EVALUATION OF EARLY DIAGNOSTIC APPROACHES FOR MALARIA AND PNEUMONIA IN CHILDREN UNDER-FIVE PRESENTING AT THE PRIMARY HEALTHCARE LEVEL IN BENIN CITY, NIGERIA: A MIXED METHODS STUDY

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ABSTRACT

Background: Malaria and pneumonia are the leading causes of under-five mortality in sub-Saharan Africa especially in Nigeria. The Integrated Management of Childhood Illness (IMCI) guidelines were developed by the World Health Organisation (WHO)/United Nations Children's Fund (UNICEF) as a strategy to reduce the burden of these and other preventable childhood diseases. However, there appears to be paucity in evidence on the diagnostic performance of the revised IMCI guidelines and whether they offer an advantage over lay diagnosis (caregiver) for malaria and pneumonia management in Nigeria.

Aim and specific objectives: This study evaluates early diagnostic approaches (IMCI guidelines and lay diagnosis) for malaria and pneumonia in children under-five at the primary healthcare level. To address the overarching aim of the study, the following four specific objectives were studied:

I. To assess the diagnostic accuracy of the IMCI guidelines and lay diagnosis (caregiver) for malaria and pneumonia in comparison to reference diagnostic approaches (microscopy and chest X-ray for malaria and pneumonia respectively). The extent of agreement between caregivers' and health workers' diagnosis of malaria and pneumonia is also assessed.
II. To estimate the burden of malaria and pneumonia among children under-five presenting to study primary healthcare centres (PHCs) according to various diagnostic approaches.
III. To determine the clinical outcomes in children diagnosed with malaria and pneumonia according to the IMCI guidelines and risk factors for severe outcomes.
IV. To qualitatively explore caregivers' and health professionals' perspectives on lay diagnosis and IMCI guidelines as diagnostic approaches for childhood malaria and pneumonia.

Methods: A mixed methods approach was used for this study. The quantitative component used a consecutive sampling approach to recruit 903 children aged 2–59 months who met study eligibility criteria for malaria and pneumonia assessment according to the IMCI guidelines at presentation to five study PHCs in Benin City,

Nigeria. Caregivers of these children were also asked what they thought the diagnosis was (lay diagnosis). Diagnostic accuracy was assessed in terms of sensitivity, specificity, positive and negative predictive values, Area under the Receiver Operating Characteristic Curves (AUROC) values and 95% Confidence Intervals (C.I). The extent of agreement was assessed in terms of Cohen's kappa statistic (k) and 95% CI. The estimated burden of malaria and pneumonia during the study period was assessed using proportions and 95% C.I. Clinical outcomes in children diagnosed with malaria and pneumonia by the IMCI guidelines were described in terms of frequency and percentages, while the potential risk factors associated with clinical outcomes were assessed using odds ratios (ORs) and 95% C.I. For the qualitative component, health stakeholders (17 health professionals and 13 caregivers) who met the study eligibility criteria were purposively recruited and interviewed using semi-structured interviews. An inductive approach to thematic analysis was used for data analysis.

Results: Compared to microscopy, the diagnosis of malaria by health workers using the IMCI guidelines was poorly accurate with an AUROC value of 0.57 (with sensitivity and specificity of 51.8% and 61.3% respectively). Similarly, caregivers' diagnosis of malaria was poor with an AUROC value of 0.55 (with sensitivity and specificity of 31.1% and 79.5% respectively) as compared to microscopy. Using the IMCI guidelines as the reference diagnostic test, caregivers' diagnosis of malaria was more accurate (AUROC 0.60) in comparison to that of pneumonia (AUROC 0.54). There was a slight or minimal level of agreement (k=0.14; 95% CI: 0.09-0.19) between caregivers and health workers in the diagnosis of malaria and pneumonia. The estimated burden of malaria and pneumonia was relatively low, varying by the study local government areas, PHCs and seasonality, irrespective of the diagnostic approach. Where follow-up data were available, approximately 57% (172/304) and 78% (81/104) of the children diagnosed with malaria and pneumonia, respectively, recovered without complications within 30 days. Self-medication prior to presenting to study PHCs and use of preventive measures against malaria were independently and significantly associated with improved clinical outcomes. In contrast, exposure to solid fuels increased the odds of severe illness following malaria or pneumonia diagnosis.

The qualitative component of the study found that caregivers rely on lay diagnosis despite the awareness of its limitations. The perceptions of malaria and pneumonia

appeared to influence caregivers' home management practices and health seeking behaviours. Caregivers showed willingness to be trained in the IMCI guidelines for improved home-based management of malaria and pneumonia. Health professionals believed that the IMCI guidelines were useful for managing both malaria and pneumonia. However, there are some recurring challenges to the wide-scale and sustainable implementation of the IMCI strategy in Nigeria. These include inaccurate diagnosis of malaria and inadequate funding.

Conclusion: The IMCI guidelines are crucial in the effective management (diagnosis and treatment) of malaria and pneumonia at the primary healthcare level in Nigeria. Although not perfect, lay diagnosis has an important contribution in the early detection and management of malaria and pneumonia at the community level in Nigeria. However, there is need for further investment in the training of both health professionals and caregivers in the IMCI guidelines for better health outcomes in under-five population. The training of caregivers in the IMCI guidelines and potential for a scale-up will benefit from careful design, piloting, implementation, and monitoring.

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LIST OF ABBREVIATIONS

95% CI	95% Confidence Interval
AGDS	Any general danger sign
AUROC	Area under the Receiver Operating Characteristic
ACT	Artemisinin based combination therapy
CHE	Community health expert
CHEW	Community health extension worker
CXR	Chest X-ray
DSNO	Disease surveillance and notification officer
EDTA	Ethylene-diamine-tetraacetic acid
JCHEW	Junior community health extension worker
HBM	Health belief model
HP	Health professional
IMCI	Integrated Management of Childhood Illness
IPT	Intermittent preventive treatment
IRS	Indoor residual spraying
ITN	Insecticide-treated mosquito net
LGA	Local government area
LLIN	Long-lasting insecticide–treated bed net
LRT	Least likelihood ratio test
NGO	Non-governmental organisation
NPV	Negative predictive value
OR	Odds ratio
ORS	Oral rehydration solution
PCR	Polymerase chain reaction
PHC	Primary healthcare centre
PHW	Primary healthcare worker
PPV	Positive predictive value
RDT	Rapid diagnostic test
ROC	Receiver operating characteristic curve
UBHC	University of Benin Health Centre
UNICEF	United Nations Children's Fund
VIF	Variance inflation factor
WBC	White blood cell
WHO	World Health Organisation

We grow up giving self-medication, everybody in Nigeria is a doctor, a doctor that's not trained – Civil servant & mother of five children

1 INTRODUCTION

1.1 Introduction to study

While the number of deaths from malaria and pneumonia in children under the age of five years is decreasing globally, the rates remain high in sub-Saharan Africa especially in Nigeria. Despite the availability of interventions such as the World Health Organisation (WHO) Integrated Management of Childhood Illness (IMCI) guidelines, Nigeria still bears the highest and second highest burden of malaria and pneumonia, respectively, in the world. Moreover, a substantial number of under-five deaths from common childhood illnesses, including malaria and pneumonia, occur at home partly because caregivers fail to recognise the seriousness of the illness and delay seeking appropriate health services. It is commonplace for caregivers to rely on their own diagnosis (lay diagnosis) for home-based management of these illnesses in Nigeria. However, there appears to be dearth of studies that have evaluated the usefulness of the IMCI guidelines and caregivers' lay diagnosis of malaria and pneumonia in children under-five in Nigeria. Motivated by the challenges of early detection and management of malaria and pneumonia in a resource-constrained setting like Nigeria, this study aims to evaluate the accuracy of early diagnostic approaches to malaria and pneumonia in children under-five. It also explores the potential of harnessing lay persons for the early detection and timely management of these diseases at the community level.

This introductory chapter provides an overview of malaria and pneumonia epidemiology in sub-Saharan Africa with a primary focus on Nigeria. This is followed by an overview of the Nigerian healthcare system especially primary healthcare, including the use of IMCI guidelines and lay diagnosis at this level of care. The chapter provides a rationale

for the research and concludes with a detailed overview of the objectives and structure of subsequent chapters of the study.

1.2 Malaria

1.2.1 Definition and causes of malaria

Malaria is a preventable and treatable life-threatening infectious disease which is caused by parasites transmitted through the bites of infected female Anopheles mosquitoes.[1] The five known Plasmodium parasites that affect humans include *Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, Plasmodium ovale* and *Plasmodium knowlesi*.[1] While *P. falciparum* and *P. vivax* are the most common, the former is the most deadly and prevalent in sub-Sahara African countries which bear the greatest burden of malaria.[1] *P. knowlesi* is predominant among monkeys in certain forested areas of South-East Asia though there have been recent reports of cases in humans.[1] The symptoms of malaria usually begin 10–15 days after a mosquito bite[1] and include fever, headache, shivering, vomiting, joint pain, haemolytic anaemia, jaundice and convulsions.[2] In severe cases malaria can cause seizures, coma or death.[3]

1.2.2 Pathogenesis and pathophysiology of malaria

Figure 1.1 below depicts the typical life cycle of the *Plasmodium species*. In brief, Plasmodium life cycle involves two phases: the exoerythrocytic phase (one that is associated with the liver) and erythrocytic phase (one that is associated with the red blood cells). When an infected female mosquito bites a person's skin during a blood meal, sporozoites in the mosquito's saliva are transferred into the bloodstream and migrate to the liver where they infect hepatocytes, multiplying asexually to produce several merozoites. The merozoites infect new red blood cells and initiate another series

of asexual reproduction cycles (blood schizogony) to produce 8–24 new infective merozoites, at which point the infected cells burst to begin the infective cycle anew. However, other merozoites develop into immature gametocytes to form the precursors of male and female gametes. During a blood meal by a fertilized mosquito on an infected person, the gametocytes are taken up with the blood and mature in the mosquito gut during which the male and female gametocytes fuse and form an ookinete (fertilized and motile zygote). Ookinetes develop into new sporozoites that migrate to the insect's salivary glands, ready to infect another individual during a bite.[4]

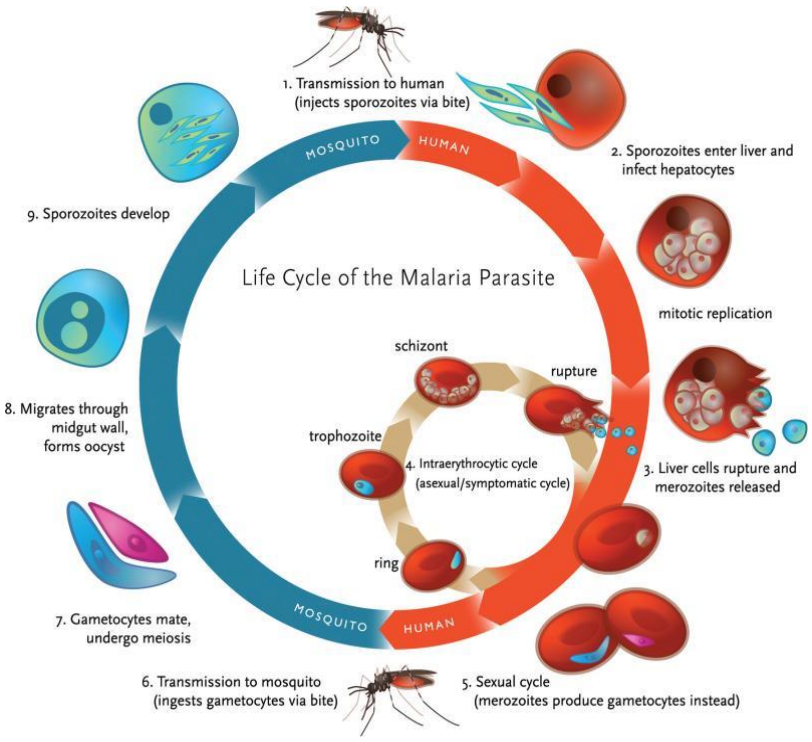


Figure 1.1: Life cycle of the malaria parasite
Source: Klein, E.Y [5]
Permission for the re-use of this figure was obtained from the original author.

1.2.3 Overlap in the clinical presentation of malaria and pneumonia in children

Despite the distinctive pathological pathways of microbial agents associated with malaria (e.g. *Plasmodium falciparum*) and pneumonia (e.g. *Streptococcus pneumoniae*), there are evidence supporting interactions between the two diseases. A study by Byass and colleagues[6] on weekly surveillance of Gambian under-five children for both clinical malaria and acute lower respiratory infections (ALRI) found high rate of coincidence between positive radiological results and high malaria parasitaemia (≥5000 µl). The authors postulated that the ARLI cases recorded may be attributable to malaria owing to the capacity of the latter to weaken the immune system thereby predisposing children to the former.[6] Conversely, ALRIs could predispose children to malaria or allow sub-clinical parasitaemia to become patent. In some situations, malaria itself may present with signs and symptoms (e.g. cough, etc.) suggestive of respiratory illness. For instance, 20% to 50% of patients with malaria have been found to present with a dry cough.[7] Moreover, increased cytoadherence between parasitized red blood cells and pulmonary endothelial cells has been suggested as a cause of respiratory distress in malaria.[8] The estimated burden of malaria and pneumonia coinfection varies across various settings ranging from 23% in Nigeria[9] to 30% in Uganda.[10]

1.2.4 Diagnosis of malaria

There are three 'broad' methods for malaria diagnosis: clinical diagnosis, laboratory diagnosis (e.g. microscopy and rapid diagnostic test) and molecular diagnosis (e.g. polymerase chain reaction). Clinical diagnosis of malaria involves an assessment of patients based on signs and symptoms by health professionals.[11] This diagnostic approach is less expensive and widely practiced especially in developing countries.

However, the diagnostic criteria (e.g. fever) are less specific and could overlap with other potentially life-threatening diseases such as septicaemia and pneumonia amongst others.[11] In addition, this diagnostic approach could potentially promote the indiscriminate use of antimalarials thereby reducing the quality of care for patients with non-malarial fevers in endemic areas.[12–14]

The laboratory and molecular diagnostic approaches can identify malaria parasites or antigens. The conventional microscopy which involves the detection and identification of *Plasmodium* species in Giemsa-stained thick blood films (for screening the presence of malaria parasite) and thin blood films (for the confirmation of *Plasmodium* species) remains the gold standard for laboratory diagnosis.[15] This diagnostic approach is appealing given its simplicity, relative low cost, ability to identify the presence, density and identity of the infecting species of plasmodium parasites.[11] However, the staining and interpretation processes associated with microscopy are labour intensive, time consuming, and require microscopists with considerable experience and training. The rapid diagnostic test (RDT) is simple, quick, relatively accurate and cost-effective (i.e. does not require electricity or specific equipment) for malaria diagnosis.[16] Regardless of the product type or manufacturer, RDTs are based on the same principle which detects malaria antigen in blood flowing along a membrane containing specific antimalarial antibodies. Most RDT products target *P. falciparum*-specific proteins such as the histidine-rich protein 2 or lactate dehydrogenase (LDH), while others detect *P. falciparum* specific and pan-specific antigens (aldolase or pan-malaria pLDH) to distinguish non-*P. falciparum* infections from mixed malaria infections.[11] Currently, there are conflicting findings on the reliability of RDT results. A group of studies reported that RDT showed excellent diagnostic performance for malaria diagnosis[17–19]

while another group reported wide variations in sensitivity in malaria-endemic settings.[16,20]

The molecular diagnostic approach is generally more sensitive and specific compared to the laboratory and clinical diagnostic approaches. Common examples of molecular diagnostic approaches include PCR, microarray and mass spectrometry. The PCR-based techniques for example, can record high diagnostic accuracy even for malaria cases with low parasitaemia or mixed infection.[21] However, PCR has limited utility in developing settings with the highest burden of malaria given the sophisticated methodologies, high cost and the requirement for equipment and highly trained technicians.[22]

1.2.5 Treatment of malaria

Diagnosed malaria cases are treated with antimalarial medications the type of which is largely dependent on the severity of infection.[1] As such, uncomplicated malaria cases may be treated with artemisinin in combination with other antimalarials (hence referred to as artemisinin based combination therapy or ACT) such as amodiaquine, lumefantrine among others.[1] The use of ACT strategy was adopted to reduce the problem of resistance in the malaria parasite to any single drug component.[23] Severe and complicated malaria cases are treated with parenteral artesunate or quinine and an appropriate antibiotic[24] to minimise morbidity and mortality especially in children under-five years.[25]

1.2.6 Prevention of malaria

The common strategies used for the prevention of malaria include the elimination of mosquitoes and prevention of mosquito bites. The use of insecticide-treated mosquito nets (ITNs) and indoor residual spraying (IRS) have been demonstrated to be highly effective in preventing childhood malaria in endemic settings.[26,27] Other preventive

measures involve community participation and health education strategies which aim to promote the level of awareness of malaria and benefits of adopting the aforementioned control measures.[28] Intermittent preventive treatment (IPT) is another preventive measure that has been used successfully to control malaria among pregnant women, infants and preschool children especially in non-endemic settings.[29] Although there is no vaccine for malaria, a vaccine called Mosquirix (RTS, S/AS01) was approved by European regulators in 2015 and is currently undergoing pilot trials in Ghana, Kenya and Malawi.[30]

1.2.7 Risk factors of malaria in children

Generally, household use of preventive measures (e.g. long lasting insecticide treated nets and indoor residual spraying) have been shown to reduce the risk of uncomplicated malaria and severe malaria in children under-five.[31,32] In contrast, living close to mosquito-breeding sites (pond, open gutter etc.), undernutrition and low socioeconomic status increase the risk of malaria in children under-five.[33–35] Moreover, household factors such as the use of irrigated land, earthen rooves, open eaves, lack of separate kitchen and a single sleeping room have been identified as risk factors for malaria among children.[36]

Evidence suggests that characteristics of the child's caregiver, usually the mother, play significant role in determining the occurrence of severe malaria. For example, a study by Safeukui-Noubissi *et al*. [37] in Bamako, Mali found that children whose caregivers had at least primary school education, showed adequate knowledge of malaria and adopted basic preventive measures, were less likely to develop severe malaria as compared with their counterparts.

1.2.8 The estimated burden of childhood malaria in Nigeria

Overall, the global burden of malaria is steadily decreasing, with malaria incidence and mortality among populations at risk (e.g. children) falling by 21% and 35%, respectively, between 2010 and 2015.[38] However, sub-Saharan Africa still accounts for about 76% and 75% of global malaria cases and deaths, respectively, with more than two thirds of deaths occurring in children under the age of five years.[38] Currently, Nigeria bears the highest burden of malaria, more than any other country in the world (Figure 1.2).[38]

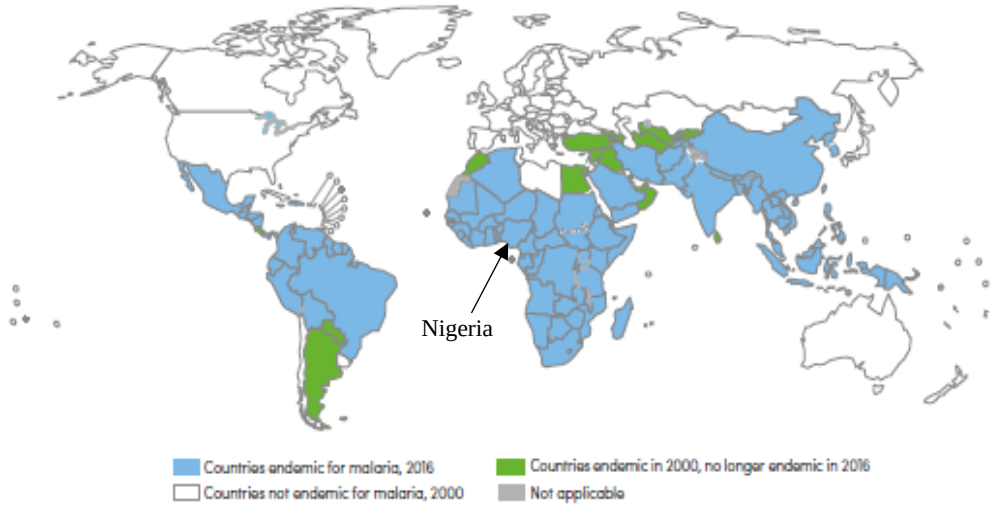


Figure 1.2: The global distribution of malaria endemicity in 2000 and 2016
Source: World Health Organization[38]
Permission to use figures from the WHO publications or website was not sought as they are allowed for research purposes such as an academic thesis or dissertation.

To assess the burden of malaria in children in Nigeria, a scoping search was carried out using the terms 'prevalence' OR 'incidence' AND 'malaria' OR 'falciparum' AND 'children' OR 'infant' AND 'Nigeria' in the PubMed database. However, the literature search was restricted to studies from 2010 till date given that the initial pilot search

yielded 2,563,799 articles. Moreover, additional studies were identified from the reference lists of papers that met the selection criteria.

All the studies on childhood malaria burden in Nigeria were cross-sectional, thereby making it impossible to ascertain incidence rates. Overall, the prevalence of childhood malaria ranged between 5% and 78%. The low prevalence (5%) of childhood malaria recorded by Oluwayemi and colleagues[39] could be explained by the focus of the study on only cerebral malaria cases. In contrast, the high proportion of malaria cases (78%) recorded in the study by Ukwaja and colleagues[9] may be due to poor specificity of the diagnostic criteria in which malaria was defined as fever or a recent history of fever. It is now mandatory for the outcome of laboratory tests (microscopy or rapid diagnostic test) to decide the treatment of suspected malaria cases.[38] Notably, most of the studies on childhood malaria were undertaken in secondary[9,40–42] and tertiary[39,43–46] hospitals. This suggests that the estimated burden of childhood malaria in Nigeria may be inaccurate given the dearth of evidence at the primary healthcare level. Table 1.1 summarises studies from 2010 to date on malaria prevalence in children in Nigeria.

Table 1.1: Estimated burden of childhood malaria in Nigeria

Author, Year	Study period	Study setting & population	Study design & identification of malaria cases	Age/age group	Prevalence of malaria (%)
Dawaki *et al*. (2016)[47]	May–June 2013	Five rural communities in Kano State: population 63	Cross-sectional study. Malaria diagnosis was based on microscopy.	<12 years	42.9 (microscopy)
Iwuafor et al. (2016)[48]	November 2012 – December 2013	Tertiary hospital, Cross-River State: population 270. However, RDT and microscopy tests were carried out on 258 and 167 patients (denominators)	Cross-sectional study. Malaria diagnosis was based on rapid diagnostic test (RDT) and microscopy.	1–59 months	32.2 (RDT) 40.1 (microscopy)
Oyeyemi et al. (2016)[49]	May–August 2014	Two secondary hospital, Lagos State: population 200. However, only 102 children were examined for malaria according to RDT and microscopy.	Cross-sectional study. Malaria diagnosis was based on RDT and microscopy.	<59 months	18.6 (RDT) 40.2 (microscopy)
National Malaria Elimination Programme, National Population Commission, National Bureau of Statistics, and ICF International (2016)[50]	October–November 2015	The six-geopolitical zone (36 States and Capital City) in Nigeria: population 6,000 and 5,748 for RDT and microscopy respectively.	Cross-sectional study. RDT (SD Bioline) in the field and microscopy in the laboratory.	6–59 months	45 (RDT) 27 (microscopy)
Adedoja et al. (2015)[51]	October 2012–May 2013	Two communities in Kwara State: population 1,017	Cross-sectional study. Malaria diagnosis was based on microscopic test.	4-15 years	20.6 (microscopy)
Adigun et al. (2015)[52]	2010 but specific details not provided.	A representative survey data of Nigeria based on the Malaria Indicator Survey: population 5,043	Cross-sectional survey. Malaria diagnosis was based on microscopic test.	<60 months	38.0 (microscopy)
Ajumobi et al. (2015)[41]	December 2010–August 2011	Secondary hospital, Kaduna State: population 295	Cross-sectional study. Malaria diagnosis was based on RDT and microscopic tests.	6–59 months	11.9 (RDT) 10.5 (microscopy)
Singh et al. (2014)[53]	July–September 2012	Secondary hospital, Kebbi State: population 198	Cross-sectional study. Malaria diagnosis was based on microscopic test.	3–15 years	59.6 (microscopy)
Oluwayemi et al. (2013)[39]	June 2009–February 2010	Tertiary hospital, Ekiti State: population 1,202	Cross-sectional study.	2–128 months	5.5 (microscopy)

			Cerebral malaria was defined as coma on admission or altered consciousness and positive test for malaria by microscopy.		
Rabiu et al. (2012)[44]	September 2010–February 2011	Tertiary hospital, Oyo State: population 209	Cross-sectional study. Malaria diagnosis was based on RDT (Cyscope mini and Paracheck-Pf) and microscopic tests.	6–144 months	85.2 (Cyscope mini) 32.1 (Paracheck-Pf) 22.0 (microscopy)
Samdi et al. (2012)[54]	2003–2004 (specific months not stated)	Tertiary hospital, Borno State: population 692	Cross-sectional study. Malaria diagnosis was based on microscopic test.	6–96 months	24.4 (microscopy)
Adesanmi et al. (2011)[46]	Not stated.	Tertiary hospital, Enugu State: population 380 (356 patients were assessed for malaria by RDT)	Cross-sectional study. Malaria diagnosis was based on RDT (Paracheck-Pf) and microscopic tests.	5–59 months	27.5 (RDT) 36.8 (microscopy)
Ukwaja, Aina and Talabi (2011)[9]	August–October 2009	Secondary hospital, Ogun State: population 1,216	A cross-sectional study. Malaria diagnosis was based on the old IMCI case definition, which was fever or recent history of fever.	2–60 months	78.0 (old IMCI)
Jeremiah, Jeremiah and Emelike (2010)[55]	March 2005–April 2006	A community in Rivers State: population 240	Cross-sectional study. Malaria diagnosis was based on microscopic test.	12–96 months	27.5 (microscopy)
Ikeh and Teclaire (2008)[56]	Unclear	Five primary healthcare centres, Plateau State: population 260	Cross-sectional study. Malaria was diagnosed by microscopy.	0-60 months	56.9 (microscopy)

Children were defined as individuals <16 years for this literature review

1.3 Pneumonia

1.3.1 Definition and causes of pneumonia

Pneumonia is an acute lower respiratory tract infection which is characterised by inflammation of the alveoli in the lungs.[57,58] Pneumonia is primarily caused by viral or bacterial infection and less commonly by fungi and parasites.[57] Bacteria and viruses are the most common causes of pneumonia in adults and children respectively.[59] Pneumonia infection in children under-five is typically characterised by cough, fever and fast or difficult breathing irrespective of the causative agents.[60,61] Common examples of bacteria that cause pneumonia include *Streptococcus pneumoniae* (nearly 50% of cases), *Haemophilus influenzae* (20% of cases), *Chlamydophila pneumoniae* (13% of cases) and *Mycoplasma pneumoniae* (3% of cases).[62,63] The commonly isolated viral agents in pneumonia cases include rhinoviruses, coronaviruses, influenza virus, respiratory syncytial virus, adenovirus, and parainfluenza.[64] It is customary for pneumonia to be classified by where it was acquired. For example, community-acquired pneumonia refers to cases acquired in the community, hospital-acquired pneumonia refers to cases that occur ≥48 hours after hospitalisation and healthcare-associated pneumonia refers to cases within hospital environment (nosocomial).[65]

1.3.2 Pathogenesis and pathophysiology of pneumonia

Essentially, pneumonia is caused by the invasion and predominance of pathogens in the lung parenchyma, resulting in inflammation and intra-alveolar exudates.[58,66] In brief, pathogens (bacteria or viruses) gain access to the lower respiratory tract through aspirations of organisms residing in the throat or nose[67] or the inhalation of contaminated airborne droplets through the mouth or nose[67] or bloodstream from other sites.[66] Once

in the lungs, pathogens invade the spaces between cells and alveoli leading to varying levels of cell deaths.[66] In an attempt to inactivate or destroy these pathogens, the immune cells –macrophages and neutrophils– further damage the lung cells.[68] Furthermore, the cytokines released by neutrophils during this phase activate the immune system, resulting in the fever, chills, and fatigue characteristic of bacterial pneumonia.[69] The immune cells (macrophages and neutrophils), pathogens and fluid from surrounding blood vessels fill the alveoli, resulting in consolidation[68] while the inflammation and congestion of the lungs reduce oxygen exchange, leading to cough and breathlessness.[70] On some occasions, infection can spread from the lungs, causing complications such as sepsis, bacteraemia, meningitis, empyema and septic embolism.[66] It should be noted that symptoms of pneumonia and malaria do overlap to present as coinfection (section 1.2.3).

1.3.3 Diagnosis of pneumonia

The diagnosis of pneumonia can be challenging given the lack of a definite diagnostic test to differentiate between bacterial and non-bacterial causes.[71] Common diagnostic approaches for pneumonia include clinical and physical examination, chest radiography (chest X-ray) and microbiological tests (e.g. culture of the sputum and blood tests).[66] According to the World Health Organization, clinical diagnosis of pneumonia in children can be based on either a cough or breathing difficulty plus increased respiratory rate (details in method chapter) or chest in-drawing.[24]

A chest radiograph is considered the gold or reference standard for pneumonia diagnosis as it can provide information on the extent of localization and exclude other causes of disease.[72] However, chest X-ray (CXR) is not ideal for routine investigation in children with signs and symptoms suggesting pneumonia who are not admitted to hospital.[73] Moreover, evidence suggests that CXR is generally less helpful in establishing whether

pneumonia is of viral or bacterial aetiology.[73] Coupled with the financial burden on patients, CXR requires a substantial level of expertise which often contributes to interpretation problem among radiologists especially in developing settings.[74]

The causative agent of pneumonia is determined in only few cases (<20%) with routine microbiological tests given the ease with which samples (e.g. nasopharyngeal swab) get contaminated.[60] However, microbiological tests, such as sputum culture, can be considered for patients who do not show a positive response to treatment, with additional blood cultures in those hospitalized for severe illness.[72] In contrast, suspected viral infections are confirmed through detection of either the virus or its antigens with culture or polymerase chain reaction (PCR).[64]

1.3.4 Treatment of pneumonia

Pneumonia was regarded in the 19th century as 'the captain of the men of death' to denote its virulence.[75] However, survival has improved since the introduction of antibiotics and vaccines in the 20th century.[64] The treatment of pneumonia is dependent on the underlying cause[65] such that cases attributed to bacteria and viruses are treated with antibiotics and antiviral medications respectively.[61] It should be noted however that children with a definite clinical diagnosis of pneumonia are required to be given antibiotics as bacterial and viral pneumonia are difficult to differentiate.[73] Amoxicillin administered according to age or weight of the child is the WHO recommended first-line drug of choice due to its efficacy and increasing high resistance to cotrimoxazole.[24]

1.3.5 Prevention of pneumonia

The primary preventive measure against some bacterial and viral pneumonia infections in children is vaccination.[65] Vaccinations against *Haemophilus influenzae* and

Streptococcus pneumoniae have been shown to be effective for the prevention of pneumonia.[66] The recent pneumococcal conjugate vaccine, typically given to children at 2, 4 and 12-13 months of age, has the advantage of being protective against 13 types of pneumococcal bacteria that cause pneumonia.[66] Other preventive measures include adequate nutrition, minimising children's exposure to indoor air pollution and effective management of other health problems such as influenza.[65,66]

1.3.6 Risk factors of pneumonia in children

Children with compromised immune systems due to malnutrition or undernourishment, especially in infants who are not exclusively breastfed for the first six months of life, are at higher risk of developing pneumonia.[76,77] Children with pre-existing illnesses or comorbidities such as symptomatic HIV infections, malaria, measles, history of wheezing or asthma and diarrhoea are also at increased risk of contracting pneumonia.[77–80] Family characteristics such as socioeconomic status, environment (e.g. indoor air pollution, living in a crowded household, exposure to cigarette smoke) have been shown to be associated with increased risk of pneumonia in children.[76,77,81,82] Other factors that have been shown to be independently associated with pneumonia in children include young age, low weight and immunisation for age, attendance of day-care centres, delay in seeking medical treatment for ≥3 days and contact with a household member with upper respiratory tract infection.[76,77,79]

1.3.7 The estimated burden of childhood pneumonia in Nigeria

Although figures on morbidity and mortality are falling, pneumonia is still the single largest infectious cause of childhood death globally (Figure 1.3).[80] The latest global estimates showed that pneumonia caused the deaths of 920,136 children under-five in

2015, equivalent to 16% of the total mortality recorded for this age group.[80] Evidence from available reports showed that Nigeria bears the highest burden of pneumonia, more than any other country in Africa.[83]

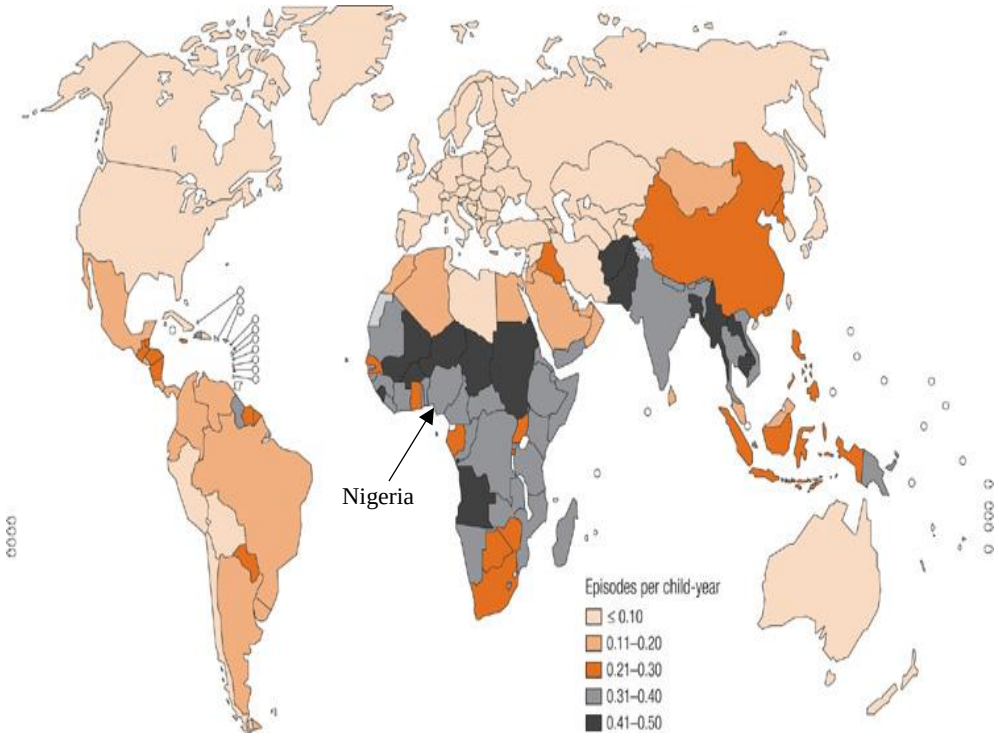


Figure 1.3: Incidence of childhood clinical pneumonia at the country level
Source: Rudan et al.[84]
Permission for the re-use of this figure was obtained from the original authors

To assess the burden in terms of prevalence and incidence of childhood pneumonia in Nigeria, a scoping search was carried out using the terms 'prevalence' OR 'incidence' OR 'cohort' OR 'longitudinal' AND 'pneumonia' OR 'respiratory disease' OR 'respiratory illness' AND 'children' OR 'infant' AND 'Nigeria' in the PubMed database. In contrast to malaria, the literature search was not restricted to studies from 2010 till date given that the initial pilot search yielded 5,963 articles. Similarly, additional studies were identified from the reference lists of papers that met the selection criteria. Overall, the prevalence of acute lower respiratory infections (ALRI) in children

in Nigeria ranged between 2% and 36%; whereas, the incidence of pneumonia was estimated to be between 270 and 364 per 1000 child population. Notably, 7 out of the nine studies were cross-sectional[9,85–92] and carried out either in tertiary[85,88–90] or secondary[9,86,90] hospitals. This suggests that the estimated burden of childhood pneumonia in Nigeria may not be reflective of the actual burden given the lack of evidence at the primary healthcare level. It should be noted however, that the inclusion of ALRI as an indication of pneumonia infection may have overestimated the true burden. For example, bronchiolitis is considered alongside pneumonia as a major component of ALRI that accounts for the global burden of disease from acute respiratory infections in children.[93] Table 1.2 summarises studies on pneumonia burden (prevalence and incidence) in children in Nigeria.

Table 1.2: Estimated burden of childhood pneumonia in Nigeria

Author, Year	Study period	Study setting & population	Study design and identification of pneumonia cases	Age/age group	Prevalence of pneumonia/ acute respiratory infections (%)
Nwolisa, Erinaugha and Ofoleta (2007)[85]	January–April 2004	Tertiary hospital, Imo State: population 829	Cross-sectional extraction of data from hospital diagnoses.	2–59 months	35.8[+]
Iloh et al. (2011)[86]	June 2008–June 2009	Secondary hospital, Imo State: population 244	Cross-sectional study. However, the approach used for case identification was unclear.	4 days–59 months	32.0[+]
Adesanya and Chiao (2016)[87]	Unclear	896 communities in Nigeria: population 28,596	Cross-sectional data from the 2013 Nigeria Demographic and Health Survey. ARI was defined by caregivers' report of cough, short, rapid breathing accompanied by a fever.	0–59 months	1.93[+]
Motayo et al. (2016)[88]	January 2010–December 2010	Tertiary hospital, Ogun State: population 263	Review of all suspected and laboratory confirmed invasive pneumococcal disease – a suspected case of pneumonia confirmed by a positive culture of *Streptococcus pneumoniae* – cases during study period.	≤12 months	1.9
Orimadegun, Ogunbosi and Carson (2013)[89]	April 2010–March 2011	Tertiary hospital, Oyo State: Population 454	A cross-sectional study. Clinical diagnoses of pneumonia were made based on history of cough or difficulty in breathing in the presence of increased respiratory rate for age. Suspected pneumonia cases were confirmed by radiography.	<2 months	6.6

Ukwaja, Aina and Talabi (2011)[9]	August–October 2009	Secondary hospital, Ogun State: population 1,216	A cross-sectional study. Diagnosis of pneumonia was based on cough or difficult breathing plus increased respiratory rates (according to the IMCI cut-offs) for age by study clinician.	2–60 months	30.0
Falade et al. (2009)[90]	February 2005–January 2006 and July 2006–June 2007	One tertiary & two secondary hospitals, Oyo State: population 1,210	A cross-sectional study. Pneumonia diagnosis was based on history of cough or difficult breathing and increased respiratory rates for age.	2–59 months	33.0
Robertson et al. (2004)[91]	June 1999–May 2001	Two communities in Oyo State: child-years of observation 1,579	A prospective cohort study of lower respiratory tract infection (LRTI). LRTI was defined based on the recording of cough or difficulty breathing and one or more of the following: fast breathing for age, lower chest wall in-drawing, stridor, wheezing or apnoea.	<12 months	323[++]
				12-59 months	270[++]
Fagbule, Parakoyi and Spiegel (1994)[92]	July 1988–June 1989	A community in Kwara State: child-years of observation 4,534	A prospective cohort study of acute respiratory infections (ARIs). ARI and severe ARI were defined as cough plus increased respiratory rate for age and cough, increased respiratory rate for age and chest wall in-drawing.	2–60 months	364[++]

[+] These findings were based on acute respiratory infections.
[++] These findings were based on acute respiratory infections and incidence rate per 1000 child-years
Children were defined as persons <16 years for this literature review

1.4 Overview of the Nigerian healthcare system

The Nigerian health care system comprises the public and private health sectors.[50] The public health sector is organised according to the three tiers of government: federal (responsible for tertiary or referral hospitals in federal institutions like universities), state (responsible for state specialist and general hospitals) and local government areas (responsible for primary healthcare centres (PHCs)).[94] The private sector is made up of the formal sector (private not-for-profit and private for-profit organisations) and the informal sector (traditional medicine providers, chemist stores etc.). Primary healthcare centres provide basic preventive, curative, promotive, and rehabilitative health care services especially in rural communities.[50] Unlike the secondary and tertiary public hospitals that are financed by the state and federal governments, underfunding and shortage of medical facilities, doctors and other important health staff are the common challenges in most of the Nigerian PHCs.[95] This could be due to the reliance of local government on states for funding. Figure 1.4 below depicts the typical organisational structure of the Nigerian primary healthcare system.

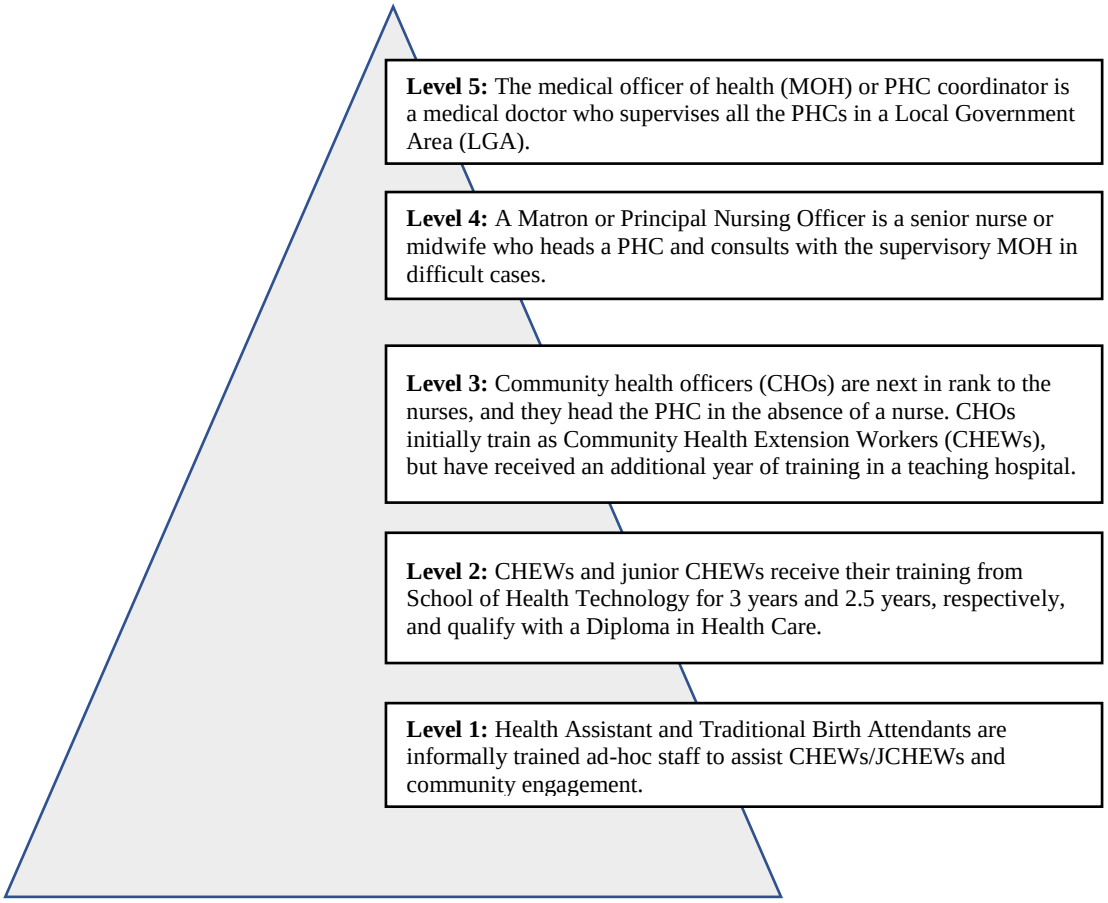


Figure 1.4: Organizational structure of the Nigerian primary healthcare system
Adapted from: Abdulmalik et al.[96]

1.5 The IMCI guidelines

The Integrated Management of Childhood Illness (IMCI) guidelines were developed by the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) in the mid-1990s to reduce morbidity and mortality, as well as promote improved growth and development in children aged 1 week up to 5 years.[97,98] Prior to the introduction of the IMCI strategy, surveys showed that many children who presented to hospitals, health centres and traditional healers in most developing countries were not properly assessed and treated by health care providers, and their caregivers were not given proper counselling.[97] The problem was more pronounced at the primary healthcare level where skilled personnel, diagnostic facilities (e.g. laboratory), essential medications and equipment were scarce or completely lacking.

The IMCI strategy includes three main components: improving case management skills of health workers, overall primary health systems and family and community health practices.[97] The guidelines follow an evidence-based approach that aims to improve the case management skills of healthcare workers with a focus on 10 common preventable diseases such as malaria, diarrhoea, pneumonia, anaemia, HIV infection among others in children under-five.[24] Being an 'integrated' approach, the IMCI strategy has the advantage of covering a variety of factors that put children at serious risk especially in developing settings where children often suffer from more than one condition, making a single diagnosis inappropriate.[97]

The IMCI guidelines describe steps for assessing, classifying and treating ill children, as well as counselling the child's caregiver. For example, the diagnosis of pneumonia could be made based on the observation of cough, fever and fast breathing assessed with the aid of minimal equipment like a timer.[99] The definition of fast breathing is presented in the assessment of pneumonia according to the IMCI guidelines of the method chapter.

Since its inception in the mid-1990s, the IMCI strategy has been introduced and implemented in more than 75 countries around the world with evidence of positive health outcomes among children under-five.[100] A multi-country evaluation to assess the impact, cost and effectiveness of the IMCI strategy following its implementation in Brazil, Bangladesh, Peru, Uganda and the United Republic of Tanzania showed positive outcomes. It was found that implementation of the IMCI guidelines improved health worker performance and their quality of care; reduced under-five death, improved nutritional level, and was more cost effective than the usual care.[97] Although there is evidence of IMCI implementation in Nigeria,[101] there seems to be lack of evaluation evidence as reported in other African countries such as Botswana and Egypt.[102,103]

1.6 Overview of lay diagnosis of illness

Lay diagnosis (also called caregivers' diagnosis or self-diagnosis) is when persons who are not formally trained to diagnose and treat medical problems nevertheless describe, explain and assign meaning to and predict a medical problem in themselves or others.[104] According to Olafsdottir & Pescosolido,[105] it is commonplace for illness to first be diagnosed by individuals experiencing symptoms and/or by family members before presenting to formal healthcare centres. These individuals, including caregivers, only decide to seek formal healthcare services when there is no improvement in health outcome or when there are complications following the administration of medications based on lay diagnosis.[106] Evidence suggests that caregivers, especially in low– and middle–income countries, rely on lay diagnosis primarily because of insufficient funds, difficulty and delays in accessing formal healthcare services, social influence from relatives or family members, unrestricted access to over-the-counter medications, among other reasons.[107,108] Overall, lay diagnosis is a commonly adopted diagnostic approach

by individuals for the diagnosis of several infectious and non-infectious diseases including progressive multiple sclerosis,[109] influenza,[110] malaria,[111] and pneumonia,[112] regardless of socioeconomic status. Depending on the context, the terms lay diagnosis and caregivers' diagnosis are used interchangeably in this study.

1.7 Justification of study

1.7.1 Evaluating diagnostic performance of the IMCI guidelines for malaria and pneumonia

Improved performance and quality of care by health workers, reduced number of under-five deaths and cost of care have been recorded as some of the health benefits following implementation of the IMCI strategy.[100] Nonetheless, the IMCI strategy has some limitations including the presumptive diagnosis of malaria based on fever (the old IMCI guidelines) and inability to distinguish between bacterial and viral pneumonia or asthma from pneumonia, as well as the consequent over-prescription of antimalarials and antibiotics.[98,113–115] This low specificity in the diagnosis of malaria and pneumonia was considered in the revised IMCI guidelines. For example, it is now mandatory for the outcome of rapid diagnostic test of all fever cases to decide the treatment of suspected malaria. However, there is the need to formally assess the actual diagnostic performance of the IMCI strategy for malaria and pneumonia as compared to reference diagnostic tests (microscopy for malaria and chest X-ray for pneumonia). Such findings will provide health policy makers with evidence on how best to tailor the IMCI strategy on childhood malaria and pneumonia for wider coverage and implementation such that there is maximum effectiveness given resource constraints in Nigeria.

1.7.2 Exploring wide-scale implementation of the IMCI strategy in Nigeria

Despite the reported benefits associated with implementation of the IMCI strategy, significant and sustainable reduction in under-five mortality is dependent on wide-scale coverage and implementation.[97] Unlike other African countries where the benefits and challenges to the wide-scale implementation of the IMCI strategy have been explored and yielded country-specific lessons for way forward,[102,103] there seems to be dearth of evidence for Nigeria in this regard. The scant evidence on IMCI guideline implementation in Nigeria is largely based on descriptive and cross-sectional studies.[116–119] Thus, a study providing an in-depth exploration of country-specific benefits and challenges to the wide-scale implementation of IMCI strategy in Nigeria seems appropriate.

1.7.3 Evaluating caregivers' diagnosis of malaria and pneumonia, and potential for training them in the IMCI guidelines

The 2016 world malaria report showed that a large proportion of children under-five are not seen in formal healthcare facilities in Nigeria (as well as other sub-Saharan Africa countries) partly due to caregivers' lack of awareness of the need to consult trained healthcare staff for febrile children.[38] Caregivers and patients often rely on lay diagnoses (either made by themselves or by family/friends) to trigger self-prescriptions of medications in Nigeria.[120] This bypassing of the formal clinical consultation often predominates either because of the inability to pay a consultation fee or the illness is considered not serious enough to warrant admission to formal healthcare facilities.[121] Interestingly, the WHO home-based management strategies aimed at reducing malaria burden relied on the presumptive treatment of fevers with an antimalarial drug.[122,123] The strategy involves training lay community members as community health workers in the

diagnosis and treatment of malaria. However, the WHO in 2010 recommended that the outcome of laboratory diagnosis (e.g. microscopy or RDT) should decide treatment of malaria.[38] The study by Mukanga and colleagues[124] in a rural Uganda district suggests that caregivers can perform diagnostic tests to decide treatments for children under-five with suspected malaria and pneumonia. This study found the diagnostic performances of 14 community health workers (three of whom had only primary school education) to be comparable to those of experienced community trainers and a laboratory scientist following an 8-day training course.

Given the health benefits of accurate and prompt diagnosis of childhood illnesses especially for malaria and pneumonia with high fatality,[38,70] it would be worthwhile to assess caregivers' diagnostic accuracy of malaria and pneumonia against standardised diagnostic approaches (e.g. the IMCI guidelines and microscopy) and develop interventions guided by findings. It would also be useful to explore caregivers' willingness to become trained in a standardised diagnostic approach for improved and prompt home-management of these and other common childhood illnesses in their children and neighbours' children. The thinking underlying such proposals is as follows: first, it is hypothesised that because of their greater stake in their children's wellbeing, caregivers will be more willing to acquire training in early and more accurate diagnosis of childhood illnesses. Second, ongoing monitoring of the child's progress following treatment to enable early intervention if any deterioration is noted, is more feasible if it is provided by the child's own caregiver in a resource constrained environment with limited professional healthcare capacity. The feasibility of implementing such a proposal would need to be explored by first, exploring the willingness of community members to undergo such training; second, acceptability of this proposal amongst healthcare professionals and third, baseline estimates of the accuracy of lay diagnosis offered by

untrained caregivers and the potential improvement in diagnostic accuracy following training in the application of IMCI guidelines.

