.2 Study population

If the results of a study are to be generalized to other groups in either the same country or other parts of the world, it is important that the study population be selected with that in mind and the characteristics of the population clearly identified. All of the study populations in the projects covered in this review were well described in baseline surveys.

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1 Report of a Working Group on Operational Research in Acute Respiratory Infections, Geneva, 21-25 June 1982 (WHO internal document)

2 Implementation of ARI Programmes and Evaluation of the Mortality Trend, Geneva, 5-8 November 1984 (WHO internal document)

1.3 Intervention

Since an ARI intervention can involve a variety of elements from the availability of antimicrobials in clinics to active case-finding and treatment at home or the implementation of a comprehensive primary health care programme, it is essential that the intervention be clearly described and, insofar as possible, documented during the study. In addition, consideration should be given to "co-interventions", such as an MCH programme, and "contamination", where the intervention spills over into the control area.

In any evaluation of a therapeutic or preventive intervention, it is important to discriminate between efficacy and effectiveness. Efficacy refers to the impact of an intervention when it is delivered and documented in the best of circumstances. Effectiveness refers to the impact of an intervention when it is delivered in the real world. As a general rule efficacy will always be greater than effectiveness since the determinants of the latter include diagnostic accuracy, provider compliance, patient compliance and coverage, as well as efficacy.

An example of the difference between efficacy and effectiveness can be seen in the use of penicillin for documented pneumonia. The efficacy of penicillin for the treatment of pneumococcal pneumonia is 95% or more and for community-acquired pneumonia may be of the order of 80%, depending on whether the responsible organisms are responsive to penicillin. Given an efficacy of 80%, what happens in the real world? Diagnostic accuracy may be only 80%; providers may prescribe correctly in only 90% of cases; only 80% of patients may take the medication; the health service may be accessible to only 80% of the population. Using a mathematical model designed for this purpose[1], it can be estimated that effectiveness would be 37% (0.8 x 0.8 x 0.9 x 0.8 x 0.8).

Although coverage, diagnostic accuracy, provider compliance and patient compliance were not documented, it is likely that all the studies were measuring ARI intervention effectiveness, not efficacy.

1.4 Risk factors for pneumonia mortality

Known risk factors for pneumonia incidence or severity include low birth weight, malnutrition and measles. It is necessary that these and other potential risk factors be evenly distributed in the intervention and control groups or at least measured. Random allocation has the potential advantage of equally distributing both known and unknown risk factors. Failure of randomization or inability to control important risk factors can alter the impact (or lack of impact) of the ARI interventions. If the risk factors are measured, their effect can be analysed.

1.5 Outcome factors

In order to be confident about the data it is necessary to use valid and reliable methods to document overall mortality, cause-specific mortality and other outcomes. Most studies have used dual reporting methods to ascertain overall mortality. However, some doubt remains about the validity of the verbal autopsy in ascertaining the cause of death. Those making a decision on cause of death should be blinded as to whether the case was from the intervention or control group/period.

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[1] Tugwell P, Bennett K.J., Sackett D.L. & Haynes R.B. The measurement iterative loop: A framework for the critical appraisal of need, benefits and costs of health interventions. Journal of chronic diseases, 38: 339-351 (1985).

1.6 Results

Statistical analysis of intervention studies involves the selection of tests that are appropriate to the type of data and their distribution. More sophisticated techniques, such as multivariate analysis, may be necessary where multiple explanatory variables are measured, e.g., immunization status, nutritional status, birth weight, etc. Where a cohort has been followed it may be appropriate to carry out a lifetable or survival analysis.

The intervention studies randomized by village (rather than by child) or made a non-random, judgemental sample of villages. The larger standard errors that may be introduced by these design effects are not taken into account by a chi-square analysis of mortality rates in the intervention and control areas (or periods). Such an analysis treats the data as if the children in the intervention area were a representative random selection from the intervention and control areas.[1] This is theoretically inaccurate and may overestimate statistical significance. It is nonetheless a familiar method of analysis and the only one that can be used at this time, given the study design and the limitations of the data currently available from the studies.

When a statistically significant difference is not found, a type 2 error may have occurred. When a number of studies are available for analysis with comparable methods, interventions and outcome measurements, it may be possible to combine the results from significant and non-significant studies in a meta-analysis.

