

Improving antimicrobial use among health workers in first-level facilities: results from the Multi-Country Evaluation of the Integrated Management of Childhood Illness strategy

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Objective The objective of this study was to assess the effect of Integrated Management of Childhood Illness (IMCI) case management training on the use of antimicrobial drugs among health-care workers treating young children at first-level facilities. Antimicrobial drugs are an essential child-survival intervention. Ensuring that children younger than five who need these drugs receive them promptly and correctly can save their lives. Prescribing these drugs only when necessary and ensuring that those who receive them complete the full course can slow the development of antimicrobial resistance.

Methods Data collected through observation-based surveys in randomly selected first-level health facilities in Brazil, Uganda and the United Republic of Tanzania were statistically analysed. The surveys were carried out as part of the multi-country evaluation of IMCI effectiveness, cost and impact (MCE).

Findings Results from three MCE sites show that children receiving care from health workers trained in IMCI are significantly more likely to receive correct prescriptions for antimicrobial drugs than those receiving care from workers not trained in IMCI. They are also more likely to receive the first dose of the drug before leaving the health facility, to have their caregiver advised how to administer the drug, and to have caregivers who are able to describe correctly how to give the drug at home as they leave the health facility.

Conclusions IMCI case management training is an effective intervention to improve the rational use of antimicrobial drugs for sick children visiting first-level health facilities in low-income and middle-income countries.

Keywords Anti-bacterial agents/administration and dosage; Antimalarials/administration and dosage; Prescriptions, Drug/standards; Child; Caregivers/education; Community health aides/education; Delivery of health care, Integrated/utilization; Primary health care; Ambulatory care facilities; Guidelines; Brazil; United Republic of Tanzania; Uganda (*source: MeSH, NLM*).

Mots clés Antibiotiques/administration et posologie; Antipaludique/administration et posologie; Ordonnance médicale médicament/normes; Enfant; Soignant/enseignement; Auxiliaire santé publique/enseignement; Distribution intégrée soins/utilisation; Programme soins courants; Services soins ambulatoires; Lignes directrices; Brésil; République-Unie de Tanzanie; Ouganda (*source: MeSH, INSERM*).

Palabras clave Antibióticos/administración y dosificación; Antimaláricos/administración y dosificación; Prescripción de medicamentos/normas; Niño; Cuidadores/educación; Auxiliares de salud comunitaria/educación; Entrega integrada de atención de salud/utilización; Atención primaria de salud; Instituciones de atención ambulatoria; Pautas; Brasil; República Unida de Tanzania; Uganda (*fuelle: DeCS, BIREME*).

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Introduction

Despite advances over the past few decades made in reducing child mortality, more than 10 million children die each year before they reach the age of five (1, 2). At least 6 in 10 of these deaths could be prevented if existing affordable interventions were available to all children who need them (3).

Antimicrobial drugs are one of the most powerful and important interventions available to reduce child mortality. Antibiotics are a proven treatment for pneumonia (4, 5), bacterial infections in neonates (6), the premature rupture of membranes (7) and for some cases of diarrhoea, including cholera, shigella dysentery, giardiasis and amoebiasis (8, 9). Antimalarials are needed to treat malaria in children (10, 11).

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The increasing rate of biological resistance to antimicrobials has been recognized as a public health emergency. Studies have documented high levels of antibiotic misuse among health-care workers, such as using antibiotics to treat viral diseases or using incorrect dosages (12, 13). Thus one important strategy for slowing the development of resistance is to reduce the unnecessary use of these drugs (14–16). Efforts to reduce the prevalence of antimicrobial resistance in low-income and middle-income countries have increasingly focused on the promising approach of providing appropriate education for health workers (12, 17, 18).

Integrated Management of Childhood Illness (IMCI) is a strategy developed by WHO and UNICEF to provide effective and affordable interventions to reduce child mortality and improve child health and development (19). IMCI includes both preventive and curative interventions, and it is designed to improve the case-management skills of health workers, to strengthen health system supports for child health-service delivery, and to improve family and community practices related to child health (20).