1.7.4 Assessing agreement between health workers and caregivers in the diagnosis of malaria and pneumonia

The extent of agreement between caregivers and health workers using the IMCI guidelines can be assessed in terms of interobserver variation. Interobserver variation is measurable in any situation in which two or more independent observers (e.g. caregivers and health workers) are evaluating the same thing (e.g. a child presenting with suspected malaria or pneumonia).[125] In addition to caregivers' diagnostic accuracy for childhood malaria and pneumonia, this study will assess the extent of agreement between caregivers' diagnoses and those of health workers using the IMCI guidelines. Thus, the extent, if any, of the role of guesswork or pure 'chance' played in caregivers' diagnosis of malaria and pneumonia would be ascertained. Moreover, this is an appropriate step given that the IMCI strategy is not considered a reference diagnostic approach like microscopy or CXR.

1.7.5 Exploring the potential for caregivers' diagnosis as a surveillance tool

Estimates of mortality from malaria and pneumonia in developing countries are often inaccurate due to lack of vital registration systems and data on cause-specific mortality.[126] It is not unusual for health monitoring especially in rural communities to be conducted based on self-reports via random spot checks and word of mouth at monthly intervals.[126] Moreover, many cases of childhood illnesses such as malaria are not presented to formal healthcare centres or, if presented, the healthcare system may not be covered by the national surveillance system.[38] Therefore, understanding the

criteria used by caregivers for malaria and pneumonia diagnosis could be used to assess the credibility of data collected in this manner. Depending on the outcome of a validation study against standardised clinical diagnostic criteria, caregivers' diagnosis of malaria and pneumonia could be considered as an adjunct surveillance tool. This will be useful in Nigeria where knowledge of disease surveillance and notification system and the use of basic surveillance recording forms among health workers at both primary and higher healthcare facilities are considerably poor.[127,128]

1.7.6 Estimating the burden of malaria and pneumonia in children under-five at the primary healthcare level

Several studies have assessed the burden of malaria and pneumonia among children under-five presenting to secondary, tertiary and private healthcare facilities in Nigeria.[118,129,130] However, there appears to be paucity of epidemiological data on the burden of these diseases in children under-five at the primary healthcare level. Most of the studies on malaria at the primary healthcare level in Nigeria appear to be focused on pregnant women[130–133] while the study of 260 children under-five assessed malaria only by microscopy.[56] Furthermore, there appears to be lack of epidemiological evidence on the burden of childhood pneumonia at the primary healthcare level in Nigeria. This suggests that the estimated burden of childhood malaria and pneumonia in Nigeria may be inaccurate and non-representative, making the allocation of scarce resources at the various levels of healthcare system inequitable and inefficient. For example, many patients who present to primary healthcare facilities in Nigeria tend to be of lower socioeconomic class compared to their counterparts who present to higher healthcare facilities (e.g. secondary, tertiary and private hospital) so previously available estimates may not be generalizable to them.[95,134,135]

1.7.7 Assessing malaria and pneumonia post-treatment outcomes and risk factors

Assessing the clinical outcomes in children diagnosed with malaria and pneumonia and risk factors associated with severe outcomes can be useful. The prevalence of clinical outcomes associated with malaria and pneumonia in children under-five in Nigeria is poorly evidenced and an understanding of the context-specific risk factors may help guide the development of or investment in appropriate public health interventions.

1.8 Study aims and specific objectives

Based on the gaps in research evidence as outlined above, this study aimed to evaluate the usefulness of the revised IMCI guidelines for the diagnosis of malaria and pneumonia in children under-five. It also explores the potential value of harnessing lay individuals for early diagnosis of these diseases at the community level. To address the overarching aims, the following specific objectives were studied:

1. To assess the diagnostic accuracy of the IMCI guidelines and lay diagnosis (caregiver) for malaria and pneumonia in comparison to reference diagnostic approaches (microscopy and CXR for malaria and pneumonia respectively). Agreement between caregivers and health workers using the IMCI guidelines in the diagnosis of malaria and pneumonia is also assessed.

2. To assess the estimated burden of malaria and pneumonia among children <5 presenting to PHCs during study period according to the various diagnostic approaches.

3. To determine the clinical outcomes in children diagnosed with malaria and pneumonia according to the IMCI guidelines and risk factors for severe outcomes.

4. To qualitatively explore caregivers' and health professionals' perspectives of lay diagnosis and IMCI guidelines as diagnostic approaches for malaria and pneumonia at the community level.

Figure 1.5 below depicts how the study specific objectives are related to each other and contribute to the ultimate study goal —improved management of childhood malaria and pneumonia at the community or primary healthcare level in Nigeria.

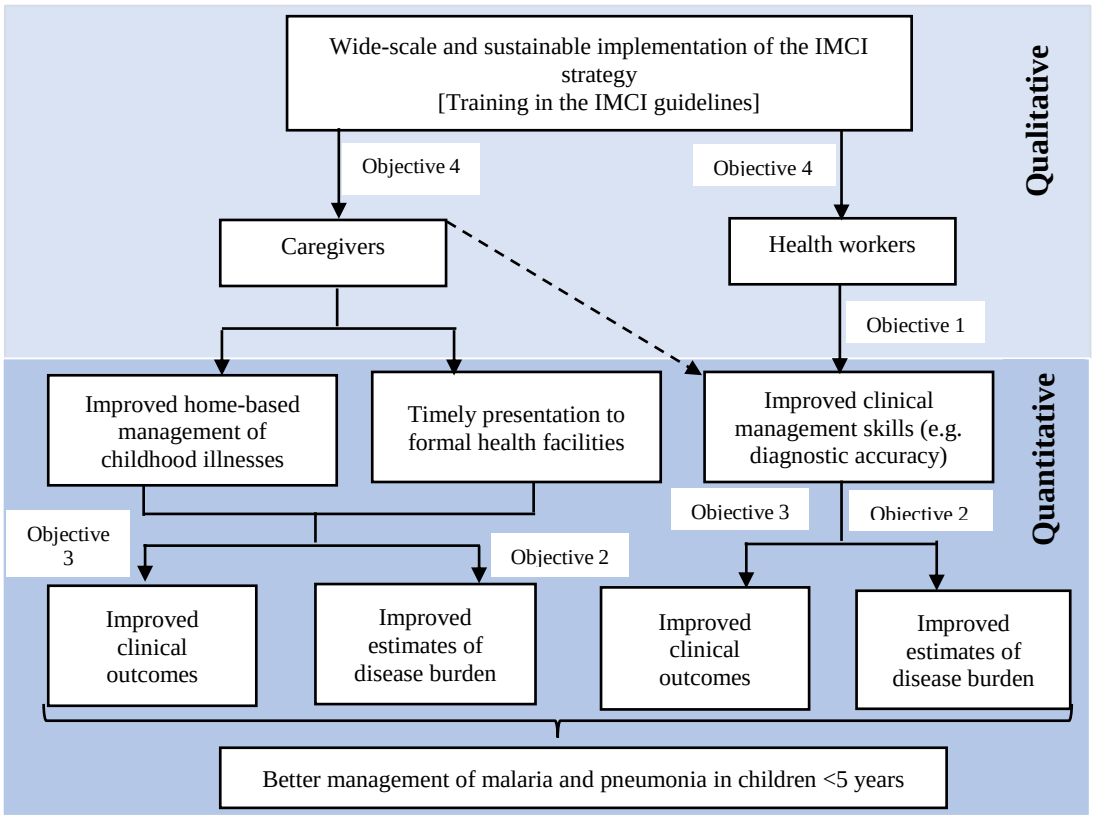


Figure 1.5: A graphical representation of the interrelationship between study specific objectives

The wide-scale and sustainable implementation of the IMCI strategy in Nigeria will require training both health workers and caregivers in the use of the guidelines. Training of health workers has the capacity to improve their diagnostic performances for malaria

and pneumonia, which in turn would result in better estimate of disease burden and clinical outcomes. Similarly, training of caregivers in the IMCI guidelines has the 'potential' to improve their recognition of malaria and pneumonia at home to institute appropriate home-based management or health seeking behaviours (e.g. timely presentation to formal health facilities).

1.9 Study outline

The study is presented as individual chapters. Chapter 2 describes the quantitative and qualitative research methods used to address each specific study objective. Chapter 3 presents the main findings of the work. Chapter 4 synthesizes the findings and discusses them with respect to the available literature. Chapter 5 concludes the study, considers the implications of findings and offers recommendations for further research.

2 METHODS

2.1 Introduction to method chapter

This study has two components (quantitative and qualitative) and four objectives. This chapter outlines the study area, centres and study design for each specific objective. This is followed by an in-depth description of the data management including collection, processing and storage for both the quantitative and qualitative components of the study. The chapter ends with a brief overview of ethical considerations and the ethical clearances sought at the outset.

2.2 Study area

This study was carried out in Benin City, the capital of Edo State in southern Nigeria. Edo State is one of the 36 States in Nigeria sharing boundaries with Kogi State in the north, Delta State in the south and Ondo State in the west. The study area, located between longitude 5.6037465°E and latitude 6.334986°N, has an estimated total area of 1,204 km^2 (465 square mile) with a population of over one million people.[136] Benin City consists of three Local Government Areas (LGAs) (Egor, Ikpoba-Okha and Oredo) out of the 18 in Edo State. The study area is within the tropical rain forest where malaria transmission is holo-endemic and stable throughout the year.[137] The area has an average annual rainfall ranging between 500mm and 2,780mm, and a relative humidity of 47.43 %.[138] Furthermore, the average annual temperature is between 24°C and 33°C.[138] The predominant occupational activities include commerce, education and health services.[139] In addition, agricultural activity is common but is largely small-scale relying mainly on manual labour.

2.3 Study centres

Prior to the commencement of study, information on the number of primary healthcare centres (PHCs) was obtained from the public health department in each of the three LGAs in Benin City. Though local government records for Benin City list a total of 34 PHCs, only eight were functioning and providing first contact care to their communities. However, only five PHCs in the three LGAs in Benin City (three in Egor, one each in Ikpoba-Okha and Oredo LGAs) were selected based on the willingness to participate in study. Each PHC is serviced by primary healthcare workers (PHWs) and provides basic prevention and curative services including immunisation, growth monitoring, health talks, antenatal and pregnancy care, as well as the diagnosis and treatment of common childhood illnesses such as malaria, pneumonia and diarrhoea. Additional services may involve family planning, promotion of sanitation and hygiene and provision of health care referrals to higher healthcare centres (secondary and tertiary hospitals) for severe illnesses. An overview of the characteristics of each study PHCs is provided in Table 2.1 below.

Table 2.1: Basic characteristics of study primary healthcare centres during study period (September 2015-July 2016).

Characteristic	Study primary healthcare centres				
	Evbuotubu	**Evbuogida**	**Uwelu**	**Ugbekun**	**Oredo**
LGA of residence	Egor	Egor	Egor	Ikpoba-Okha	Oredo
Number of staff	19	14	9	24	12
Number of staff trained in IMCI for current study (n=21)	5	6	3	4	3
Availability of medical doctor	Yes†	Yes†	No	No	No
Working time	Monday-Friday	Monday-Friday	Monday-Friday	Monday-Sunday (including night shifts)	Monday-Friday
Services provided					
In-patient	No	No	No	Yes	No
Out-patient	Yes	Yes	Yes	Yes	Yes
Immunisation	Yes	Yes	Yes	Yes	Yes
Facilities/equipment					
Number of beds	6	3	0*	8	2
Water supply	No	Yes	No	Yes	Yes
Access to electricity	No	Yes	Yes	Yes	Yes
Microscopy for malaria diagnosis	**No**	**No**	**No**	**No**	**No**
RDT for malaria diagnosis	Yes	Yes	Yes	Yes	Yes
Pharmacy store	Yes	No	No	No	No
Average number of visits by children under-five per month during study period	80	100	320	310	180

†The same medical doctor serviced both Evbuotubu and Evbuogida PHCs based on an agreed rota.

*The official PHC building had 4 beds but the actual service was delivered within the community market because of its location on a 'forbidden land'

Data were from researcher's direct observation and government information

The primary healthcare workers (PHWs) comprised of Community Health Extension Workers (CHEWs), Junior Community Health Extension Workers (JCHEWs)/Health Assistants and Nurses/Midwives. The details of academic qualifications and professional hierarchy of PHWs are presented in Table 2.2.

For the qualitative component of the study, all the caregivers and primary healthcare workers were interviewed at the study PHCs. However, the other health professionals including PHC coordinators, IMCI training facilitators and disease surveillance and notification officer were interviewed in their respective offices.

Table 2.2: Academic and professional hierarchy of primary healthcare workers

Characteristic	JCHEW[+]/Health Assistant	CHEW[++]	Nurse/Midwife	Matron/Principal Nursing Officer
Formal education	Yes for JCHEW (health assistants often lack formal education)	Yes	Yes	Yes
Minimum duration of training	2.5 years*	3 years	>3 years***	>3 years
Highest level of education	Basic school of health	Basic school of health	Tertiary degree in nursing	Tertiary degree in nursing**
Professional hierarchy	Very low	Low	High	Very high (12 out of 16 levels in nursing service)
Primary duties	Aid the CHEW in his/her duties	Provide basic public health services in PHCs and communities	Provide general health services in PHCs and communities.	Mostly an administrator or manager of PHCs.

[+]JCHEW =Junior Community Health Extension Worker

[++]CHEW =Community Health Extension Worker

*A JCHEW requires two additional years of training to be certified as CHEW given the lower academic results required for admission into training

**A CHEW could become a Matron based on the number of year of service.

*** In addition to the basic training for three years, a midwife could become a nurse after receiving 18-month additional training on competency-based nursing.

The spatial distribution of study PHCs in Benin City, Nigeria is shown in Figure 2.1 below.

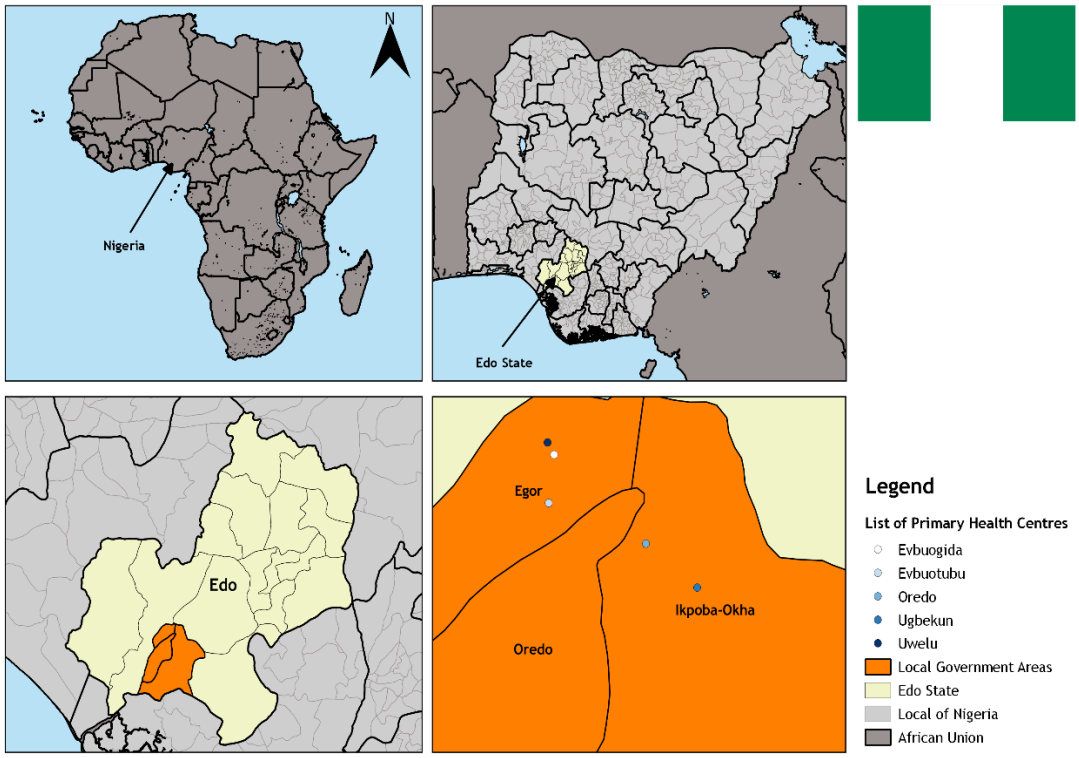


Figure 2.1: Spatial distribution of study PHCs in Benin City, Nigeria

2.4 Study design

The quantitative component consisted of two data collection points: baseline data collection at study PHCs and follow-up via telephone/home visits within 30 days of presentation at PHC. The baseline data collection point included data on clinical and socio-demographic variables while the follow-up included data on adherence to medications and occurrence of adverse clinical outcomes (severe illness). An overview of the methodological approaches adopted for each of the study objectives are presented in Table 2.3.

Table 2.3: Summary of methodological approaches adopted for specific objectives

Study objective	Study component	Data type	Analyses
1) To compare the diagnostic accuracy of the IMCI guidelines and caregivers' diagnosis of malaria as compared to microscopy, and the accuracy of caregivers' diagnosis of malaria and pneumonia as compared to diagnoses made by healthcare workers using the IMCI guidelines. In addition, agreement between caregivers' and health workers' diagnosis of malaria and pneumonia is assessed.	Quantitative	Primary	For the diagnostic accuracy findings were presented in terms of sensitivity, specificity, positive and negative predictive values and area under the receiver operating characteristic (AUROC) curve. Agreement in diagnosis was assessed by kappa statistic.
2) To assess the estimated burden of malaria and pneumonia among children <5 presenting to the study PHCs during study period according to various diagnostic approaches.	Quantitative	Primary & Secondary	The estimated burden of malaria and pneumonia were calculated as proportions and 95% Confidence Interval (C.I). The distribution of these diseases over study period was presented as percentages.
3) To determine the clinical outcomes in children diagnosed with malaria and pneumonia according to the IMCI guidelines and risk factors for severe outcomes.	Quantitative	Primary	The distribution of clinical outcomes was assessed as frequency and percentages while the risk factors for severe outcomes as odds ratio and 95% C.I.
4) To explore caregivers' and health workers' perspectives of lay diagnosis and IMCI guidelines as diagnostic approaches for malaria and pneumonia.	Qualitative	Primary	Inductive approach to thematic analysis was used to identify themes. Findings are presented in quotes with relevant explanations.

2.5 Data collection, processing, management and analyses

This section covers the data collection processes for both quantitative and qualitative components of the study. Except for follow-up data which were collected within 30 days of assessing a patient at the study PHCs, data in the quantitative component of study were collected by health workers. The lead researcher collected the qualitative data during the interviews of health stakeholders aided by semi-structured interview guide.

2.5.1 Quantitative component

2.5.1.1 Estimation of sample size

This study used the approach recommended in Obuchowski *et al.*[140] and Obuchowski [141] to determine the sample size in order to detect an area under the ROC curve (AUROC) value that exceeds 0.70 (indicating a fairly accurate test) for the diagnostic tests (IMCI guidelines and lay diagnosis) when compared to the gold standard (microscopy and chest X-ray in case of malaria and pneumonia respectively). The following assumptions were applied: k = 4[1] (i.e. 4 times as many disease cases as compared to disease negatives); type I error set at 0.05; type II error rate of 0.10 (power = 0.90); conjectured accuracy of presumptive clinical diagnosis as a predictive tool (θ) using area under the ROC curve as a measure of accuracy = 0.70; and one-sided test.

[1] Based on studies in Nigeria where the estimated prevalence of pneumonia and malaria in children under-five was 40% and 48% respectively, a more conservative estimate of 25% in both scenarios giving the broad diagnostic criteria rather than confirmed pneumonia and malaria was adopted.

The estimated sample size according to these calculations was 84 disease-free (controls) and 21 disease positive subjects (cases). If the conjectured accuracy was changed to an AUROC of 0.90 (high accuracy), the estimated sample size keeping all other parameters unchanged would be 40 disease-free (controls) and 10 disease positive (cases). However, if the conjectured accuracy was dropped such that the AUROC was under 0.60, the estimated sample size keeping all other parameters unchanged would be 339 disease-free (controls) and 85 disease positive (cases); or 424 subjects in total.

Assuming an AUROC value of under 0.60 and similar assumptions in place for both malaria and pneumonia, these estimates would need to be doubled such that the study recruited at least 424 presumed malaria and 424 presumed pneumonia cases for assessment over the course of the study. The presumed diagnosis was made based on the child's caregiver's reason for attending the primary healthcare centre. Therefore, for resource planning and costing these estimates were inflated and aimed for a total sample size of 1000 (aiming for roughly 500 cases each of presumed malaria and pneumonia). Based on discussions with healthcare staff in primary healthcare centres, it was anticipated that the study would be able to enrol at least 25 children per week to attain the estimated sample size over the proposed 12-month period for data collection.

2.5.1.2 Participant recruitment

A consecutive sampling approach (involved the selection of every child presenting to the study PHCs who met the eligibility criteria until the required sample size was attained) [142] was taken to the recruitment of eligible participants between September 2015 and July 2016. Children brought by their caregivers to the study PHCs during the study period were recruited to the study if they fulfilled all the following eligibility criteria:

- Aged 2–59 months.
- Presented to study PHCs with suspected malaria – characterised by fever or reported history of fever in the previous 24 hours OR
- Presented to study PHCs with suspected pneumonia – characterised by history of cough or difficult breathing, sign of increased respiratory rates and/or fever or reported history of fever in the previous 24 hours.
- Resided in the catchment local government area of the study PHC.
- Caregiver was willing to provide written or verbal consent in the presence of a witness (e.g. another caregiver presenting to the same PHC as the caregiver whose consent was being requested or a PHW other than the one attending to the study participant).

Children who were participating in another study or taking any treatment for diagnosed malaria or pneumonia were ineligible for study. In addition, children who had been treated for malaria or pneumonia in the 2 weeks prior to presenting to study PHCs were considered ineligible for study.

2.5.1.3 Training of study staff in IMCI guidelines and piloting of research protocol

Although the standard and short duration for IMCI training courses are ≥11 days and 5–11 days respectively,[143] a 2-day training was considered appropriate for this study given the focus on malaria and pneumonia out of the entire IMCI algorithms. An invitation letter, including information about the research, was sent to the selected PHCs with information on the time and duration for IMCI training for study. The study staff (trainees) included 23 primary healthcare workers (CHEWs, JCHEWs and nurses) who had expressed willingness and were given permission by their PHC managers (Matrons)

to attend the training. The 2-day training was facilitated by the research clinical supervisor (A.S.) and her colleague who are both Paediatricians and WHO certified IMCI facilitators.

Standardised training materials such as the WHO IMCI chart booklet, Nigerian-based IMCI assessment forms, IMCI training videos, lecture slides etc. were made available by the lead researcher before the training. On the first day of training (12th August 2015) the PHWs were trained to be proficient in the assessment, classification and treatment of children presenting with suspected malaria and pneumonia. In addition, they were trained to provide counselling to caregivers according to the IMCI guidelines.[144] On the second day of training (13th August 2015) the PHWs and the training facilitators visited a paediatric ward in a private clinic to undertake the IMCI diagnostic criteria.

Immediately after the IMCI training, the quantitative protocol was pilot tested on 17 children under-five and their caregivers between 15th and 30th August 2015. The pilot test involved data collection by the trained health workers on malaria and pneumonia diagnosis according to various diagnostic approaches (e.g. IMCI guidelines, microscopy and lay diagnosis). The lead researcher and three research assistants carried out the follow-up of children under-five assessed by the trained health workers at the study PHCs to obtain follow-up data (e.g. occurrence of clinical outcomes). The study protocol was then revised based on findings from the pilot study. Some of the changes made included choosing the most appropriate time for follow-up activity (preferably during the weekends when most caregivers were at home) and reconfiguring the study database.

Furthermore, for each study staff, independent diagnostic validation of at least two children under-five was conducted by the clinical supervisor before the commencement

of data collection. To sustain a reasonable standard for data collection, every three months the clinical supervisor (A.S.) evaluated the study staff through multiple-choice questions, clinical scenarios for interpretation and by random checking of selected recording forms for completeness. This periodic evaluation served to assess the quality or standard of data collection as well as audit how well PHWs completed recording forms.

2.5.1.4 Duration of data collection

Nigeria's rainy season is typically between April and October while its dry season is between November and March, though there have been extended periods of both rainy and dry seasons due to variations in climate.[145] Given the influence of seasonality on the burden of malaria and pneumonia,[146–148] it was decided prior to data collection that both the rainy and dry seasons would be captured. Furthermore, even when patients were recruited on the last day of data collection, they were to be followed-up for 30 days.

2.5.1.5 Data collection

Children presenting to the study PHCs who met the eligibility criteria for this study were assessed for any general danger signs, malaria and pneumonia according to the IMCI guidelines (Appendix II and XI). Following the assessment of a patient by a health worker, the caregiver was asked about his/her own diagnosis of the child's illness and any treatment administered to the child prior to presentation to study PHC. Microscopic diagnosis of malaria was carried out for both positive and negative IMCI diagnostic outcomes, while chest x-ray for confirmatory diagnosis of pneumonia was only carried out for positive IMCI diagnosis. The various diagnostic approaches and management for malaria and pneumonia are described below.

2.5.1.5.1 Assessment for 'any general danger signs' according to IMCI guidelines

Before assessing for malaria or pneumonia, a child was first assessed for any of the following general danger signs: inability to drink or breastfeed, vomiting everything, lethargic or unconscious, convulsion within the past few days and convulsion during assessment at a health facility. Observation of any general danger sign (AGDS) prompted the administration of pre-referral treatments and referral of patient to the nearest higher healthcare centre. Pre-referral treatments referred to the treatment decided by a health worker with the aid of the because of its importance in saving the patient's life (e.g. quinine for severe malaria or sugar solution for dehydration) before referral.

2.5.1.5.2 Assessment and classification of malaria according to the IMCI guidelines

Following the assessment for AGDS, the attending health worker assessed for fever by either history provided by the caregiver, touch or measurement of axillary temperature ($\geq$37.5^{o}C) with a digital clinical thermometer[2]. Duration of fever (e.g. more than 7 days) and stiff neck were also assessed and recorded. Based on recommendations of the revised WHO IMCI guidelines, a rapid diagnostic test (RDT) for malaria was carried out by the trained health workers according to the manufacturer's instructions using CareStart™ Malaria HRP2(Pf) kits (Access Bio, Inc. New Jersey, USA) in all fever cases. This RDT targets histidine-rich protein-2 (HRP2). It has the advantage of being able to withstand better than the enzyme-based RDTs the heat and temperature

[2]A single brand of digital thermometers was used across the study PHCs and these were calibrated by the principal investigator at the end of every month.

fluctuations of tropical Africa, where refrigeration and air conditioning are not always available.[149] Moreover, the RDT kit has very high performance (91.0 and 100.0 panel detection scores at the lower and the higher parasite densities respectively) as reported in the round 7 of the WHO annual RDT evaluation program [150] and is approved for public sector procurement by the National Malaria Program of Nigeria (including the study setting).[41]

Using a venepuncture method, a blood sample of about 3–4 ml was collected from patients by a trained health worker (all the health workers who participated in this study received a refresher training in this regard) in 5 ml micro-containers of ethylene-diamine-tetraacetic acid (EDTA) containers. Immediately, 5µl from the withdrawn blood sample was collected using a pipette provided with the kit and was then added into the 'S' well of the kit, followed by the addition of 60µl assay buffer solution into the 'A' well. A positive RDT with any general danger sign(s) or stiff neck indicated 'very severe febrile disease' and prompted immediate referral to the nearest higher healthcare centre. A positive RDT without any general danger sign(s) or stiff neck indicated malaria, while a negative RDT indicated non-malaria fever. Depending on the classification or diagnosis, treatments were given to patients according to age or weight as specified in the IMCI guidelines. Regardless of the diagnostic outcome, counselling on management of patients and administration of medications was provided to the caregivers by health workers in line with the IMCI guidelines. All RDT kits were stored at the recommended temperature of 4°C–30°C and were used within shelf life.

2.5.1.5.3 Laboratory diagnosis of malaria

The confirmatory diagnosis (Giemsa-stained microscopy) of malaria was carried out at the medical laboratory unit of the University of Benin Health Centre (UBHC). The

UBHC has a laboratory facility with more than five qualified microscopists and equipped with three light microscopes, one fluorescent microscope and essential laboratory reagents. In brief, the lead researcher or research assistants collected both positive and negative RDT blood samples (3-4 ml) from the five study PHCs after each working day and transported them to UBHC for microscopic diagnosis of malaria. Giemsa-stained thick and thin blood films prepared from blood samples were examined microscopically for malaria parasite using an X100 (oil immersion) objective by two microscopists to produce concordant results. However, a third scientist was called upon to resolve malaria diagnosis when the two scientists recorded contradictory results. Notably, the outcome of malaria diagnosis either by the health workers using the IMCI guidelines or caregivers was unknown to the microscopists. Positive malaria diagnosis was based on the identification of asexual stages of *Plasmodium species* on thick blood smears irrespective of parasite density. In contrast, a film was recorded as 'malaria parasite not seen' or negative after examining about 100 fields without observing *Plasmodium species*. In the case of a positive smear, the number of malaria parasites was counted against 200 white blood cells (WBCs) while parasite density was determined assuming 8,000 WBCs per microlitre (µl) of blood using the formula:[151]

$$\textbf{Malaria parasite density (per µl)} = \frac{\textbf{Number of parasites counted} \times \textbf{8000}}{\textbf{Number of WBCs counted}}$$

Thin films were used to identify the various *Plasmodium species*. The summary result findings were recorded by a microscopist using a recording form developed as part of the study protocol (Appendix XI). For quality control, a minimum of 5% of all positive and negative slides were randomly selected for internal quality control (results are used by the management of UBHC for diagnostic service improvement and training of staff).

2.5.1.5.4 Assessment and classification of pneumonia according to the IMCI guidelines

Like malaria, assessment of pneumonia was preceded by the assessment for danger signs. Thereafter, a health worker assessed for cough or difficulty breathing as well as the duration. The number of breaths per minute was counted only when the child was calm and used to define fast breathing according to the IMCI guidelines. Fast breathing was ≥50 breaths/minute if the patient was 2 months to 12 months or ≥40 breaths/minutes if the patient was 12 months to 59 months. In addition to fast breathing, chest in-drawing, stridor and wheezing were assessed by the health worker.

The presence of any general danger sign or stridor in a calm patient was classified as 'severe pneumonia' or 'very severe disease' which prompted urgent referral to the nearest higher healthcare centre after the administration of pre-referral treatment. Chest in-drawing or fast breathing was classified as pneumonia, while the absence of any pneumonia signs or very severe disease, as described above, was classified as 'cough or cold'. In both pneumonia and cough/cold classifications, treatments were provided to the sick child according to the IMCI guidelines. Counselling on patient management and proper administration of medications was provided to the caregiver according to the IMCI guidelines. Furthermore, a pulse oximeter[3] was used to measure oxygen saturation and if <90% the patient was immediately referred to the nearest hospital. If wheeze was recorded, trial of a rapid acting inhaled bronchodilator was conducted for up to three

[3] Like the clinical thermometers, pulse oximeters were calibrated at the end of every month by the researcher.

times, 15-20 minutes apart to rule out asthma. Patients with wheeze whose in-drawing resolved after bronchodilator therapy were excluded for study.

2.5.1.5.5 Radiological diagnosis of pneumonia

The gold standard test for pneumonia was a chest radiograph showing radiological changes consistent with pneumonia as assessed by a trained radiologist. Unlike malaria where blood samples were taken from both IMCI positive and negative cases for microscopy, for pneumonia only IMCI positive cases were referred to a radiological centre for antero-posterior chest radiographs or CXR as it was not considered acceptable or ethical by healthcare professionals in the study setting to refer children for CXR without a strong clinical justification.

2.5.1.5.6 Lay diagnosis of malaria and pneumonia

The caregiver, blinded to the outcome of a health worker's diagnostic outcome, was asked whether s/he knew what could be wrong with the child following the initial assessment and classification according to the IMCI guidelines. If the caregiver answered 'Yes', a follow-up question on the specific diagnosis of child's illness according to them was asked. Details on how the variables 'lay diagnosis of malaria' and 'lay diagnosis of pneumonia' were defined are presented under data management and definition of study variables.

2.5.1.6 Collection of additional study data (e.g. covariates)

A structured questionnaire was used to collect other relevant study variables[4] such as demographics, socioeconomic characteristics of patients (education and occupation of respondents), and risk factors for adverse clinical outcomes in children who met the study eligibility criteria (Appendix XI). The potential risk factors for adverse clinical outcomes in children diagnosed with malaria and pneumonia were identified based on evidence in the literature and biological plausibility. The common potential risk factors for clinical outcomes in children diagnosed with malaria were socio-demographic factors (e.g. age, caregivers' education and occupation), ownership and use of ITNs, vector control strategies in the home and surrounding area, prior intermittent preventive treatment of malaria.[152] For children diagnosed with pneumonia, information on the following potential risk factors was collected: caregivers' education and occupation, age, exclusive breastfeeding for the first 6 months of life, prelacteal feeding, living in an over-populated house (large family size), and exposure to smoke from cigarette or stove/firewood.[82,152,153] These data were collected while the patient was waiting to be attended to by a PHW or at a separate time after the consultation has been completed but concealing the diagnostic outcome from caregivers. Where a patient's caregiver could not communicate in English, Pidgin English[5] or common local dialects (e.g. Bini) were used as the language of communication.

[5] Pidgin English, commonly referred to as "Pidgin" or "Broken English", is an informal English that is spoken as a *lingua franca* across Nigeria.

2.5.1.7 Follow-up of study participants

During the initial assessment of patients at study PHCs, arrangements for follow-up were made by PHWs. Follow-up was carried out by the lead researcher or research assistants twice within 30 days of assessment of patients at the study PHCs. Given that the duration for the recommended antibiotics and antimalarials in children under five was 5 and 3 days, respectively,[154,155] the first follow-up was carried out from the sixth day of assessment at the study PHCs to ascertain the level of adherence to medications. During this initial first follow-up, caregivers were informed about the second follow-up with details of the purpose and benefits, as well as likely date and time. During the second follow-up, information on clinical outcomes (e.g. progression of illness, complications, hospitalisation, death etc.) was obtained. In scenarios where home or hospital visits (for those admitted following the initial assessment at the study PHCs) were not feasible mostly due to incorrect home addresses, the alternative approach involved contacting caregivers via phone calls to record patient outcomes. For safety purposes, the lead researcher and RAs were required to inform each other before and after follow-up visits to patients' houses. Data collected during follow-up were recorded using section three of the questionnaire previously at each study PHC (appendix XI)

2.5.1.8 Data Management: entry, validation and definition of key variables

A database was created using Microsoft Access for data entry. Data were entered into the database on an ongoing basis by the researcher and one of the research assistants

who received training to ensure standardised data entry and coding practices. While data entry errors are almost inevitable, the following steps were taken to minimise the occurrence of such errors and ensure data quality:

While the database was designed in Microsoft Access, Forms corresponding to Tables were created to minimise errors during data entry. Moreover, an initial data validation plan was put in place to assure accuracy and consistency of the data being entered in each variable field. This was done using a range of data validation features in Microsoft Access such as error alerts when incorrect values are entered in a variable field.

To ensure consistency in data entry, the initial entries by the data entry assistant were checked against entries made by the lead researcher (unique patient and PHC identifiers were used to identify the same patients). Furthermore, the lead researcher performed random periodic checks of the data entered by the assistant for errors and data completeness, albeit double-data entry was not always possible during data collection. Any errors found or queries raised by the lead researcher and data entry assistant during this process were clarified by contacting the PHWs for that PHC. The definition of key variables, including outcomes and covariates, are presented below.

2.5.1.8.1 Definition of malaria according to the IMCI guidelines

Malaria diagnosis according to the IMCI guidelines was one of the main outcome variables for this study. According to the IMCI guidelines, malaria was defined as fever (by history or touch or $\geq 37.5^{o}C$) and positive rapid diagnostic test. This was coded as a binary variable (Yes/No).

2.5.1.8.2 Definition of malaria according to microscopy

Malaria diagnosis according to microscopy was defined as the identification of asexual stages of *Plasmodium species* on thick blood smears. Similarly, this was coded as a binary variable (Yes/No).

2.5.1.8.3 Definition of pneumonia according to the IMCI guidelines

Pneumonia diagnosis according to the IMCI guidelines was defined as cough or difficulty in breathing with either chest in-drawing or fast breathing. Fast breathing was defined as ≥50 breaths/minute if the patient was 2 months to 12 months or ≥40 breaths/minutes if the patient was 12 months to 59 months. Like malaria diagnoses, pneumonia diagnosis according to the IMCI guidelines was coded as a binary variable (Yes/No).

2.5.1.8.4 Definition of pneumonia according to radiography

A chest x-ray diagnosis was classified as positive for pneumonia if new or progressive and persistent infiltrate or consolidation were observed by a trained radiologists.[156] This was coded as a binary variable (Yes/No).

2.5.1.8.5 Definition of malaria and pneumonia according to caregivers (lay diagnosis)

A similar approach used in verbal autopsy[6] was adapted for the definition of malaria and pneumonia by caregivers. In brief, after the assessment of a child for malaria or/and pneumonia by a health worker according to the IMCI guidelines at the study PHC, the caregiver was asked 'do you know what could be wrong with your child?' Only those who answered in the affirmative to the question were asked the second question: 'what do you think could be wrong with your child?' A list of caregivers' diagnoses was compiled (unedited) by the researcher and given separately to two paediatricians (each with at least five years of working experience in Nigeria) to interpret and assign classifications: malaria (Yes/No), pneumonia (Yes/No), both malaria and pneumonia (Yes/No) and neither malaria nor pneumonia (Yes/No). The independent classifications of lay diagnosis made by both paediatricians using caregivers' diagnoses were compared for agreement. Any contradicting classification between the two paediatricians was cross-checked by a third paediatrician (with over 10-year experience in Nigeria) whose classification was considered the final caregivers' diagnosis. The final classifications made by paediatricians were then used by the researcher to define the various categories of caregivers' diagnoses as previously stated. Table 2.4 (below) presents caregivers' initial diagnoses that were interpreted by paediatricians to define lay diagnosis.

[6] The interpretation and validation of the signs/symptoms reported by close relatives, friends or witnesses for the deceased prior to death with the aid of standard classification codes to assess cause-specific mortality.

Table 2.4: Caregivers' diagnoses used by paediatricians for the classification of lay diagnosis (n=903)

Caregivers' diagnoses *	Frequency (%)
Acute malaria	2 (0.22)
Anaemia & malaria	1 (0.11)
Convulsion	1 (0.11)
Cough	102 (11.30)
Cough and catarrh	5 (0.55)
Cough and fever	54 (5.98)
Cough and malaria	5 (0.55)
Cough and pneumonia	1 (0.11)
Cough and teething	1 (0.11)
Diarrhoea, malaria and fever	1 (0.11)
Difficulty breathing and fever	1 (0.11)
Difficulty in breathing	1 (0.11)
Fever	311 (34.44)
Fever and diarrhoea	1 (0.11)
Fever and catarrh	1 (0.11)
Fever and malaria	3 (0.33)
Fever and tooth problem	1 (0.11)
Hotness of the head and fever	1 (0.11)
Malaria	146 (16.17)
Malaria and cough	10 (1.11)
Malaria and diarrhoea	3 (0.33)
Malaria and upper respiratory tract infection	3 (0.33)
Malaria, fever and pneumonia	1 (0.11)
Pneumonia	5 (0.55)
Pneumonia and fever	2 (0.22)
Rashes	1 (0.11)
Ude (spleen problem) and fever **	1 (0.11)
Teething, fever and cough	1 (0.11)
Upper respiratory tract infection	1 (0.11)
Not ascertained/I don't know	236 (26.14)

* Caregivers' diagnosis when asked: what do you think is wrong with your child?
** Ude' in Benin is suggestive of hypersplenomegaly in severe malaria

The key variables for the second study objective were malaria (as per IMCI, microscopy and lay diagnosis) and pneumonia (as per IMCI and lay diagnosis). These have previously been defined in study objective 1. Given the influence of seasonal parameters on the burden of malaria and pneumonia in Nigeria,[157,158] information on average monthly temperature (^{o}C), rainfall (mm) and humidity (%) were retrospectively extrapolated from World Weather Online[159] for the study period (September 2015–July 2016). World Weather Online uses a weather forecasting model along with other metrological models like the World Meteorological Organization for research and

training purposes to deliver reliable and accurate weather forecast for any geo-point in the world.

2.5.1.8.6 Definition of malaria and pneumonia for the assessment of interobserver variation (kappa statistic)

To assess the interobserver variation in the diagnosis of malaria and pneumonia by health workers using the IMCI guidelines and caregivers, both malaria and pneumonia diagnosis according to these diagnostic approaches were classified as categorical variables. Malaria and pneumonia according to the IMCI guidelines were classified as: malaria only (Yes/No), pneumonia only (Yes/No), both malaria and pneumonia (Yes/No), neither malaria nor pneumonia (Yes/No). Similar classification approach was adopted for caregivers' diagnosis of malaria and pneumonia.

2.5.1.8.7 Definition of severe illness

Severe illness was defined as any record of complicated illness, admission to hospital and/or death within 30 days of malaria or pneumonia diagnosis according to the IMCI guidelines. The definition of complicated illness was based on the caregivers' response to the question 'Did the child develop any form of complications after assessment at study PHC?' while hospitalisation was defined as admission of child to a higher healthcare centre (e.g. private clinic or secondary hospital) or study PHCs. Severe illness was treated as a binary variable (Yes/No).

2.5.1.8.8 Definition of progression of illness

Progression of illness was formed from caregivers' responses to the question 'Please provide details about child's present state of health' during the 30-day follow-up period. Cases where caregivers mentioned that children had recovered or reported no complaints

were classified as ‘resolved illness’. In contrast, cases where caregivers stated that children had not recovered or still ill with symptoms or signs (e.g. fever; diarrhoea, vomiting, elevated temperature and cough, weakness of the body, cough and fever etc.) were classified as ‘unresolved illness’. Cases where caregivers mentioned convulsion, illness worsen, hotness of the body with convulsion and cough etc. were classified as ‘worsened illness’. However, progression of illness was restructured to form a binary variable (resolved versus unresolved-worsened) given that logistic regression is only applicable to binary outcome.

2.5.1.8.9 Definition of covariates

Age, self-medication for illness, general danger signs, preventive measures against malaria, exposure to solid fuels, family size, exclusive breastfeeding, prelacteal feeding and socioeconomic status were treated as potential risk factors for severe illness and progression of illness in children within 30 days of being diagnosed with malaria and pneumonia. These are described below

Age was presented in months and as a continuous variable. The decision to present age as a continuous variable rather than categorical or binary variable was based on the least likelihood ratio test (LRT) *p*-value (>0.05).

Self-medication refers to the intake of any medication for current illness before presenting to study PHCs. Study participants were grouped as having taken medications prior to presenting to study PHCs or not (binary variable: Yes/No).

General danger signs according to the IMCI guidelines referred to when a child was unable to drink or breastfeed, vomiting everything, lethargic or unconscious, convulsing

within the past few days or convulsing during assessment at the study PHCs. This was treated as a binary variable (Yes/No).

Protective measures against malaria included ownership of mosquito net, living in a house with netted doors/windows, living in a house where vector control measures (indoor residue spray) was practiced and receiving intermittent treatment for malaria. These were treated as binary variables (Yes/No).

Solid fuels refer to smoke from firewood or stove in the kitchen. Study participants were grouped as having been exposed to solid fuels during stay with caregivers in the kitchen while cooking or not (binary variable: Yes/No).

Study participants were categorised as living in a very small-sized family (child with one person), small-sized family (child with two persons), medium-sized family (child with 3-6 persons) or large-sized family (child with more than seven persons).

Study participants less than 6 months were grouped as currently on exclusive breastfeeding for the first six months of life or not, while those over 6 months were grouped as previously breastfed for the first 6 months of life or not. Overall, this was a binary variable (Yes/No).

Prelacteal feeds refer to water or native herbs given to babies to drink within the first days of life before lactation is established. Study participants were grouped as having been given prelacteal feeding or not (binary variable: Yes/No).

Prior to combining occupation and level of education variables of caregivers to form a socioeconomic index score, a test for collinearity[7] was done by reviewing the variance inflation factor (VIF)[8] and tolerance values of both variables. This was to ensure that occupation and level of education were independent of each other i.e., not collinear and therefore suitable for combining into a single index. Both VIF and tolerance values measure how much the regression coefficient for occupation is determined by the level of education in the model. Low VIF and high tolerance values suggest the absence of multicollinearity and vice-versa.[160] The mean VIF for both education and occupation was 1.12 suggesting that it was appropriate to combine both variables to form socioeconomic status.

Information on the caregivers' occupation and level of education was recorded in order to measure their social class using the Oyedeji's social classification approach.[161] The Oyedeji's social classification approach was considered appropriate due to its wide application in Nigerian-based epidemiological studies, hence comparability of findings. Briefly, Oyedeji's approach involved awarding socio-economic index scores to a child based on the occupation and educational attainment of parents or caregiver. In this approach, the mean of four scores (two for the father and two for the mother) to the nearest whole number, is the social class assigned to a child. For example, a father who was a university lecturer would have a score of 1 each for occupation and education. If

[7] The term collinearity implies that two variables are near perfect linear combinations of one another.

[8] This approach was also used to assess for collinearity between severe illness and progression of illness of which the mean VIF of 5.02 suggested the absence of collinearity between the two variables.

his wife was a business-woman with a school certificate level of education, she would be assigned a score 1 for occupation and 3 for education. The total of these four scores would be 6 with an average of 1.5 (i.e. 2 when taken to the nearest whole number). A lower score means higher socioeconomic status (SES) and vice-versa. Thus, the social class assigned to the child in this scenario would be II. See Table 2.5 for detail of the classifications of occupation and educational attainment.

For this study, however, the Oyedeji's approach was modified given that study participants were mostly brought to study PHCs by one of the parents or a family member (e.g. grandparent or guardian) and not both. Thus, the mean score awarded for occupation and educational attainment for the caregiver rounded to the nearest whole number was the socioeconomic class assigned to the child. For instance, a caregiver whose occupation was a trader in the market would score 4 for occupation and 4 for education if the highest educational attainment was primary school. The total of these two scores would be 8 with an average of 4 (i.e., 4 + 4 =8/2 =4). Therefore, the social class assigned to the child will be IV (Lower Class). Similar to other studies in Nigeria,[162,163] those in social class I and II were grouped as high socioeconomic class, III as middle socioeconomic class and IV and V as lower socioeconomic class.

Table 2.5: Socio-economic classification system

Oyedeji's classification approach	The classification system used for this study
Occupational classification	
I Senior Public Servants, Professionals, Managers, large-scale traders, businesspersons and contractors	**I & II** Civil servants
II Intermediate grade public servants and senior school teachers	
III Junior school teachers, professional drivers, artisans	**III** Middle-scale trading
IV Petty traders, labourers, messengers	**IV** Artisans/Traders/Subsistence farming
V Unemployed, full-time housewife, students and subsistence farmers	**V** Unemployed, full-time housewife, students
Educational classification	
I University graduates or equivalents	**I & II** Post-secondary school
II School certificate holders' ordinary level (GCE) who also had teaching or other professional training.	
III School certificate or grade II teachers' certificate holders or equivalents.	**III** Secondary school
IV Modern three and primary six certificate holders.	**IV** Primary school
V Those who could either just reads and write or were illiterate.	**V** No formal education

Regarding anthropometric measurements, weight category of study participants was based on BMI percentile Z scores. The BMI Z scores were derived by comparing the measured weights and heights of study participants to the 2006 WHO growth standards for children aged 0–5 years which adjust for child's age and sex.[164] Measurement of weight (kg) and length (cm) in infants and children aged 2–23 months old as well as those in children aged 24–59 months old were measured according to the World Health Organization (WHO) recommendations.[165] Details of BMI Z scores used for the conversion of weight categories and the generation of anthropometric variables are available in Appendix IV.

2.5.1.9 Handling missing data

It was decided prior to statistical analyses that missing data will be handled using the missing-indicator approach. This approach involved giving those with a missing value a specific missing indicator code (e.g. -9) or treating missing data as a separate category to ensure that they were not lost during analyses (e.g. fitting of multivariate model). Consequently, the estimates obtained by using this approach tend to be more precise than those obtained by the complete case analysis, thereby minimising selection bias.[166]

2.5.1.10 Statistical analyses

All quantitative data management and analyses were carried out in Stata version 14 (Stata Corp. LP, College Station, TX, United States of America). A *p*-value of <0.05 was considered statistically significant throughout this thesis.

2.5.1.10.1 Descriptive analyses

The demographic and clinical characteristics of the study population were described using frequencies and percentages (%) for binary and categorical variables. The mean (standard deviation) and median (interquartile range) were used for the description of normally and non-normally distributed continuous variables, respectively.

2.5.1.10.2 Statistical analyses for study specific objectives

Additional statistical analyses in this study are presented according to study specific objectives. The chi-square test was used to compare proportions and test for significance between proportions. Depending on the analytical approach for study objectives, Wald test or/and likelihood ratio test (LRT) were used to obtain *p*-values.

Statistical analyses for study objective 1

This study objective has three components. First, it compares the diagnostic accuracy of the IMCI guidelines and lay diagnosis (caregiver) for malaria in comparison to the reference diagnostic test (microscopy). Then it compares the accuracy of lay diagnosis of pneumonia and malaria by caregivers to the diagnoses made by healthcare workers using the IMCI guidelines. Lastly, it assesses the extent of agreement between caregivers' and health workers' diagnosis of malaria and pneumonia (interobserver reliability).

The predictive value of diagnostic methods for malaria (IMCI guidelines and lay diagnosis) with respect to the gold standard diagnostic method (Giemsa-stained microscopy) was assessed using sensitivity, specificity, area under the receiver operating characteristic curve (AUROC) values, positive predictive value (PPV) and negative predictive value (NPV).[167] Similarly, these diagnostic measures of accuracy were used to assess the predictive value of the lay diagnosis for pneumonia as compared to the IMCI guideline-based diagnosis. These diagnostic measures of accuracy are briefly described below.

