Expert Consultation on Community-Based Approaches for Neonatal Sepsis Management

September 26-28, 2007

London, UK

Meeting Report

Organizing Committee

Save the Children/Saving Newborn Lives

United States Agency for International Development

World Health Organization, Department of Child and Adolescent Health and Development

Host

University College of London, Centre for International Health and Development

Collaborating Institutions

Boston University, Center for International Health and Development
Johns Hopkins Bloomberg School of Public Health, Department of International Health

Thanks to Save the Children/Saving Newborn Lives for the cover photo.

Expert Panel

Chair: Maharaj Bhan, Department of Biotechnology, Ministry of Science and Technology, Government of India
Rappateur: Rajiv Bahl, WHO/CAH

- O. Massee Bateman, USAID/India
- Simon Cousens, London School of Hygiene and Tropical Medicine
- Kim Mulholland, London School of Hygiene and Tropical Medicine
- H.P.S. Sachdev, Sitaram Bhartia Institute of Science and Research
- Pablo Sanchez, Univesrity of Texas Southwestern Medical Center
- Jonathon Simon, Boston University
- Barbara Stoll, Emory University

Study Presenters

- Shams El Arifeen, ICDDR,B
- Abdullah Baqui, The Johns Hopkins University
- Anthony Costello, University of London
- Gary Darmstadt, The Johns Hopkins University
- Sudir Khanal, MINI Project
- Vishwajeet Kumar, King George Medical University
- David Marsh, Save the Children
- Vinod Paul, All India Institute of Medical Sciences, on behalf of Abhay Bang, SEARCH
- Judith Standley, UNICEF
- Nancy Terreri, UNICEF
- Anita Zaidi, Aga Khan University

Working Group Chairs and Rappateurs

Working Group #1: Appropriate Antibiotic Regimens and Case Management
Chair: Vinod Paul
Rappateur: Shamim Qazi

Working Group #2: Diagnostic Algorithms
Chair: Gary Darmstadt
Rappateur: Robin Houston

Working Group #3: Optimal Delivery Packages for Different Settings
Chair: O. Massee Bateman
Rappateur: Joy Lawn

Executive Summary

In September 2007, a meeting was convened to **consider program needs and identify critical research to accelerate the availability and use of safe, effective, affordable, simple, and feasible community case management approaches for neonatal sepsis/infection among families** *with no or limited access to facility-based care.* Meeting objectives were to:

I. Review the evidence from recent studies on safety, efficacy/effectiveness, feasibility, acceptability, and use of community-based management approaches to neonatal sepsis, including cross-cutting issues of (i) community identification of cases, (ii) antibiotic regimens, (iii) care-seeking behaviors, (iv) health system challenges, and (v) ethical issues.

II. Identify, review, and rank key issues that if addressed will lead to expanded access to care and facilitate development of focused short-term program approaches and a research agenda to address the issues not answered by the completed or ongoing studies.

III. Outline/design up to three priority research studies that would support the development of programs to increase access to management of newborn sepsis.

For a complete overview of the meeting background and objectives please see the agenda beginning on page 39. The meeting participants reviewed evidence from published studies, data from recently completed, but unpublished studies, and engaged in lively debate and discussion. With the assistance of an expert panel of individuals not associated with the studies, the group reached conclusions about the state of the evidence.

Points of consensus included:

Effectiveness

- In areas with limited or no access to facility-based care, home and community-based interventions involving health extension or community health workers have a substantial impact on neonatal mortality, including mortality in the first week of life. This conclusion is based on review of 6 studies conducted in south Asia- Bangladesh, India, Nepal and Pakistan.

- A positive impact on reducing neonatal mortality has been seen with three types of home and community intervention packages:
    - Community mobilization as a preventive strategy (*Makwanpur/Nepal*)
    - Community mobilization and home visits during pregnancy and neonatal period to promote optimal newborn care prevention practices including care seeking for illness (*Shivgarh/India, Hala/Pakistan, Sylhet/Bangladesh)*
    - Home visits during pregnancy and neonatal period to promote optimal essential newborn care, and management of sepsis by community health workers (*SEARCH/India, ANKUR/India, Sylhet/Bangladesh)*

- The studies presented at the consultation documented that neonatal mortality could be reduced by improving newborn care practices and identification of illnesses at home. Home visits in the first two days of life are particularly important, and there was a suggestion that visits on the first day of life may be crucial.

- Improved access to treatment of probable sepsis, either at home or at first level health facilities close to home, improves newborn care practices in general and increases identification of illnesses at home.

Antibiotic Regimens

- Available studies do not provide a full answer to the question of the best antibiotic treatment regime for neonatal sepsis at community level. Several different approaches were presented including daily administration of penicillin, gentamicin, cotrimoxazole plus gentamicin, ceftriaxone, and an ongoing study involving amoxicillin alone. One study suggests that cotrimoxazole and gentamicin treatment for young infants with possible serious bacterial infection at outpatient level may be inferior to a combination of procaine penicillin and gentamicin or to ceftriaxone alone.

- Current WHO guidelines recommend administration of penicillin and gentamicin for 14 days for suspected sepsis in newborns who present at health facilities. Actual clinical practice is 10 days. Families are often reluctant to travel to health facilities for the 10 to 14 days of administration. Research and program experience is needed on shorter-course injectable antibiotic treatment, as well as switch therapy including initial injectable antibiotic therapy followed by oral antibiotics. Each of these areas of research could contribute to improved compliance, and potentially improved treatment outcomes, in both facility and community care.

Acceptability, Feasibility and Health System Context

.

- Intervention packages in the studies presented included components targeted at birth preparedness, promotion of optimal newborn care practices at home and improved access to treatment of probable neonatal sepsis, either provided by community health workers or through referral to accessible facilities. Home visits by workers during pregnancy and the early neonatal period were a part of the intervention package in five of six studies presented that showed an impact on neonatal mortality.

- Studies reviewed during the meeting have documented that community health workers can be trained to identify and treat possible/probable neonatal sepsis.

- A pilot of an at-scale public health program in Nepal utilizing existing government community and facility workers has shown that a combination of identification of illness and treatment by community volunteers improves utilization of treatment. This program involved initiating treatment with cotrimoxazole by volunteer extension workers followed by administration of injectible gentamcin treatment by first level facility-based health workers. The meeting participants endorsed pursuing similar operations research in other settings to identify locally optimal delivery approaches.

- The impact of treatment strategies may be influenced by the wide variation in health system contexts including the access to and quality of facility based care and the intensity of community mobilization efforts.

Ethics

An unmet objective of the meeting was to review the existing evidence for community-based management approaches to neonatal sepsis through an ethical lens. The prominent issue remains: is it ethical for community-based efforts to benchmark against a different standard of care than facility based programs, in order to improve access and coverage? The meeting participants recognized two different perspectives:

- When there is no or highly limited access to facility care, infants die with no options for treatment. The standard of care should recognize this void, and provide treatment to families at the community and household level.

- It is not ethical to recommend treatment other than the gold standard of care- daily administration of penicillin/gentamicin in facilities. The potential risks of other approaches outweigh the lives saved. This position argues that pending additional evidence, research and implementation efforts should concentrate on facility based care.

Working Groups

There were many areas of agreement among consultation participants including the need to improve sepsis prevention, and to improve identification and treatment at all levels. There was endorsement by meeting participants for the need for additional research on simplified antibiotic regimens as well as guidance for early adopter countries that will move forward with community-based sepsis management approaches. The need for strategies that would engage the public and private sector to increase access were referenced in several presentations and discussions, but there was insufficient time to develop these areas. After the expert panel provided their consensus on the available evidence, three working groups were convened to consider the following issues:

1. Appropriate Antibiotic Regimens and Case Management: Needed research and potential program approaches to be undertaken
2. Diagnostic Algorithms: Recognizing the need for a simple diagnostic algorithm for use in community settings, what are the short term recommendations on the best possible algorithm. Identify and describe needed research.
3. Optimal Delivery Strategies: Issues were discussed that will need to be addressed to develop optimal delivery strategies as part of essential newborn care, and encompassing both preventive and treatment approaches in various health system scenarios.

The working group presentations are attached at the end of this report. Given the breadth and complexity of the issues discussed, there was insufficient time for the working groups to make final recommendations or for the overall participants to fully vet the working group presentations.

Next Steps in Research

Based on the expert review panel and the working group discussions, a few areas of research were determined to be the critical next steps:

1. Research on shorter course and sequential parenteral/enteral (switch) antibiotic therapies with the potential to extend access to treatment and to reduce risk associated with prolonged antibiotic administration in neonates.
2. Research on oral only regimens for geographically difficult situations.
3. Research and program pilots to develop and assess recognition of danger signs/severe illness for use by families.
4. Research in Africa on neonatal sepsis management (effective case management by first level health workers, health systems, etiology).

Program Opportunities

The group was requested at the outset of the meeting to focus their discussion on key research questions and to defer questions of program and policy. However, it was also recognized that program and policy discussions were simultaneously occurring at country level. At the time of this meeting there was an active policy debate in India about the potential for a new cadre of community health workers- ASHA - to treat sepsis, as well as an ongoing evaluation of the approach by the Indian Medical Research Council. This national discussion colored some of the interactions at the consultation. Concurrent policy discussions about moving forward with pilot programs were ongoing in Nepal and Bangladesh. In Somalia there were plans to move forward with a program, and in several other African countries including Zambia, Malawi, and Ethiopia either pilot program or evaluation studies were planned. UNICEF has developed a new training package for essential newborn care which includes community sepsis management where appropriate, based on access and services provided by the local health system and community health workers. Some participants at the meeting urged that facility strengthening and strengthening of approaches such as IMCI would also advance the program agenda.

Table of Contents

Context of Meeting

On behalf of the organizing committee, Neal Brandes opened the session and reviewed the meeting objectives. He requested that discussions build upon the evidence presented at the 2002 Karachi Newborn Sepsis WHO Consultation and recognize that an optimal situation would involve families self-identifying illness and engaging in early care seeking from quality providers. While the long term goal should be to achieve this vision through health system strengthening, the organizing committee hoped meeting participants could focus their recommendations on potential strategies for the near term.

He requested the group to consider how community sepsis management could build upon the foundation of effective community prevention approaches and essential newborn care promoted by WHO, UNICEF, the Gates Foundation funded Save the Children/Saving Newborn Lives (SNL) program, and USAID. He added that such an approach needed to involve the marriage of early identification of danger signs, high quality treatment regimens with most feasible and family acceptable approaches for different health system scenarios reflective of different country's public and private sector health care system capabilities to address access barriers. He also requested that after the participants assessed the evidence for community sepsis management that they recommend up to three potential research priorities as well as provide programmatic guidance to early adopter countries. Such recommendations should marry quality treatment with effective and feasible treatment coverage and access approaches for different health system scenarios. He requested that participants identify behavior approaches for early identification of danger signs and for care seeking, effective referral/treatment strategies; short-course treatment approaches including Uniject gentamicin, as well as considering the merits of different drug combinations and options for treatment delivery.

Saving Newborn Lives/Save the Children

The SNL program is working in 18 developing countries -- Bangladesh, Ethiopia, India, Malawi, Mali, Mozambique, Nepal, Pakistan, Afghanistan, Bolivia, Ghana, Guatemala, Indonesia, Nigeria, South Africa, Tanzania, Uganda, and Viet Nam -- to help prevent newborn illness and death with funding support from the Bill and Melinda Gates Foundation (through 2010).

Representing SNL, Shyam Thapa expressed their expectation that this meeting would review the study results and identify gaps in knowledge with respect to efficient and effective management and treatment of newborn sepsis both at home, in the community and through referral. It is important to keep in mind that many countries are moving forward with their programs in newborn health, including sepsis management. Hence, along side advancement of research, SNL is also working in many countries to simultaneously design and implement programs in newborn health, whether in the context of integrating with the larger health service delivery or scaling up proven interventions.

From the SNL perspective, the anticipated outcomes of the meeting were to help accomplish three things: (i) critical review of existing evidence that will be presented and reviewed, (ii) identify critical gaps in knowledge that SNL might be able to address through its planned research or in collaboration with other organizations, and (iii) last but not least, what guidance, though in a non-binding way, for policy and programming one might derive based on the current knowledge,

however imperfect. Cognizant of the fact that many of the study results have not been published or peer reviewed, SNL believes that the expert review panel has a unique and highly useful role to play.

