Improve outcomes of childhood pneumonia in Kenya through pneumococcal vaccination and case management
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Chapter 1

General introduction and study objectives
1.0: General introduction and study objectives

1.1: General introduction

Approximately three-quarters of global deaths among children under five years occur in Africa and Southeast Asia. The most important single cause of these deaths is Acute Respiratory Infections (ARI) and most ARI related deaths are in children with pneumonia. In 2008, an estimated 8 million childhood deaths occurred globally of which 1.6 million (18%) were caused by pneumonia. In addition, pneumonia also causes substantial morbidity across different regions of the world, and is the leading cause of the burden of disease in low income countries accounting for 9.3% of total DALYs. Recent estimates of pneumonia incidence indicate that approximately 150 million new cases of childhood pneumonia occur every year, mostly in developing countries resulting in between 11 and 20 million hospital admissions.

A series of studies conducted across several developing countries in the early 1980s identified that the main bacterial causes of pneumonia in these settings were *Streptococcus pneumoniae* and *Haemophilus influenzae type B*. In response to these aetiology studies and concurrently conducted clinical studies, The World Health Organization (WHO) developed the pneumonia case management strategy targeting common bacterial causes of pneumonia. These guidelines now contained in the IMCI strategy have underpinned the diagnosis and treatment of pneumonia among children in most developing countries for the past two decades. During the same period the profile of child health in developing countries has been raised and major new global health initiatives and partnerships have emerged. As a result considerable gains in terms of reduced childhood mortality have been recorded in several developing countries. However, a significant
number of these countries might not achieve the Millennium Development Goal 4 target of reducing child deaths by two-thirds between 1990 and 2015.\textsuperscript{16,17}

Progress toward this goal can, however, be accelerated by scaling up the delivery of existing pneumonia interventions amongst others.\textsuperscript{13,15} For one major intervention, case management, this thesis summarises and highlights data that underpin the pneumonia case management strategy in developing countries (Chapter 2). It then goes on to present the results of an intervention aimed at improving implementation of inpatient case management guidelines for common conditions responsible for most paediatric deaths including pneumonia (Chapter 3). The recent introduction of pneumococcal vaccine in Kenya is used to demonstrate the potential impact and economic consequences (cost-effectiveness) of scaling up a pneumonia prevention intervention in Kenya as an example of a low income setting (Chapter 5 and 6). The thesis also attempts to examine whether the mortality parameters used in such cost-effectiveness models that are based on very limited data, are adequate by describing inpatient case fatality rates in a number of Kenyan hospitals (Chapter 4).

**Pneumonia case management**

The WHO pneumonia case management strategy developed in the 1980s is based on a simple algorithm to identify children with pneumonia and guide initial antibiotic therapy. These protocols use age-specific respiratory rate thresholds to diagnose pneumonia at the lowest level of severity in a child with cough or difficult breathing. More severe forms of pneumonia are classified depending on the presence of either lower chest wall indrawing for severe pneumonia or danger signs for very severe pneumonia.\textsuperscript{12,18} In 2005 WHO released pneumonia case management technical updates compiled from new research evidence conducted after initial
IMCI guidelines were released in 1990. During the same year the Kenyan Ministry of health incorporated the inpatient aspect of IMCI pneumonia guidelines into its national paediatric care protocols.

These critical updates improved the initial IMCI guideline recommendations but there still remains a need to continuously evaluate case management practices for the following reasons:

1. In sub-Saharan Africa and other regions with high HIV prevalence there are rapid advances in HIV-related pneumonia research spanning pneumonia epidemiology, prevention and treatment (21-23)  
2. To keep abreast with changing disease patterns due to introduction of new pneumonia vaccines, (24) introduction of new technologies and evolution of health systems (25) and  
3. Highlight priority areas for pneumonia research. The first two studies presented in chapter two of this thesis systematically review the literature on childhood pneumonia case management practices in developing countries focusing on studies conducted after the initial WHO case management strategy was developed.

