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Infant Mortality and its Underlying Determinants in Rural Malawi

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ACADEMIC DISSERTATION

To be presented, with the permission of
the Faculty of Medicine of the University of Tampere,
for public discussion in the small auditorium of Building B,
Medical School of the University of Tampere,
Medisiinarinkatu 3, Tampere, on May 25th, 2002, at 12 o'clock.

Life is like walking on a tight rope,

first you fall and then you try to cope.

Life ahead and death behind,

joy upon and sorrow around.

With the steps of humanity,

we can beat the draw of gravity.

With eyes of imagination,

we can reach the glory of the destination.

With a child in our heart,

 heaven is never far apart.

To the families in sub-Saharan Africa

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LIST OF ORIGINAL COMMUNICATIONS

This dissertation is based on the following original papers, referred to in the text by their Roman numerals **I-V**.

I   Vaahtera M, Kulmala T, Ndekha M, Koivisto A-M, Cullinan T, Salin M-L and Ashorn P: Antenatal and perinatal predictors of infant mortality in rural Malawi. Arch Dis Child 2000;82:200-204.

II   Vaahtera M, Kulmala T, Hietanen A, Ndekha M, Cullinan T, Salin M-L and Ashorn P: Breastfeeding and complementary feeding practices in rural Malawi. Acta Paediatr 2001;90:328-332.

III   Vaahtera M, Kulmala T, Maleta K, Cullinan T, Salin M-L and Ashorn P: Epidemiology and predictors of infant morbidity in rural Malawi. Paediatr Perinat Epidemiol 2000;14:363-371.

IV   Espo(former Vaahtera) M, Kulmala T, Maleta K, Cullinan T, Salin M-L and Ashorn P: Determinants of linear growth and predictors of severe stunting during infancy in rural Malawi. Submitted for publication to Acta Paediatrica.

V   Vaahtera M, Kulmala T, Maleta K, Cullinan T, Salin M-L and Ashorn P: Childhood immunization in rural Malawi: time of administration and predictors of non-compliance. Annals Trop Pediatr 2000;20:305-312.

ABBREVIATIONS

AIDS	Acguired immunodeficiency disease syndrome
ANC	Ante-natal clinic
ARI	Acute respiratory infection
BCG	Bacillus Calmette-Guerin vaccine against tuberculosis
CFR	Case fatality rate
DHS	Demographic and health survey
DPT	Vaccine against Diphtheria, Pertussis and Tetanus
EPI	Expanded programme on immunisation
GOBI-FFF	A program of WHO focusing on growth, oral rehydration, breastfeeding and immunisation of children and family planning, female education and food supplementation.
GW	Gestational week
HAZ	Height-for-age z-score
HIV	Human immunodeficiency virus
IMR	Infant mortality rate
LBW	Low birth weight (under 2500 g)
MUAC	Mid-upper-arm circumference
OPV	Oral Polio vaccine
U/5	Under five years of age
UNICEF	United Nations Children´s Fund
WAZ	Weight-for-age z-score
WHO	World Health Organization
WHZ	Weight-for-height z-score

1. INTRODUCTION

During the past fifty-five years, childhood mortality rates have declined all over the world. Between the end of World War II and early 70´s, child death rates even in the developing countries were reduced by half (Vallin 1976). A great deal of these gains was achieved with the help of different, separate interventions targeted against communicable diseases (diarrhoea, respiratory infections, malaria, measles and other immunisable childhood infections).

However, in the late 70´s the world-wide progress was not maintained and infant mortality rates rose especially in Africa. It was noticed, that the disease-oriented vertical programmes were not effective alone. Maternal, environmental, behavioural and socio-economic factors were recognised as additional important determinants of infant survival. The GOBI-FFF interventions focusing on growth monitoring, oral rehydration as diarrhoea treatment, breastfeeding, immunisation of children, and female education, food supplements and fertility control of mothers were declared in 1982 to have the potential to prevent half of the deaths of children in the world (Cash et al. 1987).

Despite the broad approach towards the child health, the decline of child mortality in Africa has been slower since 1980 than in the 1960´s and 1970´s. Of the thirty countries with the worlds highest child mortality rates, twenty-seven are in sub-Saharan Africa (UNICEF 1999).

The region´s under-five mortality was in 1998 173/1000 live borns (UNICEF, 2000) instead of the minimum goal of 70/1000 internationally adopted in the 1990 (World Summit for Children). It is not known why the infant and child mortality rates are staying high or even increasing in many sub-Saharan African countries despite of action plans and interventions made. Malaria, respiratory and gastroenterical infections continue to be the main immediate causes of infant deaths (WHO 1995). A three-tier model of childhood deaths in developing circumstances suggest, that besides these immediate causes there may be many other underlying (behavioural, house-hold level) and ultimate/basic (socio-economic and cultural) determinants of infant mortality (Millard et al 1989, Kent 1991).

One of the new threats to infant survival is human immunodeficiency virus (HIV) infection. During the 1980s and 1990s this infection became increasingly more common among child-bearing women in sub-Saharan Africa (Preble 1990, Bloland et al. 1996, Taha et al. 1998). With the rates of over 25 % of maternal-HIV-seroprevalence perinatal HIV-infection could become the most common cause of childhood deaths, and especially the impact might become visible during infancy (Preble 1990). Although some studies have shown the importance of maternal HIV-infection on infant mortality, very few have investigated its impact on immediate causes of death, underlying determinants of death and infant mortality rates in rural communities in sub-Saharan Africa, and almost none has compared the relationships of these factors to each other.

Malawi, a sub-Saharan country in East-South Africa, has seventh highest infant mortality rates in the world (UNICEF 2000, Malawi DHS 2000). This country with

three-quarters of population living in rural circumstances, stands out with an exceptionally poor infant survival untypical for the surrounding eastern African countries. The national Plan of Action for child survival was seen as a major challenge for Malawi in the 1990´s (Government of Malawi 1991). There is not any single explanation rising from literature for the constantly high infant mortality in Malawi.

This dissertation was undertaken to investigate the immediate and underlying antenatal, maternal, socio-economic, nutritional, behavioural and infectious factors causing high infant mortality in rural Malawi. The study design was a prospective, community-based birth-cohort study with 760 live new-borns during years 1995-1998. The current study forms the second part of the larger research project called Lungwena Child Survival Study aiming at describing women´s gestational health and pregnancy outcomes, as well as children´s growth, development, morbidity and mortality during their frist five years of life in rural villages in Malawi. This was a part of research activity of primary health care programme (The Lungwena Health Project) launched by the Malawi Ministry of Health, the Medical College of the University of Malawi and a Finnish non-governmental organisation, the Mannerheim League for Child Welfare.

2. REVIEW OF THE LITERATURE

This literature review will first provide a historical perspective of global development of infant mortality and then the past and present situation in sub-Saharan Africa will be discussed. Thereafter, the current concept of infant mortality in developing countries will be reviewed in relation to the most common and important immediate causes and underlying determinants known from previous studies and literature. The global attempts to improve and promote infant survival and health are reviewed through different child health programmes, and Government of Malawi's programme on child survival is introduced. Finally, the previous longitudinal studies on infant mortality in sub-Saharan Africa are summarised, and the justification of this study assessed.

2.1 Global development of infant mortality

During year 1998, some 130 million children were born. Between 7 and 8 million of them died before reaching their first birthday, making the world infant mortality rate 59/1000 live births. 11.1 million die before their fifth birthday, contributing to under-five mortality rate of 86/1000 live births (UNICEF 2000). Despite the considerable progress achieved in infant and child mortality in recent decades, infant mortality is still responsible for a substantial proportion of deaths in most countries of sub-Saharan Africa and in South Asia. In industrialised countries, on the other hand, and particularly in Europe, infant mortality has become so low (6/1000 live births) that its influence on life expectancy is negligible (UNICEF 2000). The present situation

is very unequal; the chances of a new-born child of surviving for more than a year depends tightly on the place of birth. The following review of world trends in infant mortality since 1950 will follow estimated infant mortality ratios according to regions and continents.

The trend from 1950 to 1975 was that infant mortality fell just as quickly (4-5 % decrease annually) in the countries that were highly advanced in 1950 (for example Scandinavia) as in the countries of Eastern and Southern Europe. Despite the very different starting levels, the same rate of decline was noticed in Western Europe, Eastern Europe and South Europe and, less regularly, in Russia. Progress in Japan was even faster. Starting in the early 1950´s from a level substantially higher than that of Western Europe, the infant mortality rate in Japan fell slightly below the rate of the Scandinavian countries since 1971 (decline rate of 7-8% annually) (Vallin 1976).

On the other hand the English-speaking countries with similar culture (British Isles, Northern America and Australia/New Zealand), which in 1950 held a level of infant mortality comparable to that of Scandinavia, made slower progress (annual reduction of 2-2.5%) and were in the late 1970´s at the same level as Western Europe (Vallin 1976).

The progress achieved in the least developed regions is difficult to define. It seems to be more irregular and less rapid than in more developed areas, but in most cases it has been impossible to measure the development, since very little is known about the situation during 1950´s to 1970´s. Only Hong Kong, Singapore and Brunei in Asia

and Barbados in the Caribbean made progress comparable to Japan (about 6-8% annually). In most Latin American territories and in West Malaysia and Cyprus, the rate was the same as in Western Europe (about 4-5% annually) (Vallin 1976).

Table 1 summarises the reduction of infant mortality rates between the years 1960 and 1998 in different regions of the world. The development has been slowest in sub-Saharan Africa. During the 1980´s the child mortality declined there less than half as quickly as in South Asia, and one-fifth as rapidly as in Latin America, North Africa, and the Middle East (UNICEF 1995).

Table 1. Reduction of infant mortality rate (IMR) during 1960-1998 in the world

Region	Reduction of IMR /1000 live births
Sub-Saharan Africa	156 to 107/1000
Middle East and North Africa	153 to 51/1000
South Asia	146 to 76/1000
East Asia and the Pacific	133 to 38/1000
Latin America ans the Caribbean	102 to 32/1000
Baltic states	76 to 29/1000
Industrialised countries	31 to 6/1000

Reference: Unicef 2000.

2.2 Childhood mortality in sub-Saharan Africa

Four general features in childhood mortality trends in Sub-Saharan Africa during the period from the late 1940´s to the late 1970´s are obvious and striking. Firstly, there have been notable declines in childhood mortality since World War II in most

countries where data area available. However, there seems to be much variation among countries in the type of decline, and much variation also among countries in the level of mortality. Lastly, an overall difference in mortality levels and the rates of decline is seen between eastern and western Africa (Hill 1991). There has been also three exceptions to these general patterns: a few countries with static or rising mortality (notably Angola, Ethiopia, Mozambique, Niger, Nigeria and Rwanda); a few West African countries whose mortality has fallen to eastern African levels (Cameroon, Congo and Ghana), and finally, one eastern African country with a West African high mortality (Malawi) (Hill 1991).

In many African countries during the 1950´s 30 to 40 percent of children died before their fifth birthday, whereas in very few did less than 22 percent die. By the mid-1970´s, however, very few African countries had under-five mortality over 270/1000 live births, and many had a rate less than 220/100 live births (Hill 1991). The declines were not uniform, however, and varied greatly in size, timing, and pace. In some countries, the fall in mortality has been dramatic; for example under-five mortality almost halved in Ghana between the late 1930´s and the late 1960´s (from 370 to 200/1000), in Congo between the late 1940´s and the late 1960´s (from 290 to 150/1000), and in Kenya between the late 1940´s and early 1970´s (from 260 to 150/1000). In other countries the declines were much more gradual; for example, in Sierra Leone the decline was only 1.5 % over a decade of 1960´s (from 395 to 380/1000), in Lesotho 3% (from 210 to 180/1000) between the mid-1950´s and mid-1970´s, and Guinea and Mali dropped only with 1 % or less (Hill 1991). Childhood mortality rates were generally and initially higher in western than in eastern Africa, with a rough gradient crossing the continent from Northwest to Southeast. The

highest levels of childhood mortality were recorded still in the end of 1970´s in West Africa, the next highest in central Africa, the next to the lowest in East Africa, and the lowest in southern Africa (Hill 1991). By the 1970´s, the mortality rates dropped to 22 - 30% throughout most of West Africa, compared with 20-22 % in central and 12-20% in southern Africa (Hill 1991). The worst performers in under-five-mortality in the 1970´s included Burkina Faso, Gambia, Malawi, Mozambique, Senegal and Sierra Leone (Feachem et al. 1991).

Since the mid-1980´s, the West-East imbalance has changed the direction; numerous East African countries have experienced constant or rising infant and child mortality rates while the rates continued to decline in West Africa (Brockerhoff 1995). Child mortality rates are estimated to have risen substantially since around 1980 in Zambia, to have remained unchanged since the mid-1980´s in Kenya and Zimbabwe and since the mid-1970´s in Madagascar, and to have fallen by only 10 percent in the 1980´s from very high levels in Malawi and Tanzania (Hill 1991). At the same time, dramatic declines in child mortality since the 1980´s have been documented by the Demographic and health surveys in numerous West African countries, including Burkina Faso, Cameroon, Ghana, Guinea, and Senegal.

Malawi stands as an exceptional country in Sub-Saharan Africa with very high infant and under-five mortality rates, which have not improved in the same extent as the other neighbouring eastern African countries. In 1998, Malawi was ranked as a country with 7th highest infant mortality (134/1000) and under-five mortality rate (213/1000) in the world, with only Sierra Leone, Angola, Niger, Afghanistan, Liberia and Mali ranked higher (UNICEF 2000).

2.3 Concept of the causes of infant mortality in developing countries

In the next review the different theories of the causes of infant mortality are noted, and thereafter the most important immediate and underlying causes are separately discussed.

The causes of infant mortality are multi-factorial; especially in developing countries there are great variations between different social, economical (income and occupation) and demographical (mother's and child's age, child's sex, birth-interval) groups of people even inside one country, and the region of residence is one of the most important variable. On the other hand, similar variability can be seen among different groups of families also in industrialised countries (Vallin 1976). Thus, in order to investigate the determinants of infant mortality in a developing country, one must take into account a very broad set of different variables.

A three-tier model of causation of child mortality in developing countries, first pronounced by Millard et al in 1989, mentioned three layers of causation: proximate, intermediate and ultimate causes (Millard et al. 1989). The proximate causes inlaid the immediate biomedical causes of death. In populations with high mortality rates in early life, child death typically results from interactions of malnutrition, diarrhoea and lower respiratory infections. Many medical and public health projects have addressed the proximate causes in an attempt to improve child health (often immunisation campaigns, for example). The intermediate layer includes those behavioural/culture-specific patterns that increase exposure to the proximate causes (for example feeding and breastfeeding patterns, health-seeking behaviour etc.).

Interventions on the intermediate tier have been attempted through many nutrition, education and child care training efforts. However, the families frequently lack adequate resources (food, labour, money) to follow the recommendations (Millard et al. 1989). The ultimate layer of causes of child mortality includes economic, socio-cultural and political factors, encompassing world economy and administration of agricultural and other programmes.

A framework proposed by UNICEF and expounded by Kent continued the ideas of Millard; it included immediate, underlying and basic causes of infant mortality (Kent 1991). According to Kent, immediate factors correspond to individual level (biomedical aspects of both mother's and infant's conditions; specifically their disease and nutritional status). The underlying factors relate to the household level (for example income, access to food and health services, and marital status). Finally, the basic or macrosocial factors relate to the socio-economic development of the society or region within which the household lives (Kent 1991).

2.3.0 Immediate causes of infant death in Africa

When the trends are examined world-wide, the reduction of infant mortality has mainly concerned deaths of children over one month or even one week of age and otherwise is due to reduction of infectious diseases (mainly pneumonia, neonatal tetanus). Consequently, in the most developed regions mortality is highly concentrated in the first week of life and is mainly attributable to the "causes of perinatal mortality" and the "congenital anomalies". In the least developed regions, on the other hand, the infectious or parasitic diseases are still of decisive importance

and the risk of death remains very high throughout the first year of life and even beyond (Vallin 1976).

Of the 11 million annual under-five deaths (mostly occurring in developing countries), the majority (79%) of children die from no more than five conditions: pneumonia, diarrhoeal diseases, malaria, malnutrition and measles; and often from a combination of these conditions. These conditions typically account also for three out of four sick children seeking care at health facility (WHO 1995).