Sensitivity and specificity

Sensitivity is a measure of a screening ability to correctly identify individuals that have the disease or condition.[168] A perfect screen will be 100% sensitive i.e. all the individuals with the target conditions will be correctly identified and referred for further assessment. For example, a screening test with 80% sensitivity indicates that 80 out of 100 individuals with the target condition will be correctly identified (true positives) but 20 with the condition will have been incorrectly classified as not having the condition (false negatives). Thus, sensitivity is also called true positive fraction (TPF). On the other

hand, specificity measures the ability of a screening test to correctly identify the individuals who do not have the condition or disease.[168] A perfect screen will be 100% specific i.e. all the individuals without the target condition will not be referred for further assessment as though they had the condition. For example, a screening test with specificity of 30% means that 30 out of 100 individuals without the condition or disease will be correctly identified as such (true negatives) but 70 individuals will be incorrectly assigned as having the condition (false positives). Thus, specificity is also called true negative fraction (TNF). Ideally, a good screening test will display high specificity and sensitivity.

Positive predictive value and negative predictive value

The positive predictive value (PPV) is the proportion of individuals who are screening test positive that have the condition in question. The PPV is calculated by dividing the number of true positives by the total number of individuals who tested positive (true positives plus false positives). It is influenced by the prevalence of the condition being screened for such that the higher the prevalence value, the better the PPV and vice-versa. In contrast, the negative predictive value (NPV) is the proportion of individuals who test negative by a screening test that do not have the condition. It is calculated by dividing the number of true negatives by all the individuals who tested negative (true negatives and false negatives).

The positive and negative predictive values are very important because children with suspected condition would present with a set of symptoms rather than a diagnosis. Thus, sensitivity and specificity become less useful as the health practitioner may not know at the time of consultation whether the child has the condition or not. What would be more

useful to the health worker are the positive and negative predictive values of the screening test.

Table 2.6: An illustration of screening test

	Has disease or condition	**Doesn't have disease or condition**	**Total**
Test positive	a True positive	b False positive	**a + b**
Test negative	c False negative	d True negative	**c + d**
Total	**a + c**	**b + d**	**a + b + c + d**

Sensitivity = a/a + c, Specificity = d/b + d, Positive predictive value = a/a + b, Negative predictive value = d/c + d

Area under the receiver operating characteristic curve (AUROC)

The area under the receiver operating characteristic curve (AUROC) measures the overall accuracy of how well a screening test predicts individuals' conditions by considering both sensitivity and specificity. The receiver operating characteristic curve (ROC) shown in Figure 2, is derived by using the sensitivity and 1-specificity of a screening test to plot a curve across varying cut-offs values.[169] ROC curve of a screening test with good to excellent diagnostic capacity are located progressively closer to the upper left-hand corner in 'ROC space' and with AUROC values closer to 1.00 (>0.70). Thus, Figure 2 shows that screening test B which is closer to the left-hand corner has a better diagnostic capacity than test A. However, screening tests with an AUROC values <0.70 are said to have poor diagnostic accuracy. In contrast, an ROC curve corresponding to the diagonal line (black solid line in Figure 2) indicates the diagnostic performance of a screening test is no better than chance level and with AUROC value of 0.5 (i.e. the screening test has a useless or an extremely poor discriminative ability). It should be noted however, that the concept of perfect discrimination represented as an

AUROC value of 1.00 is purely theoretical and unattainable; it is expressed as a ROC plot with perfect sensitivity and perfect specificity. In this study, ROC curves were plotted and AUROC values calculated to compare the accuracy with which different diagnostic approaches would predict malaria and pneumonia in children under-five.

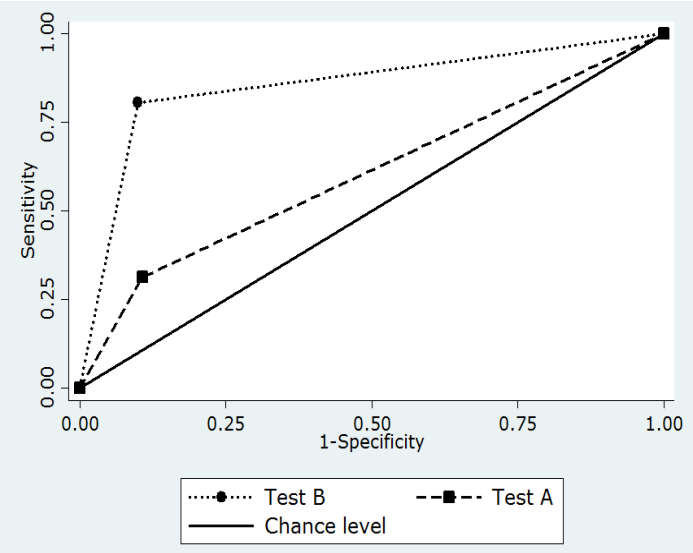


Figure 2.2: Classification of test performance using the ROC curve

Interobserver variations in the diagnosis of malaria and pneumonia

Kappa statistic (κ), proposed by Cohen in 1960,[170] is one of the measures used for assessing interobserver reliability or agreement between two or more observers. It measures the degree to which the observed agreement between two observers exceeds that which would be expected by chance alone relative to the maximum that the observers could hope to improve their agreement. Kappa statistic considers the fact that observers will sometimes agree or disagree over a diagnostic outcome simply by chance. The typical data layout used for the estimation of kappa statistic is shown in Table 2.7 below.

Table 2.7: Diagnosis of suspected malaria cases by two observers

		Observer A–Diagnosis		Totals by observer B
		Positive	**Negative**	
Observer B–	**Positive**	**a**	b	**m1**
Diagnosis	**Negative**	c	**d**	**m0**
Totals by observer A		**n1**	**n0**	**n**

In ascertaining kappa statistic, the extent to which the diagnosis of two observers agree beyond what would be expected by chance alone is first ascertained. This is done by subtracting the percent agreement observed from the percent agreement we would expect by chance alone (the numerator of kappa):

(Percent agreement observed) − (Percent agreement expected by chance alone)

Secondly, the highest level of agreement between the two observers over the agreement that would be expected by chance alone is assessed. Ideally, the maximum that the two observers could agree is 100% (i.e. the two observers agree completely). Thus, the most that they could be expected to be able to improve (the denominator of kappa) would be:

100% − (Percent agreement expected by chance alone)

$$Pe=[(n1/n) \times (m1/n)] + [(n0/n) \times (m0/n)]$$

Thus, the kappa statistic is defined by the following equation:

$$\kappa = \frac{\text{(Percent agreement observed)} - \text{(Percent agreement expected by chance alone)}}{100\% - \text{(Percent agreement expected by chance alone)}}$$

This suggests that the greater the expected chance agreement, the lower the resulting value of the kappa and vice-versa. A hypothetical scenario of the diagnosis of 75 suspected malaria cases by two observers further illustrates how kappa statistic is

calculated. Table 2.8 (below) shows the results of 75 suspected malaria diagnosed by observer A along the bottom of the table and those of observer B along the right margin. Thus, observer A identified 45 (60%) of all the 75 suspected malaria cases as positive and 30 (40%) as negative.

Table 2.8: An example showing the diagnosis of suspected malaria cases by two observers

		Observer A–Diagnosis		**Totals by observer B**
		Positive	**Negative**	
Observer B–Diagnosis	**Positive**	**41**	3	44 (58.7%)
	Negative	4	**27**	31 (41.3%
Totals by observer A		45 (60.0%)	30 (40.0%)	**75 (100%)**

Observer B identified 44 (58.7%) of all the suspected malaria cases as positive and 31 (41.3%) as negative.

The observed agreement (Po) is simply the percentage of all diagnoses for which the two observers agree, which is the sum of 'a + d' divided by the total 'n' in Table 2.9. This is 41+27/75 or 90.7%, meaning that the two observers agreed on 90.7% of their grading of suspected malaria cases.

The expected agreement (Pe) (by chance) is derived as follows:

Pe= [45/75) × (44/75)] + [(30/75) × (31/75)]

Pe=0.354 + 0.164=0.518 or 51.8%

Having calculated the figures needed for the numerator and denominator, kappa statistic is then calculated as follows:

$$\frac{90.7\% - 51.7\%}{100\% - 51.7\%} = \frac{39\%}{48.3\%} = 0.81$$

The kappa statistic is scaled to be 0 when the amount of agreement is what would be expected to be observed by chance and 1 when there is perfect agreement. A negative kappa represents agreement less than chance (worse than expected or disagreement though it's unlikely in practice). For intermediate values, the following interpretations were suggested by Landis and Koch[171]:

Kappa Statistic	*Strength of agreement*
< 0.0	Poor agreement (equivalent to chance)
0.00 – 0.20	Slight agreement
0.21 – 0.40	Fair agreement
0.41 – 0.60	Moderate agreement
0.61 – 0.80	Substantial agreement
0.81 – 1.00	Excellent agreement

Statistical analyses for study objective 2

The estimated burden was based on the proportion of children under-five who presented to study PHCs during the study period with any complaint and diagnosed to have malaria (as per the IMCI, microscopy and lay diagnosis). A similar approach was used to determine the estimated burden of pneumonia –the proportion of children under-five who presented to study PHCs during the study period with any complaint and diagnosed to have pneumonia (as per the IMCI guidelines and lay diagnosis). The denominator population for calculating both malaria and pneumonia burden, which included the total number of children aged 2–59 months who attended the study PHCs with any complaints during the study period (September 2015–July 2016), was retrospectively obtained from the records of each study PHC (details of records in Appendix V). The estimated burden of malaria or pneumonia in study setting was calculated using the formula:

$$\text{Estimated burden of disease} = \frac{\text{Children diagnosed to have malaria or pneumonia by a diagnostic approach}}{\text{Children attending the study PHCs with any complaints during the study period}}$$

The 95% confidence interval (C.I) for a proportion p was calculated using the formula:[172]

$$\mathbf{p \pm 1.96 \times \sqrt{(p \times (1 - p) / n)}}$$

Where:

p = proportion from the estimated burden of disease

√ = square root of the whole expression in brackets

n = the total number of children under-five attending the study PHCs with any complaints during the study period

The conditions for the above formula $n \times p > 5$ and $n \times (1 - p) > 5$ were met in this study. The estimated burden of malaria and pneumonia was calculated by study PHCs, local government of residence and Benin City (combination of the 3 local government areas). In addition, the distribution of malaria and pneumonia cases across study PHCs and LGAs was assessed using the chi-squared test.

Statistical analyses for study objective 3

First, the likelihood ratio test (LRT) was used to determine whether age (continuous variable) was better treated or modelled as a continuous or categorical variable. The LRT *p*-value (>0.05) was not statistically significant, suggesting that age was better retained in its original form. This was followed by descriptive analyses showing the distribution of each potential risk factor in relation to the follow-up clinical outcomes (severe illness

and progression of illness). These findings were presented as frequencies and percentages (%). The univariate association between each potential risk factor and clinical outcome was investigated, in turn, and presented as unadjusted odds ratios (ORs) and 95% confidence intervals (95% CIs). This was followed by multiple logistic regression analyses in which the association between each statistically significant risk factor from the univariate analyses and clinical outcomes was ascertained (LRT *p*-values were used to ascertain statistical significance for categorical variables while the Wald's *p*-values were used for binary and continuous variables). The results, regardless of statistical significance, consisted of variables in the final model with their adjusted ORs and 95% CI. These analyses were conducted for the clinical outcomes in children diagnosed with malaria and pneumonia separately.

2.5.2 Qualitative component

2.5.2.1 The philosophical worldviews and methodological approach for study

The philosophical world-view or paradigm that underpinned the aim and analytical approach of data for this study was social constructionism. Social constructionism considers the role that social and cultural setting play in the way that an individual perceives or makes sense of his or her world. In principle, social constructionism is the viewpoint that people's beliefs or meanings about the world or events are social inventions.[173] Social constructivists believe that meanings/beliefs held by people are many-sided and are influenced by interaction with others (hence social constructionism). Social constructivists believe that the more open-ended the questioning, the better, as the researcher listens attentively to what people say or do in their life settings.

2.5.2.2 Social constructionism and this study

The aim of the qualitative component of this study was to explore the participants' perceptions and experiences of two diagnostic approaches –lay diagnosis and IMCI guidelines– for malaria and pneumonia. The philosophical worldview underpinning this study implies that the perceptions of caregivers and HPs to the two diagnostic approaches are influenced by their social and cultural backgrounds. Hence, a qualitative study design and semi-structured interviews were deemed appropriate for this study.

The primary essence of qualitative research is its ability to describe and explain phenomena as experienced by study participants in their own words in a manner that quantitative research would neither do, nor be able to attach sufficient meaning to the experience.[174] Of importance are 'how' caregivers and HPs perceive these diagnostic approaches and not the perceived accuracy of their responses that could seem judgmental. Social constructionism believes that both the study participants and researcher are co-creators of a shared reality. The researcher believed, therefore, that through a qualitative study design, he could be flexible and open-minded as a co-participant in the meaning-generating process as he explored the perceptions that study participants had towards these diagnostic approaches.

Interviews are the most common method of obtaining qualitative data.[175] Specifically, individual face-to-face semi-structured interviews were used for this study because they were considered the most appropriate means by which participants' perceptions of the two diagnostic approaches could be explored. While focus groups could be appealing by providing insights into shared experiences,[176] there is the possibility of having dominant voice(s) whereby an individual or a group of individuals dominate or 'hijack' the discussion; in this case, perceptions of diagnostic approaches, so that theirs is the only opinion clearly articulated.[177] Furthermore, individual face-to-face interviews were

preferred to focus groups to prevent participants from being influenced by each other's responses. Given that interviews are a subjective method of inquiry, a reflexive statement was written before the interviews were conducted. Writing a reflexive statement is a way of acknowledging ways that bias may arise in qualitative research through the researcher's background and beliefs impacting on their understanding of the participants' perceptions.[178] For example, the researcher without a reflexive statement (Appendix VII) could unconsciously enforce his beliefs on study participants having practised lay diagnosis for malaria himself and participated in the 2-day IMCI training for the quantitative component of study.

Semi-structured interviews, characterised by open-ended questions, were chosen over unstructured interviews as the researcher wished to gain insight into participants' perceptions and experiences of lay diagnosis and IMCI for the diagnosis of malaria and pneumonia. In contrast, an unstructured interview would be more appropriate where there was little or no available qualitative evidence on perceptions of diagnostic approaches among health stakeholders and the researcher aimed to find out what might be the relevant questions to ask for future study.[179]

2.5.2.3 Study participants

Two groups of participants were recruited for the qualitative component of study. The first group of participants consisted of adult caregivers (≥18 years) whose children under-five had either participated in the quantitative component of study or who presented to the study PHCs for routine medical services (e.g. immunisation or treatment for other medical conditions). The second group of study participants were various HPs involved with the management and service delivery of primary healthcare

centres in Benin City. Furthermore, both group of participants needed to be residents of Benin City and willing to provide written or verbal consent.

2.5.2.4 Sampling strategy

A purposive sampling (also known as judgment or selective sampling) strategy was used for the recruitment of both HPs and caregivers for this study. Purposive sampling involves choosing individuals with the purpose or intention to meet certain criteria [174] and to ensure that a range of identified characteristics of participants is captured.[176]

Using a purposive sampling approach with the aim of achieving maximum variability within the collected data, HPs were selected to form a cross-section of various professional positions, experience, and training in IMCI. Similarly, caregivers were selected to form a cross-section of various occupations, educational attainments, parental experience as measured by the number and age of children.

According to Hardon and colleagues,[180] there are no standard rules for determining sample size in qualitative research but it depends on practical factors, research question(s) and aims of study. The authors recommend the use of pragmatic criteria in determining sample size, considering the financial implication and time required for interviewing interviewees and transcribing the interviews. Therefore, 10 and 15 interviews were specified as the minimum sample size for caregivers and HPs, respectively, in this study considering the aforementioned factors. The target number of 25 total participants (i.e. both HPs and caregivers) was considered feasible and realistic given the period and available resources for this study. However, the principles outlined

by Francis and colleagues for identifying saturation[9] in interviews were used to inform the final sample size.[181] Based on these principles, the minimum number of interviews as initially specified for both caregivers and HPs were first completed, then additional interviews were conducted until no new ideas or information emerged (i.e. observation of saturation). Overall, 13 caregivers and 17 HPs were interviewed until saturation was attained. The interviews were conducted between February and May 2016.

2.5.2.5 Development of interview guides

Interview guides or questions were developed by the researcher based on evidence in the literature and research questions. Separate interview guides, containing mostly open-ended questions to elicit deeper responses, were developed for caregivers, primary health workers, medical doctors, PHC coordinators and other local government health stakeholders, and facilitators of IMCI training. Thereafter, the developed interview guides were reviewed by two supervisors (C.P. & P.R.M.) and relevant changes were made (available in Appendix XI).

2.5.2.6 Piloting of study protocol and interview guides

The study protocol and interview guides were piloted with a caregiver and health worker, similar to the intended study participants,[182] to identify any ambiguity in questions and ensure the guides allowed for the capture of any aspect that may have been overlooked.

[9] Saturation is a term used to describe the point when study participants have provided a range of information or perceptions about research until no additional information is being provided. Hence, if a researcher is still getting additional information after several interviews, he/she is supposed to conduct more interviews until saturation is observed and vice-versa.

A review of the two audio recordings, an average of 15 minutes 45 seconds, by the researcher and two supervisors resulted in minor modifications of the interview guides. Data (i.e. audio recordings) from the pilot study were not used as part of the main study as advocated by Bowden.[182]

2.5.2.7 Participant recruitment processes

2.5.2.7.1 Recruitment of healthcare professionals

As part of the doctoral research study, a 2-day training programme on IMCI guidelines was organised for PHWs on the management of both malaria and pneumonia in children between the age of 2 months and 59 months. This was also used to enable standardised data collection for the quantitative study. Six months after the 2-day training on IMCI guidelines, an invitation letter providing information about the qualitative research was sent to the five study PHCs and relevant administrative offices (e.g. offices of PHC coordinators, administrative offices of public health units in the three local government areas in Benin City, director of health services in Edo State, medical officer of PHCs, and commissioner for health in Edo State) by the researcher. All the HPs at study PHCs and relevant administrative offices, regardless of whether they had participated in the 2-day IMCI training or not, were invited to participate in this qualitative study. Also attached to the invitation letter were participant information sheets which contained the nature and purpose of the research and an expression of interest form. HPs who expressed an interest in the study were asked by the researcher for an appropriate date and time to be interviewed.

2.5.2.7.2 Recruitment of caregivers

For the recruitment of caregivers, a letter seeking permission to post information about the research on notice boards in the study PHCs was sent to the respective directors/matrons. Following approval, the matrons then assigned at least one PHW at each study PHC to inform caregivers who presented for medical consultation or immunisation to read the research information sheet on the notice board and where necessary, explain to those who could not read in simple English, Pidgin English or the main local dialect (i.e. Bini). The contact details of the caregivers who expressed an interest in the study were recorded by a PHW and they were asked for a suitable date and time to be interviewed. Thereafter, the names and contacts details of these caregivers were collected from the PHWs at each study PHC by the researcher.

2.5.2.8 Data collection (interview procedure)

Interviews commenced according to participants' preferred date and time as stated in their expression of interest forms. However, if necessary, the researcher was flexible to reschedule interviews to dates and time most convenient for them.[183] Making reference to the study information sheets (Appendix VIII), the purpose of the interview was explained to study participants, as advocated by Bell,[184] but this was kept brief in order to avoid any potential influence on responses. It was made clear at the outset that caregivers and HPs were under no obligation to take part in the study and were free to decline the invitation. Study participants were also assured that they could decline to answer any of the questions and it was important that there was trust between the interviewee and interviewer. Before each interview, the researcher reminded the participants of the purpose of the interview, explained confidentiality, anonymity and

provided an opportunity for each participant to ask any question before completing the consent form (Appendix IX).

Consent forms (3 copies) were signed and permission given for interviews to be recorded. In the scenario where a caregiver was not literate, the participant information sheet was re-explained in simple English or Pidgin English by the researcher. Thereafter, a thumbprint was obtained or verbal consent was recorded in writing by the researcher in the presence of a witness (e.g. a caregiver presenting to PHC where the participant was interviewed or a PHW on duty during the interview). Each participant in the study kept a copy of the consent form while the other two copies were kept by the researcher and study PHC.

While it was recognised that audio recording with digital recorder of the interview could impose constraints upon the interviewee,[185] it nevertheless enabled the researcher to give the interviewees full attention, ensuring data were reliably captured, as well as saving time given that the constant writing/jotting of notes was kept to the minimum. Moreover, this can be quite distracting during conversation. For participants' comfort, interviews were held at study PHCs for caregivers and primary health workers, while PHC coordinators, IMCI training facilitators and the disease surveillance and notification officer (DSNO) were interviewed in their offices. All 30 interviews were audio recorded and participants were assigned a unique code (01–30). Prior to data analysis, any identifier, such as names of interviewees, was removed from the audio recordings.

2.5.2.9 Thematic analysis

Data were analysed using thematic analysis which allows the researcher to search, identify, analyse and report themes or repeated patterns of meaning in the data

collected.[186] Thematic analysis is a method for qualitative data analysis that encompasses several core skills and is recommended as the first method of analysis that new researchers learn.[186] It was for these reasons that thematic analysis was chosen as the method of analysis for this study. Prior to the thematic analysis of qualitative data, the researcher decided on the approach for identifying themes (i.e. inductive or deductive), and the level at which themes were to be identified (i.e. semantic or latent).

An inductive or bottom-up approach to thematic analysis was chosen for this study. In this approach, unlike the theoretical or deductive approach[10], the themes identified are strongly linked to the data themselves or data-driven. In other words, identification of themes involves coding the data without trying to fit it into a pre-existing coding frame or the researcher's analytic preconceptions.[186]

Unlike thematic analysis at the 'semantic' level that identifies themes within the surface meanings of data or that is after the literal meaning of responses, a thematic analysis at the 'latent or interpretative' level was chosen for this study. The latent approach to thematic analysis identifies or examines the underlying ideas, assumptions, and ideologies behind qualitative data.

Thematic analysis of data for this study followed the six-phased approaches recommended by Braun and Clarke,[186] bearing in mind that these phases were not a

[10] Theoretical or deductive or top-down approach to thematic tends to be driven by the researcher's theoretical or analytic interest in the research question and is thus more explicitly analyst-driven.

linear process, but more of a recursive process where one moves back and forth as needed. The six phases are described as follow:

2.5.2.9.1 Familiarisation with data

The process of familiarisation began with listening to the interview recordings followed by a rigorous verbatim transcription of audio-recordings in a way which was true to its original nature (e.g. appropriate use of punctuation). Transcriptions were carried out as soon as possible following the interviews so that they could be quickly checked against the recordings whilst fresh in the researcher's mind and errors amended when heard.[183] Following the transcription process, transcripts were compared with the original audio-recordings for accuracy. This was followed by repeated and active reading of transcripts for at least three times until the researcher became familiar with the depth and breadth of the content. During this phase, field notes that were written immediately after each interview about observations, thoughts and ideas were also referred to. The initial list of ideas and potential codes generated at the end of this phase were discussed with two research supervisors (C.P. & P.R.M) during a supervisory meeting.

2.5.2.9.2 Generating initial codes

This phase, influenced by the initial decisions made regarding approaches to thematic analysis, involved manually identifying initial codes from the transcripts and organising data into meaningful groups. This was repeated for the entire data set, ensuring that all actual data extracts were coded. To ensure consistency in coding and thereby enhance dependability and credibility, five randomly selected transcripts were independently double coded by the two research supervisors (C.P. & P.R.M.).

2.5.2.9.3 Searching for themes

Using Microsoft Excel tables as a means of visual representation, this phase involved sorting the different codes into potential themes and sub-themes and then assembling all the relevant coded data extracts within these identified themes and sub-themes into an initial thematic table.

2.5.2.9.4 Review of initial themes

This phase involved reviewing and refining of the initially identified themes. All the collated extracts from the entire data set for each initial theme were re-read again until internal homogeneity and external heterogeneity were observed in the revised thematic table. Internal homogeneity means that the data inside the themes are meaningfully related to each other, while external heterogeneity means that there are clear and identifiable differences between themes.[187]

2.5.2.9.5 Defining and naming themes

This phase involved, where necessary, defining and further refining the themes and sub-themes for analysis, and where necessary consulting both supervisors (C.P. & P.R.M.) to reach consensus. It focused on identifying the core of each theme and deciding what aspect of the data each theme represents/interprets. This phase ended with the finalising of theme and sub-theme names and the creation of a final thematic table for both caregivers and HPs.

2.5.2.9.6 Producing the report

The final themes and sub-themes were described and substantiated with appropriate data extracts from the transcripts. Throughout the text, caregivers and health stakeholders are

referred to by the unique study numbers 1–13 and 14–30 respectively, with quotations prefixed with the identification number of participant speaking.

2.6 Data confidentiality and storage

Data collected were stored in a secure password protected hard drive and a shared online password-secured study folder created within the University of Nottingham workspace that were only accessible to the researcher and the supervisors. The online folder was also used to share collected data with study supervisors during data collection in Nigeria. All hard copies of data including field notes, consent forms, interview guides and questionnaires were stored in a locked filing cabinet in Nigeria.

During management of both quantitative and qualitative data, participant details were anonymised by dropping personal identifiers (e.g. names, residential addresses, and telephone numbers). After the completion of management and analysis for study, the database versions were dated for easier identification and transferred to a secure University of Nottingham backup server for storage for a period of seven years as per the University's Code of Research Conduct and Research Ethics.

2.7 Overall ethics and ethical considerations for study

Prior to data collection, the protocol for both quantitative and qualitative components of the study was reviewed and approved by the University of Nottingham Medical School Ethics Committee (Reference number: OVS18062015 SoM EPH) and the Ethics Review Committee of Edo State Ministry of Health (Reference number: HA.577/Vol. II/126) (Appendix III).

All procedures performed in this study were in accordance with the ethical standards of institutional research committees and with the 1964 Helsinki declaration and its

amendments.[188] Though it was stated that monetary incentives should not be offered to study participants, certain services (e.g. rapid diagnosis and microscopy for suspected malaria, medications for treatment and two weighing scales) were provided in this study. Furthermore, 21 health workers were trained in the IMCI guidelines as part of the study protocol.

While waiting to be attended to by a health worker, an information sheet was given to each potential caregiver explaining the research as well as what was expected of them and their children. In the scenario where a caregiver was not literate, the participant information sheet was explained in simple English, Pidgin-English or the common local dialect. Thereafter, consent was sought from caregivers and written consent or thumbprint was obtained.

The study involved the collection of routinely collected physiological samples (e.g. blood samples for RDT and microscopy) in study PHCs and being an observational study, the researcher did not intervene in any routine diagnostic or treatment services provided to study patients. Moreover, recurrent cases of suspected malaria and pneumonia within the 30-day follow-up period were assessed as per the routine PHC protocol. The routine PHC protocol involved treating diagnosed malaria and pneumonia with recommended anti-malarial drugs and antibiotics respectively, while severe cases were referred to the nearest higher healthcare centres (e.g. secondary or tertiary hospitals).

2.8 Registration of study protocol prior to data collection

The quantitative component of the study was prospectively registered as an observational study with ClinicalTrials.gov with the unique identifier: NCT02482116.

The essence of registration was to minimise the potential for publication bias and to enhance research transparency.

2.9 Dissemination plan

Preliminary results will be made available in a study brief to be distributed to the five study PHCs, and the public health departments of the three LGAs in Benin City (December 2017). Where possible, a short workshop for sharing and discussion of findings with health workers and caregivers will also be organised.

3 RESULTS

3.1 Introduction to result chapter

This chapter begins with a description of how study participants in the quantitative studies were recruited at the study PHCs, as well as the assessment for malaria and pneumonia as per the various diagnostic approaches. Thereafter, the results are presented in three sections. The first section provides a description of study participants in the quantitative studies (children under-five and caregivers) and qualitative study (caregivers and health professionals). The second and third sections present results of quantitative and qualitative components by the study specific objectives.

3.2 Research processes, recruitment and assessment of study participants

Figure 3.1 (below) outlines the various steps involved in conducting both the quantitative and qualitative components of this study. Figure 3.2 (below) shows how the 903 children under-five in the quantitative component of the study were recruited at the five study PHCs. Figure 3.3 (below) shows the assessment of eligible children under-five for malaria and/or pneumonia according to various diagnostic approaches.

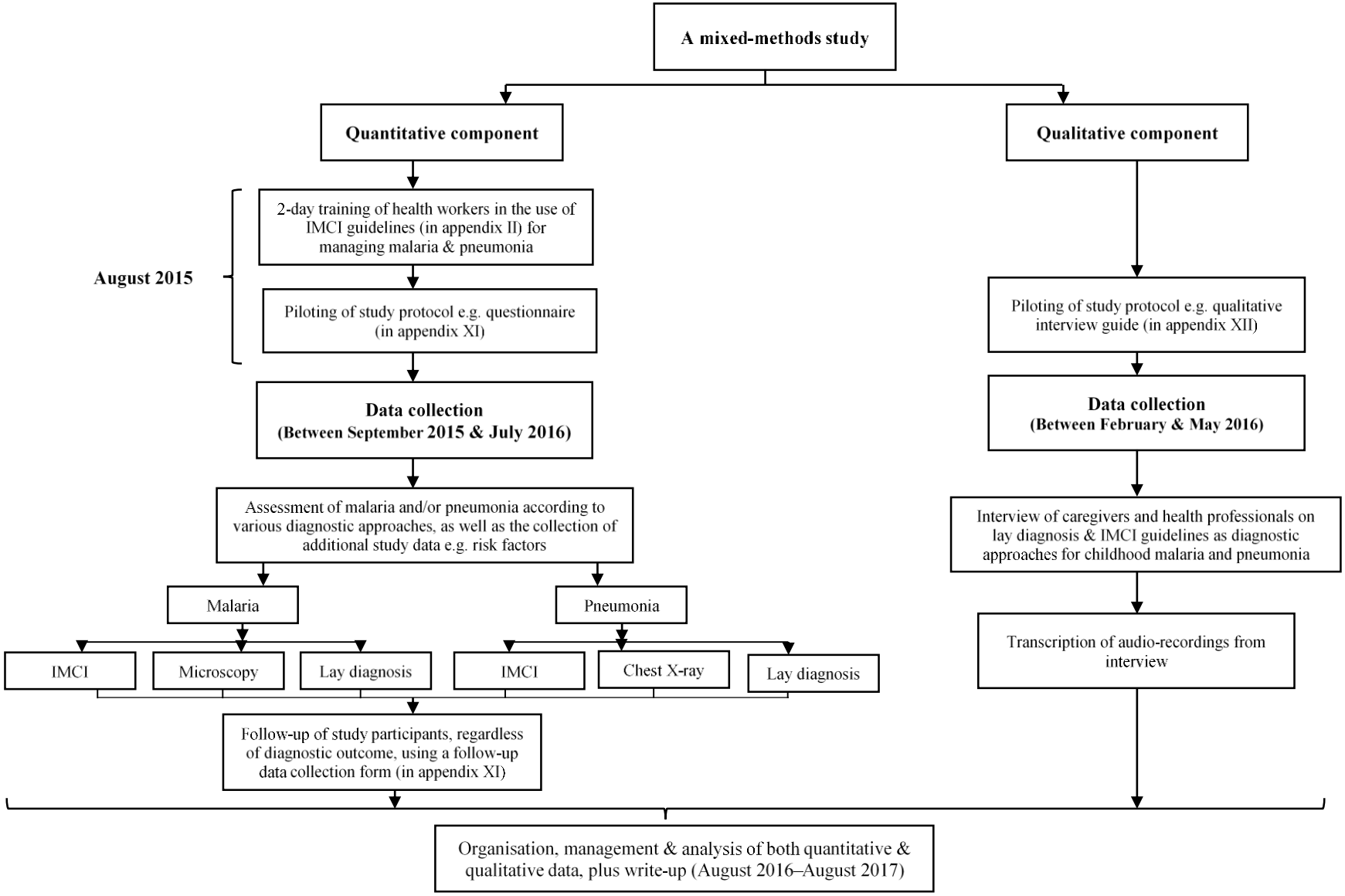


Figure 3.1: Flow charts showing the various research processes/stages

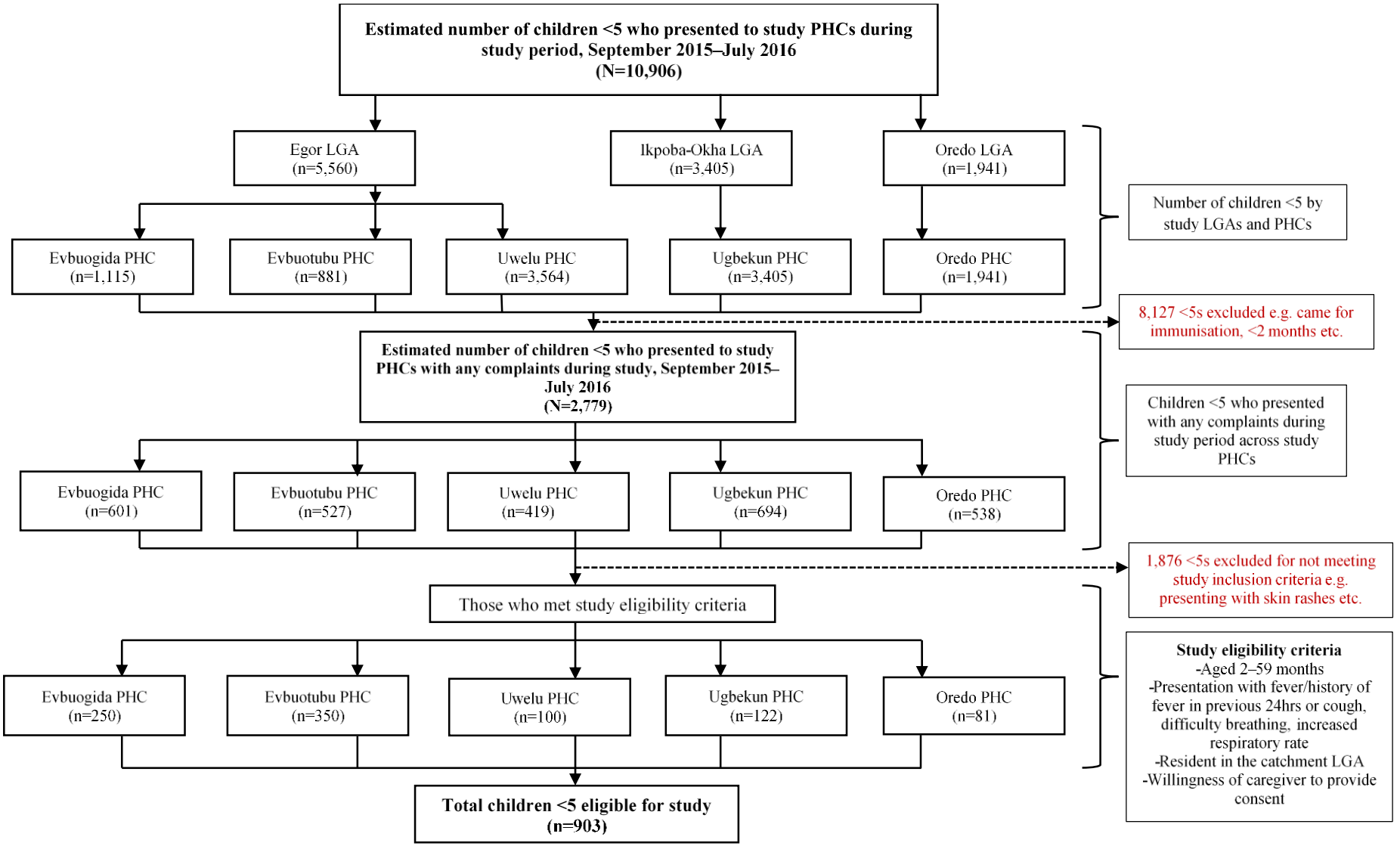


Figure 3.2: Flow charts showing the recruitment of eligible participants across study centres

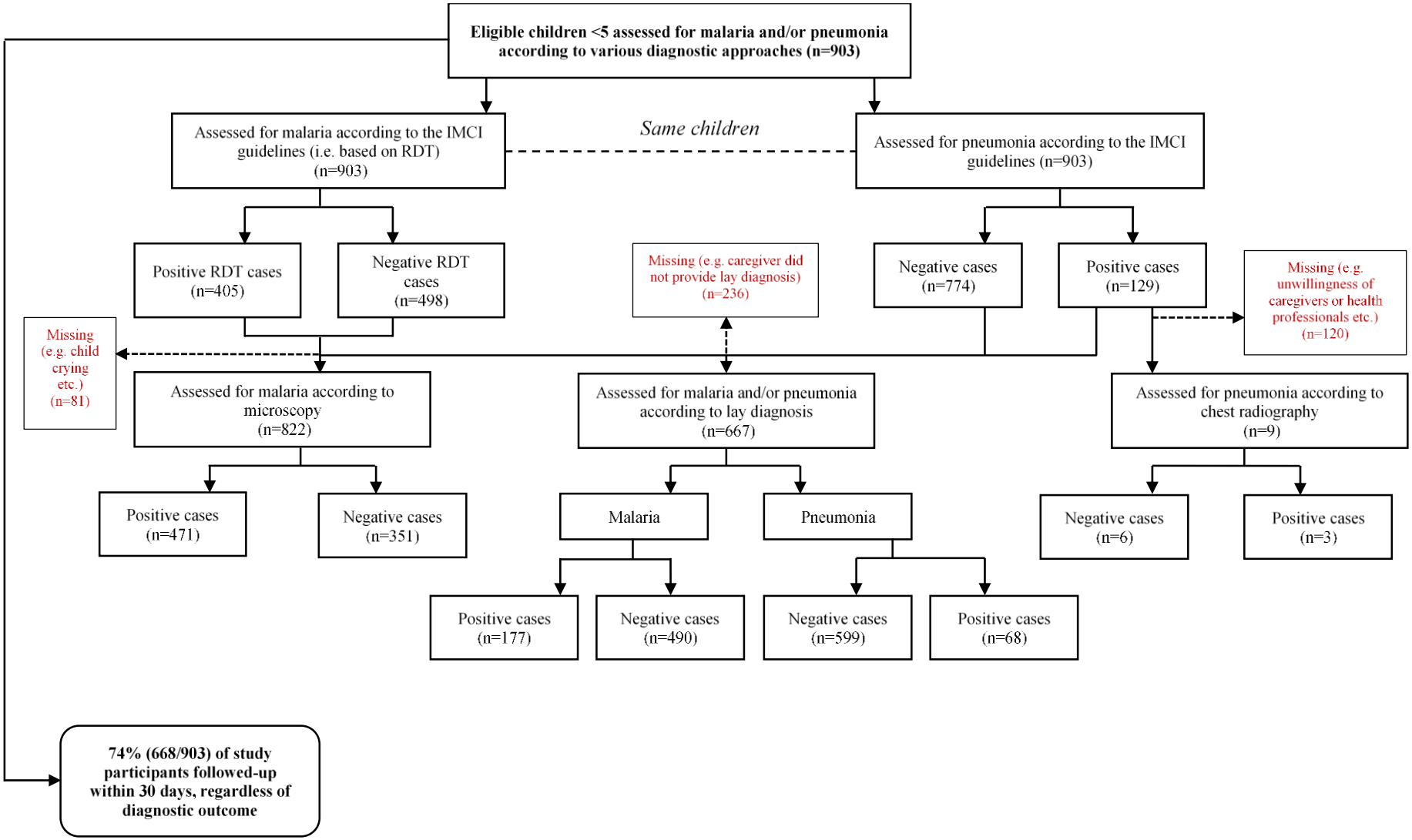


Figure 3.3: Flow charts showing the assessment of eligible children under five for malaria and/or pneumonia according to various diagnostic approaches

3.3 Description of study participants and baseline diagnostic outcomes

3.3.1 Description of study participants in the quantitative component

Table 3.1 **(**below) summarises the socio-demographic characteristics of the study participants. The mean age of study participants (children) was 20.11 months with majority between the ages of 2–11 months (36.99%). Of the 903 study participants, 55.37% were males and 668 (73.98%) were followed-up within the 30-day period following initial assessment at study PHCs.

Table 3.1: Sociodemographic characteristics of children (n= 903)

Characteristic	Frequency (%)
Mean (SD) age (months)	20.11 (14.82)
Age category (months)	
2-11	334 (36.99)
12-23	237 (26.25)
24-35	144 (15.95)
36-47	100 (11.07)
48-59	88 (9.75)
Gender	
Female	401 (44.41)
Male	500 (55.37)
Missing	2 (0.22)
Weight category*	
Normal weight	161 (17.83)
Underweight	39 (4.32)
Overweight	31 (3.43)
Obese	113 (12.51)
Missing	559 (61.90)
Estimated weight at birth as reported by caregivers (kg)	417 (46.18)
Normal (2.5-4.0)	22 (2.44)
Low (<2.5)	25 (2.77)
High (>4.0)	439 (48.62)
Missing	
Socioeconomic class	
I & II (upper class)	139 (15.39)
III	127 (14.06)
IV	314 (34.77)
V (lower class)	54 (5.98)
Missing	269 (29.79)
Local government area of residence	
Egor	696 (77.08)
Ikpoba-Okha	122 (13.51)
Oredo	80 (8.86)
Missing	5 (0.55)
Followed-up within 30-day period	
All	
No	235 (26.02)
Yes	668 (73.98)
Children diagnosed with IMCI malaria (n=405)	
No	101 (24.94)
Yes	304 (75.06)
Children diagnosed with IMCI pneumonia (n=129)	
No	25 (19.38)
Yes	104 (80.62)
Mean duration (SD) of follow-up (days)	18.3 (2.9)

* Weight category was based on BMI percentile Z scores from the 2006 WHO growth standards for children aged 0–5 years

Table 3.2 (below) summarises the socio-demographic characteristics of caregivers accompanying the study children. Most of the caregivers were females (67.00%), parents (70.43%) and between the ages of 26 and 35 years. Regarding the highest level of educational attainment and occupation, 32.45% of caregivers had completed their education at secondary school level and 33.55% were small-scale traders (i.e. artisans/traders) respectively.

Table 3.2: Sociodemographic characteristics of caregivers (n= 903)

Characteristic	Frequency (%)
Gender of caregiver	
Female	605 (67.00)
Male	67 (7.42)
Missing	231 (25.58)
Age category of caregiver (years)	
<15	3 (0.33)
15-20	7 (0.78)
21-25	88 (9.75)
26-30	189 (20.93)
31-35	216 (23.92)
36-40	98 (10.85)
41-45	16 (1.77)
46-50	9 (1.00)
>51	13 (1.44)
Missing	264 (29.24)
Relationship of caregiver to child	
Parent	636 (70.43)
Grandparent	15 (1.66)
Sibling	5 (0.55)
Other relative	2 (0.22)
Missing	245 (27.13)
Occupation of caregiver	
Artisan/Trader	303 (33.55)
Civil servant	106 (11.74)
Currently unemployed	24 (2.66)
Farmer	23 (2.55)
Housewife	75 (8.31)
Student	7 (0.78)
Retired	1 (0.11)
Self-employed/Business	127 (14.06)
Missing	237 (26.25)
Highest education of caregiver	
No formal education	37 (4.10)
Primary	144 (15.95)
Secondary	293 (32.45)

Beyond secondary	165 (18.27)
Missing	264 (29.24)

Table 3.3 (below) summarises the clinical characteristics of study participants on presentation to study PHCs and outcomes of various diagnostic approaches. Of the 903 study participants, most were brought to the study PHCs within three days of illness onset (70.21%) and the average temperature was 37.6^{o}C. Majority of the study participants were assessed for fever (97.56%) with thermometer (64.78) being the predominant method of ascertaining fever. Following assessments of study participants by health workers using the IMCI guidelines, 44.85%, 14.29% and 17.83% were classified as having malaria, pneumonia and both malaria and pneumonia respectively. As per Giemsa-stained microscopy (gold standard diagnostic test), 52.16% of the study participants were confirmed as having malaria. There were 19.60% and 7.53% malaria and pneumonia cases, respectively, according to caregivers' diagnosis (lay diagnosis).

Table 3.3: Clinical characteristics of study participants (children <5 years) (n=903)

Characteristic	Frequency (%)
Duration of illness before visiting PHCs	
≤3 days	634 (70.21)
≥4 days	269 (29.80)
Average temperature (SD) (ºC)*	37.63 (0.91)
Assessed for fever	
No	18 (1.99)
Yes	881 (97.56)
Not ascertained	4 (0.44)
Method of ascertaining fever	
Feels hot/Touch	28 (3.10)
History	286 (31.67)
Thermometer	585 (64.78)
Not ascertained	4 (0.44)
Any general danger sign (IMCI)	
No	812 (89.92)
Yes	87 (9.63)
Not ascertained	4 (0.44)
Malaria according to IMCI	
No	498 (55.15)
Yes	**405 (44.85)**
Pneumonia according to IMCI	
No	774 (85.71)
Yes	**129 (14.29)**
Both malaria and pneumonia according to IMCI	
No	742 (82.17)
Yes	**161 (17.83)**
Malaria according to microscopy	
No	351 (38.87)
Yes	**471 (52.16)**
Not ascertained	81 (8.97)
Malaria according to caregivers (lay diagnosis)	
No	490 (54.26)
Yes	**177 (19.60)**
Not ascertained	236 (26.14)
Pneumonia according to caregivers (lay diagnosis)	
No	599 (66.33)
Yes	**68 (7.53)**
Not ascertained	236 (26.14)
Complete immunisation for age	
No	96 (10.63)
Yes	571 (63.23)
Not ascertained	236 (26.14)

* Based on the total number of children assessed for fever using thermometer (n=585)

Figures 3.4 and Figure 3.5 below show the distribution of malaria and pneumonia, respectively, by the diagnostic approaches during the study period (September 2015–July 2016). The number of malaria and pneumonia cases were higher in the months corresponding to rainy season than dry season, regardless of the diagnostic approach.

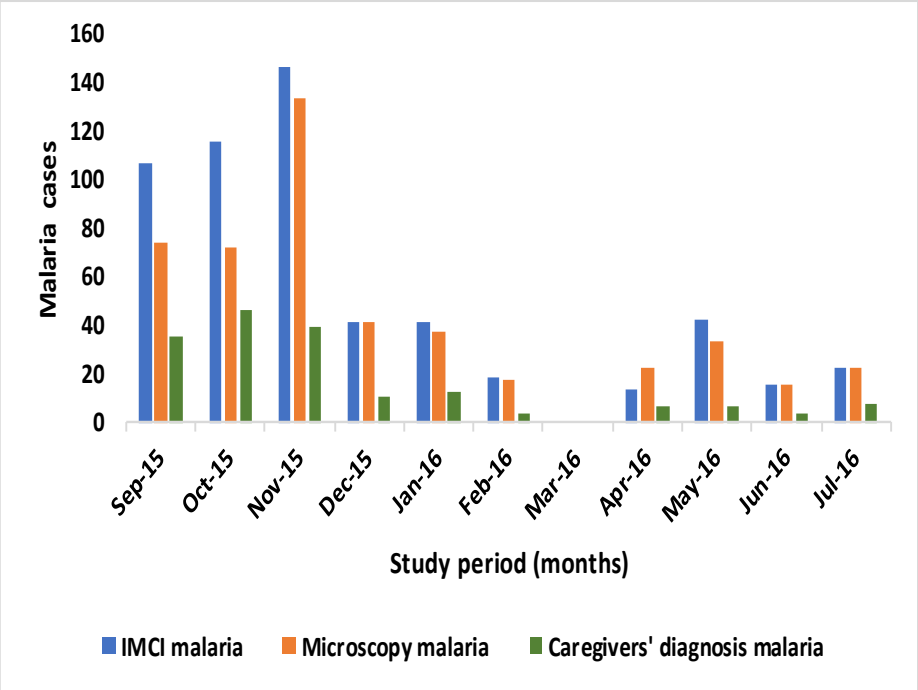


Figure 3.4: Distribution of malaria cases by diagnostic approaches during study period (September 2015–July 2016)

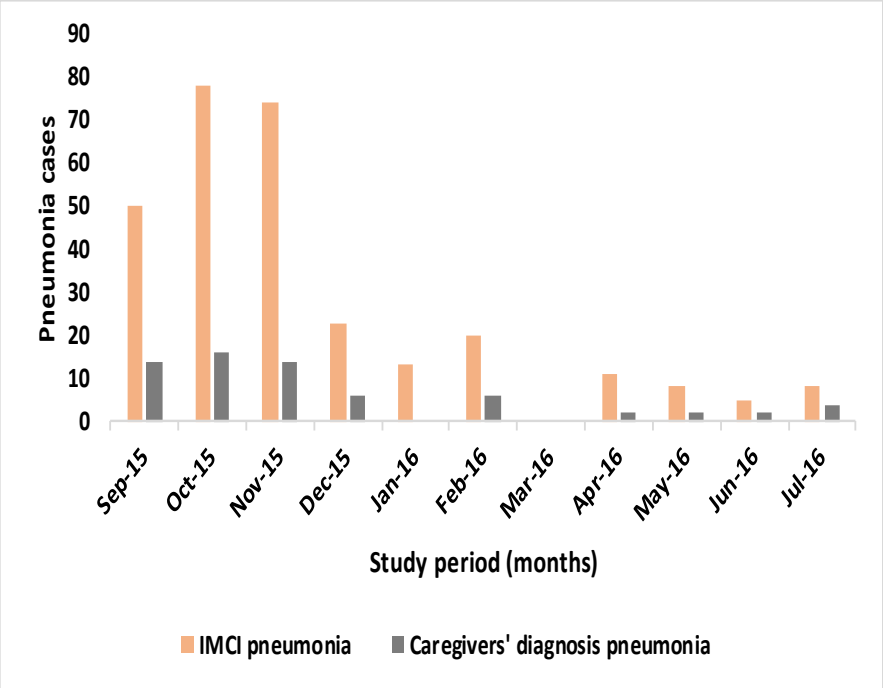


Figure 3.5: Distribution of pneumonia cases by diagnostic approaches during study period (September 2015–July 2016)

3.3.2 Description of study participants in the qualitative component

Table 3.4 (below) provides background characteristics of the thirteen caregivers (mothers) interviewed. Of the 13 mothers, eight described themselves as business women, four were government workers (lecturers, primary school teacher, and health worker) and one was a housewife. In terms of educational attainment, most of the mothers (n=7) were secondary school graduates, while four and two mothers had post-secondary and primary education respectively. The education system in Nigeria is primarily divided into primary education (six years), secondary education (six years -3 years of junior secondary school and 3 years of senior secondary school) and post-

secondary education[11] (2-6 years). The respondents had between 1 to 5 children with at least one child under the age of five years. On average, respondents reported that their children fell ill with a frequency of 1 to 5 times in a year.

Table 3.5 (below) provides background characteristics of the 17 health professionals (HPs) interviewed. Twelve of the 17 health professionals were female (70.59%). Six of the respondents interviewed were medical doctors whilst also holding other positions such as director of primary healthcare centres (n=2), coordinator of primary healthcare centres (n=2) and certified WHO facilitator of IMCI training (n=2). The respondents had between 1 to 28 years of work experience. Most of the respondents (n=10) participated in the 2-day IMCI training for this study.

[11] Post-secondary education refers to either higher technical or tertiary education.