World Health Organization

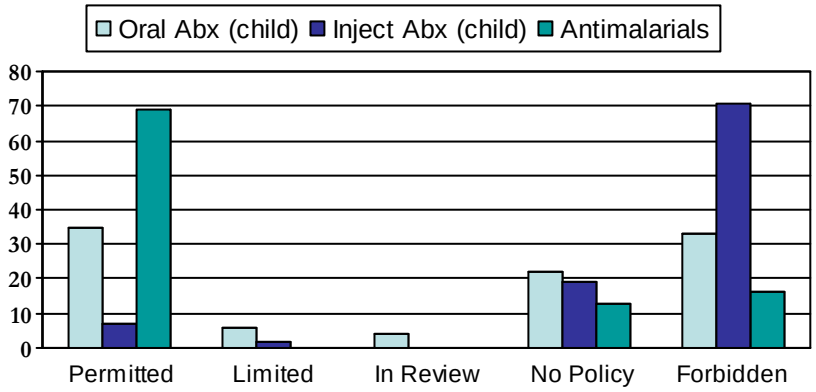
For the World Health Organization, Shamim Qazi discussed the importance of prevention and treatment of neonatal infections, which are responsible for over a quarter of all neonatal deaths globally, in improving neonatal survival. Current access to preventive and treatment interventions is very low, largely because of three reasons. First, neonates are not reached by the health system, particularly during the crucial first week of life. Second, severe neonatal infections are not readily recognized by families and health workers. Finally, even when signs of severe infection are recognized, access to treatment is poor. The WHO Department of Child and Adolescent Health and Development considers community-based strategies to be very important to increase coverage of preventive and curative interventions. The Department therefore co-organized this consultation in collaboration with USAID and SNL to review and interpret available evidence on effectiveness of community based interventions for prevention and treatment of neonatal infections, learn lessons for implementation and make recommendations for research to fill any remaining knowledge gaps.

Context: Global review of serious bacterial and acute respiratory infections among neonates and young infants

Presentation #1: Coverage/Status of ARI Programs and Policy Review
Presenter: David Marsh, Save the Children
Summary: One policy /one approach will not meet the divergent environment and needs of countries across the globe. Current national policies and levels of implementation vary dramatically.

David Marsh presented the results of an initial analysis of a survey of Millennium Development Goal (MDG) countries conducted through UNICEF and WHO country office staff. The focus of the survey was to review policies, practices, and plans regarding community-based treatment strategies or community case management (CCM) of pneumonia, malaria and neonatal sepsis. The findings highlighted significant divergence in policy, practice, and need in many of the countries. Countries accounting for 48% of mortality have some form of community case management. However, a small number of countries accounting for 20% of the burden of mortality had no community-based approaches. Some important key points were: Policies in countries are much more permissive for antimalarials than for antibiotics; Only one-third of all countries included in the survey permit oral antibiotic use at the community level; and antibiotic injections are forbidden in three-quarters of countries surveyed.

Country Policies for CHW to Dispense Three Treatments (n=54)
(preliminary data)



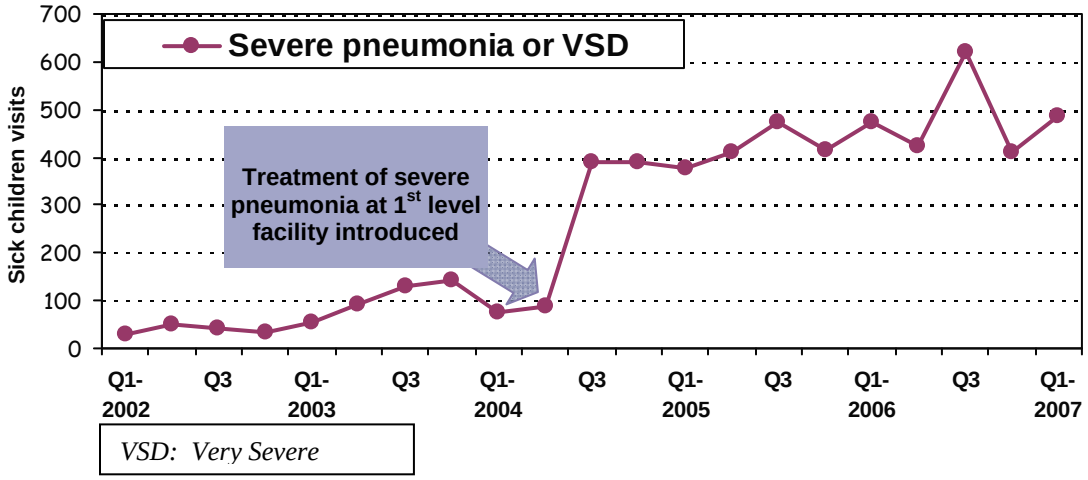
During the subsequent discussion participants identified issues for follow up including review of the tasks/workload of community health workers (CHWs), Expanded Program on Immunization (EPI) workers, and midwives; approaches to monitor quality in programs; documentation of the lessons of policy and practice from other community management strategies, notably pneumonia and malaria, and the differences in strategies in balancing the contribution of antimicrobial resistance with access to lifesaving care; and recognition that a simple diagnostic and treatment approach will be a key component for a successful program. It was also noted that such an approach should be reassuring to professional societies and governments that might raise concerns about safety.

Presentation #2: Matlab Studies: Treatment of Severe Pneumonia/Multi-Country Evaluation
Presenter: Shams El Arifeen, ICDDR, B
Summary: Revised treatment guidelines led to increased use of facilities for severe pneumonia, and improvements in care and care seeking at the facility and community level led to a decrease in case fatality from 1.1% to 0.5%. A study-related cadre of CHWs treated non-severe pneumonia in the community and referred to health facilities for severe pneumonia.

Shams El Arifeen presented an analysis from a study in the ICDDR,B Matlab surveillance area in Northern Bangladesh. The study was conducted as part of the WHO led multi-country evaluation of Integrated Management of Childhood Illness (IMCI). Recognizing that there are situations where successful referral is difficult, one impetus for the study was the low rate of correct management of children with severe illness once they reach health facilities. He suggested that families usually went to the closest point of care and avoided facilities that simply refer a sick child for care. In this study IMCI management guidelines were modified and a new study-related community health worker was introduced to treat non-severe pneumonia in the community and to facilitate referrals to newly strengthened first level facilities to treat severe pneumonia. During the last two years of this study the village health worker cadre created for this intervention began to manage significantly more non-severe pneumonia than the IMCI first level facility. Analysis of the study indicated that there were improvements in care, care seeking, utilization of first level facilities, and a decrease in case fatality from 1.1% to 0.5%.

Revised guidelines lead to increased use of facilities for severe pneumonia

Data source: Routine MIS and GoB MIS



Following the formal presentation Shams El Arifeen acknowledged in response to questions that "village doctors,"-- individuals working in the private sector with a range of knowledge levels—would continue to be the most common source of sick child care for the foreseeable future. It was recommended by some meeting participants that a hybrid approach should be considered, working with existing private sector providers and fielding a new cadre of government and NGO community health workers. While some meeting participants felt that this approach would most likely achieve coverage in a setting like Bangladesh, others cautioned that the success of this approach was premised on effective monitoring and supervision of the community health workers as well as quality assurance approaches such as social franchising for the private sector providers. Some

participants proposed that pilot research involving private sector approaches to manage community newborn sepsis management should be a priority.

Presentation #3: Global Review Serious Bacterial Infections among Neonates and Young Infants in Developing Countries: Evaluation of Etiology and Therapeutic Management Strategies in Community Settings
Presenter: Anita Zaidi, Aga Khan University
Summary: Limited data exists on etiology of infection in newborns and antimicrobial resistance to pathogens, at the community level. The policy question remains unanswered: whom to treat and appropriate antibiotic selection.

Anita Zaidi presented a literature review of the etiology of serious infections in young infants, noting the majority of data were from hospital based studies. Of the 63 studies reviewed, twenty-five had some information on community-acquired infections in young infants, and nine of those clearly focused on community-acquired infections. Organisms identified from the small percentages of newborns that were cultured and tested positive were reported for these studies, therefore lacking any data on newborns or mothers that may have tested negative due to prior antibiotic use. There were neither data on newborns who died before reaching a facility nor specific data on preterm infants.

Acknowledging the lack of data from community settings, Zaidi drew upon data collected mainly in health facilities to conclude that *Klebsiella* sp, *E.coli* and *S. aureus* were major pathogens in the first week of life in developing countries. Early onset sepsis was considered maternally acquired - but the pathogen spectrum was considered "environmentally" acquired. Group B streptococci was common in Africa and uncommon in South Asia, although inter-country variations were present and not clearly understood. Although data are limited, there appears to be a preponderance of gram negative infection and *S.aureus* in home-delivered babies.

Anita Zaidi identified few published data on infections in the seven to 59 day period of newborns and young infants. Most of the data she reported were from the Young Infant Studies conducted by WHO and a rural facility study in Kenya. The spectrum of pathogens represent the transition between the neonatal (*S.aureus, E.coli*) and post-neonatal period (*S. pyogenes, S. pneumoniae).* Gram positive organisms of which *S. pneumoniae* is the single most important pathogen, are most common in the post-natal period but are also isolated in the 7-59 day period. There was some evidence that *Salmonella* and *H. influenzae* are emerging threats.

She also conducted a review of antimicrobial resistance of pathogens causing serious infections in newborns and young infants in community settings in developing countries. Hospital-based data showed significant rates of resistance to ampicillin and gentamicin – 71% *Klebsiella* sp. and 50% *E.coli* resistant to gentamicin. There were only seven published reports of community-acquired infections: two focused on early onset sepsis or meningitis, five others used some criteria to screen community acquired infections. These very limited data make it difficult to draw conclusions. Compared to hospital settings, the reports suggested resistance rates were not as alarming in the community: gentamicin resistance may be lower, absence of methicillin resistant *S. aureus*, and *E.coli* resistance to third generation cephalosporins may be lower. There appeared to be some data to suggest high levels of resistance to cotrimoxazole for all isolates.

During the discussion participants commented on the paucity of data and struggled how to interpret the findings reported. Some participants noted confounding factors and selection bias in the data presented and the need to carefully review the data to determine if trends could be discerned. Others felt that routine monitoring of resistance, rational antibiotic use, and devising appropriate treatment guidelines were overall public health goals to preserve the health of both adults and children. As the discussion concluded, one participant noted that there was need for a policy to normalize practice, recognizing the potential need to over treat newborns as a prerequisite to reaching babies in need. An expert added that the presentation raised, but could not address, the policy question about whom to treat and appropriate antibiotic selection.

Etiology, Identification, and Diagnosis of Infection in the Community Settings

Presentation #4: Home-Based Management of Neonatal Sepsis
Presenter: Vinod Paul, on behalf of Abhay Bang, SEARCH
Summary: This work demonstrated the benefits of high case detection rates in the community by way of home visiting by community health workers. It developed a diagnosis method is simple, clinical, useable by a community health worker, valid, and provides enough time for effective treatment. This work argues for the appropriateness of using sepsis death as a 'gold standard' for treatment outcomes. It reports large reduction in the NMR, sepsis specific NMR, and case fatality. The approach was replicable in a multi-site field study.

Vinod Paul presented the SEARCH and ANKUR studies on behalf of Abhay Bang, who was unable to attend. As previously described in several published articles, the SEARCH intervention package, included diagnosis and antibiotic treatment for pneumonia and neonatal sepsis management by Village Health Workers (VHWs). This package was later replicated at much larger scale through the ANKUR study. These interventions demonstrated the benefits of high VHW surveillance rates in the community, attributed to incentives offered including recognition in the community and performance-linked payment. Bang suggested that even with active health education to suspect illness and seek care, families do not seek care on their own, and pro-active home visit contact improves detection rates, as demonstrated by the disproportionate number of diagnoses that occurred on days of home visits. The ideal clinical diagnostic method is one that is simple, usable by a CHW, valid, and provides enough lead time for effective treatment. Others emphasized that a diagnostic method appropriate for family use must also be developed and implemented. In a post-meeting communication Bang maintained that such method has been developed and published in the Journal of Pediatric Infectious Disease, 2005.

