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ABSTRACT

The incidence of preterm birth (PTB) remains high in Malawi and is currently estimated at 18.1%. Various underlying factors could contribute to PTBs in Africa, including maternal nutrition before pregnancy and during pregnancy. In Malawi, evidence is lacking making it difficult to estimate the relationship between maternal pre-pregnancy nutrition and pregnancy outcomes (duration of pregnancy and size of the newborn including weight, length and head circumference).

To address the existing gaps in knowledge on PTBs, the present study had three aims. The first aim was to describe the local perceptions of PTB, care practices for preterm infants, and challenges associated with PTB among people in a rural low-income community in Malawi. The second aim was to investigate views of the health workers about the care of the preterm infants in the health facilities and existence of any treatment guidelines such as policy documents for delivery of care to the preterm infants in Malawian health facilities. Finally, the third aim was to determine the strength of association between maternal nutritional status before and during pregnancy as well as birth outcomes among women in Malawi.

Twenty in-depth interviews and 14 focus group discussions (FGDs) were used to explore the perceived causes of PTB, care practices for preterm infants and challenges associated with PTB among community members in Mangochi district. Participants perceived that diseases such as hypertension, malaria and traditional diseases (likango and mwanamphepo) during pregnancy as well as poor diet during pregnancy, having many children and history of a PTB in the family causes/lead to PTBs. The main reported care practice for preterm infants in the community was

keeping the infant warm through dressing the infant with many warm clothes and covering an infant with wrappers, making fire inside the house and closing doors and windows to keep the house warm. Some of the reported challenges included lack of knowledge on how to properly care for preterm infants and poverty which limited the caregivers to buy the infants warm clothes and delay in seeking medical care when needed.

A total of 16 in-depth interviews with health care workers and policy makers were used to explore the care of preterm infants in the health facilities and existence of any treatment guidelines for delivery of care to the preterm infants in the health facilities. Some of the health workers reported that, policy and protocol guidelines for care of preterm infants were not available in some district hospitals and health centers, but those working in tertiary hospitals acknowledged availability of the policy and protocol guidelines. Additionally, policy makers believed that policy documents and protocol guidelines were available in all health facilities that would guide care of preterm infants. The analysis of documents also revealed that a policy document, produced by Ministry of Health (MOH) Malawi explaining care of preterm infants was available in Malawi.

The third study was a prospective cohort study nested within the International Lipid-Based Nutrient Supplement trial in Malawi (iLiNS DYAD-M) that enrolled 1,391 women with uncomplicated pregnancies in a randomized, controlled trial in Mangochi District of Malawi. Regression analysis was used to investigate the association between maternal pre-pregnancy BMI and weight gain during pregnancy with birth outcomes (duration of pregnancy and size of the newborn including weight, length and head circumference). No significant statistical associations were observed between pre-pregnancy BMI and pregnancy duration, but pre-pregnancy BMI was associated with birth weight and head circumference. Gestational weekly

weight gain (GWG) was a strong predictor for birth outcomes as it was associated with almost all measured outcomes.

In conclusion, the local perceptions of PTBs in Mangochi district include; maternal diseases, maternal behavioral related issues and social cultural practices. Participants feel that they face many challenges to care for preterm infants in the community and in the health facilities. Policy makers believe that, treatment guidelines are available in health facilities that could guide service providers to care for preterm infants. Low GWG is strongly associated with increased risk of having infants with poor outcomes in Malawi.

TIIVISTELMÄ

Ennenaikaisen syntymän ilmaantuvuus on Malawissa korkea, nykyisten arvioiden mukaan 18,1 %. Ennenaikaiseen syntymään voi Afrikassa vaikuttaa moni tekijä, kuten äidin raskautta edeltävä ja raskaudenaikainen ravinto. Äidin raskautta edeltävän ravitsemustilan ja vastasyntyneen terveyden (raskauden kesto ja vastasyntyneen koko: paino, pituus ja päänympärysmitta) välisestä yhteydestä on Malawista on vähän näyttöön perustuvaa tietoa

Tällä tutkimuksella oli kolme tavoitetta. Ensimmäisenä tavoitteena oli kuvailla käsityksiä ennenaikaisista syntymistä, ennenaikaisesti syntyneiden lasten hoitokäytäntöjä ja ennenaikaisiin syntymiin liittyviä haasteita köyhässä malawilaisessa maaseutuyhteisössä. Toisena tavoitteena oli tutkia terveydenhuollon ammattilaisten näkemyksiä ennenaikaisesti syntyneiden lasten hoidosta ja hoitoa ohjaavien dokumenttien olemassaolosta malawilaisissa terveydenhuollon yksiköissä. Kolmantena tavoitteena oli määritellä äidin raskautta edeltävän ja raskaudenaikaisen ravitsemustilan ja vastasyntyneen terveyden välisen yhteyden voimakkuus.

Käsityksiä ennenaikaisen syntymän syistä, ennenaikaisesti syntyneiden lasten hoitokäytännöistä ja ennenaikaiseen syntymään liittyvistä haasteista selvitettiin 20 syvähaastattelulla ja 14 fokusryhmähaastattelulla Mangochin alueen yhteisöissä. Haastateltavien mukaan ennenaikaista syntymää aiheuttavat raskaudenaikaiset sairaudet kuten verenpainetauti ja malaria sekä perinteiset sairaudet (likango and mwanamphepo) sekä raskaudenaikainen huono ravitsemus, monen lapsen synnyttäminen ja aikaisempi ennenaikaisen lapsen synnyttäminen. Tärkeimpinä ennenaikaisesti syntyneiden lasten kotihoitokäytäntöinä mainittiin lapsen pitäminen

lämpimänä lämpimien vaatteiden ja peitteiden avulla sekä lämmittämällä taloa avotulella ja sulkemalla ovet ja ikkunat. Haastateltavat mainitsivat ennenaikaisesti syntyneiden lasten asianmukaiseen hoitoon liittyvinä haasteina tiedonpuutteen ja köyhyyden: sairaan lapsen hoitoon vieminen viivästyi ja köyhyys rajoitti mahdollisuutta lämpimien vaatteiden hankintaan.

Terveydenhuollon ammattilaisille ja päättäjille tehtiin 16 syvähaastattelua, joilla selvitettiin ennenaikaisesti syntyneiden lasten hoitokäytäntöjä hoitoa ohjaavien dokumenttien olemassaoloa terveydenhuollon yksiköissä. Osa perusterveydenhuollossa työskentelevistä terveydenhuollon ammattilaisista kertoi, että hoitoa ohjaavia dokumentteja ei ollut joissain aluesairaaloissa ja terveyskeskuksissa, mutta yliopistosairaaloissa työskentelevät tiesivät että hoito-ohjeita on. Päätöksentekijät uskoivat, että dokumentit olivat saatavilla kaikissa terveydenhuollon yksiköissä. Lisäksi selvisi, että Malawin terveysministeriö on tehnyt ohjeen, jossa selvitetään ennenaikaisesti syntyneiden lasten hoitokäytäntöä.

Kolmas osatyö oli prospektiivinen kohorttitutkimus, joka tehtiin upotettuna satunnaistettuun, kontrolloituun iLiNS-DYAD-M -tutkimukseen, jossa mukaan otettiin 1391 naista, joilla oli normaali raskaus Mangochin alueella Malawissa. Äidin raskautta edeltävän painoindeksin sekä raskaudenaikaisen painonnousun ja vastasyntyneen terveyden välistä yhteyttä tutkittiin regressiomalleilla. Raskautta edeltävän painoindeksin ja raskauden keston välillä ei löydetty tilastollisesti merkitseviä eroja, mutta raskautta edeltävä painoindeksi oli yhteydessä lapsen syntymäpainoon ja pään ympärysmittaan. Raskaudenaikainen viikoittainen painonnousu ennusti vahvasti vastasyntyneen terveyttä, sillä se oli yhteydessä melkein kaikkiin tutkittuihin vasteisiin.

Loppupäätelmänä voidaan todeta että paikallisten ennenaikaisia syntymiä koskevien käsityksiin kuuluvat äidin sairaudet, äidin käyttäytymiseen liittyvät tekijät ja

sosiokulttuuriset tavat. Osallistujien mukaan heillä on paljon haasteita ennenaikaisesti syntyneiden lasten hoidossa sekä kotona että terveydenhuollon yksiköissä. Päättäjien mukaan terveydenhuollon yksiköissä on dokumentteja, jotka voisivat opastaa terveydenhuollon työntekijöitä ennenaikaisesti syntyneiden lasten hoidossa. Vähäinen raskaudenaikainen painonnousu on yhteydessä huonompaan vastasyntyneen terveyteen Malawissa.

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ABBREVIATIONS

ANC	Antenatal care
BMI	Body mass index
CHAM	Christian Health Association of Malawi
CI	Confidence interval
ENC	Essential newborn care
FGD	Focus group discussion
GA	Gestational age
GWG	Gestational weight gain
HCZ	Head circumference for age z-score
HSA	Health surveillance assistant
IDI	In-depth interviews
IFA	Iron and folic acid
iLiNS	International Lipid Based Nutrient Supplement
IUGR	Intrauterine Fetal Growth Restriction
KMC	Kangaroo Mother Care
LAZ	Length for age z-score
LBW	Low birth weight
LGA	Large for gestational age
LIC	Low-income country
LNS	Lipid Nutrient Supplement
MMN	Multiple micronutrients
MOH	Ministry of Health
NGO	Non-governmental organization
PTB	Preterm birth

PTD	Preterm delivery
SGA	Small for gestational age
SSC	Skin-to-skin contact
STD	Sexually transmitted disease
TBA	Traditional birth attendant
UNICEF	United Nations Children's Fund
WHO	World Health Organization
WWG	Weekly weight gain

ORIGINAL PUBLICATIONS

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1 INTRODUCTION

Preterm birth (PTB), defined as birth before 37 completed gestational weeks is one of the determinants for a child's poor health including death (1). For example, PTB is a major cause of death amongst the neonates (death in the first 28 days of life) and is associated with long-term life complications among survivors (2). Additionally, PTB is the second most common cause of death in under-five children after pneumonia (3). PTBs are likely to be influenced by several factors including maternal under-nutrition during pregnancy (4).

Evidence-based interventions on care of preterm infants especially in their first days of life have reduced mortality and morbidity related to PTBs in many countries (5). Additionally, World Health Organization (WHO) describes several low cost evidence-based interventions for care of preterm infants that are feasible for low income countries (LIC), that could possibly avert 70% of preterm deaths (5).

The low cost interventions targeting care of preterm infants in LICs include: thermal care, breast feeding, Kangaroo Mother Care (KMC) and basic hygienic care for infection prevention (1,6). Substantial evidence shows that these interventions are particularly effective in preventing death in moderately preterm infants (32 to ≤ 37 completed weeks of gestation), which accounts for more than 80% of all PTBs (1,5). For example, a recent facility-based study in Burundi shows that high survival rates of preterm infants were achieved through simple interventions such as staff training, standardized protocols and provision of KMC units (7). A recent meta-analysis has shown that KMC is associated with early initiation and effective breastfeeding which in turn reduces the incidence of necrotizing enterocolitis, a leading cause of death in

preterm infants (8). Furthermore, a randomized control trial in Zambia that targeted preterm infants between 1000 to 2500 grams reported that placement of a preterm infant in a plastic bag raised the temperature of an infant and reduced hypothermia compared to standard care (incubator care or more limited care and other specific clinical interventions according to this context) (9).

Additionally, in high-income countries neonatal mortality rates were reduced by improved care and appropriate policy changes such as improved hygienic practices around the time of birth and improved individual patient care and supportive management which may be lacking in LICs (10). Several underlying factors may contribute to neonatal mortality due to PTBs in LICs. Some of the factors include: weak health systems, limited access and utilization of health services, infections, poverty and lack of basic care (warmth and infection prevention) for preterm infants (3,11). For instance, in high income countries (with strong health systems), incidence of infections in preterm and term infants was reduced with better attention to clean care and the use of antibiotics prophylactically (12).

In Malawi, public health challenge of PTB is evident. The Born Too Soon – Global Action Report on Preterm Birth shows that rates of PTB were at 18% in 2012 and that these rates remain high as compared to other African countries (13). For example, recent estimates of PTB in Nigeria and Botswana are at 16.8% and 16.7% which is slightly lower than in Malawi (14), but higher than the estimated mean PTB rate [12.3% (9.5-15.8%)] for sub-Saharan Africa (15). In view of this public health challenge, the Government of Malawi has implemented a number of strategies to reduce PTBs such as improved data reporting system and dialogue between stakeholders and government, that newborn health should be an area of focus (16). Additionally, a recent study in two hospitals in Malawi reported that preterm infants survival was at stake in the first three days of life and that survival rates are better in better-resourced facilities (17).

Despite several efforts to reduce neonatal mortality in Malawi, recent evidence shows that neonatal death rate has been stagnant at 27/1000 deaths for more than 10 years, while other health indicators such as under-five child mortality and infant mortality have decreased (18). With exceptionally high incidence rates (18%) of PTBs in Malawi, it is important to know how these preterm infants are cared for regardless of their place of birth (facility or home). In Malawi, the available guideline on gestational age (GA) parameters for implementation of antenatal corticosteroids sets the critical minimum age for preterm infants at 24 weeks of gestation (19).

Although institutional births and deliveries attended by skilled birth attendants have increased in Malawi (90% and 91% respectively), a gap still exists on how health care workers and community members provide care to preterm infants (18). Lack of proper care for preterm infants could be one of the underlying factors contributing to limited progress of neonatal mortality in Malawi. The present study was therefore, designed to understand how preterm infants are cared in Malawi both at community and at health facility levels. The study further sought to understand the mothers' nutritional status before and during pregnancy and its association with duration of pregnancy and size of the newborn, (whether the infant is born preterm, small for gestational age (SGA), large for gestational age and size of the head).

2 A REVIEW OF LITERATURE

This chapter presents a review of literature, which includes definition of PTBs, causes of PTBs, importance of local perceptions of PTBs, consequences of PTBs, study context and justification of the present study. Multiple search strategies were used to find relevant literature including published peer reviewed papers, systematic reviews, meta-analyses and reports from Malawi Government and the United Nations agencies.

Pub Med search engine was used with Medical Subject Heading Terms (MeSH) to get an overall picture of the relevant papers in the subject area and included the following terms: PTB, causes and PTB, Africa and PTB, care and PTB, preterm community perceptions, maternal body mass index (BMI) and pregnancy outcome, low birth weight (LBW) and maternal nutrition. Additionally, unpublished reports were requested and reviewed from the following sources; Malawi Ministry of Health (MOH) offices, health development partners, non-governmental organizations (NGOs) working in maternal and child health in Malawi and various health facilities. In Malawi, development partners are directly involved in decision-making and they play a big role in funding the health sector strategic plan priority interventions through budget support and actively participating in the monitoring and implementation of the plan.

The review focused on findings describing PTB and its causes in LICs, targeting the late and moderate preterm infants (32 to ≤ 37 completed weeks of gestation) as they account for the largest numbers of PTBs (5). The review purposefully excludes still births (a baby born with no signs of life at or after 28 weeks), induced abortions

(deliberate termination of a human pregnancy, most often performed during the first 28 weeks), spontaneous abortions alternatively known as miscarriage), the extremely preterm (<28 weeks) and very preterm (28-<32 weeks) because in LICs such data may not be commonly available due to lack of mechanisms for identifying the very PTBs. Additionally, care of extremely preterm infants using high technology equipment may not be applicable to the LICs at present.

2.1 Definition and size of the problem

The WHO defines PTB as any child born before 37 completed weeks or 259 days of pregnancy (20). Time trends data suggest that incidence of PTB is increasing in many countries (21). For example, approximately 15 million babies are born preterm every year, representing more than one tenth of all new-born infants globally (22). Additionally, the majority of PTBs, over 60% is found in Asia and Africa, where access to and utilization of health services are limited, contributing to the higher risks of death and disabilities in these infants (23).

Although early recognition of the preterm infant may enhance the timely delivery of life-saving care, in sub-Saharan Africa <7% of pregnant women have access to ultrasound dating (the most accurate method currently available to assess gestational age) (24). Moreover, maternal recall of last menstrual period is often unreliable in populations with high maternal illiteracy (25). Other recommended assessment such Dubowitz score that has increased accuracy, may not be feasible in LICs because of its complexity and requires more training to perform it which may not be available in most of the LICs (25).

PTB can further be subcategorized on the basis of gestational age (GA) as discussed in the previous section (20). Additionally, an infant born preterm can also be LBW

(<2500 grams) and small for gestational age (SGA; weight less than 10th percentile for sex and GA) (26). A previous study has shown that infant mortality rate among preterm LBW infants is five times higher than those of preterm infants weighing >2500 grams and of term LBW infants (27). Additionally, a multi-country analysis in low and middle income countries reported that compared to babies born term-appropriate for GA, the relative risk for neonatal mortality was 2.4 for term-SGA births, 8.1 for preterm- appropriate for GA, and 15.4 for preterm-SGA births (28).

Despite substantial evidence on low cost interventions for care of a preterm infant, a huge survival and equity gap still exists between the poorest and the richest countries with more preterm deaths happening in the poorest countries (3). For example, the preterm cause-specific neonatal mortality rate in Europe was approximately 1.5 per 1000 births, compared with almost 10 per 1000 births in Africa (29,30).

2.2 Causes of PTB

The mechanisms leading to PTBs are not yet known but there are many underlying risk factors that trigger PTB (32). In this section, risk factors of PTBs are listed and grouped as follows: maternal nutritional status; infectious diseases (malaria and STIs including HIV/AIDS); and other maternal related factors such as diseases (diabetes, asthma and hypertension), individual or family history of PTB, young or advanced maternal age, short inter-pregnancy intervals, multiple pregnancies, mode of delivery (delivery for maternal or fetal indicators, spontaneous preterm labour with intact membranes and preterm premature rupture of the membranes, irrespective of whether delivery is vaginal or by cesarean section) (33,34). In the subsequent paragraphs, a detailed review of some of the risk factors for PTB is presented.

2.2.1 Maternal nutritional status

Recent systematic reviews clearly demonstrate that poor maternal nutrition prior to pregnancy and/or during pregnancy is associated with adverse birth outcomes including LBW and PTB (35,36). For example, women's poor nutritional status just before conception or during early pregnancy may affect critical developmental processes that begin early in pregnancy as well as the availability of nutrients (37). In addition, poor nutrition during early pregnancy may affect placental function which has been associated with adverse pregnancy outcomes such as pre-eclampsia, preterm delivery (PTD) and fetal growth retardation (37).

Most of the underlying maternal risk factors to PTB are interrelated. Systematic reviews and meta-analyses show that pre-pregnancy obesity/overweight is associated with PTB (36), yet in other studies, pre-pregnancy obesity has been associated with type 2 diabetes (38), and diabetes is also identified as an independent risk for PTB (39). Consequently, maternal underweight prior to pregnancy and during pregnancy have both remained to be the strongest independent positive predictor for PTB and LBW infants (35,40). Table 1 below presents a summary of studies that have investigated maternal nutrition related factors and their association with adverse outcomes including PTB.

Table 1: Studies investigating maternal nutritional status and its association with preterm birth

Authors	Study Design	Results
Van den Broek et al. 2014 (41)	Secondary analysis of data using collected data as part of the prevention of PTB (Apple trial (ISRCTN4023116)	Maternal undernourishment and anemia were independently associated with preterm birth, i.e anemia was associated with births <34 weeks (Adjusted OR 1.95).
McDonald et al. 2010 (36,42)	Systematic review and meta-analyses.	Overweight and obese women had an increased risk of preterm birth and induced preterm birth (RR 1.24, 1.13 to 1.37).
Han et al. 2011 (35)	Systematic review and meta-analyses	Maternal underweight was associated with preterm birth in developed countries only but not in the developing countries.
Kosa et al. 2011 (40)	Nested population-based case control study in Southern California. Retrospective case control.	Pre-term delivery was associated with both pre-pregnancy underweight and overweight.
Ramakrishnan et al. 2012 (37)	Systematic review	Mixed finding as some studies reported that maternal pre-pregnancy size, low stature; underweight and overweight were all associated with increased risks of PTD and SGA.

Ayensu, Annan, Edusei, & Badu, 2016 (43)	Systematic review	Excessive weight gain in the third trimester resulted in PTB and cesarean deliveries. The odds for preterm delivery were (2.7 and 4.3) among underweight and obese BMI, respectively.
Masho, Bisho, & Munn (44)	Multi-site prospective cohort study that enrolled pregnant women at their first prenatal visit in USA	Excessive weight gain increased the risk of spontaneous preterm births with premature rupture of membranes (PROM). Odds of indicated preterm birth were associated with underweight women who gained < 7 kg or 9.5 - 12.7 kg during pregnancy.

2.2.2 Infectious diseases

Substantial evidence shows that maternal infections during pregnancy are independent risk factors for PTBs (45). For instance, in a large population based cohort study in China, it was found that maternal pre-pregnancy hepatitis B virus infection was independently associated with higher risk of PTB and specifically early PTB (46).

Studies conducted in South Africa and Tanzania have also reported that the risk of PTBs is elevated in positive women with Human Immunodeficiency Virus (HIV) compared to women who are HIV negative (47,48). For example, in a South African study, HIV positive mothers were statistically more likely (~ 4 fold) to have preterm deliveries than their HIV negative counterparts [odds ratio (OR) 4.09, 95% CI: 1.37–12.17] ($p=0.010$) (47). On the contrary, studies conducted in Malawi and Kenya found no difference in maternal HIV infection prevalence ($p=0.30$) or syphilis prevalence ($p=0.12$) between women who delivered preterm versus term (41,49). However, in the same study, other maternal diseases such as periodontal diseases and persistent malaria (despite malaria prophylaxis) were associated with increased risk of PTB (41,50).

2.2.3 Other maternal factors

Both young and old maternal age are independent risk factors for PTB (51). For instance, a large randomized trial in Tanzania found that maternal age >30 years was independently associated with PTBs and SGA (52). While in China, it was reported that young maternal age was linked to a higher incidence of PTB (OR 1.70, 95% CI 1.18–2.43, $p < 0.01$) (53).

Clinical based studies from both high and LICs demonstrate that there are several maternal risk factors that may influence PTB and these include; history of miscarriage, pre-eclampsia, placenta previa (placenta is too close to cervix), abruption of placenta, caesarean section delivery, inadequate antenatal care (ANC) visits (less than 8 recommended visits and/or four focused ANC), multiple pregnancies and low weight gain during pregnancy (45,54). Additionally, maternal diabetes, asthma and high blood pressure are associated with adverse birth outcomes including PTB and LBW (55).

2.3 Importance of local perceptions of PTB

It is important to understand local perceptions of PTBs as they may influence the care of preterm infants in the community. Qualitative studies suggest that lay people see biomedically defined modern illnesses, traditionally defined illnesses, witchcraft, violence, impurity related to sexuality, inadequate food and inappropriate use of medicine as causing PTBs (56). In Uganda, the local explanations for PTBs included diseases (syphilis and malaria), medical complications, witchcraft and earthquakes (57). Similarly, the perceived causes of PTBs in Ghana were witchcraft, teenage pregnancies, unsafe abortions, weak sperms of men, prolonged use of family planning methods and extra marital sex by the father (58). Evidence from Malawi is lacking on local perceptions of PTBs. A recent study that investigated perceived causes of LBW in Malawi found that lack of family planning, delivering early, stress and doing too much work were reported as causes of LBW (59).