Table 3.4: Background characteristics of caregivers (*n=13*)

Caregivers' code	Sex	Occupation	Duration of occupation (year)	Highest educational qualification	Number of children	Age of children (in years)	Estimated frequency children fall ill/year
01-Caregiver	Female	Self-employed	Unknown	Secondary education	1	2	4 times
02-Caregiver	Female	Business woman	1	Secondary education	2	3 & 2	2-3 times
03-Caregiver	Female	Housewife	Unknown	Secondary education	3	5, 4 & 2	2 times
04-Caregiver	Female	Civil servant	>4	Post-secondary education	5	20, 19, 16, 12 & 4	1 time
05-Caregiver	Female	University lecturer	4	Post-secondary education	2	4 & 2	4-6 times
06-Caregiver	Female	Petty trader	2	Primary education	5	13, 10, 8, 6 & 2	2-3 times
07-Caregiver	Female	University lecturer	5	Post-secondary education	2	2 & 1.5	2-6 times
08-Caregiver	Female	Business woman	>4	Primary education	2	7 & 1	≥2 times
09-Caregiver	Female	Petty trader	3	Secondary education	3	11, 7 & 4	Last child frequently falls ill
10-Caregiver	Female	Tailor & petty trader	10	Secondary education	3	16, 9 & 4	4-5 times
11-Caregiver	Female	Primary school teacher	7-8	Post-secondary education	2	4 & 1	5 times
12-Caregiver	Female	Business woman	12	Secondary education	4	8, 6, 4 & 3	3 times
13-Caregiver	Female	Business woman	2	Secondary education	3	10, 7 & 5	3-4 times

* Average duration for interviewing caregivers = 23 minutes 24 seconds

Table 3.5: Background characteristics of health professionals (*n=17*)

HPs' unique code *	Sex	Professional qualification	Years of experience	Participation in IMCI training for study (Yes/No)
14-Doc	Female	LGA Medical Officer of Health & Medical doctor	5	No
15-PHW	Female	Junior community health extension worker	5	Yes
16-PHW	Female	Junior community health extension worker	5	Yes
17-PHW	Female	Junior community health extension worker	7	Yes
18-Nurse	Female	Nurse	26	Yes
19-DSNO	Male	Disease surveillance and notification officer (DSNO)	1	No
20-Doc	Male	Medical doctor	>13	No
21-Nurse	Female	Registered nurse mid-wife	6	Yes
22-PNO	Female	Principal nursing officer	8-9	No
23-Matron	Female	Director of nurse/matron	25	No
24-PHW	Male	Junior community health extension worker & previous owner of a chemist store	>5	Yes
25-Nurse	Female	Nurse	4	Yes
26-CDN	Male	PHC co-ordinator & Medical doctor	6	No
27-PHW	Female	Community health extension worker (CHEW)	4	Yes
28-CDN	Male	PHC co-ordinator & Medical doctor	7	No
29-FAC	Female	Consultant paediatrician & WHO IMCI training facilitator	28 9	Facilitator of IMCI training
30-FAC	Female	Consultant paediatrician & Executive secretary of Edo State Primary Healthcare Development Agency (PHDA)	7 1	Facilitator of IMCI training

*HPs' unique code: Doc =medical doctor; PHW =primary health worker; DSNO =disease surveillance and notification officer; PNO =principal nursing officer, equivalent to a matron; CDN =PHC coordinator; and FAC = IMCI training facilitator

** Average duration for interviewing health professionals = 22 minutes 10 seconds

3.3.3 Distribution of malaria and/or pneumonia cases according to various diagnostic approaches

In total, 903 children (aged 2–59 months) who presented to the study PHCs met the eligibility criteria and were included in the current study. Table 3.6 (below) summarises the number of children diagnosed with malaria, pneumonia, both malaria and pneumonia, and neither malaria nor pneumonia as per various diagnostic approaches. Of the 903 children assessed by health workers using the IMCI guidelines, 44.85% (405/903), 14.29% (129/903), 17.83 (161/903) and 23.03% (208/903) were diagnosed with malaria, pneumonia, both malaria and pneumonia, and neither malaria nor pneumonia, respectively. Caregivers of 667 children, unaware of the outcome of health workers' diagnoses with the aid of the IMCI guidelines, offered lay diagnosis when asked what they thought was the most probable cause of their child's illness. According to these caregivers' diagnoses, 26.54% (177/667), 10.19% (68/667), 0.30% (2/667) and 62.97% (420/667) of the children had malaria, pneumonia, both malaria and pneumonia, and neither malaria nor pneumonia, respectively. Of the 822 children that had their malaria status confirmed by microscopy (gold-standard test), more than half (57%) tested positive for malaria. It should be noted that there were only nine children whose diagnoses of pneumonia were confirmed by chest X-ray (results not shown but available in the flow charts showing assessment of study participants –Figure 3.3).

Table 3.6: Distribution of malaria and/or pneumonia cases as per the IMCI guidelines, microscopy and lay diagnosis

Diagnostic outcome		IMCI (%)	Microscopy (%)	Lay diagnosis (%)
		n=903	n=822	n=667
Malaria only	No	498 (55.15)	351 (42.70)	490 (73.46)
	Yes	**405 (44.85)**	**471 (57.30)**	**177 (26.54)**
Pneumonia only	No	774 (85.71)	NA	599 (89.81)
	Yes	**129 (14.29)**		**68 (10.19)**
Both malaria & pneumonia	No	742 (82.17)	NA	665 (99.70)
	Yes	**161 (17.83)**		**2 (0.30)**
Neither malaria nor pneumonia	No	695 (76.97)	NA	247 (37.03)
	Yes	**208 (23.03)**		**420 (62.97)**

NA= Not applicable

Furthermore, Tables 3.7 and 3.8 (below) provide detailed distribution of malaria and pneumonia cases according to various diagnostic approaches. Of the 903 children under-five assessed for malaria, 245 (52.0%) were diagnosed of having malaria according to both health workers using the IMCI guidelines and microscopy, whereas the number was 105 (22.3%) for lay diagnosis and microscopy (Table 3.7). Twenty-eight percent (112/903) of the total children had malaria according to both the IMCI guidelines and caregivers while 13% (17/903) had pneumonia according to both the IMCI guidelines and caregivers (Table 3.8).

Table 3.7: Distribution of malaria cases according to the IMCI guidelines and lay diagnosis compared with microscopy (n=903)

	Microscopy		
Malaria	**Negative (%)**	**Positive (%)**	**Not tested (%)**
IMCI guidelines			
Negative	**216 (61.54)**	226 (47.98)	56 (69.14)
Positive	135 (38.46)	**245 (52.02)**	25 (30.86)
Lay diagnosis			
Negative	**210 (59.83)**	234 (49.68)	46 (56.79)
Positive	55 (15.67)	**105 (22.29)**	17 (20.99)
Not ascertained	86 (24.50)	132 (28.03)	**18 (22.22)**

Table 3.8: Distribution of malaria and pneumonia cases by caregivers in relation to the IMCI guidelines (n=903)

Diagnosis	IMCI guidelines	
	Negative (%)	Positive (%)
Lay diagnosis of malaria		
Negative	**307 (61.65)**	183 (45.19)
Positive	65 (13.05)	**112 (27.65)**
Not ascertained	126 (25.30)	110 (27.16)
Lay diagnosis of pneumonia		
Negative	**519 (67.05**)	80 (62.02)
Positive	51 (6.59)	**17 (13.18**)
Not ascertained	204 (26.36)	32 (24.81)

3.4 Results of the quantitative component

3.4.1 Assessing the diagnostic accuracy of the IMCI guidelines and lay diagnosis against reference diagnostic tests

Diagnostic accuracy of the IMCI guidelines and caregivers' diagnosis of malaria as compared to microscopy

Table 3.9 (below) summarises the diagnostic performance of the IMCI guidelines and caregivers' diagnosis of malaria as compared to microscopy (reference or gold-standard diagnostic test) in terms of area under ROC curve (AUROC) values, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Compared with microscopy, the diagnosis of malaria according to the IMCI guidelines (AUROC value 0.57) and lay diagnosis by caregivers (AUROC value 0.55) was overall poor (Table 3.9). A direct comparison showed that in relation to microscopy, overall accuracy of the IMCI guidelines in the diagnosis of malaria was slightly better than caregivers' diagnosis. Specifically, in terms of diagnostic validity, the IMCI guidelines were better than caregivers' diagnosis in terms of sensitivity (51.8% versus 31.1%) in the diagnosis of malaria. In contrast, caregivers' diagnosis recorded a better specificity than the IMCI guidelines (79.5% versus 61.3%) in the diagnosis of malaria. In terms of

predictive values, both the IMCI guidelines (64.5%) and caregivers' diagnosis (66.3%) recorded moderate PPVs in the diagnosis of malaria. However, the NPVs for the IMCI guidelines (48.4%) and caregivers' diagnosis (47.1%) were much lower.

Table 3.9: Predictive value of the IMCI guidelines and caregivers' diagnosis of malaria compared to microscopy

Diagnostic approach	AUROC value (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV* % (95% CI)	NPV** % (95% CI)
IMCI guidelines (n=822)	**0.57 (0.53-0.60)**	**51.8 (47.2-56.4)**	61.3 (56.0-66.5)	64.5 (59.4-69.3)	48.4 (43.7-69.3)
Lay diagnosis (n=604) ***	0.55 (0.52-0.59)	31.1 (26.2-36.3)	**79.5 (74.1-84.2)**	66.3 (58.4-73.5)	47.1 (42.3-51.8)

*PPV= Positive predictive value; NPV**= Negative predictive value

***Calculation of predictive scores requires complete observations for both diagnostic approaches e.g. there were 604 complete diagnosis of malaria for both microscopy & lay diagnosis in this study.

Accuracy of caregivers' diagnosis of malaria and pneumonia compared to the IMCI guidelines

The study initially aimed to compare the diagnosis of pneumonia by health workers using the IMCI guidelines and lay diagnosis against the gold-standard diagnosis using chest radiography. However, the extremely low uptake of chest radiography despite it being provided free of cost to participants and its unacceptability among study PHC senior staff (matrons and doctor) made it impossible to conduct this analysis for the study. The accuracy of caregivers' diagnosis of pneumonia is therefore compared to that of the IMCI guidelines as the reference diagnostic test. Table 3.8 (below) summarises the diagnostic performance of caregivers' diagnosis for predicting malaria and pneumonia in children in terms of area under ROC curve (AUROC) values, sensitivity, specificity, PPV and NPV. The distribution of malaria and pneumonia cases as diagnosed by caregivers in relation to the IMCI guidelines is presented in Appendix VI.

Compared to the IMCI guidelines (reference diagnostic test), the overall diagnostic accuracy of caregivers in the diagnosis of malaria was moderate with an AUROC value of 0.60 (95% CI, 0.57-0.64) (Table 3.10). However, caregivers' diagnosis of malaria was close to being excellent in terms of specificity (82.5%) but poor in terms of sensitivity (38.0%). Both the PPV (63.3%) and NPV (62.7%) of caregivers' diagnosis of malaria as compared to the IMCI guidelines were moderate. Compared to the IMCI guidelines, the overall accuracy of caregivers' diagnosis of pneumonia was poor. However, the specificity (91.1) and NPV (86.6) were very good while the sensitivity (17.5) and PPV (25.0) were extremely poor. A direct comparison of caregivers' capacity to diagnose malaria and pneumonia in their children under five suggests that they are generally better at diagnosing the former (AUROC value of 0.60) than the latter (AUROC value of 0.54).

Table 3.10: Predictive value of caregivers' diagnosis of malaria and pneumonia compared to the IMCI guidelines (n=667)

Diagnostic approach	ROC Area (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)
Lay diagnosis of malaria	**0.60 (0.57-0.64)**	**38.0 (32.4-43.8)**	82.5 (78.3-86.2)	**63.3 (55.7-70.4)**	62.7 (58.2-67.0)
Lay diagnosis of pneumonia	0.54 (0.50-0.58)	17.5 (10.6-26.6)	**91.1 (88.4-93.3)**	25.0 (15.3-37.0)	**86.6 (83.7-89.3)**

The ROC curves and AUROC values showing the diagnostic performances of the IMCI guidelines and caregivers' diagnosis of malaria compared to microscopy (reference diagnostic test) are shown in Figure 3.6 (a–b) below. The ROC curves and AUROC values showing the diagnostic performances of caregivers' diagnosis of malaria and

pneumonia compared to the IMCI guidelines (reference diagnostic test) are shown in Figure 3.6 (c–d).

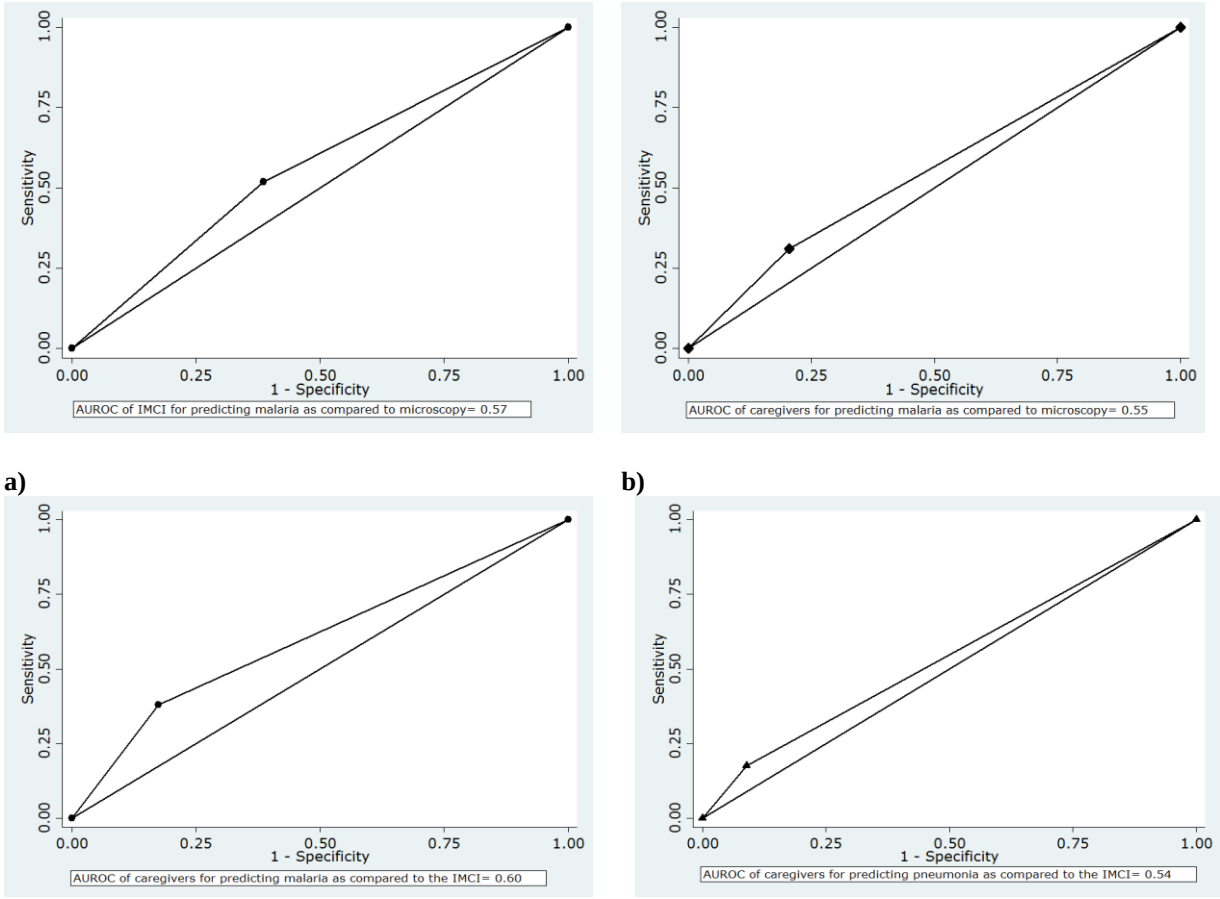


Figure 3.6: **a:** ROC curves and AUROC values of IMCI for predicting malaria as compared with microscopy (reference); **b:** ROC curves and AUROC values of caregivers' diagnosis for predicting malaria as compared with microscopy (reference); **c:** ROC curves and AUROC values of caregivers' diagnosis for predicting malaria as compared with IMCI (reference); **d:** ROC curves and AUROC values of caregivers' diagnosis for predicting pneumonia as compared with IMCI (reference)

Figure 3.7 (below) shows the ROC curves and AUROC values showing a direct comparison between the diagnostic performance of the IMCI guidelines and caregivers for predicting malaria as compared with microscopy (reference diagnostic test).

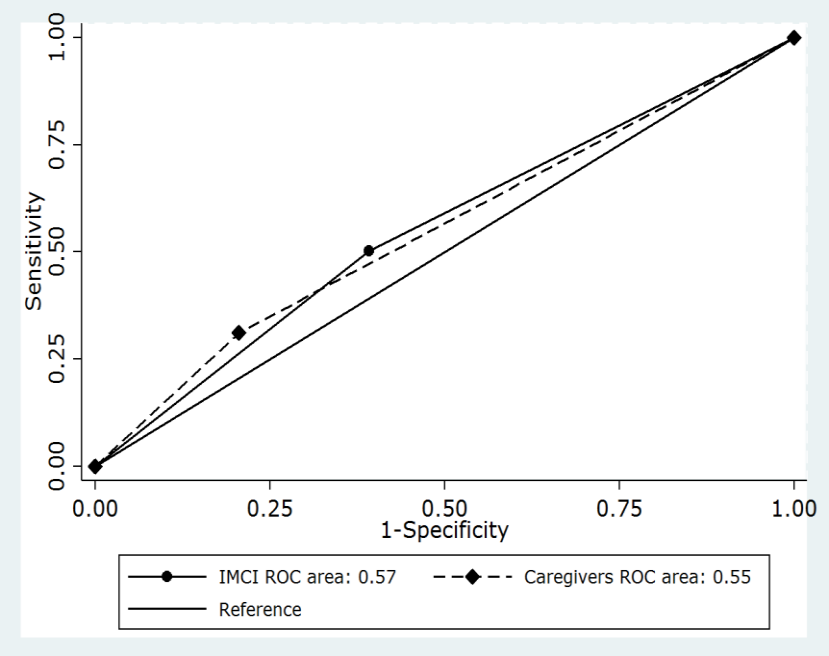


Figure 3.7: ROC curves and AUROC values of the IMCI guidelines and caregivers for predicting malaria as compared to microscopy (gold-standard)

Interobserver variation in the diagnosis of malaria and pneumonia

Table 3.11 (below) shows the results of interobserver agreement between health workers using the IMCI guidelines and caregivers (lay diagnosis) in the diagnosis of malaria and pneumonia. In total, there were 667 cases with diagnosis for both malaria and pneumonia according to the IMCI guidelines and lay diagnosis. The diagnoses made by caregivers are presented along the bottom of the table and those of health workers along the right margin. Caregivers identified 177 (26.54%), 68 (10.19%), 2 (0.30%) and 420 (62.97%) of the 667 children under-five assessed as malaria only, pneumonia only, both

malaria and pneumonia, and neither malaria nor pneumonia, respectively. Health workers with the aid of the IMCI guidelines identified 295 (44.23%), 97 (14.54%), 128 (19.02%) and 147 (22.04%) of the 667 children under-five as malaria only, pneumonia only, both malaria and pneumonia, and neither malaria nor pneumonia, respectively. Except for neither malaria nor pneumonia classification, health workers tended to diagnose more of malaria, pneumonia and both malaria and pneumonia than did caregivers.

Table 3.11: Interobserver variation in the diagnosis of malaria and pneumonia (n=667)

		Caregivers' diagnosis				
Diagnostic class		**1**	**2**	**3**	**4**	**Totals by IMCI (%)**
Health workers' diagnosis using the IMCI guidelines	**1**	**112**	10	1	172	295 (44.23)
	2	7	**17**	0	73	97 (14.54)
	3	41	32	**1**	54	128 (19.20)
	4	17	9	0	**121**	147 (22.04)
Totals by caregivers (%)		177 (26.54)	68 (10.19)	2 (0.30)	420 (62.97)	**667 (100.00)**

Legend for diagnostic classification: 1 = malaria only; 2 = pneumonia only; 3 = both malaria and pneumonia; 4 = neither malaria nor pneumonia

Percent agreement observed	**Percent agreement expected by chance**	**Kappa (95% CI)**	***P*-value**
37.78%	27.30%	**0.14 (0.09-0.19)**	0.0001

The percent agreement observed between health workers using the IMCI guidelines and caregivers seemed low as the value suggested that they both agreed on only 38% of their diagnosis of malaria and pneumonia. Furthermore, the Cohen kappa statistic of 0.14 (95% CI: 0.09-0.19) indicated slight or minimal level of agreement (generally poor) between health workers' and caregivers' diagnosis of malaria and pneumonia. The estimated kappa statistic was statistically significant ($p<0.05$).

3.4.2 Estimating malaria and pneumonia burden among children under-five who presented to PHCs

This study objective presents the estimated burden of malaria and pneumonia by study settings (three LGAs and five PHCs) in relation to various diagnostic approaches, well as by seasonal variables (average monthly temperature, rainfall and humidity) during the 11-month study period.

The estimated burden of malaria in children under-five across various study PHCs

Table 3.12 below summarises the estimated burden of malaria in children under-five who presented to study PHCs over an 11–month period. In total, 2,779 children under-five presented to study PHCs with any complaints during study period. The highest and lowest burden of malaria during the study period were recorded by microscopy with 17.0% (95% CI, 15.6-18.4) and caregivers' diagnosis with 6.4% (95% CI, 5.5-7.3) respectively. The estimated burden of malaria according to the IMCI guidelines was intermediate with 14.6% (95% CI, 13.3-16.0). These findings suggest that for every 100 children that presented to study PHCs with any complaints during the 11-month study period, approximately 15, 17 and 6 had positive diagnosis of malaria as per the IMCI guidelines, microscopy and caregivers' diagnosis respectively.

Regardless of the diagnostic approach, the estimated burden of malaria varied significantly across study Local Government Areas (LGAs) with Egor and Oredo recording the highest and lowest values respectively. A similar pattern was recorded in relation to the individual PHCs with those located in Egor LGA recording the highest number of malaria cases compared to those in Ikpoba-Okha and Oredo LGAs. Specifically, the estimated burden of malaria was overall highest at Evbuotubu PHC according to the three diagnostic approaches: 29.8%, 33.8% and 13.5% for the IMCI

guidelines, microscopy and lay diagnosis, respectively. However, the lowest number of malaria cases according to the IMCI guidelines and caregivers' diagnosis were recorded at Uwelu PHC, while Oredo PHC recorded the lowest number of malaria cases according to microscopy.

Table 3.12: Estimated burden of malaria in children under-five as per study settings (September 2015–July 2016)

Setting	Integrated Management of Childhood Illness (IMCI)		Giemsa stained microscopy		Caregivers' diagnosis	
	Cases of malaria	**Estimated burden per 100 children* (95% C.I.)**	**Cases of malaria**	**Estimated burden per 100 children* (95% C.I.)**	**Cases of malaria**	**Estimated burden per 100 children* (95% C.I.)**
All study PHCs (n=2779)	405	14.6 (13.3-16.0)	471	**17.0 (15.6-18.4)**	177	6.4 (5.5-7.3)
Local government area						
Egor (n=1547)	315	**20.4 (18.4-22.5)**	370	**24.0 (22.0-26.1)**	146	**9.4 (8.0-11.0)**
Ikpoba-Okha (n=694)	65	9.4 (7.3-11.8)	72	10.4 (8.2-12.9)	18	2.6 (1.5-4.1)
Oredo (n=538)	24	4.5 (2.9-6.6) ‡	29	5.4 (3.6-7.6) ‡	13	2.4 (1.3-4.1) ‡
Individual study PHC						
Evbuogida (n=601)	150	25.0 (21.5-28.6)	152	25.3 (21.9-29.0)	68	11.3 (8.9-14.1)
Evbuotubu (n=527)	157	**29.8 (26.0-33.9)**	178	**33.8 (29.7-38.0)**	71	**13.5 (10.7-16.7)**
Uwelu (n=419)	9	2.1 (1.0-4.0)	40	9.5 (6.9-12.8)	7	1.7 (0.7-3.4)
Ugbekun (n=694)	65	9.4 (7.3-11.8)	72	10.4 (8.2-12.9)	18	2.6 (1.5-4.1)
Oredo (n=538)	24	4.5 (2.9-6.6) ‡	29	5.4 (3.6-7.6) ‡	13	2.4 (1.3-4.1) ‡

* The estimated burden of malaria was multiplied by 100 for easier interpretation of small values.

‡ The *p*-value was < 0.001 and the result is significant at $p< 0.05$.

The highest values for malaria burden are in bold fonts.

The estimated burden of pneumonia in children under-five across various study PHCs

Table 3.13 (below) summarises the estimated burden of pneumonia in children under-five who presented to study PHCs over an 11-month period. The overall highest and lowest estimated burden of pneumonia during the 11-month study period was 4.6% (95% CI, 3.9-5.5) and 2.4% (95% CI, 1.9-3.1) according to the IMCI guidelines and caregiver' diagnosis respectively. This suggests that for every 100 children that presented to study PHCs during the 11-month study period, approximately five and two had positive diagnosis of pneumonia as per the IMCI guidelines and caregivers' diagnosis respectively.

The estimated burden of pneumonia varied significantly across the study LGAs and their respective PHCs. This was such that regardless of the diagnostic approach, the highest and lowest number of pneumonia cases were recorded in Egor and Ikpoba-Okha LGAs respectively. Moreover, the highest and lowest number of pneumonia cases at the PHC level corresponded with those located in Egor LGA (i.e. Uwelu PHC) and Ikpoba-Okha LGA (Ugbekun PHC) respectively.

Table 3.13: Estimated burden of pneumonia in children under-five as per study settings (September 2015–July 2016)

Setting	Integrated Management of Childhood Illness (IMCI)		Caregivers' lay diagnosis	
	Cases of pneumonia	Estimated burden per 100 children* (95% C.I.)	Cases of pneumonia	Estimated burden per 100 children* (95% C.I.)
All study PHCs (n=2779)	129	**4.6 (3.9-5.5)**	68	2.4 (1.9-3.1)
Local government area				
Egor (n=1547)	88	**5.7 (4.6-7.0)**	45	**2.9 (2.1-3.9)**
Ikpoba-Okha (n=694)	14	2.0 (1.1-3.4)	13	1.9 (1.0-3.2)
Oredo (n=538)	27	5.0 (3.3-7.20) ‡	10	1.9 (0.9-3.4) †
Individual study PHC				
Evbuogida (n=601)	13	2.2 (1.2-3.7)	19	3.2 (1.9-4.9)
Evbuotubu (n=527)	31	5.9 (4.0-8.2)	12	2.3 (1.2-3.9)
Uwelu (n=419)	44	**10.5 (7.7-13.8)**	14	**3.3 (1.8-5.5)**
Ugbekun (n=694)	14	2.0 (1.1-3.4)	13	1.9 (1.0-3.2)
Oredo (n=538)	27	5.0 (3.3-7.2) ‡	10	1.9 (0.9-3.4) ‡

* The estimated burden of pneumonia was multiplied by 100 for easier interpretation of small values.

‡ The *p*-value is < 0.001 and the result is significant at $p< 0.05$.

† The result is significant at $p< 0.05$.

The highest values for the estimated burden of pneumonia are in bold fonts

The estimated burden of malaria and pneumonia cases over study period, September 2015–July 2016

Table 3.14 (below) summarises the estimated burden of malaria and pneumonia cases across the 11-month study period as per the IMCI guidelines, microscopy (for malaria only) and lay diagnosis. The highest estimated burden of malaria according to the IMCI guidelines (27.4%) and microscopy (28.0%) was recorded in the month of November 2015. In contrast, the highest estimated burden of malaria according to caregivers' diagnosis (26.6%) was recorded in the month of October 2015. Generally, the estimated burden of malaria was substantially higher in the months corresponding to rainy season (September 2015—November 2015). However, there was a steady decrease in the estimated burden of malaria from December 2015 until June 2016 with a slight increase in May 2016. This pattern was evident across the three diagnostic approaches for malaria.

For the estimated burden of pneumonia over the 11-month study period, the highest number of cases according to the IMCI guidelines (30.2%) and caregivers' diagnosis (25.0%) was both recorded in the month of October 2015. Generally, the estimated burden of pneumonia was at its peak between September and November 2015, but decreased variably from December 2015 until July 2016 according to both diagnostic approaches.

Table 3.14: Estimated burden of malaria and pneumonia cases as per the IMCI, microscopy and lay diagnosis over study period (September 2015–July 2016)

Study period	IMCI				Microscopy		Lay diagnosis			
	Malaria (n=405)		Pneumonia (n=129)		Malaria (n=471)		Malaria (n=177)		Pneumonia (n=68)	
	Cases	Estimated burden (%)	Cases	Estimated burden (%)	Cases	Estimated burden (%)	Cases	Estimated burden (%)	Cases	Estimated burden (%)
September 2015	76	18.8	19	14.7	74	15.7	36	20.3	14	20.6
October 2015	77	19.0	39	**30.2**	72	15.3	47	**26.6**	17	**25.0**
November 2015	111	**27.4**	38	29.5	132	**28.0**	39	22.0	14	20.6
December 2015	26	6.4	8	6.2	41	8.7	11	6.2	6	8.8
January 2016	33	8.1	5	3.9	38	8.1	13	7.3	0	0.0
February 2016	7	1.7	8	6.2	18	3.8	4	2.3	6	8.8
March 2016 *	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
April 2016	8	2.0	5	3.9	23	4.9	7	4.0	2	2.9
May 2016	39	9.6	5	3.9	34	7.2	8	4.5	3	4.4
June 2016	12	3.0	1	0.8	16	3.4	4	2.3	2	2.9
July 2016	16	4.0	1	0.8	23	4.9	8	4.5	4	5.8

*Entries for March 2016 were missing due to an industrial action by staff of study health centres.
The highest values for malaria and pneumonia burden are in bold fonts.

The distribution of seasonal variables during study period, September 2015–July 2016

Table 3.15 (below) shows the average monthly temperature (°C), rainfall (mm) and humidity (%) during study period. The highest temperature recorded throughout the study period was in January 2016 (34°C) which corresponded with the peak of dry season in Nigeria. The highest amount of rainfall in 2015 and 2016 was recorded in October 2015 (201.68 mm) and March 2016 (203.36 mm) respectively. The values recorded for humidity during the study period was similar to the recorded pattern of rainfall. This was such that the highest and lowest values corresponded with the peak of rainy season in 2015 (88% recorded in September and October 2015) and dry season (50% in December 2015) respectively.

Table 3.15: The average monthly temperature, rainfall and humidity in Benin City, Nigeria, September 2015–July 2016

Study period	Average Temperature (°C)	Average Rainfall (mm)	Average Humidity (%)
September 2015	29	186.25	88
October 2015	30	201.68	88
November 2015	31	56.15	83
December 2015	33	2.00	50
January 2016	34	9.28	60
February 2016	33	25.70	71
March 2016	32	203.36	81
April 2016	33	140.45	79
May 2016	32	188.46	82
June 2016	30	160.59	85
July 2016	28	201.75	87

The estimated burden of malaria and pneumonia during study period in relation to seasonal variables

Figure 3.8 (below) shows the estimated burden of malaria and pneumonia in relation to the average monthly rainfall and humidity. The top left section of Figure 3.8 shows that there was an increase in the estimated burden of malaria cases as per the IMCI guidelines, microscopy and caregivers' diagnosis during high amount of rainfall in 2015 (September and October). However, there was no corresponding increase in the estimated burden of malaria with increasing amount of rainfall in 2016 (March–July). A similar pattern of association with average monthly rainfall (top right section of Figure 3.8) was recorded for the estimated burden of pneumonia as per the IMCI guidelines and caregivers' diagnosis.

The bottom left and right sections of Figure 3.8, respectively, show the estimated burden of malaria and pneumonia as per the relevant diagnostic approaches in relation to the average monthly humidity. Like the findings for rainfall, higher cases of malaria and pneumonia were recorded in the months with corresponding higher values of humidity.

Figure 3.9 below shows the estimated burden of malaria and pneumonia cases in relation to the average monthly temperature during study period. Moderate monthly temperature values appeared to be associated with higher estimated burden of malaria (top section of Figure 3.9) and pneumonia (bottom section of Figure 3.9).

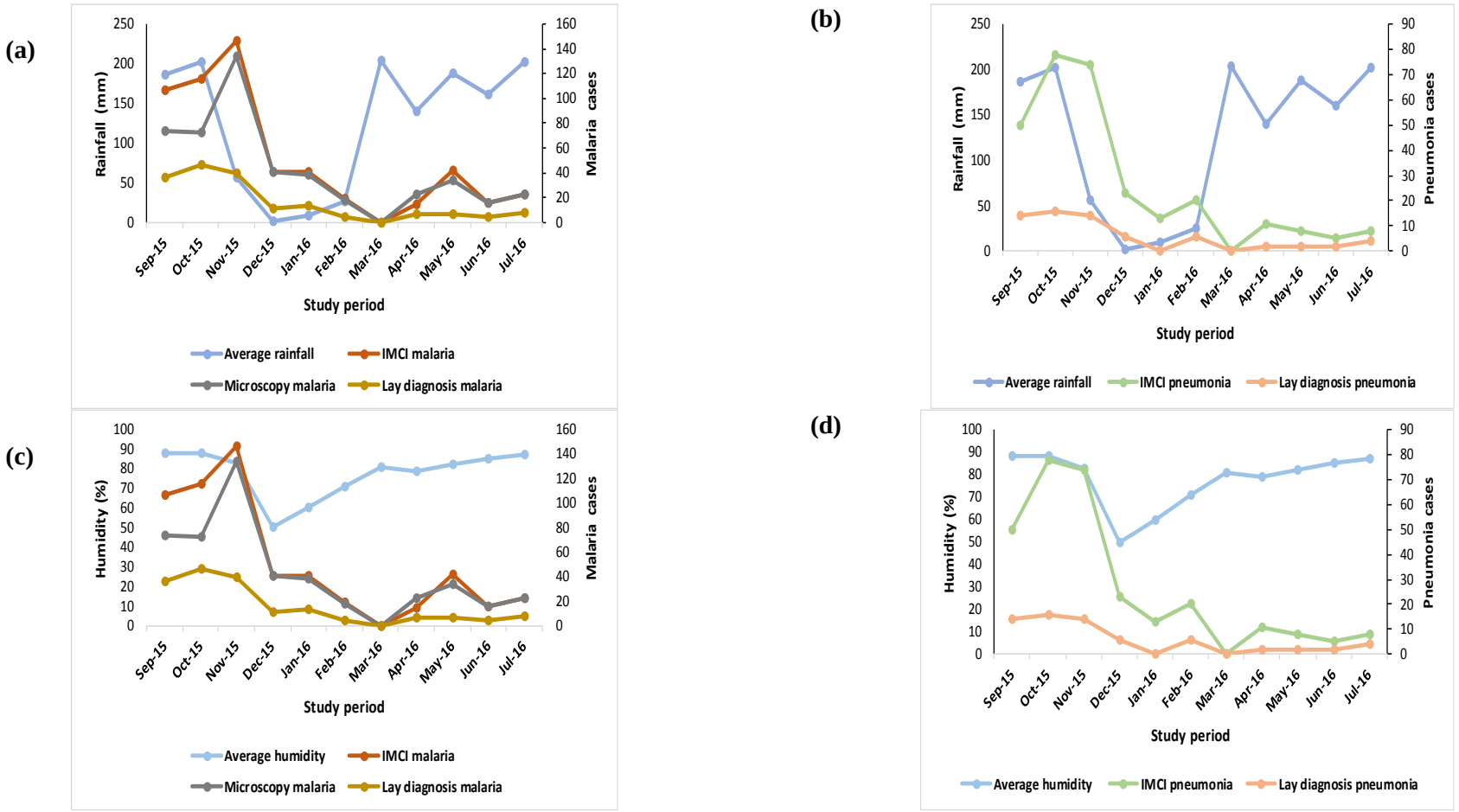
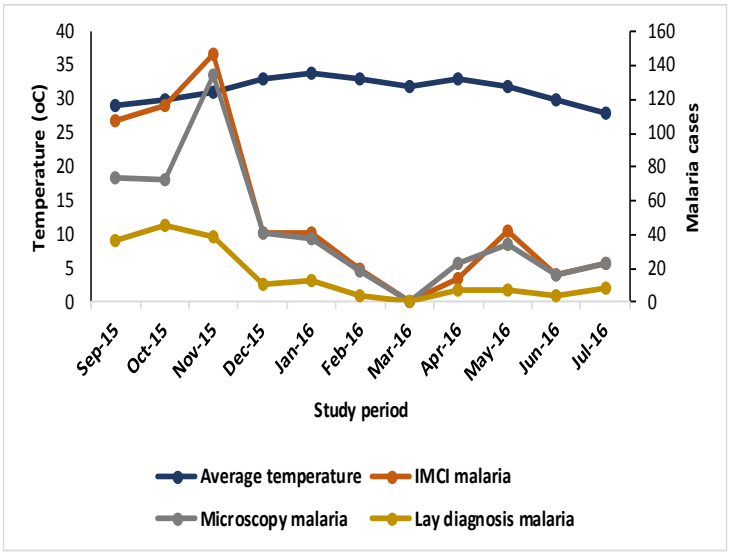


Figure 3.8: Association between average monthly rainfall (a & b) and humidity (c & d) with malaria and pneumonia cases



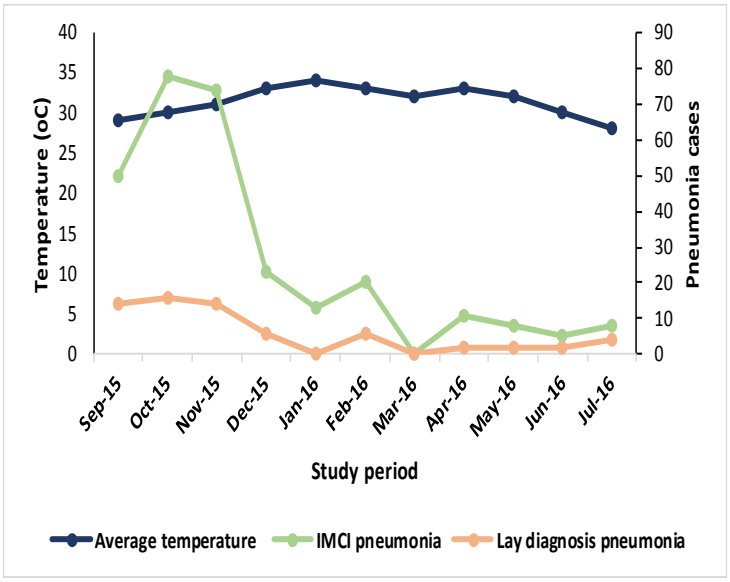


Figure 3.9: Association between average monthly temperature and malaria (a) and pneumonia (b) cases

3.4.3 Assessing clinical outcomes in children diagnosed with malaria and pneumonia and risk factors for severe outcomes

Overview of study participants that were followed-up and lost-to follow-up

Twenty-six per cent (235/903) of the total eligible children recruited into this study were lost-to follow-up during the 30 days follow-up period following initial assessment at study PHCs. Primary reasons for the loss-to follow-up were due to incorrect house addresses and mobile phone numbers (and occasionally being switched-off) provided by caregivers. There were also instances when follow-up was not possible due to inaccessible roads to caregivers' residence. On the other hand, 74% (668/903) of the total children under-five who met study eligibility criteria and assessed at the study PHCs were followed-up within 30 days for a mean duration of 18 days.

Distribution of clinical outcomes in children diagnosed with malaria and pneumonia according to the IMCI guidelines

Of the 668 children that were followed-up, 45.51% (304/668) and 15.57% (104/668) were diagnosed by the IMCI guidelines as having malaria and pneumonia respectively. Analyses in this section of the study were therefore restricted to this subsect of study participants (304 and 104 for IMCI malaria and pneumonia respectively). Table 3.16 (below) provides a summary of the follow-up (i.e. within 30-day follow-up period) clinical outcomes in children diagnosed with malaria and pneumonia according to the IMCI guidelines. The level of adherence or compliance to medications as reported by caregivers at follow-up was high in children diagnosed with both malaria 98.03% (298/304) and pneumonia 98.08% (102/104). However, the level of adherence to medications was verified in person (objective verification) only in 58.22% (177/304) and 22.12% (23/104) of the children diagnosed with malaria and pneumonia

respectively. The objective verification of medication intake involved visually inspecting drug pack or container by the researcher or research assistants during home-visits as part of the follow-up protocol. This implies that the level of adherence to medications, especially for diagnosed pneumonia cases, was mostly ascertained through phone calls to the designated caregivers.

There were four hospitalisations (4/304) and two deaths (2/304) in children diagnosed with malaria. The number of hospitalisations and deaths in children diagnosed with pneumonia were two (2/104) and one (1/104) respectively. Within the 30-day follow-up period, 43.42% (132/304) and 22.12% (23/104) of the children diagnosed with malaria and pneumonia, respectively, developed severe illness. Severe illness was defined as any form of complications, additional presentation to any PHCs or hospitals and/or death within the 30-day follow-up period. Regarding illness progression, most of the children diagnosed with malaria (186/304) and pneumonia (84/104) recovered within the 30-day follow-up period. However, illness in 2.30% (7/304) and 1.92% (2/104) of the children diagnosed with malaria and pneumonia, respectively, had not resolved but became worse or severe.

Table 3.16: Distribution of clinical outcomes in children under-five diagnosed with malaria and pneumonia according to the IMCI guidelines

Follow-up outcome	IMCI Malaria (%)	IMCI Pneumonia (%)
	n=304	***n=104***
Reported adherence to medication		
No	2 (0.66)	0 (0.00)
Yes	298 (98.03)	102 (98.08)
Missing	4 (1.32)	2 (1.92)
Objective verification of medication intake		
No	123 (40.46)	79 (75.96)
Yes	177 (58.22)	23 (22.12)
Missing	4 (1.32)	2 (1.92)
Hospitalisation		
No	300 (98.68)	102 (98.08)
Yes	4 (1.32)	2 (1.92)
Death		
No	289 (95.07)	100 (96.15)
Yes	2 (0.66)	1 (0.96)
Missing	13 (4.28)	3 (2.88)
Severe illness		
No severe illness	172 (56.58)	81 (77.88)
Severe illness	132 (43.42)	23 (22.12)
Progression of illness		
Resolved	186 (61.18)	84 (80.77)
Unresolved/Unchanging	111 (36.51)	18 (17.31)
Worsening	7 (2.30)	2 (1.92)

Potential risk factors for severe illness in children diagnosed with malaria

The unadjusted and multiple regression analyses to determine the independent predictors for severe illness of children diagnosed with malaria are presented in Table 3.17 (below). A month increase in age appeared not to be associated (p>0.05) with the occurrence of severe illness in children diagnosed with malaria by the IMCI guidelines. Overall, lower socioeconomic status appeared to offer protection to children from developing severe illness within 30 days of malaria diagnosis, but this association was not statistically significant (p>0.05). However, administration of medications prior to presenting to the study PHCs and adoption of protective measures against malaria (e.g. ownership of

mosquito long-lasting insecticide–treated bed nets (LLINs), living in houses with netted doors/windows and use of vector control measures –indoor residual spray (IRS)– and intermittent treatment of malaria) appeared to be significantly (p<0.05) associated with reduced risk of severe illness in children within 30 days of malaria diagnosis. In contrast, presentation to study PHCs with any general danger signs, exposure to solid fuels during a stay with caregiver while cooking with firewood or stove in the kitchen and living in a large family (>2 persons) appeared to increase the odds of a child developing severe illness after being diagnosed with malaria. However, the associations of family size and presentation to study PHCs with any general danger signs with the occurrence of severe illness following malaria diagnosis were not statistically significant (p>0.05). The following variables whose p-values (LRT p-values for categorical variables) were statistically significant were included in the multiple regression model: self-medication, ownership of mosquito net, netted doors/windows, intermittent treatment of malaria, vector control (i.e. use of indoor residual spray), exposure to solid fuel and family size.

Following adjustment in the multiple regression model, self-medications prior to presenting to the study PHCs [OR (95% C.I.): 0.54 (0.30-1.00)] and living in houses where vector control measures are practiced remained associated with reduced odds of a child developing severe illness following a positive diagnosis of malaria. However, these findings need to be interpreted with caution given that the statistical significance was borderline (p-values were 0.050 and 0.054 for self-medications and use of vector control measures respectively). The adoption of other preventive measures (e.g. ownership of LLINs, netting of windows/doors, and intermittent treatment of malaria) however remained significant. In contrast, only the exposure to solid fuels [OR (95%

C.I.): 2.69 (1.12-6.48)] remained significantly associated with increased odds of a child developing severe illness after a positive diagnosis of malaria.

Table 3.17: Risk factors for severe illness in children with malaria as per IMCI guidelines (n=304)

Risk factor	Severe illness		Unadjusted OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
	No (n=172)	Yes (n=132)				
Age (in months) (Mean/SD)	25.30 (15.68)	25.58 (14.48)	1.00 (0.10-1.02)	0.872		
Socioeconomic status						
Class I & II (most affluent)	25 (14.53)	35 (26.52)	1.00			
Class III	31 (18.02)	24 (18.18)	0.55 (0.26-1.16)	0.117		
Class IV	89 (51.74)	52 (39.39)	0.42 (0.23-0.77)	0.005		
Class V (worse-off)	17 (9.88)	11 (8.33)	0.46 (0.18-1.15)	0.099		
Missing	10 (5.81)	10 (7.58) NS				
Self-medication for illness						
No	38 (22.09)	45 (34.09)	1.00		1.00	
Yes	125 (72.67)	80 (60.61)	0.54 (0.32-0.90)	0.019	0.54 (0.30-1.00)	0.050
Missing	9 (5.23)	7 (5.30) NS				
Any general danger signs						
No	156 (90.70)	113 (85.61)	1.00			
Yes	16 (9.30)	18 (13.64)	1.55 (0.76-3.18)	0.228		
Missing	0 (0.00)	1 (0.76) NS				
Ownership of mosquito net						
No	86 (50.00)	97 (73.48)	1.00		1.00	
Yes	86 (50.00)	35 (26.52) ‡	0.36 (0.22-0.59)	0.001	0.46 (0.25-0.84)	0.012
Netted doors/windows						
No	56 (32.56)	83 (62.88)	1.00		1.00	
Yes	116 (67.44)	49 (37.12) ‡	0.29 (0.18-0.46)	0.001	0.53 (0.30-0.96)	0.035
Vector control measures						
No	68 (39.53)	77 (58.33)	1.00		1.00	
Yes	103 (59.88)	54 (40.91)	0.46 (0.29-0.74)	0.001	0.59 (0.35-1.00)	0.054
Missing	1 (0.58)	1 (0.76) †				
Intermittent treatment of malaria						
No	118 (68.60)	110 (83.33)	1.00		1.00	
Yes	54 (31.40)	22 (16.67) †	0.44 (0.25-0.76)	0.004	0.37 (0.20-0.70)	0.002
Exposure to solid fuels						
No	32 (18.60)	9 (6.82)	1.00		1.00	
Yes	136 (79.07)	122 (92.42)	3.19 (1.46-6.94)	0.004	2.69 (1.12-6.48)	0.027

Missing	4 (2.33)	1 (0.76) †				
Family size						
1 person	6 (3.49)	1 (0.76)	1.00		1.00	
2 persons	27 (15.70)	6 (4.55)	1.33 (0.13-13.22)	0.806	1.06 (0.97-11.50)	0.961
3-6 persons	118 (68.60)	119 (90.15)	6.05 (0.72-51.03)	0.098	4.78 (0.51-44.33)	0.169
≥7 persons	3 (1.74)	0 (0.00)	Omitted		Omitted	
Missing	18 (10.47)	6 (4.55) ‡				

†= p<0.05; ‡=p<0.001; NS=Not significant (p≥0.05)

Statistically significant results are in bold fonts, while the blank cells are indicative of variables that were not statistically significant in the unadjusted model and omitted from the adjusted model. These p-values are Wald's p-vales. P-values from LRT were used to decide which categorical variable to add onto the adjusted model.

All values are presented as the odds of having the outcome if malaria was positive according to the IMCI guidelines.

Potential risk factors for progression of illness in children diagnosed with malaria

The unadjusted and multiple regression analyses to determine the independent predictors for progression of illness in children diagnosed with malaria are presented in Table 3.18 (below). In the unadjusted analysis, a month increase in age and low socioeconomic status appeared to be contributing to lowering the risk of illness worsening within 30 days of malaria diagnosis. In addition, self-medication prior to presenting to the study PHCs, ownership of LLINs, living in houses with netted doors/windows and where control of vector and intermittent treatment of malaria were practised appeared to reduce the risk of illness becoming worse within 30 days of malaria diagnosis. In contrast, presenting to the study PHCs and staying with a caregiver while cooking with firewood or stove in the kitchen appeared to increase the risk of illness becoming worse within 30 days of malaria diagnosis.

Self-medication, preventive measures against malaria and exposure to solid fuels were included in the adjusted multivariable analysis given that they were statistically significant in the unadjusted analyses. In the adjusted multivariable analysis, self-medication prior to presenting to the study PHCs [OR (95% C.I.): 0.53 (0.29-0.97)], living in houses with netted doors/windows [OR (95% C.I.): 0.25 (0.14-0.46)] and where control of vector [OR (95% C.I.): 0.49 (0.29-0.85)] and intermittent treatment of malaria [OR (95% C.I.): 0.33 (0.16-0.66)] were practised remained significantly associated with a decreased risk of illness becoming worse within 30 days of malaria diagnosis. However, children exposed to solid fuels following a positive diagnosis of malaria were nearly thrice as likely [OR (95% C.I.): 2.96 (1.20-7.29)] to experience worsened illness compared to their counterparts whose caregivers used clean gas for cooking.