Training health workers in IMCI case management has been conducted in more than 100 developing countries in both in-service and pre-service contexts (i.e., introducing IMCI into the basic education of doctors, nurses and other health professionals) (21). The training is based on a set of case-management guidelines that is adapted in each country prior to use. The training guides the health worker through a process of assessing signs and symptoms, classifying the illness based on treatment needs and providing appropriate treatment and education of the child's caregiver. The IMCI guidelines include information on identifying malnutrition and anaemia, checking vaccination status, providing nutritional counselling, and communicating effectively with caregivers (22). The training emphasizes supervised clinical practice, and in some settings health workers are visited in their facilities shortly after training to reinforce their new IMCI skills.

The multi-country evaluation (MCE) of IMCI effectiveness, cost and impact is a global programme designed to evaluate the impact of IMCI on child health and its cost-effectiveness (23). MCE studies are under way in Bangladesh, Brazil, Peru, the United Republic of Tanzania and Uganda.

In this paper we present selected results from MCE health-facility surveys in Brazil, the United Republic of Tanzania and Uganda. Our aim is to show that large numbers of children are receiving antibiotics through health providers, and that training in IMCI case management at first-level health facilities can lead to improved practices among health workers and improved knowledge among caregivers about how to continue antimicrobial treatment at home.

Methods

MCE study designs vary across the five countries depending on the stage of IMCI implementation and the opportunities available to use existing data. All sites measure a standard set of indicators using compatible survey tools (23). These data are collected at various levels: data on mortality indicators are collected at district level through demographic surveillance systems or vital statistics; data on family behaviours, socioeconomic status, access to and utilization of health services are collected through population-based household surveys; and data on the quality of case management, health systems support for IMCI and caregiver knowledge are collected through observation-based

surveys at health facilities. Cost data are collected at household, health facility, district or municipality and national levels. Full details on study design, methods and survey tools are available on the MCE web site (<http://www.who.int/imci-mce>).

This paper draws only on data from the quality of case management survey and the caregiver knowledge survey carried out in random samples of outpatient health facilities in the United Republic of Tanzania, Uganda and Brazil. Sick children younger than five years presenting to a health facility for the first time during an episode of illness were followed by a trained observer throughout their visit. Observers recorded the care received and conducted a "gold standard" assessment of the child's condition. The caregiver accompanying each child was interviewed as she or he left the facility.

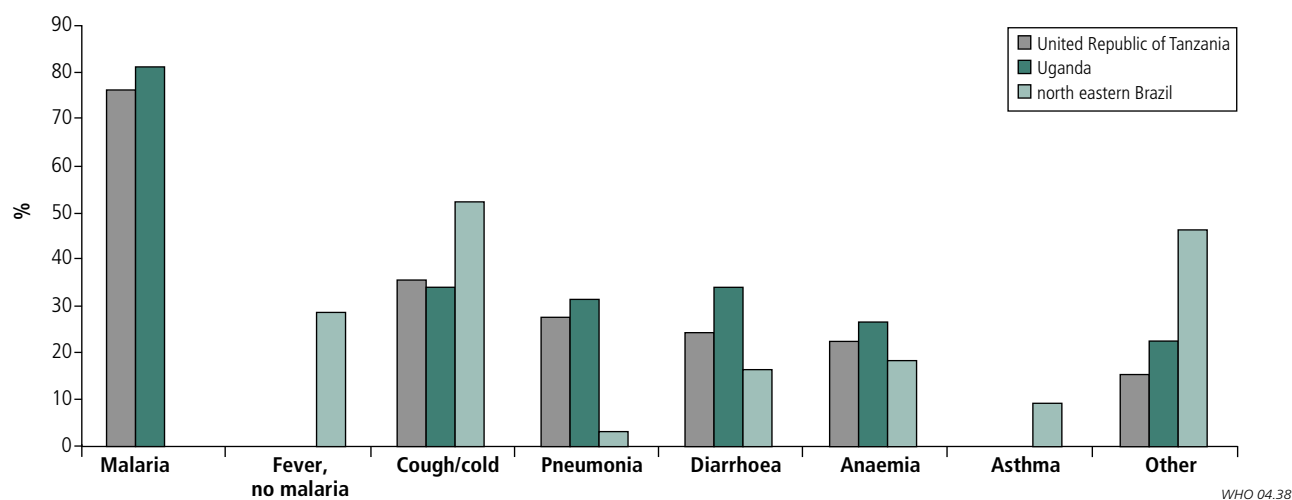
In-service training in IMCI case management had been carried out in all three sites prior to the survey. The training, which included intensive supervised clinical practise, was based on an 11-day course in the United Republic of Tanzania (24) and Uganda (unpublished data), and a 6-day or 8-day course in Brazil (25). The survey in the United Republic of Tanzania was carried out in 2000 in a sample of 75 health facilities selected from two intervention districts and two comparison districts (24); the survey in Uganda was carried out in 2000 in 80 randomly selected health facilities and was the first round of a programme of continuous monitoring in 10 districts at different stages of IMCI implementation (unpublished data); and the survey in Brazil was carried out in 2002 in 96 health facilities in four states in the north-east staffed by health-care workers with and without training in IMCI (25). Data on antibiotic needs, treatment patterns and the effects of IMCI were analysed for all three sites.