2.4 Consequences of PTB

Substantial evidence demonstrates that PTB complications are estimated to be responsible for 35% of the world's 3.1 million annual neonatal deaths, and also the second most common cause of death after pneumonia in children under 5 years of age (60). In addition to its contribution to mortality in both high and LICs, PTB may have lifelong effects on neurodevelopment functioning such as increased risk of cerebral palsy, impaired learning and visual disorders and an increased risk of chronic diseases in adulthood (61,62). Furthermore, infants born at 34 to 36 weeks have been shown to have an increased risk of neonatal and infant death when compared with those born at term (63).

Additionally, PTB has economic implications as well, since it is associated with long hospital stays if the infant is in the early preterm (<32 weeks) category, putting economic stress on the family (5). Some authors have even noted that the population attributable fractions for having hospital admissions between 9 months and 5 years were 5.7% (95% confidence interval [CI] 2.0% to 10.0%) for birth at 32-36 weeks and 7.2% (1.4% to13.6%) for birth at 37-38 weeks, compared with 3.8% (1.3% to 6.5%) for children born very preterm (<32 weeks) (64).

Recent findings reveal the consequences of both LBW and SGA and its association with PTB in LICs (65). Among those born preterm, it is well known that most of them are either of LBW infants or intrauterine growth restriction (IUGR) and are at a particular risk of illness and death in the first month of life (60). The ailments in the LBW and PTBs are exacerbated due to the risk of hypothermia, a major underlying cause of newborn deaths in LICs (20,63). Infants born both preterm and SGA have higher mortality risk than those infants with either characteristic alone

(RR15·42; [95% CI 9·11-26·12]) (28,66,67). For example, infants with combinations of being PTB and SGA have an increased risk for malnutrition and life-long complications including impaired neurodevelopment, non-communicable diseases, and psychological or emotional distress (1,68).

2.5 Recommended care for preterm infants in LICs

In the above sections, some of the risk factors for PTBs have been discussed in detail. However, addressing the burden of PTBs require a dual approach – prevention and care (29). Therefore, this section will comprise of a discussion of literature about how preterm infants can be cared especially in LIC's. Apparently, most of PTBs, about 84% occur after 32 completed weeks of gestation (15) and these infants can survive with supportive care and without intensive care (5). The simple interventions targeting late and moderate (32 to < 37 weeks) preterm infants could have a large effect on the reduction of mortality burden in preterm infants (1). For example, studies that have investigated neonatal care in high income countries indicate that the major reduction in deaths occurred even before neonatal intensive care was established (5).

In LICs, several challenges in relation to quality of newborn care including PTBs in health facilities are well documented (69,70). Meanwhile, a study that investigated perceptions and care of preterm babies in eastern Uganda similarly reported that health facilities lacked capacity to care for preterm infants in terms of protocols, health-worker's skills, basic equipment, drugs and supplies (57). Even in Malawi, a study that investigated survival of the preterm infants in two public hospitals, found that neonatal survival was lower among preterm and LBW infants in a hospital with few resources than in better resourced and specialized care facilities (17). Therefore,

the above evidence clearly shows the importance of resources in the care of preterm infants.

Results from LICs suggest that high mortality and morbidity among infants who are both SGA and preterm could be minimized with the following low cost interventions: KMC and extra support for feeding, case management of babies with signs of infection, safe oxygen management supportive for respiratory distress syndrome, use of continuous positive airway pressure and surfactant or intensive neonatal care (71). Additionally, intervention studies point to the low cost health facility-based interventions such as antenatal corticosteroids for preterm labour that could be used to prevent PTB (72). A large cohort study had also shown that women with a first stage caesarean had a decreased risk of spontaneous PTB as compared to a vaginal delivery (73). Previous studies indicate different interventions that have attributed to the decrease in neonatal deaths for asphyxia, sepsis and prematurity in LICs (74). Furthermore, the mechanisms observed in LICs for providing warmth (lighting lamps and charcoal stoves placed under the baby's bed and hot water bottles put in close proximity to the baby) might be harmful and of high risk to a preterm infant (57).

Recent studies demonstrate that recognizing LBW infants and distinguishing the ones who are preterm are essential first steps in prioritizing care for the infants at highest risk (75). Some authors have even pointed out that every infant (term and preterm) needs essential newborn care, with their mothers providing warmth, breastfeeding and a clean environment, however, a preterm infant needs extra care due to its highest concentrated risk of death (13). The WHO has described a number of priority packages and evidence based interventions for all newborn infants including PTBs described in Table 2 below.

Table 1: Lifesaving and extra newborn care, adapted from the WHO, 2012

Risk for all babies especially those who are preterm	Essential care for all babies	Extra care for preterm babies
Hypothermia = low body temperature (increased risk of infections, mortality, and for preterm babies increased risk of respiratory distress syndrome (RDS).	Thermal care Drying, warming, skin-to-skin and delayed bathing until 24 hours.	Extra thermal care Kangaroo Mother Care (KMC) for infants who are clinically stable, baby hats, blankets, overhead heaters and incubators.
Cord and skin infections, neonatal sepsis	Hygienic cord and skin care at birth and home care practices Hand washing and other hygiene. Delayed cord clamping and consider Chlorhexidine	Extra attention to infection prevention and skin care Consider Chlorhexidine and emollients
Hypoglycemia = low blood sugar (increased risk of impairment or death)	Early and exclusive breastfeeding	Extra support for breastfeeding e.g., expressing and cup or supplemented breast milk if indicated. Lack of breast milk is a risk factor for necrotizing enterocolitis in preterm babies

Hypoxia = low oxygen levels, (Increased risk of impairment or death and for preterm babies, higher risk of respiratory distress syndrome and intracranial bleeding)	Neonatal resuscitation if not breathing at birth Bag-and-mask resuscitation with room air is sufficient for >99% of babies not breathing at birth.	Safe oxygen use Monitored oxygen use e.g., in head box or with nasal cannula, routine use of pulse oximeters

Adapted from WHO, 2010 & 2012 Guidelines on recommendations on newborn health

2.5.1 Kangaroo Mother Care (KMC)

Implementation of KMC is another evidence-based intervention for care of preterm infants and LBW infants. WHO defines KMC with four components: (i) early, continuous and prolonged skin-to-skin contact between the newborn and the mother, (ii) exclusive breastfeeding, (iii) early discharge from the health facility and, (iv) close follow up at home by a health worker (76). The major component of KMC is skin-to-skin contact, by which an infant is placed vertically between the mother's breasts firmly attached to the chest and below her clothes (77).

KMC is recommended for the routine care of newborns weighing 2000g or less at birth, and should be initiated in healthcare facilities as soon as the newborns are clinically stable. Although KMC remains unavailable at large scale in most LICs, a systematic review that identified 15 studies reporting mortality and/or morbidity outcomes of which all the studies were from middle and LICs, has shown that KMC is an effective and affordable method of providing quality life-saving care to LBW/preterm infants in LICs and is effective in reducing serious morbidity in preterm and LBW infants (78).

A systematic review which included hospital-based studies, concluded that commencing KMC in the first week of life showed a statistically significant reduction in neonatal mortality [relative risk (RR) 0.49, 95% Confidence Interval (CI) 0.29-082] compared with standard care (neonatal intensive care with incubators and respiratory support) (79). In addition, a recent study similarly reported that KMC was associated with a 36% lower mortality (RR 0.64;95% [CI] 0.46, 0.89) and decreased the risk of newborn sepsis, hypothermia, hypoglycemia and hospital readmission and increased

the likelihood of exclusive breastfeeding up to four months of age, weight gain, mother-baby bonding and developmental outcomes (80).

A meta-analysis has also shown that KMC promotes early initiation of breastfeeding as compared to conventional care methods (8). Despite strong evidence that KMC reduces mortality and morbidity in preterm infants, KMC is not widely implemented in LICs (79). Studies show that there are several barriers to implementation of KCM in LICs including, health system barriers (financing, organization and service delivery), social support, medical care and family acceptance (81). For example, a systematic review has reported that the top three barriers to KMC implementation at the health facility were staffs' negative impressions such as, lack of help with KMC practice and low awareness of KMC among the staff (82). In detail, lack of resources (linens, space, staff, poor referral system) was a major barrier to implementation of KMC in most of the health facilities (81). A study from Ghana, where KMC is being implemented in over 50% of the health facilities, similarly reported challenges of space, so that all infants had to be discharged two hours after birth while for hospitals found in rural remote areas, cultural practices had an impact (83).

Despite that evidence on barriers and facilitators to implementing KMC at home is scanty, a study conducted in middle and LICs, demonstrate that implementation of community KMC is relevant as babies born in facilities are discharged early and home deliveries still occur (84). Additionally, a study conducted in Sudan suggested that KMC was feasible in LICs because it can be practiced anywhere (health facility and home) unlike standard care (incubators), which may be of high cost, difficult to maintain, shortage of skilled staff, intermittent power supply and sharing of incubators which may lead to infections among the neonates (85).

2.5.2 Infection prevention

Infections are a major cause of morbidity and mortality in preterm infants. For example, approximately 2 million neonatal death occur annually due complications of PTB and infections (28). Systematic reviews suggest that giving antibiotic therapy to women for pre-labour rupture of membranes in low and middle income countries would reduce deaths due to complications of prematurity by 12% and deaths due to sepsis by 39% (86). Additionally, in LICs, several evidence-based low cost interventions are well documented for management of infection prevention for preterm infants. Some authors have suggested that in LICs, basic hygienic practices such as hand washing, maintaining a clean environment that are meant for all newborn babies, should not be overlooked for preterm infants and unnecessary separation from the mother or sharing of incubators should be avoided for infection prevention (15).

Preterm infants have an increased susceptibility to infections because in the first weeks of their life, the preterm infants have a less developed skin barrier than term infants which may permit entry for micro-organisms leading to invasive infections (87). Results show that the application of topical emollient ointment such as sunflower oil or Aquaphor™ prevents infections in preterm infants as it reduces water loss, dermatitis and risk of sepsis (22).

A randomized clinical trial in Bangladesh reported that in the emollient arm, skin deterioration of preterm infants were statistically significantly lower ($p =< 0.05$) as compared to the untreated control arm and thus infections were reduced as well (88). Additionally, a review of studies conducted in India, Pakistan, Bangladesh, Egypt and Brazil found that topical emollient therapy significantly reduced neonatal mortality in preterm infants by 27 % (RR: 0.73, 95% CI: 0.56, 0.94) and hospital acquired infection by 50% (RR: 0.50, 95% CI: 0.36, 0.71) (87). Emollients used in

the reviewed studies included sunflower, coconut, soybean and mineral oil, of which some of them can also be found in Malawi (the study context), but various oil-based preparations can be applied depending on the availability in that particular region (87).

Randomized trials that have looked into use of chlorhexidine topical application to the infant's cord reported a significant effect in neonatal mortality especially in preterm infants if early application was done (89,90). Furthermore, in trials conducted in Egypt and Bangladesh, topical application of emollient ointment such as sunflower oil or AquaphorTM was found to reduce mortality for preterm infants and was further recommended to be a scalable simple approach to save lives even where most births were at home (90). By contrast, a systematic review which included high, medium and LICs reported that use of emollient therapy did not prevent invasive infection or death in preterm infants (91).

2.6 Malawi health system (Study context)

In Malawi, the main health care service providers are MOH and the Christian Health Association of Malawi (CHAM). Districts are the basic operational units responsible for coordinating public service delivery, which includes the delivery of health services within the district (district hospitals, health centres, health posts, dispensaries and community hospitals). The health system has three levels of care. The primary level, which is the lowest and comprises of health centres, health posts, dispensaries and community hospitals. The secondary level consists of District and CHAM hospitals. The district hospitals are in each of the 28 country's districts, which also act as referral facilities for both health centres and rural hospitals.

The tertiary level includes four central hospitals and two private hospitals with specialist services. The central hospitals are also responsible for professional training, conducting research and providing support to the districts. At community level, the health system is organized around health centres and health surveillance assistants (HSAs) serving the health care needs of villages (92). In Malawi, the HSAs comprise 30% of the health work force, working mainly on health promotion and disease prevention for a population ratio of about 1,000 per HSA (93). HSAs remain an essential cadre in driving forward efforts to achieve universal health coverage due to shortages of human resource in the health sector in Malawi (94).

Malawi's health system faces numerous challenges as recent findings show for example that overall 8.8% of Malawians aged between 15-49 are HIV positive, 37% of children under five are stunted, 12% of children are underweight, maternal mortality ratio is at 439 deaths per 100,000 live births, infant mortality and child mortality are at 42 deaths per 1000 live births and 63 deaths per 1000 live births respectively (18). Additionally, Malawi is one of the countries that have the lowest density of physicians in the world with less than 0.5 physicians per 10,000 people and an overall health worker density of 3.3 per 10,000 population which is substantially lower than the WHO standards recommendation (95).

2.7 Newborn health in Malawi

Malawi has made little progress in reducing neonatal mortality (96,97). For example, neonatal mortality has not changed for a long time as it declined from 41 deaths per 1,000 live births in 1992 to 27 deaths per 1,000 births in 2004 and has essentially remained at the same level since then (97). Three conditions including complications of PTB, severe infections and intrapartum-related birth asphyxia were reported to

be responsible for about 89% of all newborn mortality in Malawi (3). A study which had investigated the cause-specific neonatal mortality in four countries (Nepal, Bangladesh, Malawi and India), similarly reported that prematurity, birth asphyxia and infections accounted for most neonatal deaths (between 62% and 82%) in the first week of life (98).

Facility births are increasing in many LICs and in Malawi facility delivery rates have increased from 55% in 1992 to 91% in 2015-16 (97). The rapid increase in facility births has also heightened the pressure on the already few health workers in Malawi (18). Other additional initiatives might have also contributed to the increase in facility births in Malawi and these include, a shift in MOH policy from traditional birth attendants (TBAs) to skilled attendants, a comprehensive approach taken by the Malawi Road Map and Health Sector plan, which increased the supply of services through the rehabilitated facilities, encouraging communities to take an active role in maternal and newborn health and Service Legal Agreements between MOH and CHAM facilities (99). Service Legal Agreement implies an agreement between CHAM facilities and District Health Offices of the Malawi government, wherein CHAM agrees to provide critical care services, free of charge, to communities that would otherwise not be able to access critical health services, with a primary focus on maternal and neonatal interventions (100).

Others have argued that giving birth in a health facility does not guarantee care of sufficient quality to prevent newborn deaths (101,102). A cross-sectional study in Malawi found that quality of delivery facilities fall short of global standards of evidence-based care substantially (103). In this study, researchers also reported that higher-quality facilities, in the top 25% of quality scale, were associated with 2.3% fewer neonatal deaths than other facilities in Malawi (103). In addition, multiple assessments of healthcare services found that the quality of newborn care services in Malawi was lower than for other health services (96,104). Similar findings were

reported in a sub-national Performance and Quality Improvement evaluation, of which newborn survival interventions (care at birth and postnatal care) had fewer improvements in clinical standards than other interventions ANC (105).

2.8 Care of preterm infants in Malawi

Studies that have investigated care of preterm infants in Malawi are scarce. So far there is only one recent study which investigated health facility-based provider attitudes and knowledge of PTBs (106). In this study, the authors identified gaps in knowledge of PTBs which included: (i) discordance in the definition of PTB (i.e., 28–34 weeks or less than the 8th month, but with a corresponding fetal weight ranging 500 to 2,300 grams); (ii) utility and regional availability of antenatal steroids for prevention of preterm infant morbidity and mortality; (iii) need for antenatal referral for at-risk women, or with symptoms of PTB (106).

In Malawi, studies that have investigated care of preterm infants in the community are lacking. To address care of preterm infants in Malawi, the MOH has developed and implemented several guidelines adapted from the WHO. For example, a guideline on KMC that can be implemented both at health facility and community, and helping babies breathe to be implemented at the health facility level (107). However, implementation of facility KMC in Malawi has faced some challenges due to the magnitude of the countrywide KMC scale-up program to include all health facilities in the country within a short period of time (108).

2.9 Justification of present study

The reviewed literature shows that there is a gap in research of how health care staff and families provide care for preterm infants in Malawi. Recently, South Asia has

been showing a faster decline in neonatal mortality leaving Sub-Saharan Africa with greatest burden (109). Basic newborn care practices as described in the literature review above could avert as many as two thirds of neonatal deaths (110). In fact, with the current influx of facility-based deliveries in Malawi, the basic Essential Newborn Care (ENC) package are mainly simple interventions (breastfeeding, thermal care, skin to skin KMC care and infection identification) that are feasible for late preterm infants (≥32 to ≤37 gestational weeks).

Additionally, poor maternal nutrition both in pre-pregnancy and during pregnancy has shown to be associated with adverse birth outcomes. Moreover, there is little evidence from sub-Saharan Africa including Malawi that has shown the relationship between maternal nutrition and pregnancy outcomes. A study in Mangochi where the present study was conducted had previously looked at infants' nutrition from 6 to 18 months (111). With these gaps, understanding maternal pre-pregnancy nutrition and gestational weight gain (GWG) remain an important health challenge in Malawi. Unlike in the past when evidence of maternal nutrition was mostly from western countries, recent data is coming from Asian countries that describe associations between maternal nutrition and pregnancy outcomes, but lacking in sub-Saharan Africa.

3 AIMS

The current study was set to understand care of preterm infants in sub-Saharan Africa and if maternal nutrition during pregnancy and pre-pregnancy period is associated with preterm births.

The specific aims were as follows;

1. To describe local perceptions of PTB, care practices for preterm infants and challenges associated with PTB among community members of Mangochi district – Malawi (study I).
2. To understand views of policy makers and health workers'/service providers about the care of preterm infants in health facilities and existence of any policy protocol documents guiding delivery of care to the preterm infants in Malawian health facilities (study II).
3. To determine the strength of association, if any between maternal pre-pregnancy BMI and weight gain during pregnancy with birth outcomes (duration of pregnancy and size of the new born including weight, length and head circumference) among women in Malawi (study III).

4 MATERIALS AND METHODS

4.1 Approach to the study

Data from three different studies was used to achieve the aims of the present study (Fig 1). Study I was designed to understand the community perceptions of PTB and their care practices. It was a qualitative study which included 130 participants who participated in either focus group discussions (FGDs) or in-depth interviews (IDIs).

Study II was a qualitative study which assessed policy makers' and health workers' views about care of preterm infants at facility level. The study included 16 in-depth interviews and a review of available policy and protocol documents guiding management of PTBs in health facilities in Malawi.

Study III was designed to assess the association between maternal nutritional status and PTB. The study outcomes were duration of pregnancy, birthweight, birth size, length-for -age z-score (LAZ) and head circumference – for –age z –score (HCZ).

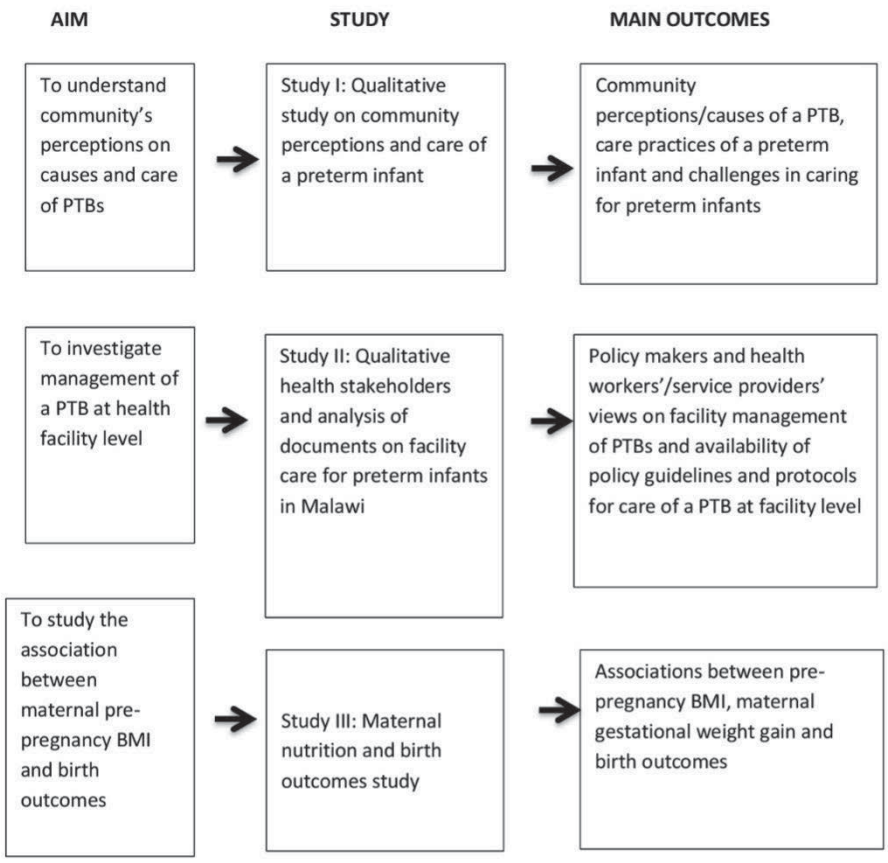

Figure 1 Overall design of the thesis

4.2 Study setting

All the three studies were conducted in Malawi, a land-locked country of about 118,484 square kilometers situated in Southern Africa. Approximately 80% of the country is covered with land and 20% is water. The United Nations' estimate of its population was approximately 17 million inhabitants for 2016, which has doubled in the last 20 years with a population density of 188.3 inhabitants per square kilometer. Approximately 84 per cent of Malawians live in rural areas (97). The country is divided into 28 districts clustered into five health zones within three regions. At the central level, the MOH takes charge of policy formulation, policy enforcement, regulation, establishment of standards, training and curriculum development and international representation on Malawi's health issues (92).

Study I took place in Mangochi district. Mangochi district is found in the Southern region of Malawi and is mainly inhabited by Yao speakers who make up 90% of the population (97). The main sources of income in the district are subsistence farming, fishing and small-scale business. The staple food is maize. Mangochi district hospital is the major referral hospital in the district. The hospital is surrounded by government health centers (Lungwena and Namwera) and Malindi private hospital, which offer both out- patient department and maternity services. The study was specifically conducted in the semi urban areas surrounding Mangochi district hospital; rural areas of the following health centres; Namwera, Lungwena and Koche; and Malindi hospital. Malindi hospital is a semi private hospital under CHAM (100). A previous study conducted in Mangochi district demonstrated a high prevalence of PTBs in the district (41). In the same study, the likelihood of death among the preterm infants was twice as compared to infants born at term (41).

Study II was a health facility based study conducted in six districts of Malawi namely; Mangochi, Zomba, Chiradzulu, Blantyre, Mulanje and Lilongwe that were purposely

selected. Capital of Malawi, Lilongwe, is located in Lilongwe district. Mangochi district hospital has been fully described under study I above. Chiradzulu district hospital is located in the Southern Malawi and serves a population of approximately 245,000 people. Prevalence of HIV in Chiradzulu district is 9.2% and 94.5% of deliveries are assisted by a skilled provider (97). Mulanje and Malosa are both semi-private hospitals under CHAM and offer both maternal and outpatient services to the surrounding population. Blantyre and Zomba are both teaching and major referral hospitals.