Acute respiratory infections (ARI) are the leading cause of mortality in children world-wide, causing approximately 4 million (one third) of all child deaths (Leowski 1986, Garenne et al. 1992). Deaths from ARI in developing countries are mainly due to bacterial pneumonia, namely due to Streptococcus pneumoniae, Haemophilus influenzae, or Staphylococcus aureus (Garenne et al. 1992).

Widely ranging figures for the incidence of pneumonia in children have been reported in community-based studies. The gross morbidity in all ARI of children less than 5 years old in developing countries varies from equal to double that of industrialised countries (Berman et al. 1985). However, in developing countries a larger proportion of ARI presents as bronchiolitits or pneumonia. Studies from six different developing countries reported incidences ranging from 0.2 to 4.0 new episodes of acute lower respiratory infections per child per year for age group under 5 years (Selwyn 1990). Children below 1 year of age have a 1.5- to 2.5-fold, sometimes as much as 5-fold higher incidence than children between the ages of 2 to 5 years in the same populations (Ruutu 1994). Pneumonia mortality is highest during

the first year of life being 3- to 10-fold higher than between the ages of 1-to 4-years, and as much as 50- to 100-fold higher than in school age. Case fatality rates of children admitted to hospital for pneumonia range from 3 to 12% (Ruutu 1994).

Diarrhoea accounts for 25% of child deaths. Globally, half of these deaths are due to acute watery diarrhoea, one third to persistent diarrhoea, and 15% to dysentery (Vesikari and Torun 1994). In general, bacterial pathogens are more important in countries with poor hygienic conditions than in industrialised countries (Vesikari and Torun 1994). Rotavirus is an important pathogen in developing countries as well as developed countries. It is the single most important causal agent of acute watery diarrhoea leading to severe dehydration. The typical age for rotavirus-diarrhoea is 6-11 months of age, but in developing countries cases begin from 2 months and extend beyond 2 years of age. It causes over 800 000 deaths per year, and is responsible for 30% of all diarrhoeal mortality in age group 6-24 months (Vesikari and Torun 1994).

Enterotoxigenic E.coli-bacteria (ETEC) are found in average in 10-20% of cases of acute diarrhoea in developing countries (Black 1993), and it may be after rotavirus the second most common cause of dehydrating diarrhoea in young children. Shigeallae-bacteria causes dysentery, and may lead to persistent diarrhoea and protein losing enteropathy. More than 500 000 children die annually from the complications of shigellosis (Vesikari and Torun 1994).

Most episodes of childhood diarrhoea resolve within one week or less, but if diarrhoea is extended to at least 14 days, it is called as persistent diarrhoea. About 10% of diarrhoeas in children from developing countries become persistent,

especially among those less than 3 years old, and more so among infants under 1 year (WHO 1990). It may be responsible for about one-third to half of all diarrhoea-related deaths. Case-fatality ranges widely, from less than 1% in community studies to 14% in hospital-based reports. Since persistent diarrhoea is a major cause of malnutrition in developing countries, even the milder, non-fatal episodes contribute to the overall high mortality rates. The risk factors for persistent diarrhoea are young age, severe protein-energy malnutrition, previous episodes of persistent diarrhoea, acute diarrhoea within the preceding two months, and presence of blood and mucus in faeces during acute diarrhoea (Vesikari and Torun 1994)

Malaria kills more than 1.5 million people a year in developing countries. Most of those deaths (90%) occur in Africa- mainly in children under five (WHO, UNICEF 1996). Plasmodium falciparum is the deadliest of malaria parasites, and it kills alone in Africa 1-2% of children and is responsible for at least one million deaths each year.

Immunoglobulin G against malaria parasites acquired transplacentally from the mother protects the infant against clinical disease during the first 6 months of life. The amount of antibody transferred from mother to child depends on the immune status of the mother so that children of partially immune or non-immune mothers are susceptible to malaria before 6 months of age. Pregnancy diminishes immunity to P. falciprum resulting in anaemia, a parasitised placenta and a lower birth weight of the baby (200 grams less than average baby in Gambia) (Alonso et al. 1991). These effects are particularly marked in primigravidas.

The duration of clinical P. falciparum-malaria is short in children and they frequently die within 2-3 days from the onset of severe neurological symptoms. In cerebral malaria the level of parasitaemia, age of less than three years and late pregnancy (third trimester) predict poor outcome. Mortality in cerebral malaria ranges even in the best hands between 10-30% (Whittle and van Hemsbroek 1994).

Measles continues to be an important cause of childhood deaths. The case fatality rate (CFR) of measles was assessed to be 3-4% through Africa and Asia (Eastern Africa being of low CFR-area) (Aaby et al., 1987). In epidemiological studies the acute mortality from measles means any death occurring within one month of the rash.

In addition to acute mortality, the five studies available from West Africa all suggest that delayed mortality is at least two to three times higher among previous measles cases than among controls (Aaby 1987). After acute infection and during the 9 months of follow-up, mortality among the previous measles cases was nine times higher than among community controls. The risk is particularly high for children who have had measles before one year of age. Most studies have emphasised the period of 1-6 months after infection as critical one.

Several studies from Guinea-Bissau have shown that children who live in houses where measles occurred during the first 6 months of their life had a mortality three to four times higher than community controls between 3 months and 5 years of age (Aaby et al. 1990). Diarrhoea deaths were particularly common among the exposed children. Children of immune mothers are usually assumed to be protected by

maternal antibodies, at least to the age of 6 months. However, in developing countries cases of measles are seen in children down to the age of 2-3 months (Aaby and Samb 1994).

2.3.1 Underlying determinants of infant death in Africa

2.3.2 Preterm birth/Low birth weight

The importance of low birthweight (LBW < 2500 g) as a cause of infant mortality and morbidity is well recognised. It has been pointed out that "birth weight is, universally and in all population groups, the single most important determinant of the chances of the new-born to survive and to experience healthy growth and development" (Cruise 1973, Hofvander 1982).

Determinants of birthweight can be divided into those associated with preterm births and those associated with small babies with intrauterine growth retardation (small for gestational age or "SGA" babies). Factors associated with preterm delivery in rural developing countries include low pre-pregnancy weight of the mother, very young maternal age, and low maternal socio-economic status and education (Kramer 1987). Poor maternal nutrition, on the other hand, is associated with SGA births rather than preterm births. Largely because of the high prevalence of maternal malnutrition, eighty per cent of LBW babies in developing countries are SGA (Lechtig et al. 1975, Villar and Belizan 1982).

LBW (< 2500 g) is a risk associated with a third of all infant deaths in developing world (two-to-three fold likelihood of death in infancy) (Lovel 1989). Also in a prospective study carried out in Kenya, Machakos, low birth weight carried a higher risk of death; mortality in LBW infants was 13% as compared to 2% in normal birth weight infants (Jansen et al. 1984). The incidence of low birth weight varies markedly, as 31% of all births in South Asia, 14% in Africa, 10% in Latin America and 6% in Europe lead to the birth of a LBW baby (UNICEF 1984). In other developing countries outside sub-Saharan Africa, estimates of the proportion of neonatal deaths attributed to preterm births have ranged from 22% to 40%. A prospective study carried out in Malawi, Mangochi district estimated that 30% of neonatal deaths were determined by preterm births (Slutsker et al. 1996). The increased risk of death in children with low birth weight and foetal growth retardation continues for years after birth in communities with low socio-economic development (Mata 1975).

2.3.3 Primiparity or high parity, short birth-interval, and previous death of other sibling

The mean birth weight is significantly lower for first births than for next births, and the perinatal and infant mortality rates for new-borns of primipara mothers are nearly double the rates for next births in a study made in a large USA hospital (Sweeney 1989).
Studies from poor and less developed countries have shown evidence that children are much more likely to die if they were born less than 2 years after their mother´s previous birth. (Hobcraft et al. 1985, Boerma and Bicego 1992, Koenig et al. 1990).

A longitudinal study from Senegal showed that a short preceding birth interval doubled the risk of an infant death, and a four-fold higher risk of dying was noticed in the second year in these children born after a short birth interval (Ronsmans 1996).

There are various mechanisms by which birth intervals might affect childhood mortality. Rapid succession of births may erode the reproductive and nutritional resources of the mother leading to a higher incidence of premature and weaker births (Pebley and Stupp 1987). Closely spaced children compete for scarce resources such as food and caring time from mother. An increased transmission of infant and child contagious infections among closely spaced siblings may also occur (Manda 1999). In addition, some studies have shown that the death of the preceding child is associated with increased risks for the index child (Cleland and Sathar 1984, De Sweemer 1984, Hobcraft et al. 1985). On the basis of a study in 25 developing countries it was determined that if the intervals between the births were at least 2 years, infant mortality was reduced by 10% and child mortality (one to four years) by 16% (UNICEF 1984).

2.3.4 Lack of socio-economic support

Whereas neonatal mortality is usually linked with health services and technological advances, postneonatal mortality is usually thought to more strongly reflect environmental (poor housing conditions, poor nutritional support for health) and social conditions (Thorburn Bird and Bauman 1998). In Malawi, a meta-analysis of Malawi demographic and health survey 1992-indicators revealed that variation of

infant mortality rates is strongly associated with a number of demographic and socio-economic factors. Geographical region of residence was found as one of the most important determinants of IMR (Kalipeni 1993). Parents´ income and parents occupation, marital status, access to safe water supply and sanitation, religion and rural residence were found to be associated with infant mortality (Kalipeni 1993).

Many studies have indicated that economic and social improvements are largely responsible for mortality decrease in low income countries initially (Gwatkin 1980, United Nations 1980; Preston 1981). Also studies in more advanced countries show that accessibility to basic sanitation, health and housing facilities play leading roles in mortality reduction (McKeown 1965).

Several studies have suggested that child mortality in developing countries is associated more closely with maternal education than with any other socio-economic factor (Caldwell 1979, Palloni 1981, Cochrane et al. 1982; review in Bicego and Boerma 1993). Education is associated with a break from traditional child-raising practices and facilitates the acquisition of information related to family planning, which through its effects on spacing and timing of births and pregnancies reduce the risk of infant mortality. In addition, mother´s schooling has been found to be related to decreased fatalism about illness, readiness to accept new ideas and increased use of modern medical facilities (Nchinda 1985). However, its impact is more strongly associated with child mortality than infant mortality in developing countries (Hobcraft et al. 1984, Cleland and Ginneken 1988).

2.3.5 Lack of modern health care or inappropriate health-seeking behaviour

Access to modern health care services, especially pre-natal care, by mothers and their children, is particularly important in reducing mortality. However, it has been argued that, due to cultural differences, availability of health care services cannot alone be pointed out to have significant decreasing effects on childhood mortality (Caldwell 1986). In fact, it has been claimed, that technological and institutional improvements of services have more impact on peri- and neonatal period, whereas socio-economic and behavioural variables have a greater role on infant morbidity and mortality.

However, there are examples of the importance of health care services on child survival. In one study children residing in villages proximate to health dispensaries were approximately 32% less likely to have died during the study period than children without access to modern health services (Magnani et al. 1996). In another study children who died had had significantly fewer contacts with the village health worker in the last six months prior to death; and also children who had had more regular contacts with the village health workers throughout the life were better protected than children for whom contact had been less systematic (Velema et al. 1991).

2.3.6 Maternal HIV-infection

The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimated that by the end of 1998 about 33 million people are living with HIV world-wide, including 22

million (67 %) in sub-Saharan Africa. In 1998, 590 000 new paediatric HIV-infections occurred (10 % of total new infections), almost all from mother-to-child transmission; ninety percent of these were in Africa (http://www.unaids.org/). Of the 2.5 million AIDS-deaths in 1998, about 510 000 (20%) occurred in children less than 15 years of age. The global epidemiology of paediatric HIV-infection so reflects the epidemiology of HIV in women. More than 80 % of the 13.8 million women living with HIV by the end of 1998 were living in Africa (http://www.unaids.org/).

Vertical transmission is the dominant mode of acquisition of HIV-infection in children. Without any intervention the risk of transmission is between 15% and 35%, and associates with maternal disease progression, preterm birth, duration of rupture of membranes, length of labour, and vaginal infection and vaginal delivery (Newell 2000). Breast-feeding approximately doubles the risk of vertical transmission; the additional risk of transmission through breastfeeding is approximately 15-28% with about one-third of it accounted for by late postnatal transmission after 3 months of age (Bobat et al. 1997, Tess et al. 1998). In Malawi, one study reported a mother-to-infant transmission rate of 35 % (Taha et al. 1995).

Studies both in developed and developing countries have shown that HIV-infection increases infant and child mortality (Blanche et al. 1989, Lallemant et al. 1989, European Collaboration study 1991). In Africa, however, mortality among children of HIV-infected mothers is higher and occurs earlier than in industrialised countries (Blanche et al. 1989, Lallemant et al. 1989, European Collaboration study 1991, Walraven et al. 1996). The probability of death by 12 months among HIV- infected children in sub-Saharan Africa ranges from 0.23 to 0.35 and by 5 years of age 0.57 to

0.68 (Lepage et al. 1998), whereas data from Europe showed probabilities of 0.1 and 0.2, respectively. In fact, one hospital-based prospective study from Malawi showed that the independent risk of under-five mortality was five times higher for infants born to HIV-infected mothers than for infants born to HIV-seronegative mothers. The study concluded that maternal HIV-infection is the main determinant of mortality in the first 30 months of life in urban community in Malawi (Taha et al. 1995).

The impact of HIV/AIDS on child morbidity and mortality is devastating, as children progress to disease and death much faster than adults. Most infected babies become ill during their first year of life, but rarely in the neonatal period (Aiken 1992). However, since symptoms of paediatric HIV/AIDS resemble other common childhood illnesses, most deaths from paediatric AIDS are not recognised as such (Preble 1990). HIV-positive children suffer more severe forms of a number of infections including bacterial infections, pneumonia, septicaemia, diarrhoea and measles (Lepage et al. 1989; Lepage and Hitimana 1991, Nkrumah et al. 1990). Although bacterial infections in HIV-infected children offer respond to medication, they may do so more slowly and require longer course of medication (Walraven et al. 1996). Incidences of specific diseases are not increased in HIV-infected children (Walraven et al. 1996). Acute and chronic diarrhoea are particularly problems in infected children (Walraven et al. 1996). Tuberculosis is less so, and malaria is not more severe in HIV-infected children than in otherwise healthy children (Nguyen-Dinh et al. 1987, Muller and Moser 1990).

2.3.7 Inappropriate breastfeeding and complementary feeding practices

Breastfeeding decreases both infant mortality and fertility, and thus is acting as an intervening variable linking infant deaths and subsequent fertility. Breastfeeding decreases morbidity and mortality in diarrhoea (Feachem and Koblinsky 1984). The risk of non-breastfed babies in a developing country to die from diarrhoea during the first months of life may be 25-fold compared with exclusively breastfed babies (Feachem and Koblinsky 1984, Victora et al. 1987).

Exclusive breastfeeding for 4-6 months was declared a global goal for optimal maternal and child health and nutrition in 1990. The exclusive breastfeeding means that an infant receives only breast milk and that "no other drink or food is given" (Innocenti Declaration 1991). Exclusive breastfeeding is important because of its contraceptive effect (Perez et al. 1992) and the protection it provides against infections (Brown et al. 1989, Wislon et al. 1998, Cesar et al. 1999, Perera et al. 1999, Raisler et al., 1999). Supplements of "non-nutritive" fluids such as water and teas have been shown to be associated with diarrhoea morbidity (Brown et al. 1989, Popkin et al. 1990) and mortality rates (Victora et al. 1989) that are two to three times higher than those observed for exclusively breast-fed infants. The beneficial effect of exclusive breastfeeding has been found to extend even beyond the actual period of exclusive breastfeeding (Howie et al. 1990, Perera et al. 1999).

A pooled meta-analysis of three studies revealed that protection provided by breast-milk against infant mortality declined steadily with age during infancy. In the first 6 months of life, protection against diarrhoea-deaths was substantially greater (odds

ratio 6.1) than against deaths due to acute respiratory infections (2.4). However, for infants aged 6-11 months, similar levels of protection were observed (1.9 and 2.5, respectively). Protection was highest when maternal education was low (WHO Collaborative Study Team 2000).

2.3.8 Malnutrition

As many as one in two childhood deaths may be related to some degree of malnutrition. Twenty-five percent of all childhood deaths (ages 1-4 years) in African countries are due to some form of malnutrition, while over 50 % may have malnutrition as a contributory cause (Uyanga 1990).