Logistic regression correcting for clustering of children at the health facility was used to calculate the odds ratio (OR) of correct performance among those with IMCI training compared with those who had not had the training. Differences in the effect of training between countries were addressed by introducing the variable "country" into the regression as a dummy variable and testing for the interaction with training. Where the interaction was not significant the ORs of the pooled data measured the effect of IMCI across all countries. Where ORs were significantly different between countries, data were not pooled. Statistical significance was set at $P < 0.05$. The significance of ORs within countries was assessed using a χ^2 test with a second-order Rao and Scott correction to account for the survey design (26).

Results

Fig. 1 summarizes the major presenting illnesses among children younger than five years visiting first-level outpatient health facilities in the three study sites. More than 60% of children in the United Republic of Tanzania and Uganda, and 46% in Brazil, presented with more than one of these illnesses. Based on the observer's "gold standard" assessment of the child's condition, about one-third of all children under five years presenting for care at outpatient facilities in the United Republic of Tanzania (32% of 419) and Uganda (35% of 516) were classified as requiring treatment with a course of antibiotics. Among children needing antibiotics, the majority needed them for pneumonia (87% in the United Republic of Tanzania, 89% in Uganda), while others needed them for acute ear infection (7% in the United Republic of Tanzania, 7% in Uganda) or dysentery (10% in the United

Fig. 1. Illnesses among children under five years of age presenting for care at first-level health facilities in the United Republic of Tanzania ($n = 419$), Uganda ($n = 516$) and north-eastern Brazil ($n = 653$)



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Republic of Tanzania, 7% in Uganda). More than two-thirds of the children presenting for care in the United Republic of Tanzania and Uganda were judged to require antimalarials, based on policies in both these countries stipulating the presumptive treatment of fever with antimalarials.

The profile of presenting illnesses was quite different in Brazil (Fig. 1), where there is no malaria in the four states participating in the MCE and where the locally-adapted IMCI guidelines include a number of conditions, such as asthma, in addition to those found in the generic IMCI case-management guidelines. Altogether 46% of children in the survey in Brazil presented with other, non-IMCI related illnesses (Fig. 1). About 10% of children (68/653) presenting for care in the health facilities in Brazil required antibiotics. In this group, 28% needed antibiotics for pneumonia, 18% for acute ear infection, and 68% for other types of infections. Sixteen per cent of children required antibiotics for more than one of these conditions.

Table 1 presents by IMCI training status of the health worker the proportion of sick children for whom health workers in the United Republic of Tanzania, Uganda and Brazil performed specific treatment and communication tasks related to antimicrobials. Pooled ORs for the effect of IMCI across all countries are also given for those indicators where the OR was not significantly different between the three countries.

High proportions of children who needed antibiotics received a prescription for them, but for many children the dosage was incorrect. Overall, children seen by IMCI-trained health-care workers were significantly more likely to receive the correct prescription of antibiotics (in terms of dose, frequency and formulation) than children seen by health workers not yet trained in IMCI. There were similar patterns in all three countries (pooled OR 2.7, 95% confidence interval (CI) = 1.5–4.8). Significantly more children seen by IMCI-trained health workers received the correct prescription for antimalarials in both Uganda and the United Republic of Tanzania (with no malaria in Brazil) than did children seen by untrained health workers, although the effect was significantly stronger in the United Republic of Tanzania (OR 17.2; 95% CI = 7.6–38.8) than in Uganda (OR 3.0; 95% CI = 1.7–5.5). IMCI training was associated with significant reductions in the unnecessary use of antibiotics in all three countries (pooled OR 2.9; 95% CI = 1.9–4.2).