Study III was conducted in Mangochi district in the catchment areas of Mangochi district hospital, Malindi hospital, Lungwena and Namwera health centres (112). This was a prospective cohort study nested within the International Lipid-Based Nutrient Supplements (iLiNS) Project DYAD trial in Malawi (iLiNS DYAD-M) that enrolled 1,391 women with uncomplicated pregnancies (<20 gestation weeks [gw] in a randomized, controlled trial in Mangochi District of Malawi (113). Current data shows that nearly 37% of children under-five in Malawi are stunted and stunting is more common in Neno and Mangochi districts (45%) and less common in Likoma district (25%) (114).

In the two studies (study I and II), the author developed the proposal, processed the ethical approval of the study, participated in the data collection, data analysis and led the development of the manuscript for publication. In the third study (III), the author participated in trial implementation and led the development of the manuscript for publication.

Figure 2 Districts where the three studies were conducted.

4.3 Study participants

4.3.1 Community perceptions of PTBs (study I)

To understand community perceptions of PTBs, the study purposefully targeted key informants comprising TBAs, traditional healers, women and men who were parents at the time of data collection and grandmothers. In this study, key informants are defined as persons with reputable knowledge in the community about care practices of a preterm infant. Additionally, the study targeted a cohort of women who were enrolled in the iLiNS DYAD-M randomized trial and had given birth to a preterm infant. In total, 130 participants were included, of which 110 were included in FGDs and 20 in in-depth interviews. None of invited people refused to take part in the study.

4.3.2 Investigating care of preterm infants at facility level (study II)

To understand care of preterm infants, the study targeted policy makers working in the maternal and child health NGOs, development partners and Reproductive Health Unit of the MOH. The NGOs, which participated in this study, were World Vision Malawi and Save the Children Malawi, while the development partners were United Nations Children's Fund, WHO and United Nations Population Fund. To understand facility care of preterm infants and its challenges, the study included front line service providers (those working in postnatal wards) in six health facilities. These service providers were from the following health facilities; health centres (Lungwena, Namwera and Koche), district hospitals (Mangochi and Chiradzulu), central hospitals (Zomba and Queens) and CHAM hospitals (Malindi, Malosa and Mulanje).

In total, 16 in-depth interviews were conducted with policy makers and service providers for this study.

4.3.3 Association between maternal BMI and birth outcomes (study III)

In this study, the associations between maternal nutrition and birth outcomes were assessed. The target population was pregnant women who were enrolled in the iLiNS DYAD-M randomized trial in Mangochi district (113). These women were enrolled at antenatal clinics of Mangochi District Hospital, Malindi Hospital, Lungwena and Namwera health centres. The iLiNS-DYAD-M was designed to study the impact on maternal and child health in rural Malawi of an intervention that provided lipid-based nutrient supplement (LNS) both to mothers during pregnancy and early lactation and to their newly born children from 6 to 18 months of age (112). In this trial, participants were randomized into three intervention groups. The women consumed from ≤ 20 gestation weeks until delivery either one daily iron and folic acid (IFA) capsule; one capsule with 18 micronutrients (MMN); or one 20 g sachet of LNS containing 118 kcal, protein, carbohydrates, essential fatty acids, and 22 micronutrients (112).

4.4 Details of data collection

4.4.1 Qualitative data (I and II)

Qualitative methods were used to study objectives I and II (i) to understand community perceptions of PTBs and their care practices for the preterm infants and (ii) policy makers and health workers' views on care of preterm infants in the health

facilities. Discussion guides were developed for the two studies that were then pre-tested and revised before actual data collection.

Community perceptions of PTBs

FGDs and in-depth interviews were used to understand community perceptions of a PTB and their care practices at community level. A total of 110 participants were interviewed through FGDs and in-depth interviews. A total of 14 FGDs were conducted as follows; fathers (n=4), mothers (n=6) and grandmothers (n=4). A total of 20 in-depth interviews were conducted with mothers to a preterm infant (n=10), TBAs (n=6), traditional healers (n=4). Women who had given birth to a preterm infant were randomly selected from a cohort of iLiNS DYAD-M trial participants (112). Saturation point was also considered to determine the actual number of interviews (115). All the discussions were conducted in local languages either Chichewa or Yao depending on the participant's preference. The author with the help of one trained research assistant conducted all the FGDs with 6 and 12 participants per discussion.

Care of preterm infants at health facility level

A total of 16 in-depth interviews were conducted to understand care of preterm infants at facility level. The author conducted all the interviews. All the participants were interviewed in their work places but in a place convenient for audio recording. English and Chichewa were used as languages for interviews based on the participant's preference. Documents were searched on internet and policy makers were consulted for existing policy and protocol documents that were available and recommended by MOH to guide service providers on facility care of preterm infants. The search engines; used were Google scholar, Google, PubMed, for available policy

and protocol guidelines on facility care of a preterm infant in Malawi. The search key words were as follows: PTB; care of a preterm infant; Malawi; preterm guidelines/protocols and preterm infants. Policy makers were also requested to share all documents and protocol guidelines that had information of PTB in Malawi, published and unpublished regardless their year of publication.

4.4.2 Quantitative data

Maternal nutrition and birth outcomes

The association between maternal nutritional status and duration of pregnancy was explored by analysing maternal pre-pregnancy BMI and weekly average gestational weight gain (WWG) and then studied their association to the duration of pregnancy. Studies indicate that nutritional status of a woman before and during pregnancy is important for a health pregnancy outcome (43). Pre-pregnancy BMI was considered an indicator of maternal nutritional status during pregnancy. The association between the exposure and outcome variables was assessed by calculating standardized coefficients using linear regression models.

The study team administered questionnaires to eligible participants on enrolment day to collect demographic information. The inclusion criteria for participants into the study were ultrasound confirmed pregnancy of no more than 20 completed gestation weeks, permanent resident of Mangochi District Hospital, Malindi Hospital or Lungwena and Namwera Health centre catchment areas, availability during the period of the study and signed an informed consent. The exclusion criteria were as follows; less than 15 years of age, need for frequent medical attention due to a chronic health condition, diagnosed asthma treated with regular medication, severe illness warranting hospital referral, history of allergy towards peanuts, history of

anaphylaxis or serious allergic reaction to any substance, requiring emergency medical care, pregnancy complications evident at enrolment visit (moderate to severe oedema, blood haemoglobin concentration <5g/dl, systolic blood pressure > 160mmHg or diastolic BP>100mmHg, earlier participation in the iLiNS-DYAD-M-trial and concurrent participation in any other clinical trial (112).

To examine the associations between maternal BMI at enrolment, maternal weight gain during pregnancy and birth outcomes, the study staff completed anthropometric measurements at enrolment (< 20 weeks), 32 weeks and 36 weeks gestational age. The anthropometrists assessed the height and weight of the mother using a high quality stadiometer (Harpenden stadiometer, Holtain Limited, Crosswell, Crymych, UK). Infant weight was assessed using an electronic infant weighing scale (SECA 381 baby scale, Seca GmbH & Co., Hamburg, Germany), infant length using length boards (Harpenden Infantometer, Holtain Limited, Crosswell, Crymych, UK) and head circumference with non-stretchable plastic insertion tapes (Shorrtape, Weigh and Measure, LLC, Olney, MD, USA).

4.5 Data analyses

Qualitative data for two studies (I & II) that sought to understand community perceptions and facility management of PTBs were transcribed and translated into English verbatim. Information relevant to facility care of PTBs in Malawi was abstracted from the documents that were collected from policy makers and searched from internet. All qualitative data were analysed using content analysis approach (116).

Associations between maternal nutrition status and birth outcomes were investigated in a cohort of pregnant women enrolled in iLiNS DYAD-M randomised trial (study

III). Data analyses were performed using STATA version 12.1 (Stata Corp, College Station, TX, USA) and SAS version 9.3 software package (SAS Institute Inc., Cary, NC, USA). Analysis of variance (ANOVA) for continuous variables and chi square test for categorical variables were applied to examine maternal weight gain and BMI at enrolment. All hypothesis tests were two-sided and P values <0.05 were considered statistically significant.

4.6 Ethical approval

The first two studies (I and II) were cleared with College of Medicine Research Ethics Committee, Malawi. College of Medicine Research Ethics Committee, University of Malawi, and the Ethics Committee of Pirkanmaa Hospital District, Finland cleared the third study. The study was registered with the following trial registration (www.clinical trials.gov, trial identification NCT01239693). Participants in all three studies had consented to take part in the study.

5 RESULTS

The results of this PhD thesis are a summary based on three studies and are presented in a sequence following the presentation of the three objectives of each study. Background information for the three studies is presented first followed by results of community perceptions of PTB, facility care of preterm infants and associations between maternal nutrition and birth outcomes.

5.1 Enrolment and background characteristics

One hundred and thirty participants were approached to be enrolled in study I (community perceptions of PTB) and none of them denied. Individual interviews were conducted in the participant's homes and all the FGDs were conducted at a centrally located place convenient for all participants in a quiet place based on the participants' preferences. More than half of the participants had some primary education, 5% had no education, and 2% had some secondary education. The mean age for mothers was 32.5, fathers 39.5, grandmothers 54, women who experienced PTB 26.5, traditional healers 51.5, and TBAs 57.5 years.

Study II was conducted between January and August 2013 with 16 participants that were involved in in-depth interviews. The informants were policy makers working in the maternal and newborn health area and frontline health workers of postnatal care services. The age range of the informants were from 24 to 58 years with the mean of 37.5 years. All policy makers were qualified to a master's degree level in health related professions and were working as heads of the newborn health unit in

their offices. In health facilities, the majority of service providers were trained midwives up to either diploma or certificate levels in nursing and one service provider had a Bachelor of Science degree in nursing.

Table 2: Background characteristics of key health stakeholders

	(n=16)
Employer of Policy makers	
Ministry of Health (Reproductive Health Unit)	1
Non-Governmental Organization (Save the Children and World Vision)	2
Development partners (UNICEF, UNFPA, WHO)	3
Health facilities service providers came from	
Central Hospital (Zomba and Queens-Blantyre)	2
CHAM Hospital (Mulanje and Malosa)	2
District Hospital (Mangochi and Chiradzulu)	2
Government health Centre's (Lungwena and Namwera)*	3
CHAM health centre (Koche)	1
Sex	
Male	1
Female	15
Age	
Median age	37.5

* Two service providers were interviewed per Government health centre

A cohort of 1391 pregnant women for study III were clinically assessed by trained study staff to be enrolled in iLiNS DYAD –M randomised controlled blinded trial between February 2011 and August 2012. There were differences in baseline characteristics of women included and excluded from the analyses of associations between BMI and weight gain and birth outcomes (Table 4). The baseline characteristics of the participants included and excluded in the study are described in the flow of participants in **Fig 3** and **Table 4** below.

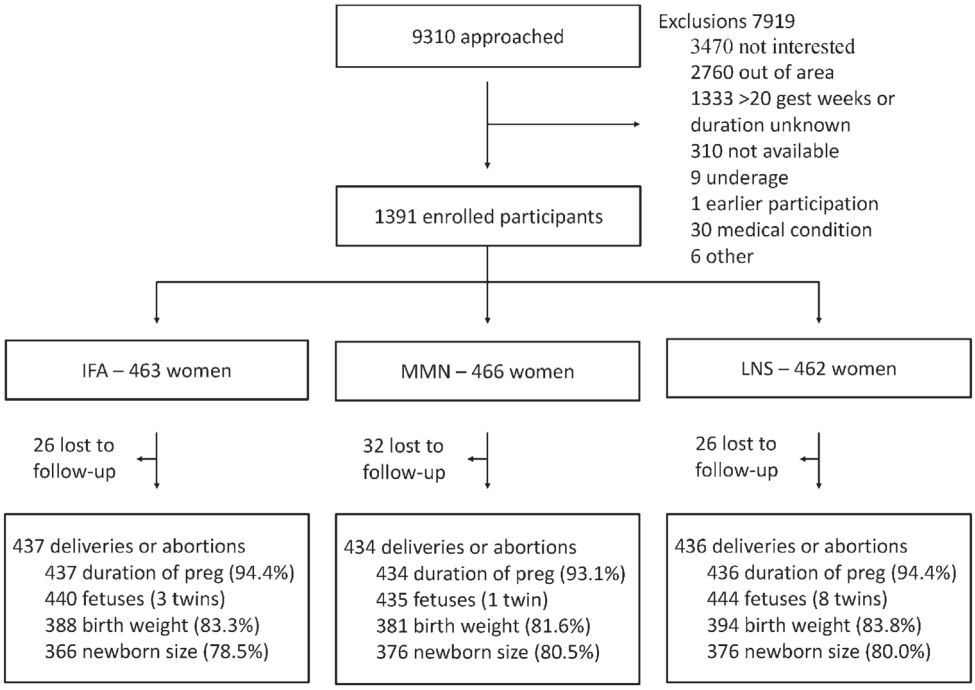

Figure 3 Flow of participants. Adapted from Ashorn et al, 2015

Table 3: Baseline characteristics of participants who were included and excluded from the analyses of associations between pre-pregnancy BMI and gestational weight gain and birth outcomes (n=1379) in Malawi

Characteristic	Included (n=1107)	Excluded (n=272)	P value[a]
Mean (SD) body-mass index, BMI (kg/m2)	22.1 (2.8)	22.4 (2.9)	0.126
Mean (SD) maternal age, years	25.1 (6.1)	24.2 (6.6)	0.025
Mean (SD) maternal education, completed years at school	3.9 (3.4)	4.5 (3.7)	0.049
Mean (SD) socio-economic score	-0.05 (0.9)	0.30 (1.1)	<0.001
Proportion of primiparous women	29.6%	20.1%	<0.001
Proportion of women with a low BMI (< 18.5 kg/m2)	4.1%	5.7%	0.367
Proportion of women with low weekly weight gain (< IOM recommendation)	70.2%	79.9%	0.008
Proportion of women with a positive HIV test	12.2%	13.9%	0.591
Number (%) of women with a positive malaria test (RDT)	22.4%	23.5%	0.749

Adapted from Gondwe et al, 2018

[a]P value obtained from ANOVA (comparison of means) or Fishers exact test (comparison of proportions

5.2 Study I: Community perceptions of PTB

This study sought to understand community perceptions of PTB and their care practices. The themes emerged from this study include, perceptions/causes of PTB, care of preterm infants and challenges of caring for preterm infants in the community. Thus, in the first part of the study, perceived causes of PTB were analysed, including care practices of preterm infants and the challenges associated with PTB among community members. The details of the findings are presented below.

Perceptions of PTB

Participants perceived diseases such as asthma, hypertension, sexually transmitted diseases (STDs), and malaria as the main causes of PTB. Additionally, they mentioned certain diseases that were mostly local such as *mwanamphepo* and *likango* which could only be treated by traditional healers. For example, participants reported that a woman that was suffering from *likango* would likely give birth to a preterm infant that would also die before reaching five years. Additionally, participants perceived anaemia, as a high risk for causing a PTB in all discussions. Participants felt that multiple sexual partners especially conducted by the husband while the wife was pregnant would cause PTB because of the belief that a man would bring *nsempho* to the wife as indicated in the following excerpt.

> *Sometimes when the woman is pregnant, the man goes out to have sex with other women and this is bad because it brings heat (nsempho) to the family, which causes the pregnant woman to deliver a preterm infant. This is because during pregnancy both the husband and wife are supposed to remain clean, and failure to do so, the wife's blood is contaminated with the hot blood of the husband taken from other women, which disturbs the fetus, and*

eventually it is forced out. Sometimes the unborn baby dies before birth. **FGD – Men, Mangochi.**

In general, participants were more concerned about the well-being of a pregnant woman as they considered pregnancy period a high risk if the woman was undergoing violence (physical and psychological). According to all participants, maternal undernutrition during pregnancy was one of the major causes of PTB. For instance, participants pointed out that a malnourished pregnant woman would not stand the pregnancy to term but may give birth to either a preterm or LBW infant and in some cases; the woman would even die in her labour.

Pregnant women are supposed to eat well and have a balanced diet such as eggs, porridge made from mgaiwa flour, vegetables and sometimes meat. However, you find that a pregnant woman is just eating okra without any other additional foods because there is no money to buy food in the family. Thus, the pregnant woman cannot survive well during pregnancy and obviously she would give birth to a preterm or LBW (onyentchera) and sometimes both the infant and the mother may die during birth. **FGD, Women - Mangochi.**

In most cases, participants perceived that both young and old maternal age as well as history of PTB in the family would cause PTB. Participants were of the view that young girls aged less than 20 years are at an increased risk because their bodies are not physically matured to carry pregnancy for nine months. On the other hand, participants felt that a pregnant woman or a family member who had previously given birth to a preterm infant had a higher risk of having a preterm infant as well. **Table 5** below shows a summary of community perceptions of PTB.

Table 4 Community perceptions of preterm birth

- *Moto* (husband or pregnant wife having other sexual partners, literally fire)
- *Chitayo* (either miscarriage or abortion): If a pregnant woman shares a dish with a woman who has recently experienced *chitayo,* can result into having a preterm infant.
- Pregnant woman being cursed by someone
- Witchcraft
- Twin pregnancy
- Young age (less than 19 years) and old age (more than 40 years)
- History of preterm birth in the family
- Gender based violence i.e husband beating pregnant wife,
- Pregnant woman doing many household chores such as pounding, cultivating in the garden all day long and searching firewood from distant places
- Woman giving birth to many children as the uterus gets tired and worn out *(Kupyapyala)*
- Small spacing between children (every year having a newborn)
- Anemia
- Poverty: Pregnant woman lacking nutritious foods or lacking enough food. i.e eating okra most of the days or having just one small meal or not having any meal at all per day because cannot afford to have proper three meals.
- Diseases: Asthma, malaria, hypertension, epilepsy, anemia, STDs such as syphilis gonorrhea and HIV/AIDs. Other diseases such *mwanamphepo* and *mauka*

*Mwanamphepo – sores in the womb as well as other parts of the body
*Mauka – itching of private parts
*Chitayo – abortion/miscarriage
*Kupyapyala – the material being too soft

Care practices for preterm infants

Participants reported that they looked at physical features of an infant and if the infant had features like pale nails, sunken forehead and frail skin, then the infant was considered preterm. Recognition of a preterm infant guided the members of the community on how to care for the infant. The commonly reported care practice for a preterm infant was providing extra warmth to protect an infant from developing pneumonia and other infections if exposed to cold weather. The participants had several mechanisms of generating warmth for a preterm infant such as making the infant sleep in between two hot bottles of water, making fire inside the house while keeping all windows and doors closed, wrapping the infant in many clothes and not bathing the infant for some months. Almost all participants reported that they cared the preterm infant by isolating the infant to protect it from diseases as one of the participants narrated.

> *A preterm infant is born too small and as such, the baby has to be kept with extra care as it can easily contract diseases because it is born early before its actual time of birth (9 months). Even its skin is not strong enough to protect the infant from infections. As such, we do not allow anyone apart from the mother to touch the infant and we keep the baby inside the bedroom away from visitors and all people living in the house. We isolate the infant for several weeks until it reaches the number of months when the infant was supposed to be born.* **IDI-TBA-Mangochi.**

Challenges in caring for preterm infants at community level

Participants mentioned that they also encountered many challenges in caring for a preterm infant. Some of the challenges were due to poverty at household level limiting them to buy only necessary items to care for the infant, transport money to take the infant to the hospital in-terms of sickness and lack of knowledge on how to properly care a preterm infant that resulted into frequent illnesses and death in some instances.

5.3 Study II: Investigating preterm care at the facility level

The second part of the qualitative study was facility based and aimed to investigate if there are any policy and protocol guidelines to guide care of preterm infants in health facilities. The study comprised of 11 health facilities (two central hospitals, 2 mission hospitals, 2 districts hospitals, 2 government health centers and 2 CHAM health centres). All the health facilities included had a maternity ward. The major themes that were evolved from this part of the study include policy makers' views about existence of policy and protocol documents on care of preterm infants, health care/service providers' views about existence of policy and protocol documents on care of preterm infants and challenges at facility level in caring for preterm infants.

Participants reported different views, such that policy makers (working in NGOs and development partners) expressed knowledge about the available policy and protocol guidelines for care of a preterm infant in the health facilities while some service providers indicated lack of knowledge on the availability of these policy documents. Additionally, policy makers reported that they do supervision in health facilities and engage service providers in workshops to equip them with upcoming knowledge on care of preterm infants including other conditions. One of the policy makers explained.

We provide all the necessary documents including policy guidelines and protocols to all health facilities but we don't know the problem, whether it is lack of reading culture or lack of communication at health facility level that service provides do not know that they have available materials in their health facilities that can assist them in caring for preterm infants. When we go for supervision, we find that these documents are just piled in the shelves full of dust implying that no one is using them. **IDI-Policy Maker - Lilongwe**.

Different views were further identified even among service providers as all those working in central hospitals reported awareness of protocols and policy guidelines in their health facilities guiding them in care of a preterm infant. On the other hand, more than half (63.3%) of the service providers working in district hospitals and health center's reported lack of knowledge of the available policy guidelines and protocols to guide them in caring for a preterm infant. One of the nurses stated.

In terms of care of a preterm infant, I cannot lie that there are documents whether policy guidelines or protocol guidelines that we can use as a reference to care for preterm infants. For example, I use my knowledge that I acquired during my training in nursing and that is what is guiding me to care for preterm infants. Of course, sometimes we also attend workshops that help us with knowledge on how to manage certain conditions including PTBs but usually personnel who go for such trainings are allocated in other sections not in the maternity or postnatal ward, so the knowledge becomes irrelevant. **IDI – Nurse (Female), Lungwena- Health Centre.**

The analysis of documents further revealed that policy and protocol guidelines were available that would guide care of a preterm infant in health facilities in Malawi. For instance, we found various documents including a sexual and reproductive health

policy booklet, compiled and approved by Malawi MOH that had information on care of preterm infants in health facilities in Malawi (Table 4 of article II).

Facility care challenges of preterm infants.

Participants in all facilities reported several challenges in relation to facility care of a preterm infant and these included lack of resources such as space to implement KMC, limited staff, medicine, uncoordinated system at facility level and poor referral system. For instance, in health centers, service providers indicated that they did not have electricity, hence no oxygen supply for preterm infants.

5.4 Association between pre-pregnancy BMI, weekly gestational weight gain with birth outcomes (study III)

In the third part of the study, an association between maternal nutritional status and birth outcomes (duration of gestation, birth weight, LAZ, and HCZ) was analysed. Of the 1,391 pregnant women enrolled to the iLiNS-DYAD-M clinical trial, 1,287 women were included in the analysis. Among those excluded in the analyses, 84 were lost to follow up, 12 had twin pregnancies and 8 had incomplete data set. We calculated body mass index (BMI) from weight and height measurements conducted at the enrolment visit for all women who enrolled in the iLiNS-DYAD-M trial. We used the estimated BMI at 13.7 wg as the proxy for pre-pregnancy BMI and assumed that minimal change in BMI occurred between pre-pregnancy and 13.7gw as described in the methodology chapter. The mean (SD) pre-pregnancy BMI for those included in the analyses was 21.8 (2.7) kg/m^2. The proportion of women who were underweight (BMI < 18.5 kg/m^2) was 5.9 %, while the prevalence of overweight (BMI ≥ 25.0 kg/m^2) was 10.9 %. The proportion of women who had low average

GWG (< IOM recommendation) was 71.8%, while the prevalence of high GWG was 5.2%.