Table 3.18: Risk factors for progression of illness in children diagnosed with malaria according to the IMCI guidelines (n=304)

Risk factor	Progression of illness (%)		Unadjusted OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
	Resolved (n=186)	Unresolved/Worsening (n=118)				
Age (months) (Mean/SD)	25.44 (15.57)	25.40 (14.53)	0.99 (0.98-1.02)	0.981		
Socioeconomic status						
Class I & II (most affluent)	28 (15.05)	32 (27.12)	1.00			
Class III	35 (18.82)	20 (16.95)	0.50 (0.24-1.06)	0.069		
Class IV	93 (50.00)	48 (40.68)	0.45 (0.24-0.84)	0.011		
Class V (worse-off)	18 (9.68)	10 (8.47)	0.49 (0.20-1.23)	0.126		
Missing	12 (6.45)	8 (6.78) **NS**				
Self-medication for illness						
No	**40 (21.51)**	**63 (36.44)**	**1.00**		**1.00**	
Yes	**136 (73.12)**	**69 (58.47)**	**0.47 (0.28-.080)**	**0.005**	**0.53 (0.29-0.97)**	**0.041**
Missing	**10 (5.38)**	**6 (5.08)** †				
Any general danger signs						
No	168 (90.32)	101 (85.59)	1.00			
Yes	18 (9.68)	16 (13.56)	1.47 (0.72-3.03)	0.285		
Missing	0 (0.00)	1 (0.85) NS				
Ownership of mosquito net						
No	94 (50.54)	89 (75.42)	1.00		1.00	
Yes	92 (49.46)	29 (24.58) ‡	0.33 (0.20-0.55)	0.001	0.62 (0.33-1.15)	0.126
Netted doors/windows						
No	**58 (31.18)**	**81 (68.64)**	**1.00**		**1.00**	
Yes	**128 (68.82)**	**37 (31.36)** ‡	**0.21 (0.13-0.34)**	**0.001**	**0.25 (0.14-0.46)**	**0.001**
Vector control measures						
No	**71 (38.17)**	**74 (62.71)**	**1.00**		**1.00**	
Yes	**114 (61.29)**	**43 (36.44)**	**0.36 (0.22-0.58)**	**0.001**	**0.49 (0.29-0.85)**	**0.011**
Missing	**1 (0.54)**	**1 (0.85)** ‡				
Intermittent treatment of malaria						
No	**126 (67.74)**	**102 (86.44)**	**1.00**		**1.00**	
Yes	**60 (32.26)**	**16 (13.56)** ‡	**0.33 (0.18-0.61)**	**0.001**	**0.33 (0.16-0.66)**	**0.002**
Exposure to solid fuels						
No	**33 (17.74)**	**8 (6.78)**	**1.00**		**1.00**	

Yes	**148 (79.57)**	**110 (93.22)**	**3.07 (1.36-6.90)**	**0.007**	**2.96 (1.20-7.29)**	**0.019**
Missing	**5 (2.69)**	**0 (0.00) †**				

†= $p<0.05$; ‡=$p<0.001$; NS=Not significant ($p\geq0.05$)

Statistically significant results are in bold fonts, while the blank cells are indicative of variables that were not statistically significant in the unadjusted model and omitted from the adjusted model. These *p*-values are Wald's p-vales. P-values from LRT were used to decide which categorical variable to add onto the adjusted model.

All values are presented as the odds of having the outcome if malaria was positive according to the IMCI guidelines.

Potential risk factors for severe illness in children diagnosed with pneumonia

The results of the unadjusted analyses to determine the independent predictors for severe illness in children diagnosed with pneumonia are presented in Table 3.19 (below). In the unadjusted analyses, a month increase in age does not seem to be associated with the occurrence of severe illness within 30 days of pneumonia diagnosis according to the IMCI guidelines. While lower socioeconomic status appeared to be generally associated with increased risk of severe illness, being in Class III (average socioeconomic status) however seemed to offer some level of protection compared to the most affluent children (Class I and II). Children who had taken medications before presenting to the study PHCs, presented to the study PHCs with any general danger signs and were exclusively breastfed for the first six months of life appeared to have lower odds of developing severe illness within 30 days of being diagnosed with pneumonia. However, these associations were not statistically significant ($p>0.05$). In contrast, living with a family member who smoke, being exposed to solid fuels in the kitchen and having been given prelacteal feeding within the first six months of life appeared to increase the risk of a child developing severe illness after being diagnosed with pneumonia. Similarly, the association between severe illness and these variables were not statistically significant. Thus, none of these variables was considered for adjustment in a multiple regression model to identify independent predictors for severe within 30 days of pneumonia diagnosis.

Table 3.19: Risk factors for severe illness in children diagnosed with pneumonia according to the IMCI guidelines (n=104)

Risk factors	Severe illness (%)		Unadjusted OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
	No (n=81)	Yes (n=23)				
Age (in months) (Mean/SD)	13.70 (13.06)	13.78 (14.80)	1.00 (0.97-1.04)	0.980		
Socioeconomic status						
Class I & II (most affluent)	17 (20.99)	4 (17.39)	1.00			
Class III	17 (20.99)	3 (13.04)	0.75 (0.15-3.88)	0.731		
Class IV	36 (44.44)	14 (60.87)	1.65 (0.47-3.87)	0.432		
Class V (worse-off)	5 (6.17)	2 (8.70)	1.70 (0.24-12.17)	0.597		
Missing	6 (7.41)	0 (0.00) NS				
Self-medication for illness						
No	21 (25.93)	7 (30.43)	1.00			
Yes	57 (70.37)	16 (69.57)	0.84 (0.31-2.33)	0.741		
Missing	3 (3.70)	0 (0.00) NS				
Any general danger signs						
No	73 (90.12)	21 (91.30)	1.00			
Yes	7 (8.64)	2 (8.70)	0.99 (0.20-5.14)	0.994		
Missing	1 (1.23)	0 (0.00) NS				
Family member smoke						
No	66 (81.48)	17 (73.91)	1.00			
Yes	15 (18.52)	6 (26.09) NS	1.55 (0.52-4.60)	0.427		
Exposure to solid fuels						
No	33 (40.74)	6 (26.09)	1.00			
Yes	45 (55.56)	17 (73.91)	2.08 (0.74-5.84)	0.165		
Missing	3 (3.70)	0 (0.00) NS				
Prelacteal feeding within first 6 months						
No	54 (66.67)	14 (60.87)	1.00			
Yes	27 (33.33)	9 (39.13) NS	1.29 (0.49-3.35)	0.607		
Exclusive breastfeeding for first 6 months						
No	27 (33.33)	9 (39.13)	1.00			
Yes	54 (66.67)	14 (60.87) NS	0.78 (0.30-2.02)	0.607		

NS=Not significant ($p \geq 0.05$)

The blank cells are indicative of variables that were not statistically significant in the unadjusted model and omitted from the adjusted model. These *p*-values are Wald's p-vales.
All values are presented as the odds of having the outcome if malaria was positive according to the IMCI guidelines.

Potential risk factors for progression of illness in children diagnosed with pneumonia

Table 3.20 **(**below) presents the results of the unadjusted and multiple regression analyses to determine independent predictors for the progression of illness in children diagnosed with pneumonia. In the unadjusted analyses, a month increase in age does not seem to be associated with the occurrence of severe illness within 30 days of pneumonia diagnosis according to the IMCI guidelines. Children who had taken medications prior to presenting to the study PHCs and were exclusively breastfed within the first six-month of life appeared to be less likely to develop worsened illness within 30 days of being diagnosed with pneumonia. In contrast, lower socioeconomic status, presenting to the study PHCs with any general danger signs, living in houses where family member smoke, exposure to solid fuels in the kitchen and having been given prelacteal feed within the first six months of life appeared to increase the risk of illness worsening within 30 days of pneumonia diagnosis. The associations between progression of illness and these variables were not statistically significant (p>0.05). Thus, none of these variables was considered for adjustment in multiple regression analysis model to identify independent predictors for worsened illness within 30 days of pneumonia diagnosis.

Table 3.20: Risk factors for progression of illness in children diagnosed with pneumonia according to IMCI (n=104)

Risk factors	Progression of illness (%)		Unadjusted OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
	Resolved (n=84)	Unresolved/Worsening (n=20)				
Age (months) (Mean/SD)	13.58 (12.96)	14.30 (15.44)	1.00 (0.97-1.04)	0.829		
Socioeconomic status						
Class I & II (most affluent)	18 (21.43)	3 (15.00)	1.00			
Class III	17 (20.24)	3 (15.00)	1.06 (0.19-5.98)	0.948		
Class IV	38 (45.24)	12 (60.00)	1.89 (0.47-7.56)	0.365		
Class V (worse-off)	5 (5.95)	2 (10.00)	2.30 (0.31-18.55)	0.401		
Missing	6 (7.14)	0 (0.00) NS				
Self-medication for illness						
No	21 (25.00)	7 (35.00)	1.00			
Yes	60 (71.43)	13 (65.00)	0.65 (0.23-1.85)	0.419		
Missing	3 (3.57)	0 (0.00) NS				
Any general danger signs						
No	76 (90.48)	18 (90.00)	1.00			
Yes	7 (8.33)	2 (10.00)	1.21 (0.23-6.30)	0.824		
Missing	1 (1.19)	0 (0.00) NS				
Exposure to solid fuels						
No	34 (40.48)	5 (25.00)	1.00			
Yes	47 (55.95)	15 (75.00)	2.17 (0.72 -6.55)	0.169		
Missing	3 (3.57)	0 (0.00) NS				
Family member smoke						
No	68 (80.95)	15 (75.00)	1.00			
Yes	16 (19.05)	5 (25.00) NS	1.42 (0.45-4.47)	0.553		
Prelacteal feeding within first 6 months						
No	56 (66.67)	12 (60.00)	1.00			
Yes	28 (33.33)	8 (40.00) NS	1.33 (0.49-3.64)	0. 574		
Exclusive breastfeeding for first 6 months						
No	28 (33.33)	8 (40.00)	1.00			
Yes	56 (66.67)	12 (60.00) NS	0.75 (0.28-2.04)	0.574		

NS=Not significant ($p \geq 0.05$)
The blank cells are indicative of variables that were not statistically significant in the unadjusted model and omitted from the adjusted model. These *p*-values are Wald's p-vales.
All values are presented as the odds of having the outcome if malaria was positive according to the IMCI guidelines.

3.5 Results of the qualitative component

3.5.1 Exploring stakeholder perspectives of lay diagnosis and IMCI guidelines as diagnostic approaches for malaria and pneumonia

Following an overview of the interviews, findings of this study objective are presented in two sections: 1) stakeholder perspectives on lay diagnosis of malaria and pneumonia (primarily caregivers' views with reference to the views of health professionals where relevant) and 2) stakeholder perspectives of the IMCI guidelines (only health professionals' perspectives). Unless otherwise stated, primary healthcare workers (PHWs) (including junior and senior community health extension workers, matrons and nurses) and other health professionals (PHC coordinators, clinicians, disease surveillance & notification officer, and IMCI training facilitators) are collectively referred to as 'health professionals' (HPs) in this study. Additionally, caregivers in this study refer to parents, guardians or relatives.

3.5.2 Interviews

The interviews of both caregivers (n=13) and HPs (n=17) in the qualitative component were conducted between February 2016 and May 2016. The average durations for interviewing caregivers and HPs were 23 minutes 24 seconds (range between 17 minutes 53 seconds and 33 minutes 12 seconds) and 22 minutes 10 seconds (range between 13 minutes 12 seconds and 44 minutes 22 seconds) respectively.

3.5.3 Stakeholder perspectives on lay diagnosis of malaria and pneumonia

Overall, four themes (bold and italicized fonts) were identified as shown in Table 3.21 below.

Table 3.21: Overview of main themes and sub-themes of stakeholder perspectives on lay diagnosis of malaria and pneumonia

Themes	Sub-theme 1	Sub-theme 2	Sub-theme 3
Perceptions of lay diagnosis	Meaning of lay diagnosis	Appropriateness & benefits of lay diagnosis	Contributing factors to the practice of lay diagnosis
Perceived severity, self-efficacy and diagnostic criteria for malaria & pneumonia	Perceived severity of malaria & pneumonia	Perceived self-efficacy	Diagnostic criteria
Lay management of malaria and pneumonia	Treatment pathways for suspected malaria	Treatment pathways for suspected pneumonia	Role of faith in seeking healthcare services
Perceptions on training caregivers to use the IMCI guidelines	Perceived benefits of training caregivers in IMCI guidelines	Receptiveness and challenges to training caregivers in the IMCI guidelines	

3.5.3.1 Perceptions on lay diagnosis

The following three sub-themes were identified: meaning of lay diagnosis; appropriateness & benefits of lay diagnosis; and contributing factors to the practice of lay diagnosis.

3.5.3.1.1 Meaning of lay diagnosis

Twelve of the respondents described lay diagnosis to be routine, convenient and cultural practice. Lay diagnosis, admittedly practiced by most of the caregivers, was regarded as being important for early intervention that would, in turn, prevent the development of

severe illnesses and consequent high expenditure on medications and other related health services.

> **04:** "I don't know what the factors are, just that we're used to it. I don't know if there is any factors (sic). We grow up giving self-medication, everybody in Nigeria is a doctor, a doctor that's not trained." *Civil servant & mother of five children*

Moreover, three caregivers seemed to believe that lay diagnosis was a mother's duty and aided by her perceptiveness to recognise early signs and symptoms of illnesses in children.

> **05:** "I feel that the children, for children that have not started school, they are always with their parents and most times parents have, they are very perceptive when their child start (sic) changing in behaviour." *University lecturer & mother of two children*

3.5.3.1.2 Appropriateness & benefits of lay diagnosis

Caregiver views

While most of the caregivers believed that lay diagnosis was not appropriate, it was nevertheless found to be relied on by caregivers in the study setting. Some caregivers provided a detailed description of the signs and symptoms for the lay diagnosis of malaria but admitted that the approach was limited, unreliable and could be deceptive.

> **07:** "Generally, I think I will say self-diagnosis is not safe because it may not be reliable as you think because there are certain signs that are common with different illnesses. However, it is a major practice especially in this part of the country. I'm also guilty of it." *University lecturer & mother of two children*

Five of the respondents were concerned that if lay diagnosis was inaccurate it could cause adverse side-effects following the administration of medications purchased from chemist stores. Hence, there was the belief that instead of lay diagnosis, standard diagnostic test results ought to guide the choice of medications for treatment.

> **11:** "My view is, it's not good to diagnose for ourselves because it leads to so many things. If our children are sick, we're supposed to meet a doctor to prescribe the drugs for us. It's not good and can cause many things because some drugs, if you buy some drugs yourself it might lead to, maybe the drug is not for the sickness and the child takes the drugs, it might lead to bad effects." *Primary school teacher & mother of two children*

While two caregivers mentioned that they would not attempt to diagnose their children themselves, the incidence of fever or suspected malaria at night prompted them to resort to lay diagnosis. As such, lay diagnosis was reported to be beneficial particularly at night when the community primary healthcare centre (PHCs) would have closed and there was no nearby alternative health centre.

> **01:** "…self-diagnosis can help you at night especially when you don't have mobility to take your child out [to a nearby healthcare centre]." *Self-employed & mother of a child*

Health professional views

Four HPs agreed with the views of most caregivers on the inappropriateness of lay diagnosis. According to these HPs, lay diagnosis contributed to the waste of limited funds in purchasing wrong medications, and this, in turn, could contribute to late presentation to a health centre and development of severe clinical outcomes.

> **15:** "It is not good. I see some women running down and say they want to have malaria test before any treatment. By the time we do the test, at times we will see them (sic) negative or positive and we will say yes, because they have been treating this child, there is no improvement. I will say this child has malaria, where are the drugs that you have been using? At times they brought some that you don't even know the names, they brought about six and I will say all these ones are not for malaria. These are to relieve you from pain." *Junior community health extension worker*

However, a disease surveillance and notification officer believed that there was a possibility of using validated lay diagnosis by caregivers for the surveillance of malaria. The HP believed that once validated with a standard diagnostic test, he would be willing and confident to use the lay diagnosis of malaria by caregivers for surveillance purpose.

19: "…if it is reliable and the equipment have been tested and ok, that self-diagnosis in respect of malaria will be more effective. I, as a disease surveillance officer, will yield to such services." *Disease surveillance and notification officer*

3.5.3.1.3 Factors contributing to the practice of lay diagnosis

Caregiver views

There was consensus amongst caregivers that financial hardship was the primary reason for reliance on lay diagnosis. Despite the awareness of its limitations, it seemed caregivers relied on lay diagnosis to economize on limited financial resources. Unlike lay diagnosis that mostly culminates in the purchase of medications at chemist or pharmacy stores at a relatively cheap cost, many caregivers believed that presenting to a formal healthcare centre involved spending more money for various medical services such as registration, diagnosis, treatment and consultation.

02: "Well, because sometimes it's not everybody that have that money. When you come to hospital, they say, you must come and give injection. It's not everybody that have that money for injection." *Business woman & mother of 2 children*

10 Pidgin-English: "…maybe na the money, dem say come do test, come do this one. Maybe because of that one you go just guess then go buy medicine." *Tailor/petty trader & mother of three children*

English translation: *Maybe it's because of money needed to cover the cost of tests and other expenses. As a result, you'd rather guess and purchase medications.*

Interestingly, three caregivers believed that money was not the primary determining factor for the reliance on lay diagnosis for suspected malaria; rather, it was the widespread practice to first try to manage illness at home before seeking professional health care.

04: "…but naturally, even if the money is there, they would first of all treat before they would now look for the doctor." *Civil servant & mother of five children*

Moreover, the perception of malaria being a 'common' illness was identified as a contributing factor to the reliance on lay diagnosis. This could partly be explained by the endemicity of malaria in Nigeria and the consequent familiarity by many people with basic symptoms and medications for treatment. A quote from one of the caregivers buttresses this argument.

> **11:** "Some people have the habit of, even though they have money, they will say abeg [common] is it not common malaria? Let me just go to the chemist and buy malaria medicine for her, the malaria will go." *Primary school teacher & mother of two children*

Challenges in accessing formal healthcare services or frequent delays were also reported as a contributing factor to the practice of lay diagnosis. According to five caregivers, accessing formal healthcare services was stressful and often involved considerable time and money given the distance from their residence.

> **07:** "Accessing healthcare could be a very long and tedious process. The way it is here, you have a sick child, you go to the hospital, you even have to go through a lot of stress to get to the hospital in the first place because the roads are bad and getting to the hospital you have to wait a long queue to get your card and then you queue up again probably for hours to see the doctor. You know it's a very cumbersome and very discouraging process." *University lecturer & mother of two children*

The potential impact of delay was more prominent among business women, some of whom were the breadwinners of their families. To avoid experiencing loss in their businesses, these caregivers reported they would prefer to purchase medications at nearby chemist stores.

> **06 Pidgin-English:** "Reason wen me still know again be say as some wan take come hospital, e get as e be, dem go dey look am say time, no chance, dem go say before I go go hospital again come sit down there, time go don go, that time this work when I dey work I nor go see chance tey come. Make I kuku buy for chemist here make this work nor come pass me because I nor go see chance tey go hospital because if I go hospital today before I come do everything, evening go reach. That time this work this market nor go get head." *Petty trader & mother of five children*
>
> **English translation:** *Another reason I know for the reliance on lay diagnosis is the delays at hospitals. Instead of spending so much time at the hospital, I would prefer to just buy some medications at a*

nearby chemist store so that my business will not be affected. If I visit the hospital, I may return to the market by evening time and by then the business may not be productive.

Social influence from neighbours, friends, family members or relatives was recognised as a reason for the practice of lay diagnosis. Some caregivers seemed confident about their lay diagnosis because of 'validation' by someone making a reference to previous illnesses like that experienced by their children and therefore, did not feel the need to go to the PHC or other healthcare professionals for a formal diagnosis. Social influence seemed to be dependent on caregivers' level of awareness of common illnesses and financial power, as well as educational attainment. Compared with caregivers who had post-secondary school education, those with primary school education and mostly petty traders had relatively poor knowledge of malaria and were more willing to seek advice from neighbours. Unrestricted access to over-the-counter (OTC) medications and the availability of native herbs were identified as contributing factors to the reliance on lay diagnosis.

06 Pidgin-English: "Some dey ask questions, maybe leg dey pain am, all this leg all this joints, as e dey waka joints dey pain am then e fit ask people: if I dey waka joints dey pain me. Some go say na rheumatism, some go say this one, dem go dey give am different different names. Dem e go come ask which kind medicine e go buy as e be say no money as person talk am. E go come ask say which kind medicine I go fit buy when go cure am, then maybe dem go tell am buy this one buy this one buy that one." *Petty trader & mother of five children*
English translation: *Some persons ask questions regarding leg and joint pains. For example, a person could tell a neighbour or relatives that he/she experiences pains around the joints when walking. The neighbours or relatives asked would then provide a lay diagnosis of rheumatism and all sorts. The person experiencing the pain would then ask for the most effective and cheapest medication given the lack of sufficient funds. Similar to the lay diagnosis, there will be several suggestions of medications.*

Health professional views

Fourteen of the HPs agreed with the caregivers' views that having limited finance was the major reason for the practice of lay diagnosis. In addition, three of the HPs believed

that difficulty accessing healthcare services and proximity to chemist stores were influential to caregivers' reliance on lay diagnosis.

> **29:** "When they come to the hospital or the health centres, they have to be away from work. Then they sit on a long queue before it gets to their turn and then when they finish, the drugs are probably not available in the health centre so they have to go and buy it in the chemist. So why don't you just go straight to the chemist and remove all that long queue and all that." *Consultant paediatrician & IMCI training facilitator*
>
> **23:** "Chemist [store] is closer to them than health facility because they have it at their compound and nearby while health facility is about few miles from the setting. Not everyone is closer to it, but we have chemist almost two, two houses. It's easier for them to get to." *Matron & manager of a PHC*

3.5.3.2 Perceived severity, self-efficacy and diagnostic criteria for malaria & pneumonia

This theme explores caregivers' perceived severity, self-efficacy, and diagnostic criteria used for the lay diagnosis of malaria and pneumonia.

3.5.3.2.1 Perceived severity of malaria and pneumonia

Malaria was regarded by most caregivers as a 'common' illness that could be managed at home. In contrast, caregivers seemed afraid of the prospect of their children having pneumonia. In few instances, the existence of pneumonia was denied and seen as a curse with the fear that, from a religious point of view, acceptance of even the notion of pneumonia could make it a reality. For instance, five caregivers vehemently rejected the prospect of their children having pneumonia and would rather seek for immediate treatment at the nearest PHC to avert possible adverse outcomes such as admission to critical care or death.

> **07:** "I think malaria is endemic to us, so over time we have a lot of experience in handling malaria. It is easy for us to spot the signs of malaria and then if malaria is handled early, it is easy to curb it and if it is not, if the medications are not working, it still gives you some time to go to the hospital unlike pneumonia. Pneumonia may be more tragic, if you waste too much time guessing what the problem is and what the treatment will be." *University lecturer & mother of two children*

> **02:** "…No. God forbid! They will not get it [pneumonia] in Jesus name! Because me I don't have it and I don't know where they get it. It is not in my family at all, I reject it. That's the thing I hate mostly. I hated it with passion. It will not be my portion in Jesus name. I hear it, but I pretend like the name is not existing." *Business woman & mother of two children*

Unlike malaria, for which most mothers were willing to take full responsibility by visiting the nearest chemist store for medications, two of 13 interviewed mothers admitted they were not willing to do same for pneumonia without their husbands' 'approval'. This could be regarded as a protective strategy adopted by these caregivers to avoid being responsible for the possible occurrence of adverse outcomes. The reluctance of five caregivers to accept the diagnosis of pneumonia by perceived junior health workers or opting to go 'straight[12]' to standard healthcare centres (e.g. secondary hospitals) instead of chemist stores further confirms the fear of pneumonia.

> **02:** "It's just that I can't just conclude alone because I have a husband. I can't just say ok. It's what both persons will stand and do." *Business woman & mother of two children*

> **03:** "I will say I have to wait for the doctor to confirm or the matron. She [health worker] say (sic) no it's pneumonia. I say ma, I don't know if it's pneumonia as for me my husband says until the doctor says or the matron says it's pneumonia before I [can believe]." *Housewife & mother of three children*

3.5.3.2.2 Perceived self-efficacy for malaria and pneumonia diagnosis

Eleven of the 13 interviewed caregivers were confident they could diagnose malaria in themselves and in their children. However, compared to diagnosis in themselves, two caregivers admitted lacking certainty and confidence in the lay diagnosis of malaria in their children and hence could only 'suspect' malaria, as well as being more willing to

[12] In the study context, straight connotes emergency

seek professional healthcare services for confirmation. This low efficacy in diagnosis of malaria could be due to the perception of children being more vulnerable and the need to take extra care to avoid causing more harm rather than alleviating the illness.

> **Interviewer: What about your children, can you tell if they have malaria?**
>
> **05:** "Yes I can tell at least to an extent, even if I don't know at what extent of the malaria." *University lecturer & mother of two children*

Unlike malaria, nine of the caregivers said they could not and were unwilling to diagnose pneumonia in their children. Couple with perceived fear, caregivers' unwillingness and inability to diagnose pneumonia seemed to be associated with their relatively low level of awareness and knowledge of pneumonia. For instance, eight of the respondents who were unwilling and unable to diagnose pneumonia admitted that their knowledge was mostly from hearsay. Only one of the caregivers said her knowledge was based on when the child was diagnosed with pneumonia on a previous occasion.

> **06 Pidgin English:** I nor go fit know. I go just carry am go hospital make dem check am for me since I never see am before." *Petty trader & mother of five children*
> **English translation:** *I will not know how to. Instead I will just take him to the hospital for proper diagnosis since I have no prior experience.*

3.5.3.2.3 Diagnostic criteria for malaria and pneumonia

In addition to being able to lay-diagnose malaria in themselves and their children, many of the caregivers went further to provide a detailed description of symptoms such as fever, weakness of the body, joint pains and bitter taste in the mouth for the lay diagnosis of malaria in themselves. Of the symptoms, a bitter taste in the mouth was reported by eight out of the 13 caregivers as the most convincing indication of malaria. Bitter taste in the mouth seemed to aid the certainty for the lay diagnosis of malaria and suggest that

the suspected malaria was severe and required urgent self-medication or visit to a healthcare centre.

> **09 Pidgin-English:** "If I get malaria, I go just weak, to get up go be problem to me. Before my mouth go dey bitter, you go know say that malaria don hit me well well. Nai I tey dey know." *Petty trader & mother of three children*
>
> **09 English translation:** *If I have malaria I will be weak and find it difficult to get up from bed in the morning. Having bitter taste in the mouth means the malaria is very severe. That's how I know.*

Whilst acknowledging the fact that most infants and children under the age of five years were unable to adequately express their feelings, most caregivers believed that they could perceive minor changes in their children's behaviours alerting them of possible illness such as malaria that may be otherwise missed by healthcare professionals during early phases of illness when clinical signs and symptoms may be absent. For instance, malaria was suspected when children suddenly became less physically active and showed less appetite for food. Other reported signs used for the lay diagnosis of malaria in children were fever and incessant cry.

> **07:** "For my son, prior to when he falls very ill, his appetite drops, let's say about four or five days before he breaks down, his appetite drops and then when the full signs come, he starts running temperature. He is not as active as he used to be and then sometimes he could even start vomiting, then I suspect malaria." *University lecturer & mother of two children*
>
> **03:** "I'm the one taking care of her every day so if she falls sick, I do know because she will not be playing the way she is playing before and she will be doing somehow, crying mummy mummy, even though you're giving her things she will not like to pick it." *Housewife & mother of three children*

For the few caregivers who were confident of being able to diagnose pneumonia in children, the common signs mentioned were difficulty in breathing, fast breathing and persistent cough. Two of the caregivers also mentioned signs (e.g. chest raising and falling or stomach cutting into two) suggestive of 'chest in-drawing'.

08 Pidgin-English: "I fit know, I dey know. If my baby get pneumonia, e go dey cough and e go dey cough continuously, e nor dey stop and here [pointing towards her stomach], e belle go dey cut into two, e go dey breathe fast fast. Nai I take dey know say na pneumonia." *Business woman & mother of two children*

English translation: *I can, I do know. If my child has pneumonia, he will be coughing continuously and his stomach will be dividing into two sections and he will be breathing fast. That's how I know it's pneumonia.*

07: "My child has never had pneumonia but I know about it. I have seen children that had pneumonia. They have this very deep breathing like they are struggling to breathe and then you see their chest raising and falling and then they breathe very deeply trying to drag air in and out and then, of course, they are also very ill maybe it will be accompanied with temperature and fever." *University lecturer & mother of two children*

It is worth noting that the willingness and ability to diagnose pneumonia in children seemed independent of socioeconomic status (i.e. measured by educational status and occupation) as the caregivers that provided details of signs and symptoms for the diagnosis of pneumonia came from different socioeconomic backgrounds.

3.5.3.3 Lay management of malaria and pneumonia

This theme explores specifically the 'typical pathways' taken by caregivers for the management of suspected malaria and pneumonia.

3.5.3.3.1 Treatment pathways for suspected malaria

It was customary for most caregivers to have medications including paracetamol and antimalarials at home for the treatment of illness especially at night. Hence, the suspicion of malaria in children prompted the administration of paracetamol and antimalarial or native herbs.

03: "…but at times, their body do hot (sic), I go for paracetamol. I always have paracetamol at home for them." *Housewife & mother of three children*

> **05:** "The first thing I do is try and get an antimalarial, basic antimalarial maybe not the one that's being prescribed, just the normal one that you get across the counter and I will administer it to the child, that's what I do." *University lecturer & mother of two children*

For the caregivers that seemed aware of the potential harm of an elevated temperature on children (e.g. convulsions), they reported practicing tepid sponging at night before presenting to healthcare centres the following morning.

> **10 Pidgin-English:** "If I see say e body dey hot well well, I go pour am water. Like sometimes now, maybe when I come here [PHC] in the night e body come still dey hot. I come put small towel dey put water for e head, make e temperature dey cool down, make e nor too high. Early morning, I just carry am, pour am water, give am medicine, come carry am come health centre." *Tailor/trader & mother of three children*
> **English translation:** *If I notice he has high fever, I will bath him. Sometimes, like the day I came here [PHC] his body was hot at night. I now used a small soaked towel to clean his head in a bid to bring down the temperature. After bathing and giving him medications in the morning, we came to the health centre.*

Many caregivers considered seeking homecare services provided by health workers or pharmacists/chemists when the suspected malaria was not improving or worsening following the home-based management. Sometimes, the choice to seek the homecare services provided by a health worker or visit a chemist store was out of convenience.

> **01:** "…sometimes I won't be able to come down here [PHC], so I will take him to her house [house of a PHW]. Sometimes she prescribes drugs, gives him drugs and I pay for it. I go to her house and I will tell her and she will say don't worry. As far she's close to me I have no problem. I have access to her. If she's not available, she's here [PHC]. I will run down." *Self-employed & mother of a child*

These treatment options seemed particularly appealing to caregivers because of proximity to their residence and the flexibility of health providers. For instance, four caregivers liked the fact that they could purchase medications from chemist stores anytime (including mid-night) or manage high fever through the guidance of a health worker via a mobile phone.

> **02:** "…because it's your first child, you don't know what to do, what will I do? What help (sic) me is that some of the health workers, I have some phone numbers in (sic) my phone, I will just call them in (sic) mid night. I'll call them and they will tell me what to do. That was the method I kept." *Business woman & mother of two children*

When the suspected malaria persisted, or showed signs of worsening, most caregivers reported presenting to the nearest PHCs where proper diagnosis and treatment could be accessed.

> **07:** "Well, it is not usually the first thing I do. I do that when maybe after giving him drugs, of course, if it's malaria, after giving the first dose, you notice the child starts recovery. But after giving the first and the second and then I notice the child is still sick, then I take him to the primary healthcare before the child gets better." *University lecturer & mother of two children*

Regardless of the severity of suspected malaria, most of the interviewed caregivers said they were reluctant to visit higher healthcare centres (e.g. specialist private clinic, secondary and tertiary hospitals) possibly due to the perceived financial implications or fear of their children being admitted to critical care. However, three caregivers mentioned that the primary reasons they would take their children to a higher healthcare centre were if referred by PHCs following diagnosis of a severe outcome (e.g. severe pneumonia) or observation of a traumatic condition/injury due to a fall.

> **01:** "Except they decide that it's beyond them, if it's beyond them they will definitely direct me or refer me to another hospital." *Self-employed & mother of a child*

3.5.3.3.2 Treatment pathways for suspected pneumonia

Eight of the interviewed caregivers believed that pneumonia in children was caused by the penetration of the chest region by cold or breeze. Hence, there was an emphasis on the need to provide children with very thick or several layers of clothes, especially during rainy season when the weather is usually cold. Nonetheless, most of the

caregivers admitted that their knowledge of pneumonia was based on hearsay and they did not really understand its exact cause. Interestingly, only one caregiver mentioned the bacterial cause but recognised pneumonia as being associated with feeling cold.

> **11:** "Pneumonia, is it not the one that's caused by cold? I don't really know much about that sickness, that pneumonia, but what I only know is that they say always wear your child clothes because of pneumonia. But I feel that maybe it's because of cold but I don't really know the cause." *Primary school teacher & mother of two children*

> **07:** "Well pneumonia as I know, is caused by certain bacteria in the air and then they make people prone to cold, yes, cold in both children and adults." *University lecturer & mother of two children*

Regarding diagnosis of pneumonia, some caregivers showed awareness of the role of CXR. However, willingness to accept CXR recommended by a HP seemed to be dependent on perceived health hazards, severity of pneumonia and socioeconomic status in terms of the level of education or occupation. For instance, caregivers who had post-secondary school education and working in healthcare or educational settings showed awareness of the role of CXR for the diagnosis of pneumonia, potential side-effects of radiation from CXR and willingness to question the rationale for CXR. In contrast, their counterparts who had only secondary or primary education and were mostly petty traders seemed ignorant of the role of CXR for the diagnosis of pneumonia and were more willing to accept a doctor's recommendation without question. This group of caregivers were also more likely to assume that 'doctors know everything' and therefore should not be questioned.

> **01:** "Well, like I said earlier I don't know anything about chest x-ray, if it's expensive or not, but whereby the doctor or on your own you felt pains and you complain to a doctor and the doctor says you should go for a chest x-ray, why not, you go for it." *Self-employed & mother of a child*

Contrary to the typical pathways adopted for the management of malaria, that of pneumonia seemed to be influenced by the perceived severity and level of awareness. For instance, 11 of the caregivers were not willing to consider home management, visit chemist stores and homecare services provided by health workers for suspected pneumonia. Moreover, the perceived danger and difficulty in the administration of antibiotics for suspected pneumonia further discouraged some caregivers from considering these healthcare services.

> **05:** "I can buy antimalarial over the counter but when it comes to antibiotics, I'm very careful. I feel I need a practitioner to be able to tell me what I should take. Most times these antibiotics that I take have doses and you must calculate the child's weight to be able to administer antibiotics. Most antimalarial, you just get it across the counter, they will tell you it's 5ml from 0 month to 1 year or from 6 months to 1 year as the case may be, but for antibiotics, they don't really specify especially for the dosage and administration." *University lecturer & mother of two children*

It also appeared that pneumonia was regarded as an illness that could cause sudden and severe adverse outcomes. Hence, presenting to chemist stores was considered 'risky' and instead caregivers reported they would go 'straight' to a PHC. In the context of the study setting, the use of words like 'going straight' to a PHC or hospital suggests the need to take an immediate action to resolve an imminent danger.

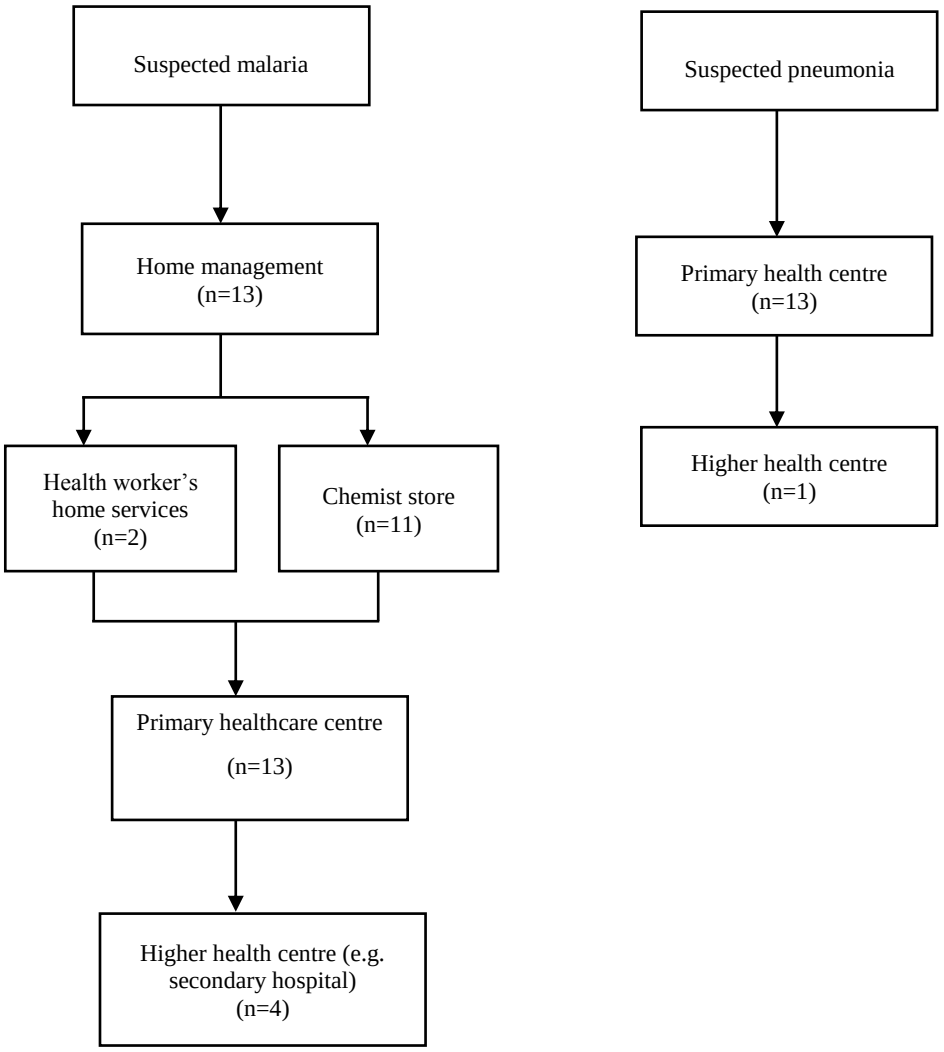
> **07:** "I don't have any information on how to manage pneumonia at home, and if I notice my child has pneumonia, I will take the child straight to the hospital because I know it will be administered with antibiotics and I can't do that at home." *University lecturer & mother of two children*

PHCs were considered the best option for suspected pneumonia because of the availability of doctors and other health professionals believed to have the relevant knowledge of appropriate treatment.

> **13:** "There's a health centre here. I will go to the health centre and consult the doctor. Chemist do not know about pneumonia. It's only the doctor that can know how far about pneumonia (sic)." *Business woman*

Interestingly, two caregivers believed that following the initial management of pneumonia by a doctor or health worker, they were confident of being able to manage suspected pneumonia in the future thereby saving limited financial resources. This suggests that caregivers were open to the idea of lay management for pneumonia but the main barrier seemed to be self-efficacy relating to pneumonia diagnosis and treatment.

> **09 Pidgin-English:** "If doctor come give me medicine, I don know say na this kind drugs nai dey work am. I go write am down, na so I take dey do so that if I come across that sickness, I go just go chemist buy the drugs instead of me to come throway big money here." *Petty trader & mother of three children*
>
> **English translation:** *With a doctor's prescription, I would know the right medication for pneumonia. I will write the name of the medication down, that's what I do so that upon the reoccurrence of the illness, I will go to the chemist store to purchase the medication thereby saving money.*



(a) **(b)**

Figure 3.10: Typical treatment pathways as reported by participants for suspected malaria (a) and pneumonia (b)

3.5.3.3.3 Role of faith in seeking healthcare services

Faith seemed to play a significant role in influencing some caregivers' health seeking behaviours. All the interviewed caregivers were Christians and some of them stated or implied on several occasions that they relied more on prayers than medications. For instance, four caregivers reported praying over medications before administering them to their children. They seemed to believe that God's power, not medication, was responsible for healing. According to these caregivers, medications were merely the media through which God performed healing. Although not explicitly stated, based on the responses of some caregivers, it seemed that dependence on medications rather than on God portrayed lack of faith. The influence of faith appeared more predominant for illnesses that were perceived less serious and non-threatening.

> **02:** "Sometimes when you see that the thing is not serious like that, as a Christian, the first thing I do when I see my child running up (sic), I put him in my lap and pray. I take the paracetamol and pray, Baba [Almighty] God as I'm giving him this paracetamol, baba God let it work." *Business woman & mother of two children*

> **03:** "At times when your children fall sick as for me I don't come to buy drugs like that because I don't believe on drugs. I do pray for them. That's how I do take care of my kids, I do pray for them and say let God take control. I will be giving her paracetamol, I will be praying because I believe there is nothing God cannot do. I will pray for her." *Housewife & mother of three children*

3.5.3.4 Perceptions of training caregivers to use the IMCI guidelines

This theme focuses on perceptions of training lay persons (e.g. caregivers) to use the IMCI guidelines for home management of common illnesses in their children and their

neighbours' children in the capacity of community health experts (CHEs). The following two sub-themes were identified: perceived benefits of training caregivers in the IMCI guidelines and receptiveness to and perceived challenges of training caregivers in IMCI.

3.5.3.4.1 Perceived benefits of training caregivers in the IMCI guidelines

Caregiver views

Most of the caregivers seemed to value the prospect of being trained to use the IMCI guidelines and believed that training could make them 'popular' and have increased 'knowledge', as well as help them to save money as they become informed on the appropriate medications for the management of common childhood illnesses. Most caregivers, especially the first-time mothers, also believed that training could help boost their confidence in the home management of common childhood illnesses. For instance, a caregiver remarked that the first-time mothers would be enthusiastic at the prospect of being trained given their lack of experience and tendency to panic when managing common childhood illnesses.

> **12 Pidgin-English:** "E dey very good. You know say some women don use their brain waka far. So when you get the brain, dem call you say dem wan train you, e good. E go make you popular and know more, e go make you reach where you nor first reach, dey save people lives, do many things. E go make me happy." *Business woman & mother of four children*
>
> **English translation:** *It is very good. You know some women have gone to places based on their intelligence. So, it is good when you're intelligent and invited for training. It will make you popular and know more, take you to places you have not been to before, saving lives and doing many things. It will make me happy.*

> **13:** "The idea good for us (sic), if they train parents for it, it's not every time parents will have a lot of money at home. We can easily take care of our children at home." *Business woman & mother of three children*

Health professional views

Six HPs believed that caregivers could easily be trained to use the IMCI guidelines. These HPs believed training could encourage mothers to be more proactive to recognise early signs and symptoms of illnesses, thereby preventing severe outcomes due to late presentation to health facilities. Furthermore, five HPs believed that training could raise caregivers' level of awareness of appropriate medications for common illnesses, thereby minimising the existing problem of over-administration of medications. Three HPs showed their optimism in this regard by stating that given the special interest in their children's wellbeing, caregivers would be willing to observe best medical practices in terms of administration of medications.

> **20:** "These people are already buying it without consultation, without knowledge. So this knowledge no matter how little we think it is, will benefit the parents. When you get to the place that you cannot treat, see the doctor. They will know their limit." *Medical doctor*

> **22:** "If they do that it will be very good because some mothers especially the lay women in the streets or at home, if their child is sick, the first thing they do is just give only paracetamol and rest. If they are able to train these lay women from these guidelines, that if your baby is sick, from 2 years to this age and you have paracetamol at home, you have the knowledge of these ACT drugs and the knowledge of some of these antibiotics that you can easily get in chemist shops or pharmacy shops close to them, then it will reduce the disease in the community and the effect it will have on the children if they are really taken care of on time." *Principal nursing officer*

Lastly, two HPs believed that if caregivers were trained to recognise and manage common childhood illnesses, they would have a lesser workload as only unresolved cases would be presented to PHCs. This expectation could be attributed to the reported low health workers–patient ratio in Nigeria.

> **24:** "I buy the idea if they can do it, it will work. It's not everything that the health worker will do." *Junior community health extension worker*

3.5.3.4.2 Receptiveness and perceived challenges to training caregivers in the IMCI

Caregiver views

All the interviewed caregivers seemed enthusiastic and willing to become trained in the IMCI guidelines for home management of common illnesses in their own children.

> **01:** "It's good. It will also help you as a mother because you have your own kids also, so it will definitely help you." *Self-employed & mother of a child*

However, responses on the willingness to be trained to become community health experts[13] (CHEs) to assist their neighbours' children was mixed. While seven caregivers were confident and willing to receive training to become CHEs, a group consisting of three caregivers were willing to be trained 'only' for their immediate families. This latter group of caregivers expressed fear of being held responsible or branded as 'evil' in the advent of severe outcomes (e.g. admission to critical care and/or death). The fear expressed by these caregivers was based on the belief that their neighbours could fail to adhere strictly to given instructions or read prescription notes due to educational level, as well as choosing to buy different medications due to insufficient funds. In addition, these caregivers seemed to think that medications were potentially harmful and therefore

[13] A community health expert was defined as someone in the community who parents could seek advice from if they were worried about their child's illness. This advice could be whether it was safe to treat the illness with medicines from the pharmacy or if they needed to go immediately to the PHC. S/he could also advise parents on suitable medicines, and their services would usually be free of charge. This definition was provided by the interviewer to the parents before asking them questions on becoming CHEs.

were reluctant to prescribe treatment, although may be willing to assist with diagnosis and make a referral to the nearest PHC.

> **08 Pidgin English:** "E good to do am, but the world when we dey so, they are dangerous. Why I say they are dangerous, you fit tell am now say, see wetin you go do, see drugs wen you go buy give your pikin. E fit go buy another one now give am. May God nor let bad thing happen, something happen to that child, e go say na so so person like this nai tell me say buy so so medicine give am." *Business woman & mother of two children*
>
> **English translation:** *It is good to do it, but we live in a world where people are dangerous. Why I said they are dangerous is because you might tell someone what to do, these are the drug to buy for your child. The person may go and buy a different drug. God forbid if anything should happen to that child, the person will say it was that person that prescribed the drugs for me.*

> **03:** "As for me, anything health they are very risky. I don't think if you're not a matron or doctor, you can be doing those things at home. What about one day you told a woman how to treat her child maybe she lost that child? That will cause you trouble. Even though am trained, I don't think I can do it, because this is children we're talking about because you might tell person to do something like this and he may go home and do another thing. He say you're the one that told him, from there? No! Even though I'm trained, I will use it for my children alone, I will tell you to go to health centre in case, because I don't want trouble in my life." *Housewife & mother of three children*

For the few caregivers that were willing to prescribe medications in addition to other services, they reported the need to adopt protective measures such as documenting (i.e. in writing) their prescriptions for future reference or, if possible, purchasing medications themselves for their neighbours. Furthermore, a caregiver expressed concern that despite her willingness to work as a CHE, she might not receive the needed support from health workers and they could choose to disregard her recommendations. For this reason, she would only agree to volunteer as a CHE on the condition that her referrals to PHCs were respected by health workers.

> **10 Pidgin-English:** "I nor go just tell am go like that, as e be say I know the medicine. Wetin I go do I go just write am give am cos I nor go use mouth talk am make e nor go buy another thing make e nor go put me for trouble. If you fit give me money, I fit go help am go buy am or I write am for am. I nor go fit tell am why because medicine now nor be the one wetin person dey eat anyhow, even common water now e dey hard to drink anyhow. So I nor go fit just tell am say go buy, I nor want trouble." *Tailor/petty trader & mother of three children*
> **English translation:** *I will not just tell her to go or send her away without providing help since I know the right medication. I would write the prescription because telling her the medication verbally could cause trouble for me. If given the money I could go and buy the medication or I prescribe on a paper.*

> *I can't tell her verbally because medications are not what one should buy indiscriminately. So, I cannot rely on verbal prescription, I don't want trouble.*

Two caregivers suggested the potential benefits of incorporating their husbands in IMCI training. According to these caregivers, literate husbands could provide a supportive role to their wives with less education (and unable to read) especially with regards to the administration of medications. In addition to having the final say as head of the family, it is reasonable to assert that application of the skills and knowledge gained from IMCI training may ultimately depend on the husband's approval in a developing setting.

> **01:** "A mother who is not well educated cannot do it except maybe the man is very educated, in terms of education the man can also help the woman out. I mean some persons not even end up going to primary at all or when one find oneself in that kind of situation, you can easily have access to the man, educate the man, probably from there the woman can get more knowledge from the man." *Self-employed & mother of a child*

When asked whether monetary incentives would influence their decision to receive IMCI training to become CHEs, most of the caregivers answered in the negative. Becoming a CHE was believed as a selfless service to mankind and an opportunity to do God's will. According to these caregivers, gratitude from neighbours and blessings from God were more than enough rewards for them.

> **02:** "Well, if I look at it, it's good because you're helping human being because God has already said that when you see your neighbour, you have to stay with him and help. I can do it because money is not everything. It is better you do something they tell you thank you. It's God that rewards, it's not the money. If they give you money you will eat [spend] the money, what's the need? When they say thank you, that thank you, who want to reward you is somewhere, it's not the person." *Business woman & mother of two children*

Two of the caregivers noted that their willingness to provide free services to their neighbours could depend on receiving IMCI training free of charge. However, a

caregiver noted that being offered monetary stipends would only be a further incentive rather than the primary determinant for her services. Moreover, another caregiver said that being offered monetary stipends would motivate her to devote more hours of services as a CHE to other caregivers.

> **11:** "Yes I can, provided I didn't pay money for the training. I can render the services free of charge. …that's encouragement so that I will be willing anytime they [parents] need my help." *Primary school teacher & mother of two children*

Health professional views

The interviewed HPs had divided views regarding the training of caregivers in the IMCI guidelines for home management of common illnesses in their children and neighbours' children. Six of the HPs believed the IMCI guidelines were simple enough to be used by caregivers and that training could result in the appropriate use of medications and consequently reduce morbidity and mortality associated with childhood illnesses. To buttress their position, two HPs referred to the successful training of mothers in the use of oral rehydration solution (ORS) for home management of diarrhoea in Nigeria. These HPs believed that caregivers could equally be trained to use the IMCI guidelines for other common childhood illnesses.

> **20:** "The more people that are trained, the better. In Nigeria now, the issue of management of childhood diseases like diarrhoea disease, parents were taught then, ORS sachet that is formulated now was not readily available. Every parent that comes for antenatal is taught before they deliver. When they finally deliver, they come for immunisation, they are taught. They come for infant clinic, they are taught. Today, diarrhoea disease is less common in those areas that had access, just train the parents. So if lay people are also trained in IMCI guidelines so that they can do something more objective rather than being 100% subjective, I think the community is better off. So, the more people we train, the better." *Medical doctor*

An HP who supported the idea of training caregivers believed that focusing training on CHEs for communities rather than immediate families would be more effective. According to the HP, training caregivers for their immediate family would not be effective given that some childhood diseases were infectious and could easily be transmitted from children of untrained caregivers to those of trained caregivers. This HP also believed that trained CHEs live closer to communities than professional health workers and were therefore more likely to make positive impacts.

> **21:** "I feel, they are close to the community more, as in, more than the health workers. They will spread whatever good thing they learned from that training more than the health workers, because they live with the people in that community. They live directly with the people in that community." *Registered nurse midwife*

The four HPs who did not support the idea of training caregivers in the IMCI guidelines were concerned that training could amplify the already existing problem of over-administration of medications. They also expressed concern about caregivers' capacity to differentiate malaria symptoms (e.g. fever) from those of other infectious diseases such as pneumonia, as well as determine the appropriate dosing of medications by weight and age. Furthermore, these HPs questioned the ethical appropriateness of training a caregiver to treat his/her child given the tendency to become emotional when their children were ill. They made references to instances where mothers had administered excessive doses of medications to expedite recovery in their children.