Based on Gadchiroli observational data, neonates receiving cotrimoxazole and gentamicin suffered a lower mortality rate from sepsis (6.9%) than neonates receiving only cotrimoxazole (12.6%). During the same period the mortality rate of 26% was reported for neonates receiving no treatment. In the ANKUR project, mortality was at 4.6% with a combination of the algorithm-based approach and treatment by community care workers. High risk groups for sepsis management included infants who became symptomatic in the first four days of life (clinical diagnosis of early-onset sepsis CF 16.8%), birth weight under 1750 grams (CF 22.9%), and gestational age under 34 weeks (CF 35.3%).

The sepsis specific NMR in the internvetion areas showed large reduction in both studies: by 90% in Gadchiroli and by 79% in the ANKUR project.

During group discussion some participants expressed concerns about the study methodology and potential for further replication and scale-up of these models. Issues discussed included a potential reporting bias as the studies only looked at death while the neonate was on therapy and did not provide data on death for those who do not get treatment. (In a subsequent communication Bang maintained that his article in the Journal of Perinatalogy did report this information. The period in which the treated and untreated cases occurred was the same, i.e. 1995 to 2003. Similarly, the reported reduction in the sepsis specific NMR was population based and hence included all neonatal deaths in the community irrespective of treatment.) Also voiced was a concern that use of the IMCI algorithm in the community led to over-diagnosis. Some participants argued that the Gadchiroli untreated baseline group, which suffered a mortality rate of 26%, may not be comparable to the groups receiving cotrimoxazole or cotrimoxazole plus gentamicin. They maintained that this was because the detection criteria for the baseline group was not the same as for the other groups; the baseline group had refused treatment and so were likely to be more ill than the other groups who had been found through active illness-seeking. Infact, the three groups were adjusted for the major risk factors and hance were comparable. Moreover, the diagnosis criteria used to diagnose the untreated and treated groups were similar. However, it was argued that the case fatality of the three groups – untreated, receiving cotrimoxazole and cotrimoxazole plus gentamicin – had been adjusted for risk factors. Finally, issues that were discussed in this presentation and in others included the appropriateness of using sepsis death as a 'gold standard'. This represented a divergence of opinion with some maintaining that due to ethical concerns and practical difficulties, the ideal gold standard (bacterial culture) is not available in community-based studies. The gold standard of 'death due to sepsis' was used by Bang because it is more definitive and specific than a pediatrician's judgment (unvalidated) that the neonate is sick or conducing the study on hospital based population. The SEARCH and ANKUR teams noted that in Gadchiroli 7% of neonates were selected for treatment and one out of four to six treated were true positive. This compares favorably to statistics from Boston nurseries that indicate 4-10% of neonates are treated, but only one out of 15 to 25 of the treated were true positive.

Presentation #5: Studies on Maternal and Infant Survival and Neonatal Sepsis in Nepal
Presenter: Anthony Costello, University College of London
Summary: The Makwanpur study utilized women's groups to impact birth outcomes and resulted in reductions in maternal and newborn mortality larger than expected. The Janakpur study found no significant impact of antenatal multi-micronutrient supplementation on birth outcomes. A new study, Dhanusha, will look at the impact of training community health volunteers on the recognition and management of neonatal sepsis with oral amoxicillin.

Anthony Costello presented data from three studies. He first reviewed the findings from the Makwanpur study, a participatory intervention study looking at the effect of women's groups on birth outcomes (demand side research) with non-health worker facilitators. He also referenced the Janakpur study which was a double-blind, randomized control study looking at the effect of antenatal micronutrient supplementation on birth weight and gestational duration. He also shared the impetus and design of Dhanusha, an ongoing cluster randomized controlled trial with two new nested studies examining the impact of sepsis management by community volunteers on newborn

survival and the impact of community women's groups on newborn survival and maternal and infant nutrition. By conducting these studies simultaneously, the study utilized a four-arm comparison to address interaction between the above two interventions.

Dhanusha was developed in the context of the Nepal health system, i.e. that Female Community Health Volunteers (FCHVs) have a long history of treating infection in older infants with oral antibiotics at community level, matched with referral failure for newborn care in areas with access barriers. The decision to use oral amoxicillin in the study came through an expert meeting of key stakeholders recognizing the health system context and access constraints in Nepal. Within the context of an existing longstanding community mobilization and care package, FCHVs treat for possible infection, with infants less than two months of age with suspected severe bacterial infection getting initial treatment and then being referred to health workers. Referral to paid health-center based health workers will be followed by treatment with gentamicin at a dose of five mg/kg intramuscularly, daily for seven days. Cases of local infection which are treated without referral and suspected severe infection will be followed up in the community four times over the next month. Data analysis will look at the difference between the existing system (a volunteer that has basic knowledge) and giving a volunteer an additional package of care (i.e. training for diagnosis and treatment). Additionally, the study looks at the impact of women's groups with and without the above intervention.

Some participants encouraged the Dhanusha team to consider how to analyze the interactions between the intervention groups and the potential benefit of adding a fifth arm whereby volunteers are encouraged to make home visits, not provide initial treatment and only refer after diagnosis. Anthony Costello was also requested to undertake strong process documentation to record the activities of the FCHVs. Some participants suggested that the addition of a control group would also facilitate addressing the issue of optimal time for the first home visit to make a difference in health outcomes. There was interest expressed by some in understanding the value added of each component of the intervention package.

Presentation #6: Community-Based Newborn Care: Evidence from Hala, Pakistan
Presenter: Anita Zaidi, Aga Khan University, on behalf of Zulfiqar Bhutta
Summary: Through improved training of Lady Health Workers and community support strategies, community mobilization and community care improved maternal and newborn care and care-seeking.

Anita Zaidi presented an Aga Khan University study in Hala district, rural Sindh province on behalf of Zulfiqar Bhutta, who was unable to attend the consultation. This study is testing a community-based prevention and referral approach. Results from the pilot phase demonstrated that improving the training of Lady Health Workers (LHWs), in coordination with the creation of community support strategies i.e. new formed women's support groups, can significantly reduce neonatal mortality in rural Pakistan. The new women's groups meet every three to four months. This project is in three phases: baseline, introduction of care package in intervention communities, and scale up of the intervention to all clusters through mid-2008.

Each LHW has a catchment area of 100 – 150 households to which they provide basic maternal and child health and reproductive care. They received a stipend of $30/month, six months of basic training and refresher trainings.

Health systems strengthening efforts occurred in both control and intervention clusters. These efforts included training of care providers in the public sector (LHWs/Doctors/Paramedics) in resuscitation and essential newborn care, improving the referral pathway and linkage to facilities, and improving drug availability and management information systems (MIS). Whereas newborn pneumonia/fast breathing were treated in the community, newborns with potential sepsis were referred to facilities. LHW were sometimes present at time of birth and some participants offered that despite the difficulties, not training the LHWs might be a missed intervention opportunity to save lives.

Intervention area LHW Training	**Control LHWs**
Core curriculum	**Core curriculum**
Promotion of antenatal care	**Promotion of antenatal care**
Iron folate use in pregnancy	**Iron folate use in pregnancy**
Immediate newborn care	**Immediate newborn care**
Cord care (cleaning and avoidance of traditional material application)	**Cord care (cleaning and avoidance of traditional material application)**
Promotion of exclusive breastfeeding	**Promotion of exclusive breastfeeding**
Additional curricular content	
Promotion of adequate maternal nutrition and rest	
Early breastfeeding (within the first hour) and avoidance of pre lacteal feeds)	
Home care of the low birth weight infants	
Recognition of sick newborns and danger signs	
Treatment of neonatal pneumonia with oral TMP-SX	

Data were presented from the pilot phase suggesting that community mobilization and community care through the LHW program improved maternal and newborn care and care-seeking. In addition to a baseline survey, an independent team conducted two cross sectional surveys of all households to collect data on births, deaths, and care-seeking behaviors during the previous 12 months.

Pilot Phase Impact of Intervention

(intervention versus control clusters)

Indicator	**RR (95% CI)**	**% change**
Stillbirth rate	0.74 (0.64-0.86)	26%
Early neonatal mortality rate	0.82 (0.71-0.95)	18%
Late neonatal mortality rate	0.72 (0.53-0.98)	28%
Perinatal mortality rate	0.78 (0.70-0.87)	22%
Neonatal mortality rate	0.80 (0.70-0.91)	20%

The principle investigator was not present, so discussion did not reach closure on the following issue: the context, coverage, timing, and dose of oral antibiotics provided (trimethoprim/sulfamethoxazole (cotrimoxazole)) by LHWs.

Care Seeking Behaviors

Presentation #7: Experiences from Shivgarh, India
Presenter: Vishwajeet Kumar, King George Medical University
Summary: In the study community, perceived cause of neonatal death was the single most important determinant of preventive behaviors and care/care seeking for newborns. Community mobilization to prevent newborn mortality reduced NMR by 50%, and increased care seeking from health facilities by 12%.

Vishwajeet Kumar presented the results from the Shivgarh study, a community-based cluster randomized controlled trial, in Uttar Pradesh, India. The study investigated impact of community health workers through home visits and community mobilization to prevent newborn mortality. Workers offered neither referral nor treatment services and only educated families about essential newborn care including prevention of hypothermia. Community perceptions of the cause of neonatal death - predominantly evils spirits- was found to be very different than a clinical model. Perceived cause of neonatal deaths was the single most important determinant of preventive behaviors and care/care seeking for newborns. The majority of newborns in the study catchment area were given some form of medication and care was predominantly sought from the unqualified medical practitioners (40-50%), government doctors (10-15%) and self (20-25%).

The intervention involved seven days of training and a cadre of predominantly male community health workers, who identified pregnant women and educated them in essential newborn care. Two antenatal and two postnatal visits were conducted, with the first postnatal visit on day one and the second on day three or four. There was one community health worker per 3500 and one supervisor for every seven workers. The trial was stopped by the study Data Study Monitoring Board when early analysis of the intervention arm suggested a 50% reduction in NMR. Analysis of the study results also indicated a 12% increase in care seeking from health facilities.

Much of the post presentation discussion focused on why mainly males were recruited as intervention workers and the impact of their home visits during the postnatal period as this is neither usual practice nor culturally acceptable in regular programs. Several participants felt further analysis of this issue would be helpful. There was also discussion about the unusually high baseline NMR – 81 (in fact the baseline NMR in the intervention area was 63, and it was 81 in the control area) - in this community and the impact of the intervention to reduce mortality to average levels in India. Further analysis of data is anticipated on the main effects of this trial. The reduction in the NMR from the baseline was of the order of one third (from 63 to 42) and not by 50%.

Delivery/Treatment Strategies in Health System Scenarios

Presentation #8: MINI Project: Increased Access Through Innovation: Community Based Management of Neonatal Infections in Nepal
Presenter: Sudhir Khanal, MINI Project
Summary: In this pilot effort, in the context of an existing Nepalese government public health program, Female Community Health Volunteers visiting newborns in the

home were successful in the identification, treatment, and referral for infection. Strategies need to be developed to reach infants earlier.

Sudhir Khanal presented the Morang Innovative Neonatal Intervention (MINI), a community-based pilot program (2005-2007) in a population of 300,000 to improve rates of early identification and correct management of infections in young children under two months in Morang district, Nepal. Prior to this program, no community-based services for newborns existed in the district. A baseline survey suggested care seeking from health facilities for this age group ranged from 2-5%. Similar to the findings of other studies discussed earlier during the meeting, 70% of newborn deaths in the study area occurred during the first week of life. MINI was undertaken in partnership with the existing Ministry of Health and Population (MoHP) system infrastructure in Morang district including the MoHP staff based in health facilities and the female community health volunteers (FCHVs) based in the community. The FCHV cadre have, since the 1980s, been providing selected community-based health services including antenatal care (ANC) visits, vitamin A distribution and management of acute respiratory infection (ARI) and non-severe pneumonia.

There was no active case detection and FCHVs depended upon families to contact them when they suspected illness. As part of the MINI study FCHVs were encouraged to visit newborns within 3 days after birth, but as unpaid volunteers they were not compelled to do so. Twenty-two percent of the deaths occurred before the FCHVs visited the home. The study demonstrated that low skilled FCHVs can diagnosis danger signs in newborns and treat with an oral antibiotic. FCHVs followed an algorithm for classification of sick neonates, provided cotrimoxazole and instructed families on its use, and facilitated referral to facility-based Village Health Workers (VHWs) and Maternal and Child Health Workers (MCHWs). These VHWs and MCHWs used a simple scale and administered 15 mg injectable gentamicin to normal weight and 10 mg to low birth weight newborns once daily for seven days. In cases where the family refused referral, the FCHV offered the family treatment of the newborn with cotrimoxazole.