GWG was a strong predictor for birth outcomes as it was associated with almost all measured outcomes as follows; pregnancy duration, birth weight, LAZ and HCZ (Table 5). Additionally, there were no significant statistical associations between pre-pregnancy BMI and pregnancy duration but pre-pregnancy BMI was positively associated with birth weight and HCZ in both unadjusted (β=0.11, p=0.001and β=0.09, p=0.003, respectively) and adjusted models (β=0.11, p=0.001 and β=0.09, p=0.003).

Table 5 Associations between maternal pre-pregnancy body-mass index (BMI) and average weekly gestational weight gain and birth outcomes in rural Malawi

Outcome	Pre-pregnancy BMI (kg/m^2)				Weekly weight gain (g/wk)			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	Regression co-efficient (SE)a	P-value[b]	Regression co-efficient (SE)[a]	P-value[b,c]	Regression co-efficient (SE)[a]	P-value[b]	Regression co-efficient (SE)[a]	P-value[b,c]
Pregnancy duration	-0.01 (0.03)	0.686	-0.003 (0.03)	0.926	0.08 (0.03)	<0.002	0.06 (0.03)	0.031
Birthweight	0.11(0.03)	<0.001	**0.11(0.03)**	<0.001	0.22 (0.03)	<0.001	**0.20 (0.03)**	<0.001
Newborn length-for-age z-score	0.065 (0.03)	0.040	0.056 (0.03)	0.067	0.19 (0.03)	<0.001	**0.13 (0.03)**	<0.001
Newborn head circumference z-score	0.09(0.03)	<0.003	**0.09 (0.03)**	0.003	0.15 (0.03)	<0.001	**0.15 (0.03)**	<0.001

Adapted from Gondwe et al, 2018

[a] Standardized coefficient with standardized standard errors. Standardized coefficients are the number of standard deviations the outcome variable changes per standard deviation change in the predictor variable.

[b] P-values were determined by linear regression models.

[c] Models were adjusted for covariates found in bivariate analysis to be associated with the birth outcome (P<0.10). Model for pregnancy duration was adjusted for gestational age at enrollment, parity, maternal height and HIV status. Model for birthweight was adjusted for number of previous pregnancies, HIV status, primparity, site of enrollment, season of enrollment, and maternal. Model for length age z score (LAZ) was adjusted for number of previous pregnancies, HIV status, child sex, maternal height, parity, and maternal age. Model for head circumference was adjusted for number of previous pregnancies, maternal height, parity and site of enrollment. Models for the associations between weekly weight gain and duration of pregnancy, birthweight, LAZ, and head circumference were also adjusted for maternal pre-pregnancy BMI.

Additionally, underweight women had no increased risk of giving birth to a preterm infant [RR (95% CI): 0.6 (0.2 to 1.4), p=0.202], LBW [RR (95% CI): 1.5 (0.9 to 2.5) p=0.100], and small head circumference [RR (95% CI): 0.9 (0.3 to 2.8), p=0.827] but were at an increased risk of giving birth to a SGA infant [RR (95% CI): 1.5 (1.2 to 2.0) , p=0.002] as compared to normal weight women. There was no increase or decrease in risk of stunting, SGA, or small head circumference when comparing infants of overweight and normal weight women.

Table 7 below shows the results of the prevalence of adverse birth outcomes among women with normal, low or high average weekly gestational weight gain. Although the proportion of overweight women was higher (10.9% versus 5.9%) than those of underweight women, infants born to underweight women below IOM recommendations, had a higher risk of stunting [RR (95% CI): 1.6 (1.0 to 2.5), p=0.029) when compared to infants born to normal weight women. Additionally, there was no risk of adverse birth outcomes among women with high GWG (above the IOM recommendations) compared to women with normal GWG.

Table 6 Prevalence of adverse birth outcomes among women with normal, low, or high average weekly gestational weight gain in rural Malawi

Outcome				Comparison between women with low and normal weight gain		Comparison between women with high and normal weight gain	
	Maternal weight gain during pregnancy			Unadjusted	Adjusted	Unadjusted	Adjusted
	Normal weight gain within IOM[c] recommendations	Low (below IOM recommendations	High (above IOM recommendations)	RR (95% CI)	RR (95% CI)[a]	RR (95% CI)	RR (95% CI)[a]
Incidence of preterm birth (GA <37 weeks)	21/302 (7.0 %)	106/916 (11.6 %)	2/69 (2.9 %)	1.7 (1.0 to 2.7)	1.5 (0.9 to 2.3)	0.4 (0.1 to 1.8)	0.4 (0.1 to 1.6)
Incidence of (low birth weight) LBW (<2,500 g)	21/278 (7.6 %)	124/797 (15.6 %)	0/61 (0.0 %)	**2.1 (1.3 to 3.3)**	**2.0 (1.2 to 3.2)**	N/A	N/A
Prevalence of newborn stunting (LAZ <-2)	35/257 (13.6 %)	138/767 (18.0 %)	0/58 (0.0 %)	1.3 (0.9 to 1.9)	1.1 (0.7 to 1.6)	N/A	N/A
Incidence of small for gestational age (SGA)[b]	64/278 (23.0 %)	265/797 (24.7 %)	6/61 (9.8 %)	**1.4 (1.1 to 1.9)**	**1.4 (1.0 to 1.8)**	0.4 (0.2 to 1.0)	0.5 (0.2 to 1.2)
Prevalence of small head circumference (HCZ <-2)	4/261(1.5 %)	39/765 (5.1 %)	0/58 (0.0 %)	**3.3 (1.2 to 9.3)**	**3.4 (1.2 to 9.7)**	N/A	N/A

Adapted from Gondwe et al, 2018

[a] Model for preterm birth was adjusted for gestational age at enrollment, HIV status, primiparity, and site of enrollment. Model for LBW was adjusted for child sex, HIV status, maternal height, primiparity, household food insecurity score, and site of enrollment. Model for newborn stunting was adjusted for HIV status, maternal age, maternal height, primiparity, and site of enrollment. Model for SGA was adjusted for child sex, gestational age at enrollment, HIV status, maternal age, maternal height, primiparity, season of enrollment, and site of enrollment. Model for small head circumference was adjusted for maternal age, maternal height, primiparity, season of enrollment, and site of enrollment

[b] Defined as having birth weight <10th percentile for infants of the same gestational age from INTERGROWTH-21st standard

[c] IOM: Institute of Medicine

6 DISCUSSION

The overall aim of the present study was to understand care of preterm infants in sub-Saharan Africa and whether maternal nutrition during pregnancy and pre-pregnancy period is associated with birth outcomes. The study was set first to explore community perceptions of PTBs and care practices for preterm infants. The second part of the study was set to explore the care of preterm infants in health facilities by understanding the views of policy makers and health care workers providing front line services in the health facilities. The third part of the study investigated the associations between maternal BMI and birth outcomes. In the subsequent sections, the results of each study are discussed. The limitations and the strengths of the study are presented at the end of the discussion.

6.1 Community perceptions of PTB and care of preterm infants

Some of the findings on community perceptions of PTB in this study are consistent with a previous study conducted in Malawi, which investigated perceptions of LBW. Our findings are also similar with an epidemiological study which reported that STDs, malaria, history of PTB in the family were some of the risk factors of a PTB (54). The finding that community members were able to recognize a PTB by just looking at the physical features of the infant is important in providing care for a preterm infant at home. The physical features reported in the present study to identify the preterm infant are similar to those reported by community members in Ghana and Uganda (57,58). However, more evidence from hospital-based studies is needed to clinically verify if the reported physical features describe a preterm infant.

Others have also suggested that recognizing whether the newborn is preterm or term are the first steps in saving the preterm infant which in most cases require just basic care (6).

WHO recommends thermal protection in the initial days of life for all infants. Inadequate thermal care increases the risk of hypothermia specifically in low weight and preterm infants (12). Our results indicate that provision of warmth was the preferred care for preterm infants among the community members. However, in the present study, participants reported some dangerous and harmful care practices such as putting the infant in between two hot water bottles and making fire inside the house with windows and doors closed as mechanisms for providing warmth. If not well handled, such mechanisms can cause immediate death to an infant or long-term disabilities. Studies conducted in other parts of sub-Saharan Africa such as Zambia similarly observed that some care practices (use of heated water bottles to provide external warmth) for preterm infants maybe harmful if not well handled (117). Additionally, a systematic review that investigated umbilical cord care practices for preterm infants in low- and middle-income countries reported that most of the care practices for preterm infants were harmful and needed immediate attention. The review included 8 countries in sub-Saharan Africa, 5 countries in Asia, one country in Latin America and the Caribbean (118). Furthermore, a qualitative study conducted in Zambia has demonstrated that putting powder or dung on the umbilical stump, may increase exposure to harmful pathogens (119).

The present study shows that poverty was a major challenge in caring for preterm infants in terms of purchasing warm materials for the infant and financial costs to meet hospital bills in case of a sickness of the infant. Others have equally noted that PTB does not only affect infants but also their family members because of financial costs to ensure care for their preterm infants, having an increased cost implications for both families and health services (120). Studies that have investigated cost

effectiveness of caring for preterm infants in the health facilities have found that length of hospital stay was positively associated with increased hospital costs in relation to both human and material resources (121).

Challenges of lack of knowledge in caring for preterm infants in the community requires multi sectoral coordination to sensitize the community on simple evidence based interventions for care of preterm infants. Similarly, in Ghana it was reported that lack of awareness in the community was the main barrier in providing care for preterm infants (58). In other LICs, adoption of home-based neonatal care provided by community health workers has being effective in improving neonatal and perinatal mortality in general (122). Additionally, health education to mothers and caretakers of preterm infants would equip them with proper knowledge about how to care for their preterm infants and eventually prevent illnesses and mortality among preterm infants.

6.2 Stakeholder analysis on facility care of preterm infants

This study aimed at investigating care of preterm infants at facility level by exploring the views of policy makers and service providers working in the study catchment areas. Existing policy and protocol documents were also searched through internet, especially those that would provide guidance to care of a preterm infant in the health facilities. The limitations of the present study are that health facilities in remote areas that had no electricity were included and therefore the care of preterm infants in such facilities could not be comparable to those facilities with electricity. No wonder, all health facilities without electricity had reported challenges related to electricity such as lack of incubators, heaters and oxygen supply for preterm infants.

In the present study, the availability of protocols and guidelines was not consistent among health facilities, such that central hospitals had guidelines and protocols to guide them in preterm care unlike in district hospitals and health centres. In Kenya, irrespective of facility type, no hospital was found with clinical management guidelines for management of newborns in general (123). Policy makers felt that some service providers were not using the available policy and protocol guidelines to guide them in caring for preterm infants in the health facilities. A previous study has similarly reported that failure to use evidence informed protocols for care of preterm infants may lead to inconsistent care by health care professionals (124). In LICs, studies that have investigated the effectiveness of adherence to use of the available protocol and guidelines for care of preterm infants are scarce. However, a study that evaluated compliance to international guidelines for parental nutrition in preterm infants across neonatal intensive care units of four European countries found that most of the clinical practice was based on common available guidelines (125).

One other observation was that some service providers (63.3%) especially those working in health centres and district hospitals had no specific knowledge and competencies of how to care for a preterm infant. Several factors could have contributed to this finding. One of the reasons could be lack of coordination and information sharing amongst the staff within the health facility because in some facilities, service providers expressed that they were knowledgeable about care of a preterm infant. The second reason could probably be lack of empowerment among staff members to demand materials that would help them do their work properly. Capacity building to frontline health-care workers about care of preterm infants, continuous supervision and feedback to health workers would probably help in alleviating the challenge of lack of knowledge in care of preterm infants in the health facilities. Russel and colleagues similarly suggested that parents require nurses with

specialized knowledge of the preterm infant to support them with proper guidance and care of their preterm infants (126).

Our findings are similar to several studies from LICs that have reported numerous health facility-based challenges in caring for preterm infants including, health worker shortages, space, lack of incubators and insufficient incubators in caring for preterm infants (85,127). The problem of health worker shortage is inevitable in most LICs. Previous studies have shown that even other mechanisms for managing a preterm infant such as the introduction of continuous positive airway pressure device were found challenging to provide in a country like Malawi due to low staffing levels to ensure adequate monitoring (128). Furthermore, due to intermittent power supply especially in rural areas of LICs, the availability of incubators may not necessarily have a large impact on treatment.

KMC is underutilized in most LICs despite that it is a low cost evidence based recommended care for preterm infants (85,129). In the present study, participants reported that KMC was not widely implemented due to lack of space especially in health centres and district hospitals. A KMC multi-country analysis study of health system bottlenecks similarly noted that KMC services were mainly introduced in tertiary facilities despite most facility deliveries taking place at lower facility levels (130). Additionally, a systematic review of barriers and enablers of implementing KMC reported lack of private space for mothers to perform KMC and to remain in the hospital with the newborn for a long time (81). Strengthening the community by educating mothers and community mobilization about KMC would probably solve the problems of space in the health facilities so that most of the preterm infant care should happen at home. Moreover, a study in Sudan reported that lack of awareness among health staff and the community were the two main obstacles to KMC implementation (85). Information sheets about KMC in local languages in health facilities, health education, and sensitization of the communities and staff workshops

about KMC would probably alleviate the challenges of lack of awareness about KMC.

6.3 Associations between pre-pregnancy BMI and birth outcomes (III)

Recent findings suggest that maternal nutritional status, reflected by maternal BMI either before or during pregnancy and GWG, is perceived as a significant predictor of perinatal and long-term outcomes for mothers and children (131,132). However, evidence linking associations of pre-pregnancy BMI and birth outcomes in sub-Saharan Africa, including Malawi is lacking. In the present study, the associations between maternal pre-pregnancy BMI and GWG and birth outcomes were investigated. The study also determined whether women with low or high pre-pregnancy BMI or women with inadequate or excessive GWG were at increased risk of adverse birth outcomes.

GWG was an important predictor for birth outcomes as it was significantly associated with most of the birth outcomes assessed (duration of gestation, birth weight, LAZ and HCZ). Furthermore, there was a higher proportion of women with inadequate GWG (70%) than women with low pre-pregnancy BMI (5.9%). The high prevalence of inadequate GWG in the present study highlights serious need for investigating factors associated with poor GWG during pregnancy especially in rural LICs. Several factors could have influenced low GWG in the present study, including loss of appetite, stress due to overworking, poor living conditions and cultural beliefs about food choices during pregnancy. A recent review of studies in low and middle income countries indicate that apart from economic hardships, inadequate dietary and nutritious intakes, and poor access to health facilities; women chose deliberately to eat less food during pregnancy for fear of having a large baby and enduring hard

labour (133,134). Additionally, our findings are consistent with various studies showing that low GWG below the IOM recommendations is an important risk for adverse birth outcomes including preterm and LBW infants (135). On the other hand, an excessive GWG is also associated with negative birth outcomes such as a longer infant hospital stay and excessive birth weight (136). Thus, emphasizing health living among pregnant women and all reproductive age women is probably important for positive birth outcomes.

In the present study, low pre-pregnancy BMI was not a strong predictor for adverse birth outcomes, perhaps because the mean pre-pregnancy BMI was so good to see the effect. These findings are different from what was reported from Asian countries (131,132). Additionally, a recent systematic review conducted in Asia had also reported that maternal under nutrition increased the risk and incidence of intrauterine growth retardation, anaemia, preterm delivery, LBW and delivery of SGA infants (43). Therefore, it is advisable that a woman should enter into pregnancy with normal weight (within IOM recommendations) and maintain it throughout pregnancy for positive birth outcomes. Another systematic review further indicates that a pregnant woman with pre-pregnancy underweight and who is unable to gain adequate weight throughout pregnancy is at risk of adverse birth outcomes (preterm birth, LBW, intrauterine growth restrictions and SGA) (137).

Understanding pre-pregnancy BMI is complex as it may be influenced by several factors such as a woman's life style, socio cultural factors, economic status and whether the pregnancy was planned or unplanned. The results of the present study show that pre-pregnancy BMI was significantly associated with birthweight and HCZ. By contrast, a previous study found no significant associations between maternal BMI and head circumference (131). Furthermore, previous studies have relied on using self-reported BMI in determining pre-pregnancy BMI unlike in the

present study whereby BMI was measured during each and every clinic visit by trained study staff.

The present study did not show a significant risk of giving birth to a LBW and SGA infant among underweight women. Contrary, a systematic review and meta-analysis of a population-based cohort study in low and medium income countries reported that maternal underweight was significantly associated with higher risk of PTB, LBW and SGA (138). Additionally, in another systematic review which included 78 studies from both developed and developing countries, underweight women were reported at increased risk of having a LBW infant (137). The differences could be due to lower power as only 5.9% had the predictor characteristics in the present study. Underweight women were again found at significant risk of giving birth to an infant with stunting.

The results also show no significant risk of adverse birth outcomes among women who were overweight (above IOM recommendations). Similarly, no significant differences in the risk of LBW by maternal overweight was reported in a retrospective study of Thai women (139). Use of different cut-off points for maternal BMI could have an effect on the differences in the findings.

In summary, the three studies demonstrate that the well –being of an infant is probably influenced by several underlying factors that are inter related. The present study has shown that good infant health starts before birth. For example, in our current study, maternal nutrition is important in the birth outcomes, as poor maternal weight gain is associated with negative birth outcomes. Additionally, girls and women empowerment with prior knowledge surrounding childbirth would probably be important in pregnancy management and care of the infants. The present study has also revealed the gap that exists between policy makers and implementers that may negatively affect the performance of front line health

workers. Generally, in rural Malawi, interventions aiming at improving infant health should equally focus on people living in the rural community where the majority of Malawian population is found.

7 STRENGTHS AND LIMITATIONS OF THE STUDY

The main strengths of the present study are related to its design. The study used mixed methods in its approach to collect data. For instance, it used both qualitative and quantitative methods to answer the research questions. For the qualitative part, the study was implemented by a qualitative researcher and well trained research assistants in qualitative study designs. Qualitative tools were pretested, revised and saturation was reached during data collection to determine the quantity and quality of data. In addition, the study included key informants that were knowledgeable about the subject matter. Secondly, for the quantitative part, a well-trained study group was used in the implementation of the study and all study instruments were standardized.

The study had also its weaknesses that are worthy to acknowledge and point out. Some of the weaknesses are as follows; the study was conducted during the period when there was an alarm by the '2012 Global Action Report on Preterm Birth,' indicating that Malawi was one of the countries with highest rates of PTB (18%) which may have influenced some response bias especially from policy makers who were aware of the report on PTB (13). However, the inclusion of front line service providers with hands on experience supplemented the findings as front line service providers are not directly linked to policy formulation. Additionally, use of in-depth interviews minimized response bias as respondents would not influence each other unlike in the FGDs.

Furthermore, the inclusion of some participants who had given birth to a preterm infant in the catchment area of the parent trial may have created a response bias,

since participants got used to frequent visits by the study group on different issues concerning their health. Another major limitation is that the present study as a sub study of the parent trial was conducted in the catchment area that has been overwhelmed by different studies in the previous years. Thus, participation in the study may be influenced by several factors including the study incentives. However, the study team explained the details of the study to all potential participants to enable them understand the study and make informed decisions before consenting their participation in the study.

For the qualitative study about community perceptions and care practices of PTB, the findings of the current study focused on a small sample within one district and their care practices might be different from other regions. Some studies have also noted that different cultural practices have a strong influence on the upbringing of an infant (140). Secondly, much as we included grandmothers in this study, grandfathers were excluded to get their perceptions on PTB. Considering that, women are in the frontline providing care, they take more responsibility in the care of the newborn other than men. Similarly, studies conducted in four African countries found that newborn care was considered as a woman's domain (141). Additionally, the participants were mainly from the rural with low education status that may also have influenced their perceptions about preterm infants. Lastly, apart from including women who had given birth to preterm infants, participants who had never had an experience of a PTB were also included to express their perceptions on PTB as well.

8 SCIENTIFIC CONCLUSIONS

Based on the study findings above, the following conclusions are made.

1. The local perceptions of PTBs among community members of Mangochi district include maternal diseases, behavioral related issues and social cultural practices. Provision of warmth is commonly reported care practice for preterm infants despite that some mechanisms for providing warmth are poorly done. Generally, community members face several challenges in caring for preterm infants including lack of proper knowledge on how to care for preterm infants.

2. Policy makers and health workers'/service providers are of the view that care of preterm infants in some of the health facilities in Malawi is challenging due to lack of resources such as staff, incubators, space and limited knowledge in caring for preterm infants. Policy makers feel that documents and policy guidelines guiding delivery of care to preterm infants are available in health facilities, but service providers are of the view that the policy documents are not available in some of the health facilities.

3. In Malawi, maternal nutritional status before pregnancy is associated with birth weight and the incidence of small head circumferences in the newborn. Maternal nutritional status during pregnancy, as measured by GWG is more strongly associated with multiple birth outcomes, including duration of pregnancy, as well as newborn weight, length and head circumference.

9 PUBLIC HEALTH IMPLICATIONS AND FUTURE RESEARCH

The present study has indicated that community members have some knowledge of possible causes of PTB, which sets a good foundation for programs with an interest in improving PTB at community level. Additionally, people in the community have knowledge on recognition of PTB that is important for decision making on how to care for a preterm infant. However, some of the knowledge in identification of preterm infants needs to be questioned as it may wrongly guide people in the community in care of these infants. Additionally, with numerous health facility challenges in caring for preterm infants, it is important to equip people in the community with knowledge in care of preterm infants using low cost evidence based interventions such as KMC and basic hygienic care practices. The limited knowledge among front line service providers about KMC for preterm infants in some of the health facilities probably suggests that there is need to include KMC in the training curriculum. Moreover, the lack of access to guidelines and protocols for PTB in health facilities provides an opportunity of revisiting some of the routine practices of how policy makers works with implementers to ensure that policies and treatment guidelines are implemented accordingly.

The present study has also revealed some challenges that people in the community face in caring for preterm infants. The poor care practices highlighted in this study also need to be addressed as they may continuously drag the nation's success towards improving neonatal deaths in Malawi. For instance, use of hot water bottles and making fire inside the house to warm preterm infants is risky to the health of an infant if not well managed. Lack of knowledge reported by service providers about

the existing protocol and policy documents in some health facilities is also worrisome as it points to the knowledge gap that service providers may not properly care for preterm infants according to set recommendations. Although, limited staff is a major challenge in Malawi, good coordination within the health facilities, provision of training and supervision to frontline service providers working in maternal and neonatal wards is important in ensuring improved neonatal care including a preterm infant.