> **29:** "If you take the algorithm for malaria for example, you have to do testing before you treat. So, if you teach mothers that when a child has fever the child may possibly have malaria, what about the testing? And as it is now, there are so many other things that can cause fever other than malaria, which is one of the limitations of the fever algorithm on the IMCI." *Paediatric consultant & IMCI training facilitator*

> **27:** "Some of them will, we have been seeing some. If you tell them to give your child 5 ml of paracetamol because of the age, we know drugs go with body weight and age, because they want the drugs to work faster, they will increase the dose." *Community health extension worker*

An HP advised that even if caregivers were to be trained in the IMCI guidelines, treatment should be excluded to avoid over-administration of medications. According to this HP, training of caregivers should focus on the recognition of severe signs and symptoms for better health outcomes.

> **29:** "It is not advisable that mothers should start treating their children at home, but they can be taught to recognise signs of illness in their children. One of the major reasons why outcomes of children who have malaria and pneumonia is poor, is because parents delay in bringing their children to the hospital. So, if mothers are taught to recognise signs of potentially severe illness, so when the child is breathing fast and has a fever it is likely that the child has a pneumonia, mothers should bring the child to hospital, and then we will have better outcomes." *Paediatric consultant & IMCI training facilitator*

For suspected pneumonia, three HPs believed caregivers should not be trained either for home diagnosis or treatment. These HPs believed that a caregiver whose child had suspected pneumonia may be too anxious and find it difficult to properly count the respiratory rate as part of the diagnostic processes.

> **18:** "I don't think they can manage pneumonia at home. Will they be able to count the breath like we are going to do here? Some will feel like I'm not a doctor, I'm not a nurse, how will I do this? To me, I don't think they will be able to manage pneumonia." *Nurse*

In contrast, four HPs believed that it would be easier to train caregivers to manage pneumonia than malaria. These HPs noted that the diagnosis of malaria involved many subjective steps that could easily be mistaken for other illnesses, whereas steps involved in the diagnosis of pneumonia such as counting of respiratory rates were more objective and easy to carry out. However, these HPs believed that caregivers may find the

diagnosis of severe pneumonia difficult given that some of the diagnostic steps (e.g. assessment of stridor and chest in-drawing) were difficult and subjective.

> **25:** "Like a child that's coughing, having difficulty in breathing, coughing for about two days and maybe breathing fast, you will just tell them in plain language it's signs and symptoms of pneumonia. But for that of malaria, sometimes the child will be vomiting and I don't know how they will manage it at home." *Nurse*

> **24:** "Good, that one [pneumonia] is easier, it's easier to do than that aspect of malaria. You know why? Counting of breathes an inexperienced person can do it when the person is calm. It doesn't take a health worker to do it, just to train the person, just like I'm counting 1 2 3 4 5 6 7 8 9 10 now, I will be able to count it without being trained as a health worker." *Junior community health extension worker*

Instead of training caregivers in the use of IMCI guidelines for home management of common childhood illnesses, two HPs believed it would be more beneficial for resources and efforts to be channelled into the training of paramedics, employing more health workers and equipping available health facilities. This position appeared to be based on the premise that caregivers lacked the capacity to carry out accurate diagnosis and which in turn could exacerbate the problem of over-medications.

> **14:** "For me I think it will be better to get more health facilities, employ more people, we have a lot of trained health personnel in the country. Instead of investing in training lay people, let's make use of the ones that have already been trained, get them employed, and build more facilities." *Medical officer of health*

Notwithstanding the conflicting views, there appeared to be consensus among the health professionals that training of caregivers in the IMCI guidelines and the potential benefits may be more feasible for those with considerable level of education who could read and write.

> **25:** "I think, it is not all parents that are literate, that can read. So that will be a kind of, there will be difficulty here in training all, except those that are literate, those that can read and use the guideline." *Nurse*

3.5.4 Stakeholder perspectives on IMCI guidelines

Table 3.22 below provides an overview of the main themes and related sub-themes identified from the thematic analysis of transcripts from HPs perspectives on IMCI guidelines.

Table 3.22: HPs perspectives on acceptability and implementation of IMCI guidelines in Nigeria -overview of the main themes and sub-themes

Theme	Sub-theme 1	Sub-theme 2
Perceptions of IMCI guidelines	Delivery of IMCI training	Perceived benefits of IMCI training
Acceptability of & attitudes to IMCI for managing malaria & pneumonia	Management of malaria	Management of pneumonia
Perceptions of wide-scale implementation of IMCI in Nigeria	Stakeholders & proposed pathways for the wide-scale implementation of IMCI	Perceived challenges to the wide-scale implementation of IMCI

3.5.4.1 Perceptions of IMCI guidelines

This theme explores HPs' experiences during the 2-day training in IMCI guidelines for this study.

3.5.4.1.1 Delivery of IMCI training

All the trained PHWs reported that they were satisfied with the facilitation of the IMCI training. Specifically, PHWs felt the facilitators were approachable and where necessary made the training material more comprehensible by using Pidgin-English (improper English) and local dialect (i.e. Bini in study setting) interchangeably. The facilitators were also reported to have shown awareness of the diversity of educational attainment and work experience amongst the PHWs. For example, the PHWs had various positions and levels of experiences.

> **15:** "The way she introduced her own teachings. You know there are some students that will say this particular lecturer I love this one, but that one I don't understand. But she will break it to your own knowledge (sic). Even using the Pidgin to teach you so that everybody will be carried along." *Junior community health extension worker*

> **24:** "They quite understood the level of the people whom they have taught, they put themselves to our level and did very well. The woman was very friendly, they were all friendly, not only the woman, both the assistant and the doctor, you know that's another key element for someone to learn very fast. You must be friendly to somebody or the participants. When you are so harsh to participants you won't be able to get something, that love, that friendly love that they've gotten, it made us to concentrate, it made us to show (sic) that love in that study. That's why you see today now we're making an impact through this study." *Junior community health extension worker*

PHWs valued the usefulness of training materials, such as the Nigerian adapted IMCI chart booklets and assessment notebooks, videos, and recording forms, for the management of childhood malaria and pneumonia. Following the 2-day training, nine health workers said they were constantly referring to the training materials for guidance during the assessment of patients and for clarification.

> **27:** "The training material was ok, it helps a lot. Even after the training if we have anything that we have to remember, we fall back to our training material." *community health extension worker*

The manuals used for the 2-day training did not have a hardcover and two of the health workers complained that their copies got damaged after a while. Hence, they suggested that subsequent training manuals should have hardcovers for better preservation.

> **21:** "They [the training materials] were ok. But the only area, I don't know, if they were hard cover for the training materials, I personally would have preferred it more, I feel with that the materials can last longer. It's what you can always refer back to." *Registered nurse midwife*

Five health workers reported that translation of the learning from the 2-day training to practice was not easy as they had to frequently refer to the IMCI chart booklets. Eight health workers agreed that the duration of training being two days was intensive and insufficient to consolidate the information from both the practical and theory sessions.

> **25:** "They were ok, but the thing there was that the training was kind of compounded. You know they trained us for two days, like rush rush rush." *Nurse*

Furthermore, five of the eight health workers complained about the length of the training (9:00 am–5:00 pm) as they reported arriving home late and not having enough time for domestic chores. Given that 7 of the interviewed 8 health workers that participated in the 2-day IMCI training were women, this may be a crucial factor to consider in rolling out the training on a wide-scale if most of the people being trained are women.

> **17:** "The training was good but the only thing I see is that the day for the training was too long…that day we stayed long, it took a full day." *Junior community health extension worker*

Interestingly, six health workers unanimously suggested a duration of 5–7 days for subsequent IMCI training, regardless of the focus being only malaria and pneumonia algorithms. They proposed 3–4 days for the theory while the remaining days focused on practical sessions. These health workers believed that a longer training duration would allow for timely completion of the daily training session while creating enough time for personal duties.

> **15:** "But what I will say is that the training, the period of the training was not enough. Maybe if this kind of thing comes up again it should be five days. For five days, we will come early and go back early." *Junior community health extension worker*

From the two facilitators' perspectives, training for this study was an abridged version given that the typical IMCI training covers several algorithms (e.g. malaria, pneumonia, diarrhoea, measles, anaemia, ear infection etc.) for an average duration of one week. The facilitators believed that IMCI training was generally intensive, regardless of the duration and version.

> **30:** "The IMCI [training] usually is a 6 day training, even that 6 days is usually loaded. From morning till evening, you are in one place with little or no breaks at all." *Consultant paediatrician & IMCI training facilitator*

3.5.4.1.2 Perceived benefits of IMCI training

Apart from two health workers who mentioned they had previously received training on rapid diagnosis of malaria, the IMCI guidelines seemed relatively new to the trained PHWs. After the 2-day training, most of the trained health workers said they were better able to assess and classify (diagnose) children with suspected malaria and pneumonia correctly, as well as administer relevant treatments and counseling. In addition, most of the health workers stated that they valued the training on communication skills for counselling of parents. Despite the awareness of the need to provide counselling to caregivers, it seemed it was not a routine practice at most study PHCs prior to this study. Health workers reported that the IMCI training reinforced the need to provide counselling using appropriate language to better communicate follow-up care to caregivers.

> **21:** "In the aspect of how we can communicate properly with the mothers of the kids, that aspect was really demonstrated very well. They [the facilitators] demonstrated it very well, the kind of, how we can come down to their level, using the right words to them, allowing them to equally ask us questions, giving them listening ears, being patient with them." *Registered nurse midwife*

3.5.4.2 Acceptability of & attitudes to the IMCI guidelines for managing malaria & pneumonia

This theme explores HPs' acceptability and attitudes towards the IMCI guidelines for diagnosing and treating malaria and pneumonia.

3.5.4.2.1 Management of malaria with the IMCI guidelines

Health workers reported that they valued the IMCI for its objectiveness and enabling them to manage suspected malaria much more easily as they knew the right step to take at the right time. Four health workers found the colour-coding of illness severity in the IMCI chart booklet very helpful. For instance, very severe febrile illness (fever and any general danger sign[14] or stiff neck), malaria (fever and positive RDT) and fever (fever and negative RDT) are coded as pink, yellow and green respectively. Overall, health workers believed that the IMCI chart booklet directed them to provide better assessment, classification and treatment of suspected malaria.

> **16:** "The guidelines is ok. It really helps a lot in the classification. Maybe, probably, you are looking for how to classify, just check the book and you will be able to classify properly. Those colours, because like this patient that was brought now when you just look at the convulsing now, you just know that the child has a danger sign, you will know that this is the first thing you are to classify for not the second line, it was easy." *Junior community health extension worker*

However, 13 of the HPs, including primary health workers and clinicians, disagreed with the IMCI guidelines regarding the outcome of rapid diagnostic test (RDT) for deciding malaria treatment. These HPs believed the RDT results were not accurate given the contradiction with classical signs and symptoms of malaria. One of the health workers supported this opinion by recounting how the RDT she conducted contradicted the result of microscopy (reference diagnostic test for malaria) brought along by a parent.

> **27:** "I have seen such cases, RDT test will show negative but if you go to the lab you will see positive or if you test the temperature, it will tell you that this child has malaria. Even the physical appearance,

[14] Any general danger sign is when a child is unable to drink or breastfeed, vomits everything, lethargic or unconscious, has had convulsions or currently convulsing.

history, hotness of the body, those ones will give you the signs that this child has malaria, but RDT test will still show you negative. There is one case like that, she brought lab result. I don't know she had done it before, so I just did RDT and it tested negative and the result she brought was even 2+ and the temperature was even above 38 [degree Celsius]. She came here straight." *Community health extension worker*

In contrast, an HP argued that when properly conducted according to manufacturer's instructions, RDT was a sensitive and specific test for malaria. This HP went on further to say that the accuracy of RDT for diagnosing malaria was comparable to that of microscopy, if not better. He believed that the observed contradictory results between RDT and clinical signs and symptoms for malaria could be due to a low level of malaria parasitaemia. According to this HP, RDT was more likely to be negative for low malaria parasitaemia regardless of presenting signs and symptoms and vice-versa.

26: "Well, that test, the rapid test is a specific test and very sensitive test. Now, there are other causes of elevated temperature apart from malaria. Stress from the environment, pneumonia, coughing, rhinitis, viral infections, other viral infections can cause fever in the child. Since that test is very sensitive, I want to disagree with those health workers who are saying that they noticed fever and the test is saying negative. The test will say negative once the malaria parasite in the blood is low. If malaria parasites are in the body, it will reflect in the result. If it's not there it will not reflect. And I want to let you know that that rapid test is even more reliable than laboratory test of malaria parasites. I just came back from Ibadan, from a seminar where this rapid test comparing the results vis-à-vis the laboratory test was done and it was so clear than the laboratory test (sic)." *PHC coordinator & medical doctor*

For the treatment of malaria, health workers liked the recommended choice of ACT and artesunate/quinine for treating non-severe and severe cases respectively. According to health workers, the recommended medications for diagnosed malaria agreed with their current choice of medications. They also liked the fact that the IMCI guidelines provided details about the specific dosage of medications to use for children of different age groups and weights.

> **27:** "The treatment is ok, because that's the best treatment for now, the ACT. When we use ACT for all the patients we saw during the exercise, we always have positive change if they come for the first or second day, the next day they will come for check-up, they are better than the first day they came." *Community health extension worker*

The IMCI guidelines recommend the use of an appropriate antibiotic for the treatment of malaria when a bacterial cause of fever is 'known' or 'identified'. However, it appeared that some health workers preferred a combination of antimalarial and antibiotics for the treatment of 'all' malaria cases, irrespective of whether the alternative cause of fever was identified or not. Five health workers seemed to believe that combined antimalarial and antibiotics functioned as broad-spectrum medication with the potential to act against both malaria parasites and bacterial causes of fever. Furthermore, many health workers felt that the IMCI guidelines were inflexible as treatment for malaria was based solely on RDT outcome. Seven health workers admitted that there were times when they needed to treat suspected malaria cases based on experience which they were not able to do as they were required to strictly adhere to the IMCI guidelines.

The decision whether to include antibiotics for the treatment of malaria seemed to be influence by the routine practices of these health workers and caregivers' demand for several medications believed to be more effective. Hence, antibiotics were not prescribed because they were believed to be effective for malaria; rather, they were being prescribed possibly as a 'placebo' to meet the patient expectations.

> 16: "Most patients, if they come to the hospital maybe just give them few drugs, they will think maybe you have done nothing, until you have given them to their satisfaction. So, there are some patients who are used to taking antibiotics always." *Junior community health extension worker*

In contrast, a health worker agreed with the IMCI recommendation of including antibiotics to the treatment of malaria only when an alternative cause of fever had been identified.

> **18:** "If the treatment is just plain fever, just treat for that. Only when you have associated causes, other reasons why you should add antibiotics." *Nurse*

3.5.4.2.2 Management of pneumonia with the IMCI guidelines

All the HPs agreed that the IMCI guidelines were useful for the diagnosis of pneumonia given the lack of radiological facilities for chest x-ray (CXR) at the primary healthcare level in study setting. Although not routinely recommended, health professionals, mostly clinicians, believed CXR had a role in the diagnosis of pneumonia. However, three clinicians admitted relying on clinical diagnosis of pneumonia largely due to the low socioeconomic status of many patients who present to PHCs.

> **14:** "…since I see patients mostly from the low class, usually they might not be able to afford the chest x-ray. So, from signs and symptoms and from my examination of the patient, if I'm sure it's pneumonia, I will treat." *Medical officer of health*

> **20:** "There are issues with chest x-rays, one finance. Let's assume you are not going to take care of the health hazard, how many of them will be able to afford it at that level of practice? An x-ray can cause more than 2000 Naira [Nigerian currency], so they don't have the money. They tell you, this 2000 Naira can buy drugs, most antibiotics you are going to use are less than 500 Naira. So, if that x-ray is not critically indicated, you can negotiate because if you don't and say go and do a chest x-ray, they can leave, they won't do the x-ray, they will go to quarks." *Medical doctor*

Fear by caregivers over the potential health hazards of exposure to CXR, rather than insufficient finance, was also identified as a contributing factor to HPs' reluctance in recommending CXR for pneumonia diagnosis. An HP reported that in such a scenario, there was a need to explain the benefits of accepting CXR to caregivers. Nevertheless, it seemed that prior to this study, some health workers expected the diagnosis of

pneumonia by the IMCI guidelines to be very difficult. However, many health workers believed that the diagnosis of pneumonia was easy following the 2-day training and knowing the guidelines were based on research evidence boosted their confidence during application.

> **24:** "I never knew it will be easier to diagnose pneumonia, I never knew before I came in contact with you people. It's very simple, it makes it easier, it makes you stress less. Before when you see the way children breath, you will think they want to give up. But with this programme, this IMCI guidelines, it's very easy." *Junior community health extension worker*

One of the health workers however complained that the inability of caregivers to accurately report signs and symptoms of pneumonia affected her diagnostic capability. It seems that the better the information on signs and symptoms of pneumonia provided by caregivers, the more informed the health worker would be in providing diagnosis and appropriate treatment.

> **15:** "Because at times, when they brought in the baby, when we test and it's reading positive or negative [RDT], before we will turn our eyes, we will start hearing noise and we will say madam, raise up the shirt of your son or daughter. Then we will now see the chest going up and down [chest in-drawing]. When did it start and they will say about two weeks ago. And I will say this is what you should have complained, not saying it's malaria or fever, and she will say I don't, they say it's malaria that's causing it and I will say everything will be ok." *Junior community health extension worker*

Six health workers reported that the recommended choice of antibiotic –amoxicillin– in the IMCI guidelines for pneumonia treatment was not their preference. They believed that other antibiotics, such as augmentin (an oral antibacterial consisting of amoxicillin and the beta-lactamase inhibitor, clavulanate potassium), were better and more effective than amoxicillin. The inclination of these health workers toward other antibiotics could be due to the perception that the more expensive antibiotics were more effective than the relatively cheaper amoxicillin. Three of the health workers believed that instead of

prescribing a single antibiotic for the treatment of pneumonia (i.e. amoxicillin), they would prefer a combination of two types of antibiotics. It seemed to them that amoxicillin was narrow-spectrum (effective against specific group of bacteria) while combined antibiotics were broad-spectrum (acts against a wide range of disease-causing bacteria).

> **15:** "My view about that is that the amoxicillin is not high enough for that pneumonia. That is the level of the antibiotics, we have zinnat, we have augmentin, we have sefazo." *Junior community health extension worker*

Two health workers admitted to having changed their attitude towards amoxicillin for the treatment of pneumonia. Following the training and use of the IMCI guidelines, these HPs considered amoxicillin to be an effective antibiotic for the treatment of all the pneumonia cases they managed.

> **18:** "Before now, I never thought we could use amoxicillin. We go for cephalexin, all these fancy drugs, but with this amoxicillin, we began having good result. When they [parents] come two, three days for check-up, they will say we are better now." *Nurse*

However, two health workers suggested the inclusion of alternative antibiotics in the IMCI guidelines given the likelihood for failure in the supply of amoxicillin and the attendant effects on healthcare delivery.

> **24:** "…there are other antibiotics that will be able to help in combating the menace of this pneumonia that the IMCI guidelines should also captured those kinds of antibiotics. That is, there must be an alternative for something. If there's no this, let us use this and both work for the same purpose. It will help in terms of emergency purposes." *Junior community health extension worker*

3.5.4.3 Perceptions on the wide-scale implementation of IMCI in Nigeria

This theme explores the perceptions of HPs on the wide-scale implementation of IMCI in Nigeria.

3.5.4.3.1 Stakeholders & proposed pathways for the wide-scale implementation of IMCI

To drive the wide-scale implementation of IMCI in Nigeria, the active participation of the following stakeholders was identified: public health physicians, public health officer associations, the executive Governors of States, states house of assembly (legislative arm of government in Nigeria), tertiary institutions, local government Chairpersons, various local government workers, and non-governmental organisations (NGOs).

To achieve wide-scale adoption of IMCI guidelines in Nigeria, one of the HPs suggested that few local government areas should first be selected for piloting. Then, there should be a wide-scale adoption in an entire State based on the lessons learned from the pilot study. At the State level, an HP suggested a top-down approach which would involve first inviting and briefing the Executive Governor of the State before seeking the support of other stakeholders. According to this HP, adopting this approach has the capacity to make stakeholders with both financial resources and responsibility for formulating policies committed to the IMCI project. In contrast, a bottom-up approach (e.g. starting from the primary health facility) was anticipated to be less efficient given the lack of financial support and political will-power at this level.

> **28:** "Yes, if we want to implement it in Benin City, we should target the top so that the programme, interest in the programme will now scale down to the bottom. If you want to start with the grassroots, it will not see the light of the day." *PHC coordinator & medical doctor*

> **22:** "Before implementation of anything can be done, there are processes you pass through, you will go through the secretariat, the council secretariat, the PHC coordinator first, before anything can be implemented in the health facility. You don't just come to the facility like that and want to implement anything, no." *Principal nursing officer*

3.5.4.3.2 Perceived challenges to the wide-scale implementation of IMCI in Nigeria

Several challenges were identified by the HPs to the wide-scale implementation of IMCI strategy in Nigeria with inadequate funds identified as the primary challenge. Primary healthcare centres are primarily financed and managed by local governments (LGs) in Nigeria. Given the reliance of LGs on State governments for finance, many HPs believed that adequate funds may not be readily available to sponsor the wide-scale implementation of the IMCI strategy. According to these HPs, funds would be required for all activities including training and re-training of health workers, as well as procurement of essential materials as part of the wide-scale implementation.

> **26:** "Funding, funding to carry out such large scale training is what will be the major setback." *PHC coordinator & medical doctor*

> **28:** "The first thing that I will see that may be a challenge is if local government is required to contribute its quota. If local government is required to contribute its quota maybe finance, that's the number one challenge. I mean, 12 months, we are into 12 months now, no salary. So, anything that will require local government to contribute will die, may draw the system back or the programme back." *PHC coordinator & medical doctor*

Another identified challenge was the political-will or willingness of government at various levels (federal, state and local) to actively participate in the wide-scale implementation of IMCI strategy in Nigeria.

> **28:** "Then another one [challenge], will there be political will? It depends on the man on seat. If the man on seat has that political will to drive the force, well we can. But if the political will is not there that's gonna be a very serious challenge." *PHC coordinator & medical doctor*

Five HPs believed that sustaining the IMCI programme was a bigger challenge than the initial implementation. For example, the frequent disruption in the supply of relevant materials was cited as a possible challenge to the sustainable implementation of the

IMCI strategy. These HPs expressed concern about the financial burden of treatment on caregivers in the absence of regular supply of materials such as medications. As such, it was believed that caregivers may lose interest in seeking formal health care.

> **18:** "Like I know we had training for malaria fever somewhere at a time. So, we were taught how to use RDT. But at a time, they don't supply us stripes [RDT kits] and most of the parents have known that this thing is free, we don't pay for it but when we now ask them, maybe we now go and buy to continue doing that process, they will say, but you used to do it free, why are you now asking for money?" *Nurse*

> **22:** "To implement is not the problem, the sustainability is what matters. If you [researcher] leave now, people that have benefited from this programme are still coming back because maybe their child was two months when you came. By the time you tell the patient to pay for services given to them, they will start complaining or the patient might not even have money, what will you do? That's just the problem. It is sustainability that matters in any, in the implementation of any new programme." *Principal nursing officer*

The low level of employment of young PHWs, partly due to the governments' inability to fund the salaries, was also identified as a possible challenge to the wide-scale implementation of IMCI strategy. An HP believed that the employment and training in IMCI guidelines should focus on young PHWs who were more likely to be employed for a longer duration than older PHWs nearing retirement.

> **30:** "The factors, top most on the list is lack of man power, you find out that some of these people that were trained in IMCI have since retired and they retired without training the younger ones coming behind them. So, there is need for training and retraining of health workers and then admittance into the health facilities of new and younger health workers so that each facility has an IMCI trained worker that will be there for a long time. Not the one that's about to retire, the one that still has several years to go." *Consultant paediatrician & IMCI training facilitator*

The perceived poor diagnostic accuracy of RDT for malaria was reported as a potential determining factor for HPs' willingness to use the IMCI guidelines. One of the HPs advised that issues with the diagnostic accuracy of RDT for malaria need to be addressed to enhance health workers' compliance with the IMCI guidelines.

> **14:** "I have my own reservation fully based on the use of RDT. If it's strict that when the RDT are negatives we won't treat for malaria, we might run into a lot of problems because majority of the films, the RDT will give you negative and for those children when you do the investigation, you might find out that they are positive with malaria." *Medical officer of health*

The challenge of applying the IMCI was further compounded by the reports that some health workers had a general negative or biased attitude to health guidelines. Two HPs believed that this could contribute to non-compliance to the IMCI guidelines by health workers. To address this problem, four HPs advocated for continuous training and follow-up supervision of trained health workers.

> **26:** "Now if we eventually get the funds to carry out the training, some of the health workers are already having a bias [mind] against the guidelines. Until they are trained before that bias can be erased." *PHC coordinator & medical doctor*

> **29:** "What essentially happens is that many workers utilize the training for just soon after they have been trained, and after a while, they go back to their old ways. So supportive supervision is required to ensure that they continue to use these materials until it becomes a system or way of doing things." *Consultant paediatrician & IMCI training facilitator*

Two HPs believed that positive attitudes of communities to the IMCI strategy can significantly contribute to the successful wide-scale implementation and vice-versa. Referring to a previously 'failed' community intervention in the use of mosquito nets, an HP believed that to ensure acceptance and uptake, there was need to properly educate the community on the IMCI strategy and potential benefits.

4 DISCUSSION

4.1 Recap of study and introduction to discussion chapter

This study used a mixed-methods approach to evaluate early diagnostic approaches for malaria and pneumonia (IMCI guidelines and lay diagnosis) in children under the age of five years presenting to five primary healthcare centres in Benin City, Nigeria. Using quantitative data prospectively collected between September 2015 and July 2016, the study assessed both the accuracy and reliability of these diagnostic approaches and estimated the burden of malaria and pneumonia over an 11-month period. The study also assessed clinical outcomes of children diagnosed with malaria and pneumonia according to the IMCI guidelines and the risk factors.

The qualitative component of the study used semi-structured interviews conducted between February and May 2016 to explore caregivers' (n=13) and HPs' (n=17) perspectives of lay diagnosis and IMCI guidelines as diagnostic approaches for childhood malaria and pneumonia. Specifically, the first section of the qualitative study explored the perceptions of caregivers, and where relevant, HPs, regarding lay diagnosis of malaria and pneumonia. This section also sought to explore the feasibility and acceptability of caregivers being trained in the use of the IMCI guidelines for improved home management of common childhood malaria and pneumonia. The second section of the qualitative component explored the perceptions of HPs regarding acceptability of managing malaria and pneumonia with the IMCI guidelines and the feasibility of its wide-scale implementation in Nigeria.

This penultimate chapter begins by discussing the distribution of both malaria and pneumonia cases with an emphasis on the potential implications of coinfection. It then discusses the findings of the four study specific objectives in view of available literature.

It then synthesises the overall findings across the four study objectives using the approach of triangulation to mixed-methods research. The chapter concludes with strengths and limitations of the study, including the generalisability and transferability of findings.

4.2 Overlap in the classification of malaria and pneumonia and potential implications

Eighteen percent of the 903 children assessed by health workers using the IMCI guidelines met the classification for both malaria and pneumonia. In contrast, only 2 (0.30%) of the 667 caregivers that provided lay diagnosis of malaria and pneumonia provided a classification of both diseases. While symptoms overlap –the basis for the dual classification in the current study– does not equal disease overlap, evidence suggests it's a strong indication of malaria and pneumonia coinfection.[9,10] Whilst dual diagnoses are possible, it is also likely that some children will have malaria with pulmonary involvement, which may present as, but is not, pneumonia. The opposite scenario is equally possible. Clinical malaria has the tendency to weaken the immune system thereby predisposing children to pneumonia.[6] Conversely, pneumonia may predispose children to malaria or allow sub-clinical parasitaemia to become patent.[6] Byass and colleagues[6] argued that malaria itself may, in some situations, present with signs and symptoms (e.g. cough, catarrh etc.) suggestive of respiratory illness, in which case additional diagnosis of pneumonia according to the IMCI guidelines is likely. For instance, 20% to 50% of patients with malaria have been documented to present with a dry cough [7] while high fever, anaemia, and lung involvement have been implicated with the occurrence of tachypnoea (increased respiratory rate).[8]

The 18% mixed malaria-pneumonia classification recorded in the current study is lower than the 23% (284/1,216) recorded by Ukwaja *et al*[9] in Nigeria and 30% (1,099/3671) recorded by Källander *et al*[10] in Uganda. The differences may be attributable to the IMCI diagnostic criteria for malaria. While the definition of pneumonia was similar across all studies, the definition of malaria varied. Unlike the current study that defined malaria as fever (based on caregivers' report or ≥37.5 ^{o}C) plus positive RDT, the other studies defined malaria as fever during presentation to the health facility or recent history of fever. Findings of this study have implications for malaria and pneumonia management (diagnosis and treatment) especially at the community level.

The extremely small number of both malaria and pneumonia cases according to lay diagnosis suggests that caregivers may be less likely to recognise both diseases and adopt dual home-based treatments (antimalarials and antibiotics). This would lead to a focus on one of the diseases, most likely malaria, while the deleterious effects of the other remain unabated. This is a likely scenario in sub-Saharan settings, such as Nigeria, where caregivers' knowledge of and care seeking for malaria are better in comparison to pneumonia.[190,191] The possibility of overlap in malaria and pneumonia symptoms needs therefore to be reiterated in community interventions against common childhood illnesses. Currently, the IMCI guidelines appear to treat malaria and pneumonia as mutually exclusive diseases. This is justifiable in sub-Saharan Africa where children present with overlapping malaria and pneumonia symptoms, which necessitates dual IMCI classifications and treatments.[9] However, the current findings suggest the need for health workers to always look beyond a single classification and consider the feasibility of mixed infections. Certainly, overlap in symptoms and possible coinfection would prolong the time spent in diagnosing a patient and consequently the cost of medications

for dual positive cases. Nonetheless, this will need emphasising during the training of health workers in the use of IMCI guidelines.

4.3 Assessing the diagnostic accuracy and reliability of the IMCI guidelines and lay diagnosis for malaria and pneumonia diagnosis

Summary of main findings

This study objective assessed both the diagnostic accuracy and reliability of the IMCI guidelines and lay diagnosis for malaria and pneumonia in children under-five presenting to the study PHCs. First, it compared the diagnostic accuracy of the IMCI guidelines and lay diagnosis to microscopy (reference diagnostic approach). It also compared the accuracy of lay diagnosis of malaria and pneumonia by caregivers against the diagnoses made by healthcare workers using the IMCI guidelines. Lastly, the extent of agreement between caregivers' and health workers' diagnoses of malaria and pneumonia was assessed. The overall diagnostic accuracy of both the IMCI guidelines (AUROC value 0.57; 95% CI: 0.53–0.60) and lay diagnosis (AUROC value 0.55; 95% CI: 0.52–0.59) was poor in comparison to microscopy. Specifically, the IMCI guidelines showed better sensitivity than caregivers in the diagnosis of malaria (51.8% versus 31.1%) as compared to microscopy, whereas, reverse was the case with regards to specificity (79.5% and 61.3% for lay diagnosis and IMCI respectively). When the IMCI guidelines were considered as the reference diagnostic test, caregivers' diagnosis of malaria (AUROC value 0.60) was more accurate than their diagnosis of pneumonia (AUROC value 0.54). There was minimal level of agreement between caregivers and health workers in the diagnosis of malaria and pneumonia (kappa statistic 0.14; 95% CI: 0.09–0.19).

Validity of the IMCI guidelines and lay diagnosis

The validity of a diagnostic test, described by its sensitivity and specificity, is the ability to detect a person with disease or exclude a person without disease.[192,193] Compared with microscopy, both the sensitivity (52%) and specificity (61%) of the IMCI guidelines were relatively low. These values are below the WHO recommended ≥95% and ≥90%, respectively, for sensitivity and specificity of HRP2-based RDT kit in a clinical setting in Nigeria.[41] Furthermore, the low sensitivity of the IMCI guidelines compared to specificity is contrary to the normal expectation in which the IMCI guidelines show superiority in sensitivity for the diagnosis of childhood illnesses even at the expense of specificity.[113] This is justifiable given the severity and deleterious impact of common childhood illnesses (e.g. malaria and pneumonia) in children under-five with less developed immune system.

Findings in the current study contradict with previous studies in the Gambia,[98] Kenya [113] and India [194] where compared to microscopy, specificity of the IMCI guidelines was consistently lower than sensitivity in the diagnosis of malaria. In contrast, the findings are consistent with those recorded by Simoes and colleagues in Ethiopia where the specificity of the IMCI guidelines was higher than sensitivity for malaria diagnosis.[195] Nevertheless, these contrasting findings may be attributed to the methodological differences between the current study and the others. Unlike the current study where the diagnosis of malaria by the IMCI guidelines was based on positive RDT (the revised IMCI guidelines), the Kenyan and Gambian studies [98,113] based malaria diagnosis on only fever (the initial IMCI guidelines). Thus, the low specificities of 8% and 0% in the Gambian and Kenyan studies, respectively, could be attributed to high number of false positive cases owing to the inability of fever to accurately predict malaria. This limitation of the old IMCI guidelines and attendant consequences (e.g. occurrence of

antimalaria resistance) have been addressed through the mandatory undertaking of RDT to decide malaria treatment. Conversely, basing malaria diagnosis on only fever may explain why the sensitivity for malaria diagnosis was higher in the Kenyan (100%) and the Gambian (87%) studies as compared to the current study (51.8%). Furthermore, the high specificity (71%) recorded by Mittal *et al* [194] for malaria diagnosis compared to the 61.3% recorded in the current study may be attributable to differences in study settings. Unlike the current study that was carried out in primary healthcare facilities, that of Mittal and colleagues was carried out in a tertiary healthcare centre where malaria cases were more likely to be severe and readily identified based on presenting signs and symptoms. The marked difference between specificity (99%) and sensitivity (39%) for malaria diagnosis (also based on fever) recorded by Simoes and colleagues [195] was attributed to difficulty in using the IMCI guidelines in areas with varying malaria risk, as well as the confusion between axillary and rectal temperature thresholds. The current study was carried out in a setting that is endemic for malaria and relied only on axially temperature.

The moderate specificity of the IMCI guidelines in the diagnosis of malaria indicates feasibility of a substantial number of false positive cases especially during the rainy season when transmission of malaria is at its peak.[41] Nevertheless, the recorded specificity in the current study could be partly explained by the brand of RDT kit used. CareStart Malaria HRP2 (Pf) kit for the rapid diagnosis of malaria targets *Plasmodium falciparum* histidine-rich protein-2 (*Pf*HRP2) which can persist in the bloodstream for as long as 2–5 weeks after treatment.[196–199] Evidence suggests that this is a limitation of this kit and a major cause of false-positive results (low specificity).[196–199] It could be argued that the diagnostic accuracy of the IMCI guidelines in the current study might

have been different, perhaps better, if an RDT kit which targets plasmodial lactate dehydrogenase (pLDH) had been used. The pLDH is produced by live parasites and RDT kits which target this antigen have been shown to be more accurate in diagnosing malaria than *Pf*HRP2-specific kit.[201] However, this argument may not be sufficient to explain the observed findings in the current study. This is because several studies [41,149] in which distinct brands of RDT kits targeting *Pf*HRP2 were used for malaria diagnosis recorded far better specificity values relative to microscopy. For example, the evaluation of SD Bioline RDT kit (which targets *Pf*HRP2) in northern Nigeria recorded 98.5% specificity, as well as 100% sensitivity, in comparison to microscopy.[41] It could be asserted therefore that the brand (product quality) of an RDT kit, in addition to the target antigen, contributes to its diagnostic performance.

The moderate specificity of the IMCI guidelines has potential impacts on both caregivers and health workers. High false positives by the IMCI guidelines could result in the needless prescription of antimalarial drugs for the treatment of non-malaria febrile illnesses.[204] This would, in turn, lead to an increased financial burden on caregivers at the primary healthcare level many of whom are of lower socioeconomic status in Nigeria.[95,205] Moreover, false positive cases could increase the time spent by health workers on a patient and consequently their workload. This would be more impactful in Nigeria where the health worker–patient ratio is extremely low.[206] For example, health workers are less compliant to the IMCI guidelines when there are too many patients waiting healthcare services.[102,207–209]

The poor sensitivity of the IMCI guidelines in diagnosing malaria (51.8%) as compared to microscopy in the current study implies high false negatives. The low sensitivity of RDT in the current study is comparable to those recorded in Zamfara (40.3%) and Enugu

(42.3%) States [210,211] in Nigeria where similar brand of RDT kit was used. The missed opportunity to treat children with malaria due to false negative diagnostic outcome could result in adverse clinical outcomes such as convulsion and death. There are several possible explanations for high false negatives. Quite often, false negative results arise due to low parasite density (<200/µL) especially for RDTs that target HRP-2.[211,212] Thus, undertaking this study over an 11-month period, which covered the dry season, may have contributed to the recorded sensitivity given low parasitaemia during this period. Deletion of the HRP2 gene in *P. falciparum* (when parasites fail to express the target antigen) has been reported to contribute to the occurrence of false negative results with RDTs that are HRP2-specific.[213,214] However, this may not be feasible given the lack of record of HRP-2 deletion in study setting. Furthermore, CareStart being a *P. falciparum*–specific RDT kit may have failed to detect other *Plasmodium species* (e.g. *P. ovale* and *P. malariae*) that are in circulation in Nigeria.[215] The potential impact of negatively affecting sensitivity is supported by research evidence. Using a CareStart™ Malaria HRP2/pLDH Combo RDT kit in a 'low transmission region' of Senegal, Diallo and colleagues[216] recorded excellent sensitivity (97.3%) and specificity (94.1%) relative to PCR. Unlike the brand used in the current study, that of Diallo and colleagues is designed to detect both *PfHRP*-2 and pLDH of all malarial species. Similar findings have been reported in China-Myanmar endemic borders [217] and Ethiopia using microscopy as the reference diagnostic test.[218] Lastly, false negative RDT results could arise in samples with high Plasmodium parasitemia attributable to a phenomenon called 'prozone effect' or 'high-dose hook effect. [219,220] Prozone effect is when false negatives occur as a result of high antibody concentration, which saturates antigens thereby preventing lattice formation and precipitation –positive reaction.[220] In such a scenario, antimalarial treatments could be withheld from patients who have very high parasite

density.[219] The feasibility of prozone effect in the current study is however difficult to ascertain as parasitaemia density was not assessed either by RDT or microscopy.

Compared to microscopy, caregivers' diagnosis of malaria recorded low sensitivity, possibly resulting in failure or delay to initiate appropriate home-based management or seek care at formal healthcare settings for suspected childhood malaria. This has been found to contribute to the occurrence of adverse outcomes such as admission to critical care or death.[31] The low sensitivity could be attributed to the endemicity of malaria in this study setting as it becomes readily dismissed as a common and non-threatening illness.[221–223] In contrast, caregivers' diagnosis of malaria was highly specific suggesting they were good at ruling out malaria. However, the notably poor NPV of caregivers' diagnosis of malaria suggests the need to carry out a confirmatory diagnostic test before dismissing negative diagnosis.

Compared to the IMCI guidelines, the sensitivities of caregivers' diagnosis of malaria (38.0%) and pneumonia (17.5%) were extremely low in the current study. This is worrisome given the availability of effective treatment for two leading causes of morbidity and mortality in children under-five. The approach used in this study to ascertain caregivers' diagnosis of malaria and pneumonia may have contributed in underestimating their diagnostic performances as compared to the IMCI guidelines. In addition to basing caregivers' diagnoses on a single event, diagnoses of 'fever' and 'cough' were classified by paediatricians as non-malaria and non-pneumonia, respectively, despite the possibility of these being actual malaria and pneumonia cases. Evidence suggests that caregivers tend to use 'fever' and 'malaria' [224] or 'cough' and 'pneumonia' interchangeably.[225] For example, the study of malaria assessment by 131 women in Benin City Nigeria found that more than half of the study participants (59%)

considered fever as an indication of malaria.[137] When fever and cough were considered as indicators of malaria and pneumonia, respectively, in the current study (results available in Appendix VII), caregivers' overall diagnostic accuracy improved significantly especially for pneumonia. Compared to the IMCI guidelines, the AUROC for caregivers' diagnostic of pneumonia increased from 0.54 (poor) when cough was considered as non-pneumonia to 0.79 (excellent) when it was considered as pneumonia. Treating fever as an indicator of malaria also improved caregivers' diagnostic accuracy (AUROC 0.60 to 0.69), albeit the improvement was lesser compared to that of pneumonia. While the possible underestimation of caregivers' diagnostic capacity in the current study may be feasible, the findings equally suggest that some malaria and pneumonia cases as diagnosed by caregivers might have been mere fever and/or cough. In such a scenario, caregivers' diagnostic accuracy may have been overestimated.

Predictive capacity of the IMCI guidelines and lay diagnosis

The positive predictive value (PPV) and negative predictive value (NPV) are more relevant to the health professional in estimating the probability of a disease condition in individual patients than sensitivity and specificity.[192] While the classification of sensitivity and specificity are based on individuals with or without a disease condition, the PPV and NPV can describe an individual's chance of having a condition once the test results are known.[192,226] The NPVs of the IMCI guidelines (48.4%) and lay diagnosis (47.1%) were relatively low, suggesting that a negative result according to these diagnostic approaches may not be sufficient to confirm the absence of malaria (high false negatives). This has a few implications for both health workers and caregivers. The low NPV of the IMCI guidelines implies that despite a negative diagnostic outcome, health workers may choose to administer anti-malarial drugs especially when a child

presents with signs and symptoms suggestive of malaria. Consequently, health workers may be less willing to strictly comply with diagnostic outcomes of the IMCI guidelines for childhood malaria management. The issue of non-compliance by health workers based on diagnostic outcome of the IMCI guidelines is not new as it has previously been reported by other studies.[204,208,227] Conversely, the low NPV of lay diagnosis suggests the need for further confirmatory diagnosis regardless of a negative lay diagnosis. In addition to the cost of double diagnosis, the low NPV could hamper the feasibility of relying on lay diagnosis for surveillance purpose especially in developing countries where standard services are either unavailable or unsustainable. However, a negative diagnosis of pneumonia by caregivers is firmly supported by the IMCI guidelines given the excellent NPV (86.6%).

While sensitivity and specificity are stable properties of diagnostic approaches, most of the gain in the PPV is dependent on the underlying disease prevalence.[168] This might possibly explain why the PPV for caregivers' diagnosis of malaria (prevalence of 19.6%) was 63.3% compared to that of pneumonia 25.0% (prevalence of 7.5%). Moreover, this suggests that the predictive values of the IMCI guidelines and lay diagnosis for malaria and pneumonia based in PHCs may not be applicable at the higher healthcare centres (e.g. secondary hospital) where the prevalence of these diseases is likely to be different.

Interobserver agreement for malaria and pneumonia diagnosis between caregivers and health workers using the IMCI guidelines

There was poor agreement between health workers using the IMCI guidelines and caregivers regarding malaria and pneumonia diagnosis in the current study (k=0.14; 95% CI: 0.09-0.19). This may be indicative of poor understanding of the clinical features of these diseases (especially pneumonia) by caregivers and grounds for concern. Poor

parental understanding of malaria and/or pneumonia could negatively affect both the diagnostic processes by health workers and clinical outcome of children. This underlines the need to train caregivers in in standard diagnostic approach (e.g. the IMCI guidelines) for better recognition and reporting of childhood malaria and pneumonia at the community level. However, the low level of agreement between caregiver-health workers is less likely to introduce bias due to interobserver variability. This is because of the blinding of caregivers' diagnoses to the diagnostic outcomes of IMCI guidelines. It is worth noting that the minimal level of agreement recorded in the current study does not equates to poor diagnostic accuracy. Even when caregivers' and health workers' classification of malaria and pneumonia differ (poor agreement), diagnostic accuracy may not.

4.4 Estimating malaria and pneumonia burden among children under-five

Summary of main findings

This study objective provided an estimated burden of malaria and pneumonia among children under-five presenting to the study PHCs during study period according to various diagnostic approaches. The estimated burden of malaria during the study period was 14.6%, 17.0% and 6.4% according to the IMCI guidelines, microscopy and lay diagnosis respectively. The estimated burden of pneumonia over the same period was 4.6% and 2.4% according to the IMCI guidelines and lay diagnosis respectively. In terms of study setting, the estimated burden of malaria and pneumonia was significantly higher in Egor LGA compared to Ikpoba-Okha and Oredo LGAs, regardless of the diagnostic approach. A similar pattern was recorded for the estimated burden of malaria and pneumonia at individual PHCs in these LGAs. It was also found that seasonal variables

(average monthly temperature, rainfall and humidity) appeared to influence the estimated burden of malaria and pneumonia during the study period. The highest and lowest number of malaria and pneumonia cases were recorded during the rainy season (September–October 2015) and dry season (December 2015–February 2016) respectively.

Estimated burden of malaria and pneumonia compared to national estimates

The estimated burden of malaria according to the IMCI guidelines and microscopy in the current study were relatively low compared to the national estimates for children under-five in Nigeria.[50] However, this needs to be interpreted with caution because, unlike the current study, the estimates for Nigeria were based on surveys carried out between October and November when the number of malaria cases tend to be high. Similarly, the estimated burden of pneumonia in the current study was lower than the values recorded by studies for children under-five in Nigeria which were carried out in secondary and tertiary hospitals.[9,85,86,90] The extremely low burden of malaria based on caregivers' diagnosis in the current study appears to reflect the level of knowledge of malaria among women in study seting.[50] The 2016 national survey on knowledge of malaria survey showed that the proportion of women from Edo State (where this study was undertaken) recorded the lowest level of knowledge of malaria as compared to their counterparts from neighbouring States in Southern Nigeria.

Estimated burden of malaria and pneumonia across study setting

The estimated burden of malaria and pneumonia was not evenly distributed across the three LGAs and five PHCs, despite the proximity. This underlines the complexity of disease burden in a setting of similar climatic and environment conditions.[228] Despite

the apparent similar climatic conditions across the study LGAs and PHCs, the estimated burden of malaria was substantially higher in Egor compared to Ikpoba-Okha and Oredo LGAs, as were the corresponding PHCs. While the factors that influence variation in the epidemiology of malaria within the same geographical setting are not completely understood, proximity to mosquito breeding sites or vegetation has been identified.[229] The drainage system in Egor communities seemed less efficient compared to those in Oredo and Ikpoba-Okha communities, hence creating more breeding sites for mosquitoes. An alternative explanation for the higher burden of malaria and pneumonia in Egor LGA could be due to the number of health workers who participated in the 2-day IMCI training for this study. There were more trained health workers in Egor LGA (n=14) than in Ikpoba-Okha (n=4) and Oredo (n=3) making it more likely for potential eligible children to be recruited into study at this location. Other potential factor includes the number of viable PHCs in each study LGA (three in Egor and one each in Ikpoba-Okha and Oredo), which may have influenced the patient load in these LGAs. This underlines the importance of wide-scale implementation of the IMCI training across PHCs in a setting.

Impact of variation in diagnostic accuracy on estimated burden

It appears that variation in the estimated burden of malaria in the current study was dependent of the degree of sensitivity of various diagnostic approaches. As such, it appears that the type of RDT kit used in the current study contributed to the estimated burden of malaria according to the IMCI guidelines. As previously explained in the discussion of first study objective, the RDT kit used in this study targets *Plasmodium falciparum* histidine-rich protein 2 (*Pf*HRP2) which can persist in the bloodstream 2–5 weeks after parasite clearance or successful treatment.[196–198,230] It is therefore possible

for antigens from previous malaria infections to have been wrongly identified as active part of the current infection, which in turn would inflate the number of positive malaria cases (false positives). In contrast, the *Pf*HRP2 antigens would be unrecognised by microscopy and classified as negatives. Furthermore, it is possible that health workers' diagnostic performance and consequently the estimated disease burden may have been influenced by the adopted longitudinal approach to study. This is such that the assessment of children for malaria and/or pneumonia may become less accurate with time due to loss of diagnostic skills or principles.[231]

It was surprising that despite the reported endemicity of malaria and pneumonia in study setting, caregivers' estimation of these diseases was not comparable to the values recorded by the other diagnostic approaches. A possible explanation could be due to the approach used for classifying caregivers' diagnosis of malaria and pneumonia. As previously explained in the discussion of caregivers' diagnostic accuracy (discussion of first study), it is possible that some of the fever and cough cases were malaria and pneumonia. This is interesting given that more than half of the total diagnoses made by caregivers were 'cough' and fever and classified as non-pneumonia and non-malaria, respectively. Nonetheless, these findings suggest that a surveillance system that relies on caregivers' reported cases of malaria and pneumonia may seriously underestimate their prevalence. This would be particularly challenging in developing countries where self-reports of morbidities and mortalities (verbal autopsy) are becoming complementary diagnostic tools to the often limited surveillance systems and medical records from health facilities.[126]

Association of seasonal variables with estimated burden of malaria and pneumonia

The pattern to the distribution of malaria cases in the current study are congruent with previous studies in Nigeria where low and high number of cases were recorded during the dry season and rainy season, respectively, with peaks toward the end of the rainy season.[232,233] Rainfall provides habitat for breeding,[232] prolongs the longevity of malaria vectors due to the increase in humidity and facilitate the growth of vegetation which serve as niche for mosquito larval proliferation.[234] This may explain why the estimated number of malaria cases was higher in September and October 2015 when the average rainfall for these months was high. Interestingly, November 2015 accounted for the highest episodes of malaria according to the IMCI guidelines and microscopy despite recording lower amount of rainfall as compared to September and October 2015. The number of malaria cases tend to peak immediately after the rainy season when water bodies can retain pockets of stagnant water and floods have receded to facilitate the breeding of mosquito and burgeoning population.[235] In addition, mosquitoes are more productive during this period as their eggs or larvae become less likely to be washed away by floods or rain drops.[236] Regarding the influence of temperature on the distribution of malaria, it appears the anopheles mosquitoes reproduce and mature faster at an increased temperature of 27.5–30ºC. For example, on average, it takes about 22–23 days at 20ºC and half the time at 27.5–30ºC for mosquitoes to reproduce and mature.[237] This corresponds with the high number of malaria cases recorded between September and October 2015 when the average temperature was 29ºC and 30ºC respectively.