This presentation led to some discussion as to the optimal timing of the first postpartum neonatal visit to prevent or identify and treat severe illness. The JHU team indicated they were undertaking this analysis using the Projahnmo data, but were not prepared to present it at this meeting.

Work Load Added to Community Health Workers

Worker to Population ratio

FCHVs (1:1283; Min 238, Max 7114)
VHW/MCHW (1:6414; Min 2673, Max 28584)

FCHV Case Load

Birth	= 2.52	(~5 in 2 months)
Local Bacterial Infections (LBI)	= 0.55	(~1 in 2 months)
Possible Sever bacterial Infections (PSBI)	= 0.23	(~1 in 4 months)
Low Weight	= 0.25	(~1 in 4 months)

VHW/MCHW case load

Gentamicin injection = 1.88 (~2 each per month)

Increased responsibility towards society, sometimes working on Saturdays
Recording and Reporting

There was also some concern expressed as to the decision to exclude 22% of deaths—i.e. mortality that occurred before the visit of a FCHV- from the data analysis presented. During the discussion it was noted that the Morang NMR was low compared to Nepal's average, and reflective of the better health status of Morang than other Nepali districts.

However, Khanal noted that this was a deliberate program decision to test this approach in a politically stable and accessible community prior to expanding to areas with weaker monitoring systems. One participant raised a concern about dose-related gentamicin toxicity and the presenter reported no adverse events related to dosage. Khanal also responded to a concern about potential misuse of the antibiotics and noted there was none. In response to a question why FCHVs were successful in treatment and referrals to health facilities, he noted that by their presence and credibility in the community the FCHVs were effective representatives of the health system. At the conclusion of the presentation it appeared that many meeting participants were appreciative of the potential of the MINI approach to be employed in health systems such as Nepal with special reference to areas of low access to facility-based care.

Presentation #9: Projahnmo Projects, Mirzapur and Sylhet/Bangladesh: Introduction
Presenter: Shams El Arifeen, ICDDR, B
Summary: A package of obstetric and neonatal care interventions by community health workers showed an increase in the use of antenatal care services, use of clean cord cutting instruments, immediate breastfeeding, and delayed bathing (>3 days). Change in care seeking behaviors included an increased use of qualified providers, facilities and CHWs, as well as use of referral facilities for care of the sick neonate. Sylhet data indicated a 34% reduction in neonatal mortality in the home-care arm of the study.

Shams El Arifeen began the presentation on the Projahnmo Project in Bangladesh by reviewing the objectives of the two cluster randomized trials in Sylhet and Mirzapur. Objectives included: evaluate the impact of a package of obstetric and neonatal care interventions with varying delivery strategies; evaluate the impact of antibiotic use in the community on colonization of neonates with antibiotic-resistant bacteria (Sylhet only); and identify the principal agents of serious bacterial infections in the community (Mirzapur only). Facilities were strengthened by training of staff on essential newborn care, supply of logistics for management of sick newborn and mothers, joint supervision by the government of Bangladesh and project staff and regular coordination at sub-district and district levels.

Initial formative research in these sites documented a lack of family knowledge about planning or preparedness for birth, clean delivery practices, and no individual designated for essential care of the newborn immediately after delivery; no recognition of danger signs, delayed cord cutting, drying and wrapping and improper cord care.

These interventions showed an increase in the following practices: use of antenatal care services, use of clean cord cutting instruments, immediate breastfeeding, and delayed bathing (>3 days). Change in care seeking behaviors included an increased use of qualified providers, facilities and CHWs, as well as use of referral facilities for care of the sick neonate. There was no change in the use of village doctors, homeopaths and other unqualified providers. Although the home-care arm of the Sylhet trial showed significant reductions in neonatal mortality, the community-care arm (facility-based care) did not.

El-Arifeen reiterated that care seeking is determined by convenience, cost and confidence and trust in the available services. In considering scaling up of this intervention, the project team recommended the following principles be attainable: good quality care as close as possible to communities, one point of care (minimize referral needs), ensure referral facilities are well

functioning and elicit confidence, and utilize context-specific mixed service delivery strategy. Community-based workers are needed for birth preparedness and newborn care. Community-based sepsis management in areas of weak health facilities and high mortality, but with strong links with the health system, may only be needed for a limited time period until health facility-based care is available, accessible and reliable.

Projahnmo Intervention Activities			
Activities	**Sylhet**		**Mirzapur**
	Home Care (TX and education by CHWs)	**Community Care (facility outreach education)**	
CHWs: Surveillance to identify pregnant women	√		√
CHWs: 2 Antenatal home visits for birth/newborn care preparedness	√		√
CHWs: 3/4 Postnatal home visits days 1,2,7, and 9 (for Mirzapur)	√		√
CHWs: Home screening/management of sick child	√		
CHWs: Home screening/referral of sick child			√
Community mobilizers: Meetings for men/women	√	√	
Orientation for TBAs on newborn care	√	√	√
Strengthened health facilities for routine maternal/neonatal care and management of maternal/newborn complications	√	√	√
Usual care through government health facilities and outreach services, private providers	√	√	√

In the subsequent group discussion several participants questioned whether the study team had sufficiently invested in the community care arm. The investigators concurred that despite significant investment, health system strengthening would have required additional time and investment beyond the three years of the study to potentially achieve a mortality impact.

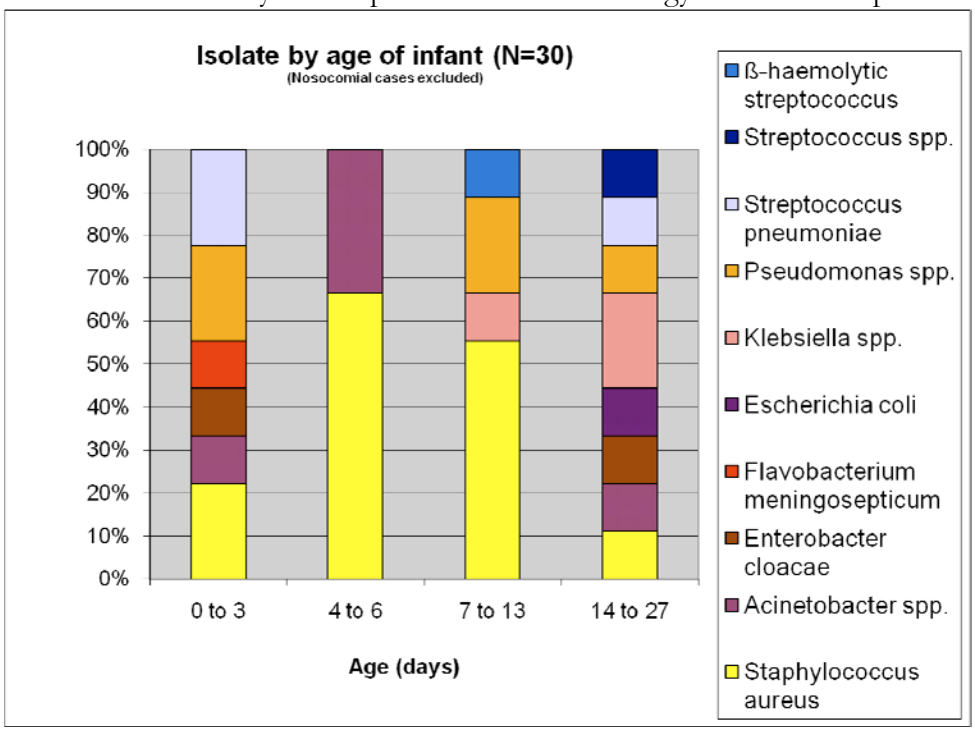
During the discussion El-Arifeen also acknowledged high attrition of study community health workers due to more lucrative and permanent employment opportunities being offered to these workers; an important consideration for scale up decisions. He added that the impact of CHWs may be higher in stable communities. CHWs were accepted over a period of time. Families will only interact with a CHW if they see value in doing so. Separating the natural improvement of CHWs due to increased trust over time versus measuring the effect of better project management developed is challenging. Future research will need to consider how to measure the effect of these different components, or accept that supervisory meetings and the ability to intervene and improve is also part of intervention.

Presentation #10: Community Acquired Newborn Infections: Lessons from Projahnmo-2, Mirzapur, Bangladesh

Presenter: Gary Darmstadt, The Johns Hopkins University

Summary: CHWs were able to use a clinical algorithm to identify sick newborns needing urgent referral-level care as compared to physician assessment. A simplified algorithm was developed for use during routine household surveillance to identify severely ill neonates.

Gary Darmstadt continued the Projahnmo presentation with a discussion on the community acquired newborn infection study at the Mirzapur site. As a component of the studies described by Shams El-Arifeen, the observational study in Mirzpur examined the etiology of neonatal sepsis and the effectiveness of a clinical algorithm for identification of severe neonatal illness during routine household surveillance by community health workers (CHWs). Specifically, the goal of the study was to determine if a simplified algorithm for use by a CHW could predict the need for urgent referral-level evaluation or treatment for severe neonatal illness.



A study of the etiology of pathogens in newborns in Mirzapur found that both gram positive and a mixture of gram negative organisms were important community-acquired agents of neonatal sepsis. Treatment regimens need to cover *S. aureus*.

CHWs were trained to promote preventive care and to assess newborns in the home (88% home-born) on days 1, 3, 7 and 9 of life, and to classify and manage illness using an algorithm adapted from Bangladesh neonatal IMCI. CHWs referred sick newborns to Kumudini Hospital, with the costs for care borne by the project. If referral failed and patients met criteria for very severe disease or had continuing illness with two signs of possible very severe disease, CHWs were authorized to provide oral antibiotics (cotrimoxazole).

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and Kappa statistics were calculated using physician assessment of severe illness needing urgent referral-level evaluation as the gold standard. Validity of the CHWs' assessment was compared across various algorithms for identification of severe neonatal illness, including the initial 8-sign algorithm, the revised 11-sign revised algorithm, and additional algorithms.

This study demonstrated that household surveillance for severe neonatal illness with facilitated referral to hospital was accepted by most families in Mirzapur. CHWs were able to use a clinical algorithm to identify sick newborns needing urgent referral-level care as compared to physician assessment. A simplified algorithm was developed for use during routine household surveillance to

identify severely ill neonates in a population where previously most neonates who died in the first 24 hours of life were missed.

While there was appreciation for the immediate program utility of the simplified diagnostic algorithm by some and acknowledgment by study authors that some refinement of the algorithm would be necessary (e.g. jaundice, and respiratory rate and temperature cut-offs), other meeting participants suggest the need for a larger scale replication study. The group agreed this issue could be revisited after the studies were published.

Presentation #11: Community-Based Management of Newborn Infections: Lessons from Projahnmo - Sylhet District, Bangladesh
Presenter: Abdullah Baqui, The Johns Hopkins University
Summary: Treatment by CHWs was associated with lower fatality, and is as safe and effective as the control arm (no side effects reported).

Abdullah Baqui completed the discussion of the Projahnmo project with a focus on community acquired newborn infections at the Sylhet site. In the Sylhet home care cohort, there were 10,585 live births, the NMR was 47.0 per 1000 live births at baseline and 29.2 per 1000 live births in the last six months of the intervention. Of these live births, 19.5% were preterm, and the NMR in this group was 74.3 per 1000. Although data from a randomized trial, this analysis is based on observation data.

The study trained CHW to assess newborns on days 1, 3 and 7 of life, using an algorithm similar to IMCI, MINI, and SEARCH. CHWs referred newborns with severe infection to government sub-district hospitals or to a qualified health care provider. If referral failed but parents consented to home treatment, CHWs treated these cases at home using injectable antibiotics for ten days.

These observational data demonstrated that CHWs were able to use the clinical algorithm to assess, identify, and manage neonates in community with potentially serious illnesses. CHW treatment is safe and effective, as it was associated with the lowest case fatality rate and no complications were reported. The community generally accepted CHWs giving injectable antibiotics (also confirmed by qualitative study). CHWs worked with and were accepted most by the poorest households.