The study further demonstrated that low GWG was a strong predictor for most of the birth outcomes in our study including LBW, LAZ and SGA. Therefore, the findings of the present study unveil some suggestions for further research as described below.

Conduct a study to investigate community management of preterm labour. The present study focused on community perceptions of a PTB and care of a preterm infant without actually finding out how preterm labour, which may lead to PTB, is managed at community level. Therefore, understanding how community members perceive preterm labour would probably lead into interventions that can help people at community level to know high-risk pregnancies and its management.

Conduct a study to investigate interventions targeting behavior change in the communities that would help to address harmful care practices for preterm infants. Some care practices reported in the present study may be harmful and it was not known if there are any interventions promoting evidence based care practices in the communities. Interventions targeting evidence based care practices of preterm infants would not only promote good infant care practices but would also alleviate the public health challenges including hospital costs and infant morbidity and mortality in Malawi.

Conduct a study to investigate how health facilities are prepared to manage PTB including preterm labour at health facility level. The present study focused on facility care of PTBs not taking into consideration how high risk pregnancies are managed. Having evidence based information on facility preparedness of preterm labour including PTB would help to find mechanisms to lower the high incidence of PTBs in Malawi.

Conduct a study to investigate causes of low average weekly weight gain in pregnant women in rural areas. Since gestational weekly weight gain was a strong predictor for all negative birth outcomes that we studied, investigating the underlying causes of low GWG would be important to inform on new interventions to address the challenges of poor gestational weight and improve the negative pregnancy outcomes.

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Perceptions and experiences of community members on caring for preterm newborns in rural Mangochi, Malawi: a qualitative study

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Abstract

Background: The number of preterm birth is increasing worldwide, especially in low income countries. Malawi has the highest incidence of preterm birth in the world, currently estimated at 18.1 percent. The aim of this study was to explore the perceived causes of preterm birth, care practices for preterm newborn babies and challenges associated with preterm birth among community members in Mangochi District, southern Malawi.

Methods: We conducted 14 focus group discussions with the following groups of participants: mothers (n = 4), fathers (n = 6) and grandmothers (n = 4) for 110 participants. We conducted 20 IDIs with mothers to preterm newborns (n = 10), TBAs (n = 6) and traditional healers (n = 4). A discussion guide was used to facilitate the focus group and in-depth interview sessions. Data collection took place between October 2012 and January 2013. We used content analysis to analyze data.

Results: Participants mentioned a number of perceptions of preterm birth and these included young and old maternal age, heredity, sexual impurity and maternal illness during pregnancy. Provision of warmth was the most commonly reported component of care for preterm newborns. Participants reported several challenges to caring for preterm newborns such as lack of knowledge on how to provide care, poverty, and the high time burden of care leading to neglect of household, farming and business duties. Women had the main responsibility for caring for preterm newborns.

Conclusion: In this community, the reported poor care practices for preterm newborns were associated with poverty and lack of knowledge of how to properly care for these babies at home. Action is needed to address the current care practices for preterm babies among the community members.

Keywords: Malawi, Preterm, Newborn care practices, Perceptions of preterm, Newborn community care

Background

Recent estimates indicate that there are 15 million preterm newborns annually and the number is increasing each year [1]. South Asia and sub-Saharan Africa accounts for almost two-thirds of the world's preterm newborns and over three-quarters of the world's newborn deaths due to preterm birth complications [1]. Worldwide almost half of preterm newborns are born at home and even for those born in facilities; essential newborn care (ENC) is often lacking [2]. Consequently, most of the preterm deaths occur at home in low-income and medium-income countries against a backdrop of poverty, sub-optimal care seeking and weak health systems [3]. It has been argued that most of these deaths would be averted by ensuring clean delivery, treating infections with antibiotics, promoting early and exclusive breastfeeding and keeping babies warm [4,5].

Malawi has the highest incidence of preterm birth in the world, estimated at 18.1 percent [1]. A previous study about preterm birth in rural communities in Malawi, described that neonatal and perinatal mortality was twice as high in preterm newborns as compared to term newborns [6]. Additionally, newborn survival interventions in Malawi such as care at birth and postnatal care

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have fewer improvements as compared to other interventions such as antenatal care and family planning [7]. Yet most newborn deaths happen in the first week and half of those in the first 24 hours of life [8] and among preterm newborns the lack of ENC may lead to death [9].

To our knowledge, there is a lack of evidence that people at community level in Malawi can easily care for preterm newborns. Information on local perceptions of preterm birth and care practices is important for programs aiming at improving preterm newborn health at the community level. Two studies in Malawi have previously reported on community concepts of preterm birth and knowledge of preterm birth respectively [10,11]. However, these studies did not investigate how preterm newborns were cared for. Thus, to improve newborn health outcomes in a resource poor setting currently challenged with a high incidence of preterm births [1], we undertook a qualitative study to explore the perceived causes of preterm birth among community members, recognition of preterm newborns, the reported care practices for preterm newborns and what people perceive as challenges in caring for preterm newborns at community level in Mangochi District in southern Malawi.

Methods

We used a qualitative study design [12] to describe the community members' perceptions about preterm birth and care practices for preterm babies. This was a substudy of a randomized controlled trial testing the impact of lipid based nutrient supplements provided to women during pregnancy on birth outcomes. The randomized controlled trial was carried out in areas served by a government district hospital (Mangochi), two health centers (Lungwena and Namwera), and St Martin's Hospital located in Malindi run by the Christian Health Association in Malawi (CHAM) [13]. The government district hospital is the major referral hospital in the district providing curative, preventive and maternal services.

Sampling and recruitment procedures

Different sampling strategies were used for different groups of participants. Firstly, we used purposeful sampling for recruiting women, men, grandmothers, traditional birth attendants (TBAs) and traditional healers. We introduced the aim of the study to the local leaders in the community and engaged them to help in identifying potential participants to be included in the study. These local leaders were village heads in the catchment areas and because of their knowledge about the population in their communities; they were in a good position to locate the potential participants. For instance, we asked for men who were not yet grandfathers and had at least one infant at home born in the previous year and women who had given birth in the previous year. The criteria for selecting parents with an infant of less than one year was to explore their current care practices and experiences for newborn babies including their knowledge on the care for preterm babies. We included grandmothers who were staying with their grandchildren in the same household for focus group discussions (FGDs) because we assumed that they would have a greater role to support and advise the parents on how to care for a newborn baby including a preterm. We randomly selected the women who had given birth to a preterm newborn baby for in-depth interviews (IDIs) from the existing list of participants enrolled in the on-going randomized controlled trial to specifically explore the preterm care practices. Pregnancy outcomes for participants enrolled in the clinical trial were well documented and preterm newborn babies were defined as those born before 37 weeks gestational age.

Data collection

Data collection took place between October 2012 and January 2013. Focus group discussions (FGDs) and in-depth interviews (IDIs) were used for data collection. A discussion guide was developed in English and translated into two local languages: *Chiyao*- the common local language in the catchment areas and *Chichewa* – the national language in Malawi. The same discussion guide was used for both FGDs and IDIs. Topics covered in the discussion guide were: perceived causes of preterm birth, definition of preterm birth, recognition of preterm newborns, care practices of preterm newborns and the associated challenges. We used IDIs mainly with TBAs, traditional healers and mothers of preterm newborns to get individual perspectives on the issues discussed. We conducted ten IDIs with mothers of preterm newborns, six TBAs and four traditional healers. We conducted a total of 14 FGDs, with a total of 110 participants from the following groups: women (four groups), grandmothers (four groups) and men (six groups). Each focus group consisted of 4 to 12 members. FGDs [14,15] were mainly conducted with grandmothers, fathers and mothers to explore their group views. We planned 5 focus groups with men, more than women focus groups based on the assumption that men are rarely involved in taking care of newborns. However, we conducted 6 FGDs with men instead of the planned 5, because in one site we received more participants than we could include in one group. None of the approached participants refused to take part in the interviews. A summary of the total number of interviews conducted is presented in Table 1.

The interviews were carried out in one of the local languages based on the interviewees' preference. In FGDs, we encouraged all participants to contribute to the discussions and each session took approximately 40 to 50 minutes. The interviewers briefed the participants on the aim of the study. All the interviews were recorded digitally. One

Table 1 Interview type

	n = 130
FGD (women)	4 groups (49)
FGD (men)	6 groups (29)
FGD (Grandmothers)	4 groups (32)
In-depth interview with mothers to preterm babies	10
In-depth interview with TBAs	6
In-depth interview with traditional healers	4

researcher with experience in conducting qualitative studies (AG) and two research assistants (moderator/note taker), fluent in both local languages conducted all the FGDs and IDIs. All the IDIs were held in participants' homes and FGDs in either a school or a place selected by a group away from disturbances. All participants received two bars of soap to compensate for their time.

Data management, analysis and ethical considerations

The recorded interviews were transcribed verbatim and then translated into English because some of the authors were not familiar with the local languages. The transcribed text was then compared with handwritten notes by the note-taker. We manually analyzed data using a content analysis approach [16]. The lead author read through the transcripts to get a sense of the whole text identifying themes, coding and assigning them to categories [17]. A summary of the findings was made, shared among the authors and agreed upon. We obtained oral and written consent from all the participants before the start of each interview. The College of Medicine Research Ethics Committee (COMREC) approved the study.

Results

Perceived causes of preterm birth

Participants reported a number of causes of preterm birth, which can be grouped into two aspects: maternal factors during pregnancy and general social factors as detailed in Table 2. The maternal factors included pregnant woman not eating good quality and enough food, pregnant woman doing excess household chores, husband beating his pregnant wife, frequent illnesses of the pregnant woman, having a previous abortion, history of preterm birth in the family, early and late childbearing. One male FGD participant noted that early childbearing was becoming more common in their communities, which many agreed to.

> *"Nowadays girls as young as under 16 years have already started child bearing and they are too young and not physically developed. These girls usually give birth to preterm newborns because their body organs are not well developed".* **FGD, Men.**

Table 2 Summary on perceived causes of preterm birth in the community

Causes of preterm birth	
Maternal factors	Frequent illnesses during pregnancy
	Pregnant woman overworking during pregnancy i.e. farming, fetching firewood
	Husband beating the pregnant wife
	Pregnant woman eating too little and poor quality food, i.e. always eating okra, sometimes sleeping without food
	Young and old maternal age
	The history of a preterm birth in the family
	Attempted abortion or previous abortion using traditional medicine
	Giving birth to many children
	Short intervals between births
	Pregnant woman delays in starting antenatal care
	Sexually transmitted infections (*matenda opatsirana pogonana*) i.e. syphilis (*chindoko*), gonorrhea (*chinzonono*) and HIV/AIDs
	Traditional diseases such as *Moto/tsempho* or *ndaka/nsanjiko*
	Malaria, epilepsy, high blood pressure, anemia
General social factors	Use of family planning methods, especially injections
	Will of God
	Witchcraft
	Use of local medicine during pregnancy

Furthermore, during FGDs, several women reported that a woman having too many births, especially eight or more times was dangerous because the uterus was much utilized and could lead to preterm birth.

> *"The uterus has weight but when you have given birth so many times, it loses the weight and becomes lighter (kupyapyala) failing to hold the pregnancy".* **FGD, Women.**

Participants further reported a number of illnesses during pregnancy that would lead to preterm birth, such as malaria, high blood pressure *(matenda a mtima)*, anemia *(kuchepa magazi)*, asthma *(mphumu)* and epilepsy *(khunyu)*. In addition, all participants emphasized that sexually transmitted infections (STIs) (*matenda opatsirana pogonana*) such as gonorrhea (*chinzonono*), syphilis (*chindoko*) and HIV/AIDS were the main cause, if left untreated as the quote below explains:

> *"If a woman has a disease in the her womb and if it is transmitted to the baby inside the womb, then the baby doesn't stay longer in the womb - move out of*

place, and eventually the baby comes out too soon before it is ripe. Most of these diseases are sexually transmitted diseases such as syphilis, gonorrhea and HIV/AIDs. **IDI, TBA.**

Participants also perceived traditional illnesses, i.e. *mwanamphepo* explained in Table 3 among women and *likango* for both women and men that would lead to a preterm birth or miscarriage. The participants also emphasized *moto*/*tsempho* in *Chichewa* language or *ndaka*/*nsanjiko* in *Yao* language that caused preterm birth because the pregnant woman carelessly shared utensils and ate food prepared by a woman who recently had a miscarriage, had a preterm birth and who has frequently engaged in sex with a man. Participants felt that a husband having a sexual relationship outside marriage causes miscarriage or preterm birth because there is contamination of blood through sexual intercourse of the husband with another woman outside marriage believed to be 'hot' which is then mixed with the blood of the pregnant wife through sex also believed to be 'hot'. Participants further reported that a pregnant woman could also give birth to a preterm newborn if having sex outside marriage. The two quotes below help to explain more:

"Some of the women could go and sleep with other men (nsanjiko) when their pregnancy is already tired and we happen to know such women because when delivering, they start by pouring out a lot of water and then delivers a preterm newborn ..." **IDI, TBA.**

"We know that the man had sex with another woman so that made the wife to lose the pregnancy because the blood from the other woman is different from the wife's blood and sometimes the woman who slept with the husband had miscarried before". **FGD, Men.**

The general social factors were heredity, the use of family planning methods, witchcraft and that the pregnant woman might not have spoken respectfully to elderly people who in turn cursed (*anamutemberedza*) her. Mothers with a previous preterm birth commonly reported that it was God's will. However, one mother of a preterm newborn emphasized that use of the traditional medicine whilst pregnant would also cause a preterm birth because the system in the uterus '*is disturbed*'.

Recognition of preterm newborns

All participants perceived preterm newborn as a baby who was born before the pregnancy had lasted for nine complete months. Participants reported that they counted the number of months from the last menstrual period as highlighted in the quote below:

"If born at home and when we count months and find that the months are not adding up to 9 months, we know that the baby is born preterm and we take the baby to the hospital". **FGD, Men.**

Furthermore, participants reported using physical features 'see a summary of points on recognition of preterm newborns' to recognize a preterm baby. Grandmothers and TBAs commonly reported that the skin of preterm newborn is too soft, has many wrinkles, is transparent and weak (*kupyapyala*) in the *Chichewa* language just like a piece of paper.

Summary on recognition of preterm babies

- Baby is too small, fails to breathe properly and have transparent lips which are soft
- Baby fails to breastfeed, sunken forehead and skin having many wrinkles
- Baby born with few hairs, have few eye lashes and nails not fully developed

Table 3 Definitions of vernacular terms related to perceived causes and care of preterm baby

Most common words	Meaning
Mwanamphepo *(Chichewa/Chiyao)*	Traditional illness found in women believed to cause sores inside the womb and causes miscarriage or preterm birth
Likango (*Chichewa/Chiyao*)	Traditional illness found both in men and women. Causes preterm birth and also death to the newborn before the preterm newborn reaches one year. Can be cured by traditional medicine.
Ndaka/nsanjiko (*Chiyao*) or tsempho/moto (*Chichewa*)	Caused by sexual impurity if the husband of a pregnant woman is having sex outside marriage while the wife is pregnant.
	Sometimes caused by the pregnant woman herself if she is having sex with other men besides the husband
	Causes preterm birth if the pregnant woman carelessly eats or shares utensils with a woman who had miscarried before, had a preterm newborn or a woman who is engaging in sex
Kupyapyala (*Chichewa*)	A state of being weak and thin
Anamutembereza (*Chichewa*)	Expression of been cursed by someone

- Body looks watery to show that it is not fully developed
- Looks malnourished and anemic
- Counting the number of the months if less than 9 months corrected gestational age
- Baby looks sick, has a pale body with pale teats and soft body scaring people to hold
- Fails to pass stool in the first day of life

Care practices for preterm newborns

All participants emphasized that preterm newborns received extra care compared to term newborns because most of them could easily die if not well cared for. The majority of participants commonly reported providing warmth as the main method of care. It could be provided by wrapping the newborn with warm materials, making fire inside the house, closing windows, doors and keeping the baby inside the house all the time. Grandmothers and TBAs advised women to squeeze milk from their breasts and give it to the baby because preterm newborns could not suckle enough milk on their own. TBAs mainly reported encouraging mothers to preterm babies to use plastic bottles and bags with hot water inside as explained in the quote below:

> *"Sometimes, we fill hot water into two plastic bottles, and a plastic bag. We lay the preterm newborn on top of the plastic bag and the two bottles are placed side by side of the newborn. In that way, the newborn is like still into her mother's womb, feeling warm*". **IDI, TBA.**

The majority of participants reported that the preterm newborn was not bathed until it reached 9 months corrected gestational age. Additionally, almost all women in the FGDs and IDIs reported that most families with preterm newborns did not allow other people to see the newborn until it had reached 9 months corrected gestational age as explained below.

> *"We restrict the people who come to see the baby. We do not allow anyone to come and see the baby because we are afraid of those who could do something bad – such as bewitching the baby, the way they hold or carry the baby and some are coughing as well so we get scared that they would infect the baby. So we only allow those people within the family, but not anyone else".* **FGD, Women.**

A few women in the FGDS reported that care involved maintaining good hygiene i.e. keeping the house clean, washing the newborn clothes and sprinkling water on the house surroundings to control dust. The other reason for confining the preterm newborn indoors was that parents feared discouragements from other people as one of the mothers to preterm newborn babies explained in the quote below:

> *"We just tell them that you are not going to see the baby because it is preterm. In a normal situation, it means it is not yet born. Because when you allow them, they start gossiping that the baby is too tiny and cannot survive".* **IDI, Mother of a preterm newborn.**

None of the participants reported using skin-to-skin kangaroo care for preterm newborns. When asked, some acknowledged to have heard of it from the radio but did not know how to do it. However, a mother of a preterm newborn said that she practiced it in the hospital, but at home, it was difficult because of several household chores. A summary of reported care practices is presented in Table 4.

Challenges of caring for preterm newborns in the community.

Almost all participants reported that the care of a preterm newborn was demanding, requiring the mother to be available all the time, thereby affecting business, farming and household chores. Men reported that they did not take part in carrying the baby, but provided support by fetching firewood, paraffin (a liquid which is used for a lamp to give light at night), and relish (a dish that is served with the Malawian staple food - *nsima*). Paraffin helps the mother to constantly check on the newborn at night while fetching for the relish and firewood are duties that a woman normally does so that the family can have something to eat. The women agreed with this assessment stating that having a preterm newborn was a burden on women because men did not help much in caring for the newborn. The majority of women further complained that instead of helping, their husbands started seeing other women which disturbed their marriages. The quote below explains more about how a preterm newborn in the family influenced men having sexual partners outside marriage.

> *"A preterm birth is considered like a miscarriage (chitayo); requiring the family to wait for the appropriate time to take local medicine for chitayo before the family resumes sex, failing to do so the husband can die and this waiting time forces some men to go for other women".* **FGD, Women.**

Participants reported challenges of poverty and lack of knowledge on caring for preterm newborns. Because of poverty, parents failed to buy warm materials, lived in cold houses with grass thatched leaking roofs and failed to rush the baby to the hospital because of lack of

Table 4 Summary of care practices and challenges

Care practice for preterm newborns	The preterm newborn is not bathed until it reaches 9 months corrected gestational age
	Keeping the baby inside the house until it reaches 9 months corrected gestational age
	Windows and doors of the house are kept closed all the time
	Maintaining a clean environment (washing newborn clothes and sprinkling water around the house to control dust)
	Use of plastic bottles and bags with hot water inside to provide warmth
	Make fire inside the house to keep the house warm
	Wrap the baby with blankets
	Expressing breast milk (mothers squeezing the breast milk into a cup and using a spoon to feed the newborn)
	Couples with a preterm newborn refrain from sex until required time when couples take traditional medicine
Challenges faced in caring for preterm newborns	The preterm newborns fall sick often times
	Poverty- no money to buy paraffin, to pay hospital bills and transport, to buy warm materials and to improve the condition of the house if leaking
	Mother to preterm baby fails to do business and household chores i.e. farming and fetching firewood
	Men start having other sexual affairs outside marriage
	Lack of knowledge on how to properly care for preterm newborns

money for transport and to pay for the hospital bills. In one of the catchment areas, the nearest health facility was a pay for-service hospital and participants complained of lack of money to access the facility.

> *"Because of lack of money when your child falls sick, you wait first so that you can do piece work to find money – poverty is a problem here and these kind of babies when they fall sick, it means you have to rush to the hospital but this doesn't happen because the nearest hospital is a paying one".* **FGD, Men.**

All participants concurred that many preterm newborns had failed to survive because of lack of proper care in the homes. However, the majority of participants mentioned that they were able to tell that the preterm newborn was sick because the baby would develop a fever, not breath normally, change skin color to yellow, coughing and crying often times when the mother tries to hold the newborn. Grandmothers and TBAs said that they always provided traditional medicine to the preterm newborns before going to the hospital.

> *"We find long queues at the hospital and a preterm baby can die whilst waiting to be attended so after giving it local medicine, we then decide to start off for the hospital because even if you go sometimes they tell you that there is no medicine".* **IDI, TBA.**

Discussion

In our study, we used FGDs and IDIs to explore perceptions of preterm birth and care practices for preterm newborns among community members in the Mangochi district in southern Malawi. Some of the perceptions of preterm birth reported in our study, such as maternal factors are similarly reported as risk factors for preterm birth in previous qualitative and epidemiological studies in Malawi and elsewhere [10,18-21]. Tolhurst *et al.*, in a study on 'perceptions of preterm birth in Malawi' similarly reported witchcraft, sexual impurity, traditional illnesses such as *mwanamphepo* and *likango* as causes of preterm birth and miscarriages [10]. Although it is well known that early pregnancies have public health consequences for both the mother and the newborn, in our study areas participants reported that early childbearing was common and was associated with preterm birth. Similar findings were reported by 78% of the respondents in a study conducted in Dowa district of Malawi who were concerned that teenage pregnancies were becoming common in their area [22]. Furthermore, several studies have reported higher rates of preterm deliveries among adolescent mothers as compared to adults [23,24]. Additionally, we found that participants in our study perceived the use of family planning methods such as injections, use of traditional medicine whilst the woman is pregnant and previous abortion to cause preterm birth.

We found that the majority of participants reported the concept of providing warmth as the most common care practice for preterm newborns. Other studies also recommend that simple care practice such as provision of warmth to preterm newborns should be universal [9,25-27]. However, some reported practices of generating warmth in our study, especially use of plastic bottles with hot water inside could be dangerous to the newborn if not properly handled. In contrast, the use of skin to skin contact for providing warmth was not mentioned and the majority of participants when asked reported lack of knowledge about skin to skin kangaroo mother care. Another qualitative hospital based study in Uganda also reported that participants did not know why and how skin to skin care should be done [28]. Furthermore, we suggest that the period of delayed bathing (until the baby reaches 9 months of corrected gestational age) is over emphasized and there is a need for further research

to investigate the exact period of delayed bathing. However, we did not find out if the delayed bathing was after the first bath or that the baby was not bathed at all. Another study has also reported lack of evidence as to how long to delay, especially if the bath can be warm and in a warm room [29]. In our study, keeping the preterm newborn baby indoors and not allowing other people outside family members to see the baby was the most reported care practice in order to protect the baby from infections and discouragement from other people. This was also reported in Tanzania, where families secluded both baby and mother for 40 days so as to protect the newborn from witchcraft [30]. Maintaining a clean environment of the preterm newborn, such as washing the newborn clothes, keeping the house and its surroundings clean was another care practice reported in this study.