Communication with children's caregivers about how to administer antimicrobials at home was significantly better for children seen by IMCI-trained health workers than for children seen by health workers who had not yet been trained (Table 1). Caregivers whose children were seen by workers not trained in IMCI received little or no information about how to administer antibiotics or antimalarials. For example, 98% of caregivers of children who received an antibiotic from an IMCI-trained health worker in the United Republic of Tanzania were advised correctly on how to administer the drug, while only 18% of caregivers served by a health worker not yet trained in IMCI received this advice (Table 1). Also in the United Republic of Tanzania, caregivers whose child was seen by an IMCI-trained health worker were significantly more likely to be able to report correctly as they left the facility how and when the drugs should be given to the child than were those caregivers whose child was seen by a health worker who had not been trained in IMCI. This was not the case in Uganda and Brazil.

Finally, there were significant differences by IMCI training status in the proportion of children prescribed an antibiotic or antimalarial who received the first dose before leaving the health facility in all three countries (Table 1). However, the effect was significantly stronger in the United Republic of Tanzania than in Uganda and in Brazil. In the latter two countries the proportion of children who received the first dose of medication at the facility was low (21% in Uganda and 27% in Brazil) even after training in IMCI, leaving much room for improvement. Administering the first dose at the facility is recommended in the generic IMCI case-management guidelines because it ensures that the treatment begins immediately and provides an opportunity for the health care worker to demonstrate to the caregiver the correct way to administer the drug.

Discussion

Large numbers of children attending first-level health facilities in the three MCE study sites are receiving antibiotics from both IMCI-trained health care workers and health-care workers who have not been trained in IMCI case management. In facilities where health workers have not been trained in IMCI, antibiotics are not prescribed when they should be; they are prescribed when

Table 1. Indicators of appropriate antimicrobial treatment given to children and advice given to their caregivers by health workers with and without training in Integrated Management of Childhood Illness (IMCI) in the United Republic of Tanzania, Uganda and north-eastern Brazil. All results adjusted for clustering at health-facility level.

	United Republic of Tanzania			Uganda			Brazil			Pooled country data		
	IMCI trained ^a	Not trained ^a	OR ^b	IMCI trained	Not trained	OR	IMCI trained	Not trained	OR	IMCI trained	Not trained	Adjusted OR
Treatment indicators												
Child needs antibiotics and receives correct prescription	77 (69)	43 (58)	4.4 ^d	41 (68)	25 (83)	2.1	67 (33)	51 (35)	1.9	61 (170)	36 (176)	2.7 ^d (1.5–4.8)
Child needs antimalarials and receives correct prescription	85 (175)	25 (136)	17.2 ^d	49 (139)	24 (221)	3.0 ^d	No malaria in Brazil at study sites					
Child does not need antibiotics and leaves without them	86 (150)	57 (117)	4.6 ^d	59 (108)	38 (170)	2.4 ^d	94 (261)	87 (323)	2.4 ^d	84 (519)	68 (613)	2.9 ^d (1.9–4.2)
Child receives the first dose of treatment at the facility	84 (179)	1 (145)	369 ^d	21 (153)	3 (231)	8.5 ^d	27 (33)	0 (35)	$P=0.028^e$			
Communication indicators												
Caregiver of child who is prescribed antibiotic is advised how to use it	98 (73)	18 (77)	323 ^d	31 (80)	29 (144)	1.1	54 (41)	9 (70)	12.4 ^d			
Caregiver of child who is prescribed antimalarials is advised how to use them	96 (156)	13 (83)	164 ^d	46 (127)	22 (156)	2.9 ^d	No malaria					
Caregiver of child who is prescribed antibiotic knows how to give it	68 (78)	46 (77)	2.4 ^d	15 (62)	9 (123)	1.7	62 (50)	63 (63)	0.9	49 (190)	33 (263)	1.7 (1.0–2.8)
Caregiver of child who is prescribed antimalarials knows how to give them	80 (158)	38 (81)	6.4 ^d	33 (121)	25 (140)	1.5	No malaria					

^a Values are percentages (numbers).