For very severe disease, the rate of referral compliance was 34% and home treatment acceptance was 43%. The case fatality rate was 4.4% for those treated by CHWs, 14.2% for those treated by qualified medical providers, and 28.5% for those who received no treatment or who were treated by other providers. After controlling for differences in background characteristics and illness signs among treatment groups, newborns treated by CHWs had a hazard ratio of 0.22 (95% confidence interval 0.07 – 0.71) for death during neonatal period and those treated by qualified providers had a hazard ratio of 0.61 (95% confidence interval of 0.37 – 0.99), compared to newborns who received no treatment or were treated by untrained providers. Where health systems are weak, CHWs should be considered at least in the short term. Social status, community engagement and strength of backup systems all have potential to effect the success of CHWs.

Abdullah Baqui recommended that mechanism to identify pregnant women and newborns need to be in place so that the local health worker can assess the newborn soon after birth. Community education and mobilization need to occur to create awareness and demand for services.

Case fatality rate by type of management

Classification	Referral successful d/n (%)	Treated by CHWs d/n (%)	Treated by other* providers or no care d/n (%)
VSD	23/162 (14.2%)	9/204 (4.4%)	32/112 (28.6%)
PVSD-MS	1/32 (3.1%)	0/49 (0.0%)	10/50 (20.0%)
PVSD-SS	0/79 (0.0%)	2/522 (0.4%)	6/219 (2.7%)

*Other includes village doctor, pharmacist, homeopath
*d=# of death, n=# in category

VSD: Very Severe Disease
PVSD-MS: Possible Very Severe Disease – Multiple Symptoms
PVSD-SS: Possible Very Severe Disease – Single Symptom

This study did not collect data on what happened when the family complied with referral beyond being seen by a physician (e.g. detailed encounter data on care provided, compliance with care). The sickest neonates were referred, and therefore may have had the poorer prognosis (see accompanying case fatality rate table). In anticipating a future program, the role of the CHW when a referred neonate returns home (treated or untreated) needs to be defined in the context of the broader health system.

Abdullah Baqui concluded his presentation with several comments on future research needs. Noting that all newborn infections are not same, he reiterated the need to further improve the algorithm and offered that all suspected newborn infections do not need injectable antibiotics – perhaps only neonates that the study classified as very severe disease or possibly very severe disease, which was approximately 7-8% of the study population, a finding that was consistent with SEARCH/ANKUR and MINI data.

Presentation #12: Karachi Young Infant Studies
Presenter: Anita Zaidi, Aga Khan University
Summary: Out-patient therapy with once-daily injectable antibiotics is a potentially effective option in countries with high NMR where hospitalization of sick young infants is not feasible.

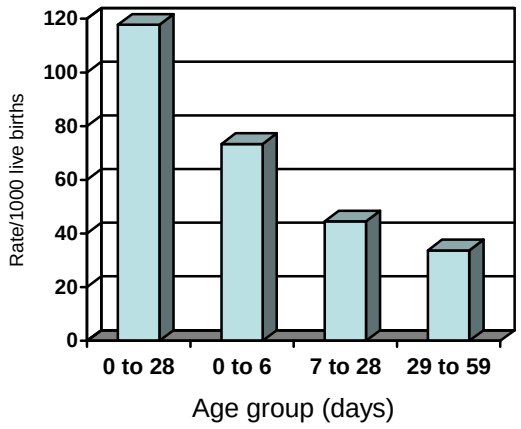
Anita Zaidi provided data from the Karachi study in a peri-urban slum, where special satellite clinics were set up as part of the multi-site Young Infant Studies (YIS), 2003 – 2007. This was the only site of YIS to collect from a non-hospital setting and the primary objective of this randomized controlled trial was to evaluate success, cured or improved and failure rates, of following regimens for community-based management of suspected serious bacterial infections (SSBI) among patients whose families refused hospital referral:

- intramuscular procaine penicillin plus gentamicin (OD)
- intramuscular ceftriaxone (once daily)
- oral cotrimoxazole and intramuscular gentamicin (OD)

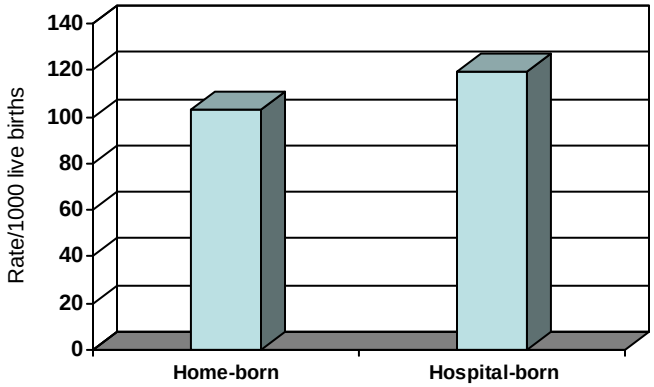
The study involved both hospital and clinic outpatient management of sepsis. Additional sub-studies at this site included disease burden, etiology and antimicrobial resistance and the impact of

case-management approach. This site has a home based delivery rate of 75%. Seventy percent of families refused referral to a tertiary public sector nursery located within one hour of the site despite provision by the study of transport and assistance in registration at the hospital, a dedicated day time physician and medications, and a 93% acceptance of referral to PHC center by CHW. A qualitative assessment of the determinants of care-seeking at this site outlined the following as the common determinants: father's availability and agreement; number of children, caretaker availability; past experience with hospital care and perceptions of quality; distance from place of residence; maternal engagement and health status; and clinical condition and perceived vulnerability of baby.

Clinical Sepsis Rates (9916 live births)



Clinical sepsis rates
9916 live births
(home-born 7521, hospital-born 2395)



[1]Used standardized case definition

[2] Includes 7% diagnosed by CHWs (if excluded, sepsis rate is **106.8**)

Excludes CHW diagnosed sepsis

Drug Regimens

Group 'A'	Procaine penicillin 50,000 units/kg/day OD IM & gentamicin 5 mg/kg day OD IM
Group 'B'	Ceftriaxone 50 mg/kg/day OD IM
Group 'C'	Cotrimoxazole 10 mg/kg divided bid & gentamicin 5 mg/kg day OD IM

OD = once daily

All regimens given for 7 days

Outcomes – Intention to treat analysis: 1 week

Outcome	A N=145	B N=145	C N=143*	Total N=433
Cured or improved	132 (91%)	123 (84.8%)	117 (81.8%)	373 (86%)
Treatment failure or death**	13 (9%)	22 (15.2%)	26 (18.2%)	61 (14%)

*1 loss to follow-up excluded

**2 deaths in A, 3 in B, and 7 in C

***A = penicillin and gentamicin, B = ceftriaxone, C = cotrimoxazole and gentamicin

Anita Zaidi concluded from this data that out-patient therapy with once-daily injectable antibiotics was a potentially effective option in countries with high NMR where hospitalization of sick young infants is not feasible. She noted that penicillin and gentamicin were highly effective and safe for management of suspected severe bacterial infection (SSBI) in first level facilities, however there was

a higher withdrawal rate associated with use of procaine penicillin and gentamicin than other regimens. She argued that this regimen was superior to oral cotrimoxazole plus intramuscular gentamicin but also acknowledged that oral antibiotic therapy may have a potential role in settings where injectable antibiotics are not feasible. Intramuscular (IM) ceftriaxone was a satisfactory alternative to a penicillin/gentamicin regimen, but more expensive. Data suggested that infants receiving shorter courses of penicillin and gentamicin also did well. Zaidi stated that there was a high degree of compliance with out-patient injectable therapy for SSBI in young infants at first level facilities. In the study site, newborns with severe umbilical infections were 2.5 times more likely to suffer treatment failure with penicillin and gentamicin than those without severe umbilical infection.

In the subsequent discussion some participants suggested that poor infection control in the hospital and sicker newborns being admitted to hospitals contributed to a multi-factoral interaction that would need to be considered in the final analysis of study results. Some participants questioned the analysis of the culture positive sepsis. Zaidi noted that despite the study paying for treatment participants in the study catchment area sought care from private sector providers including approximately 4% of the enrolled study participants who withdrew to seek care from private providers. Zaidi offered that anecdotal evidence suggested that treatment by quacks may have reduced mortality in the study area.

Presentation #13: UNICEF Training Package
Presenters: Nancy Terreri and Judith Standley
Summary: UNICEF has a new training package for essential newborn care that includes community sepsis management where appropriate based on access to and services provided by the local health system and community health workers. Regional and country activities to address neonatal sepsis are underway in South Asia and East and Southern Africa.

The formal presentations concluded with Nancy Terreri and Judith Standley providing an overview of a new UNICEF training package for essential newborn care that included community sepsis management. They also reviewed current options for community based care, and provided a summary of efforts by UNICEF, selected countries, and NGO efforts to reduce newborn mortality as noted below.

Program targets for maternal and newborn health have been set and include nine components that focus on antenatal and postnatal visits, emergency obstetric and newborn care, and integrated management of newborn and child illness (IMNCI). The training package is based on the premise that, as permitted by country policies, trained community health workers can provide community surveillance for pregnancy, make home visits to prepare the mother and family for delivery, provide immediate care to a newborn if delivered at home, and make a home postnatal visit within 24 hours, and 2-3 times in the first week of life.

The most appropriate and effective treatment of sepsis can occur in the health system or by a CHW, depending on access, skills and supervision of workers, availability of drugs, and the relationship with the community.

The level of community health worker interventions depends on the factors above, and can include simple health education and prevention practices to illness identification and referral, screening for complications, provision of first dose of oral antibiotics to full treatment and follow-up.

UNICEF Regional and Country Activities include:

South Asia

- India
  - Implementing IMNCI in 250 districts; identification of sepsis, first dose and referral
  - Accredited Social Health Activists (ASHAs) to be trained to identify danger signs; some ASHAs to treat depending on location and local policy

- Bangladesh and Nepal
  - UNICEF supports scale up of models developed through local research

East and Southern Africa

- Zambia
  - Testing the feasibility of providing community based newborn care, including management of newborn complications by CHW in two learning districts

- Malawi
  - Implementing a phase-in strategy of providing community based newborn care, including treatment of newborn sepsis by health extension workers in three learning districts

- Eritrea
  - Adding identification and treatment of newborn sepsis by CHW to community based integrated management of childhood illness (C-IMCI)

- Madagascar
  - National newborn policy and community/home based identification and treatment in remote areas

- Somalia
  - Planning small pilot in Somaliland with community treatment before phase-in

- Tanzania
  - C-IMCI to include home-based newborn care; identification of danger signs and Referral

- Uganda
  - Community-based resource persons (CORPS) in internally displaced persons (IDP) camps to expand community pneumonia treatment to include newborn sepsis

Expert Review

The Expert Panel was asked to review the data presented, and provide summary conclusions and recommendations to the meeting participants that reflect:

1. What are the policy-relevant conclusions that can be drawn from the presented studies?
2. What research/management aspects of neonatal sepsis won't be addressed or won't be addressed adequately by the presented research?
3. What are the main research gaps/needs to advance community based management of neonatal sepsis?

The expert panel provided the following summary, as a guide to consider the evidence presented:

Intervention Trials

Study	Design	Intervention (intensity)	NMR impact (95% CI)
SEARCH	One intervention and one control area	Home visits (*****) Treatment of sepsis by village worker (*****) Community mobilization activities (**)	70% (59% to 81%) Ref : J.of Perinat. 2005;25:S92-S107 57% (33% to 73%) Lancet 1999; 354: 1955-61
ANKUR	Before-after	Home visits (*****) Treatment of sepsis by village worker/health facility in urban areas (*****) Community mobilization activities (**)	51% (36% to 65%) Unpublished
Sylhet	Cluster randomized trial	Home visits (***) Treatment of sepsis by village worker (*****) Community mobilization activities + Health facility strengthening (*)	34% (8% to 53%) Ref: Lancet 2008; Jun 7;371(9628):1936-44.
Shivgarh	Cluster randomized trial	Home visits (***) Community mobilization activities (****) Skin to Skin contact ? Referral	50% (xx% to xx%) Unpublished
Hala	Pilot: 4 vs. 4 clusters	Home visits (***) Community mobilization activities (***)	20% (9% to 30%) Unpublished
Makwanpur	Cluster randomized trial	Community mobilization activities (*****)	30% (6% to 47%) Lancet. 2004 Sep 11-17;364(9438):970-9

*Efforts and success for health facility strengthening varied between studies

The points of consensus for the expert panel are listed in the executive summary (pages 4 and 5). Based on the evidence presented, expertise assembled, and approximately four hours for deliberation, the group was unable to endorse global recommendations for community case management for neonatal sepsis/infection among families with no or limited access to facility-based care. The expert panel's summary comments, however, are a guide for next steps in research, program development, and policy consideration.