**Implementing guidelines to improve admission paediatric care**

Community case management of pneumonia has been successfully implemented in several studies conducted in low- and middle-income countries. A meta-analysis of these studies showed that successful implementation of case management reduced neonatal mortality by 27%, while infant and child mortality reduced by 20% and 24%, respectively.26

There had, however, been limited apparent effort to implement the hospital-level case management approaches to treatment of severe forms of pneumonia. Yet studies have identified significant challenges that need to be addressed in order to reduce pneumonia-related deaths through implementation of case management guidelines in health facilities. These challenges
include clinical overlap of pneumonia and other common conditions including malaria, effective referral for inpatient care, management of at-risk groups including neonates, HIV positive and severely malnourished children, and transforming guidelines into widespread practice.\textsuperscript{27} In view of these findings, it is not surprising that a recently published systematic review reported insufficient published data to estimate the effect of hospital case management on pneumonia mortality.\textsuperscript{28}

In Uganda, Simoes and colleagues reported that it was possible to implement the inpatient IMCI component in primary care in areas where referral to hospitals is difficult.\textsuperscript{29} Even where children complete referral to hospitals Nolan et al established that resources for delivering such care are commonly missing in developing countries.\textsuperscript{30} Apart from inadequate resources, a survey of 14 district hospitals conducted in Kenya confirmed that case management practices not requiring additional resources within district hospitals are poor.\textsuperscript{31} Assessment and classification of pneumonia episodes were incomplete across hospitals and there were significant problems with antibiotic choice, dose prescription and oxygen administration for very severe pneumonia. Similar problems with assessment and treatment of children have also been reported in district hospitals in Tanzania.\textsuperscript{32}

Studies in developed countries have shown that guideline dissemination is a necessary but not an adequate component of interventions aimed at changing clinical practice.\textsuperscript{33} This observation could possibly explain the poor case management practices reported above in the Kenyan and Tanzanian studies conducted several years after the countries had adopted IMCI guidelines.\textsuperscript{31,32} It has been suggested that multifaceted interventions are more likely to improve adoption of guidelines and therefore quality of care.\textsuperscript{33} For pneumonia a recent review recommended that wider implementation of guidelines built around training, provision and use of effective
antibiotics and improving use of oxygen provided the greatest potential for reducing pneumonia related deaths at health facilities.\textsuperscript{27} In this thesis the findings of a study (Chapter 3) employing a multifaceted intervention aimed at improving paediatric care within hospitals is presented and the impact of the intervention on inpatient pneumonia case management practices, one of the key targets for intervention, is highlighted.

**Mortality in children admitted to hospital with pneumonia**

It has been demonstrated that the MDGs for child survival are achievable if proven child survival interventions are made universally available.\textsuperscript{13,15} In settings with high infant and child mortality rates the impact of an intervention on mortality is a key consideration in allocating limited healthcare resources. This is particularly true in Africa where approximately half of all global childhood pneumonia deaths occur.\textsuperscript{1} To optimise resource allocation for pneumonia interventions evaluation of the impact of such interventions should be based on robust model assumptions and accurate mortality estimates.

While it is generally accepted that pneumonia admissions in paediatric wards have a higher case fatality rate compared to other less severe diagnoses,\textsuperscript{34} it is increasingly recognised that the outcome of inpatient care within each hospital is determined by several factors including case mix.\textsuperscript{35-37}

There are, however, very few studies comparing pneumonia outcome across different inpatient populations and most studies used for decision making commonly assume that pneumonia case fatality rates are homogeneous across hospitals, countries and even across entire regions. The study presented in chapter 4 examines this assumption of homogeneous mortality by comparing hospital case fatality rates in several facilities and across time in one facility.
Economic burden of inpatient paediatric care

The cost of care is among the identified access barriers to health care in Kenya and other settings in which patients make direct payments prior to receiving treatment. Improving access to basic health care is essential if the outcomes of children with pneumonia are to be improved. The impact of cost on accessibility is more pronounced among the poorest population and while such populations and children are often exempted from payment schemes in the public sector at the policy level a number of studies document poor adherence to user fees policies in primary healthcare. Cost may therefore remain a significant barrier to accessing care, or, may cause considerable hardship once incurred for those with very low incomes.