Studies that set out to test for a 10-20% change in efficacy or effectiveness require several hundred events in each group. Hence, in the context of ARI intervention studies for which the prevailing mortality rate per annum is around 10 per thousand, some 10 to 20 thousand child-years of exposure are required in each group.

In reviewing these studies it was observed that, in most of them, sample size was determined on the assumption of a 30% or 50% reduction in mortality. If this was an optimistic assessment, most studies will end up with differences that are not significant. Moreover, if the actual impact is of the order of 10-30%, bias attributable to selection or the distribution of other risk factors can easily obliterate such an effect in non-randomized comparisons. Indeed, it will always be difficult to disentangle a real effect from an artefact of this kind in such studies. Hence, a single study of such an association will be insufficient to demonstrate efficacy unless it is large and the artefact can be convincingly shown to be unimportant. In general this is extremely difficult.

1.7 Conclusion

Despite the fact that methodological issues such as controlling for other risk factors, measurement bias and adequacy of statistical analysis made interpretation problematic, it was necessary to decide whether each study provided evidence to support or refute the hypothesis that ARI case management reduces overall and ALRI-specific childhood mortality. The conclusions for each study reflect a consensus of those attending the meeting in the light of the methodological strengths and weaknesses of each study.

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[1] Kirkwood, B.: Community-based intervention trials. Presentation at the British Society for Population Studies Conference "Health Interventions and Mortality Change in Developing Countries", University of Sheffield (1987).

2. SUMMARIES OF SEVEN ARI INTERVENTION STUDIES

2.1 Haryana, India. (Low-birth-weight infant study).[1,2]

Principal Investigator: V. Kumar, Department of Community Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh-160 012.

2.1.1 Study design: Controlled trial of active case-finding and management for low-birth-weight infants.

2.1.2 Study population: Low-birth-weight infants from 37 villages in the state of Haryana were included in the study over the period January 1982 to September 1983. Twenty-one of the villages served as an intervention area and 16 as a control area. Sociodemographic characteristics were similar in the two areas.

2.1.3 Interventions: Primary health care workers were trained in ARI case management and oral rehydration therapy. Immunization against diphtheria, pertussis, tetanus, BCG and polio (but not measles) resulted in significantly higher coverage levels in the intervention area than in the control area.

2.1.4 Risk factors: The intervention and control groups were similar, apart from the interventions.

2.1.5 Outcome factors:

(a) Overall mortality was detected through visits by a primary health care worker to each home at weekly intervals.

(b) Cause-specific mortality was estimated by verbal autopsy, using information obtained by a trained field worker. Validation of the diagnosis was assured by supervisory staff.

(c) Morbidity was recorded by the primary health care field workers. These data were used to calculate and compare case-fatality rates in the intervention and control areas.

2.1.6 Results: There was evidence of reduced total and ALRI-specific mortality in the intervention group as compared with the control group, but it was of borderline significance (p=0.06). This result probably reflects the relatively small sample size. There was a significant reduction in case-fatality rate.

2.1.7 Conclusion: On the basis of the case-fatality data, this study provides evidence that the case management approach reduces mortality from ARI in this high-risk group.

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[1] Datta, N., Kumar, V., Kumar, L., & Singhi, S.: Application of case management to the control of acute respiratory infections in low-birth-weight infants: a feasibility study. Bulletin of the World Health Organization, 65: 77-82 (1987).

[2] Final results are pending from a subsequent ARI intervention study targeted at all children under 5 in the same area.

2.2 Jumla, Nepal

Principal Investigator: M.R. Pandey, Mrigendra Medical Trust, Kathmandu; Advisors: N. Daulaire and E. Starbuck, John Snow Incorporated, Integrated Rural Health/Family Planning Services Project, Patan Dhokha, Lalitpur, Kathmandu.

2.2.1 Study design: A controlled trial of ARI detection and management by community health workers. A control group was provided by phased introduction of the intervention.

2.2.2 Study population: An exceptionally isolated community in Nepal with very high mortality rates for mothers and children and virtually no health services. The intervention was phased in over the course of one year to cover a population of 75 000. Outcome measurements were carried out in 18 of 30 sub-divisions of the district (6600 children). The intervention initially covered 4 of the outcome measurement sub-divisions and was phased into an additional 8 during the course of the first year; the remaining 6 were phased in at the beginning of year 2.