Interestingly, we found that grandmothers encouraged mothers to squeeze milk from the breast and feed the newborn using a spoon and a cup in agreement with preterm newborn care recommendations [31]. However, none of the participants reported promoting early and exclusive breastfeeding for preterm newborns. The role of grandmothers in newborn feeding practices, including breastfeeding has also been reported in many studies [32-34]. Similarly, perceptions of sexual impurity around pregnancy and childbirth have been reported in some parts of Malawi and Bangladesh [10,34-37]. According to Bezner's study in the northern part of Malawi, grandmothers and other elders of the village report that they would recognize if a child is suffering from *'moto'* or has died of *'moto'* - a disease described traditionally to be associated with sexual impurity [34]. In Bangladesh, families similarly know that children are vulnerable and at increased risk for serious health problems during the first weeks of life and take action to protect them [38]. The similarities of these studies from Malawi and Bangladesh are that they both report on sexual impurity in relation to care practices for any newborn not specifically for preterm babies. However, the similarities of these findings across these two countries probably suggest that programs targeting newborn health should consider such deep rooted perceptions in order to be successful.

In the present study participants report diverse challenges, including economic and health system related issues such as the lack of medication in public facilities and long queues. Lack of money was cited as the major challenge as many families are reportedly poor and could not afford to properly care for the preterm newborns including taking them to the hospital in case of sickness. In one of the catchment areas, the nearest health facility is a pay for-service hospital and this delays decision making to access medical care for a sick preterm newborn. This finding is in line with what others have found [39,40]. Actually, it has been acknowledged that poverty undermines maternal, newborn and child health through numerous pathways, including reduced care-seeking and access to health care services [40,41]. In order to mitigate the impact of poverty on maternal and infant health, there is a policy in Malawi that allows free access to services at CHAM hospitals with a focus on maternal and neonatal interventions [42]. However, the CHAM hospital in the catchment areas was not yet a beneficiary at the time of data collection. Similar interventions are reported in India, where the government has introduced a program that entitles all pregnant women and neonates to free care at public facilities, including free drugs and free transport to and from home [36].

The strength of this study is that we triangulated the data by using both FGDs and IDIs to explore community perceptions and care practices of preterm newborns. In addition, we included male participants in our study in a society which specifies gender roles assuming that men are not expected to know much about caring for newborn babies. The limitation of our study is that we did not include grandfathers who may have different opinions on preterm birth and care practices. Furthermore, the findings of this study cannot be generalized to all communities in Malawi as the study was conducted among a few people within the catchment areas of an active clinical trial. Although the present study was conducted in catchment areas that have had multiple studies, we believe that the response bias was minimized because no similar study had been conducted before. In addition, some of the participants in our present study were not involved in the ongoing clinical trial. Another limitation is that we did not ask for a place of delivery, so those who gave birth at home might have different views from those who delivered in a health facility on care practices. Possibly those who delivered at the facility had different care practices. However, even when mothers deliver at the health facility, they are quickly discharged and most of the newborn care happens at home.

Conclusions

In this community, the reported poor care practices to preterm babies were associated with many challenges such as poverty and lack of knowledge on how to properly care for these babies at home. There is a need for action to address the current care practices for preterm newborn babies among the community members in order to improve survival of the increasing numbers of preterm babies in Malawi. These findings add new knowledge to the existing literature on the preterm newborn care which can foster appropriate preterm newborn care practices in the rural communities.

Abbreviations
TBA: Traditional birth attendant; CHAM: Christian Health Association in Malawi; IDIs: In-depth interviews; FGDs: Focus Group Discussions; MoH: Ministry of Health; ENC: Essential Newborn Care; STI: Sexually Transmitted Infections; WHO: World Health Organization.

Competing interests
The authors declare that they have no competing interests.

Authors' contributions
PA, AG, UA designed the study. AG collected the data, did the analysis and drafted the manuscript. PA, AM, and UA participated in data interpretation and critically edited the paper. All authors approved the final manuscript to be submitted to *BMC Pregnancy and Childbirth*.

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Investigating Preterm Care at the Facility Level: Stakeholder Qualitative Study in Central and Southern Malawi

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Abstract *Objectives* Malawi is estimated to have one of the highest preterm birth rates in the world. However, care of preterm infants at facility level in Malawi has not been explored. We aimed to explore the views of health stakeholders about the care of preterm infants in health facilities and the existence of any policy protocol documents guiding the delivery of care to these infants. *Methods* We conducted 16 in-depth interviews with health stakeholders (11 service providers and 5 policy makers) using an interview guide and asked for any existing policy protocol documents guiding care for preterm infants in the health facilities in Malawi. The collected documents were reviewed and all the interviews were digitally recorded, transcribed and translated. All data were analysed using content analysis approach. *Results* We identified four policy protocol documents and out of these, one had detailed information explaining the care of preterm infants. Policy makers reported that policy protocol documents to guide care for preterm infants were available in the health facilities but majority (63.6 %) of the service providers lacked knowledge about the existence of these documents. Health stakeholders reported several challenges in caring for preterm infants including lack of trained staff in preterm infant care, antibiotics, space, supervision and poor referral system. *Conclusions* Our study highlights that improving health care service provider knowledge of preterm infant care is an integral part in preterm child birth. Our findings suggests that policy makers and health decision makers should retain those trained in preterm new born care in the health facility's preterm unit.

Keywords Policy and guidelines · Preterm care · Health facilities · Malawi

Significance

These findings are important to the field of public health because they highlight the current situation about the care of preterm infants in some of the health facilities in Central and Southern Malawi. The findings can be used by public health researchers and policy makers to improve maternal and child health outcomes, especially in preterm infant care.

Introduction

Globally, South Asia and sub-Saharan Africa account for approximately two-thirds of the 15 million preterm newborns that are born annually and over three-quarters of the world's newborn deaths is due to preterm birth complications [1]. Most of these newborns (>80 %) are born between 32 and 37 weeks of gestation and could be saved with simple care, such as warmth, feeding support and provision of antibiotics [2, 3]. Other priority interventions

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addressing infant care include extra care for sick and small newborns, skilled care at birth, neonatal resuscitation, Kangaroo Mother Care (KMC) and infection prevention [4–6]. Additionally, the World Health Organisation (WHO) recommends affordable and essential newborn care (ENC) practices (clean cord care, thermal care, and initiating early and exclusive breastfeeding) for handling preterm birth [4]. However, the uptake of these low cost interventions in many low-income countries (LICs) remains relatively low [7].

In LICs, several challenges in relation to quality of care in health facilities are well documented (i.e. lack of equipment, supplies and drugs, outdated clinical protocols and staff shortages) [8]. To help parents and health professionals in the management of preterm births, various guidelines have been developed and approved by many scientific societies in various countries [9]. Additionally, recognising low birth weight (LBW) infants and distinguishing the ones who are preterm are essential first steps in prioritizing care for the highest risk infants [3].

Malawi is one of the countries estimated to have the highest preterm birth rate in the world [7]. However, there is limited evidence to show how preterm births are handled at the health facility level in Malawi. A literature review reveals few studies that have investigated care of preterm infants at health facilities in Malawi other than one recent study which looked at provider attitudes and knowledge of preterm birth [10]. Therefore, an in-depth understanding of health stakeholders' experiences about current preterm infants care is significant in improving care of preterm infants, and consequently infant health at health facility level. The aim of this qualitative study was to explore views of preterm infant care among health stakeholders and investigate if there were any policy protocol documents guiding service providers to care for these infants at the facility level. The findings from this study will inform health decision makers and policy makers in Malawi on the current care practices of preterm infants in health care facilities.

Methods

Study Location

This study was conducted in the Central and Southern regions of Malawi. In the central region, the study focused on five policy makers who were from the Ministry of Health headquarters office, health developmental partners and one non-governmental organization (NGO) that are currently working on infant health activities. For the purpose of this study, "policy makers" imply those health stakeholders who are not providing clinical care in the health facilities but are partners to Ministry of Health (MoH) and are currently involved in infant health activities. These policy makers are also responsible for developing health protocol documents and providing technical support. In Malawi, there are three levels of health care: primary, secondary and tertiary, and this study included health facilities from all three levels [11]. In the southern region, the study focused on 10 health facilities in 5 districts. These districts were Mangochi, Zomba, Blantyre, Chiradzulu and Mulanje.

Sampling and Data Collection

We used purposeful sampling to select health stakeholders in 10 health facilities (Table 1) and 5 health stakeholder offices. The health facilities included 2 government health centres, 2 Christian Health Association of Malawi (CHAM) health centres, 2 district hospitals, 2 CHAM hospitals and 2 central hospitals. The 5 health stakeholder offices were: the Ministry of Health headquarters (Reproductive Health Unit), Save the Children International, World Health Organisation, United Nations Population Fund and United Nations Children's Fund. The health stakeholders in the health facilities were service providers working in the clinical care of preterm infants.

We used semi-structured interviews with open-ended questions to collect data. We conducted 16 face to face in-depth interviews with health stakeholders of whom 11 were service providers in the health facilities and 5 were policy makers from health stakeholder offices. Detailed characteristics of health stakeholders are reported in Table 1. Although we pre-planned the number of interviews, we also considered saturation point. The issues discussed with policy makers included their knowledge about existing policy protocol documents which guides the management of preterm infants in health facilities, their role in preterm infant care, and associated challenges with preterm infant care. We discussed with service providers how they and other service providers cared for preterm infants, if they had policy protocol documents to guide them in the care of preterm infants, recognition of preterm infants and challenges in caring for these infants. Interviews took approximately 40–60 minutes.

Originally, the plan was to interview three people at each health facility as follows: the in-charge of the postnatal ward, the service provider in the postnatal ward, and the matron. During the pilot, we found that the service provider working in the postnatal ward was the most appropriate person to interview. The findings from the pilot study showed that service providers were managing preterm infants without guidance from policy protocol documents but revealed that they encouraged extra warmth for preterm infants. One researcher experienced in qualitative research conducted all the interviews. These interviews

Table 1 Background characteristics of key health stakeholders

	(n = 16)
Policy makers	
Department of Health (Reproductive health unit)	1
Non-governmental organisation	1
Developmental partners	3
Health care facilities	
Central hospital (Zomba and Queens-Blantyre)	2
CHAM hospital (Mulanje mission and Malosa)	2
District hospital (Chiradzulu and Mangochi[a])	3
Government health centres (Lungwena, Namwera)	2
CHAM health centres (Nkoche and Malindi)	2
Sex	
Male	1
Female	15
Age	
Years in range	24–58 years, median age 37.5

[a] In one district hospital, we interviewed two service providers because they were both interested to take part in the discussion

were conducted either in *Chichewa* or English based on the interviewees' preference. *Chichewa* is Malawi's most widely spoken local language.

We actively searched for any existing policy protocol documents by asking health stakeholders to share a copy of the documents that guided service providers to care for preterm infants in the facilities. The documents reviewed were only those that were confined to Malawi health care system and were approved by Ministry of Health, Malawi. In this study, policy protocol documents are defined as any systematically written statements that set clear direction to assist service providers about specific care for preterm infants.

The interviews were digitally recorded and transcribed verbatim. We translated the Chichewa transcripts into English. The first author systematically read and re-read through the transcripts looking for patterns. We analyzed all data using a content analysis approach [12], identifying emerging themes in categories and sub-categories. The first author compiled a summary of the main findings and shared with other authors who agreed on the results.

One investigator reviewed all the identified documents and abstracted the following information: recognition of preterm infants, management of preterm labour, management of preterm infants, facility management of sick preterm infants and recommendations for home care. The first author made a summary table of the findings and shared with other authors for comments until a consensus was reached.

Ethical Consideration

Ethical approval was obtained from the College of Medicine Research and Ethics Committee (COMREC) in Malawi. All participants received written and detailed verbal information about the aim of the study and the procedure of data collection during the time of booking appointments with interviewees. Participants consented verbally to participate in the study and also accepted that the interviews should be digitally recorded. We did not compensate participants for their participation in the study. We assured all participants that the information discussed through interviews will remain anonymous and person information will not be identified with any of the results.

Results

Existing Policy Protocol Documents on Facility Care for Preterm Infants

Table 2 presents a summary of the findings from the 4 policy protocol documents identified from health stakeholders on the management of preterm infants. All documents had information on management of preterm infants. For instance, the 'National Sexual and Reproductive Health and Rights' (SRHR) policy had one statement under the theme of **Maternal and Neonatal Health** describing that '*Kangaroo mother care shall be routinely used in the management of premature infants'*. The second document that described the care of preterm infants in detail was the 'Malawi National Guidelines for Kangaroo Mother Care' developed in 2005 and revised in 2009. This document described care for LBW and preterm infants at different levels of health care including referral procedures, discharge criteria, re-admission, and recommendations for

Table 2 Summary of policy protocol documents identified from policy makers on preterm care

Document name	Document type	Key points discussed on preterm care
National and sexual reproductive health rights (SRHR)	Policy	KMC shall be routinely used for managing preterm and low birth weight infants
road map for accelerating the reduction of maternal and newborn mortality and morbidity in Malawi	Road Map	Documents percentages of newborns that receive ENC, including neonatal resuscitation, percentage of health facilities with newborn resuscitation services, skilled birth attendant at birth, document number of health facilities providing KMC
Malawi national guidelines for Kangaroo mother care	Guideline	Explains the importance of KMC, eligibility criteria for admission of infants on KMC in the health facilities, referral procedures, Initiation of KMC at community level, KMC position and nutrition, care of the baby during KMC, discharge and follow up
Evaluation of kangaroo mother care services in Malawi	Report	Scaling up of KMC facilities by facility numbers, progress with KMC implementation and KMC facilities, services and practices

home care. The other two documents namely: 'Road Map for Accelerating the Reduction of Maternal and Newborn Mortality and Morbidity in Malawi' and an 'Evaluation Report of Kangaroo Mother Care Services in Malawi' also had information on both maternal and newborn care, including Essential Newborn Care (ENC) such as thermal care, feeding support and infection prevention.

Policy Makers Views on Care for Preterm Infants

All (5) policy makers reported that there was SRHR policy protocol document and quoted its policy statement that '*Kangaroo mother care shall be routinely used in the management of premature infants'*. The policy makers further reported that there was no separate policy other than SRHR document, addressing care for preterm infants at health care facility level in Malawi. Additionally, policy makers reported that copies of the SRHR policy were distributed to all health facilities in Malawi. One of the policy makers explained how KMC was conducted in practice. *'KMC involves the mother carrying the newborn baby skin to skin tight in-between her breasts wrapped with a piece of cloth. This helps to keep the baby warm and encourages breastfeeding, so that preterm and LBW infants can easily gain weight'* (Policy-Maker—Lilongwe). However, one (20 %) of the policy makers further reported that in the previous years, much attention was on maternal health and preterm birth was rarely mentioned during antenatal care.

Service Provider's Views on Care for Preterm Infants

Primary Levels and Secondary Levels

Seven (63.6 %) of the service providers in health centres and district hospitals reported lack of knowledge of the existing policy protocol documents that could guide them to properly manage preterm infants. Probing on how they provided care for these infants, they reported to use knowledge gained through their nursing training period, meetings, and workshops. However, one (9.1 %) of the service providers expressed concern that even knowledge gained through workshops was not well utilized in many health facilities because of how service providers were allocated in the hospital wards. As asserted by one service provider, *'Sometimes there is one person selected to attend a training or workshop on KMC but you find that the person is no longer working in the postnatal ward to manage preterm infants. In this way, it does not help because the information is not well utilised'*. (Service provider - District Hospital).

Tertiary Level (Central and CHAM Hospitals)

All (4) of the service providers working in tertiary level facilities reported awareness of the existing documents and was already implementing KMC for LBW and preterm infants, as recommended in the SRHR policy and the national KMC guideline. Service providers in these facilities also reported to advise mothers/guardians of preterm infants to breastfeed often and keep the infants warm. However, none of them had a copy of the existing documents and they reported that the policy protocol documents were kept somewhere in other offices. As one of them narrated, '*We have the policy and some guidelines on preterm care, but we have them in the other offices…, but when we are looking for information, we usually try to find out wherever they are'*. (Service provider—Central Hospital).

Challenges in Caring for Preterm Infants in Health Facilities

Table 3 presents a summary of challenges that health stakeholders had reported, and some of the cross cutting

Table 3 Summary of reported challenges for caring preterm infants

Policy makers
Lack of timely supervision to all healthy facilities due to logistics problems
Less budgeting towards preterm infant health than other areas at the district level to buy antibiotics
Many service providers failing to utilise the available policy protocol documents with information on care of preterm infants
Health centres
Insufficient resources (no heaters, incubators, staff and space)
Poor transport system for referring preterm infants to other hospitals
Lack of proper coordination between referral hospitals and health centres
Lack of knowledge on preterm care
Mothers to preterm infants failing to take advice from service providers on caring infants
District hospitals
Few/no incubators, non-functioning heaters
Lack of follow up on discharged preterm infants
Misallocation of trained staff in preterm care to other hospital wards
No antibiotics and oxygen supply
Poor attitude among some service providers towards survival of preterm infants
Lack of trained staff on preterm care
Central Hospital/CHAM hospitals
Lack of follow up on discharged preterm infants
Fewer staff, incubators and space compared to number of preterm infants

challenges in the health facilities were shortage of staff, space, and antibiotics. Challenges reported in district hospitals and health centres were almost similar and are grouped under primary/secondary level while those reported in Central and CHAM hospitals are presented under tertiary level. Policy makers reported their own challenges (Table 3).

Primary and Secondary Levels

In these facilities, (63.6 %) of the service providers reported similar challenges, such as poor referral system, lack of coordination, lack of follow up system, oxygen supply, non-functional heaters, lack of knowledge on preterm care, and space to initiate KMC. In addition, there was an attitude problem among some of the service providers that a preterm infant would not survive. The service provider said, *'As nurses, we also should accept that sometimes we have bad attitude …by just looking at the preterm baby and see how it looks, we say but is this one going to survive? Instead of either instructing the mother on what to do or checking on the baby you just stay, that the mother will come and ask, we sometimes have a problem as well'*. (Service provider—District Hospital).

Three (27.3 %) of the service providers described work load as the main limiting factor to properly manage the preterm infants. One of them highlighted, '*You find yourself that you did not sleep the whole night, and the following morning you are also on duty doing antenatal care, working in the maternity and other areas… and yet there is a mother with a preterm infant who needs constant supervision, so it becomes difficult because you are tired and there is a lot of work'*. (Service provider—Health Centre).

Few service providers (27.3 %) felt challenged because some women were reported too poor to afford linen to cover their preterm infants. In addition, two (18.2 %) of the service providers reported that low education amongst the majority of mothers made care for preterm infants difficult because most mothers would not follow instructions from service providers but rather listen to their guardians on caring for their preterm infants.

Tertiary Level

The service providers felt that the number of resources per preterm infant contributed more to the difficulty in caring for these infants, rather than the availability of such resources. One service provider explained: *'Most of the times we have a lot of preterm infants and the beds for these infants are few that sometimes we combine three or four of them on one bed which can also cause infections. If there is any way of helping, we could appreciate additional beds and heaters'* Service provider-CHAM hospital.

Additionally, service providers explained that there was no follow up system if preterm infants were discharged to their respective homes.

Policy Makers

Three (60 %) of the policy makers reported logistics problems that limited them to conduct timely supervision to health facilities. One (20 %) of the policy makers reported that preterm birth was not an area of focus until recently due to an alarm from the 2012 'Born Too Soon' report on preterm birth. Another explained that there was little attention on the issue of managing preterm infants at district level resulting into less budgeting towards preterm infants. However, three (60 %) of the policy makers described that there was an attitude problem among some of the health workers as they were not willing to learn from colleagues and utilise the available policy protocol documents to guide them on appropriate care. For instance, policy makers described providing enough support, including trainings and materials to health workers on care for preterm infants, but when monitoring them, care was not conducted as expected. Although shortage of staff was widely acknowledged by the 5 policy makers interviewed, one (20 %) of them felt that duty allocation, especially in the health centres, accelerated the problem because service providers wanted to have long off duty hours. The policy maker elaborated, *'In some of the health centres it is really difficult for one person to be committed to many activities, but sometimes there are two or three people and they give each other* 1 *week duty allocation day and night so that they can be off duty for a longer time which is tiresome and makes them ineffective'*. (Policy Maker—Lilongwe).

Discussion

In this study, we found that most (63.6 %) of the service providers were not aware about the existence of the policy protocol documents to guide them on care of preterm infants in their health facilities. Additionally, the identified documents lacked detailed information on how service providers would recognise preterm infants and information that could guide them to determine appropriate care for these infants. Lawn et al. [3, 6] suggests that recognition of LBW and distinguishing which ones are preterm are essential first steps in prioritizing care for the highest risk infants. Furthermore, the documents did not have information on the management of preterm labour which could improve the health outcome of preterm infants [13].

Our study reveals that primary knowledge of care for preterm infants tends to vary among health facilities. For instance, the majority (63.6 %) of the service providers in district and health centres lacked knowledge of preterm infant care, which suggests that there is a lack of training in preterm infant care based on the available policy protocol documents. Another study similarly found that for almost 78 % of the guidelines, more than 10 % of the physicians were not aware of their existence [14]. In Kenya and Uganda, it was also found that there were no protocols guiding appropriate care for preterm infants in the health care facilities and that no hospital had clinical management guidelines for common causes of serious illness in infants [15, 16].

Furthermore, our findings suggest that there is a gap between the recommended simple care for preterm infants [13] and what is relevant for health care facilities to care for these infants. In our study, KMC was not promoted in some health care facilities due to lack of knowledge of how to implement it and lack of space. Similarly, in Uganda, service providers lacked adequate KMC rooms for preterm care in the health care facilities [16]. Challenges in relation to space imply that KMC may not suit all health care facilities in Malawi. Others have also noted that KMC remains unavailable at-scale in most low income countries [2, 5]. However, evidence shows that if KMC is initiated in good time it reduces neonatal mortality with approximately more than half, unlike the incubators and standard care [17, 18].

Specific problems such as lack of timely supervision to health facilities are important because they can help to identify areas which need further improvement in the management of preterm infants. In fact, lack of resources such as essential antibiotics, space, poor referral system, shortage of staff and lack of follow-up system are not unique to this study. Some additional studies have documented the same findings, including poor infrastructures in many low resource settings [19, 20]. Others have suggested that giving proper resources for health workers can enable them to provide good quality services [15].

In our study, poor attitudes among service providers who reported that the death of preterm infants is inevitable can affect the health outcome of these infants. Thus, changing service providers' attitudes in this area is crucial because history of neonatal care in high income countries shows that the major reduction in deaths occurred before neonatal intensive care was established [3]. We did not find any study specifically reporting negative attitudes towards care for preterm infants. However, a study which investigated parents and health professionals attitudes towards KMC for preterm infants showed that the majority of the mothers felt positively about KMC but professional staff considered KMC to be sub-standard care and that it increased staff workload [21]. Other studies suggest that training in general improves the provider's knowledge and level of confidence [22, 23].