^b OR = odds ratio.

^c Value in parentheses is 95% confidence interval. Combined country estimates were adjusted for clustering at facility level and for country effect. The pooled result is not reported in cases in which odds ratios were significantly different between countries.

^d Statistically significant at 5% level of significance.

^e Corrected *P*-value. OR cannot be calculated because there were no observations.

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they should not be; and the health workers do not communicate adequately with the child's caregiver about how to give the drugs at home and the importance of completing a full course of antibiotics.

We have shown that IMCI case-management training can improve the use of antimicrobial drugs significantly among health workers who treat sick children in first-level outpatient health facilities in low-income and middle-income countries. IMCI-trained health workers were more likely than their colleagues who had not had training in IMCI to prescribe antibiotics and antimalarials correctly, to communicate effectively to caregivers about how these drugs should be administered after leaving the facility, and to provide the first dose of the drug at the health facility. IMCI training was also found to be associated with more rational use of these drugs, with fewer children receiving antibiotics unnecessarily.

The effect of IMCI training on indicators measuring correct treatment and communication was significantly different between countries for five of the eight reported indicators, and in general showed a much stronger effect in the United Republic of Tanzania. One possible explanation for this difference between the three countries is that the study design in the United Republic of Tanzania included two intervention districts with high training coverage in which all the health workers observed had been trained in IMCI and two comparison districts in which none of the health workers had been trained. IMCI implementation in Uganda and Brazil was less well controlled. In Uganda, IMCI has been implemented at a national level and in a phased manner, and in Brazil IMCI has been implemented at a municipal level. The quality of training, supervision and follow-up in the United Republic of Tanzania would therefore be expected to be much better than in Uganda and Brazil. A second possible explanation for the weaker effect of IMCI in Uganda and Brazil may be related to factors such as the abolition of user fees and low morale of health workers in Uganda (unpublished data) and the high turnover of staff in Brazil (25).

Health workers' performance may be affected by several factors in addition to training. However, country-specific reports on the performance of health workers in general have shown that IMCI improves performance significantly, even after adjustment for type of health worker and geographical area (25).

Given the effectiveness of IMCI case-management training in improving the performance of health workers, a major challenge facing developing countries is how to increase training coverage in first-level facilities, especially given the rapid turnover

of staff in some settings (27). The inclusion of IMCI guidelines in the pre-service training of health workers is one promising option that has been adopted by many countries. In addition, however, major new efforts are needed at community level to improve care-seeking behaviour and to strengthen the roles of community-based health workers in settings where they are available.

Conclusion

Data from three of the MCE sites have shown that the use of antimicrobial drugs among health workers treating children at first-level health facilities can be significantly improved through IMCI case-management training. However, the strength of the effect depends on the intensity with which IMCI is being implemented.

Ministries of Health and their technical assistance partners, including WHO, should support IMCI case-management training as an effective intervention not only to improve the management of childhood illness but also to reduce the inappropriate use of antimicrobials. ■

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Conflicts of interest: none declared.

Résumé

Amélioration de l'utilisation des antimicrobiens par les agents de santé des établissements de premier niveau : résultats de l'évaluation multipays du programme de prise en charge intégrée des maladies de l'enfant

Objectif La présente étude avait pour objet d'évaluer l'effet de la formation à la prise en charge intégrée des maladies de l'enfant (PCIME) sur l'utilisation des antimicrobiens par les agents de santé soignant les jeunes enfants dans des établissements de premier niveau. L'administration d'antimicrobiens constitue une intervention essentielle en matière de survie de l'enfant. Chez l'enfant de moins de cinq ans, ces médicaments administrés sans retard et de façon correcte lorsque la situation l'exige peuvent sauver la vie. En ne les prescrivant qu'à bon escient et en veillant à ce que les malades suivent leur traitement

jusqu'au bout on peut freiner le développement de la résistance aux antimicrobiens.

Méthodes Les données recueillies au cours d'enquêtes d'observation dans des établissements de soins de premier niveau choisis par tirage au sort au Brésil, en Ouganda et en République-Unie de Tanzanie ont fait l'objet d'une analyse statistique. Ces enquêtes ont été réalisées dans le cadre de l'évaluation multipays de l'efficacité, du coût et de l'impact de la PCIME.