2.2.3 Intervention: Only one intervention was tested in this study where workers were trained to detect pneumonia, assess its severity, and administer cotrimoxazole according to an algorithm. Severe cases had to be treated at home rather than referred due to the inadequacy of the health services.

2.2.4 Risk factors: A strength of this study is that by having a single intervention for ARI there was no apparent change in potential risk factors for ARI. For instance, measles immunization coverage was stable at 15 to 20%. Low birth weight (<2500 g) was common. Nutritional status was very poor and possibly included Vitamin A deficiency. Heavy domestic smoke pollution was documented. Potential effects of seasonality (including seasonal variations in malnutrition) were adjusted for in calculating annual mortality rates; this adjustment will be reviewed by a statistician.

2.2.5 Outcome factors:

(a) Overall mortality in the under-5 age group was documented by the independent Vital Events for Child Survival system. From August 1986 to March 1988, 970 deaths and 3322 births were registered. During the first 12 months, during which there were both intervention and control groups, data were collected on 6572 children and included 2107 births and 575 childhood deaths. Retrospective surveys covering approximately one-third of the events in question found only 6 events which had been missed by the village enumerators.

(b) Cause-specific mortality was estimated by verbal autopsy with initial data collection by field supervisors and decision-making by physicians blinded to whether the death was from the control or the intervention group.

2.2.6 Results:

(a) Overall mortality was calculated on a monthly basis for the children under study and converted to an annual basis using a standardized population to account for the seasonal variation in mortality. Deaths per 1000 child-years at risk were 18% lower in the intervention group for the under-5 age group (100 per 1000 compared with 83). The rate in infants was 25% less in the intervention group (250 per 1000 compared with 188). The most striking difference was in the 3-5 month age group where the intervention was associated with a 44% reduction in mortality (150 per 1000 compared with 84). The infant mortality rate was 19% less in the intervention group (201 per 1000 live births compared with 162).

(b) The ALRI-specific mortality fell only in infants less than 6 months of age. The ALRI-specific reduction could only partially account for the reduction in overall mortality and a fall in overall mortality was seen in infants 6-11 months of age and in children 1-4 years old despite there being no reduction in ALRI-specific mortality in these age groups. This may reflect inaccuracies in the verbal autopsies or an impact of cotrimoxazole use on other causes of death, even though the drug was given only for fast breathing or chest indrawing. Diarrhoea-specific death rates were 28% less in the intervention group.

2.2.7 Conclusion: While statistical analysis and further consideration of the rate adjustments are required, the study is a unique demonstration of the potential impact of active case-finding and management alone in a population with a high prevalence of pneumonia risk factors. The possible impact on diarrhoeal disease mortality deserves further study.

2.3 Abbottabad, Pakistan

Principal Investigators: A.J. Khan, Ayub Medical College, Abbottabad; J.A. Khan, PMRC Research Centre, Abbottabad.

2.3.1 Study design: A controlled trial of ARI case detection and management with a before-and-after analysis of the control area where the intervention was started after 2 years.

2.3.2 Study population: Three clusters of villages in mountainous areas were selected. Thirty-one of 40 villages were allocated to the intervention, after which 9 other villages were identified as controls.

2.3.3 Intervention: The major thrust of the programme was the implementation of ARI case management with active case-finding. Immunization, a nutritional programme (food supplements for pregnant women), and diarrhoeal disease control through improved access to ORT were under way at the same time, but were implemented to an equal extent in both the intervention and the control areas. Immunization coverage increased in the intervention area in the first year of the study from 5% in January 1985 to 77% in January 1986. Community health workers (CHW) were trained to identify ARI and use an algorithm for initial management with antimicrobials if appropriate. Subsequent treatment was expected to be provided by a medical graduate.

2.3.4 Risk factors: The level of measles immunization was similar in both areas.

2.3.5 Outcome factors:

(a) Overall mortality was detected by CHWs in the intervention area, but by a quarterly survey in the control area.

(b) Cause-specific mortality was estimated by verbal autopsy. In view of the different methods used to determine mortality in the two areas, the interval between death and verbal autopsy was longer in the control area.