Basic care practices such as warmth [1] for managing preterm infants was promoted in all health facilities we visited in this study. The main strength of this study is that we triangulated our data by using in-depth interviews and sourced existing documents on preterm care so that we could compare the two in addressing our research question. This study was conducted within the following limitations: we did not discuss the contents of the existing documents with the policy makers to obtain a true picture of the gaps that exists in these documents about care of preterm infants in the health care facility in Malawi. In addition, we had a good representation of central hospitals as we included 2 out of the 4 hospitals in Malawi, but other facilities such as health centres, district hospitals and CHAM hospitals were under represented, therefore our results cannot be generalised to all health facilities in Malawi.

Conclusion

Despite policy makers' acknowledgement of the available policy protocol documents that could guide care for preterm infants at facility level, majority (63.7 %) of the service providers lacked knowledge on how to properly care for these infants. Improving service providers' knowledge on care of preterm infants is an integral part in providing appropriate care for preterm infants at the facility level. Our study suggests that policy makers and health decision makers should retain those trained in preterm new born care in the health facility's preterm unit.

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PLOS ONE

RESEARCH ARTICLE

Pre-pregnancy body mass index (BMI) and maternal gestational weight gain are positively associated with birth outcomes in rural Malawi

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Abstract

Background

Whereas poor maternal nutritional status before and during pregnancy is widely associated with adverse birth outcomes, studies quantifying this association in low income countries are scarce. We examined whether maternal pre-pregnancy body mass index (BMI) and weight gain during pregnancy are associated with birth outcomes in rural Malawi.

Methods

We analyzed the associations between pre-pregnancy BMI and average weekly gestational weight gain (WWG) and birth outcomes [duration of gestation, birth weight, length-for-age z-score (LAZ), and head circumference-for-age z-score (HCZ)]. We also determined whether women with low or high pre-pregnancy BMI or women with inadequate or excessive WWG were at increased risk of adverse birth outcomes.

Results

The analyses included 1287 women with a mean BMI of 21.8 kg/m^2, of whom 5.9% were underweight (< 18.5 kg/m^2), 10.9% were overweight ($\geq$ 25 kg/m^2), 71.8% had low WWG [below the lower limit of the Institute of Medicine (IOM) recommendation], and 5.2% had high WWG (above IOM recommendation). In adjusted models, pre-pregnancy BMI was not associated with duration of pregnancy ($p = 0.926$), but was positively associated with birth weight and HCZ (<0.001 and $p = 0.003$, respectively). WWG was positively associated with duration of gestation ($p = 0.031$), birth weight ($p<0.001$), LAZ ($p<0.001$), and HCZ ($p<0.001$). Compared to normal weight women, underweight women were at increased risk of having stunted infants ($p = 0.029$). Women with low WWG were at increased risk of having infants with low birth weight ($p = 0.006$) and small head circumference ($p = 0.024$)

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compared to those with normal weight gain. Those with high BMI or high WWG were not at increased risk of adverse birth outcomes.

Conclusions

WWG is an important predictor of birth outcomes in rural Malawi. The high prevalence of inadequate WWG compared to low pre-pregnancy BMI highlights the need to investigate causes of inadequate weight gain in this region.

Introduction

The nutritional status of a woman before and during pregnancy is important for a healthy pregnancy outcome [1]. Maternal malnutrition may play a key role with regard to poor fetal growth including low birth weight (LBW), short- and long-term infant morbidity and mortality, and long term, potentially irreversible cognitive, motor and health impairments [2,3]. Pregnant women in sub-Saharan Africa are at a particular nutritional risk as a result of poverty, food insecurity, political and economic instabilities, frequent infections and frequent pregnancies [4].

The effects of pre-pregnancy anthropometric status (estimated by maternal BMI) are well documented [4–6]. In low income countries (LICs), maternal underweight in early pregnancy is a leading risk factor for adverse birth outcomes, including LBW, preterm birth, small for gestational age (SGA), and stillbirth [5,6]. There is some evidence suggesting that high BMI prior to pregnancy is associated with an increased risk of preeclampsia, gestational diabetes, caesarean section, postpartum haemorrhage, and fetal macrosomia [7]. Additionally, entering pregnancy with high pre-pregnancy BMI increases the risk for pregnancy complications and adverse outcomes for both mother and infant [8–10].

Maternal gestational weight gain (GWG) has also been widely studied as an independent predictor of adverse pregnancy outcomes [11,12]. Multiple studies from middle and high income countries have found that women with inadequate GWG were at a higher risk of giving birth to LBW and preterm infants [5,12–16]. Women in LICs generally have lower weight and GWG than those in high income countries [17]. More than 95% of LBW infants are born in LICs—sub-Saharan Africa alone has a 15% incidence of LBW [18]. In Malawi, the incidence of LBW is 12% [19]. Additionally, Malawi is one of the poorest countries in sub–Saharan Africa with approximately 80% of the population living in rural communities that are faced with various health challenges including malnutrition [19]. However, recent reports show an increase in obesity/overweight from 9% in 1992 to 21% in 2015–16 among urban Malawian women of reproductive age (15–45 years) [19,20]. Studies that have examined the impact of pre-pregnancy BMI (either low or high) or inadequate or excessive GWG on birth outcomes in Malawi are lacking. In the present study, we tested the hypothesis that maternal pre-pregnancy BMI and weight gain during pregnancy are positively associated with birth outcomes (duration of pregnancy and size of the newborn including weight, length and head circumference). We also aimed to examine the impact of pre-pregnancy BMI (either underweight or overweight) and average weekly gestational weight gain (WWG;(inadequate or excessive) on risk of adverse birth outcomes (preterm birth, stunting, LBW, small head circumference and SGA). In an exploratory analysis, we examined whether a lipid-based nutrient supplement or a multiple micronutrient supplement consumed during pregnancy modulated the associations between pre-pregnancy BMI and birth outcomes compared to an iron-folic acid supplement.

Materials and methods

Study design and setting

This was a prospective cohort study, nested within the International Lipid-Based Nutrient Supplements (iLiNS) Project DYAD trial in Malawi (iLiNS-DYAD-M), which was a randomised controlled trial that was carried out in Mangochi District. Mangochi district is a semi-urban, semi-rural area of southern Malawi with subsistence farming and fishing as the main sources of income. Participants were recruited between 14 and 20 gestation weeks, seen again at 32 and 36 gestation weeks, and soon after birth, to determine weight gain during pregnancy and birth outcomes.

Participants were recruited from 1 district hospital (Mangochi), 1 semi-private hospital (Malindi) and 2 public health centres (Lungwena and Namwera) from February 2011 to August 2012. The inclusion criteria were being a permanent resident of the catchment areas, not more than 20 weeks gestational age, identified through antenatal clinics and signed or thumb-printed informed consent. The exclusion criteria were being less than 15 years of age, chronic medical conditions requiring frequent medical attention, history of allergies, evident pregnancy complications, earlier participation in the same trial or concurrent participation in any other clinical trial. Participants in the trial were randomized into three intervention groups. The women consumed from $\leq$ 20 gestation weeks until delivery either one daily iron and folic acid (IFA) capsule; one capsule with 18 micronutrients (MMN); or one 20 g sachet of lipid-based nutrient supplement (LNS) containing 118 kcal, protein, carbohydrates, essential fatty acids, and 22 micronutrients [21] (**S1 Table**). The intervention had a limited impact on birth outcomes [22]. The trial was performed according to Good Clinical Practice guidelines and the ethical standards of the Helsinki Declaration. The study (Trial registration: www.clinicaltrials.gov, trial identification NCT01239693) was conducted under approval of College of Medicine Research Ethics Committee (COMREC), University of Malawi, and the Ethics Committee of Pirkanmaa Hospital District, Finland.

The study nurses determined the women's gestational age through obstetric ultrasound assessment. We obtained participants' background information and details of their home location at enrolment day. To examine maternal BMI and maternal weight gain during pregnancy, the study staff completed clinic anthropometric measurements at enrolment ($\leq$ 20 weeks), 32 weeks and 36 weeks gestational age. The anthropometrists assessed the weight and height of the mother using a high quality scale (SECA 874 flat scale, Seca GmbH & Co., Hamburg, Germany) and stadiometer (Harpenden stadiometer, Holtain Limited, Crosswell, Crymych, UK). We assessed infant weight using an electronic infant weighing scale (SECA 381 baby scale, Seca GmbH & Co.), infant length using length boards (Harpenden Infantometer, Holtain Limited) and head circumference with non-stretchable plastic insertion tapes (Shorrtape, Weigh and Measure, LLC, Olney, MD, USA).

Definitions

Maternal pre-pregnancy BMI was categorised into underweight ($<$18.5 kg/m^2), normal (18.5–24.9 kg/m^2), and overweight ($\geq$ 25 kg/m^2), according to the classification by the World Health Organisation (WHO) [23]. Average WWG was defined as the average weight gained per week during pregnancy based on Institute of Medicine (IOM) for weight gain during pregnancy [24]. The IOM guidelines were developed to minimise the negative health consequences for the mother and fetus of inadequate or excessive gain. The guidelines recommend that underweight women gain more weight, and overweight women gain less weight, compared to women within the "normal" weight category at the time of conception [25]. Inadequate weight

gain was defined as average weekly weight gained below the IOM guidelines for average weekly weight gain during pregnancy and excess weight gain was defined as average weekly weight gained above the IOM guidelines for weight gain during pregnancy [25]. The cut-off for inadequate rate of WWG was the lower limit of the IOM's recommended range of average weekly weight gain during pregnancy, which takes the pre-pregnancy BMI into consideration [25]. Preterm birth was defined as < 37 weeks of gestation, newborn underweight as < 2500 g, stunting as newborn length for age z-score (LAZ) < -2, small head circumference as newborn head circumference z-score (HCZ) < –2, and small for gestational age (SGA) as weight $<10^{th}$ percentile for gestational age and sex using the INTERGROWTH -21^{st} standards [26]. We used the WHO Child Growth Standards to calculate the weight-for-age, length-for-age, and head circumference-for-age z-scores [27].

Statistical analysis

Since pre-pregnancy BMI was not available for study participants, we used regression modelling to create a proxy for pre-pregnancy BMI. We created a regression curve of maternal BMI against gestational age at enrolment and determined that 13.7 gestational weeks (gw) was the lower limit of the curve at which the 95% CI fit closely to the regression curve. We therefore used the estimated BMI at 13.7 gw as the proxy for pre-pregnancy BMI and assumed that minimal change in BMI occurred between pre-pregnancy and 13.7 gw, based on IOM assumptions of weight gain in the first trimester (0.5–2.0 kg) [25]. WWG as a continuous variable was estimated using a mixed modelling method. This method allowed us to calculate the average weekly weight gain for all women from whom weight measurement was performed at each clinic visit (enrolment, 32 gw, or 36 gw), and impute weekly weight gain for those from whom one or two weight measurements were missing.

We used analysis of variance (ANOVA) for continuous variables and Fisher's exact test for categorical variables to examine differences between those included and excluded from the analyses of associations between maternal weight gain and pre-pregnancy BMI and birth outcomes. We used linear regression models to examine the associations between pre-pregnancy BMI, weekly weight gain and continuous birth outcome variables (duration of gestation, birth weight, LAZ, and HCZ). We used logistic regression to examine the association between categorical and continuous variables. We also examined the interaction between pre-pregnancy BMI and weekly weight gain (as both continuous and categorical variables) with regard to maternal birth outcomes. Linear regression coefficients are presented as standardized coefficients, which are the number of standard deviations a dependent variable will change, per standard deviation increase in the predictor variable. We used standardized coefficients in order to assess the strength of association between the predictor and birth outcome in a given model in comparison with the association between another predictor and that same birth outcome in a different model. The use of standardized coefficients allows for such comparisons between predictor variables for the same outcome, even though the units of the predictor variables differ (i.e. BMI vs. weekly weight gain). We computed standardized coefficients from the regression analysis using standardized dependent and independent variables. We used Poisson regression models to estimate the relative risk for dichotomous birth outcomes (preterm birth, LBW, stunting, SGA, and small head circumference) by categorical predictors of pre-pregnancy BMI (<18.5 vs. between 18.5 and 24.9, and ≥ 25.0 vs. between 18.5 and ≥ 25.0) and average WWG. Potential confounders such as maternal age, maternal height, haemoglobin (HB) at enrolment, HIV status, season of enrolment, site of enrolment, primiparity, marital status and education years were selected *a priori* based on their reported associations with birth outcomes and examined as covariates. Those that were associated with the birth

outcomes ($p<0.10$) in bivariate analysis were included in the adjusted models. All hypothesis tests were two-sided and P values <0.05 were considered statistically significant. Data analyses were performed using STATA version 12.1 (Stata Corp, College Station, TX, USA) and SAS version 9.3 software package (SAS Institute Inc., Cary, NC, USA).

Results

A total of 1391 participants were enrolled in the iLiNS-DYAD-M study between February 2011 and August 2012. Of the 1391 participants enrolled, we had complete information on height and weight for 1382 participants (99.4%). After excluding 12 women with twin pregnancies, BMI at enrolment was available for 1370 (98.5%) participants. Data on the duration of pregnancy were available for 1287 (93.9% of those from whom BMI data were available) and birth weight, length, and head circumference were available for 79.7%, 79.0%, and 79.1% of those from whom BMI data were available, respectively. Birth outcome data were not available for approximately 20% of newborns of the enrolled participants because some died, some moved out of the area, some weren't found at the time of measurements, and some newborns didn't cooperate (stay still) for the weighing or measuring.

The mean (SD) pre-pregnancy BMI of all participants was 21.8 (2.7) kg/m^2. The proportion of women who were underweight (BMI $<$ 18.5 kg/m^2) was 5.9%, while the prevalence of overweight (BMI $\geq$ 25.0 kg/m^2) was 10.9%. The proportion of women who had low WWG ($<$ IOM recommendation) was 71.8%, while the prevalence of high WWG was 5.2%. There were differences in baseline characteristics of women included and excluded from the analyses of associations between BMI and weight gain and birth outcomes (Table 1). Those who were included in the analyses were older, less educated, of lower socio-economic status, more likely to be primiparous, and less likely to have had low WWG compared to women who were excluded from the analyses.

Associations between pre-pregnancy BMI and weekly GWG and duration of pregnancy and newborn size

Pre-pregnancy BMI was positively associated with birth weight and HCZ in both unadjusted ($\beta = 0.11$, $p = 0.001$and $\beta = 0.09$, $p = 0.003$, respectively) and adjusted models ($\beta = 0.11$, $p = 0.001$ and $\beta = 0.09$, $p = 0.003$, respectively) (Table 2). No statistical associations were seen between pre-pregnancy BMI and pregnancy duration in either unadjusted ($\beta = -0.01$, $p = 0.686$) or adjusted models ($\beta = -0.003$, $p = 0.926$). However, in unadjusted models pre-pregnancy BMI was associated with LAZ ($\beta = -0.065$, $p = 0.040$) and HCZ ($\beta = 0.09$, $p = <0.003$) but the association with LAZ was no longer significant after adjusting for covariates ($\beta = -0.056$, $p = 0.067$). WWG was significantly associated with pregnancy duration, birthweight, LAZ and HCZ in both unadjusted ($\beta = 0.08$, $p = 0.002$; $\beta = 0.22$, $p = 0.001$; $\beta = 0.19$, $p = 0.001$ and $\beta = 0.15$, $p = 0.001$) and adjusted models ($\beta = 0.06$, $p = 0.031$; $\beta = 0.20$, $p = 0.001$; $\beta = 0.13$, $p = 0.001$; and $\beta = 0.15$, $p = 0.001$, respectively). There were no significant interactions between pre-pregnancy BMI and WWG for any of the birth outcomes.

Associations between low or high BMI and birth outcomes

The associations between low and high BMI and birth outcomes are presented in Table 3 and Table 4. Mean duration of pregnancy and LAZ were not different between women who were underweight compared to women of normal weight [mean difference (95% CI): -0.22 wk (-0.93 to 0.50), $p = 0.536$; and -0.25 z-score (-0.08 to 0.57), $p = 0.137$, respectively). Similarly, no significant differences were noted in either average birth weight [mean difference (95% CI): 66 g (-64 to 196 g), $p = 0.320$] or HCZ [mean difference (95% CI): 0.20 z-score (-0.16 to 0.48),

Table 1. Baseline characteristics of the participants who were included and excluded from the analyses of associations between pre-pregnancy BMI and gestational weight gain and birth outcomes (n = 1379) in Malawi.

Characteristic	Included (n = 1107)	Excluded (n = 272)	*P* value[a]
Mean (SD) body-mass index, BMI (kg/m2)	22.1 (2.8)	22.4 (2.9)	0.126
Mean (SD) maternal age, years	25.1 (6.1)	24.2 (6.6)	0.025
Mean (SD) maternal education, completed years at school	3.9 (3.4)	4.5 (3.7)	0.049
Mean (SD) socio-economic score	-0.05 (0.9)	0.30 (1.1)	<0.001
Proportion of primiparous women	29.6%	20.1%	<0.001
Proportion of women with a low BMI (< 18.5 kg/m^2)	4.1%	5.7%	0.367
Proportion of women with low weekly weight gain (< IOM recommendation)	70.2%	79.9%	0.008
Proportion of women with a positive HIV test	12.2%	13.9%	0.591
Number (%) of women with a positive malaria test (RDT)	22.4%	23.5%	0.749

[a] *P* value obtained from ANOVA (comparison of means) or Fishers exact test (comparison of proportions)

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$p = 0.333$] among infants born to underweight women and normal weight women (Table 3). However, we found that infants born to underweight women were at a greater risk of stunting [RR (95% CI): 1.6 (1.0 to 2.5), $p = 0.029$] and being SGA [RR (95% CI): 1.5 (1.2 to 2.0), $p = 0.002$] but no significant risk was noted for small head circumference [RR (95% CI): 0.9 (0.3 to 2.8), $p = 0.827$] when compared to infants born to normal weight women (Table 4). We found no increase or decrease in risk of stunting, SGA, or small head circumference when comparing infants of overweight and normal weight women in adjusted models [RR, (95% CI): 0.9 (0.5 to 1.5), $p = 0.634$; 0.7 (0.5 to1.0), $p = 0.075$; and 0.7 (0.2 to 2.4), $p = 0.620$, respectively].

Table 2. Associations between maternal pre-pregnancy body-mass index (BMI) and average weekly gestational weight gain and duration of pregnancy and newborn size in rural Malawi.

Outcome	Pre-pregnancy BMI (kg/m^2)				Weekly weight gain (g/wk)			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	Regression co-efficient (SE)[a]	P-value[b]	Regression co-efficient (SE)[a]	P-value[b,c]	Regression co-efficient (SE)[a]	P-value[b]	Regression co-efficient (SE)[a]	P-value[b,c]
Pregnancy duration	-0.01 (0.03)	0.686	-0.003 (0.03)	0.926	0.08 (0.03)	<0.002	0.06 (0.03)	0.031
Birthweight	0.11(0.03)	<0.001	0.11(0.03)	<0.001	0.22 (0.03)	<0.001	0.20 (0.03)	<0.001
Newborn length-for-age z-score	0.065 (0.03)	0.040	0.056 (0.03)	0.067	0.19 (0.03)	<0.001	0.13 (0.03)	<0.001
Newborn head circumference z-score	0.09(0.03)	<0.003	0.09 (0.03)	0.003	0.15 (0.03)	<0.001	0.15 (0.03)	<0.001

[a] Standardized coefficient with standardized standard errors. Standardized coefficients are the number of standard deviations the outcome variable changes per standard deviation change in the predictor variable.

[b] P-values were determined by linear regression models.

[c]Models were adjusted for covariates found in bivariate analysis to be associated with the birth outcome (P<0.10). Model for pregnancy duration was adjusted for gestational age at enrollment, parity, maternal height and HIV status. Model for birthweight was adjusted for number of previous pregnancies, HIV status, primparity, site of enrollment, season of enrollment, and maternal. Model for length age z score (LAZ) was adjusted for number of previous pregnancies, HIV status, child sex, maternal height, parity, and maternal age. Model for head circumference was adjusted for number of previous pregnancies, maternal height, parity and site of enrollment. Models for the associations between weekly weight gain and duration of pregnancy, birthweight, LAZ, and head circumference were also adjusted for maternal pre-pregnancy BMI.

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Table 3. Continuous birth outcomes among normal weight, underweight, and overweight women in rural Malawi.

Outcome	Maternal nutritional status before pregnancy (based on body-mass-index BMI)			Comparison between underweight and normal weight participants				Comparison between overweight and normal weight participants			
	Normal BMI (18.5–25.0 kg/m^2)	Underweight (BMI < 18.5 kg/m^2)	Overweight (BMI ≥25.0 kg/m^2)	Unadjusted		Adjusted		Unadjusted		Adjusted	
				Mean Difference (95% CI)	p-value[a]	Mean Difference (95% CI)	p-value[a,b]	Mean Difference (95% CI)	p-value[a]	Mean Difference (95% CI)	p-value[a,b]
Mean (SD)[c] duration of pregnancy, weeks	39.1 (3.0) *n = 1058*	39.5 (2.2) *n = 71*	39.2 (2.7) *n = 158*	-0.46 (-1.17 to 0.25)	0.200	-0.22 (-0.93 to 0.50)	0.536	-0.16 (-0.34 to 0.66)	0.527	- 0.08 (-0.57 to 0.42)	0.761
Mean (SD) birthweight (grams)	2973 (446.8) *n = 941*	2939 (446.9) *n = 62*	3012 (439.9) *n = 133*	134 (20 to 249)	0.022	66 (-64 to 196)	0.320	-39 (-120 to -42)	0.350	108.0 (- 9 to 225)	0.070
Mean (SD) length for age z-score	-1.00 (1.11) *n = 893*	-1.21 (1.09) *n = 60*	-0.87 (1.10) *n = 129*	0.21 (-0.08 to 0.50)	0.163	0.25 (-0.08 to 0.57)	0.137	- 0.13 (-0.34 to 0.07)	0.211	0.02 (-0.27 to 0.31)	0.898
Mean (SD) head circumference z-score	*-0.14 (1.08) n = 894*	-0.47 (0.92) *n = 61*	-0.06 (1.17) *n = 129*	0.34 (0.06 to 0.62)	0.018	0.20 (-0.16 to 0.48)	0.333	-0.08 (-0.28 to 0.12)	0.429	0.21 (-0.08 to 0.51)	0.160

[a] P-values obtained from Poisson regression models.

[b] Models were adjusted for covariates found in bivariate analysis to be associated with the birth outcome (P<0.10). Model for gestational age at delivery was adjusted for gestational age at enrollment, parity, maternal height and HIV status. Model for birthweight was adjusted for number of previous pregnancies, HIV status, primparity, site of enrollment, season of enrollment, maternal age and gestational age at enrolment. Model for length for age-z score was adjusted for number of previous pregnancies, HIV status, child sex, maternal height, parity, maternal age, and gestational age at enrolment. Model for head circumference was adjusted for number of previous pregnancies, maternal height, parity and site of enrollment.