Résultats Les résultats des trois sites retenus montrent que les enfants pris en charge par des agents de santé formés à la PCIME

ont une probabilité sensiblement plus élevée de recevoir une prescription correcte d'antimicrobiens que ceux qui sont soignés par des personnels de santé n'ayant pas reçu cette formation. Ils ont également davantage de chances de recevoir leur première dose de médicament avant de quitter l'établissement de soins, et que la personne qui s'occupe d'eux reçoive des explications sur

la façon d'administrer le médicament et soit en mesure de décrire correctement la façon de faire avant de quitter l'établissement.

Conclusion La formation à la PCIME est une intervention efficace pour améliorer l'usage rationnel des antimicrobiens chez les enfants malades vus dans les établissements de soins de premier niveau dans les pays à faible revenu et à revenu intermédiaire.

Resumen

Mejora del uso de los antimicrobianos entre los agentes de salud de los servicios de primer nivel: resultados de la Evaluación Multipaíses de la estrategia de Atención Integrada a las Enfermedades Prevalentes de la Infancia

Objetivo El objetivo del presente estudio fue evaluar el efecto de la capacitación para el manejo de casos conforme a la Atención Integrada a las Enfermedades Prevalentes de la Infancia en el uso de antimicrobianos entre los agentes de salud que trataban a niños de corta edad en servicios de primer nivel. La administración de antimicrobianos constituye una intervención esencial para la supervivencia infantil. Es posible salvar la vida de los menores de cinco años que necesitan esos fármacos si se garantiza que los reciban rápida y correctamente. La aparición de resistencia a los antimicrobianos se puede frenar prescribiéndolos únicamente cuando sean necesarios y asegurándose de que quienes los reciben completen el régimen terapéutico.

Métodos Se analizaron estadísticamente los datos reunidos mediante encuestas observacionales llevadas a cabo en servicios de salud de primer nivel seleccionados aleatoriamente en el Brasil, Uganda y la República Unida de Tanzania. Las encuestas se realizaron como parte de la evaluación multipaíses de la eficacia, el costo y el impacto de la AIEPI.

Resultados Los resultados obtenidos en los tres sitios evaluados muestran que los niños atendidos por personal sanitario capacitado para dispensar AIEPI tienen más probabilidades de recibir prescripciones correctas de antimicrobianos que los atendidos por personal no capacitado para ello. Asimismo, en su caso hay más probabilidades de que reciban la primera dosis antes de abandonar el servicio de salud, de que su cuidador reciba instrucciones sobre la manera de administrar el fármaco, y de que, al abandonar el servicio de salud, su cuidador sea capaz de describir correctamente la manera de administrar el medicamento en su domicilio.

Conclusión La capacitación para el manejo de casos en el marco de la AIEPI es una intervención eficaz para fomentar una administración más racional de los antimicrobianos a los niños enfermos atendidos en los servicios de salud de primer nivel en los países de ingresos bajos o medios.

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References

1. Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? *Lancet* 2003;361:2226-34.
2. Ahmad OB, Lopez AD, Inoue M. The decline in child mortality: a reappraisal. *Bulletin of the World Health Organization* 2000;78:1175-91.
3. Jones G, Steketee RW, Black RE, Bhutta Z, Morris SS, Bellagio Child Survival Study Group. How many child deaths can we prevent this year? *Lancet* 2003;362:65-71.
4. Sazawal S, Black RE. Meta-analysis of intervention trials on case management of pneumonia in community settings. *Lancet* 1992;340:528-33.
5. Boerma JT, Sommerfelt AE, Rutstein SO. *Childhood morbidity and treatment patterns*. Columbia (MD): Institute for Reserve Development/Macro International, 1991. (Demographic and Health Surveys Comparative Studies No. 4.)