The following information is taken directly from the expert panel presentation back to the participants. It represents a summary and commentary on the evidence presented.

Effectiveness of community based interventions

- Home and community-based interventions involving health extension or community health workers have a substantial impact on neonatal mortality, including mortality in the first week of life. This conclusion is based on studies conducted in South Asia- Bangladesh, India, Nepal and Pakistan.

- Interventions packages in the studies presented included components targeted at birth preparedness, promotion of optimal newborn care practices at home and improved access to treatment of probable neonatal sepsis, either provided by community health workers or through referral to accessible facilities.

- A positive impact on reducing neonatal mortality has been seen with three types of home and community intervention packages:
  - Community mobilization (*Makwanpur*)
  - Community mobilization and home visits during pregnancy and neonatal period to promote optimal newborn care practices including care seeking for illness (*Shivgarh, Hala, Sylhet*)
  - Home visits during pregnancy and neonatal period to promote optimal newborn care, and management of sepsis by community health workers (*SEARCH, ANKUR, Sylhet*)

- Direct comparisons of the three different types of community interventions would be useful, but not generally available. Only one study (Sylhet) compared two intervention approaches with controls. The first intervention approach consisted of home visit and treatment at home, and the second approach was community mobilization and health facility strengthening with controls. In this three-cell trial, only the former approach was effective. The community mobilization and facility strengthening intervention in the Sylhet trial was limited, when compared to other community mobilization interventions evaluated earlier (e.g. Makwanpur).

Home visits for newborn care

- Home visits during pregnancy and early neonatal period were a part of the intervention package in 5 of 6 studies showing an impact on neonatal mortality.

- All studies utilizing community health workers had contact with the family during pregnancy and in the first week of life. However, the intensity of home visitation varied across studies that showed mortality reduction.

- Home visits made in the first week of life are particularly important, and there is a suggestion that visits during the first two days of life may be crucial.

Access to treatment for neonatal sepsis

- Considering all the presented studies, neonatal mortality can be reduced by improving newborn care practices and identification of illnesses at home.

- Improved access to treatment of probable sepsis, either at home or at first level health facilities close to home, has impact additional to improving newborn care practices and identification of illnesses at home.

- It is important to recognize that the impact of treatment strategies may be influenced by the access to and quality of facility based care and the intensity of community mobilization efforts.

- Studies have shown that community health workers can be trained in identification and treatment of probable neonatal sepsis

- A pilot scale program in Nepal through existing community and facility workers has also shown that a combination of identification of illness and treatment by community volunteers in conjunction with treatment by first level facility-based health workers can improve access to treatment

- The group endorsed similar operation research in other settings to identify locally optimal delivery approaches

.

- Available studies do not allow us to answer the question of the appropriate antibiotic treatment regime for neonatal sepsis at community level.

- One study suggests that cotrimoxazole and gentamicin treatment for young infants with possible serious bacterial infection at outpatient level may be inferior to a combination of procaine penicillin and gentamicin or to ceftriaxone alone.

Etiology

- Data on etiology of community-acquired neonatal sepsis from developing countries is very limited.

- Even the available data from out-born newborns admitted in hospitals does not reflect the true picture in the community due to referral bias.

- It is unclear if there are important differences in etiology between Asian and African settings.

Clinical Algorithms to Identify Serious Infection in the Community

- Two different approaches have been used to validate clinical algorithms for use at community level. The first approach uses death as a gold standard (e.g. SEARCH), presence of two signs of illness. The second approach uses decision by a paediatrician to admit in a hospital as the gold standard (e.g. YIS, Mirzapur).

- We feel that the second approach is more appropriate but more research is needed to refine the current algorithms to make them as simple as possible while retaining high sensitivity and specificity.

- Further analysis of existing data and new data to refine clinical algorithms for diagnosis of neonatal sepsis at community level.

Research priorities identified by the expert panel

- Assess effectiveness of oral antibiotics in treatment of subgroup of infants identified to have possible sepsis.

- Assess the effect of possible additional benefit of presence at birth to a later home visit on the first day of life.

- Intervention studies need to be replicated in Africa, particularly in high HIV settings.

- Development of strategies for improving care for neonatal sepsis in urban poor.

- Etiology studies to help decide effective antibiotic regimes for treatment of suspected neonatal sepsis and monitor resistance.

- Operational research to develop a well-standardized protocol for improving the quality of referral care.

- Operations research to understand coverage and practices of private providers and develop strategies to use them in improving access to care.

- Operational research to facilitate scale up access to care using different delivery strategies (MINI type studies).

- Operation research studies to refine strategies to reach newborns on the first day of life and the most vulnerable populations.

As early parts of the consultation involved rich discussion that ran over, there was limited time for the working groups to vet and make well developed recommendations on research priorities as well as recommendations for early adopter countries. The presentations for each of the three working groups follow.

Working Group 1: Appropriate Antibiotic Regimens and case management

Objectives:

- Develop recommendations for possible antibiotic regimens for treatment of neonatal sepsis and pneumonia for research studies
- Other potential research issues regarding management of neonatal sepsis
- Suggest possible antibiotic regimens for early adopter countries as well as operational research programme/projects for community treatment of neonatal sepsis.

Summary Discussion

The discussion started with etiology of neonatal sepsis and antimicrobial resistance and covered briefly efficacy and effectiveness studies, diagnosis of the neonatal sepsis and pneumonia regional variations with African sites to be included in any future research. Future research questions should address community case management approaches for neonatal sepsis/infection among families with no or limited access to facility-based care. There was also consensus on the benefit of research on shorter course and switch therapies both from the perspective of extending access to treatment and for the potential reduction of risk due to long-term toxicity that may be associated with prolonged antibiotic administration in neonates.

I. Antibiotic regimens for treatment of sepsis and pneumonia in infants under 2 months
The following recommendations were made on the basis of some published and some unpublished data e.g., Zaidi et al PAS 2006; Straus et al lancet 1998; Addo-Yobo et al Lancet 2004; Sazawal and Black Lancet Inf Dis 2003, and WHO expert meeting report on neonatal sepsis 2003. The group based their recommendations on past consultations and professional judgements and did not have time to systematically review all possible antibiotic treatment regimens.

Community based efficacy study neonatal sepsis:

2 arm or 3 arm study in a well controlled community environment (e.g., Karachi type)

- Injectable procaine penicillin plus gentamicin for 7 days

vs.

- Injection gentamicin plus procaine penicillin for 2-3 days followed by continuation of intramuscular once daily gentamicin plus oral amoxicillin twice daily to complete 7 days

vs.

- Injectable procaine penicillin plus gentamicin for 2-3 days followed by oral amoxicillin-clavunic acid to complete 7 days

To randomize when the child is improving.

Community based effectiveness neonatal sepsis study:

2 arm study in a well surveillanced community setting (e.g., Sylhet type)

- Injectable procaine penicillin plus gentamicin for 7 days

vs.

- Injectable procaine penicillin plus gentamicin for 2-3 days followed by oral amoxicillin-clavunic acid to complete 7 days

To randomize when the child is improving.

Efficacy study for treatment of pneumonia in 0-2 months:

2 arm study
In children with only fast breathing and chest indrawing (community acquired pneumonia)

- Injectable procaine penicillin plus gentamicin for 7 days

vs.

- Oral amoxicillin for 7 days

(Newborns with complications starting on Day One to be excluded)

II. Etiology of neonatal sepsis and antimicrobial resistance

- Molecular epidemiology of the organisms causing neonatal sepsis is needed, particularly for home born babies; including early onset
- Determinants of rampant antimicrobial resistance among organisms causing neonatal sepsis need to be identified
- Low bacterial isolation rates makes it challenging (new technologies/donors would help)
- Blood culture, umbilical and skin cultures could be collected from infants and genital cultures from the mother.
- Linkages could be developed with the existing networks that are looking at etiology in other ages
- Sentinel centres at from the first/second level facility and community
- Interventions and strategies that can avert antimicrobial resistance among organisms causing neonatal sepsis need to be investigated

III. Other potential research issues (not rank ordered)

- Role of omphalitis (incidence and treatment outcome of NS); start with further analyses of existing datasets (e.g. the GAVI Pneumo ADIP has identified relevant studies)
- Research on other conditions that can be treated with oral antibiotics e.g, skin , eye, umbilical infections
- Prevention of neonatal sepsis
  - Maternal prophylaxis (vaginal washes)
  - Chlorhexidine use in mother and babies
  - Skin emollient
  - Maternal immunization
  - Probiotics
  - Use of infection control programmes in the hospital to reduce/control NS
- Appropriate indicators for assessing community effectiveness, apart from NMR: i.e. percent coverage of sepsis cases with treatment and case fatality in treated cases and sepsis specific NMR.
- Long term toxicity of gentamicin
- Long acting antibiotic/other candidate antibiotics
- Uniject (could be part of the clinical trials); safety of uniject in fixed and high doses
- Rapid simple non-invasive diagnostics for small facilities and in community settings

- Effectiveness of tele-consultation in managing neonatal sepsis in the community
- Develop antimicrobial agents/molecules suited to the community management of neonatal sepsis (e.g.: a broad spectrum , safe agent that is oral, or long acting injectable
- Pharmacokinetic studies to look at the serum levels of antibiotics
- Prevention of sepsis: including hand-washing by caregivers
- Opportunities for research should be capitalized in other on-going operational research programme projects
- Role of private providers and other delivery strategies
- Long term follow-up of children treated with oral or short course antibiotics for NS

IV. Possible antibiotic regimens for early adopter countries as well as operational research programme/projects for community treatment of neonatal sepsis.

While recognizing the WHO concern that it was premature to provide any recommendations without additional research, participants in this group felt it important to provide some guidance relevant for the next 5-10 years on possible regiments for settings or countries where a decision has been made to move forward with programs or pilot projects. With these suggestions the group reiterated its appreciation of the WHO and noted the following possibilities:

- Parenteral or oral-parenteral combination therapy
  - Procaine penicillin once daily (OD) intramuscular (IM) plus gentamicin OD IM (delivery of gentamicin could be through use of Uniject)
  - Amoxicillin twice daily (BID) orally (PO) plus gentamicin OD IM
  - Cotrimoxazole BID PO plus gentamicin OD IM
- If injection is not available, use available oral antibiotic

In the subsequent discussion it was agreed that research in Africa on neonatal sepsis should be prioritized for future studies as previous research was predominately in Asia. Two participants felt some research on antibiotic toxicity would be appropriate. The group also discussed the merits of 1-4 days of injectable antibiotics prior to switching to oral treatment. In areas with high quality facilities a community mobilization a strategy should be tested to refer newborns to facilities as soon as possible after diagnosis of suspected severe bacterial infection, within first three days. Other participants championed the need for oral only regimens- amoxicillin or amoxicillin-clavulanic acid in geographically difficult situations, while some were uncomfortable recommending a specific antibiotic. Concern was raised that evidence was needed before any recommendations could be offered. It was suggested that at a minimum, efforts using oral antibiotics should be encouraged to document the outcomes. The WHO multi-center trial demonstrating equivalence of injectable ampicillin and oral amoxicillin to treat severe pneumonia was noted and WHO would be interested in research on oral only treatment of pneumonia in neonates. There is a need to establish population-based surveillance to properly test regimens in real world conditions. In addition to existing funders the Wellcome Trust and Gates foundations could be approached for potential support.

Working Group 2: Diagnostic Algorithms

Objectives:

- Develop short term recommendations on best possible algorithm for use at facilities and community levels
- Define further research that may be needed
- Describe general methodology that might be used for the recommended research

Summary Discussion:

It was agreed that some promising evidence presented at the meeting from Mirzapur, Bangladesh combined the published Young Infant Study facility-based analyses should be carefully reviewed and validated in other settings. Some working group members felt it would be appropriate to develop an interim algorithm for use in the near term while concurrently undertaking research to refine and validate the algorithm through in more controlled research sites. It was noted that research was also needed to reduce the need for home visits and train families to recognize danger signs in newborns.