(c) Information on the incidence of childhood ARI morbidity in the preceding 14 days was obtained by the supervising teams through scheduled home visits. Besides those visits, each CHW daily visited 20-25 houses to identify ARI.

2.3.6 Results: There was a reduction in overall and ALRI-specific mortality when comparisons were made between the control area and the intervention area for concurrent years and between control and intervention periods for the control area. Comparison of the 1985/86 data for control and intervention areas revealed a 52% (statistically significant) fall in ALRI-specific infant mortality (32.5 vs 15.5/1000 live births, p=0.01) and a fall of 55% for under-5 mortality (28.7 vs 12.8/1000, p=.001).

2.3.7 Conclusion: The project has provided evidence to support the hypothesis that case management of ARI reduces mortality.

2.4 Bohol, Philippines

Principal Investigator: M.G. Lucero, Research Institute for Tropical Medicine, Alabang, Metro Manila.

2.4.1 Study design: A before-and-after and concurrent controlled trial of ARI case management without active case-finding.

2.4.2 Study population: The island of Bohol had been the site of MCH programmes in the 1970s and had fairly good health services as reflected in infant mortality rates of approximately 50 per 1000 live births. Prior to the study, antimicrobials were available for serious ARI from doctors at the health centre. Baseline data indicated that the two areas were similar in most sociodemographic measures, although the control area had fewer homes with electricity, less safe water and a higher occurrence of measles. Each area consisted of approximately 10 000 children under 5 years of age with approximately 1000 infants. Baseline studies were carried out in both areas in 1984. The intervention took place in 1985 and 1986.

2.4.3 Intervention: Case management of ARI was provided by midwives who had been trained to detect severe ARI and to prescribe antimicrobials according to an algorithm. Case-finding was not active. Maternal education had been planned but not carried out by the time of the current analysis. Questions were raised concerning the degree of implementation of the case management protocol.

2.4.4 Risk factors: This was probably not a major problem. Measles immunization coverage was high in both areas: approximately 90%.

2.4.5 Outcome factors:

(a) Overall mortality was detected by two complementary methods: periodic household surveys and a continuous monitoring system.

(b) Cause-specific mortality was analysed by verbal autopsy as soon after death as possible, using a standardized questionnaire.

2.4.6 Results:

Analysis is complicated by differences in baseline status between the areas. The control area had significantly lower total IMR, ALRI-specific IMR and non-measles associated ALRI-specific IMR.

(a) Overall under-5 mortality fell by approximately 13% and 10% in the intervention and the control area, respectively, between the pre-intervention and intervention years. A fall in infant mortality of approximately 20% was recorded for the intervention area but not for the control area, where the infant mortality rate was at the same level at the start of the study as it was in the intervention area at the end of the study.

(b) ALRI-specific under-5 mortality, exclusive of measles, fell by 28% in the intervention area compared with 10% in the control area (p=0.07). ALRI-specific infant mortality, exclusive of measles, fell by 30% in the intervention area but increased by 1.5% in the control area.

2.4.7 Conclusions: This study shows a possible effect of a case management programme in which the sick children were brought to a clinic rather than detected by deliberate case-finding. It is possible that the impact has been under-estimated due to doubts about the extent of the coverage.

2.5 Bagamoyo, United Republic of Tanzania[1]

Principal Investigators: F.D.E. Mtango, Department of Epidemiology, Muhimbili Medical Centre, Dar es Salaam, and D. Neuvians, German Agency for Technical Cooperation, Dar-es-Salaam.

2.5.1 Study design: A controlled trial of case management for ARI, without active case-finding, in randomly selected intervention and control areas with the addition of a before-and-after study for the control area.

2.5.2 Study population: Eight of the 16 sub-districts of the district of Bagamoyo were randomly selected for the intervention. The other districts constituted the control area in which the intervention was started one year later. The district was a typical rural area. In the first year of the study there were 8098 children under the age of 5 in the control area and 8028 in the intervention area. A survey in 1984 revealed a 53% immunization level for measles and a nutrition survey in 1986 detected 35% moderately and 3% severely malnourished children.