Similar to findings in the current study, influence of seasonality on the burden of pneumonia has been noted elsewhere in Nigeria with higher number of cases recorded during the rainy season.[158] During the rainy season, people tend to stay indoors to avoid

cold, which in turn enhances the transmission of potential pathogens (e.g. *Streptococcus pneumoniae*) from infected to healthy individuals. Furthermore, the high number of pneumonia cases recorded between October and November 2015 corresponded with harmattan during study period. Harmattan in Nigeria is characterized by cold-dry air and dusty north-east trade wind with occasional cold depending on the location.[238] The increased dust particles during this period can facilitate the spread of pneumonia infection through droplets.[239]

Worth noting was the marked difference in the estimated burden of malaria and pneumonia diagnosed by caregivers in the months coinciding with rainy and dry seasons. Like the standard diagnostic approaches, there were more malaria and pneumonia cases according to lay diagnosis in the months corresponding to rainy season than dry season. This suggests that caregivers have awareness of the influence of seasonality on the occurrence of childhood malaria and pneumonia. This is demonstrated by the clothing, often with sweaters, on children during the rainy season as compared with dry season in study setting.

4.5 Assessing clinical outcomes in children diagnosed with malaria and pneumonia and risk factors for severe outcomes

Summary of main findings

This study objective sought to determine the clinical outcomes in children within 30 days of being diagnosed with malaria and pneumonia according to the IMCI guidelines and risk factors for severe outcomes. Most of the children diagnosed with malaria and pneumonia by health workers using the IMCI guidelines recovered within 30 days. In addition, the level of adherence or compliance by caregivers to medications for diagnosed malaria and pneumonia was generally high. Living in houses that adopted

preventive measures (e.g. ownership of LLINs, netting of windows/doors and intermittent treatment of malaria) were independently and significantly ($p<0.05$) related to reduced odds of severe and worsened illness within 30 days of malaria diagnosis. However, self-medication prior to presenting to the study PHCs appeared to be protective for adverse clinical outcomes especially in relation to the occurrence of worsened illness within 30 days of malaria diagnosis. In contrast, exposure to solid fuels was independently and significantly ($p<0.05$) associated with increased odds of severe and worsened illness within 30 days of malaria diagnosis. Notably, none of the identified independent predictors of severe and worsened clinical outcomes within 30 days of malaria diagnosis was statistically significant in pneumonia cases. Nonetheless, self-medication prior to presenting to the study PHCs any exclusive breast feeding for the first six months of life appeared protective against the occurrence of severe and worsened illness within 30 days of pneumonia diagnosis. In contrast, exposure to solid fuels in the kitchen while staying with a caregiver during cooking and smoke from a family member who smoke increased the risk of adverse clinical outcomes.

Distribution of clinical outcomes

The relatively small number of severe outcomes in children diagnosed with malaria and pneumonia in the current study could be indicative of how well the IMCI guidelines are able to manage childhood illnesses. Evidence suggests that children with suspected malaria and pneumonia who are managed by health workers using the IMCI guidelines tend to have better clinical outcomes compared to those managed with the traditional approach (non–IMCI).[240,241] The extremely high level of adherence to medications among caregivers in this study may be partly explained by the post-treatment counselling provided by health workers in line with the IMCI guidelines. Health workers

who have been trained in the IMCI guidelines are better at prescribing medications and providing the necessary follow-up advice to caregivers.[242,243] During the IMCI training, health workers are taught effective communication skills (e.g. use of praise and assessing caregivers' level of comprehension) and the provision of follow-up advice including dosage regimen. However, the number of objectively verified compliance to medications in the current study was low. This underlines one of the possible challenges in conducting prospective follow-up study in a developing setting. For instance, a major challenge to the follow-up of participants in the current study was the lack of verifiable house addresses provided by caregivers. Nevertheless, findings in the current study are consistent with those in Ghana where there was a significant improvement in clinical outcomes among 94% of 593 under-five febrile children 7–10-days after being managed by health workers using the IMCI guidelines.[244]

Association of self-medication with clinical outcomes

Although specific details were not ascertained, protection conferred by the intake of medications prior to presenting to health facilities is indicative of the potential health benefits of prompt treatment of malaria. This is congruent with the findings by Sirima *et al.*[245] in Burkina Faso where children who had taken antimalarials before presenting to health facilities were less likely to develop severe illness compared to their counterparts. The specific mechanism by which self-medication confers protection on children diagnosed with malaria is not well understood. However, it appears the prior intake of antimalarials prolongs the incubation period of malaria parasite and its multiplication rates, thereby lowering parasitaemia and occurrence of adverse clinical manifestations.[246] Notwithstanding the recorded health benefits, the association between self-medication and occurrence of severe illness following malaria diagnosis was almost

statistically insignificant (p=0.050). This is indicative of finding being by chance and needs to be considered during interpretation. Moreover, self-medication is often based on presumptive diagnosis with several deleterious impacts ranging from exacerbation of drug resistance[247] to financial losses to caregivers.[248] A potential strategy to minimise this impact however would be to train caregivers in standard clinical guidelines (e.g. the IMCI guidelines) so that the practice of self-medication is guided by research evidence.

Association of preventive and control measures for malaria with clinical outcomes

The common preventive and control measures (i.e. ownership of insecticide treated mosquito nets, living in houses with netted doors/windows, use of IRS and intermittent treatment of malaria) were protective against the occurrence of severe and worsened illness within 30 days of malaria diagnosis. These protective measures seem to function by preventing the infective bites from mosquitoes and initiation of 'reinfection' following malaria diagnosis. This is a plausible explanation given the short incubation period of 9–14 days for *Plasmodium falciparum*.[249] This is a serious problem for children under-five whose acquired immunity against reinfection becomes weak after an initial cure from malaria infection.[250] Nonetheless, in contrast to the assumption in this study, evidence suggests that the ownership of LLINs does not necessarily translates into usage especially during the dry season when weather is hot and uncomfortable in Nigeria.[48,251] It is possible therefore that the observed association between the use of LLINs and clinical outcomes in the current finding may be biased as the ownership of LLINs was assumed to be equate actual usage. Also, worth noting is the potential effect of confounding in these findings. The protection conferred by these protective measures was by far higher in the univariate analyses as compared to the multivariable model with adjusted ORs.

Association of exposure to solid fuels with clinical outcomes

Solid fuels (e.g. smoke from firewood or stove in the kitchen) produce high amount of household air pollution containing health–damaging pollutants such as small soot particles and gasses (e.g. carbon monoxide, nitrous oxides etc.) capable of penetrating deep into the lungs.[252] These pollutants cause health problems by altering the defense mechanisms of the lungs, for example, decreasing mucociliary clearance or macrophage responses to pathogens.[253–255] Similar to findings in the current study, a prospective cohort study in the Dominican Republic found that compared to their counterparts whose caregivers used clean gas for cooking, the risk of acute lower respiratory infections in children exposed to charcoal smoke increased by 56% during a 12-month follow-up period.[256] Despite the associated risk, preventing children under-five from being exposed to solid fuels in developing settings may be a challenge as they often stay with their caregivers in the kitchen while cooking.[257,258]

Unlike pneumonia, the association of solid fuels with malaria is not clear-cut given the conflicting evidence.[36,259] Yamamoto and colleagues [259] in a case-control study found that exposure to particulate matter from biomass smoke in sleeping rooms of 283 children (aged <9 years) in Burkina Faso reduced the risk of malaria by more than 50%. The authors postulated that protection from solid fuels could be due to the toxic environments created by smoke which affected the transmission of mosquitoes. In contrast, Ghebreyesus and colleagues [36] in a prospective study found greater risk of malaria among Ethiopian children living in (presumably smokier) houses without separate kitchens. The authors believed that the increased risk of malaria was partly due to entrance by mosquitoes to houses through open eaves. Ghebreyesus and colleagues believed the repellent effect of smoke on mosquitoes had less effect as main feeding

activities were carried out throughout the night when cooking would have been completed. Notwithstanding, both studies investigated the impact of exposure to solid fuels as a risk factor for malaria, rather than the potential impact on post-treatment outcomes (severe and worsened illness). However, the explanations provided by Ghebreyesus and colleagues may be applicable to the current study given the availability of open eaves in houses in study setting. It is interesting to note the potential confounding effect on the risks posed by exposure to solid fuel in the current study. For example, the odds of severe illness in children diagnosed with malaria decreased from 3.19 in the univariate analysis to 2.69 after adjusting for other potential risk factors.

4.6 Exploring stakeholder perspectives of lay diagnosis and IMCI guidelines as diagnostic approaches for malaria and pneumonia

Summary of main findings

This study objective explored stakeholder's (caregivers and health professionals) perspectives of lay diagnosis and IMCI guidelines as diagnostic approaches for malaria and pneumonia. Lay diagnosis was found to be a widely practised diagnostic approach by caregivers despite the awareness of its limitations. Caregivers were generally more confident in diagnosing malaria compared to pneumonia and this was largely due to their perceived severity and beliefs. Suspected malaria was managed hierarchically by caregivers beginning from the home and then to the chemist stores or healthcare services operated by health workers. Formal healthcare services, preferably PHCs, were explored when illness was not improving or becoming worse. Conversely, suspicion of pneumonia prompted visit to the nearest formal healthcare centre without exploration of the initial line of care in the case of suspected malaria. For improved home-based management of common childhood illnesses in their children and neighbours' children,

most caregivers expressed enthusiasm and willingness to become trained in the use of the IMCI guidelines. However, some caregivers and health professionals were concerned over the safety and appropriateness of this approach.

There was a general sense of satisfaction among health workers over the delivery of the 2-day IMCI training for the current study. However, many health workers believed the duration was insufficient to consolidate what they were taught and unanimously suggested 5–7 days as an appropriate duration for subsequent IMCI trainings. Notably, HPs expressed concerns on the reliability of RDT results given the observed contradictions with common signs and symptoms of malaria. Generally, HPs believed that the wide-scale implementation of IMCI in Nigeria was feasible but identified inadequate finance, political–will and sustainability as important recurrent challenges that needed to be addressed.

4.6.1 Stakeholder perspectives on lay diagnosis of malaria and pneumonia

Perceptions of lay diagnosis

Lay diagnosis was a widely practised diagnostic approach used by caregivers as an early intervention measure against common childhood illnesses. Findings in the current study are consistent with other studies which found that though lay diagnosis was regarded by caregivers as unreliable, it was nevertheless widely practised.[112,260] In addition, the current study showed that lay diagnosis was more like an inherent response to illness in the self or family. In some instances, the 'lay diagnosis' may be a much more nebulous decision pathway leading to referral to a healthcare provider (as seems to be the case in pneumonia), while in other instances, like malaria (an endemic and more commonly

experienced disease), the lay diagnosis may be more definitive and lead to self-treatment.

Diagnostic criteria for malaria & pneumonia

In terms of diagnostic criteria, the signs and symptoms mentioned by caregivers for the lay diagnosis of malaria in themselves and in their children are consistent with those in the clinical medical literature.[246] Interestingly, most of the caregivers in this study reported having bitter taste in the mouth as the most characteristic and convincing symptom for malaria in themselves. While few studies have reported bitter taste in the mouth as a symptom of malaria, most do not.[261,262] Currently, there are reports of how the non-specificity of malaria signs and symptoms contribute to the indiscriminate use of antimalarials.[12,14] It may be worthwhile therefore to validate bitter taste in the mouth to address this challenge. Depending on the outcome, this symptom could be re-emphasised in clinical guidelines and public health awareness campaigns.

Caregivers reported using signs such as decreased physical activity, loss of appetite, fever and incessant crying to 'suspect' malaria in their children. These are consistent with those reported in the medical literature.[246,263] However, observations of these signs support the notion that caregivers may be able to detect minor changes in their children's behaviours as possible diagnostic clues that may be otherwise missed by healthcare professionals during early phases of malaria when more specific clinical signs and symptoms may be absent.

For the few caregivers who were confident they could offer a diagnosis of pneumonia in their children, the common signs and symptoms (e.g. difficulty in breathing, fast breathing, fever) are in accordance with those in medical literature.[264–267] Interestingly,

fast breathing (tachypnoea) mentioned by caregivers in this study has been shown to have a high accuracy with 74% sensitivity and 67% specificity for radiologically defined pneumonia.[268] The belief that pneumonia in children was caused by the penetration of chest region by cold or breeze has been previously reported by other studies in Nigeria.[190,269] Regarding preventive and control measures against pneumonia, most caregivers in this study believed that adequate clothing and avoidance of cold would suffice. However, it is worrying that caregivers seemed to lack knowledge of essential preventive measures such as the common Pneumococcal Conjugate Vaccine (PCV) given the burden of childhood pneumonia in Nigeria. This apparent poor knowledge of basic preventable measures among caregivers may be indicative of low coverage or uptake of interventions against pneumonia.

Perceived severity, self-efficacy and lay management of malaria and pneumonia

Overall, this study showed that caregivers' perceived severity of both malaria and pneumonia influenced their self-efficacy and ultimately the typical pathway taken for managing these diseases. Malaria was regarded by caregivers as a common and mild illness. This phenomenon has previously been reported in Kenya,[270,271] Tanzania [222] and Nigeria.[223] Conversely, pneumonia was regarded as a very dangerous illness as demonstrated by caregivers' preference for formal healthcare centre where doctors and qualified health professionals were believed to be available. These perceptions of malaria and pneumonia by caregivers appeared to influence their perceived self-efficacy to manage these diseases. This is in line with other studies [272,273] where the perceived severity of pneumonia was found to have negatively affected caregivers' ability to manage the illness in their children. It is worth noting that low diagnostic accuracy in caregivers does not necessarily translates into a low degree of confidence or sense of

self-efficacy to provide diagnosis. It was unsurprising therefore that lower education levels appeared to be associated with lower diagnostic accuracy but not with self-efficacy in this study. While health literacy and general literacy both share similar attributes in terms of acquisition, processing and application of information to specific needs in life, the former is more specific.[274] For example, it is possible for a more educated caregiver (generally literate) to be more aware of the signs/symptoms and complexities around diagnosis (i.e. high diagnostic accuracy) and be less confident in diagnosing an illness (i.e. low self-efficacy) and vice-versa.

Furthermore, caregivers' perceptions of malaria influenced their choice of first exploring home-based management or other home-based health services (chemist stores) as the initial line of care. This trend has also been reported by other studies where the more severe caregivers perceived the child's malaria to be, the more likely they were to seek professional healthcare services.[275–277] In contrast, the perception of pneumonia appeared to influence caregivers' preference for formal healthcare centres (e.g. PHCs) as the first line of care for suspected cases. This typical pathway is corroborated by studies in Sierra Leone [278] and Nigeria [190] where caregivers described pneumonia as a 'hospital sickness' that could lead to serious complications if not promptly addressed. The typical pathways taken by caregivers for managing suspected childhood malaria and pneumonia could be explained by the health belief model (HBM). Based on the HBM, caregivers were more likely to take prompt action, in this case seek professional healthcare services, for suspected pneumonia that was perceived to be very severe than malaria perceived as a 'common' illness.[279] In terms of self-efficacy, caregivers felt more confident in their ability to diagnose and treat malaria due to its endemicity in the study setting and the frequent interactions with health service providers; suggesting that

affected children were more likely to receive prompt treatment for malaria at home and not for pneumonia.

It should be noted that the treatment pathways adopted for suspected malaria and pneumonia may not be a simple linear one as depicted by Figure 3.10 in the result chapter, where caregivers alter healthcare seeking behaviour depending on perceived severity of illness or referral by a health professional. Instead, the process is most likely iterative with caregivers constantly reappraising signs and symptoms and possibly proffering a lay diagnosis and, in many cases, seeking professional healthcare based on the perceived severity of the illness.[280,281]

Perceptions on training caregivers to use the IMCI guidelines

The health impact of an intervention based on the home management of malaria among caregivers of children under-five in Ogun State Nigeria provides insights on the potential benefits of training caregivers in the IMCI.[282] Using the course contents of the Nigeria National Malaria Control Program, caregivers in the intervention group were provided a two-week training on three courses that consisted of malaria transmission, prevention and treatment, and malaria prevention and treatment practices. Following a 3-month training, caregivers in the intervention group were better at administering the right dose of medications and recognising danger signs to prompt immediate presentation to health centres than their counterparts in the control group. The shifting of tasks from professional health workers to community members is rooted in the philosophy endorsed in the 1978 Alma-Ata Declaration, which called for 'bringing health care as close as possible to where people live and work'.[283] The approach of home-based management was adopted by the WHO to reduce malaria burden.[122] It involves training lay

community members as health workers to diagnose and provide treatment for malaria, and provide education to caregivers on malaria. Reduction in malaria burden has been reported with the implementation of this approach.[123] Training caregivers to use the IMCI guidelines however has potential challenges that need to be addressed. Some caregivers in the current study expressed fear of being held responsible or branded 'evil' in the event of adverse clinical outcomes. This is understandable given the influence of superstitious or traditional beliefs in Nigeria.[284,285] The training of caregivers in standard guidelines for improved management of common childhood illnesses would therefore benefit from specific interventions on counteracting harmful superstitious beliefs to health in Nigerian communities. Moreover, some HPs were concerned that caregivers may be less professional to adhere strictly to specified drug dosages in the IMCI guidelines, thereby amplifying the problem of over-administration of medications. This is equally worth addressing.

4.6.2 Stakeholder perspectives on IMCI guidelines

Perceptions of IMCI guidelines

Findings in the current study are consistent with other studies [209,286] where training in the IMCI guidelines was adjudged informative and empowering by health workers. Despite the initial challenges experienced shortly after training, improved management of patients and counselling of caregivers as reported by health workers in the current study have also been reported in a systematic review.[242] Ideally, the IMCI training modules require health workers to be trained for 11 days and then followed-up by the trainers for 5 weeks averagely to consolidate their new skills.[287] However, a 2-day training course was adopted for the current study for pragmatic reasons and research objectives, thus may not reflect the true capacity building needs in Nigeria. Interestingly,

the 5–7 days duration of IMCI training that was unanimously recommended by health workers for future roll-out is similar to the shorter training course (i.e. 6 days) adopted by several countries to save cost.[288] An alternative approach to address the challenges associated with standard training may be for future roll-out to consider focusing on selected diseases with higher morbidity and mortality rather than the entire IMCI algorithms. In Nigeria for example, IMCI training could focus on malaria, pneumonia and diarrhoea which are responsible for most cases of under-five admission to healthcare facilities.[289] A potential problem with this approach however is that common childhood illnesses in developing settings rarely occur alone, which necessitated the 'integrated' approach to management (i.e. the IMCI strategy) in the first place. Thus, it may be inappropriate to isolate the management of individual disease in the IMCI algorithm given that the benefits of an integrated approach to management would outweigh the training cost.

Malaria and pneumonia management with the IMCI guidelines

Despite the several benefits in terms of affordability and portability,[290] most of the HPs (including clinicians) in this study believed the RDT results for malaria diagnosis were unreliable. According to these HPs, this position was based on the contradiction of RDT results with typical signs and symptoms of malaria. Contrary to the recommendations in the IMCI guidelines of deciding malaria treatment based on an RDT outcome,[97] most HPs in the current study expressed willingness to prescribe antimalarials solely based on clinical diagnosis. This is not an uncommon phenomenon as several studies have reported similar findings.[208,291–293] Furthermore, there was uncertainty among health workers over when to administer antibiotics for children diagnosed with malaria based on the IMCI guidelines. Some health workers appeared to favour the concurrent

administration of antibiotics and antimalarials for malaria treatment. In addition to possibly increasing the financial burden on caregivers (a potential reason to rely on lay diagnosis), this practice could potentially exacerbate the problem of over-prescription of medications and the attendant problems. In contrast to this and other studies,[115,292] Senn *et al.* [115] in Papua New Guinea and Bisoffi *et al.* [294] in Burkina Faso found that health workers were more likely to withhold antibiotics when malaria (with similar symptoms to pneumonia at initial stages) was diagnosed. This needs to be addressed as it would not only serve to endear health workers to complying with the IMCI guidelines but enforce the appropriate prescription of medications. Moreover, the IMCI recommendation for the administration of antibiotics only when other causes of fever (e.g. bacterial infections) were identified,[24] there is need for an explicit explanation on how this confirmatory test should be carried out needs to be explicitly explained in the IMCI guidelines.

Regarding the management of pneumonia, health workers generally believed the IMCI guidelines were adequate and reliable for diagnosis. In terms of treatment however, two of the HP suggested the inclusion of alternative antibiotics in the IMCI guidelines. This is logical and worth addressing given the likelihood for failure in the supply chain of medications, including amoxicillin, in developing countries.[295]

Perceptions of wide-scale implementation of IMCI in Nigeria

Of the identified challenges to the wide-scale implementation of the IMCI strategy in Nigeria, inadequate funding, lack of political-will and sustainability were eminent. These challenges are not peculiar to Nigeria as they have been reported in African and other countries.[102,208,209,296,297] The annual budget for healthcare sector has been

generally poor in Nigeria. Despite pledging to commit at least 15% of its total annual budget to public health during the special summit of the Organisation of African Unity on health in 2001, Nigeria is still unable to meet this target with allocations of 4.13% and 4.17% of its 2016 and 2017 annual budgets respectively.[298] Moreover, the reliance of local governments –responsible for managing PHCs in Nigeria– on state governments, federal government and non-governmental organisations often results in limited or delayed finance for primary healthcare projects.[299] In addition to determining the quality of healthcare services, health workers play a significant role in the successful implementation of interventions at the primary health care level.[300] Their non-compliance with the IMCI guidelines due to the perception to RDT results could pose a significant challenge to the wide-scale and sustainable implementation even with adequate finance and political-will. This belief by HPs was identified as a challenge to the wide-scale implementation of the IMCI strategy in Ghana.[208] The wide-scale and sustainable implementation of the IMCI strategy in Nigeria would therefore benefit more from addressing the identified challenges in their entirety rather than focusing on individual factors.

4.7 Synthesis of main findings

This section seeks to provide a more in-depth understanding of the research findings and clarify disparate quantitative and qualitative findings by placing them in dialogue with one another.

Caregivers' and health professionals' experiences for early detection of malaria and pneumonia

Findings of the thesis suggest that compared to microscopy, the overall diagnostic accuracy of the IMCI guidelines (AUROC 0.57) for malaria was slightly better than

caregivers' diagnosis (AUROC 0.55). The superiority of the evidence-based IMCI strategy to lay diagnosis is expected [240] given that it was also applied by trained health professionals. Nonetheless, what is more important is the overall predictive performance of the IMCI guidelines in comparison to microscopy (as demonstrated by the AUROC values). This is important and underlines the need to adopt measures to improve the diagnostic performance of the IMCI guidelines as functioning microscopes are often unavailable at the primary healthcare level in many developing countries.[240] A proven strategy to improving and ensuring sustainability of the IMCI guidelines will require continuous training and regular follow-up of health workers.[301] However, the country-specific challenges (e.g. inadequate finance, lack of political-will, sustainability, suboptimal reliability of RDT results for malaria diagnosis and community perceptions amongst others) identified in the current study will need to be addressed.

Findings in this thesis on malaria diagnosis by the IMCI guidelines are contrary to previous validation studies[98,113,194] where sensitivity was found to be superior to specificity. While the recorded moderate specificity of the IMCI guidelines is good given the potential economic burden of false positive result to caregivers, the low sensitivity and negative predictive value (NPV) (both connoting high false negatives) have serious implications. There is tendency for low compliance by health workers with the IMCI guidelines in the diagnosis of malaria. This is more likely when there is a negative diagnostic outcome for a child presenting with classical signs and symptoms of malaria. This was affirmed by the complaints by most of the HPs in the qualitative component where the RDT was considered unreliable and inaccurate. The HPs further believed this to be a limitation of the IMCI guidelines that needed to be addressed if adequate compliance was to be achieved. This issue is not peculiar to the current study

as similar findings have been recorded in other countries.[204,208,227] To minimise the occurrence of missed opportunities to treat children with malaria, and in turn enhance compliance, it may be worthwhile exploring the feasibility of including health workers' intuition as a component of the IMCI guidelines. The use of intuition is helpful where a health worker may have strong clinical suspicion regarding the condition of a child despite seemingly normal diagnostic results.[302] This was reiterated by some HPS in the qualitative component of the study where they believed that the strict adherence to the IMCI guidelines restricted their use of acquired clinical experience and expertise.

From the qualitative component of study, caregivers were more confident of their ability to predict childhood malaria than pneumonia. This was mirrored by the findings of the quantitative data where the diagnostic accuracy for and the estimated burden of malaria were better in comparison to those of pneumonia. Similar findings on caregivers' perceptions of malaria and pneumonia have been reported by other studies in Nigeria,[190] Tanzania [222] and Sierra Leone.[278] It could be argued that caregivers' perceived threats of malaria and pneumonia influenced both the diagnostic accuracy and estimated burden of these diseases according to lay diagnosis. These findings could be further explained by some of the variables in the health belief model (HBM). According to the HBM, the perceived severity of, and susceptibility to a disease influence individual's perceived threat of the disease.[303] In terms of perceived severity, pneumonia was perceived to be a severe illness with the potential to result in adverse clinical outcomes (e.g. death or admission to critical care) and best managed at formal healthcare centres where experienced HPs were available (e.g. PHCs). Furthermore, some caregivers believed that children were particularly susceptible to pneumonia and could easily develop adverse outcomes following an infection. It is possible therefore that the suboptimal

accuracy of lay diagnosis of pneumonia and hence the estimated burden in the current study were partly due to fear or perceived threat. Five caregivers suggested that they sometimes knowingly deny the possibility of their children having pneumonia as evidenced by the quote: "*No. God forbid! They will not get it [pneumonia] in Jesus name! That's the thing I hate mostly…I hear it, but I pretend like the name is not existing."* Nonetheless, majority would rather seek immediate treatment at the nearest PHC to avert possible adverse outcomes.

Malaria was perceived to be a common and mild infection that could easily be managed without consulting HPs. Similar to the current findings, a study on health seeking behaviour among caregivers of children under-five in Kenya found that malaria was considered as non-life-threatening illness while pneumonia was considered as a more sudden and serious illness.[304] In contrast, a Nigerian study that focused only on malaria found that it was regarded by caregivers as a serious health problem and life-threatening.[305] Giving the contrasting evidence, it would have been interesting to explore caregivers' perceptions of malaria and pneumonia individually rather than the concurrent approach adopted in the current study.

Using lay diagnosis for early management and routine surveillance of malaria and pneumonia at the community level

It has been recognised that the optimal care for ill children will benefit from the integration of care delivered by health workers using the IMCI guidelines with basic healthcare provided by caregivers.[113] Indeed, the safety concerns expressed by caregivers and health professionals over the prospect of training lay persons in standard diagnostic approach are cogent and worth addressing. The minimal level of agreement between caregivers and health workers in the diagnosis of malaria and pneumonia

further underlines the need to train caregivers in a standard diagnostic approach (e.g. IMCI guidelines). However, the high specificity and ability to recognise subtle signs/symptoms of malaria early on recorded by caregivers as well as their willingness and enthusiasm are positive indicators for the feasibility of training them in the IMCI guidelines. Training caregivers in the IMCI guidelines has potential benefits. First, it could improve their timely recognition and prompt treatment of childhood malaria and pneumonia or, presentation to the nearest health facility. This is supported by findings in the current study where the administration of medications (though specific details were not ascertained) to children prior to presenting to health facilities was protective against the occurrence of severe illness. Additionally, studies in Nigeria have shown that caregivers who have undergone training in malaria management have improved knowledge for home management and referral practices for severe cases.[306,307]

Regarding the surveillance of malaria and pneumonia (and possibly other common childhood illnesses), lay diagnosis could be adopted as part of the Integrated Disease Surveillance and Response (IDSR) system in Nigeria. In this approach, the community is considered one of the channels through which surveillance data are collected and reported.[308] For instance, members of the community including birth attendants, community or village leaders, health extension workers, traditional healers among others are often relied on for surveillance data. Training caregivers in the IMCI guidelines may therefore help to improve the reliability of data collected at this level. However, surveillance data collected through this approach may not be reproducible over time and place partly due to the somewhat subjective approach taken to the interpretation of caregivers' diagnoses by paediatricians. Thus, it may be worthwhile exploring the

prospect of adopting a probabilistic modelling approach similar to that used for interpreting verbal autopsy data in this regard.

4.8 Strengths and limitations

The use of a mixed methods approach addressed the overarching study aims more comprehensively than by using either quantitative or qualitative method alone. By adopting a mixed methods approach, a common limitation of quantitative study which is the limited ability to explain the 'how' or 'why' of research findings was compensated by the qualitative study. Similarly, the quantitative component of the study counterbalanced a common limitation of qualitative study which is the limited applicability of findings due to the small sample sizes required for an in-depth exploration of a research question.

This study has the advantages of collecting data over an 11-month period which accounted for the influence of seasonality on the estimated burden of malaria and pneumonia, first collecting data on risk factors at study PHCs and then following-up study participants within 30 days to assess the occurrence of clinical outcomes (thereby minimising the problem of reverse causality), and being the first of its kind in Nigeria to explore both caregivers' and HPs' perspectives on lay diagnosis and the IMCI guidelines.

This study ensured the integrity of various diagnostic approaches by assessing caregivers' diagnosis of malaria or/and malaria after health workers had classified children using the IMCI guidelines. The microscopists were also blinded to the diagnostic outcomes of malaria diagnoses made by health workers and caregivers at study PHCs. Moreover, to standardise malaria diagnosis across the study PHCs, thereby

ensuring uniformity of RDT results and comparability of findings, the brand of RDT kit already in use by health workers was adopted for this study.

Depending on caregivers' preference, interviews were conducted in both English and Pidgin-English to prevent imposing constraints of views upon the interviewees (or to allow participants to express themselves more freely). When Pidgin-English was used as the language of interview, the study sought to retain participants' original viewpoints by presenting findings in both original language and English translation. Furthermore, triangulation was done by comparing the identified themes from thematic analysis by researcher with those of two research supervisors (C.P. & P.R.M.) to validate study findings.

To ensure findings of the qualitative component of the study were reliable and credible, good practice in qualitative research such as the provision of a clear and detailed account of philosophical worldviews underpinning the research, processes of data collection and analytical approaches[309,310] were observed. To further enhance credibility, a reflexive statement (Appendix VIII) was written prior to the fieldwork being undertaken to express possible ways in which the values, personal and intellectual biases, prior assumptions and experience of the researcher may influence the study.

Unlike malaria where confirmatory tests using microscopy were undertaken regardless of the RDT outcome, only IMCI positive pneumonia cases were referred to a radiological centre for CXR as it was not considered acceptable or ethical by HPs to refer children for CXR without a strong clinical justification. The IMCI guidelines tend to be subjective given the influence of training on diagnostic performance.[311] As such, findings in the current study may not be sufficient to explain the diagnostic accuracy of

lay diagnosis of pneumonia in comparison to the IMCI guidelines (the reference diagnostic test). This needs to be considered in the interpretation of current findings. Nonetheless, this study adopted a pragmatic approach which reflected the existing conditions in the Nigerian primary healthcare system. For instance, findings from the qualitative component of study indicated that HPs, particularly the clinicians, may be reluctant to recommend CXR largely due to economic considerations rather than potential health hazards. These findings would be useful in planning public health interventions toward mitigating the burden of childhood pneumonia at the community level in Nigeria.

In exploring the association between potential risk factors for severe and worsened illness in children diagnosed with malaria and pneumonia during the 30-day follow-up period, a sub-sample consisting of only those with positive diagnosis was used for analyses. That is, the sample size for analyses was reduced as only 45.5% (304/668) and 15.6% (104/668), respectively, of the children diagnosed with malaria and pneumonia were used for analyses. Evidence suggests that studies using logistic regression as analytical tool to explore the association of exposure variables and the outcome tend to overestimate or bias the effect (e.g. odds ratios shift away from one or are overestimated) when the sample size is small or moderate.[312] However, based on Long's estimation, sample size of under 100 should be avoided while samples above 500 are adequate.[313] Thus, the estimated measure of effect (odds ratio) for study objective 3 should be interpreted with caution given the potential effect of reduced sample size on findings.

Some variables in this study had substantial number of missing data (e.g. socioeconomic status had 30% of missing data) which were handled by treating missing data as a separate category. There are some flaws with this strategy though, mainly due to not

knowing how the missing data are divided amongst the real categories. Therefore, it is not clear what the relationship is between the probability of a value being missing and the other variables in the dataset. Additionally, there is some evidence that adopting this approach to missing data leads to unpredictable bias since very dissimilar groups of participants can be grouped together. However, other than complete case analysis it is the most appropriate alternative to the somewhat complicated multiple imputation approaches. Thus, findings on the association between socioeconomic status and adverse clinical outcomes (severe and worsened illness) within 30 days of malaria and pneumonia diagnosis should be interpreted with caution. Nonetheless, the missing data in socioeconomic status may be attributable to the sensitive nature of educational and occupational status in study setting. Regarding missing data, the findings of study objective three may be biased if those lost to follow-up were systematically different from those that were successfully followed up. However, unavoidable challenges, ranging from inaccurate house addresses and mobile phone numbers to inaccessible roads, during data collection are possible explanations for the recorded loss-to-follow-up.

The duration spent on IMCI training has the potential to affect the diagnostic performances of health workers, with longer duration favouring better diagnostic performance and vice-versa.[311] It is likely therefore that the duration of two days adopted for the current study may have underestimated the diagnostic performances of health workers using the IMCI guidelines. While there are findings indicating that long training duration provide no substantial benefits,[117,314] many health workers in the current study believed the training was ‘rushed’ and inadequate to consolidate what they were taught.

Thus, the potential impact of training duration on the diagnostic performances of health workers needs to be considered in the interpretation of findings.

There was no data for March 2016 due to the industrial action by PHWs across the five study PHCs. Following an industrial strike, it takes a while before caregivers' confidence in the health care system is restored. This may explain why a corresponding rise in the estimated burden of malaria and pneumonia cases following the onset of rainfall in March 2016 (which coincided with the industrial action and highest amount of rainfall) did not occur as expected.

Lay diagnosis was a term that the researcher introduced to the respondents during the interviews before asking them what their views were. There is therefore the possibility for framing bias such that responses could be influenced based on how questions were phrased or presented.[315] Reporting bias is also likely during the interviews whereby caregivers' responses to questions on lay diagnosis will be dependent on the perceived appropriateness of practice. However, it is possible that the use of the formal term 'lay diagnosis' by the researcher could have replaced the natural process of caregivers trying to make sense of what may be wrong with oneself or one's child when they are not feeling well. Furthermore, observer bias during the assessment of caregivers' diagnosis of malaria and/or pneumonia by health workers is likely. Despite being trained, health workers may be more likely to report lay diagnosis of malaria or pneumonia knowing the IMCI diagnostic outcome. Perhaps, the occurrence of observer bias could have been minimised by first confirming caregivers diagnoses prior to IMCI assessment and classification by health workers.

In assessing the estimated burden of malaria and pneumonia, a major assumption was that the recruitment of eligible study participants had captured all potential cases. Although there was no record to show how many potential eligible participants were not recruited into the study and assessed for malaria or/and pneumonia, this assumption, however, has limitations. It is possible that children who met the study eligibility criteria presented to the study PHCs when health workers trained in the IMCI guidelines were off-duty. If systematically different from those that were recruited and participated in study, this may lead to non-response bias. Such a scenario could also lead to an underestimation of malaria and pneumonia burden in the five study PHCs.

4.9 Generalisability and transferability of findings

Findings in this study may have limited generalisability to the population of children under-five in study setting as data were collected at five of the eight functioning PHCs. Furthermore, it may not be appropriate to generalise findings in this study beyond the primary healthcare level as most patients who present to higher healthcare centres (e.g. secondary and tertiary hospitals) in Nigeria tend to be of higher socioeconomic class.[95,205] Nonetheless, the study contributes to the literature especially regarding to the burden of childhood malaria and pneumonia at the PHC level.

Findings in the qualitative study may have limited transferability across the primary healthcare system as there seemed to be an over-representation of health workers. However, the study explored the perspectives of HPs with diverse backgrounds (e.g. PHC coordinators, surveillance officer, medical doctors, IMCI training facilitators etc.) involved with the running of primary healthcare system in Nigeria.

The views expressed by the interviewed mothers in the qualitative component of study may not be applicable to those of fathers. Fathers are known to significantly influence

the decision making and health seeking behaviours of mothers and ultimately the health of the child.[316] It would have been interesting to explore fathers' perceptions and willingness to become trained and/or support their wives to become trained in the IMCI guidelines.

5 CONCLUSION, IMPLICATIONS and RECOMMENDATIONS

5.1 Conclusion

Findings of this study suggest that the IMCI guidelines are crucial in the effective management (diagnosis and treatment) of malaria and pneumonia at the primary healthcare level in Nigeria. However, there is need to improve the case management skills of health professionals through investment in training in the IMCI guidelines for management of childhood malaria and pneumonia in Nigeria.

Lay diagnosis is widely relied on by caregivers for the management of common childhood illnesses, although the diagnostic accuracy seems poor compared to standard diagnostics. There is potential for harnessing lay diagnosis through training of caregivers in the IMCI guidelines for improved management of common childhood illnesses at the community level. However, training caregivers in the IMCI guidelines and potential for a scale-up will require careful design, piloting, implementation, and monitoring.

The main conclusions drawn are:

- The overall diagnostic accuracy of the IMCI guidelines and lay diagnosis for malaria diagnosis was relatively poor as compared to microscopy. However, the IMCI guidelines were slightly better at diagnosing malaria than lay diagnosis in comparison to microscopy.
- Using the IMCI guidelines as the reference diagnostic test, caregivers were better at diagnosing malaria than pneumonia.
- The estimated burden of malaria and pneumonia over an 11-month period was relatively low and varied by diagnostic approach, setting (LGAs and PHCs) and seasonality during the study period.

- Children under-five generally recovered well within 30 days of being diagnosed with malaria or pneumonia according to the IMCI guidelines. Self-medication and the adoption of preventive measures against malaria appeared protective against the occurrence of severe illness, whereas, exposure to solid fuel worsened illness within 30 days of malaria or pneumonia diagnosis.
- Caregivers' perceived severity of malaria (less severe illness) and pneumonia (serious and life-threatening illness) influenced the adoption of lay diagnosis for home-based management and health seeking behaviours.
- Caregivers were willing to be trained in the IMCI guidelines for better management of common childhood illnesses. However, challenges identified by caregivers and healthcare professionals need addressing.
- Training of health workers in the IMCI guidelines appeared to improve their clinical skills in managing children with malaria and pneumonia, as well as counselling of caregivers. However, recurrent factors including short duration of training, perceived unreliability of RDT for malaria diagnosis, and inadequate funding are potential challenges to the wide-scale and sustainable implementation of the IMCI strategy in Nigeria.

5.2 Implications of study findings

Implications for diagnosis and treatment

- The overall accuracy of rapid diagnostic test for malaria diagnosis seems to partly depend on the brand or product quality. Thus, RDT for malaria diagnosis (by extension the IMCI guidelines) may have improved clinical utility and consequently compliance by health workers if its diagnostic accuracy is considered before usage.

- The IMCI guidelines could benefit from the inclusion of an alternative or second line antibiotic for pneumonia treatment given the likelihood for the recommended amoxicillin to go out of stock especially in developing countries, including Nigeria.
- Training caregivers in the IMCI guidelines could improve the home-based management of childhood illnesses. It could also reduce the burden on available few health workers and improve their case management skills due to better reporting of clinical symptoms and prompt presentation to health facilities.

Implications for improved clinical outcomes in children under-five

- A post-treatment health benefit of adopting preventive measures against malaria (e.g. netting of windows/doors) is reduction of the likelihood of children under-five developing severe illness after malaria diagnosis and treatment.
- Children diagnosed with malaria and pneumonia should be prevented, as much as possible, from being exposed to sources of smoke such as firewood in the kitchen and cigarette to ensure better treatment outcome.
- Counselling of caregivers according to the IMCI guidelines could enhance adherence to prescribed medications, thereby minimising the occurrence of adverse clinical outcomes.

Implications for the cost of IMCI scale-up

- Achieving an effective and sustainable wide-scale implementation of the IMCI strategy in Nigeria will require adequate and consistent financial investment from local governments and relevant healthcare stakeholders.

- Training of caregivers in the IMCI guidelines will require substantial financial investments for training, diagnostic kits, medications, monitoring etc.

Implications for research and policy

- Data on the estimated burden of malaria and pneumonia could be useful to the Nigerian health services policy-makers in public health planning and allocation of resources.
- The study-specific prevalence of malaria and pneumonia will be useful to researchers for sample size calculations for similar studies based in primary healthcare in Nigeria.
- Findings on the accuracy of various diagnostic approaches for malaria and pneumonia have provided evidence for researchers to assess the extent of misclassification bias associated with a specific diagnostic approach.

5.3 Recommendations for public health practice and future research

- The rapid diagnosis of malaria according to the IMCI guidelines should consider using kits with better sensitivity and specificity for better health outcomes and to enhance compliance by health workers.
- The duration and length (hours spent per day) of IMCI training course should be considered in future research despite the associated financial cost. For example, a duration of at least five days may be appropriate.
- The feasibility of training caregivers in the use of IMCI guidelines for improved home-based management of malaria and pneumonia, as well as the potential for

a scale up should be explored. However, a step-wise approach involving careful design, piloting, implementation, and monitoring should be adopted.

- A similar approach to the interpretation of verbal autopsy data into causes of death should be explored for improving lay diagnosis for research and surveillance purposes.

APPENDICES

Appendix I: Dissemination of research findings

Manuscripts submitted for publication and conferences attended

Elimian OK, Myles P, Phalkey R, Sadoh A, Pritchard C. 'Everybody in Nigeria is a doctor…': a qualitative study of stakeholder perspectives on lay-diagnosis of malaria and pneumonia in southern Nigeria. International Journal of Public Health. Forthcoming 2017.

The abstract for the above manuscript has been accepted for an oral presentation at the International Conference on Tropical Medicine and Infectious Diseases (07–09 Sep 2017), Edinburgh, Scotland.

Elimian OK, Phalkey R, Sadoh A, Pritchard C, Myles P. A comparison of accuracy of early diagnostic approaches for malaria and pneumonia. Manuscript under review.

Elimian OK, Phalkey R, Myles P, Pritchard C, Sadoh A. How accurate is parents' lay diagnosis of pneumonia and malaria in children under-five years in Nigeria? Proceedings of the University of Nottingham Faculty of Medicine Postgraduate Research Conference; 2016 October 18; Nottingham, United Kingdom.

Appendix II: A cross-section of the 2014 revised IMCI guidelines: focus on pneumonia & malaria in children aged 2-59 months

SICK CHILD AGE 2 MONTHS UP TO 5 YEARS

ASSESS AND CLASSIFY THE SICK CHILD

ASSESS | CLASSIFY | IDENTIFY TREATMENT

ASK THE MOTHER WHAT THE CHILD'S PROBLEMS ARE

- Determine if this is an initial or follow-up visit for this problem.
  - if follow-up visit, use the follow-up instructions on TREAT THE CHILD chart.
  - if initial visit, assess the child as follows:

USE ALL BOXES THAT MATCH THE CHILD'S SYMPTOMS AND PROBLEMS TO CLASSIFY THE ILLNESS

CHECK FOR GENERAL DANGER SIGNS

Ask:
- Is the child able to drink or breastfeed?
- Does the child vomit everything?
- Has the child had convulsions?

Look:
- See if the child is lethargic or unconscious.
- Is the child convulsing now?

URGENT attention

• Any general danger sign	***Pink:*** **VERY SEVERE DISEASE**	■ Give diazepam if convulsing now ■ Quickly complete the assessment ■ Give any pre-referal treatment immediately ■ Treat to prevent low blood sugar ■ Keep the child warm ■ Refer URGENTLY.

A child with any general danger sign needs *URGENT* attention; complete the assessment and any pre-referral treatment immediately so referral is not delayed.

THEN ASK ABOUT MAIN SYMPTOMS:
Does the child have cough or difficult breathing?

If yes, ask:
- For how long?

Look, listen, feel*:
- Count the breaths in one minute.
- Look for chest indrawing.
- Look and listen for stridor.
- Look and listen for wheezing.

CHILD MUST BE CALM

If wheezing with either fast breathing or chest indrawing:

Give a trial of rapid acting inhaled bronchodilator for up to three times 15-20 minutes apart. Count the breaths and look for chest indrawing again, and then classify.

If the child is:	***Fast breathing is:***
2 months up to 12 months	**50** breaths per minute or more
12 Months up to 5 years	**40** breaths per minute or more

Classify COUGH or DIFFICULT BREATHING

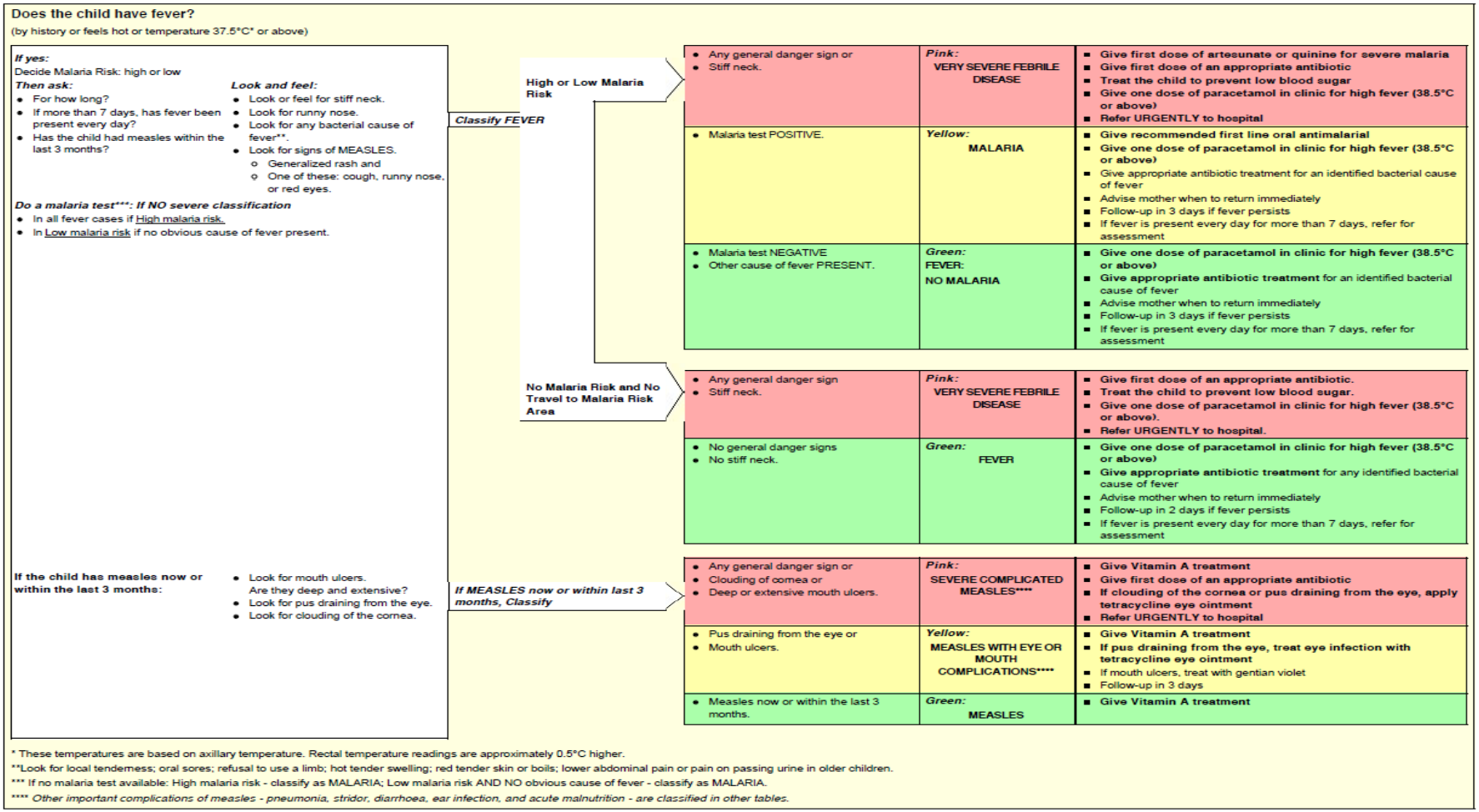
• Any general danger sign or • Stridor in calm child.	***Pink:*** **SEVERE PNEUMONIA OR VERY SEVERE DISEASE**	■ **Give first dose of an appropriate antibiotic** ■ **Refer URGENTLY to hospital****
• Chest indrawing or • Fast breathing.	***Yellow:*** **PNEUMONIA**	■ **Give oral Amoxicillin for 5 days***** ■ If wheezing (or disappeared after rapidly acting bronchodilator) give an inhaled bronchodilator for 5 days****** ■ If chest indrawing in HIV exposed/infected child, give first dose of amoxicillin and refer. ■ Soothe the throat and relieve the cough with a safe remedy ■ If coughing for more than 14 days or recurrent wheeze, refer for possible TB or asthma assessment ■ Advise mother when to return immediately ■ Follow-up in 3 days
• No signs of pneumonia or very severe disease.	***Green:*** **COUGH OR COLD**	■ If wheezing (or disappeared after rapidly acting bronchodilator) give an inhaled bronchodilator for 5 days****** ■ Soothe the throat and relieve the cough with a safe remedy ■ If coughing for more than 14 days or recurrent wheezing, refer for possible TB or asthma assessment ■ Advise mother when to return immediately ■ Follow-up in 5 days if not improving

**If pulse oximeter is available, determine oxygen saturation and refer if < 90%.*

*** If referral is not possible, manage the child as described in the pneumonia section of the national referral guidelines or as in WHO Pocket Book for hospital care for children.*

****Oral Amoxicillin for 3 days could be used in patients with fast breathing but no chest indrawing in low HIV settings.*

***** In settings where inhaled bronchodilator is not available, oral salbutamol may be tried but not recommended for treatement of severe acute wheeze.*



* These temperatures are based on axillary temperature. Rectal temperature readings are approximately 0.5°C higher.
**Look for local tenderness; oral sores; refusal to use a limb; hot tender swelling; red tender skin or boils; lower abdominal pain or pain on passing urine in older children.
*** If no malaria test available: High malaria risk - classify as MALARIA; Low malaria risk AND NO obvious cause of fever - classify as MALARIA.
**** *Other important complications of measles - pneumonia, stridor, diarrhoea, ear infection, and acute malnutrition - are classified in other tables.*

Appendix III: Ethical approval from the University of Nottingham and Edo State Ministry of Health

The University of Nottingham

Faculty of Medicine and Health Sciences

Research Ethics Committee
School of Medicine Education Centre
B Floor, Medical School
Queen's Medical Centre Campus
Nottingham University Hospitals
Nottingham
NG7 2UH

Direct line/e-mail
+44 (0) 115 8232561
Louise.Sabir@nottingham.ac.uk

14th July 2015

Kelly Elimian
PhD Student
Room B104 , Epidemiology and Public Health
Clinical Sciences Building
City Hospital Campus
Nottingham University Hospitals
Hucknall Road
Nottingham
NG5 1PB

Dear Kelly

Ethics Reference No: OVS18062015 SoM EPH – **please always quote**
Study Title: Malaria and pneumonia in children under the age of five years old presenting to primary healthcare centres in Benin City, Nigeria: an estimation of disease burden and a comparison of early diagnostic approaches.
Chief Investigators/Academic Supervisors: Dr Puja Myles, Associate Professor, Dr Catherine Pritchard, Non Clinical Professor in Public Health, Epidemiology and Public Health, School of Medicine, University of Nottingham, Dr Ayebo Sadoh, Associate Professor/Consultant Paediatrician, Institute of Child Health, University of Benin, Nigeria.
Lead Researcher/student: Kelly Elimian, PhD Student, Epidemiology & Public Health, School of Medicine.
Duration of Study: 01/08/2015-30/07/2016 – 12 months
No of Subjects: 1,000

Thank you for you submitting the above which has been reviewed by the Committee at its meeting on 18th June 2015 and the following documents were received:

- Letter of Ethical Approval from Dr HI Eboreime, Director of Medical Service For: Hon Commissioner, Ministry of Health, Benin City, EDO State, Nigeria dated 18th February 2015. Ref: HA.577/Vol.II/126.
- FMHS Research Ethics Application form dated 08/05/2015.
- Study Protocol, dated 08/05/2015
- Clinical Management/Outcomes, Baseline Assessment and Caregiver questionnaire Forms, dated 08/05/2015
- Interview Guide/Schedules for Qualitative Studies dated 08/05/2015
- Information Sheet for Patients, dated 08/05/2015
- Information Sheet for Health Stakeholder, dated 08/05/2015
- Information Sheet for Caregivers, dated 08/05/2015
- Consent Form- dated 08/05/2015
- Consent Form – Health Stakeholders, dated 08/05/2015
- Consent Form – for Caregivers, dated 08/05/2015

These have been reviewed and are satisfactory and the study has been given a favourable opinion.