Working Group slides follow:

Comment on terminology: "danger signs"

- Terminology commonly used for signs to be taught to mothers to trigger referral, but terms were originally used for IMCI algorithm, and this confusion needs to be clarified
- Further research is needed to determine the optimal signs and messages for mothers for home identification of sick infants
- These may differ from signs used in algorithm
- This issue was beyond the scope for our group

Algorithm for use in instances of self referral

- Self referral may be to facility or to health worker in formal health sector
- Algorithm from YIS is acceptable for application for these instances
- Algorithm presumes a 'trigger', that is, that cases are referred because CHW or mother feels infant is not well

Recommendations for further monitoring in instances of self referral

- Establish working group to define standardized protocol for monitoring the application of YIS algorithm in instances of self referral:
  - Defining the additional monitoring needed when algorithm is applied in existing or new settings
  - Research will be prospective to determine how well algorithm is working in different settings
  - Further exploration of how algorithm works in settings of HIV/AIDs or high malaria prevalence

Algorithm for use for household screening

- Example: identification of a sick infant during a routine postnatal visit by a CHW
- In these cases, use existing YIS algorithm to identify infants sick enough to warrant referral

- In situations where referral is not possible and management (treatment) decisions are required, programs **must** have a strong monitoring system

↓

2. Community household screening (YIS)

↓

Screen positives for referral

↓ → 3. Trigger for management if referral refused

<u>Research for screening situations</u>

1. Should a trigger be used to stimulate use of algorithm?
    - No trigger suggests true surveillance of all infants
    - For example, 'Is your baby sick' or Is your baby feeding well?
2. Is the YIS algorithm adequately valid when not all babies will receive referral and management decisions need to be made?
    - Explore variations in certain signs (temp, RR) and potential inclusion of additional signs (feeding assmt vs. history)
    - Sites should monitor treatment given and outcomes
3. Can we identify the sub-set of infants who need antibiotic treatment on the basis of a subset of signs within YIS algorithm?
    - Oral, injectable, or no treatment w/ follow-up left to other group

<u>Further analysis on existing datasets</u>

- Jaundice (YIS and Projahnmo)
- Local infections—eye, umbilical, skin pustules (Karachi, Sylhet, Mirzapur, MINI)
- Narrowing the algorithm to identify those needing antibiotic treatment (Karachi, Mirzapur, Sylhet, MINI): based on cultures and deaths

<u>Specific weaknesses within algorithm requiring further research</u>

- Jaundice
- Local infections—eye, umbilical, skin pustules

<u>Prospective research in sites with complete surveillance and where community treatment is taking place</u>

- Is the algorithm sensitive enough or too broad?
- Can we further improve the algorithm by evaluating a larger number of signs and symptoms?
    - Are we applying screen fully, are we following up on all babies?
    - Identification of false positives/negatives
- Can algorithm be subdivided to identify those needing injectable/oral/topical treatment?

In the subsequent discussion there were suggestions that the algorithms would benefit from evaluation in larger populations. In addition to the program evaluation and additional research to refine an algorithm for health worker use, there was consensus on the need for research to assess and potentially develop a simple approach to facilitate the ability of families identification of danger signs including sepsis; recognizing the balance between over referral as well as program challenges in achieving a scaled up effort with community health workers.

Working Group 3: Optimal delivery packages for different settings

Introductory Discussion:

There are now more than 190 separate interventions for the newborn. Which ones should be scaled-up? It is more achievable for programs to implement a package of strategic interventions versus adopting single interventions and layering them at different times. Community care is currently not systematic. To consider scaling-up sepsis interventions, the experts need to think about how they will be integrated. It can not be done in a vacuum.

Implementation Questions

Overall package implementation questions

- Choice of packages/context/adaptation
- Varying delivery strategies for packages
- Health facility quality of care, triage
- Integration and making integration work

Specific package questions

- Postnatal care – number and timing of visits, identifying small babies, and incremental benefit/cost
- Intrapartum care – the gap for home births, how to implement and incremental benefit/cost
- Care of small babies and Kangaroo Mother Care (KMC)

Continuum of care questions

- Demand side generation especially for newborn case management

Cross cutting

- Monitoring and Evaluation especially quality of postnatal care (e.g. delayed bathing)
- Working with private sector including non qualified

Priority Questions

A. Pathway for survival of baby with danger signs (family/community/facility)
B. Package for visits at home and presence at birth for home births

Also important but not covered:

- Identification of small babies
- Quality improvement in facilities
- Private sector role

A. Pathway for survival of baby with danger signs

- Recommendation for Continuum of Care
- Current coverage and quality along the continuum from home to facilities for sepsis prevention and management is low
- Neonatal Mortality can be reduced by:
  - improving newborn care practices
  - identification of illness at home

- improved access to treatment of illness

Rationale:
- Improved access to treatment providers will only lead to health impact if the quality of care delivered is adequate

Objectives:
- To identify effective approaches for the delivery of appropriate treatment of suspected newborn sepsis

Research Question:
- Conditional to appropriate illness recognition, what are the benefits of alternative mechanisms of delivering anti-microbial treatment of suspected sepsis?

Methods:
- Multi-site operational studies
- Comparison groups: CHW, Health Facility workers (level 1), Private providers incl. pharmacists
- Key outcomes: Appropriate and complete anti-microbial treatment (adequate choice of antimicrobial, dose and duration)
- (It was noted that evidence that does not include mortality impact may be insufficient for influencing policy decision)

Time frame/Budgets/Logistics:
- Adequacy – 2 years ~ US$ XX0,000
- Impact – 4-5 years ~ USD XX,000,000

B. Community-based visit package
- Context is the community level package
- Linking to other levels e.g. Antenatal care and skilled attendance
- The cadre may be very context specific e.g. CHW, extension worker, community nurse midwife

Current priorities for reducing neonatal infections (also NMR and potentially MMR):
- Early postnatal visit is crucial and is unlikely without contact during pregnancy
- The intra-partum contact is crucial but more complex to deal with for home births

Home Visit Package

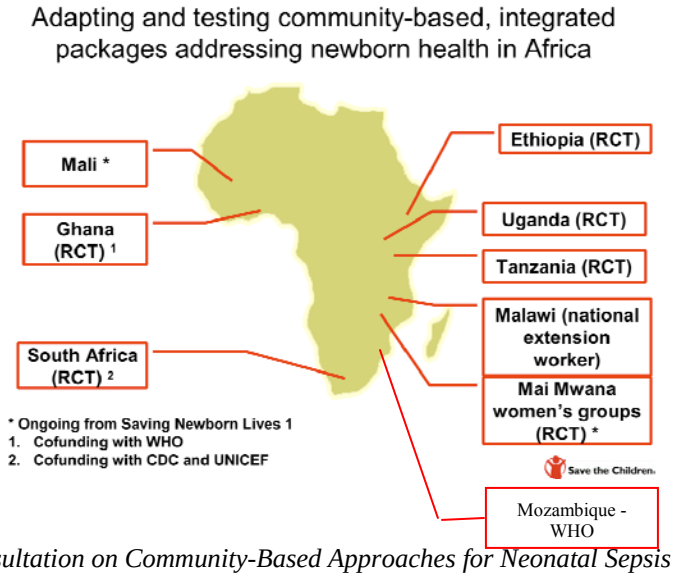
Programme Priority:
Home visit package and aiming for postnatal contact in the 24 hrs of birth followed by at least 2 more contacts in the first week, and extra visits for small babies
with systematic links to facilities

Research Priority:
Testing a home visit package in a variety of contexts and assessing impact and cost and feasibility/sustainability

Time period	Number of home visits	Timing of home visits	Facility/ outreach contact	Content
Pregnancy	Min 2*	As early as possible 3rd trimester	4	Birth planning Danger signs Newborn care preparation
Intra-partum	Multiple issues to discuss		Promote facility births	Clean delivery kit?
Postnatal	Priority of early Number is for Research Extra (2 visit?) for LBW babies (how to identify)	1. < 24-hr after birth or discharge from Facility 2. Day 2 to 4 3. Day 7 (could be at facility) Later e.g. 4 weeks to promote the 6 week mother and baby visit	Context specific but may be possible e.g. at 7 days if not far to walk	Illness recognition Prevention messages (clean, warm, feed) Danger signs recognition and plan
Child and Family Planning			6 weeks	

Home visit package Study design

- Multi country – range of countries to reflect contexts
- Intervention - core aspects of package the same but some context specific add-ons e.g. home management of sepsis, or PMTCT integration
- Outcomes – NMR, and other process and intermediaries
- Cost – comparable costing of packages across contexts, incremental costs, also linked health facility strengthening costs in some contexts



Expert Consultation on
Community-Based Approaches for Neonatal Sepsis Management

September 26-28, 2007
Room B, 2nd floor, Wellcome Trust Building
Institute of Child Health, University College London
30 Guilford Street

Draft Agenda

Wednesday, September 26, 2007

Meeting Objectives: Respond to program needs and identify the critical research to accelerate the availability and use of safe, effective, affordable, simple, and feasible community case management approaches for neonatal sepsis/infection among families with no or limited access to facility-based care as follows:

IV. Review the evidence from recent studies on safety, efficacy/effectiveness, feasibility, acceptability, and use of community-based management approaches to neonatal sepsis, including cross-cutting issues of (i) community identification of cases, (ii) antibiotic regimens, (iii) care-seeking behaviors, (iv) health system challenges, and (v) ethical issues.

V. Identify, review, and rank key issues that if addressed will lead to expanded access to care and facilitate development of focused short-term program approaches and a research agenda of (1-3) studies to address the issues not answered by the completed or ongoing studies.

VI. Outline/design up to three priority research studies that would support the development of programmes to increase access to management of newborn sepsis.

Expected Outcomes:

I. Review of the evidence from the presented data and list policy and programming relevant conclusions for different health system scenarios.

II. Outline research/management aspects of neonatal sepsis that have not been addressed adequately by the presented research. Prioritize three key questions.

III. Develop outlines of the research question, scope and methodology of the three priority research projects.

8:45am **Welcome, Introductions, and Review Agenda**

9:05am Overview Presentation: Neal Brandes

9:15am – 10:30am **Session I: Review of Evidence and Program Needs**
Chairs: SNL, USAID, WHO

Using the 2002 WHO/CAH sepsis consultation as a point of departure, consultation participants will review research finding and consider program developments as the basis for recommendations later in the consultation on priority research that will inform expanded access to treatment of newborn sepsis in areas with no or low access to facility care.

Presenters will be requested present focused talks with the assumption that participants will have read background material in advance. They will be requested to ensure that the following categories of information are addressed with reference to meeting objective I:

- Etiology, identification, and diagnosis of infection in the community settings
- Care seeking behaviors
- Delivery/treatment strategies in health system scenarios
- Other relevant findings that would inform discussion of key objectives of Meeting
- Programmatic and research recommendations

Presentations:

- Brief summary of coverage/status of ARI programs and policy review
  (David Marsh – 10 minutes)

- Summary on Matlab Studies: Treatment of Severe Pneumonia/MCE evaluation
  (Shams El Arifeen – 15 minutes)

- Brief summary of research review
  (Anita Zaidi – 20 minutes)

Group Discussion

10:30am -10:45am **Tea Break**

10:45am – 12:30pm **Continuation of Session I**

- ANKUR/SEARCH/ICMR
  (Vinod Paul – 30 minutes)

Group Discussion

- Mira/Dhanusha/Makwanpur
  (Anthony Costello – 15 minutes)

Group Discussion

- Hala
  (Anita Zaidi – 20 minutes)

Group Discussion

12:30pm - 1:30pm Lunch

1:30pm – 3:30pm Continuation of Session I

- Shivgarh
  (Vishwajeet Kumar – 20 minutes)

Group Discussion

- MINI
  (Sudhir Khanal and Penny Dawson - 25 minutes)

Group Discussion

- Projahnmo: Sylhet and Mirzapur
  (Shams El Arifeen, Gary Darmstadt, Abdullah Baqui - 1 hour)

3:30pm – 3:45pm Tea Break

Group Discussion (Projahnmo)

- Young Infant Study: Bacterial Agents, Antibiotic Comparison, Determinants of Compliance
  (Anita Zaidi, 30 minutes)

Group Discussion

5:00pm – 5:30pm Charge to Expert Panel

Room G, 5th floor, Wellcome Trust Building, Institute of Child Health is available until 9pm for the panel to meet together.