According to epidemiological studies from 53 developing countries, fifty-six percentage of child deaths were attributable to malnutrition's potentiating effects, and 83% of these were attributable to mild-to-moderate as opposed to severe malnutrition. Severe malnutrition accounts for 1-5% of deaths in hospital-based mortality from developing countries (Pelletier et al. 1994, Pelletier et al. 1995). The cornerstone of the methodology Pelletier used was based on the results of eight community-based, prospective studies, one of which was carried out in Malawi.

The anthropometric indicators of nutritional status are significantly associated with the risk of death (Pelletier et al. 1994). This is consistent with the vast majority of the 28 studies from Africa and Asia (Pelletier 1994). The only exception is a study from Zaire (Kasongo Project Team 1983), which found no significant relationship between mortality and any anthropometric indicators. The other studies in Sub-

Saharan Africa (from Tanzania, Uganda,Guinea-Bissau, Senegal, southern Malawi) have all reported a significant association between malnutrition and child mortality (Pelletier 1994).

Among infants dying within 1 year of measurement, all indicators (weight-for-age, weight-for-height, height-for-age and arm-circumference-for-age) predict mortality with approximately equal strength, with some preference for arm circumference - and weight-for-age indicators. However, the child anthropometry-mortality relationship is likely to be modified by a number of factors, for example the age of the child, possibly sex of the child in some settings, length of follow-up after measurement, season and breastfeeding (Pelletier 1994).

The course of infection in malnourished children is more severe, more prolonged, and more likely to be fatal than in well-nourished controls. Prospective field studies have shown that growth faltering related to infections begins at approximately 3-6 months for breast fed infants, or earlier for those bottle-fed (Mata 1978). There have been discussions about whether this phenomenon is related to inadequate food supplementation after the mother´s milk becomes insufficient, to repetitive infectious diseases, or to both factors combined (Waterlow 1981). In traditional societies, the rule is a decline in the supply of breastmilk when the infant is 4-6 months of age, which may not be accompanied by adequate food supplementation. At the same time the onset of recurrent enteric infections occurs with the start of the complementary feeds (Mata 1975, Mata 1978).

Diarrhoea is both a cause and an effect of malnutrition. Diarrhoeal diseases impair weight as well as height gains, with the greatest effects being seen with recurrent or prolonged illnesses, which reduce the critical catch-up growth that otherwise occurs after diarrhoeal illnesses or severe malnutrition. Malnutrition (whether assessed by impaired weight or height for age) leads to increased frequencies and durations of diarrhoeal illnesses (James 1972, Palmer et al. 1976, Tomkins 1981, Black et al. 1984, Biaragi et al. 1985, Henry et al. 1987).

2.3.9 Lack of immunisation

The World Health Assembly in 1974 set the goals to provide immunisation for all children of the world by 1990. At that time less than 5% were immunised. The expanded programme on immunisation (EPI) was called expanded, because DPT and measles vaccines were added to former polio and BCG-immunisation programmes. EPI prevents around 2 million deaths from measles, pertussis, and neonatal tetanus and almost a quarter of a million cases of paralytic poliomyelitis each year (WHO 1989). There are still, however, nearly three million children who die by diseases that can be prevented though immunisation.

Results from a prospective cohort study in Guinea-Bissau showed, that both BCG and measles vaccines halved child mortality in the cohort. In areas of high mortality, vaccines may have substantial effects on mortality from all causes through non-specific effects on deaths from diseases other than those targeted by the vaccines (Shann, 2000). Mortality was lower in the group vaccinated with any vaccine than in those not vaccinated, the mortality ratio being 0.74. Recipients of measles vaccine

were protected from all other causes of deaths than measles also, the ratio being 0.51 (Kristensen et al. 2000). Standard measles vaccine may associate with a non-specific beneficial activation of the immune system (Aaby et al. 1995), but this effect is observed only in areas with high mortality (Aaby et al. 1996).

The immunisation schedule for infants recommended by the WHO Expanded Programme on Immunisation is: at birth BCG and if possible, the Polio zero, OPV0; at 6 weeks DPT1 and OPV1; at 10 weeks DPT2 and OPV2; at 14 weeks DPT3 and OPV3; and finally Measles at 9 months (WHO, UNICEF 1996).

2.4 Global programmes on infant health

The different approaches to improve the infant survival globally are summarised in table 1. The first four (EPI-, ARI-, Diarrhoeal Diseases- and Malaria- programmes) are focusing on controlling single infectious diseases and improving the prevention and treatment of the infections. The next two (GOBI-FFF and World summit for the children´s survival) have a broader vision of integrated prevention of ill-health of infants and management of a sick child, and they also consider the environmental, house-hold level, maternal and nutritional factors as determinants of infant health and survival.

Table 2. Global programmes on infant health

Name of the programme	Start time and the key objectives	Impact on infant mortality	Ref.
1. The Expanded programme on Immunisation (EPI)	The world Health Assembly in 1974 set the goals to provide immunisation (DPT, measles, polio and BCG) for all children of the world by 1990. National strategies based on outreach components such as mobile units and improved cold chains were implemented in the mid-1980s.	Measles vaccination decreases the infant and later mortality to measles and also for non-measles diseases; no precise estimates of effects of BCG on mortality exist.	Ewbank and Gribble 1993
2. ARI control	Emphasises early detection of pneumonia and bronchitis and appropriate antibiotic treatment made available through primary health care.	A meta-analysis of case-management intervention trials estimated a reduction of infant mortality rate of 15.9 per 1000 and an U/5 mortality rate reduction of 36 per 1000.	Ewbank and Gribble 1993
3. Diarrhoeal Diseases control	Focus on a case-management strategy that promotes the use of oral rehydration therapy, continued breastfeeding, safe weaning practices, the use of potable water, personal and domestic hygiene.	Few studies of the mortality impact of ORT programs have been done, and none in sub-Saharan Africa. The available studies suggest that childhood mortality can be reduced by diarrhoeal case-management programs that achieve a level of coverage of over 50% of ORT. The rate use in sub-Saharan Africa is estimated by WHO to be 36% of diarrhoeal episodes. However, the dysentery and persistent diarrhoea continue to keep the diarrhoea-related mortality high in the absence of proper antimicrobial and nutritional treatment.	Ewbank and Gribble 1993

4. Malaria control	Strategies include eliminating breeding places for mosquitoes, direct killing of mosquitoes with insecticide, preventing mosquito bites by means of barriers such as bednets, drug prevention, and treating fevers that may be due to malaria.	Infant mortality could be reduced substantially if malaria were eliminated or greatly reduced, but the diversity of ecologies and the spread of chloroquine-resistency complicates the impact. Chemoprofylaxis for pregnant women can increase mean birthweights among first births.	Ewbank and Gribble 1993
5. GOBI-FFF	Started in 1982, focused on growth surveillance, oral rehydration therapy of gastrointestinal diseases, breastfeeding and better weaning, and universal immunisation (GOBI), and Food supplementation of pregnant mothers and malnourished children, female education, and family planning (-FFF). Communication between health instances, communities and families should be enhanced.		Cash et al. 1987
6. World summit for Children; Declaration of infant survival	1990, the main themes were based on the GOBI-elements, but the responsibility of promoting and maintaining good infant care fell upon communities. Central objectives: 1) reduction of IMR and U/5 mortality rates by 1/3 of the 1990 levels, or to 50 and 70 per 1000 live birth by the year 2000; 2) reduction of severe and moderate malnutrition among U/5 children to half of the 1990 levels by year 2000; 3) universal access to safe drinking water and to sanitary means of excreta disposal.	The national governments in sub-Saharan Africa prepared national Action plans with exact objectives and startegies for achieving goals in children´s health by the year 2000.	

2.5 Government of Malawi-National programme of action for the survival, protection and development of children in the 1990`s

Malawi signed the Convention on the Rights of the child and the World Declaration for child survival in January, 1991, to demonstrate the Government´s commitment to the achievements of the Goals of the Summit (Government of Malawi 1991). The Plan of Action was a further demonstration of this commitment and it was seen as a major challenge for Malawi in the 1990`s (Government of Malawi 1991).

Central themes of the Plan were: 1) a reduction of all deaths due to malaria by 50 % among children under 5 years of age by the year 2000; 2) a reduction by one third of all deaths due to acute respiratory infections in children under 5 years of age by the year 2000; 3) strengthening information, education and communication activities which emphasise the prevention of AIDS; and 4) a 50 % reduction of deaths due to diarrhoea in children under 5 years of age by the year 2000. The more detailed information on Malawi´s Action Plan is given in the Appendix.

2.6 Previous longitudinal studies on infant mortality in sub-Saharan Africa

A Medline search in October 2001 of English articles, with the words infant mortality/Africa south of the Sahara/longitudinal or community based studies, resulted in 100 longitudinal studies on infant and child health and mortality. Of these, only twelve were accepted by the author as truly examining infant mortality. In addition, seven longitudinal community based cohort studies have been conducted before the medline-publications. These nineteen prospective longitudinal studies are

summarised in table 2 and their objectives, participants, methodology and main results are reviewed.

The earliest studies from the 1950-1960`s, the Keneba-study in the Gambia and Pare-Taveta from Kenya and Tanzania found infections to be very common and a principal cause for malnutrition among children. The next three studies in the 1970´s; namely Machakos, Malumfashi and Kilombero in Kenya, Nigeria and Tanzania assessed nine months as optimal age for measles immunisation and noticed the importance of malaria.

In the late 1970´s-1980´s there were several longitudinal studies carried out in sub-Saharan Africa; the Juba-study in Sudan, two studies in Guinea-Bissau, one urban study in Zambia, one in Malawi and one in Uganda. These studies recognised maternal malaria as an important cause of preterm births and malaria and respiratory infections as causes of neonatal deaths. Diarrhoea was reported in four out of six studies as the main cause of postneonatal deaths, but measles and malnutrition were also noticed as important determinants of infant mortality. The reasons for common growth faltering and malnutrition were diarrhoea in Sudan and too few complementary feeds in Zambia, and mid-upper arm circumference was mentioned as the most sensitive indicator for child survival in two studies (Malawi and Uganda), and height-for-age in one (Guinea-Bissau).

During the 1990´s six prospective, longitudinal studies considering infant mortality issues were performed, out of which three were completed in Malawi. Most of these studies reported diarrhoea, respiratory infections and malaria as the immediate

causes of infant deaths. Three of the studies detected underlying determinants of childhood deaths, and these were high parity of mother, long distance to health centre and ill mother (risks for 30-months mortality in Zaire) and on the other hand, primiparity or old age of mother and female-gender of the infant in Nigeria. Results from Malawi are given later. The Jimma study in Ethiopia found poor sanitation, unsafe water source, low income of family, illiteracy and infections as the risk factors for poor growth.

The studies from Malawi reported HIV-infection and very low maternal vitamin-A serum levels as risk factors, which increased infant mortality three-fold, and preterm births as risk for neonatal deaths. Bloland et al. found in their study in Mangochi district that low birth weight, primiparity, maternal HIV and combination of low education and low socio-economic status were the most important determinants of infant mortality. Maternal HIV predominated for postneonatal deaths. Factors that were significant in univariate analysis but not significant in the final multivariate models included preterm birth, previous adverse reproductive outcome, dying during high malaria transmission season, and being born at home (Bloland et al. 1996, Mangochi Malaria Research project 1987-1989).

All of these longitudinal studies have provided some important data on infant mortality rates and immediate causes of morbidity and infant deaths. However, only 3 studies have investigated the independent risk factors of infant mortality, and only one longitudinal study, carried out in the end of 1980´s in Malawi, has analysed the impact of HIV epidemic on infant mortality and compared it to other early underlying antenatal, maternal, perinatal and socio-economic predictors of death.

The women enrolled into that study were mostly delivering at the Mangochi hospital, and the results were published few years later, in 1996.

None of the longitudinal studies reviewed has included data about other important underlying determinants of infant survival, such as rural infant´s breastfeeding and complementary feeding status, health-care seeking, immunisation behaviour and detailed data on morbidity and case-fatality of acute illness episodes.

Table 3. Summary of the **longitudinal (prospective, rural and urban)** studies on infant health/mortality in Sub-Saharan Africa

Time	Place of study	Objectives	Subjects and methods	Main results/ conclusions	Reference
1950 onwards	Keneba, **the Gambia**	To gather data on communicable diseases and to relate infection to malnutrition.	700-900 persons; Prospective, rural, annual demographic surveys	Infections very common among children; rainy season-peaks in morbidity and child mortality; concluded that malnutrition resulted principally from infection.	Ewbank and Gribble 1993, McGregor 1991
1954-66	Pare-Taveta, **Kenya and Tanzania**	To assess the public health importance of malaria, the efficacy of insectisides for control.	1500 households, Prospective, rural community	Insecticides reduced infant mortality from 200 to 100/1000 live births, but the levels rose again after stopping of spraying mosquitoes.	Ewbank and Gribble 1993, Bradley 1991
1969-79	Danfa, **Ghana**	To assess cost-effective health and family planning.	4000 persons, Prospective, rural community	Family planning was best delivered through health services; polio morbidity significant; malaria chemoprofylaxis effective but induced resistance.	Ewbank and Gribble 1993, Neumann et al., 1991
1974-81	Machakos, **Kenya**	To obtain data on childhood morbidity, mortality and malnutrition.	4000 households visited biweekly and later monthly, Prospective, rural	Nine months as optimum age for measles immunisation; causes of child death; no seasonal variation in morbidity/mortality; levels and risks for perinatal mortality.	Ewbank and Gribble 1993, Muller and Ginneken 1991
1974-79	Malnumfashi, **Nigeria**	To study effects of chronic malaria and epidemiology of meningococcal infections.	43 000 persons, Prospective, rural community	Malaria´s adverse consequences were indirect; chemoprofylaxis highly effective in improving haemoglobin levels in children; morbidity and mortality peaked in rainy season.	Ewbank and Gribble 1993, Tomkins et al. 1991

Date	Location	Objective	Study details	Findings	Reference
1982 onwards	Kilombero, Tanzania	To assess levels, trends and causes of malnutrition, morbidity and mortality.	1900 persons, Prospective (annual morbidity/mortality in one village), 132 000 persons' data from health centre.	Extensive local data on morbidity and malnutrition; importance of malaria, hookworm, schistosomiasis and malnutrition; most deaths occurred in rainy season.	Ewbank and Gribble 1993, Tanner et al., 1991
Stopped in 1984	Juba, Sudan	To gather data on morbidity, mortality (causes and mortality rate) and growth of infants.	233 pregnant women and their offspring, visited monthly, Prospective, rural	IMR 118/1000 live births; diarrhoea the main cause of death; maternal malaria associated with preterm births; children's growth much impaired by diarrhoea; the children had high ARI morbidity; mean weight was at 3rd centile at year 1 among infants studied.	Woodruff et al., 1984
Stopped in 1986	Guinea-Bissau	To study under-five survival of children.	2228 children 6-59 months of age, Prospective, 8-12 months follow-up, periurban and rural	Under-five mortality double in periurban compared to rural communities because of measles outbreak; HAZ positively correlated to U/5 survival.	Smedman et al., 1986-7
Stopped in 1988	Malawi	To study growth and nutritional status, morbidity, and mortality of under-five children.	1178 children U/5, for infant morbidity and growth study 46 infants, measures twice a year in 3 seasons, Prospective, rural	U/5 mortality 270/1000 (137 deaths); MUAC, WHZ and triceps skinfold as indicators of survival; improvement of water supply did not improve U/5 survival; growth faltering from 3 months of age onwards; ARI and malaria common during the first five months of age, then diarrhoeal diseases dominated.	Lindskog et al., 1988 and 1994
Stopped in 1990	Lusaka, Zambia	To describe the immediate causes of deaths and the infant growth.	257 children, Prospective, urban	Prematurity and respiratory problems the main causes of neonatal death; then diarrhoea, measles and malnutrition. Growth faltered after 8 months of age; too few complementary feeds to infants; immunisation coverage over 70%.	Watts et al., 1990
1987-90	Guinea-Bissau	To assess the infant and under-five mortality rates and main causes of death.	1426 children, Prospective, semi-urban	IMR 94/1000 and U/5-mortality 215/1000 live births; Persistent and acute diarrhoea the main causes of death; 75% of children brought to health facility before death.	Molbak et al., 1992