6. Bang A, Bang RA, Baitule SB, Reddy MH, Dashmukh MD. Effect of home-based neonatal care and management of sepsis on neonatal mortality: field trial in rural India. *Lancet* 1999;354:1955-61.
7. Kenyon S, Boulvain M, Neilson J. Antibiotics for preterm premature rupture of membranes. *Cochrane Library*. Issue 2. Oxford: Update Software, 2002.
8. Salam MA, Bennish ML. Antimicrobial therapy for shigellosis. *Review of Infectious Diseases* 1991;13 Suppl 4:S332-41.
9. Muhuri PK, Anker M, Bryce J. Treatment patterns for childhood diarrhoea: evidence from demographic and health surveys. *Bulletin of the World Health Organization* 1996;74:135-46.
10. Kidane G, Morrow R. Teaching mothers to provide home treatment of malaria in Tigray Ethiopia: a randomized trial. *Lancet* 2000;356:550-5.
11. Schellenberg D, Menendez C, Kahigwa E, Aponte J, Vidal J, Tanner M, et al. Intermittent treatment for malaria and anaemia control at time of routine vaccinations in Tanzanian infants: a randomised, placebo-controlled trial. *Lancet* 2001;357:1471-7.
12. Smith RD, Coast J, Millar MR, Wilton P, Karcher AM. *Interventions against antimicrobial resistance: A review of the literature and exploration of modelling cost-effectiveness*. Geneva: Global Forum for Health Research, 2001.
13. Hui L, Li XS, Zeng XJ, Dai YH, Foy HM. Patterns and determinants of use of antibiotics for acute respiratory tract infection in children in China. *Pediatric Infectious Disease Journal* 1997;16:560-4.
14. Sack RB, Rahman M, Yunus M, Khan EH. Antimicrobial resistance in organisms causing diarrhoeal disease. *Clinical Infectious Diseases* 1997;24 Suppl 1:S102-5.
15. Bartoloni A, Cutts F, Leoni S, Austin CC, Mantella A, Guglielmetti P, et al. Patterns of antimicrobial use and antimicrobial resistance among healthy children in Bolivia. *Tropical Medicine and International Health* 1998;3:116-23.
16. Vila J, Vargas M, Casals C, Urassa H, Mshinda H, Schellenberg D, et al. Antimicrobial resistance of diarrheagenic *Escherichia coli* isolated from children under the age of 5 years from Ifakara, United Republic of Tanzania. *Antimicrobial Agents and Chemotherapy* 1999;43:3022-4.
17. Santoso B, Suryawati S, Prawaitasari JE. Small group intervention vs formal seminar for improving appropriate drug use. *Social Science and Medicine* 1996;42:1163-8.
18. Bexell A, Lwando E, Von Hofsten B, Tembo S, Eriksson B, Diwan VK. Improving drug use through continuing education: a randomised controlled trial in Zambia. *Journal of Clinical Epidemiology* 1996;49:355-7.
19. Gove S. Integrated management of childhood illnesses by outpatient health workers: technical basis and overview. *Bulletin of the World Health Organization* 1997;75 Suppl 1:7-16.
20. Lambrechts T, Bryce J, Orinda V. Integrated management of childhood illnesses: a summary of first experiences. *Bulletin of the World Health Organization* 1999;77:582-94.
21. WHO, Child and Adolescent Health and Development. *Integrated Management of Childhood Illness (IMCI)*. Available from <http://www.who.int/child-adolescent-health>
22. WHO, UNICEF. *Handbook IMCI: Integrated Management of Childhood Illness*. Geneva: World Health Organization; 2000. WHO document WHO/FCH/CAH/00.12.
23. Bryce JB, Victora CG, Habicht JP, Vaughan JP, Black RE. The multi-country evaluation of the Integrated Management of Childhood Illness Strategy: Lessons for the evaluation of public health interventions. *American Journal of Public Health* 2004;94:406-15.
24. Tanzania IMCI multi-country evaluation health facility survey study group. Health care for under-fives in rural Tanzania: effect of Integrated Management of Childhood Illnesses on observed quality of care. *Health Policy and Planning* 2004;19:1-10.
25. Amaral J, Gouws E, Bryce J, Leite AJM, Cunha ALA, Victora CG. Effect of Integrated Management of Childhood Illness (IMCI) on health worker performance in Brazil. *Cadernos de Saude Publica*. In press 2004.
26. StataCorp. *Stata Statistical Software: Release 7.0*. College Station (TX): Stata Corporation; 2001.
27. Bryce J, El Arifeen S, Pariyo G, Lanata CF, Gwatkin D, Habicht JP, et al. Reducing child mortality: can public health deliver? *Lancet* 2003;362:159-64.