5:30pm End of Session I

Thursday, September 27, 2007

Session II: Identify, review, and rank key issues focused on expanding access to care and facilitate development of a focused short-term program approaches and research agenda

The expert group will present their conclusions and chair of the expert group will lead the plenary discussion of all participants towards the outputs of the meeting. i.e:

1. What are the policy and program-relevant conclusions that can be drawn from the presented studies?

2. What are the critical issues related to community management of neonatal sepsis that have not been addressed adequately by the presented research?

3. What are the main research gaps/needs

From this session three research projects of highest priority would be identified from among a longer list, which can then be discussed by the three working groups

9:30am **Synthesis of the state of the of the evidence and conclusions on issues by external commentators**
Chair: Maharaj Bhan

10:30am – 10:45am Tea Break

10:45am – 12:30pm Programmatic Relevance

- UNICEF activities involving Community and home-based prevention and treatment of newborn sepsis
  (Nancy Terreri and Judith Standley, 10 minutes)

Group Discussion

12:30pm – 1:30pm Lunch

1:30pm Session III: Working groups to define programmatic priorities to strengthen community management of sepsis and outline priority studies

The consultation participants will divide into three working groups to work on the three topics that will be identified based on the decisions made by the group during the morning session. The expected outcome of the group work should be to develop an outline of the research question, scope and methods.

Concept paper and group presentation will need to be transferred to the organizing committee at the beginning of the report out session on Friday.

1:30pm – 2:00pm Development of the working groups

(topics, participants, chairs, rapporteurs)

2:00pm – 3:30pm **Working Groups convene**

- Group 1: Room B
- Group 2: Room E, 2nd floor, Wellcome Trust Building, Institute of Child Health
- Group 3: Philip Ullman Seminar Room 2, Ground Floor, Institute of Child Health
- *Group 4: If Needed*

3:30pm – 3:45pm **Tea Break**

3:45pm – 5:00pm **Working Groups reconvene**

5:00pm – 5:30pm **Working Group Chairs and Rapporteurs meet with Organizing Committee to review progress, any issues of the groups**

Friday, September 28, 2007

8:00am – 10:30am **Continuation of Working Groups**

10:30am – 10:45am **Tea Break**

10:45am – 12:30pm **Continuation of Working Groups**

12:30pm – 1:30pm **Lunch** (working or otherwise)

1:30pm - 3:30pm **Working Group Presentations**
Chair: Simon Cousens

Room B, 2nd floor, Wellcome Trust Building, Institute of Child Health

- Group 1: 30 minutes

Group Discussion (30 minutes)

- Group 2: 30 minutes

Group Discussion (30 minutes)

3:30pm – 3:45pm **Tea Break**

3:45pm – 4:45pm **Working Group Presentations continued**

- Group 3: 30 minutes

Group Discussion (30 minutes)

- Group 4: 30 minutes

Group Discussion

5:45pm Next Steps and Adjourn

Acronyms

ALRI	Acute Lower Respiratory Infection
ARI	Acute Respiratory Infection
ASHA	Accredited Societal Health Activist
C-IMCI	Community – Integrated Management of Childhood Illness
CA	Community Acquired
CFR	Case Fatality Rate
CHW	Community Health Worker
CHX	Chlorhexidine
CORPS	Community-based resource persons
EPI	Expanded Program on Immunization
FCHV	Female Community Health Volunteers
FP	Family Planning
GoB	Government of Bangladesh
GoI	Government of India
ICMR	Indian Council of Medical Research
IDP	Internally Displaced Persons
IM	Intra-muscular (injection)
IMCI	Integrated Management of Childhood Illness
LHW	Lady Health Worker
MCHW	Maternal and Child Health Worker
MINI	Morang Innovative Neonatal Intervention (Nepal)
MIS	Management Information Systems
MMR	Maternal mortality rate
MOHP	Ministry of Health and Population
MRSA	Methcillin resistant *Staphylococcus aureus*
NMR	Neonatal mortality rate
PHC	Public Health Center
SEARCH	Society for Education Action and Research in Community Health
SNL	Saving Newborn Lives
TMP-SX	Trimethoprim/sulfamethoxazole (oral antibiotic)
USAID	United States Agency for International Development
VHW	Village Health Worker (Nepal)
VSD	Very Severe Disease
WHO	World Health Organization
YIS	Young Infant Study

Acknowledgements

Each of the presenters, for their longs hours of preparation and willingness to share their data

Members of the Expert Panel for their unbiased review of the presented data and long hours

Rapporteurs: Vicki Pollit and Pascal Odent – a monumental task, handled with grace and professionalism

Madeleine Green, Sarah Ball and Anthony Costello for coordinating logistics, problem solving and overall hosting of an ever growing meeting

Investigators who were unable to attend but were willing to share their data

All participants for their thoughtful consideration of the complex issues at hand

Participant list

Shams El Arifeen
ICDDR,B: Centre for Health and Population Research
Mail: GPO Box 128, Dhaka 1000
Bangladesh
shams@icddrb.org

Narendra Arora
INCLEN Trust and INCLEN Inc.
5th Floor, 18 Ramnath Building
Yusuf Saraj Community Centre
New Delhi, 110 049, India
nkarora@inclentrust.org

Kishore Azad
Diabetic Association of Bangladesh
122 Kazi Nazrul Islam Avenue
Dhaka-1000, Bangladesh
pcp@dab-bd.org

Rajiv Bahl
Child and Adolescent Health and Development
World Health Organization
20 Avenue Appia
Geneva, Switzerland
bahlr@who.int

Abdullah Baqui
The Johns Hopkins University
School of Public Health
615 N. Wolfe Street Building E8132
Baltimore, MD 21205, USA
abaqui@jhsph.edu

O. Massee Bateman
MCH and Urban Health Division
Office of Population Health and Nutrition
USAID/India
mbateman@usaid.gov

Maharaj Bhan
Department of Biotechnology
Ministry of Science and Technology
Government of India
Block 2, C.G.O. Complex
Lodi Road,
New Delhi, India
Community.research@cih.uib.no

Neal Brandes
Office of Health, Infectious Disease and Nutrition
USAID
1300 Pennsylvania Ave. NW
Washington, DC 20523, USA
nbrandes@usaid.gov

Wally Carlo
University of Alabama at Birmingham
619 South 20th Street
525 New Hillman Building
Birmingham, AL 35233 USA
WCarlo@peds.uab.edu

Edward Chigwedere
Save the Children/Malawi
P.O Box 30374
Lilongwe, Malawi
echigwedere@llmw.savechildren.org

Ellen Cooper
Boston University
Department of Pediatrics
670 Albany, Bio III
Boston, MA 02118, USA
ercooper@bu.edu

Anthony Costello
Centre for International Health and Development
Institute of Child Health
University College London
30 Guilford Street, London WC1N 1EH UK
a.costello@ich.ucl.ac.uk

Simon Cousens
London School of Hygiene and Tropical Medicine
367, Keppel Street
London WC1E 7HT, UK
simon.cousens@lshtm.ac.uk

Gary Darmstadt
The Johns Hopkins University
School of Public Health
615 N. Wolfe Street Building E8132
Baltimore, MD 21205, USA
gdarmsta@jhsph.edu

Penny Dawson
Nepal Family Health Program
P.O. Box 1600
Kathmandu, Nepal
pdawson@nfhp.org.np

Karen Edmond
London School of Hygiene and Tropical Medicine
Keppel Street
London WC1E 7HT, UK
Karen.Edmond@lshtm.ac.uk

Heather Haberle
Office of Health, Infectious Disease and Nutrition
USAID
1300 Pennsylvania Ave. NW
Washington, DC 20523, USA
hhaberle@usaid.gov

Robin Houston
P.O. Box 665
Bozeman, MT 59771-0665
houstonr@theglobal.net

Angela Hwang
Global Health Program
Bill and Melinda Gates Foundation
PO Box 23350
Seattle, WA 98102
Angela.Hwang@gatesfoundation.org

Lily Kak
Office of Health, Infectious Disease and Nutrition
USAID
1300 Pennsylvania Ave. NW
Washington, DC 20523, USA
lkak@usaid.gov

Sudhir Khanal
MINI Project
JSI/Nepal Family Health Project
Kathmandu, Nepal
sudhirkhanal@hotmail.com

Vishwajeet Kumar
Clinical Epidemiology Unit
King George Medical University
Lucknow, India
vkumar@jhsph.edu

Joy Lawn
Saving Newborn Lives/Save the Children USA
11 South Way
Cape Town 7405, South Africa
joylawn@yahoo.co.uk

Dharma S. Manandhar
Dept. of Pediatrics, Kathmandu Medical College
755 Prasuti Marg, Thapathali
GPO Box 921, Kathmandu, Nepal
dsm@healthnet.org.np

David Marsh
Save the Children
54 Wilton Road
Westport, CT 06880, USA
dmarsh@savechildren.org

Jose Martines
Child and Adolescent Health and Development
World Health Organization
20 Avenue Appia
Geneva, Switzerland
martinesj@who.int

Kim Mulholland
London School of Hygiene and Tropical Medicine
Keppel Street
London WC1E 7HT, UK
Kim.mulholland@lshtm.ac.uk

Charles Mwansambo
Pediatrics Department
Kamuzu Central Hospital
P. O. Box 149
Lilongwe, Malawi
cmwansambo@malawi.net

Vinod Paul
Department of Pediatrics and
WHO Collaborating Centre for Training and
Research in Newborn Care
All India Institute of Medical Sciences
New Delhi – 110029, India
vinodkpaul@hotmail.com

Razia Pendse
Department of Making Pregnancy Safer (MPS)
World Health Organization
20 avenue Appia - 1211 Genève 27
pendsera@who.int

Shamim Qazi
Child and Adolescent Health and Development
World Health Organization
20 Avenue Appia
Geneva, Switzerland
Qazis@who.int

H.P.S. Sachdev
Pediatrics and Clinical Epidemiology
Sitaram Bhartia Institute of Science and Research
B-16 Qutab Institutional Area
New Delhi 110016, India
hpssachdev@gmail.com

Salim Sadruddin
Save the Children
House No. 5, Street 29, F-7/1
Islamabad, Pakistan
ssadruddin@savechildren.org.pk

Pablo J. Sanchez
University of Texas Southwestern Medical Center
Dept. of Pediatrics
5323 Harry Hines Blvd. (Room E3.508)
Dallas, TX 75390-9063, USA
Pablo.Sanchez@UTSouthwestern.edu

Mohammad Shahidullah
Department of Pediatrics
BSMMU, Shahbag
Dhaka, Bangladesh
neonatal@bdcom.com

Jonathon Simon
Boston University
Center for International Health and Development
85 E. Concord Street
Boston, MA 02118, USA
jsimon@bu.edu

Judith Standley
CNM, MPH Health Section, Room 839-1 UNICEF
3 United Nations Plaza
New York, New York 10017, USA
jstandley@unicef.org

Barbara J. Stoll
Department of Pediatrics
Emory University
School of Medicine
Atlanta, GA 30303, USA
barbara_stoll@oz.ped.emory.edu

Nancy Terreri
Health Section, PD H-8F (Room 884)
UNICEF HQ, 3 UN Plaza
NY, NY 10017, USA
nterreri@unicef.org

Shyam Thapa
Saving Newborn Lives Program, Save the Children
2000 M Street, Suite 500, NW
Washington, DC 20036
sthapa@savechildren.org

Donald Thea
Boston University
Center for International Health and Development
85 E. Concord Street
Boston, MA 02118, USA
dthea@bu.edu

Steve Wall
Saving Newborn Lives Program
Save the Children
2000 M Street, Suite 500, NW
Washington, DC 20036, USA
swall@savechildren.org

Boagle Worku
Department of Pediatrics and Child Health
Addis Ababa University
PO Box 9086
Addis Ababa, Ethiopia
bogalewo@yahoo.com

Linda Wright
National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Boulevard, Room 4B05J
wrightl@mail.nih.gov

Anita K.M. Zaidi
Department of Pediatrics and Child Health
Aga Khan University
Stadium Road; PO Box 3500
Karachi 74800, Pakistan
anita.zaidi@aku.edu