2.5.3 Intervention: Although the ARI programme was comprehensive in that it included a full nutrition education programme and information about oral rehydration for diarrhoeal disease, the major thrust of the intervention was case management of ARI through the existing health service. The other parts of the package were phased in over a number of years. Village health workers were trained at a 2-month course. The initial year of the study was 1983/84 and data were available until 1986/87.

2.5.4 Risk factors: It is difficult to determine whether the programme components other than case management of ARI are likely to have altered significant risk factors for ARI. The impact of these other interventions may have been limited due to the delay in starting them and the good level of health services at the time of the study.

2.5.5 Outcome factors:

(a) Overall mortality data were collected through continuous reporting by village health workers and a yearly survey. Data from the latter indicated that only 50% of deaths were being detected by the village health workers.

(b) Cause-specific mortality was measured by verbal autopsy; the information was collected by a medical assistant, who recorded a probable cause of death which was reviewed by the principal researchers.

(c) Morbidity was recorded by the village health workers when they saw children with ARI and also during a specifically designed community survey.

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[1] Mtango, F.D.E. & Neuvians D.: Acute respiratory infections in children under five years. Control project in Bagamoyo, Tanzania. Transactions of the Royal Society of Tropical Medicine & Hygiene, 80: 851-858 (1986).

2.5.6 Results:

(a) Overall under-5 mortality is significantly reduced when the control and intervention areas are compared for 1983 (40.1/1000 vs 32.4/1000, $p<0.01$) and when the control year and the average of the subsequent intervention years for the control area are compared (40.1/1000 vs 35.5/1000, $p<0.05$).

(b) There was a reduction in under-5 ALRI-specific mortality between the control area and the intervention area for 1983 (14.4/1000 vs 11.5/1000), but this was not statistically significant. However, when the control year and the average of the subsequent intervention years for the control area are compared, there is a significant difference (14.4/1000 vs 9.8/1000, $p<0.001$). Furthermore, when the control and intervention areas are compared for the first 2 years (1983 and 1984) there is also a significant difference (13.2/1000 vs 10.9/1000, $p<0.05$). However, this needs careful interpretation since the intervention was implemented in the control area in 1984. ALRI mortality not associated with measles decreases significantly only when the first 2 years in the control area are compared with the last 2 years in the intervention and the control area (9.5/1000 vs 7.1/1000 in 1985-1986 when the intervention was applied in the control area, $p=0.01$; 9.5/1000 vs 6.6/1000 in 1985-1986 in the intervention area, $p<0.01$).

2.5.7 Conclusion: The study was quite well designed and the impact of the programme seems significant. Although some of the reduction in ALRI mortality was due to a decline in measles-associated pneumonia deaths, it was argued that much of this reduction was attributable to better case management, and that the impact has been on pneumonia mortality, irrespective of whether the pneumonia was a consequence of measles.

2.6 Kathmandu Valley, Nepal

Principal Investigator: M.R. Pandey, Mrigendra Medical Trust, Thapathali, Kathmandu.

2.6.1 Study design: A before-and-after trial of a comprehensive programme of active case-finding and management of ARI, maternal ARI-specific education, immunization and case management of diarrhoeal disease.

2.6.2 Study population: A rural Nepalese community close to Kathmandu, with a low level of health care and high occurrence of ARI. According to the initial census, in January 1984, the community was composed of 1127 families, a total population of 6332 and an under-5 population of 1019. Other characteristics were an economy of subsistence agriculture and a low level of maternal literacy (6%). Population changes were followed throughout the surveillance and intervention years of the study by recording the number of births, deaths, immigrants and emigrants.

2.6.3 Intervention:

(a) Case management of ARI by community health workers (CHW), who had been trained at a 13-day course to diagnose and treat or refer ARI, under the supervision of health assistants.

(b) Case management of acute diarrhoea.

(c) Implementation of EPI.

(d) Provision of education to mothers on ARI, breast-feeding, domestic smoke pollution and cigarette smoking.

2.6.4 Risk factors: A change in measles immunization coverage was the major potential change in risk factors, although other changes in risk factors may have occurred given the comprehensive nature of the intervention.

2.6.5 Outcome factors:

(a) Mortality was detected by the CHW and checked by a local committee.

(b) Cause-specific mortality was ascertained by verbal autopsy, using information obtained by a health assistant from another field station. A decision on cause was made by 2 paediatricians contemporaneously with each phase of the study and could not be considered to be blind.