1988-89	Uganda	Anthropometry as a predictor for under-five mortality.	4320 0-59 months old children, Prospective, rural	MUAC the most sensitive predictor of mortality, followed by weight-for age measurements.	Vella et al., 1994
Stopped in 1994	Blantyre, **Malawi**	To assess the impact of HIV-infection on birthweight, infant and child mortality.	1385 children, Prospective hospital-based case-control study, urban, regular check-ups and HIV-testing.	Infant mortality 3 times higher among HIV-positive infants, also preterm births and intrauterine growth retardation more common among infected infants, but the mean birth weights did not differ. Diarrhoea, ARI and failure to thrive the main causes of death in HIV-positive babies.	Taha et al., 1995
1992-93	Jimma, **Ethiopia**	To describe the socio-economic environments of households, to assess the nutritional status and infant mortality rate.	Birth-cohort of 1563 children, Prospective, urban, bimonthly visits	IMR 115/1000 live births (141 deaths); the mean HAZ and WAZ at 12 months were −1.4 and −1.5 SD. Risk factors for poor growth were poor sanitation/unsafe water source, low income of family, illiteracy. Diarrhoea, fever and ARI common infections, which impaired weight gain.	Asefa et al., 1996 and 1998
Stopped in 1996	**Zaire**	To assess the maternal determinants of child survival. The inclusion criteria were exclusively breastfed children, who had no severe malnutrition or ARI/diarrhoea episodes, and were not born as preterm babies.	776 children aged 0-3 months, random-cluster sample, Prospectively followed for 30 months, rural	Risk factors for 30-month mortality were high parity of mother, over 5 km distance to health centre and invalidating maternal disease. Maternal school education was also a risk for child death.	van den Broeck et al., 1996
1987-89	Mangochi-Malaria project, **Malawi**	To assess the causes and epidemiology of infant and second-year mortality.	3274 liveborn infants, Prospective birth-cohort, rural, bimonthly home visits	578 infant deaths, 30% of neonatal deaths related to preterm births. Diarrhoea, fever and ARI the main immediate causes of postneonatal deaths, illnesses lasted 1 week or less and 2/3 of deaths occurred at home, although 80% were brought to health facility during illness. Low birth weight, primiparity, maternal HIV and low education and socio-economic status the independent	Slutsker et al., 1996; Bloland et al., 1996

				factors of infant mortality. Maternal HIV predominated for postneonatal deaths.	
Stopped in 1988	Blantyre, **Malawi**	To assess the importance of maternal vitamin A deficiency on infant mortality.	377 HIV-negative mothers and their offspring, Prospective birth-cohort, hospital-based, urban	IMR 48/1000 live births (18 infant deaths); if maternal vitamin A-serum levels were very low during pregnancy, the infants had three-fold risk for mortality.	Semba et al., 1998
1993-97	**Nigeria**	To assess the risk factors for infant mortality and the causes and seasonality of deaths.	3308 population, Prospective, rural community	IMR 68/1000 live births. Primiparity, old mother and female-gender risk factors for infant mortality. More neonatal deaths in rainy season, infections the main causes for postneonatal deaths.	Lowoyin, 2001

2.7 Justification of the study

The literature review revealed that infant survival has not improved in sub-Saharan Africa as much as in other parts of the world in spite of several global and national infant survival plans and programmes. Especially Malawi stands out with an exceptionally poor infant survival untypical for the surrounding eastern African neighbour countries. There is not any single explanation rising from the literature for the constant and even increasing infant mortality in Malawi.

Literature review also offers a very long list of possible causes and underlying factors, which predispose infants to preterm deaths in developing countries. It also shows, that maternal HIV-infection has become a growing threat to infant survival in Africa. The earlier longitudinal attempts to study infant mortality in sub-Saharan Africa and in Malawi have shown that infectious diseases such as diarrhoea, malaria and respiratory infections form the main causes of postneonatal deaths. However, none of the studies has carried out an organised comparison of the impact of different underlying determinants, such as maternal infections (also HIV-infection), antenatal and perinatal factors, health-seeking behaviour, nutritional, breast-feeding and immunisation status of an infant, and household characteristics.

To improve child health in Malawi, it is important to understand the relationships between the different factors of infant health especially in rural communities of the country, as three quarters of the Malawian population live in distant villages.

Figure 1. Theoretical frame for the justification of the study.

Basic causes of infant mortality
(economic/socio-cultural aspects of society)

Underlying causes of infant mortality
(behavioural and household level factors such as breastfeeding and other feeding habits, immunisation behaviour, especially measles immunisation coverage, asccess to food and health services, income, occupation and living circumstances of families etc.)

Immediate causes of infant mortality
(biomedical aspects of mother and child such as infectious diseases, mainly diarrhoea, malaria, respiratory infections, measles and HIV-morbidity, and nutritional status, birth interval, birth weight)

Sub-Saharan Africa has the lowest infant survival status in the world. Total reduction of IMR in 1960-1998 was from 156 to 107, whereas in other less developed regions the decline was 133-153 to 38-76 infants per 1000 live births. Malawi and Niger has the highest peacetime infant mortality in the world.

Why has Malawi exceptionally high IMR despite the national programme of action for the survival for children in the 1990´s? What are the independent immediate, underlying and basic determinants of infant mortality in rural Malawi? Does the HIV-epidemic explain the constantly high mortality?

3. HYPOTHESIS AND AIMS OF THE STUDY

The main goal of this study was to describe the common health hazards during the first year of life in rural Malawi, and especially to investigate the immediate and underlying antenatal, socio-economic, nutritional, behavioural and infectious factors causing high infant mortality.

As the initial **hypothesis** of risk factors for infant mortality in Lungwena we assumed on the basis of literature review and previous studies, that the high infant mortality in Lungwena is a result of:

1. High morbidity to infectious diseases
2. Late health-seeking behaviour when the child become sick
3. High proportion of maternal HIV
4. Poor maternal weight gain during pregnancy
5. Low birth weight of the baby and
6. Malnutrition of children

We assumed, that the infections are the main immediate causes of infant death, but the relationship of maternal and child infections to other underlying and basic causes of infant mortality was not known as there were no previous studies available from rural sub-Saharan Africa.

The specific **aims** investigating the risk factors of infant mortality were:

1. To measure the infant mortality rate, and to detect the place, timing and immediate causes of infant death.

2. To describe the case-fatality rates and health-seeking behaviour during acute fatal illness episodes.

3. To analyse the impact of HIV-epidemic on infant mortality and to compare it to other early underlying antenatal, maternal, perinatal and socio-economic predictors of death.

4. To investigate the magnitude and predictors of exclusive breastfeeding and to describe the changes in infant diets during the first 18 months of life.

5. To analyse the epidemiology, health-seeking behaviour and predictors of acute illness episodes among the infants.

6. To describe children´s growth during infancy in rural Malawi.

7. To analyse factors that predict linear growth faltering (severe stunting, i.e chronic malnutrition) at twelve months of age.

8. To describe the population coverage and time of administration of childhood vaccinations, with a specific focus on measles immunisation.

4. SUBJECTS AND METHODS

4.1 Setting of studies and follow-up

4.1.1 Study area

The study was performed in Malawi, a country situated in the south-eastern, sub-Saharan Africa. Malawi shares boarders with Tanzania in north, Zambia in west, and Mozambique in east. The map of Malawi and the study area are illustrated in Figure 2. Malawi belongs to the least developed countries in the world, measured with many different ways. Table 3 presents the most important health and socio-economic statistics of Malawi.

Figure 2. The map of Malawi
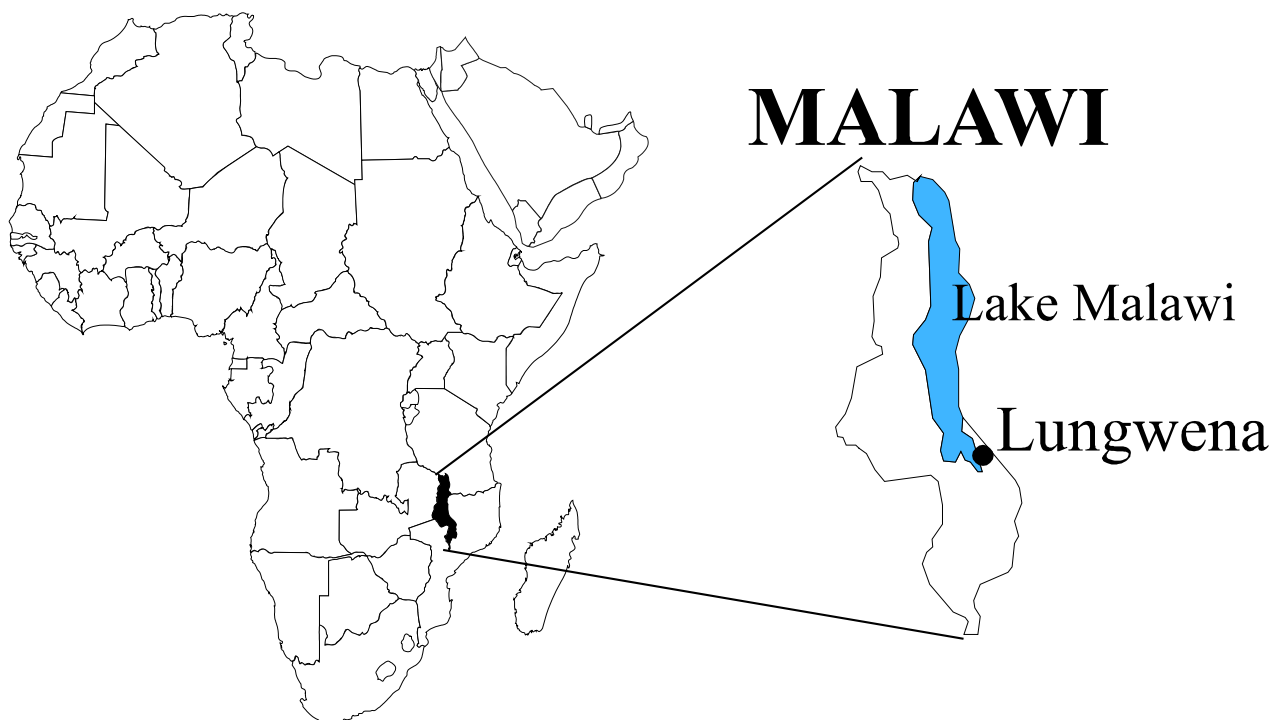
The study was carried out in Lungwena of Mangochi district, rural area in southern Malawi. Lungwena is a 20 km long and about 5 km wide rural area in the Rift Valley between the mountains and the eastern shore of Lake Malawi. Approximately 17,000 people occupy a total of 4,200 households in the 23 villages of this area. The predominant religion is Islam and the major ethnic group is the Yaos, Chi-Yao being the main language in the area. Most of the inhabitants are subsistence farmers, but fishing is also common. The most important staple agricultural product is maize, normally harvested in April-May. Family organisation is matrilineal. Traditionally, the land is inherited by the women who remain near their mother´s home even when married. However, men are normally considered as heads of households.

A demographic and health survey in 1994 revealed that the health situation, as measured by childhood mortality figures, was even worse in Lungwena than in other parts of Malawi. To improve the situation, the Malawi Ministry of Health, the Medical College of the University of Malawi and a Finnish non-governmental organisation, the Mannerheim League for Child Welfare, launched a primary health care programme in the area. The Lungwena Health Project aimed to provide improved health services, develop a field training site for community health professionals and carry out appropriate research. The present project is part of the research activity.

The Lungwena Training Health Centre located in the middle of the Lungwena area provided normal preventive and curative modern health services like family planning, antenatal and delivery care, growth monitoring, vaccinations, and treatment of common illnesses. Modern care could also be obtained from the

Namalaka Health Centre (private religious centre), Malindi hospital (private religious hospital) or Mangochi District Hospital (governmental), situated some 23 km, 15 km and 32 km respectively from the health centre. Climatically, there are three seasons: a rainy season between December and March-April, a subsequent dry and cool period when temperatures can occasionally fall below 20°C, and a hot and dry period from September to November. Falciparum malaria is endemic throughout the year, with peak prevalence being seen during the rainy season between December and March.

For administrative purposes, the Lungwena region was divided into four separate areas surrounding the health centre. The mean distance between the study participant's homes and the health centre was 5.2 km and the usual transport was on foot. The northern area (area 4, the furthest from the health centre) was visited monthly by a mobile well-baby clinic and vaccination team and the eastern area (area 3) was served irregularly by a similar mobile team. However, inhabitants of the other two areas (south, area 2; west, area 1) had no access to mobile clinics. Vaccinations were regularly given free of charge in health facilities and outreach clinics. During occasional national campaigns, vaccinations were also provided at extended outreach clinics in villages. In the study area, vaccinations were available daily (except at weekends).

Under-five clinics were commonly used and monthly growth of weight was recorded to under-five cards, which were found from almost every family. If the growth had monitored as faltered, the infant was sent to Outpatients´ department visit, and the medical assistant referred the child to nutrition clinic for an outpatient visit.

According to Malawian standard treatment guidelines, diarrhoea should be treated with oral rehydration solutions and fever without any other symptoms with anti-malarial drugs. There were no functioning village extensions of outpatient treatment possibilities, and no special HIV-home treatment programmes were available.

All 23 villages in Lungwena area were served by a traditional birth attendant who had attended a training course on modern antenatal and delivery care. There were also numerous traditional and religious healers in Lungwena.

Figure 3 . Educational session at antenatal clinics in Lungwena health centre

Table 4. Malawi health and wealth indicators

Indicator	Measure
Total population	10.3 million (year 1998)
Total number of surviving infants	460 000 (year 1997)
Urbanisation rate	15% (year 1997)
Infant mortality rate	134/1000 live births (7th highest in world; year 1998)
Life expectancy at birth	39 years (2nd lowest in world; year 1998)
Female literacy rate	42% (year 1997)
GNP per capita (USD)	170 (year 1997)
Immunisation coverage among 1-year-old infants:	
Tuberculosis (BCG)	100%
Polio	94%
Diphtheria, pertussis, tetanus	95%
Measles	87%

Reference: State of the World children 2000.

4.1.2 Preparatory phase of the study

The main study project was preceded by a three-month pilot study and an information campaign. During this period altogether twelve research assistants were hired and trained, and study questionnaires as well as laboratory procedures were

tested. In addition the purpose and consequences of the study were discussed in the local management committee for the Lungwena Health Project, each of the 23 village chiefs as well as the heads of the two traditional authorities in the area were met individually and finally a total of 44 village meetings were arranged.

Initial information on local diets for infants was obtained from focus group discussions attended by local mothers, a research assistant and one scientist. The data were used to develop a vernacular structured questionnaire. A verbal autopsy technique was tested in nearby yao-communities and validated in surroundings similar to the present study site during year 1994 by the author of this thesis. Based on the experience from the test and the similar interviews used elsewhere, the verbal autopsy criteria and vernacular questionnaire were developed (Nykänen et al. 1995).

4.1.3 Sequence of study examinations

Figure 3. llustrates the sequence of the study examinations, child follow-up and the endpoints analysed in sub-studies. Within approximately one week of delivery a research assistant visited the mothers to collect information on delivery events and pregnancy outcomes and to measure the baby. In addition, the surviving new-borns were medically examined within four weeks from birth by a member of the research team at Lungwena health centre. After the first visit, the home visits to villages were carried out on monthly basis until the child was 18 months old, and then every three months.

Figure 4. Sequence of study examinations and endpoints studied.