Studies conducted in Kenya have reported both inpatient and outpatient paediatric treatment costs for common conditions including malaria. There are no local studies on treatment costs of childhood pneumonia, and existing studies for other illnesses rarely include indirect costs such as caretaker time and transport costs. The study presented in chapter five set out to describe treatment costs for paediatric inpatient pneumonia from a societal perspective, incorporating both direct and indirect cost of illness, and compare these costs across facility type and with the cost of other illnesses namely malaria and meningitis.

Cost effectiveness of pneumococcal conjugate vaccination

The pneumococcus is the most important cause of bacterial pneumonia in developing countries. Pneumococcal disease was estimated to have caused approximately 821,000 deaths among children worldwide in 2000 of which 16,000 occurred in Kenya. Trials in Africa, and elsewhere, have demonstrated that pneumococcal conjugate vaccines (PCV) are effective in
preventing episodes of pneumococcal illness and many of these childhood deaths are preventable by vaccination.

The high cost of these vaccines remains a major obstacle to their widespread use in developing countries. A few African countries including Kenya, The Gambia, and Rwanda have introduced the pneumococcal vaccine into routine immunization using external donor funds availed through the GAVI Alliance (GAVI). The introduction experience of these early adopters can thus provide essential data to support introduction of the vaccines in other countries that are considering vaccine introduction. Information on the cost-effectiveness of such vaccines can also support decisions for continued funding of vaccination programmes by national governments at the end of donor funded initiatives. The final study presented in chapter six of this thesis summarises the projected health benefits and cost effectiveness of pneumococcal vaccination among Kenyan infants born in 2010.

**Study location**

The studies presented in this thesis were conducted in Kenya, an East African country with a population of approximately 38.6 million people. In common with most developing countries, the Kenyan population is predominantly young and approximately 16 million people are aged 15 years and below. The current child mortality rate is 74 per 1000 live births.46

The country is divided into eight administrative provinces. Thirteen hospitals located in six out of these eight administrative provinces were used as sites for the studies. These six provinces represent diverse geographical, climatic and ecological conditions. There is also marked variation in child health indicators across the provinces. Central province situated in the Kenyan highlands has rich agricultural potential and better economic indicators than the remaining
provinces and the estimated child mortality rate is 51 per 1000 live births. The region also has among the lowest HIV prevalence (4.6%) in the country and is non endemic for malaria. On the other hand, Nyanza and Western provinces have child mortality rates of 145 and 121 per 1000 live births, respectively.46 These regions have higher HIV prevalence (6.6% in western and 13.9% in Nyanza,46) and malaria endemicity ranges from moderate to intense for most areas within the two provinces.

With the exception of one site the remaining hospitals were rural district hospitals providing first level referral inpatient care or equivalent. The teaching and national referral hospital was included in a single study (costs) only. Two Faith Based Hospitals equivalent to district hospitals were also included in the study on treatment costs only.
1.2: Study objectives

1.2.1 General objective

The main aim of this study was to explore the evidence supporting current pneumonia case management practice and assess the potential for improving case management of severe forms of pneumonia among Kenyan children admitted to hospital while examining the likely costs and effectiveness of prevention resulting from introduction of the pneumococcal conjugate vaccination.

1.2.2 Specific objectives

To conduct a systematic review describing the evidence base that supports childhood pneumonia case management practices in developing countries

To assess the impact of an intervention to improve paediatric inpatient care for common childhood illnesses including pneumonia case management in eight district hospitals in Kenya

To describe case fatalities in Kenyan children admitted to nine rural district hospitals with pneumonia and explore its variability

To determine the economic costs of inpatient care during admission for common childhood illnesses including pneumonia in Kenyan hospitals

To estimate the cost effectiveness of universal infant vaccination with pneumococcal conjugate vaccine in Kenya

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