(c) Episodes of ARI were recorded by the CHWs.

2.6.6 Results:

(a) Overall under-5 mortality fell by 40%. A similar fall occurred in the infant mortality rate.

(b) ALRI-specific under-5 mortality fell by 60-70% ($p<0.01$ when the intervention years are combined). A similar fall occurred in ALRI-specific infant mortality ($p<0.01$ when the intervention years are combined).

(c) The incidence of ARI was stable (4.6 episodes per child per year during the surveillance year and 5.8 and 5.3 episodes in the intervention years). Data on treatment outcome indicted that 92% of discovered episodes were being treated by the study team with 1% or less case fatality; a higher case fatality was observed in the small number of children treated exclusively by traditional faith healers.

(d) Measles immunization coverage increased from 11% to 71% to 82% and the occurrence of measles declined from 18% to 8% to 4% in the surveillance and intervention years, respectively. Few of the pneumonia deaths were measles-associated.

2.6.7 Conclusion: Most of the reduction in ALRI mortality was accounted for by pneumonia not associated with measles. This study is considered to provide evidence in support of the use of active case-finding and management by CHWs.

2.7 Kediri, Indonesia

Principal Investigator: R. Roesin, Directorate General of Communicable Disease Control, Ministry of Health, Jakarta Pusat.

2.7.1 Study design: A before-and-after trial of active ARI case-finding and management, with increased primary health care.

2.7.2 Study population: The Kediri subdistrict of the West Nusa Tengagara province was selected because it fulfilled the criteria of having approximately 5000 under-5 children, adequate primary health care and practising village volunteer health workers. A pre-study census revealed the presence of 12 074 households, a total population of 56 688 and an under-5 child population of 8624 with 3547 infants. Measles immunization coverage was very low in the baseline study (1.5%). Maternal literacy was 23%.

2.7.3 Intervention: The programme was a broad one involving the implementation of case-finding and management of ARI together with EPI, diarrhoeal disease control, nutrition, maternal and child health and family planning. A substantial effort was put into optimizing coverage and compliance.

2.7.4 Risk factors: A large measles epidemic occurred during the control year of the study and measles immunization coverage was improved. However, all measles-associated pneumonia and diarrhoea deaths were classified as measles only.

2.7.5 Outcome factors:

(a) Overall mortality in children was measured by the community team in the first instance and checked by a 3-monthly retrospective survey.

(b) Cause-specific mortality was measured by verbal autopsy, for which information was obtained by a full-time supervisor (an experienced health inspector) and a 3-member review committee (all doctors, including one paediatrician).

(c) The occurrence of moderate and severe ARI was recorded by village health workers and staff members of the local health and sub-health centres.

2.7.6 Results: Results have been provided for the first 6 months of the intervention and are considered as preliminary. ALRI-specific infant and under-5 mortality rates fell by more than 50% only 6 months after the start of the intervention ($p<0.001$). There was also a dramatic reduction in measles-related mortality in the first year of the intervention as a result of a crash immunization programme which raised the immunization coverage to 90%.

2.7.7 Conclusions: Allowing for the preliminary nature of the results, there seems to have been a substantial reduction in ARI mortality which cannot be explained by the reduction in measles-associated mortality.

ANNEX 2

GLOSSARY

ARI	Acute respiratory infection(s). Includes both acute upper and lower respiratory infections.
AURI	Acute upper respiratory infection(s). Includes common cold, pharyngitis and otitis media.
ALRI	Acute lower respiratory infection(s). Includes pneumonia, bronchiolitis, croup, epiglottitis and bronchitis.
ALRI-specific mortality	Deaths preceded by symptoms of acute lower respiratory infection (such as cough, breathing difficulty, fast or noisy breathing, air hunger) on verbal autopsy. Most of these deaths would be expected to be from pneumonia.
ARI case management	Assessment and management of children with acute respiratory infection according to signs of severity. In the studies, antimicrobials were provided only for children with signs suggesting serious acute lower respiratory infection (tachypnea or chest indrawing, see Table 2) which usually would be due to pneumonia. Acute upper respiratory infections and bronchitis were treated with supportive care only except in Abbottabad where antimicrobials were also recommended for otitis media and purulent pharyngitis.

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