DELIVERY AND FOLLOW-UP IN LUNGWENA INFANT STUDY
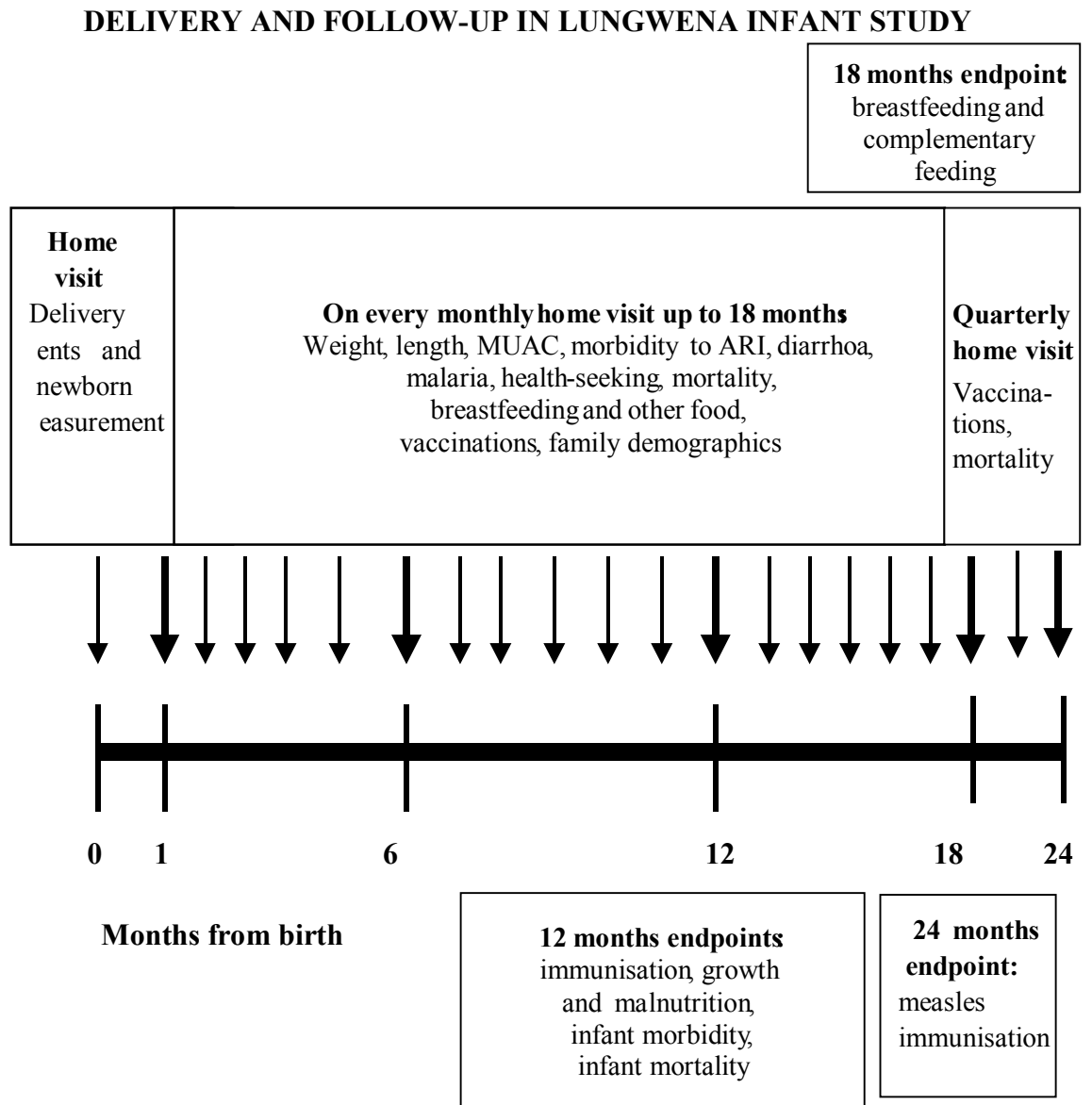
MUAC= mid-upper arm circumeference, ARI= Acute respiratory infection.

4.1.4 General set-up of studies

Within the present sub-studies, the follow-up time started from the birth and ended

up at first birthday of cohort children in sub-studies of infant mortality (I), infant

morbidity and health-seeking (III) and infant growth and development of

malnutrition (IV). In a sub-study of feeding practices the follow-up period was extended from birth to 18 months of age (II), and in the last sub-study of immunisation practices the children were followed up to two years of age (V).

All the live born infants who had not dropped out from the follow-up by one year of age (both singletons and twins) were included into the study I of infant mortality rates and causes of deaths. In the analysis of predictors of infant mortality (I) the study group was restricted to singletons born alive. The live-born infants with at least one month of follow-up were included in the feeding (II) analysis (both singletons and twins). From morbidity study (III) children with less than 2 months of observation were excluded from the analysis, but those infants who died, but had at least 2 months of observation of morbidity were included (III). The live-born singleton babies, who survived and were followed-up to 1 year of age, were taken into the growth and malnutrition study (IV). In the immunisation study, infants (both singletons and twins) surviving and followed at 6, 12 and 24 months were included into the study of vaccination coverage rates, and the infants who survived and were followed at 12 months of age were analysed for the predictors of incomplete immunisation status at twelve months of age (V).

4.1.5 Study subjects

The study subjects included live-born offspring of a cohort of 795 pregnant women recruited from an antenatal clinic at the Lungwena health centre between June 1995 and September 1996. The last child of the cohort was born in February 1997. Owing to a very high antenatal care coverage and comprehensive enrolment to the study, the

birth cohort comprised approximately 95% of all new-borns in the area. The sample size was based on our wish to study the effect of human immunodeficiency virus infection on infant mortality.

The research protocol was reviewed and approved by the Malawi National Health Science Research Committee and informed consent was obtained verbally from each pregnant women before enrolment.

The author of this thesis was responsible for field supervision, training and co-ordination of the study and collection of data for two years in Lungwena. The author of this dissertation has also conducted all the data entry, analyses and writing of the five publications derived from the sub-studies introduced in this thesis.

Fig 5. The author examining a study child at one-year-old clinic outreach.

4.2 Methods

4.2.1 Summary of studied variables

Table 4. shows the summary of socio-economic, antenatal, obstetric, perinatal, nutritional and other infancy-time variables studied and tested for their association with infant mortality (I), morbidity (III), malnutrition (IV), uncompleted immunisation status (V), and inappropriate feeding methods (II). The methods used in the separate sub-studies are explained in detail later.

Fig 6. A research assistant interviewing a study mother by local Chi-Yao language during a monthly home visit

Table 5. Variables analysed as predictors of infant mortality, inappropriate feeding methods, morbidity, malnutrition and incomplete immunisation status among studied children.

Socio-economic variables	Antenatal variables	Obstetric/new-born variables	Infancy-time variables
Age of parents (years)	Mother's parity		Monthly weight of the child
Education of parents (years at school)	Maternal height		Monthly length of the child
Literacy of parents	Maternal weight gain		Monthly MUAC of the child
Occupation of parents	Maternal anaemia in pregnancy		Monthly number / duration of illness episodes
Religion of parents	Maternal malaria at ANC		Monthly place and timing of health-seeking
Number of people in the household	Maternal HIV infection		Survival status monthly
Gender of the head of the family	Maternal syphilis status at ANC		Causes of infant deaths
Present and past marriages of parents	Total energy intake of mother at pregnancy (at 32nd gestational week)		Season and age of morbidity
Building material of house		**Obstetric/new-born variables**	Monthly immunisation status
Source of used water (safe/unsafe)		Birth before 38th gestational weeks	Monthly recording of type and frequency of given food items

Absence of adequate sanitation	Month of birth	Monthly recording of breastfeeding
Ownership/size of the cultivated land	Place of delivery	Monthly recording of demographic changes in the family
Ownership of domestic animals	Attendant of delivery	Father's absence from home (months)
Distance between home and health centre	Mode of delivery	Age when complementary and family foods first given to child
Age of mother at first pregnancy	Delivery complications	Duration of exclusive breastfeeding
Birth interval between last two babies	Gender of the child	
Number of people in household	Birth order	
Number of previous infants in family	New-born weight	
Number of deaths to < 5-year-olds	New-born length	
Residential area (village)	New-born MUAC	
	Head circumference of the new-born	
	Mean weight (WAZ) at age 1-3 months	
	Singleton/ twin baby	

4.2.4 Study participants´ background information

Data on the socio-economic background of the participants were collected through personal interviews at enrolment. Cultivated farm areas were measured by the agricultural extension workers. Tests for maternal human immunodeficiency virus infection (ELISA antibody test), syphilis reactivity (rapid plasma reagin, RPR test), malaria (peripheral blood parasitaemia) and anaemia (haematocrit < 0.34) were assessed with routine laboratory methods from a blood sample taken at antenatal care enrolment. All participants received malaria prophylaxis with suphadoxine-pyrimethamine. Those women with a positive syphilis test as well as their sexual partners and the new-born infants were treated with an intramuscular injection of bentzathine penicillin.

Delivery events and child characteristics were recorded during home visits carried out as soon as possible after birth and later at monthly intervals. Length of gestation at birth was determined from maternal fundal height at antenatal visits. Because a large proportion of deliveries took place at home, maturity scores were not able to be used.

4.2.5   Infant mortality, causes of deaths

If an infant death was discovered, the assistant reported the death to the research team. A verbal autopsy interview was carried out usually by the researcher and the research assistant, and the guardians were interviewed about the child´s preceding symptoms and signs. Based on the answers, three doctors using predefined diagnostic criteria determined causes of death.

4.2.6 Breastfeeding and complementary feeding methods

Individual food items included in the form were grouped into new-born foods, complementary foods and family foods. The first group included breast-milk and those non-milk liquids, that were typically given to babies early after birth. Complementary foods included various types of thin maize porridges (6-7 % dry matter). Family foods included items that were also consumed by others in the family (thick maize porridge being the most important item). Infants were considered to have been exclusively breastfed up to the date when they first received anything other than breastmilk.

For the first 18 months of their life, every child was monthly visited by one of the ten local research assistants. The structured questionnaire was used to interview the guardian (usually mother) about food items ever given to the infant and the frequency of their consumption during the day preceding the interview.

For the purposes of the associations with malnutrition-study, infant weaning was categorised as "appropriate" when thin maize porridges were introduced only after 2 months of age and family foods before 7 months of age, "one risk characteristic" if porridges were introduced before 2 months or family foods after 7 months of age, and "two risk characteristics" if porridges were given early and family foods late.

4.2.7 Infant morbidity and health-seeking behaviour

The guardian was monthly asked about the number and length of illness episodes that had occurred since the last visit. If any episodes were recorded, health-seeking behaviour was also inquired. Illnesses were classified into diarrhoea, ARI (as defined by fever with coryza or cough), malaria (fever without any other symptoms) and other illness episodes. Because the time of observation differed from one individual to another, we used follow-up month adjusted means to describe average morbidity.

For the assessments of associations, morbidity was defined as the total number of all disease episodes that the child was calculated to have had during the first year of life. This figure was obtained by dividing the number of observed episodes by the number of months the child was in follow-up and then multiplying this value by a factor of 12. According to the number of disease episodes the children were categorised as having no (0 episodes), some (1-6 episodes/year) or many illness episodes (more than 6 episodes / year). Both fatal and non-fatal illness episodes were included in the morbidity statistics. Comparable category ranges for diarrhoea-specific morbidity were (0) none, 0.1 to 2.4 (some) and > 2.4 (many) episodes per child per year. These categories were used in the analysis for the determinants of malnutrition.

4.2.8 Growth and development of malnutrition during infancy

Weights, lengths, and mid-upper arm circumferences (MUAC) were measured with portable spring-scales, self-made length boards and non-elastic tape measures. Anthropometric indices (WAZ, weight for age; HAZ, height for age and WHZ,

weight for height) were calculated with EPI-INFO 6.04b software. Because birth weight (within 48 hours of birth) were known only for 32% of the participants, we used a surrogate marker (WAZ_{1-3}) for birth size. This variable was calculated by taking a mean of WAZ-score obtained at first three monthly weight measurements after birth.

Malnutrition was categorised into underweight (WAZ < -2), stunting (HAZ < -2) or wasting (WHZ < -2). If the index value was below -3, malnutrition was considered severe. For MUAC, a cut-off values of 13.5 cm (at risk) and 12.5 cm (malnourished) were used. To study the predictors of poor growth, malnutrition was defined as low weight for age (WAZ < -2) at 12 months of age.

4.2.9 Immunisation practices

Information about vaccinations given was obtained verbally from the guardian at each visit. Research assistants verified the information using the U/5 cards carried by the guardians. Finally the primary investigator double-checked the accuracy of the data from health centre records. If given before the age of 32 days, the first dose of polio vaccination was defined as polio 0 and as polio 1 if given later. For assessment of factors associated with vaccination frequency, a child who had not received one or more of the recommended doses (except polio) by 1 year of age was considered not to have completed her immunisations appropriately.

4.3 Statistical methods

Data entry was done with Microsoft Excel 7.0 while analyses were carried out with SPSS 9.0 statistical software. In addition, EPI-INFO 6.04b was used in sub-study of infant growth and BMDP for infant morbidity-study.

Identification of variables associated with infant deaths, uncompleted immunisation programme and malnutrition (univariate analysis) was carried out with cross-tabulation of dichotomous variables. Relative risks and their 95% confidence intervals were calculated using routine methodology and statistical significance, evaluated at 0.05 level, was assessed with Pearson chi-square test. For continuous variables, univariate logistic regression and Wald test were used. For assessing associations between morbidity and various linear or dichotomous predictor variables, the Kruskall-Wallis non-parametric independent sample test and cross-tabulation with chi-square tests for statistical significance were used. Non-parametric Mann-Whitney rank sum test and calculation of medians and percentiles were used when comparing morbidity and health–seeking in different populations. Assessments of associations between various predictor variables and duration of exclusive breastfeeding or age at onset of complementary feeding was done using univariate and multivariate linear regression.

Logistic regression with stepwise exclusion based on likelihood testing was used for multivariate modelling of infant mortality, uncompleted immunisation programme and malnutrition at one year of age. The initial model included usually those variables that were significantly ($p < 0.05$) associated with mortality in univariate

analysis, as well as those known from the literature to be associated with the parameter tested. The least significant variables were excluded from the model in a stepwise manner until all remaining variables were significant at $p < 0.1$. To test the independent effect of the important predictors of morbidity, a polychotomous logistic regression was performed.

5. RESULTS

5.1 Enrolment and follow-up

The enrolment of the study children and the numbers of children remaining in the follow-up of the five sub-studies of this dissertation are shown in Fig. 7.

Active surveillance through local traditional birth attendants and study participants identified only 37 pregnant women whodid not receive antenatal services from Lungwena. Thus, 95.2% (795/834) of all pregnant women in the area were eligible for study. There were no socio-economic differences between those women who attended the Lungwena health centre and those who did not (I).

Table 5 shows a summary of background information of the families studied, and selected information on maternal and new-born infant data.

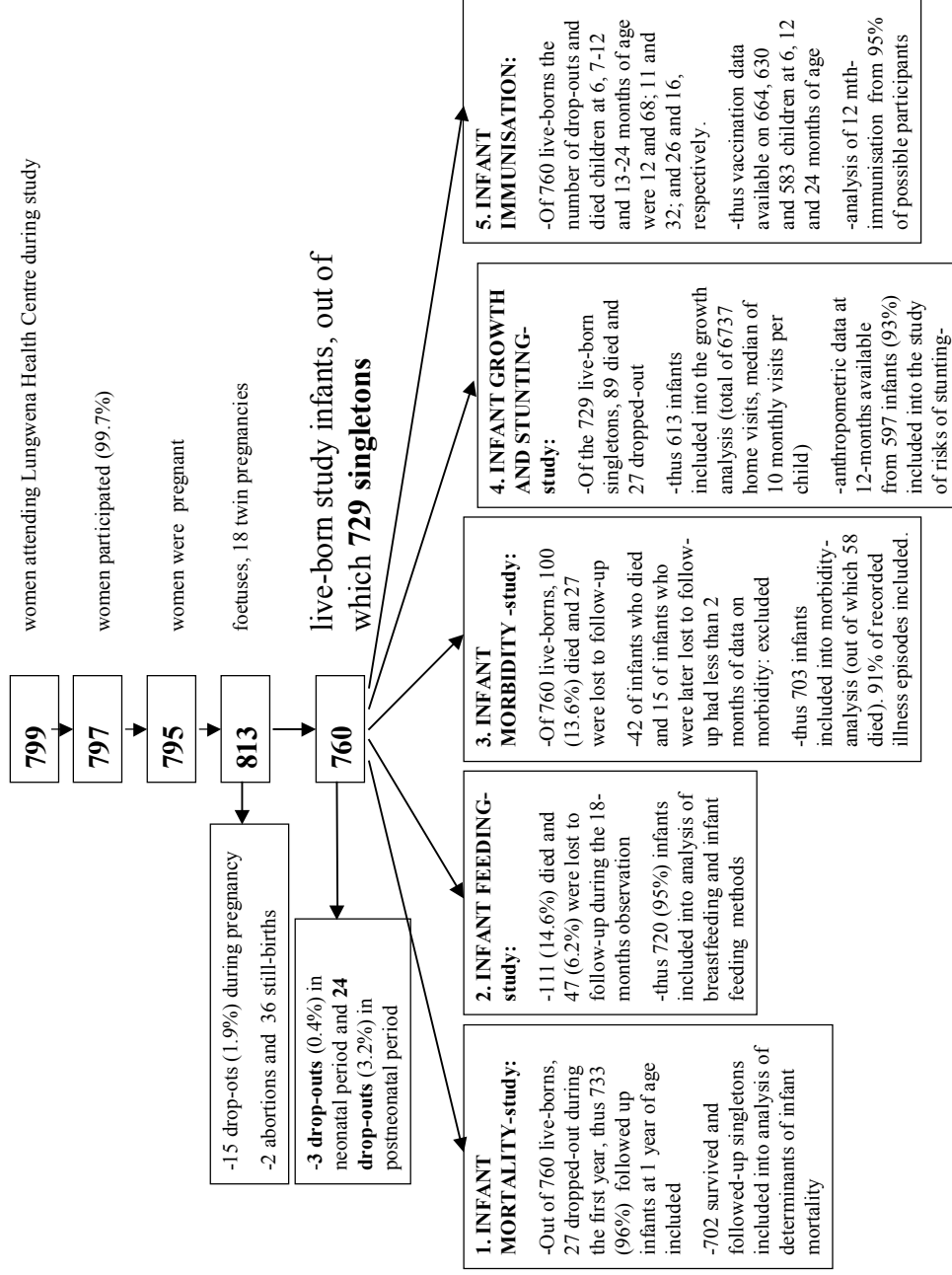**Fig. 7.** Enrolment and follow-up in the five sub-studies of this thesis.