The University of Nottingham

A favourable opinion is given on the understanding that the Conditions set out below are followed.

1. A Favourable opinion is given on the understanding that all appropriate ethical and regulatory permissions are respected and followed in accordance with all local laws of the country in which the study is being conducted and those required by the host organisation/s involved.

2. You must follow the protocol agreed and inform the Committee of any changes using a notification of amendment form (please request a form).

3. You must notify the Chair of any serious or unexpected event.

4. This study is approved for the period of active recruitment requested. The Committee also provides a further 5 year approval for any necessary work to be performed on the study which may arise in the process of publication and peer review.

5. An End of Project Progress Report is completed and returned when the study has finished (Please request a form).

Yours sincerely

Dr Clodagh Dugdale
Chair, Faculty of Medicine & Health Sciences Research Ethics Committee

Telegrams: PERM HEALTH

Telephone: 200030

EDO STATE

MINISTRY OF HEALTH

P.M.B. 1103,
BENIN CITY
EDO STATE OF NIGERIA

Our Ref: HA. 577/Vol. II/126
Your Ref:
Date: **18th February, 2015**

Kelly Elimian
Department of Microbiology
Faculty of Life Sciences
University of Benin
P.M.B. 1154 Benin City.

RE: APPLICATION FOR ETHICAL APPROVAL

I am directed to acknowledge the receipt of your letter dated 9th February, 2015 on the above subject matter. Consequent upon the review of your proposal and recommendations by the State Ethical Clearance Committee, you are hereby given approval by the Honourable Commissioner to conduct the research on **"malaria and pneumonia in children under the age of five years old presenting to primary healthcare centres in Edo State, Nigeria: an estimation of disease burden and a comparison of early diagnostic approaches and models."**

You are to ensure confidentiality of the respondents and make available to the library of the Ministry of Health, a copy of your research findings.

Accept the assurances of the highest esteem of the Honourable Commissioner.

Dr. (Mrs.) H.I. Eboreime
(Director Medical Services)
for: Honourable Commissioner.

Cc: The Director
PHCs
Ministry of Health, Benin City

Above is for your information and necessary action

Dr H.I. Eboreime
Director Medical Service
For: Hon Commissioner

Appendix IV: BMI Z scores and percentile equivalents used for anthropometry

A: Body Mass Index (BMI) Z-scores used for the conversion of weight categories

Weight category	Z-scores	Percentile equivalents
Underweight	-4.53 to -1.71	$<5^{th}$
Normal/Healthy weight	-1.72 to 1.02	5^{th} to $<85^{th}$
Overweight	1.03 to 1.63	85^{th} to $<95^{th}$
Obese	1.64 to 4.98	$\geq 95^{th}$

B: Conversion values for Percentile and Z-scores

Z-scores	Percentile equivalents
-3	0.2^{nd}
-2	2.3^{rd}
-1.96	2.5^{th}
-1.64	5^{th}
-1.04	15^{th}
-1	16^{th}
0	50^{th} (median)
+1	84^{th}
+1.04	85^{th}
+1.64	95^{th}
+1.96	97.5^{th}
+2	97.7^{th}
+3	99.8^{th}

Appendix V: Total estimated number of children under-five who presented to study PHCs during the study period

Total estimated number of children <5 years who presented to study PHCs during study period (September 2015–July 2016)						
Study period	**Egor LGA**			**Ikpoba-Okha LGA**	**Oredo LGA**	**Total**
	Evbuogida PHC	**Evbuotubu PHC**	**Uwelu PHC**	**Ugbekun PHC**	**Oredo PHC**	
September 2015	211	125	408	398	245	**1387**
October 2015	169	130	488	455	198	**1440**
November 2015	159	107	390	382	253	**1291**
December 2015	106	93	375	311	260	**1145**
January 2016	78	92	401	385	241	**1197**
February 2016	91	74	456	297	220	**1138**
March 2016†	0	0	0	0	0	**0**
April 2016	45	39	98	110	0	**292**
May 2016	59	57	249	342	117	**824**
June 2016	87	86	309	411	164	**1057**
July 2016	110	78	390	314	243	**1135**
Total children <5 visits	**1115**	**881**	**3564**	**3405**	**1941**	**10906**
Total children <5 visits with any complaints	**601**	**527**	**419**	**694**	**538**	**2779**
† There was no data for March 2016 due to an industrial action						

Appendix VI: Predictive capacity of lay diagnosis with fever and cough as proxies for malaria and pneumonia respectively

Predictive capacity of lay diagnosis when fever and cough were considered malaria and pneumonia diagnoses respectively

	AUROC value (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)
Caregivers' diagnosis of malaria					
Compared to microscopy (n=604)	0.53 (0.49-0.56)	78.0 (73.2-82.3)	27.4 (22.1-33.2)	58.2 (53.5-62.8)	49.0 (40.7-57.3)
Compared to the IMCI guidelines (n=667)	0.69 (0.66-0.72)	94.6 (91.3-96.9)	43.8 (38.7-49.0)	57.2 (52.6-61.6)	91.1 (85.9-94.8)
Caregivers' diagnosis of pneumonia					
Compared to the IMCI guidelines (n=667)	0.79 (0.75-0.84)	75.3 (65.5-83.5)	83.0 (79.6-86.0)	42.9 (35.4-50.7)	95.2 (92.9-96.9)

Appendix VII: Reflexive statement

As part of this doctoral study, children between the age of two months and 59 months were assessed for malaria and pneumonia using various diagnostic approaches (e.g. IMCI guidelines) and depending on the outcome, provided treatment for free. It is therefore likely that this may have influenced some caregivers' participation regarding willingness and responses (e.g. the tendency to provide positive responses to questions in attempt to give something back to the study).

The researcher had practised lay diagnosis for suspected malaria and believed his personal beliefs and preferences might have been brought into the research thereby biasing participants' responses. However, undertaking a formal training in a qualitative module and reviewing the interview guide with two of the study supervisors (C.P. and P.R.M.) prior to data collection helped to minimise such a scenario.

Given the availability of formal healthcare services (e.g. PHCs) in study setting, there could be a sense of 'guilt' with reliance on lay diagnosis and may influence some participants to hold back certain information. However, the use of relevant prompts during interviews was useful in this regard.

Appendix VIII: Information sheets for study participants (caregivers and health professionals)

Information Sheet for Caregivers

Title of study: A study of burden of malaria and pneumonia in children under the age of five years in Nigeria and comparison of diagnostic approaches or methods.

Name of Researcher(s): Kelly Elimian

Dear Sir/Madam,

We would like to invite you and your child to take part in this research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team members will go through the information sheet with you and answer any questions you have. Talk to others about the study if you wish. Ask us if there is anything that is not clear. Please take as much time as you need to decide whether you wish to take part or not. If you decide to take part please keep this leaflet safely. Thank you for reading this.

What is the purpose of the study?

Among the common preventable and treatable diseases in Nigeria (e.g., HIV, malnutrition, diarrhoea, malaria, pneumonia etc.), malaria and pneumonia contribute more to the recorded deaths and related problems from these diseases. We found that lay-diagnosis of these diseases by caregivers is a common practice in Nigeria. By lay-diagnosis we mean people who are not medically qualified deciding treatment of an illness solely based on signs and symptoms. Therefore, with this study, we would like to know your views on lay-diagnosis of malaria and pneumonia in children under the age of five years old in Nigeria.

Why have you been invited for this study?

You are being invited to take part in this study because you are a caregiver (e.g., parent, guardian etc.) of children between the ages of 2 months to 4 years. Your participation completely depends on you.

Do I have to take part?

It is up to you to decide whether or not you take part in this study. If you do decide to take part you will be given this information sheet to keep and be asked to provide formal approval of your willingness to participate in the study (i.e., to sign a consent form). You will provide your approval either by a written signature or saying you have agreed to take part in the study in the presence of a witness. If you decide to take part, you are still free to withdraw at any time and without giving a reason. This would not affect your legal rights.

What will happen to me if I take part in this study?

You will be asked in a person-to-person interview open ended questions (i.e. questions that will allow you to express your views on the topic without necessarily being restricted). The interview will be audio-taped or recorded to make it much easier for us to use the information you provide after the interview. You may end the interview at any time. For the interview, Kelly Elimian will administer the open-ended questions at your convenient time and place.

What are the possible disadvantages and risks of taking part?

There are no obvious disadvantages or risks that will likely arise from this study. However, you may spend up to 30-40 minutes of your time for the interview.

What are the possible benefits of taking part?

Your participation could help provide useful information for better management of malaria and pneumonia in children under the age of five years in Nigeria.

What if there is a problem?

In case you have a complaint on your treatment by the interviewer or anything to do with the study, you can initially approach the researchers who will do their best to answer your questions or the observed issue. The researchers' contact details are given at the

end of this information sheet. If this achieves no satisfactory outcome, you should then contact the Director of Health Services Department, University of Benin **Dr (Mrs) C. Enofe** via her mobile number: +2348163104400. Alternatively, if something serious happened as a result of your child's participation in the study please report to the Ethics Committee Secretary, **Mrs Louise Sabir** via: louise.sabir@nottingham.ac.uk or **Dr (Mrs) H.I. Eboreime**, Director of Medical Services, Edo State Ministry of Health.

Will my taking part in the study be kept confidential?

We will follow ethical and legal practice and all information about you will be handled in confidence. If you join the study, the data collected for the study will be looked at by authorised persons from the University of Nottingham and University of Benin who are organising the research. They may also be looked at by authorised people to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

All information which is collected about you during the course of the research will be kept **strictly confidential**, stored in a secure and locked office, and on a password protected computer database. Any information about you which leaves the research unit will have your name and address **removed** (anonymised) and a unique code will be used so that you cannot be recognised from it.

All research data (including an anonymised copy of the audio recording) will be kept securely for 7 years. After this time individual data records will be disposed of securely. During this time all precautions will be taken by all those involved to maintain your confidentiality, only members of the research team will have access to your personal data. The written information will not be stored with the tape recording. No information will be written in any case file and all physical information collected will be stored in a locked filing cabinet and all electronic data collected will be stored on a password protected computer.

In line with safeguarding or security policies, if you disclose something that indicates that you or someone else may be at risk of serious harm then we may need to follow guidelines and report it. We will, where appropriate, inform you of our actions before we undertake them.

What will happen if I don't want to carry on with the study?

Your participation is voluntary and you are free to withdraw at any time, without giving any reason, and without your legal rights being affected. However, if you withdraw then the information collected so far cannot be erased and this information may still be used in the project analysis.

What will happen to the results of the research study?

The results of this study will be written up as part of an educational degree at the University of Nottingham. The results of the study will also hopefully be provided to Edo State Primary Healthcare Services, Ministry of Health and possibly published in academic journals of public health. No participants will be able to be identified from the research or publication.

Who is organising the research?

This research is being organised by the University of Nottingham in collaboration with the University of Benin and is being conducted as part of the lead investigator's doctoral study at the Division of Public Health and Epidemiology at the University of Nottingham.

Who has reviewed the study?

All research in the Division of Public Health and Epidemiology, University of Nottingham is looked at by the Medical School Research Ethics Committee, to protect your interests. In addition, this study has been reviewed and approved by the Honourable Commissioner for Health, Edo State ministry of Health through the Director of Medical Services.

Further information and contact details

Chief investigator – Kelly Elimian, Department of Public Health and Epidemiology, The University of Nottingham, Clinical Sciences Building phase 2, City Hospital Campus, Nottingham. NG5 1PB. Tel: +44115 8231390/+2348052754088

Co-Investigator-Dr Ayebo Sadoh, Institute of Child Health, University of Benin/University of Benin Teaching Hospital, Benin City, Nigeria. Tel: +2348033435312

Co-investigator –Dr Puja Myles, Department of Public Health and Epidemiology, The University of Nottingham, Room B116 Clinical Sciences Building Phase 2, City Hospital Campus, Nottingham. NG5 1PB. Tel: +44115 823 1348

Co-Investigator- Dr Catherine Pritchard, Department of Public Health and Epidemiology, The University of Nottingham, Room B117 Clinical Science Building Phase 2, City Hospital Campus, Nottingham. NG5 1PB. Tel: +44115 823 1368

Information Sheet for Health Professionals

Title of study: A study of burden of malaria and pneumonia in children under the age of five years in Nigeria and comparison of diagnostic approaches.

Name of Researcher(s): Kelly Elimian

Dear Sir/Madam,

We would like to invite you to take part in this research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. A member of the research team will go through the information sheet with you and answer any questions you have. Talk to others about the study if you wish. Ask us if there is anything that is not clear. Take as much time as you need to decide whether you wish to take part or not. If you decide to take part please keep this leaflet safely.
Thank you for reading this.

What is the purpose of the study?

Of all the common preventable and treatable diseases in Nigeria (e.g., HIV, malnutrition, diarrhoea, malaria, pneumonia etc.), malaria and pneumonia contribute to more than half of the recorded deaths and related problems from these diseases. The World Health Organization (WHO) Integrated Management of Childhood Illness (IMCI) guidelines were developed to reduce the problems from these diseases and **some** benefits have been recorded.
That said, problems from these diseases remain unacceptably high in Nigeria, suggesting that efforts such as the WHO IMCI guidelines have had limited effectiveness and coverage. Therefore, with this study, we would like to explore the feasibility and acceptability of the WHO IMCI guidelines in primary healthcare centres in Benin City, Nigeria.

Why have I been invited?

You are being invited to take part in this study because you are a healthcare stakeholder in the primary healthcare system in Benin City, Edo State of Nigeria. The stakeholders we intend to invite for participation in this study include: primary healthcare workers, coordinators/supervisors of primary healthcare centres, clinicians, facilitators of the WHO IMCI training programme, caregivers of study patients etc.

Do I have to take part?

It is up to you to decide whether or not you take part in the research. If you do decide to take part you will be given this information sheet to keep and be asked to sign a **consent form** to indicate your willingness to participate. If you decide to take part, you

are still free to withdraw at any time and without giving a reason. This would not affect your legal rights.

What will happen to me if I take part?

Following the 2-day training on the assessment and classification of under-five children for malaria and pneumonia according to the WHO Integrated Management of Childhood Illness (IMCI) guidelines, you will be asked to provide your opinion/s on the feasibility and applicability of the guidelines in primary healthcare centres in an individual face-to-face interview. The interview will be audio-taped or recorded, because this will make it much easier for us to use the information you provide after the interview. However, if you do not want to be audiotaped, the interview can still continue but for longer period of time as the interviewer and his assistant will take down notes. Please know that you are free to end the interview at any time. You will be interviewed by **Kelly Elimian** who is a student of the University of Nottingham and a lecturer in the Department of Microbiology, University of Benin.

What are the possible disadvantages and risks of taking part?

There are no obvious disadvantages or risks to you that will likely arise from this study, and this study will not interfere with or endanger your job security as your identity will **NOT** be disclosed to anyone outside the research team. However, you will spend about 30-40 minutes of your time during the interview.

What are the possible benefits of taking part?

We cannot promise the study will help you directly but the information we get from this study as a result of your participation could help improve the management of malaria and pneumonia in children, and improve primary healthcare services for under five Nigerian children.

What if there is a problem?

In case you have a complaint on your treatment by a member of staff or anything to do with the study, you can initially approach the researchers who will do their best to answer your questions or address any issue of concern to you. The researchers' contact details are given at the end of this information sheet. If this achieves no satisfactory outcome, you should then contact the Director of Health Services Department, University of Benin **Dr (Mrs) C. Enofe** via her mobile number: +2348163104400. Alternatively, if something serious happened as a result of your child's participation in the study please report to the Ethics Committee Secretary, **Mrs Louise Sabir** via: louise.sabir@nottingham.ac.uk or **Dr (Mrs) H.I. Eboreime**, Director of Medical Services, Edo State Ministry of Health.

Will my taking part in the study be kept confidential?

We will follow ethical and legal practice and all information about you will be handled in confidence. If you join the study, the data collected for the study will be looked at by authorised persons from the University of Nottingham and University of Benin who are organising the research. They may also be looked at by authorised people to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a participant and we will do our best to meet this duty.

All information which is collected about you during the course of the research will be kept **strictly confidential**, stored in a secure and locked office, and on a password protected database. Any information about you which leaves the research unit will have your name and address **removed** (anonymised) and a unique code will be used so that you cannot be recognised from it.

All research data (including an anonymised copy of the audio recording) will be kept securely for 7 years. After this time it will be disposed of securely. During this time all precautions will be taken by all those involved to maintain your confidentiality and only members of the research team will have access to your personal data.

In line with safeguarding or security policies, if you disclose something that indicates that you or someone else may be at risk of serious harm then we may need to follow guidelines and report it. We will, where appropriate, inform you of our actions before we undertake them.

What will happen if I don't want to carry on with the study?

Your participation is voluntary and you are free to withdraw at any time, without giving any reason, and without your legal rights being affected. However, if you withdraw then the information collected so far cannot be erased and this information may still be used in the project analysis.

What will happen to the results of the research study?

The results of this study will be written up as part of a higher education degree at the University of Nottingham. The results of the study will also be provided to Edo State Primary Healthcare Services, Ministry of Health and possibly published in local and international academic journals of public health. You will **NOT** be identifiable from the research or publication.

Who is organising the research?

This research is being organised by the University of Nottingham in collaboration with the University of Benin and is being conducted as part of the lead investigator's doctoral study at the Division of Public Health and Epidemiology at the University of Nottingham.

Who has reviewed the study?

All research in the Division of Public Health and Epidemiology, University of Nottingham is looked at by an independent Medical School Research Ethics Committee, to protect your interests. In addition, this study has been reviewed and approved by the Honourable Commissioner for Health, Edo State ministry of Health through the Director of Medical Services.

Further information and contact details

Chief investigator – Kelly Elimian, Department of Public Health and Epidemiology, The University of Nottingham, Clinical Sciences Building phase 2, City Hospital Campus, Nottingham. NG5 1PB. Tel: +44115 8231390/+2348052754088

Co-Investigator-Dr Ayebo Sadoh, Institute of Child Health, University of Benin/University of Benin Teaching Hospital, Benin City, Nigeria. Tel: +2348033435312

Co-investigator –Dr Puja Myles, Department of Public Health and Epidemiology, The University of Nottingham, Room B116 Clinical Sciences Building Phase 2, City Hospital Campus, Nottingham. NG5 1PB. Tel: +44115 823 1348

Co-Investigator- Dr Catherine Pritchard, Department of Public Health and Epidemiology, The University of Nottingham, Room B117 Clinical Science Building Phase 2, City Hospital Campus, Nottingham. NG5 1PB. Tel: +44115 823 1368

Information Sheet for Patients (caregivers)

Title of study: A study of burden of malaria and pneumonia in children under the age of five years in Nigeria and comparison of diagnostic approaches or methods.

Name of Researcher(s): Kelly Elimian

Dear Sir/Madam,

We would like to invite you and your child to take part in this research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team members will go through the information sheet with you and answer any questions you have. Talk to others about the study if you wish. Ask us if there is anything that is not clear. Please take as much time as you need to decide whether you wish to take part or not. If you decide to take part please keep this leaflet safely. Thank you for reading this.

What is the purpose of the study?

Among the common preventable and treatable diseases in Nigeria (e.g., HIV, malnutrition, diarrhoea, malaria, pneumonia etc.), malaria and pneumonia contribute more to the recorded deaths and related problems from these diseases. The World Health Organization (WHO) Integrated Management of Childhood Illness (IMCI) guidelines were developed to reduce the problems from these diseases in children under the age of five years presenting to primary healthcare centres (PHCs) in developing countries such as Nigeria. Therefore, with this study, we would like to study the problems from childhood malaria and pneumonia and compare different methods of diagnoses so as to improve the control and prevention of these diseases.

Why has my child been invited?

You and your child are being invited to take part in this study because your child is between the age of 2 months to 4 years, presenting to a primary healthcare centre (PHC) in Benin City and presently living in the local government area of PHCs for this study. The participation of your child completely depends on whether you agree or not for him/her to take part in this study.

Does my child have to take part?

It is up to you to decide whether or not your child takes part. If you do decide to take part you will be given this information sheet to keep and be asked to provide formal approval of your willingness to participate in the study (i.e., to sign a consent form). You will provide your approval either by a written signature or saying you have agreed for your child to take part in the study in the presence of a witness. If you decide for your child to take part, you are still free to withdraw him/her at any time and without giving a reason. This would not affect your legal rights.

What will happen to my child if he/she takes part?

Your child will be checked for the presence of malaria and pneumonia according to the WHO IMCI guidelines. To avoid giving your child drugs unnecessarily, a rapid diagnostic test for malaria will be carried out to decide whether antimalarial drugs should be given or not. Because we are comparing the accuracy of different methods of diagnoses, we would also take your child's blood (through the vein) to view under the microscope (the gold standard test for malaria), and only if the doctor says so, carry out chest x-ray (the gold standard test for pneumonia). Either the same day as the first visit or within 30 days after presentation to the PHC, you will be administered a questionnaire to get other important information about the child and this might take up to 40-50 minutes. The interview will be audio-taped or recorded to make it much easier for us to use the information you provide after the interview. You may end the interview at any time. For the interview, either a primary healthcare worker (PHW) or one of the researchers will administer the questionnaire at your convenient time.

Expenses and payments

For participating in this study, the cost of all the tests (malaria and pneumonia) and drugs (antimalarial, antibiotics and other necessary drugs) will be provided to you free of charge.

What are the possible disadvantages and risks of taking part?

There are no obvious disadvantages or risks that will likely arise from this study, and this study will not interfere with or change any diagnostic or treatment services that are routinely provided to your child. However, apart from your time taken to take part in completing the questionnaires and participating in an interview, your child may feel a little discomfort during the collection of blood sample and/or may experience discomfort from the cool temperature in the examination room and coldness of the recording plate during chest x-ray test.
Please note that blood taken from your child will **ONLY** be tested for malaria and pneumonia.

What are the possible benefits of taking part?

In addition to the cost of tests and drugs being provided to you free of charge, your participation could help provide useful information for better management of malaria and pneumonia in children under the age of five years who present to primary healthcare centres in Nigeria.

What if there is a problem?

In case you have a complaint on your treatment or that of your child by a member of staff or anything to do with the study, you can initially approach the researchers who will do their best to answer your questions. The researchers' contact details are given at the end of this information sheet. If this achieves no satisfactory outcome, you should then contact the Director of Health Services Department, University of Benin **Dr (Mrs) C. Enofe** via her mobile number: +2348163104400. Alternatively, if something serious happened as a result of your child's participation in the study please report to the Ethics Committee Secretary, **Mrs Louise Sabir** via: louise.sabir@nottingham.ac.uk or **Dr (Mrs) H.I. Eboreime**, Director of Medical Services, Edo State Ministry of Health.

Will my child taking part in the study be kept confidential?

We will follow ethical and legal practice and all information about you and child will be handled in confidence. If you join the study, the data collected for the study will be looked at by authorised persons from the University of Nottingham and University of Benin who are organising the research. They may also be looked at by authorised people to check that the study is being carried out correctly. All will have a duty of confidentiality to you and child as research participants and we will do our best to meet this duty.

All information which is collected about you and child during the course of the research will be kept **strictly confidential**, stored in a secure and locked office, and on a password protected computer database. Any information about you and child which leaves the research unit will have your name and address **removed** (anonymised) and a unique code will be used so that you and your child cannot be recognised from it.

All research data (including an anonymised copy of the audio recording) will be kept securely for 7 years. After this time individual data records will be disposed of securely. During this time all precautions will be taken by all those involved to maintain the confidentiality of you and your child, only members of the research team will have access to these data. The written information will not be stored with the tape recording. No information will be written in any case file and all physical information collected will be stored in a locked filing cabinet and all electronic data collected will be stored on a password protected computer.

In line with safeguarding or security policies, if you disclose something that indicates that you, your child or someone else may be at risk of serious harm then we may need to follow guidelines and report it. We will, where appropriate, inform you of our actions before we undertake them.

What will happen if I don't want my child to carry on with the study?

Your participation and that of your child is voluntary and you are free to withdraw at any time, without giving any reason, and without your legal rights being affected. However, if you withdraw then the information collected so far cannot be erased and this information may still be used in the project analysis.

What will happen to the results of the research study?

The results of this study will be written up as part of an educational degree at the University of Nottingham. The results of the study will also hopefully be provided to Edo State Primary Healthcare Services, Ministry of Health and possibly published in academic journals of public health. No participants will be able to be identified from the research or publication.

Who is organising the research?

This research is being organised by the University of Nottingham in collaboration with the University of Benin and is being conducted as part of the lead investigator's doctoral study at the Division of Public Health and Epidemiology at the University of Nottingham.

Who has reviewed the study?

All research in the Division of Public Health and Epidemiology, University of Nottingham is looked at by the Medical School Research Ethics Committee, to protect your interests. In addition, this study has been reviewed and approved by the Honourable Commissioner for Health, Edo State ministry of Health through the Director of Medical Services.

Further information and contact details

Chief investigator – Kelly Elimian, Department of Public Health and Epidemiology, The University of Nottingham, Clinical Sciences Building phase 2, City Hospital Campus, Nottingham. NG5 1PB. Tel: +44115 8231390/+2348052754088

Co-Investigator-Dr Ayebo Sadoh, Institute of Child Health, University of Benin/University of Benin Teaching Hospital, Benin City, Nigeria. Tel: +2348033435312

Co-investigator –Dr Puja Myles, Department of Public Health and Epidemiology, The University of Nottingham, Room B116 Clinical Sciences Building Phase 2, City Hospital Campus, Nottingham. NG5 1PB. Tel: +44115 823 1348

Co-Investigator- Dr Catherine Pritchard, Department of Public Health and Epidemiology, The University of Nottingham, Room B117 Clinical Science Building Phase 2, City Hospital Campus, Nottingham. NG5 1PB. Tel: +44115 823 1368

Appendix IX: Consent forms for study participants (caregivers and health professionals)

CONSENT FORM FOR CAREGIVERS

Name of Researcher: Kelly Elimian

Title of Project: A study of burden of malaria and pneumonia in children under the age of five years in Nigeria and comparison of diagnostic approaches.

Please read this form and sign it once the above named or designated representative has explained fully the aims and procedures of the study (in the information sheet) to you.

	Tick ✓ for 'Yes'
• I voluntarily agree to take part in this study	
• I confirm that I have read (or have read out to me) and understand the information sheet for the above study and have had the opportunity to ask questions and discuss the study with one of the above investigators all aspects of the study and have understood the advice and information given as a result.	
• I understand that data collected in the study may be looked at by authorised individuals from the University of Nottingham, the research group and relevant regulatory authorities. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from the participant's participation in this study. I understand that my personal details will be kept confidential.	
• I understand that information about me recorded during the study will be kept in a secure database. If data is transferred to others it will be made anonymous. Individual data records will be kept for 7 years after the results of this study have been published.	
• I understand that I can ask for further instructions or explanations at any time.	
• I understand that the interview will be audio taped and that anonymous direct quotes from the interview may be used in the study reports.	
• I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis.	

…… …… ……

Name(s) of Caregiver **Date** **Signature or Thumbprint**

I confirm that I have fully explained the purpose of the study and what is involved to:

……

I have given the above named a copy of this form together with the information sheet.

_____ _____ _____

Name of Person taking consent **Date** **Signature**

3 copies: a copy each for the caregiver, project note/record and researcher

CONSENT FORM FOR HEALTH STAKEHOLDERS

Name of Researcher: Kelly Elimian

Title of Project: A study of burden of malaria and pneumonia in children under the age of five years in Nigeria and comparison of diagnostic approaches.

Please read this form and sign it once the above named or designated representative has explained fully the aims and procedures of the study (in the information sheet) to you.

	Tick ✓ for 'Yes'
• I voluntarily agree to take part in this study	
• I confirm that I have read (or have read out to me) and understand the information sheet for the above study and have had the opportunity to ask questions and discuss the study with one of the above investigators all aspects of the study and have understood the advice and information given as a result.	
• I understand that data collected in the study may be looked at by authorised individuals from the University of Nottingham, the research group and relevant regulatory authorities. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from the participant's participation in this study. I understand that my personal details will be kept confidential.	
• I understand that information about me recorded during the study will be kept in a secure database. If data is transferred to others it will be made anonymous. Individual data records will be kept for 7 years after the results of this study have been published.	
• I understand that I can ask for further instructions or explanations at any time.	
• I understand that the interview will be audio taped and that anonymous direct quotes from the interview may be used in the study reports.	
• I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis.	

…….. …… ……

Name of Health Stakeholder **Date** **Signature or Thumbprint**

I confirm that I have fully explained the purpose of the study and what is involved to:

…….

I have given the above named a copy of this form together with the information sheet.

_____	_____	_____
Name of Person taking consent	**Date**	**Signature**

3 copies: a copy each for health professional, project note/record and researcher

Appendix X: Questionnaire for quantitative component of study

IMCI STUDY IN BENIN CITY

Patient ID: _____ **PHC ID:** _____ **Name of PHC** _____

Name of patient: _____ **Age:** _____ (months)

Date: _____ **Initial visit?** ☐ **Follow-up visit?** ☐

Sex: ____ **Weight:** _____ (kg) **Height:** _____ (cm) **MUAC:** _____ (cm) **Temperature:** _____ (°C)

Ethnicity: Bini ☐ Ishan ☐ Afemai ☐ Other ☐ ***Specify*** _____

Religion: Christian ☐ Muslim ☐ Traditional ☐ Other ☐ ***Specify*** _____

LGA of residence: Egor ☐ Oredo ☐ Ikpoba-Okha ☐

Home address: _____

Phone number: _____

Ask: What are the child's problems? _____

_____

_____

ASSESS *(Tick all signs present)*	**CLASSIFY**
CHECK FOR GENERAL DANGER SIGNS **Yes** ☐ **No** ☐ *(Remember to use IMCI Chart Booklet when selecting classification)* **FOR HOW LONG?** NOT ABLE TO DRINK/BREASTFEED ☐ _____ Days LETHARGIC/UNCONSCIOUS ☐ _____ Days VOMITS EVERYTHING ☐ _____ Days CONVULSION(in the past 1 week) ☐ _____ Days CONVULSING NOW ☐ _____ Days	
DOES THE CHILD HAVE A COUGH OR DIFFICULT BREATHING? **Yes** ☐ **No** ☐ Count the breaths in one minute : _____ Breaths per minute *Remember: 2 months to 12 months; 50 breaths per minute or more = fast breathing* *12 months - 5 years; 40 breaths per minute or more = fast breathing* **FOR HOW LONG?** FAST BREATHING ☐ _____ Days Look for CHEST INDRAWING ☐ _____ Days Look and listen for STRIDOR ☐ _____ Days Look and listen for WHEEZE ☐ _____ Days OXYGEN SATURATION (<92%) value: _____ % _____ Days	
DOES THE CHILD HAVE FEVER (by history/feels hot/temperature 37.5 C or above?) **Yes** ☐ **No** ☐ If yes, for how long _____ Days If more than 7 days, has fever been present everyday? Yes ☐ No ☐ **RDT test:** Positive ☐ Negative ☐ Unconfirmed ☐ Look or feel for STIFF NECK: Yes ☐ No ☐ If yes, for how long ..... Days	

①

INTERVENTION AT TIME OF ASSESSMENT

1. What was the action taken after the patient was assessed? Patient was discharged ☐
   Patient was referred ☐

2. If the patient was referred, indicate the referral centre? Secondary hospital (e.g. Central Hospital) ☐
   Tertiary hospital (e.g. UBTH) ☐ Private Clinic (e.g. MODIC CLINIC) ☐

3. Was the patient given drug/s after assessment? Yes ☐ No ☐
   If the patient was given drug, please complete the table below
   Please always check your IMCI Chart booklet for Treatment

IDENTIFY TREATMENT
(Tick ✓ for YES)

No.	Name of Drug	Age Group	Dosage	Duration (Days)	Cost (₦)
1.	Oral Antibiotics (Amoxycillin) ☐	2 Months - 12 Months ☐ 12 Months - 5 Years ☐	Syrup (125mg/5ml) / Tablets (250mg) 10ml ☐ 1 ☐ 20ml ☐ 2 ☐	No. of times/day × Days 2 × 5 *Note: For two times daily, divide the dosage by two eg. 10ml will be 5ml taken twice.*	____
2.	Oral Antimalaria (Artemeter-Lumefantrine) ☐	3 Months - 3 Years ☐ 4 Years - 5 Years ☐	Syrup / Tablets 7ml ☐ 1 ☐ 10ml ☐ 14ml ☐ 20ml ☐ 2 ☐	2 × 3	____
3.	Paracetamol ☐	2 Months - 2 Years ☐ 2 Years - 5 Years ☐	Syrup ☐ Tablet ☐ Intramuscular (IM) or Injection ☐ *(A Patient can be given both syrup & IM)*	*As shown in the drug pack*	____
4.	Salbutamol ☐ (For wheezing)	*As shown in the drug pack*	Syrup ☐ Tablet ☐	*As shown in the drug pack*	____
5.	Any other Drug *Write the Name below:* (i) ____ (ii) ____ (iii) ____ (iv) ____	*Reason for giving other drug(s)* ____ ____ ____ ____	*Tick Necessary Boxes* Syrup ☐ Tablet ☐ Intramuscular (IM) or Injection ☐	*As shown in the drug pack*	____

②

4. If oxygen saturation is less than 92%, was the patient given supplemental oxygen? Yes ☐ No ☐
   If the patient was given supplemental oxygen, record the cost: ₦ _____
5. Was the patient given inhaled salbutamol bronchodilator with a spacer for wheezing? Yes ☐ No ☐
   If the patient was given inhaled salbutamol bronchodilator, record the cost: ₦ _____
6. Was the parent given counsel according to the IMCI guidelines? Yes ☐ No ☐

Return for follow-up on: ____/____/_____

WHAT ARE THE CHILD'S OTHER PROBLEMS (COMORBIDITIES)?

(examples include: ear problem, malnutrition, running nose, rashes, jaundice, etc.)

No.	Medical condition	Duration (Days)
1.		
2.		
3.		
4.		

ASSESSMENT FOR LAY-DIAGNOSIS & HEALTH BEHAVIOUR AMONG PARENTS

Q1: Do you know what is wrong with the patient? Yes ☐ No ☐

If yes to Q1, what do you think is wrong with the patient? _____

_____

It is possible for a caregiver/parent to provide more than one classification of illness e.g. FEVER AND COUGH.

Q2: When you suspect that your child is ill/sick, do you visit the nearest chemist/ pharmacy store to buy drugs? Yes ☐ No ☐

If Yes to Q2, did you visit a chemist/pharmacy store for the child's present illness before reporting to this primary healthcare centre? Yes ☐ No ☐

Remarks

④

SECTION TWO

TO BE COMPLETED BY LABORATORY/RADIOLOGY STAFF

Patient ID:_____Nameof Patient:_____Date:_____

Diagnostic tests	Results/Description	Cost (₦)
Malaria Status	Positive ☐ Negative ☐ If positive, score:_____	
Parasite density	_____(µL)	
Distribution of *Plasmodium species*	*P. falciparum* ☐ *P. ovale* ☐ *P. vivax* ☐ *P. Malariae* ☐	
PCV/Haemoglobin Conc.	_____(%)	
Chest x-ray (CXR) Result	Normal ☐ Remarks:_____	
	Pneumonia ☐ Remarks:_____	
	Other diagnosis ☐ Remarks:_____	

SECTION THREE

TO BE COMPLETED BY PI/RAs

Patient ID:_____**Name of patient:**_____

Date first follow-up:_____**Date of last follow-up:**_____ **Number of follow-up:**_____

1. Title of respondent:_____Name (*surname last*):_____
2. Gender of Respondent:_____
3. Respondent marital status: Married ☐ Single ☐ Separated/Divorced ☐ Windowed ☐
4. Respondent's relationship to patient: Parent ☐ Sibling ☐ Grandparent ☐ Other Relative ☐ None ☐
5. Respondent age group: <15 ☐ 15-20 ☐ 21-25 ☐ 26-30 ☐ 31-35 ☐ 36-40 ☐ 41-45 ☐ 46-50 ☐ >51 ☐
6. Caregiver's occupation: Artisan/Trader ☐ Farmer ☐ Civil-servant ☐ Self-employed/Business ☐ Retired ☐ Currently unemployed ☐ Housewife ☐ Others ☐ if others, specify_____
7. Caregiver's educational qualification: No formal education ☐ 1° school ☐ 2° school ☐ >Secondary school ☐
8. Mother's education (If diff from caregiver): No formal education ☐ 1° school ☐ 2° school ☐ >Secondary school ☐
9. Caregiver's monthly income: <5,000 Naira ☐ 5,000-20,000 Naira ☐ >20,000 ☐ Naira ☐

COMPLIANCE WITH DRUG PRESCRIPTIONS

10. Has the patient completed the prescribed antimalarial drug? Yes ☐ No ☐ NA ☐
11. If yes to **Q10**, was this objectively verified? Yes ☐ No ☐ NA ☐
12. Has the patient completed the prescribed antibiotic drug? Yes ☐ No ☐ NA ☐
13. If yes to **Q**12, was this objectively verified? Yes ☐ No ☐ NA ☐
14. Has the patient completed any other prescribed drugs? Yes ☐ No ☐ NA ☐
15. If yes to **Q**14, was this objectively verified? Yes ☐ No ☐ NA ☐

FOR PATIENTS REFERRED AND ADMITTED TO HOSPITAL

16. Was the patient hospitalised for this illness? Yes ☐ No ☐
    If yes, for how long?:_____ Days
17. Was the patient admitted to critical care/ICU during hospitalisation? Yes ☐ No ☐
    If yes, for how long?:_____ Days
    Indicate the level of critical care: Level 2 ☐ Level 3 ☐
18. How much did you spend for patient's admission to critical care? ₦_____
19. Was the patient given infusion during hospitalisation? Yes ☐ No ☐
    If yes, how much did infusion cost? ₦ _____
20. Was the patient given oxygen during admission in hospital? Yes ☐ No ☐
    If the patient was given oxygen, how much did it cost? ₦_____
21. Did you or relatives have to lodge near the hospital to take care of the patient while on admission? Yes ☐
    No ☐
    If yes, about how much did it cost you/them? ₦_____
22. In addition to the above cost, did you incur other expenses during patient's admission in hospital?
    Yes ☐ No ☐
    If you did, how much money did you incur ? ₦_____

FOR ALL PATIENTS

23. Did you miss work caring for patient? Yes ☐ No ☐
    If yes, for how long? _____ Days
24. Did you lose money because you were not working (Probe for loss of wages, business days lost, leave without pay, helper & driver wages etc.)? Yes ☐ No ☐
    If yes, how much money did you lose? ?_____
25. How did you pay for medical expenses? Own finance ☐ Family members ☐ Meeting/Club ☐
    Loan/Burrowed ☐
    If you paid through loan, what was the % interest?_____%
26. Did the patient miss school or out of home care during illness? Yes ☐ No ☐
    If yes, for how long?_____ Days
27. Did the patient develop any side effect/s or complication/s during the course of this illness? Yes ☐ No ☐
28. If yes to Q27, please state the side effect/s or complication/s: (i) _____
    (ii)_____
29. Complete records on mortality/death: Death: Yes ☐ No ☐
    Cause of death:_____
    Location: PHC ☐ Hospital ☐ Home ☐

RISK FACTORS FOR MALARIA AND PNEUMONIA)

30. What was the patient's weight at birth (Attempt to verify from birth record/card)? _____(Kg)
31. Did patient have medical problem/s (i.e. neonatal) at birth?: Yes ☐ No ☐
    If yes, please provide detail:_____

Malaria:

32. Does the patient own a mosquito net or long lasting insecticidal net (LLIN)? Yes ☐ No ☐
33. Does the patient sleep under mosquito net or Long lasting insecticidal net (LLIN)? Yes ☐ No ☐
    If yes to Q33, can mosquito nets be objectively verified (Ask the respondent to show you the nets in the household)? Observed, hanged ☐ Observed, not hanged ☐ Not observed ☐
34. Does the patient's (household) windows and doors have mosquito nets? Yes ☐ No ☐
    If yes to Q34, can nets on windows and doors be objectively verified (Ask the respondent to take you round the house if possible)? Observed, hanged ☐ Observed, not hanged ☐ Not observed ☐
35. How many mosquito nets (both bed, windows/doors) does your household have? Specify_____ [If 7 or More Nets, Record '7']
36. Does the patient live close to aquatic habitats (e.g., Vehicle tyres, domestic containers and tree holes/ leaves)? Yes ☐ No ☐
    If yes to Q36, specify the type: Open-gutters/pot-holes ☐ Pool/pond ☐ Domestic containers ☐
    Other environmental habitats (vehicle tyres) ☐
    What is the distance of patient's residence from aquatic environment (e.g. open gutter)? _____ (m)
37. Does the patient regularly use vector or mosquito control measures or practice indoor residual spraying (e.g., insecticide spray or repellent) at home and surrounding area? Yes ☐ No ☐
38. Does the patient practice intermittent preventive treatment for malaria (e.g. every two weeks without malaria signs/symptoms)?
    Yes ☐ No ☐
39. Are there community preventive measures such as environmental sanitation and waste collection services in patient's neighbourhood? Yes ☐ No ☐

Pneumonia:

40. Does any member of family residing in the same house as patient smoke any form of tobacco or other types of compounds that can be smoked in this area? Yes ☐ No ☐
41. How often does anyone smoke inside a patient's house? Daily ☐ 2-3 times/wk. ☐ >3 times/wk. ☐ Never ☐
42. Does patient's parent use stove or firewood to cook? Yes ☐ No ☐
43. Does the patient come to the kitchen during cooking? Yes ☐ No ☐
44. Was (Is) patient (being) exclusively breastfed for the first 6 months of life? Yes ☐ No ☐
45. Was (Is) patient given prelacteal feeding? Yes ☐ No ☐
46. Does the patient attend any out-of-home care? Yes ☐ No ☐

If yes to Q46, which of the following care centre? Preschool ☐ family care ☐ Crèche attendance or Day-care ☐ Nursery ☐

47. How many children 0-10 years of age live with the patient? Please specify:_____
48. How many people sleep in the same room as the patient? Please specify: _____
49. Has patient completed immunisation regimen for his/her age? Yes ☐ No ☐

Use the revised Nigerian immunization schedule below as a guild

1. 10 weeks (2 months 2 weeks) [OPV2, Pentavalent 2, PCV (optional)]
2. 14 weeks (3 months 2 weeks) [OPV3, Pentavalent 3, PCV, Rotavirus 2 (optional)]
3. 9 months [Measles]
4. 12 months (1 year) [Yellow fever]
5. 15-18 months [MMR, OPV, chicken pox (optional)]
6. 24 months [Meningitis, Typhoid fever (optional)]

Appendix XII: Interview guide for the qualitative component of study

INTERVIEW GUIDE FOR QUALITATIVE STUDY

To explore the feasibility and acceptability of early diagnostic approaches and programme delivery models according to relevant stakeholders (health professionals and caregivers)

Assessment of the WHO IMCI guidelines by Primary Healthcare Stakeholders

Thank you for agreeing to participate in this interview. I am interviewing a range of people involved in primary healthcare services in Benin City. The interview will last approximately 40 minutes.

Can I just confirm that you have read the information sheet and have signed the consent form?

If there are any questions you do not wish to answer then please let me know.

Can I confirm your name?

Organisation that you represent:

I was planning to record this interview so that I can transcribe it and then look across interviews for themes. I will ensure that the transcripts are made anonymous so I won't be able to identify you or your organisation individually. Are you happy with this? (Start recording at this point). If interviewee is unhappy with being recorded, explain that the interview might take longer as notes will be taken as the interview progresses.

Primary Health Workers

1. How long have you been working as a PHW in this PHC?
2. Can you tell me about your role in primary healthcare services? (Emphasis on routine *health assessment*)
3. Could you describe your *general* experience during the IMCI training for this study
4. What is your view about the delivery of the IMCI training in terms of the:
    a. Facilitators b) Training materials c) Training schedule

5. Tell me about your experience using the IMCI guidelines to assess and classify pneumonia
6. Tell me about your experience using the IMCI guidelines to assess and classify malaria
7. How would you compare your experience in using the IMCI guidelines for malaria and pneumonia?
8. How would you describe the role of the IMCI guidelines on your ability to prescribe drugs for patients?
9. From your experience, would you consider recommending the IMCI guidelines for use to 'every' PHWs in PHCs? In the whole of Edo State/Nigeria? (*Practicality/Feasibility/Generalisability*)
10. If we were to repeat this study, do you have any suggestions as to how we might perform better?

Clinicians/Medical Officer of Health: Observe introductory protocol before asking questions

1. How long have you been working as a clinician in this PHC?
2. Can you tell me about your role in primary healthcare services? (Emphasis on routine *health assessment*)
3. What is your view about the assessment and classification of malaria and pneumonia according to the IMCI guidelines?
4. Tell me about your experience in assessing patients simultaneously/alongside with PHWs who used the IMCI guidelines. What do you think about the comparison in the assessment?
5. How would you describe the possible role of the IMCI guidelines on treatment of malaria and pneumonia? (Emphasis on drug prescriptions)
6. From your experience, would you consider recommending the ICMI guidelines for use to 'every' PHWs (*Practicality/Feasibility*)?

7. Do you consider the IMCI as a potential alternative for the management of malaria and pneumonia especially in a resource-constrained setting (i.e., where clinicians and qualified nurses are not readily available)?
8. If we were to repeat this study, do you have any suggestions as to how we might perform better?

IMCI facilitators/trainers: Observe introductory protocol before asking questions

1. Tell me about your experience as a WHO IMCI trainer/facilitator
2. Could you describe your *general* experience as a facilitator/trainer during the IMCI training for this study
3. What is your view about the IMCI training in terms of the:
    a. Training materials b) Training schedule c) Participants
4. Following the training, do you think the IMCI guidelines were sufficient for the assessment and classification of malaria (*Practicality/Feasibility/Generalisability*)?
5. Following the training, do you think the IMCI guidelines were sufficient for the assessment and classification of pneumonia?
6. If we were to repeat this study, do you have any suggestions as to how we might perform better?

PHC coordinators: Observe introductory protocol before asking questions

1. How long have you been working as a PHC coordinator?
2. Can you tell me about your role in primary healthcare services? (Emphasis on *administrative duties*)
3. Could you describe your *overall experience* during the IMCI training for this study (*if applicable*)?
4. What is your view about the IMCI training in terms of the:
    a) Training materials c) Training schedule

5. How would you describe the possible role of the IMCI guidelines on the assessment and classification of malaria in your PHC?
6. How would you describe the possible role of the IMCI guidelines on treatment of pneumonia? (Emphasis on drug prescriptions)
7. From your experience, would you want to recommend the IMCI guidelines use to ‘every’ PHWs in PHCs? In the whole of Edo State/Nigeria?
8. If we were to repeat this study, do you have any suggestions as to how we might perform better?

Assessing the diagnostic criteria used by <u>caregivers</u> for lay-diagnosis in ascertaining malaria and pneumonia

Thank you for agreeing to participate in this interview. I am interviewing a range of caregivers of children under the age of five years old in Benin City. The interview will last about 40 minutes.

Can I just confirm that you have read the information sheet and have signed the consent form?

If there are any questions you do not wish to answer then please let me know.

Can I confirm your name?

Lastly can I confirm your occupation?

I was planning to record this interview so that I can transcribe it and then look across interviews for themes. I will ensure that the transcripts are made anonymous so I won't be able to identify you or your organisation individually. Are you happy with this? (Start recording at this point). If interviewee is unhappy with being recorded, explain that the interview might take longer as notes will be taken as the interview progresses. In case of language barrier, explain to the interviewee why a translator is needed during the interview.

Do you have any questions before we commence the interview?

May I begin the interview now?

15-20 caregivers (*Including caregivers of non-participants)*

1. Please tell me about your child/ren
2. How often does your child/do your children fall ill (say in a year)?
3. Could you describe how you typically manage your child/ren when ill?
4. What do you think about lay-diagnosis?
5. How do you see the lay-diagnosis of malaria?
6. How do you see the lay-diagnosis of pneumonia (Emphasis difference from common cold)?

7. Tell me about your experience in using lay-diagnosis to assess and classify pneumonia
8. Tell me about your experience in using lay-diagnosis to assess and classify malaria
9. What diagnostic criteria or clinical factor(s) influence your lay-diagnosis for malaria?
10. What diagnostic criteria or clinical factor(s) influence your lay-diagnosis for pneumonia?
11. What non-clinical factors do you think contribute to lay-diagnosis of malaria and pneumonia?
12. What do you do after diagnosing malaria?
13. What do you do after diagnosing pneumonia?
14. Could you please describe your willingness to receive standardised trainings such as the WHO IMCI (this would have been explained at the initial stage) to improve the certainty/accuracy of your diagnosis?
15. Following the standard training, what do you think about acting as an enforcer/referrer of severe malaria/pneumonia cases in your locality/area?
16. Thank you again for your time.

These semi-structured questions will be used as a guide rather than a script. Probes or follow-up questions will be used when necessary. Examples of common probes or follow-up questions are: who, what, when, what did you do then? When did this happen? What do you mean? Tell me more about that, walk me through the experience etc. Also, various forms or probes, ranging from silence, sounds, to a single word, will be used when necessary.

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