[c] SD: standard deviation

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Associations between low or high WWG and birth outcomes

Compared to women whose WWG was normal (within IOM recommendations), women with low WWG (below the IOM recommendations) in adjusted models had a shorter average duration of pregnancy [mean difference (95% CI): 0.56 wk (0.17 to 0.95), $p = 0.005$]; lower average infant birth weight [mean difference (95% CI): 142 g (80 to 204), $p = 0.001$]; LAZ [mean difference (95% CI): 0.26 z-score (0.11 to 0.41), $p = 0.001$]; and head circumference z-score [mean difference (95% CI): 0.33 z-score (0.18 to 0.49), $p = 0.001$] (Table 5). Similarly, women with low WWG were at a greater risk of having an infant with LBW, SGA and small head circumference in adjusted models [RR (95% CI): 2.0 (1.2 to 3.2), $p = 0.006$; 1.4 (1.0 to 1.8), $p = 0.037$; and 3.4 (1.2 to 9.7), p = 0.024, respectively], but not significantly more likely to have a stunted infant or give birth preterm [RR (95% CI): 1.1(0.7 to 1.6), $p = 0.681$; and 1.5 (0.9 to 2.3), $p = 0.124$, respectively] (Table 6). There were no differences in birth outcomes or risk of adverse birth outcomes among women with high WWG (above the IOM recommendations) compared to women with normal WWG.

Associations between pre-pregnancy BMI and birth outcomes within each intervention group

There were no significant associations between pre-pregnancy BMI and either pregnancy duration or LAZ when stratified by intervention group after adjusting for covariates (Table 7). However, the covariate adjusted association between pre-pregnancy BMI and birth weight was significantly positive among all 3 intervention groups (IFA: p = 0.012; MMN: p = 0.007; LNS: p = 0.033). There was a significantly positive association between pre-pregnancy BMI and

Table 4. The prevalence of adverse birth outcomes among normal weight, underweight, and overweight women in rural Malawi.

Outcome	Maternal nutritional status before pregnancy (based on body-mass-index BMI)			Comparison between underweight and normal weight participants				Comparison between overweight and normal weight participants			
				Unadjusted		Adjusted		Unadjusted		Adjusted	
	Normal BMI (18.5–25.0 kg/m^2)	Underweight (BMI < 18.5 kg/m^2)	Overweight (BMI ≥25.0 kg/m^2)	RR (95% CI)	P-value[a]	RR (95% CI)	p-value[a,b]	RR (95% CI)	p-value[a]	RR (95% CI)	p-value[a,b]
Incidence of preterm (GA<37wk)	110/1060 (10.4%)	5/93 (5.4%)	14/134 (10.5%)	0.5 (0.2 to 1.2)	0.139	0.6 (0.2 to 1.4)	0.202	1.0 (0.6 to 1.7)	0.980	1.0 (0.6 to 1.7)	0.908
Incidence of low birth weight (<2500 g)	118/942 (12.5%)	15/81 (18.5%)	12/113 (10.6%)	1.5 (0.9 to 2.4)	0.115	1.5 (0.9 to 2.5)	0.100	0.8 (0.5 to 1.5)	0.560	0.8 (0.5 to 1.4)	0.464
Prevalence of stunting (LAZ<-2)	140/894 (15.7%)	20/80 (25%)	13/108 (12.0%)	1.6 (1.1 to 2.4)	0.024	1.6 (1.0 to 2.5)	0.029	0.8 (0.5 to 1.3)	0.332	0.9 (0.5 to 1.5)	0.634
Prevalence of small for gestational age (SGA)[c]	279/942 (29.6%)	34/81 (42.0%)	22/113 (19.5%)	1.4 (1.1 to 1.9)	0.013	1.5 (1.2to 2.0)	0.002	0.7 (0.4 to 1.0)	0.034	0.7 (0.5 to 1.0)	0.075
Prevalence of small head circumference (HCZ<-2)	37/894 (4.1%)	3/81 (3.7%)	3/109 (2.8%)	0.9 (0.3 to 2.8)	0.850	0.9 (0.3 to 2.8)	0.827	0.7 (0.2 to 2.1)	0.491	0.7 (0.2 to 2.4)	0.620

[a] P-values obtained from Poisson regression models.

[b] Models were adjusted for covariates found in bivariate analysis to be associated with the birth outcome (P<0.10). Model for preterm birth was adjusted for gestational age at enrollment, HIV status, primiparity, and site of enrollment. Model for LBW was adjusted for child sex, HIV status, maternal height, primiparity, household food insecurity score, and site of enrollment. Model for newborn stunting was adjusted for HIV status, maternal age, maternal height, primiparity, and site of enrollment. Model for SGA was adjusted for child sex, gestational age at enrollment, HIV status, maternal age, maternal height, primiparity, season of enrollment, and site of enrollment. Model for small head circumference was adjusted for maternal age, maternal height, primiparity, season of enrollment, and site of enrollment

[c] Defined as having birth weight <10th percentile for infants of the same gestational age from INTERGROWTH-21st standard

GA: Gestational age

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HCZ only among women in the MMN group (p = 0.019), but not the IFA (p = 0.096) or LNS (p = 0.140) groups.

Within each intervention group, the risk of preterm birth, low birthweight, stunting, and small head circumference was not different between women with a BMI in the normal range compared to women with either a low or high BMI after adjusting for covariates. The risk of SGA was significantly higher among women with a low compared to normal BMI for women in both the IFA [RR (95% CI): 1.6 (1.01 to 2.4), p = 0.047)] and MMN [RR (95%CI): 1.9 (1.2 to 3.1), p = 0.008] groups, but not among women in the LNS group [RR (95%CI): 1.3 (0.7 to 2.1), p = 0.404]. There were no significant differences in adverse birth outcomes between women with low vs higher BMI within any of the intervention groups (p>0.05 for all) (Table 8).

Discussion

Our findings from a cohort of pregnant women in rural Malawi indicate that pre-pregnancy BMI was positively associated with birth weight and HCZ, and women with low pre-pregnancy BMI had a 60% increased risk of giving birth to stunted newborns. We further observed that average weekly gestational weight gain (WWG) was strongly associated with pregnancy duration, birth weight, LAZ, and HCZ, and women who gained inadequate weight during pregnancy were at higher risk of giving birth to newborns with LBW, SGA, and small head circumference. We did not find increased risk of adverse birth outcomes among women with high pre-pregnancy BMI or WWG above IOM recommendations. These results are of public health importance as they emphasize the need for addressing proper nutrition amongst

Table 5. Continuous birth outcomes among women with normal, low, or high average weekly gestational weight gain in rural Malawi.

Outcome				Comparison between women with low and normal weight gain				Comparison between women with high and normal weight gain			
	Maternal weight during pregnancy			Unadjusted		Adjusted		Unadjusted		Adjusted	
	Normal weight gain within IOM recommendations	Low (below IOM recommendations	High (above IOM recommendations)	Difference in means (95% CI)	P-value[a]	Difference in means (95% CI)	P-value[a,b]	Difference in means (95% CI)	P-value[a]	Difference in means (95% CI)	P-value[a,b]
Mean (SD)[c] duration of pregnancy, weeks	39.63 (2.18) *n = 302*	38.89 (3.18) *n = 916*	40.04 (1.61) *n = 69*	0.74 (0.35 to 1.12)	<0.002	0.56 (0.17 to 0.95)	0.005	-0.41 (-0.91 to 0.13)	0.138	-0.45 (-0.99 to 0.08)	0.099
Mean (SD) birthweight (grams)	3098 (451) *n = 278*	2908 (440) *n = 797*	3203 (311) *n = 61*	190 (130 to 251)	<0.001	142 (80 to 204)	<0.001	-105 (-224 to 15)	0.086	-88.51 (-212 to 35)	0.158
Mean (SD) length for age z score	-0.72 (1.04) *n = 257*	-1.13 (1.12) *n = 767*	-0.47 (0.83) *n = 58*	0.41 (0.25 to 0.56)	<0.001	0.26 (0.11 to 0.41)	<0.001	- 0.25 (-0.54 to 0.03)	0.084	-0.24 (-0.54 to 0.05)	0.102
Mean (SD) head circumference headz	0.07 (0.95) *n = 261*	0.26 (1.12) *n = 765*	0.34 (0.91) *n = 58*	0.31 (0.2 to 0.5)	<0.001	0.33 (0.18 to 0.49)	<0.001	-0.26 (-0.53 to 0.01)	0.055	-0.26 (-0.49 to 0.07)	0.139

[a] P-values obtained from Poisson regression models.

[b] Models were adjusted for covariates found in bivariate analysis to be associated with the birth outcome (P<0.10). Model for gestational age at delivery was adjusted for gestational age at enrollment, parity, maternal height and HIV status. Model for birthweight was adjusted for number of previous pregnancies, HIV status, primparity, site of enrollment, season of enrollment, maternal age and maternal BMI. Model for length for age-z score was adjusted for number of previous pregnancies, HIV status, child sex, maternal height, parity and maternal age. Model for head circumference was adjusted for number of previous pregnancies, maternal height, parity and site of enrollment.

[c] SD: standard deviation

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Table 6. The prevalence of adverse birth outcomes among women with normal, low, or high average weekly gestational weight gain in rural Malawi.

Outcome				Comparison between women with low and normal weight gain				Comparison between women with high and normal weight gain			
	Maternal weight gain during pregnancy			Unadjusted		Adjusted		Unadjusted		Adjusted	
	Normal weight gain within IOM[d] recommendations	Low (below IOM recommendations	High (above IOM recommendations)	RR (95% CI)	P-value[a]	RR (95% CI)	P-value[a,b]	RR (95% CI)	P-value[a]	RR (95% CI)	P-value[a,b]
Incidence of preterm birth (GA <37 weeks)	21/302 (7.0%)	106/916 (11.6%)	2/69 (2.9%)	1.7 (1.0 to 2.7)	0.033	1.5 (0.9 to 2.3)	0.124	0.4 (0.1 to 1.8)	0.237	0.4 (0.1 to 1.6)	0.178
Incidence of (low birth weight) LBW (<2,500 g)	21/278 (7.6%)	124/797 (15.6%)	0/61 (0.0%)	2.1 (1.3 to 3.3)	0.002	2.0 (1.2 to 3.2)	0.006	N/A	N/A	N/A	N/A
Prevalence of newborn stunting (LAZ <-2)	35/257 (13.6%)	138/767 (18.0%)	0/58 (0.0%)	1.3 (0.9 to 1.9)	0.141	1.1 (0.7 to 1.6)	0.681	N/A	N/A	N/A	N/A
Incidence of small for gestational age (SGA)[c]	64/278 (23.0%)	265/797 (24.7%)	6/61 (9.8%)	1.4 (1.1 to 1.9)	0.008	1.4 (1.0 to 1.8)	0.037	0.4 (0.2 to 1.0)	0.046	0.5 (0.2 to 1.2)	0.120
Prevalence of small head circumference (HCZ <-2)	4/261 (1.5%)	39/765 (5.1%)	0/58 (0.0%)	3.3 (1.2 to 9.3)	0.022	3.4 (1.2 to 9.7)	0.024	N/A	N/A	N/A	N/A

[a] P-values for incidence of preterm birth and prevalence of small for gestational age newborns were obtained from Poisson regression models. P-values for unadjusted incidence of LBW, and prevalence of stunting and small head circumference were obtained by Fisher's exact test, as no 'women who gained excess weight gave birth to a LBW or stunted infant or an infant with a small head circumference.

[b] Models were adjusted for covariates found in bivariate analysis to be associated with the birth outcome (P<0.10). Model for preterm birth was adjusted for gestational age at enrollment, HIV status, primiparity, and site of enrollment. Model for LBW was adjusted for child sex, HIV status, maternal height, primiparity, household food insecurity score, and site of enrollment. Model for newborn stunting was adjusted for HIV status, maternal age, maternal height, primiparity, and site of enrollment. Model for SGA was adjusted for child sex, gestational age at enrollment, HIV status, maternal age, maternal height, primiparity, season of enrollment, and site of enrollment. Model for small head circumference was adjusted for maternal age, maternal height, primiparity, season of enrollment, and site of enrollment

[c] Defined as having birth weight <10th percentile for infants of the same gestational age from INTERGROWTH-21st standard

[d] IOM: Institute of Medicine

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women not only during pregnancy and in the pre-pregnancy period, but also exploring other underlying factors that may influence low WWG among pregnant women in rural Malawi.

We found few other studies that have reported associations between pre-pregnancy BMI and birth outcomes in developing countries. A 2011 meta-analysis of 78 studies showed increased risks of preterm birth and LBW among underweight women, however, only a handful of the studies were from developing countries [28]. The 4 studies from developing countries included in the analysis of preterm birth showed no increased risk among underweight compared to normal weight women [28], which is in line with our findings. Although the authors of the meta-analysis did not examine newborn stunting, the 9 studies from developing countries included in the analysis of LBW showed an increased risk of LBW among underweight women [28]. While the incidence of LBW was higher among underweight compared to overweight women in our study, the difference was not significant. The relatively low prevalence of pre-pregnancy underweight in our sample limited our statistical power to detect such a difference. We did, however, find a greater prevalence of infant stunting among underweight women. More recent studies in developing countries have shown increased risks of adverse birth outcomes among women with low pre-pregnancy BMI [5,15,29]. Additionally, a prospective cohort study of over 500,000 women in rural China indicated increased risks of preterm birth and LBW among women with low pre-pregnancy BMI [28]. However, compared to

Table 7. Associations between maternal pre-pregnancy body-mass index (BMI) and duration of pregnancy and newborn size within each intervention group.

Outcome	Group	Pre-pregnancy BMI (kg/m^2)	
		Regression co-efficient (SE)[a]	P-value[b]
Pregnancy duration	IFA	-0.08 (0.05)	0.129
	MMN	0.01 (0.05)	0.816
	LNS	0.03 (0.05)	0.561
Birthweight	IFA	0.14 (0.06)	0.012
	MMN	0.14 (0.05)	0.007
	LNS	0.11 (0.05)	0.033
Newborn length-for-age z-score	IFA	0.08 (0.06)	0.225
	MMN	0.08 (0.05)	0.094
	LNS	0.04 (0.05)	0.364
Newborn head circumference z-score	IFA	0.11 (0.06)	0.096
	MMN	0.13 (0.05)	0.019
	LNS	0.07 (0.05)	0.140

[a] Standardized coefficient with standardized standard errors. Standardized coefficients are the number of standard deviations the outcome variable changes per standard deviation change in the predictor variable.

[b] P-values were determined by linear regression models. Models were adjusted for covariates found in bivariate analysis to be associated with the birth outcome ($P<0.10$). Model for gestational age at delivery was adjusted for gestational age at enrollment, parity, maternal height and HIV status. Model for birthweight was adjusted for number of previous pregnancies, HIV status, primiparity, site of enrollment, season of enrollment, and maternal age. Model for length for age z score was adjusted for number of previous pregnancies, HIV status, child sex, maternal height, parity, and maternal age. Model for head circumference was adjusted for number of previous pregnancies, maternal height, parity and site of enrollment.

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our study population, the prevalence of pre-pregnancy underweight was much higher in the Chinese population, and increased from 10.4% to 14.1% in the 3-year time period of their study [30]. Similar to the meta-analysis, they didn't examine newborn stunting.

Our observation of no increased risk of adverse birth outcomes (preterm birth, LBW, stunting and small head circumference) among high pre-pregnancy BMI women is consistent with a retrospective study of Thai women [31]. By contrast, several other studies, as well as a systematic review, reported that high pre-pregnancy BMI (>25kg/m^2) increased the risk of preterm delivery [7,28,32]. However, it is important to note that some of those studies used different cut off points in describing BMI categories. Additionally, some studies relied on self-reported pre-pregnancy BMI [31,33]. Thus, more research is needed to investigate associations between high pre-pregnancy maternal BMI and birth outcomes in LICs, specifically in sub-Saharan Africa.

A key finding of our study was that low average WWG is an important risk factor for adverse birth outcomes, which aligns with previous studies [15,33]. For example, in our cohort of pregnant women, low WWG was associated with most of the outcomes we assessed (LBW, SGA, and small head circumference). A recent systematic review and meta-analysis reported that women with low GWG had a 3.4 times greater risk of LBW, regardless of the maternal pre-pregnancy BMI category [16] whereas in our study the relative risk was a bit lower [RR 2.0 (95% CI), 1.2 to 3.2]. Inadequate GWG was also found to be positively associated with risks of both LBW and preterm birth in a systematic review and a large retrospective cohort of Chinese nulliparous women [13,28]. However, in these studies, excessive GWG was associated with decreased risks of preterm delivery, SGA and LBW [13,28,32], which we did not find, perhaps

Table 8. The prevalence of adverse birth outcomes among normal weight, underweight, and overweight women within each intervention group.

Outcome		Maternal nutritional status before pregnancy (based on body-mass-index BMI)			Comparison between underweight and normal weight participants		Comparison between overweight and normal weight participants	
	Group	Normal BMI (18.5–25.0 kg/m^2)	Underweight (BMI < 18.5 kg/m^2)	Overweight (BMI ≥25.0 kg/m^2)	RR (95% CI)	Adjusted p-value[a]	RR (95% CI)	Adjusted p-value[a]
Incidence of preterm (GA<37wk)	IFA	42/355 (11.8%)	3/32 (9.4%)	4/44 (9.1%)	1.1 (0.4 to 3.4)	0.881	0.7 (0.2 to 1.9)	0.474
	MMN	34/355 (9.6%)	0/27 (0%)	7/40 (14.9%)		0.978		0.133
	LNS	34/350 (9.7%)	2/34 (5.9%)	3/43 (7.0%)	0.8 (0.2 to 2.9)	0.681	0.8 (0.3 to 2.5)	0.762
Incidence of low birth weight (<2500 g)	IFA	41/319 (12.9%)	7/27 (25.9%)	1/36 (2.8%)	1.9 (0.9 to 4.0)	0.078	0.2 (0.03 to 1.3)	0.084
	MMN	41/310 (13.2%)	3/25 (12.0%)	7/40 (17.5%)	0.9 (0.4 to 2.3)	0.895	1.4 (0.6 to 3.1)	0.417
	LNS	36/313 (11.5%)	5/29 (17.2%)	4/37 (10.8%)	2.3 (0.9 to 5.9)	0.077	0.97 (0.4 to 2.5)	0.947
Prevalence of stunting (LAZ<-2)	IFA	56/300 (18.7%)	8/26 (30.1%)	4/32 (12.5%)	1.7 (0.8 to 3.4)	0.141	0.7 (0.3 to 1.7)	0.423
	MMN	42/302 (13.9%)	4/24 (16.7%)	6/42 (14.3%)	1.3 (0.5 to 3.7)	0.555	1.1 (0.5 to 2.4)	0.766
	LNS	42/292 (14.4%)	8/30 (26.7%)	3/34 (8.8%)	1.7 (0.9 to 3.4)	0.114	0.7 (0.2 to 2.3)	0.605
Prevalence of small for gestational age (SGA)[b]	IFA	98/319 (30.7%)	13/27 (48.2%)	5/36 (13.9%)	1.6 (1.01 to 2.4)	0.047	0.4 (0.2 to 0.97)	0.042
	MMN	88/310 (28.4%)	11/25 (44.0%)	9/40 (22.5%)	1.9 (1.2 to 3.1)	0.008	0.9 (0.5 to 1.6)	0.772
	LNS	93/313 (29.7%)	10/29 (34.5%)	8/37 (21.6%)	1.3 (0.7 to 2.1)	0.404	0.8 (0.4 to 1.4)	0.405
Prevalence of small head circumference (HCZ<-2)	IFA	20/300 (6.7%)	1/26 (3.9%)	0/32 (0%)		0.600		0.977
	MMN	8/301 (72.7%)	1/25 (4.0%)	2/42 (4.8%)	1.7 (0.3 to 12.0)	0.575	1.9 (0.4 to 9.8)	0.435
	LNS	9/293 (3.1%)	1/30 (3.3%)	1/35 (2.9%)		0.953		0.843

[a] P-values obtained from Poisson regression models. Models without RR did not converge due to the small incidence of adverse birth outcomes, so those P-values were obtained from multiple linear regression. Models were adjusted for covariates found in bivariate analysis to be associated with the birth outcome (P<0.10). Model for preterm birth was adjusted for gestational age at enrollment, HIV status, primiparity, and site of enrollment. Model for LBW was adjusted for child sex, HIV status, maternal height, primiparity, household food insecurity score, and site of enrollment. Model for newborn stunting was adjusted for HIV status, maternal age, maternal height, primiparity, and site of enrollment. Model for SGA was adjusted for child sex, gestational age at enrollment, HIV status, maternal age, maternal height, primiparity, season of enrollment, and site of enrollment. Model for small head circumference was adjusted for maternal age, maternal height, primiparity, season of enrollment, and site of enrollment

[b] Defined as having birth weight <10th percentile for infants of the same gestational age from INTERGROWTH-21st standard

GA: Gestational age

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due to the low proportion of women with excessive GWG. Given the lack of interaction between pre-pregnancy BMI and WWG, it seems that weight gain within the IOM recommendations is beneficial to all women, regardless of their BMI at the time of conception.

We explored the associations between pre-pregnancy BMI and birth outcomes within each of the intervention groups to get a sense of whether the nutritional intervention during pregnancy helped to prevent adverse birth outcomes among women with low or high pre-pregnancy BMI. Interestingly, underweight women in the iron-folic acid and multiple micronutrient supplement groups were at greater risk of giving birth to a SGA infant than normal

weight women, while there was no such association among women in the lipid-based nutrient supplement (LNS) group. LNS was the only supplement of the 3 that contained calories, protein, and essential fatty acids, which may have helped protect infants of underweight women from being SGA.

One limitation of the current study is that we used BMI, a proxy for body composition, rather than the more direct methods of assessing body composition. Another limitation was that we calculated pre-pregnancy BMI from BMI at enrolment using regression modelling, rather than directly measuring pre-pregnancy BMI. The generalizability of these findings may be limited, as those included in the study were of older age, less educated, lower socio-economic status, and had a higher prevalence of primiparity compared to those excluded from the study. Additionally, the proportions with low WWG and low BMI among excluded women were slightly higher than among those included (79.9% vs 70.2% and 5.7% vs 4.1%), which may have some impact on generalizing the findings of the present study to the larger population. The strengths of this study are that it was a prospective study with a large sample size, and highly trained study staff was used to perform study protocols.

Conclusion

Our findings support our hypothesis that low maternal WWG is an important risk factor for adverse pregnancy outcomes. These findings highlight the need for a better understanding of the reasons behind such a high prevalence of low GWG in rural Mangochi and how to improve the situation. There was a large discrepancy between the rates of pre-pregnancy underweight (5.9%) and low average WWG (71.8%), suggesting that factors other than lack of food contributes to low WWG. Therefore, programs should aim at investigating other underlying factors such as maternal infections during pregnancy that may impair appetite. Nevertheless, linear associations between pre-pregnancy BMI and birth weight and child head circumference, and increased risk of stunting among women with low pre-pregnancy BMI suggest that the importance of adequate nutrition in the pre-pregnancy period shouldn't be overlooked.

Supporting information

S1 Table. Dietary supplements consumed by women enrolled in the iLiNS Project.
(PDF)

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