799 women attending Lungwena Health Centre during study

797 women participated (99.7%)

795 women were pregnant

813 foetuses, 18 twin pregnancies

760 live-born study infants, out of which **729 singletons**

-15 drop-ots (1.9%) during pregnancy
-2 abortions and 36 still-births

-**3 drop-outs** (0.4%) in neonatal period and **24 drop-outs** (3.2%) in postneonatal period

1. INFANT MORTALITY-study:

-Out of 760 live-borns, 27 dropped-out during the the first year, thus 733 (96%) followed up infants at 1 year of age included

-702 survived and followed-up singletons included into analysis of determinants of infant mortality

2. INFANT FEEDING-study:

-111 (14.6%) died and 47 (6.2%) were lost to follow-up during the 18-months observation

-thus 720 (95%) infants included into analysis of breastfeeding and infant feeding methods

3. INFANT MORBIDITY -study:

-Of 760 live-borns, 100 (13.6%) died and 27 were lost to follow-up

-42 of infants who died and 15 of infants who were later lost to follow-up had less than 2 months of data on morbidity: excluded

-thus 703 infants included into morbidity-analysis (out of which 58 died). 91% of recorded illness episodes included.

4. INFANT GROWTH AND STUNTING-study:

-Of the 729 live-born singletons, 89 died and 27 dropped-out

-thus 613 infants included into the growth analysis (total of 6737 home visits, median of 10 monthly visits per child)

-anthropometric data at 12-months available from 597 infants (93%) included into the study of risks of stunting-

5. INFANT IMMUNISATION:

-Of 760 live-borns the number of drop-outs and died children at 6, 7-12 and 13-24 months of age were 12 and 68; 11 and 32; and 26 and 16, respectively.

-thus vaccination data available on 664, 630 and 583 children at 6, 12 and 24 months of age

-analysis of 12 mth-immunisation from 95% of possible participants

Table 6. Background data of the live-born children (760) included into the study.

Variable	Proportion (%)
Mother < 20 years of age	22
Mother single, divorced or widowed	3
Mother non-Muslim (Christian, other)	6
Mother illiterate	86
Mother HIV-infected	19
Child´s birth order 1st (primiparas)	24
2nd/3rd	35
4th/5th	22
>5th	19
Age of previous child in the family < 36 months	20
36 months or over	56
Child´s gender (girl)	49
Month of birth Jan-March	17
Apr-Jun	15
July-Sept	33
Oct-Dec	35
Home delivery	59
Preterm deliveries, child born < 38 gestational weeks	20
Distance to health care (km) < 2.5	25
2.5-4.9	23
5-7.4	23
> 7.4 km	29
Residential area: Area 1 (4.2)*	12
Area 2 (6.2)	22
Area 3 (2.3)	33
Area 4 (7.8)	33

Cultivated land (hectares)< 0.5		63
	0.5-0.9	21
	1.0-1.4	8
	>1.4	8
Family owns some animals		50
The household has more than one room		15
The family owns a bike, car, mattress or a radio		46
The household has a latrine		76
The family gets the drinking water from unsafe source		64

*The Lungwena villlages were divided into 4 different areas ("Gulu"s), and the average distance to the health centre form the mid-point of the area is shown in the parenthesis.

5.2 Levels, immediate causes and predictors of infant mortality (Articles I and III)

Infant mortality rate (IMR) was 136 deaths / 1000 live born children. Mortality was slightly higher among boys than among girls and more than twice as common for twins than singletons (table 2 in Article I). Of the 760 infants born alive, 733 were singletons and sixty percent of all births were home births. Sixty-five percent of children who died, died at home. More than a quarter of deaths occurred neonatally, but thereafter mortality remained constant. There was no seasonal clustering of infant deaths.

Table 7 shows the disease-specific causes of infant deaths among the studied cohort. Acute respiratory infections, malaria and diarrhoeal diseases formed almost two-thirds of the immediate causes of death. Those infants who died at home had more respiratory infections as a cause of death (15 (24%) compared to 2 (8%) among those infants who died at hospital), but this difference did not reach significance (p=0.085).

Table 7. Disease-specific causes of infant deaths of study cohort.

Diagnosis	Girls % (n)	Boys % (n)	All % (n)
Acute resiratory infection	*27 (12)	29 (16)	28 (28)
Malaria	27 (12)	18 (10)	22 (22)
Diarrhoea	7 (3)	18 (10)	13 (13)
Preterm baby or low birth weight	4 (2)	5 (3)	5 (5)
AIDS	0 (0)	7 (4)	4 (4)
Birth injury or asphyxia	2 (1)	5 (3)	4 (4)
Other	20 (9)	9 (5)	14 (14)
Not known	13 (6)	7 (4)	10 (10)
Total	100 (45)	100 (55)	100 (100)

* Proportion (absolute number) of children dying because of the defined condition.

The case fatality rates were 4% for malaria, 2% for ARI, 1% for diarrhoea and 5% for other illness episodes. There were no differences in the total morbidity or the duration of illnesses among the survivors and the non-survivors (Article III).

During the acute illness episodes, traditional healers were significantly more commonly consulted by those families whose infants died than by those families whose infants did not die (OR 1.8, 95% confidence interval 1.1 to 3.0, p = 0.02, Pearson chi-square test). This trend was apparent for all illness categories, but most notable during ARI episodes (OR 2.8; 95% CI 1.0 to 7.7, p = 0.04, Fisher's exact chi-square test) (Article III).

*Determinants of infant mortality (***Article I****)*

Univariate analyses indicated that among singleton live-born infants maternal primiparity, poor maternal weight gain, low birth weight and birth between May and July, maternal HIV infection, preterm birth of child and young age of mother, as well as some socio-economic variables were associated with deaths in infancy (Table 4, Article I).

In a multivariate analysis controlling for gender of child, source of drinking water, sanitation facilities, ownership of domestic animals, presence of fishermen in the household and some other variables, season of the child´s birth was the strongest predictor of infant mortality (adjusted OR 2.5). Other independent predictors were maternal HIV-infection (adjusted OR 2.0) and primiparity (adjusted OR 2.0), preterm birth of child (adjusted OR 2.0), smaller cultivated land areas (each additional hectare increased the survival probabilities of an infant by 50%) and longer distance to the health centre (each extra kilometre to health centre increased the risk for mortality by 10 %) (Table 5, Article I).

Based on the prevalences and adjusted odds ratios, maternal primiparity accounted for 22%, birth in May-July for 22%, preterm births for 17% and maternal HIV-infection for 15% of the population attributable risk (PAR%) for infant mortality in Lungwena. When multivariate analysis was restricted to infants surviving the neonatal period, strongest independent predictors of mortality were birth between May and July (adjusted OR 2.4), maternal HIV-infection (OR 2.3) and maternal

primiparity (OR 2.3). In contrast, preterm birth was not associated with post-neonatal mortality.

5.3 Determinants of breastfeeding and complementary feeding (Article II)

Every child in the cohort was breastfed throughout the follow-up period, i.e. from the first month of life to 18 months of age. The exclusive breastfeeding rates at one, two, three and four months of age were 19%, 8%, 2% and 0%, respectively. The corresponding rates for predominant breastfeeding at the same ages were 44%, 31%, 11% and 4% respectively (Article II).

As many as 30% of all infants were receiving complementary porridges already during their first month of life. The median ages when complementary foods and family foods were introduced were 2.5 and 6.3 months, respectively. At the age of four months virtually every infant in the cohort was receiving complementary foods, and by ten months of age, almost all children were eating family foods (Table 2, Article II).

Predictors of exclusive breastfeeding or delayed onset of complementary foods

According to multivariate analysis better adherence to infant feeding recommendations was associated with increased maternal education, greater number of children in the family, larger size of family's cultivated land area and delivery at health facility. In most cases, one unit increase in the predictor variable was

associated with a 2 - 8 day prolongation of exclusive breastfeeding period or in a similar delay in the onset of complementary feeding (Table 3, Article II).

5.4 Infant morbidity and health-seeking (Article III)

The average infant in this study, which comprised 703 children, suffered from 3.8 illness episodes during the first year of life. The most common entity was diarrhoea (1.3 episodes / child / year), followed by ARI (1.1 episodes), malaria (0.7 episodes) and other diseases (0.6 episodes). On average, each participant was ill for 2.7 days per month, corresponding to 32 days during the first year of life. Categorised according to the disease, the yearly number of illness days for diarrhoea, ARI, malaria, and other diseases were eleven, nine, five and seven, respectively (Table 2, Article III).

The median (25th; 75th percentile) duration of all illness episodes was 7 (4;9) days. In approximately half of the illnesses the symptoms lasted for more than seven days and in 13% for more than two weeks. Ten percent of diarrhoea episodes were persistent (i.e. lasted for more than 14 days) (Table 2, Article III). One third (37%) of the illness episodes were managed at home without external help. The traditional healer was consulted in 16% and a medical professional in 55% of the episodes (Table 5, Article III).

Distribution of morbidity according to infant´s age and calendar month

The frequency of illnesses increased steadily during the first six months of life, mainly due to increasing numbers of diarrhoea episodes. Acute respiratory infections were most frequent during the first three months of life, and malaria episodes were more common later in infancy (Figure 1, Article III). The morbidity was highest in April-May, just after the rainy season, when ARI and malaria episodes were common. The rainy months were the peak season for diarrhoea (Figure 2, Article III)

Independent predictors of morbidity

According to multivariate logistic analysis, residential area far away from the health centre was the strongest predictor of morbidity (AOR 4.4). Other independent determinants included baby's weight during first three months of age, number of children in household, safety of drinking water, and paternal monogamy. Unsafe drinking water increased the morbidity risk by 50% and each child in the family by 20%. On the other hand, morbidity risk was lowered by 23% for each additional Z-score unit (approximately 800 g) in the baby's weight during the first three months of life (Table 4, Article III).

5.5 Infant growth, the development of malnutrition and determinants of severe stunting (Article IV)

Low weight for age (WAZ<2) was often found already during the first six months of life, but became much more frequent during the rest of infancy. Moderate and even severe stunting (HAZ < -2 and <-3, respectively) was occasionally recognised already at three months, and increased in prevalence throughout the follow-up period. At one year of age, 40% of infants were underweight (WAZ<-2), over 70% stunted (HAZ<-2), 35% both underweight and stunted and 31% severely stunted. More than 30% had a MUAC below 13.5 cm but very few were markedly wasted (WHZ < -2) (Table 2, Article IV).

Despite the slightly faster average growth, boys were more frequently underweight or stunted, especially after 6 months of age. The prevalence of moderate underweight (WAZ < -2) was 33% vs. 27% at nine months and 44% vs. 35% at 12 months for boys and girls, respectively. At one year of age, 15% of boys and 8% of girls were severely underweight (WAZ<-3, 95% CI$_{diff}$ 3 to 13%). Similarly, 37% of boys and 24% of girls were severely stunted at this age (HAZ<-3, 95% CI$_{diff}$ 6 to 21%) (Article IV).

Independent predictors of severe stunting

According to the multivariate modelling with logistic regression, the strongest predictor of severe stunting at twelve months of age was low weight during the first three months after birth. Additional independent risk factors included inappropriate weaning pattern (adjusted odds ratio 3.1), high morbidity (AOR 2.8), maternal height

under 150 cm (AOR 2.2), male gender (AOR 1.9), and home delivery (AOR 1.7)
(Table 4, Article IV).

5.6 Timing and risk factors for incomplete immunisation (Article V)

The coverage for EPI-vaccinations among study infants was high, except for
measles. At one year of age, the proportion of children who had received BCG, three
doses of polio, three doses of DPT and measles vaccination were 99%, 91%, 90%
and 64% (Table II and Figure 1, Article V).

The three doses of DPT were given at a median (range) age of 10 (0 - 52), 16 (7 - 57)
and 24 (13 - 103) weeks, respectively, i.e. at 2, 4 and 6 months. The three doses of
polio vaccination were given at 9 (2 - 52), 16 (7 - 57) and 23 (11 - 103) weeks. The
median (range) age when the children received measles vaccination was 44 (25 -
104) weeks, i.e. 10 months (Figure 1, Article V).

Eighty infants (9.7 %) received measles vaccination before the age of nine months
and 15 (2.0 %) before the age of eight months. Of all children who remained in the
follow-up at two years of age, eighty-one per cent received measles vaccination
through normal health centre services and 3% during the national outreach campaign
(Article V).

In early 1996, when the oldest study children were 7 to 9 months old, there was an
epidemic of measles in the area. Altogether 42 children (8 study infants) were
reported to have had a severe disease. The mean age of the study infants who fell

sick was 5.4 months and they were all unvaccinated against measles. One study infant died. There were no reported cases of polio, diphtheria or tetanus (Article V).

Independent predictors of non-compliance with recommended vaccination schedule

A multivariate analysis controlling for a number of socio-economic variables indicated that residence in areas with no mobile under-five outreach clinic, birth between April and June and birth at home were all independently and statistically significantly associated with failure to receive all appropriate immunisations by the age of one year (each factor doubled the risk for lacking proper immunisation)(Table III, Article V).

6. DISCUSSION

This community-based prospective study was conducted to investigate the immediate causes of deaths, the patterns of morbidity, and the underlying determinants of infant mortality among a cohort rural Malawian infants. On the basis of literature review and previous studies from Africa, our initial starting hypothesis were that high infant mortality in Lungwena might be a result of high morbidity to infectious diseases, late health-seeking behaviour when the child become sick, maternal HIV and poor maternal weight gain during pregnancy, low birth weight of the baby and malnutrition of the children.

Carrying out a prospective follow-up study in a rural sub-Saharan country with the help of local community assistants and families succeeded very well. Malawian people were very co-operative and very few refused participation or were lost to follow-up so that 91% to 96% follow-up was reached in the different sub-studies.

Infant survival is still an important task for health care in Malawi. A very high infant mortality rate of 136 per 1000 live births was exactly the same than the national figure often given for Malawi (UNICEF 2000). The 760 live-born infants and one hundred infant deaths in our study cohort formed the basis for the analysis of the mortality-related issues. Our prospective, longitudinal birth-cohort with exactly known birth and death places and dates and our monthly interviews gave a good opportunity to obtain reliable information on mortality in a rural community in sub-Saharan Africa.

Two out of three infants who died, died from a quite acute, short infectious disease. Most of the episodes except malaria were not of any tropical origin, but common respiratory and gastroenterical infections, which cause a lot of morbidity in infants also in developed countries. With all the capacity we had for defining the immediate causes of deaths by verbal autopsies and interviews by home visits, the illnesses seemed to be treatable episodes of respiratory infections, malaria and diarrhoea. Verbal autopsy was possible to carry out among these mostly illiterate yao-muslim families in Lungwena, as the parents were quite open to answer the questions. In fact, these interviews were the only way to know the possible immediate causes, as most of the infants who died (65%) died at home.

6.1 The hypothesis of high morbidity leading to mortality

Respiratory infections, malaria and diarrhoea formed also the main morbidity (two-thirds of the episodes) in infancy in Lungwena. However, slightly more than one episode of diarrhoea, malaria and ARI per year is not much, and far less than what we expected. One of our starting hypothesis for this study was that the children die because they are so often ill. However, the morbidity seems to be the same than in developed countries. The observed number of illness episodes was lower in Lungwena (mean 3.8 episodes/child/year) than morbidity in some earlier reports from Sub-Saharan Africa (2.3-6.5 episodes / year) (Oni et al.1991, Lindtjoern et al. 1992, Muhe et al. 1995).

This can be explained by the fact that our study period covered only the first year of life, whereas other cohorts have included also older children i.e under-five morbidity

(Lang et al. 1986, Oyedije and Osinusi 1990, Selwyn 1990, Wafula et al. 1990, Oni et al. 1991, Lindtjoern et al. 1992, Dikassa et al. 1993, Manun´ebo et al. 1994, Muhe et al. 1995). During the first year, infants are still partially protected against infectious diseases both through maternally acquired humoral immunity as well as through reduced exposure to microbes whilst breastfeeding. In our material, under-six-month-old babies were all partially breastfed and had significantly fewer illnesses than the older infants.

There were no differences in the total morbidity or the duration of illnesses amongst the survivors and the non-survivors. It seems that the high number of infection episodes per se is not the main problem that makes the infectious attacks lethal. Instead, the duration of illnesses is in general long, the children are not treated at all or not properly or not in time, or the illness episodes are very severe because of other underlying health problems predominant in the region. The average of thirty-two days of illnesses per year is a very high figure. The episodes were long-lasting with the median duration of one week and 13 % (10 % of diarrhoea) of all episodes lasted longer than two weeks. Such persistent illnesses place infants into the dangers of malnutrition. Especially recovery from long and severe diarrhoea episodes demands proper care and should include continued breastfeeding, rehydration and complementary feeding for catch-up growth.

Among those 58 infants who died and of whom we knew at least two months morbidity follow-up information, the case fatality rates found were 4% for malaria, 2% for ARI, 1% for diarrhoea and 5% for other illness episodes. The number of

infants in this analysis is quite low, but still these data suggest that at the community level such fatalities are common, especially those caused by malaria.

While reported cases of malaria have remained constant elsewhere in the world, incidence rates in tropical Africa, where 90 percent of global cases occur, has grown 5 to 20 % annually since the emergence of chloroquine-resistant parasites in the late 1970´s (Brinkman and Brinkman, 1991). The disease continues to have a high case-fatality rate among young children, who account for more than half of the cases in Africa.

6.2 The hypothesis of late health-seeking behaviour

Our other hypothesis was, that the infants die in Malawi because they are brought to modern health care too late or not at all. The results address indeed the importance of health-seeking behaviour, as the traditional healers were signifantly more commonly consulted by families whose infants died than by those whose infants did not die. This was especially true for infants with respiratory infections. However, modern health care was reported to be used surprisingly often, as a medical professional was consulted in over half of the illness episodes (lethal and none-lethal). On the other hand, one-third of the illnesses were managed at home without external help and a traditional healer was consulted in 16%. A very scary finding was, that many infants died at home shortly after visiting a modern health facility.

6.3 Vaccine-preventable diseases

Although infectious diseases continued to be a major problem in Lungwena, very few infants died from a vaccine-preventable disease, as only one infant died of measles, and there were no reported cases of polio, diphtheria or tetanus. Only one pertussis-like disease was recorded, and which did not lead to death of the infant. The over ninety percent coverage of BCG, DPT and polio vaccinations are high, and are in accordance with findings from recent cross-sectional surveys (Malawi DHS 1992, Malawi Social Indicators Survey 1995).

However, the measles vaccination covered only 64 % of the cohort at the age of one year, a figure that is somewhat lower than that of a recent national surveys or that reported by UNICEF (UNICEF 1999, Malawi DHS 1992, Malawi Social Indicators survey 1996). By the age of two years, eighty-one percent of the children had received measles vaccination either at the health centre or outreach clinics. With such vaccination coverage, measles virus can still spread in a community, as also evidenced by the miniepidemic in our study area. During a 5-day national campaign, one-fourth of the unvaccinated children who were younger than two years of age were identified and immunised. An even higher proportion (46/82) of previously unimmunised children who were over 2 years old were also reached during this vertical intervention. So the campaign complemented regular health services in the study area by raising measles vaccination coverage closer to the 85-90% normally required to achieve herd immunity (Anderson and May 1990, Schlenker et al. 1992).

6.4 The hypothesis of maternal HIV-infection increasing the infant mortality

One initial hypothesis was, that maternal HIV-infection is a major underlying cause for infant mortality in Lungwena. In the end of 1980, vertical HIV-infection was suggested to have increased infant mortality rates in some sub-Saharan African countries by 15-26% (Lallemant et al. 1989, Ryder et al. 1989). Subsequent studies, many carried out in Malawi, indicated that children born to HIV-positive mothers had at least two-fold mortality rates compared to children whose mothers were HIV-negative (Aiken 1992, Miotti et al. 1992, Lepage et al. 1993, Bloland et al. 1995, Taha et al. 1995, Bloland et al. 1996).

Our study of singleton children confirmed this finding and indicated that on a population level, maternal HIV-infections accounted for 15 % of all infant deaths, approximately as many as maternal primiparity (22%), births between May and July (22%) and preterm births (17%). Thus, HIV infection was an important, but not the main determinant of infant mortality in this cohort, despite the almost 20% infection prevalence among the mothers.

Despite these somewhat comforting results, the impact of maternal HIV on infant mortality may still increase in future. Perinatal transmission rates can possibly increase over time as more HIV-positive mothers develop more advanced HIV-infection, and thus will be more infectious to their offspring (Preble 1990). HIV-seroprevalence among pregnant women in urban Malawi rose from 2.0 % in 1985 to 32.8 % in 1996, i.e., a 16-fold increase in 11 years. Young women with fewer pregnancies and more education are most likely to be HIV-infected (Taha et al.

1998). Because this region is mostly rural, two-thirds of additional deaths will be in the rural areas, despite the fact that urban HIV-infection rates have currently been considerably higher than the rural rates. It is possible that after 5-10 years maternal HIV-infection is a far more stronger predictor of infant mortality even among rural communities, than it was during the years 1995-1998.

6.5 Other underlying determinants of infant mortality

Maternal primiparity as an underlying risk factor for infant mortality has been noticed also in earlier cross-sectional and cohort studies from developing countries. Part of this effect has been suggested to be attributable to younger maternal age, more frequent maternal infections and larger share of preterm deliveries and low-birth-weight babies among the primiparous women (Arkutu 1978, Brabin 1991, Bloland et al. 1995, Bouvier et al. 1997). In our material, primiparity remained an independent and important risk factor even after adjustment for maternal age, child's preterm birth and numerous socio-economic variables.

A defined season of birth (May to July in the studied cohort) as an underlying determinant of mortality was a new finding. The explanation for this may be, that rural agricultural communities in southern Malawi, with their main staple food being maize, are very dependent on seasonal weather-changes, which influences food intakes of both mothers and their offspring (food shortage in the beginning of rainy season November-February, then maize-and other crop-harvesting in March-May). Maternal and infant malaria-infection are also more common when the rainy season changes to cold season (April-June). Maternal malaria-infection and poor weight

gain especially during the last trimester of pregnancy places the offspring in the danger of preterm births, intra-uterine growth retardation and anaemia.

Bloland et al. found in their study in rural Malawi, that low birth weight, primiparity, maternal HIV and combination of low education and low socio-economic status were the most important determinants of infant mortality. Maternal HIV predominated for postneonatal deaths. Factors that were significant in univariate analysis but not significant in the final multivariate models included preterm birth, previous adverse reproductive outcome, dying during high malaria transmission season, and being born at home (Bloland et al. 1996, Mangochi Malaria Research project 1987-1989). However, in that study hospital births accounted for 63.8% of the births among enrolled women, and thus there could have been a bias of having more risk-pregnancy mothers and more LBW-babies than in our study carried out in rural Mangochi with over 60% of births occurring at home.

The other two earlier studies conducted in Malawi found low maternal education, father´s occupation, geographical area, first births and higher birth orders (Madise and Diamond 1995, Manda 1999) and dead of the preceding birth/child, low birth weight and no safe drinking water (Manda 1999) as the underlying determinants associated with infant mortality. In the study of Manda (which used Malawi DHS 1992 indicators) maternal schooling had only a marginal impact on infant mortality in the whole Malawi. Region and safe water were stronger predictors of IMR (Manda 1999). We did not find an association between higher maternal school education and lower risk of infant mortality. In fact, univariate analysis revealed, that maternal education was a risk for infant mortality in Lungwena, although the numbers of

mothers with such schooling were not large enough for meaningful statistical analysis. This result may be a sign of increased risk of maternal HIV-infection among higher educated persons in Malawi. In fact, the same kind of result was found by Miotti and Dallabetta in Malawi (1992); an educational level above grade school (Standard 8) for both the mother and her spouse were significantly and positively correlated with HIV-1-infection.

Male children tend to have higher mortality than female children especially in the neonatal period, but also slightly higher among postneonatal age groups in sub-Saharan Africa (Mirza et al. 1990, Madise and Diamond 1995, Jaffar et al. 1997). A similar slight gender difference was found also in our study, although the difference was not significant. Birth order and maternal age have been recognised in many studies to have a J-shaped relationship with IMR (Madise and Diamond 1995). In our study of singleton infants higher birth order, birth interval or maternal age did not come up as independent predictors of mortality.

The results of our cohort study also revealed, that inappropriate breastfeeding and complementary feeding methods were important underlying risk factors for increased morbidity and malnutrition, and thus placed infants into risk of infant death. The exclusive breastfeeding period was short (mostly one month), complementary foods were started very early and the diets for older infants were not very diverse. Early complementary feeding increases the risk of enteric infections and mortality, and also risk for postnatal transmission of human immunodeficiency virus infection from the breast milk of an infected mother (Coutsoudis et al. 2000). Since almost 20% of mothers in Lungwena were HIV-infected and only one third of families had access to

safe drinking water (Kulmala et al. 2000), the short periods of exclusive or even predominant breastfeeding were likely predisposing the infants to health problems.

Breast-feeding provides infants with complete nutrition to age 4-6 months, about half of the nutritional needs for life months 6-12, and up to one-third of needs for life months 12 to 24 (de Cock et al. 2000). Breastfeeding even after 6 months of age up to 24 months provides the growing child important additional nutrition if the available food otherwise is insufficient. The local instructions suggest, that if breastmilk substitute is not available (6 months of formula feeding costs US 300 $ and the heating or treating the necessary water is also far too expensive for families in Lungwena), nutrient enriched family foods (oil and sugar added) should be provided to infants from the age of six months to two years five times a day (de Cock et al. 2000). This is clearly unreachable advise for families in Lungwena where the infants get hardly twice a day some thin maize-porridge especially during food-shortage-months.

Non-appropriate infant feeding methods are very common in Lungwena, as 59 % of families gave complementary porridges too early or family foods too late to their children, and 13 % of families had both non-appropriate behaviours. In this study we showed, that non-compliance with infant feeding guidelines resulted in more than doubling of the malnutrition risk at 1 year of age. Other studies in Africa and Malawi have also addressed the inappropriate and inadequate infant feeding methods as major risk factors for malnutrition after six months of age (Burgess et al, 1975; Lindskog et al, 1988; Shrestha et al., 1990). Consequently, if the baby is born with birth weight over 2500 g and breastfeeding is exclusive for the first 4 to 6 months of

life, and is accompanied by adequate complementary foods, faltering in weight does not occur before nine month of age among low-income infants (Cohen et al., 1995).

6.6 The hypothesis of malnutrition as underlying cause of infant mortality

At one year of age, forty per cent of infants were underweight, over two-thirds stunted, thirty-five per cent both underweight and stunted, and 12 % and 31 % severely underweight and stunted. On the other hand, only 2 % were acutely wasted at twelve months. The results indicate, that chronic stunting and mild-to-moderate underweight starts early and is far more common than acute or severe malnutrition in Malawi. The prevalence of moderate malnutrition is higher among this cohort of rural infants than among urban Malawians. According to Malawi DHS only 27 % of 6- to 11- month-olds were stunted and 9 % were severely underweight (Malawi DHS 1992). The strong imbalance between rural and urban Malawians has also been noticed by other studies (Malawi DHS 1992, Pelletier and Msukwa 1991).

One unexpected finding in our study was that the male infants had more severe growth faltering after 6 months of age than the females. The reasons behind this were not fully investigated, but the gender difference has been noticed previously by cross-sectional studies (Malawi DHS, 1992). In addition, a longitudinal cohort study from Northern Malawi showed that the mean height-for-age of female infants was higher than that of boys (Pelletier and Msukwa, 1991). One explanation given earlier by Pelletier has been that among girls, proximate factors like feeding practices and use of health care may mitigate against the effects of household resource factors to a greater extent than among boys.

The low weight in the first three months of life was found to be the strongest predictor of malnutrition (chronic malnutrition, i.e. stunting) at 1 year of age in our cohort, but also non-appropriate infant feeding methods, birth between March and May, many diarrhoea episodes during infancy and home delivery were significant risk factors.

We did not investigate the association between growth faltering (stunting) and infant mortality in this thesis. However, it is known from many previous studies, that malnutrition is a determinant of infant mortality, and also low height-for-age predicts the risk of infant death within a year after a measurement (Pelletier 1994). In our cohort, the males had a slightly higher risk of infant mortality between the age of 1 and 3 years (unpublished finding), and a higher proportion of severely stunted and underweight male infants between the ages 6 and 12 months of age might have contributed to this. However, it was beyond the scope of this thesis to examine this hypothesis any further.

6.6 Strengths and limitations of the study

The main strength of the present study lies in its prospective, community based and rural setting as few such studies have been performed in sub-Saharan Africa. The study design facilitates production of data that represent the majority of population, as only a fraction of the population lives in urban circumstances in sub-Saharan Africa and Malawi. In addition, the high antenatal coverage and minimal loss to follow-up ensures a highly representative study sample in the present cohort. As only a few such prospective cohort studies have previously been carried out in low-income countries, both the descriptive and analytical results of this study are of interest.

For most sub-Saharan countries accurate measures of infant health, morbidity and mortality have remained unknown, and the socio-economic determinants behind them have not been explored. The fact that this study was conducted in one of the least developed countries in the world, in Eastern sub-Saharan Africa, by repeated monthly home-visits to rural families and that it considered several aspects of infant health instead of just concentrating on one or a few of them, makes this study valuable.

However, there are limitations that should be born in mind when interpreting the results. It may be that the results are not generalizable to whole Malawi as such. Malawi is divided into three different districts, and the cultural and behavioural habits, environment, season, staple food and educational and socio-economic variables differ from one district to another. Lungwena in Southern district, where

this study was conducted, suffers from hot and dry seasons and endemic malaria, has mainly yao-muslim people with matrilineal culture and the families are poorest and of lowest education of the districts. The people in Northern district for example are mostly Christians, more educated and use cassawa instead of maize as a staple food.

One major limitation of the study was the absence of complete birthweight data. The high number of unknown birthweights prevented the inclusion of birthweight in the analysis which we used to examine the predictors of infant mortality and malnutrition. The average weight (z-score) during the first three months of life was used instead. This procedure might have left some small for gestational age- babies unrecognised.

The data about the infant mortality rates and the age and season of infant mortality are probably highly reliable. One of the strengths of this study is that the exact birth and death dates were recorded. The exactly known ages of the children were essential also for the other analyses. However, the causes of infant death were for obvious reasons less than accurately recorded, as they were diagnosed using interviews of the parents. Verbal autopsy method carries a recall bias, and sometimes it is not easy to distinguish between the symptoms of e.g. acute malaria, dehydration or meningitis. Also some recall biases and methodological problems in categorising the diseases and separating episodes from persistent diseases are likely to have occurred in the analysis of morbidity. However, both verbal autopsies and the information on morbidity were usually gathered within a month after the child had fallen ill or had deceased, and both interview forms included prompted vernacular questions of different symptoms and signs. Also, the relative proportions

of different diseases and death diagnosis were very similar to those recognised elsewhere in Malawi and Africa.

The fact that not many socio-economic variables were found to be associated with adverse outcomes of infant health may have been due to the homogeneity of the study population. Most of the studied mothers were illiterate, had no significant possessions, were from matrilineal yao-muslim families, and were subsistence farmers with very small cultivated land area, and hence the socio-economic influence on infant life could not be really detected. The same homogeneity applies to the breastfeeding habits, as all the mothers universally breastfed their new-borns for the first 18 months of life and gave supplements to breastmilk almost allways already during the first month. This hindered us to analyse the impacts of breastfeeding and non-breastfeeding on infant growth and mortality. Nevertheless, the importance of breastfeeding on infant mortality is already well documented in other studies, and it was not our aim to investigate it further.

The importance of maternal HIV on determining the infant mortality was shown in our study and the fact that it was tested at least from pregnant mothers is a strength of this study. However, in the absence of paediatric HIV-testing, we could not detect directly the impact of the disease on rural malawian infant´s growth, morbidity, mortality and health-seeking behaviour. Another limitation to health-seeking behaviour analysis is that we did not ask the guardians about the exact treatments given to infants with different illnesses. Especially the knowledge on the use of oral rehydration therapy for diarrhoeal diseases, antimicrobial treatment for pneumonia,

antimalarial therapies for malaria and nutritional rehabilitation of malnutrition would

have added a great deal to analysis.

7. KEY FINDINGS AND CONCLUSIONS

The following eight points highlight the most important results of the studies comprising this thesis. The findings are mentioned in the same numerical order as the aims of the study.

1. The infant mortality in Lungwena, Malawi was 136 per 1000 live births between 1995 and 1998. Over two thirds of deaths took place at home. After the perinatal period, the risk of dying continued at the same level for the whole infancy period. The three most important immediate causes contributing 2/3 of the deaths were acute respiratory infections, diarrhoea and malaria.

2. The case fatality rates were 4% for malaria, 2% for ARI, 1% for diarrhoea and 5% for other illness episodes. There were no differences in the total morbidity or the duration of illnesses amongst the survivors and the non-survivors. During the acute illness episodes, traditional healers were significantly more commonly consulted by those families whose infants died than by those whose infants did not die.

3. The determinants of infant mortality were mother´s primiparity, maternal HIV-infection, preterm birth, long distance to health centre from home and small farm land area for cultivation. The birth season was the strongest predictor of infant mortality. Preterm birth was a risk factor only for neonatal period. Maternal primiparity accounted for 22%, birth in May-July for 22%, preterm births for 17% and maternal HIV-infection for 15% of the population attributable risk for infant mortality in Lungwena.

4. Breastfeeding was universal up to 18 months of age in Malawi, but the culture of exclusive breastfeeding was missing. The exclusive breastfeeding rates at one, two, three and four months of age were only 19%, 8%, 2% and 0%, respectively. The mothers with more education and experience of previous children were more attached to exclusive breastfeeding, but still supplements to breastfeeding (water and thin porridges) were universally started too early.

5. Diarrhoea, respiratory infections and malaria were the main causes of morbidity in Lungwena. The number of illness episodes was rather low (3.8 episodes per year), but the episodes lasted usually long, at least one week. Ten per cent of diarrhoea episodes were persistent. One third of the illness episodes were managed at home without external help, and traditional healer was consulted in 16% and a medical professional in 55% of episodes. The residential area, unsafe source of water, low birth weight and crowding in family were risk factors for increased morbidity.

6. Moderate and even severe stunting were present in several children already at three months of age, and its prevalence increased steadily throughout infancy. Decline in relative weight started usually between 6 and 9 months of age. At one year of age, fourty percent of infants were underweight (WAZ<-2), over 70% stunted (HAZ<-2), 31% severely stunted (HAZ<-3), and 35% both underweight and stunted. Boys were significantly more commonly underweight and stunted at one year of age than girls.

7. The independent risk factors for severe stunting (HAZ <-3) at 12 months of age were small birth size (AOR 14.3), inappropriate weaning pattern (AOR 3.1), high morbidity to illnesses (AOR 2.8), male gender (AOR 1.9), and home delivery (AOR 1.7).

8. Over 90% of studied infants were vaccinated against tuberculosis, polio and diphtheria-pertussis-tetanus with three doses at one year of age, but only 64% were vaccinated against measles. National campaigns and mobile out-reach clinics were important methods which increased vaccination coverage closer to the needed over 80 % herd immunity against measles.

Maternal HIV infection was an important, but not the main determinant of infant mortality in this cohort, despite the almost 20% infection prevalence among the mothers. The lack of exclusive breastfeeding and deliveries at home increased the theoretical risk of vertical transmission of HIV to newborn infants. The infants of HIV-infected mothers deceased two times more often during infancy than the infants of non-infective mothers. On the other hand, the birth during months after rainy season (May-July) increased the infant mortality risk by a factor of 2.5, and maternal primiparity by a factor of 2.2.

In addition to HIV, the other infectious diseases (acute respiratory infections, diarrhoea and malaria) and many underlying determinants (primipara mother, low maternal weight gain during pregnancy, low birth weight, chronic malnutrition (stunting) and behavioural aspects associated to breastfeeding and health-seeking habits) still keep the infant mortality high in rural Malawi.

Fig 8. Independent risk factors of infant mortality in Lungwena

BASIC CAUSES
(economic or socio-cultural)   - Could not be found

UNDERLYING CAUSES
(behavioural or house-hold level)   -Health-seeking first to traditional healer when
                                       the infant fell sick

                                      -Lack of exclusive breastfeeding and too late start
                                      of family foods to infant (leading to stunting,
                                      chronic malnutrition of infants). Boys were more
                                      severely malnourished

                                      -Birth at home instead of health facility

                                      -Long distance to health centre and lack of
                                      outreach clinic

                                      -Low measles-immunisation coverage leading to
                                      increased risk of measles-episodes, malnutrition
                                      and later mortality of the contacts

                                      -Small cultivated farm land

IMMEDIATE CAUSES

          <u>Infant</u>   <u>Mother</u>

          -Respiratory infections   -Maternal HIV-infection

          -Malaria   -Maternal malaria at pregnancy

          -Diarrhoea   -Primiparity

          -Season of birth in Maly-July   -Low weight gain at pregnancy

          -Low birth weight

                                   ↓

          INFANT MORTALITY

                        (136/1000 live births, 2/3 died at home)

8. PUBLIC HEALTH IMPLICATIONS AND TARGETS FOR FUTURE RESEARCH

Neonatal mortality was high in rural Malawi, and mortality stayed high even for the rest of infancy. Preterm births, respiratory infections and delivery complications were the main reasons for the high neonatal mortality, and infections (respiratory infections, diarrhoea, malaria) predominated during the postneonatal period as causes of mortality. Therefore methods that improve diagnosis and treatment of these acute infections should be carefully searched for. The signs of pneumonia especially in malnourished infants should be recognised by community, as these infants carry high risk for respiratory infection -related deaths. Also the proportion of infants with dehydrating diarrhoea and dysentery and the treatment given could be investigated.

Endemic falciparum malaria is often fatal for young infants. In our study the case-fatality rate was 4%, being the highest of the infectious diseases. The children frequently die from this species of malaria within 2-3 days from the onset of neurological symptoms and coma, which therefore should be recognised by the families early.

Traditional healers were significantly more commonly consulted by those families whose infants died than those whose infants did not die, especially if the infant fell ill with respiratory infection. The reasons, why some families choose to use traditional healers in stead of modern health care, would be important to know.

Birth in May, June or July, being a first-born child, maternal HIV-infection and long distance from home to health centre predicted infant mortality in the cohort. The

perinatal medication against HIV for mother and new-born child could have a positive impact on infant survival. This would mean, that special waiting huts should be available for pregnant women and their near (also traditional birth) assistants next to health centre, and labour in health facilities should be encouraged. A culture of giving special advise for young mothers with their first baby on child-raising practices, including health-seeking behaviour during acute illnesses and exclusive breastfeeding, should be supported both in communities and health facilities.

Exclusive breastfeeding was very rare in Lungwena. However, from previous studies it is known that it prevents infants from diarrhoeal and respiratory morbidity and mortality, and it also protects infants from vertical transmission of HIV, compared to mixed feeding. Thus the quality of educational sessions of antenatal clinics on breast-feeding would be important to investigate, and the reasons for not following the recommendations should be inquired. The intervention with exclusive breastfeeding education, and the evaluation of growth, morbidity and mortality among rural malawian infants after better feeding practices could have a potential strategy for future research.

Ten percent of diarrhoea episodes in the cohort were persistent. The risk factors for persistent diarrhoea found in previous studies are severe malnutrition, previous similar episodes, acute diarrhoea within the preceding two months and presence of mucus and blood in faeces during acute diarrhoea. Thus antimicrobial treatment in the case of dysentery and continued support and follow-up of catch-up growth of infants should be promoted. The residential area, unsafe source of water used and crowding in family were risk factors for increased morbidity in this cohort, and

therefore building the environment more healthier with sanitation, protected water sources, better housing and family spacing continue to be important.

Faltering of linear growth is a severe problem in Lungwena. Stunting was prevalent already during the first months of life, indicating that the chronic malnutrition may start during the foetal period. Further investigations are needed on reasons of stunting, and to explain why males are more severely stunted and underweight than female babies during infancy in Lungwena, and what are the consequences of stunting for early childhood.

Measles immunisation is not yet optimal in rural Lungwena. With the coverage of 64% the herd immunity for measles is not reached, which was proven by an epidemic of measles in the community studied. From other studies it is known, that recipients of measles vaccine were partly protected from other causes of deaths than measles also, especially in areas of high mortality. Thirty-six percent of infants under one year of age and one-fifth of children under two years of age are not covered by measles vaccination in Lungwena. In the light of this knowledge, every opportunity should be used to give measles immunisation in Lungwena, with the help of functioning outreaches.

Finally, the goals of the Action Plan of Malawi´s government to decrease the amount of morbidity and mortality from respiratory infections, malaria, diarrhoea, malnutrition and AIDS, are not yet reached in this rural southern Malawian community. The continued support of GOBI-FFF programmes is needed in rural Malawi. Growth monitoring focusing on finding the severely stunted and

underweight infants during early months of life, and treatment of gastroenterical diseases with oral rehydrating solution for preventing dehydration and enhancing the catch-up growth should be promoted, and the importance of exclusive breastfeeding and measles vaccination highlighted.

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Government of Malawi-National programme of action for the survival, protection and development of children in the 1990`s

Growth monitoring

Food security and nutrition was one important sector in the Plan of Action. The current policy for the 1990´s was to reduce malnutrition, micronutrient deficiencies and to improve food security at all levels. This was predicated on the fact that malnutrition in Malawi was widespread; for example 56 % of children under 5 years of age were stunted and about 6.9% of the total visits to under-five clinics were due to micronutrient deficiencies. Although there have been impressive achievements in national crop production, 55 % of the smallholder households were food insecure. In addition, smallholders with less than one hectare of land were unable to meet their food requirements (Government of Malawi 1991).

To address these problems, The Plan outlined several objectives and strategies which included the strengthening and expanding growth monitoring and nutrition education programmes (especially nutritional status of female children); strengthening and expanding community-based child care centres and conducting applied and operational research on nutritional deficiencies including food security (Government of Malawi 1991).

Monitoring diseases like malaria, diarrhoea, respiratory infections and AIDS

Malaria has been the leading cause of morbidity and mortality of children under-five years in Malawi for a long time (19 % of deaths were due to malaria). In recent years, there have been rising incidence rates and widespread resistance to

chloroquine. Strategies to reduce the malaria deaths of U/5 children to 50 % by the year 2000 included effective case management (Government of Malawi 1991). The activities were focused on ensuring the availability of effective anti-malarial drugs at all levels of health care, expanding training of community health workers in diagnosis and treatment of malaria, and provision of microscopes for confirming diagnosing. Prophylactic treatment against malaria was ordered to be given to all pregnant women in order to minimise problems of low birth weight which is a risk factor for infant mortality. The vector control was focused on intensifying the drainage of mosquito breeding areas and promoting the use of impregnated mosquito nets and use of pesticides.

Diarrhoea has been another major killer (8 % of all deaths in children U/5 in health facilities) and is compounded by low levels of access to safe water supply, adequate sanitation and poor hygienic practices. The goals of reduction by 50 % of deaths due to diarrhoea in children u/5 and 25 % reduction in diarrhoea incidence rate pronounced in the Plan were believed to be reached by effective case management at health facility and community levels, and by education of parents on control of diarrhoeal diseases. Central objective has been the improvement of environmental health, water and promotion of use of sanitation platform latrines. The effective case management was also mentioned, but not the methods how to carry out it. The importance of early provision of oral rehydration therapy (ORT) and Intra-Veneous fluids and training communities in ORT were launched in the Plan (Government of Malawi 1991).

Respiratory infections have been also endemic with tuberculosis and pneumonia taking heavy death toll on children in Malawi (ARI accounts for 13 % of deaths in children U/5). The reduction by 1/3 of deaths due to acute respiratory infections in children mentioned in the Plan was declared to be achieved by effective case management and widespread use of recommended drugs and expanded training of communities on ARI. The more detailed recommendations of how to do these actions were missing from the plan (Government of Malawi 1991).

The Acquired Immune Deficiency Syndrome (AIDS) was noticed to have an increasing importance as a cause of deaths in the u/5 children in the Plan. Since the first case was diagnosed in 1985, nearly 10 000 cases have been reported in Malawi. The strategies for decreasing the HIV-infections in Malawi during the 1990´s included identification of information, education and communication activities, prevention of the spread of HIV/AIDS by providing condoms, screening of blood before transfusion, and by early treatment of opportunistic infections such as tuberculosis. Also the importance of conducting research to know how many children are infected by AIDS/HIV was declared in the Plan (Government of Malawi 1991).

Breast-feeding and complementary feeding

The major threats to child health from which breast-feeding provides protection in developing countries are malnutrition, gastrointestinal infections, other infections secondary to malnutrition, poor psychosocial and intellectual development, and short birth spacing. According to national Malawian guidelines an infant should be

exclusively breastfed up to 4 to 6 months of age, then the proper complementary foods should be given to a child and at 7-8 months an infant can gradually turn to family foods. Breast-feeding is advised to be continued up to two years of age of a child.

Expanded Programme on Immunization in Malawi

EPI in Malawi was launched in 1979. UNICEF in Malawi has channelled extensive external funding, which has enabled major acceleration of the national immunization programme. The result has been an impressive improvement in vaccination coverage throughout Malawi and the global Universal Child Immunization (UCI) goal of 80 % coverage for all childhood antigens was exceeded by the end of 1989 as one of the first countries in Africa (Government of Malawi 1991). Since then high coverage levels have been maintained. Measles rates in the under fives have fallen by 73 % from 1985-1991, polio cases have reduced by 96 % from 1985 with only 3 cases reported in 1991, and neonatal tetanus rates have fallen by two thirds from 1983-1990. While measles attack rates had fallen, there was an intensive drive to raise coverage to 90 %, to improve surveillance and to respond rapidly to contain outbreaks.

The success of the programme has been built up over many years. The initial smallpox immunisation of the early 1970´s led to mass campaigns against measles in the mid 1970´s and the phased introduction of other vaccines with gradual extension of services through fixed and mobile vaccination units in the 1980`s. Today EPI is one component of the family health programme of the Ministry of Health which is

fully integrated into the national health system. Ideally vaccinations would be offered side by side with other MCH services such as child-spacing, growth monitoring and antenatal care. Where possible, services are offered on a daily basis and widespread outreach services cover areas remote from health units.

The Action plan for 1990´s reminded of the maintenance of high level of immunisation coverage of at least 90 % of children under 1 year of age by the year 2000. The Malawi Immunisation strategy aimed at immunising every new-born against all six EPI target diseases before the child attains 12 months of age. The more specific targets were elimination of neonatal tetanus by the year 2000, to reduce deaths due to measles by 95 % and measles cases by 90 % by 1995, eradication of poliomyelitis by the Year 2000 (Government of Malawi 1991).

As Malawi reported 4 polio cases in 1989 and only 3 in 1990 (Government of Malawi 1991), WHO graded Malawi at stage B where it states the following condition: Any country which has over 50 % immunisation coverage and reports less than 10 cases of poliomyelitis in a year, that country is at stage B and needs to strengthen its immunisation, surveillance and control activities. Strategies for achieving the goals were immunisation of children under 1 year, identifying unserved areas and provision of regular outreach services where possible. Also ensuring adequate supply of U/5 cards as well as intensifying information and education activities for health workers and communities were seen as important methods in the Plan of action (Government of Malawi 1991).