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Non-CTIMP Study Protocol

To document pneumonia case management practices in selected communities in Pakistan; A qualitative study

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CONTENTS

1 INTRODUCTION 8
1.1 BACKGROUND 8
1.2 1.2. RATIONALE FOR STUDY 8
2 STUDY OBJECTIVES 10
2.1 OBJECTIVES 10
2.1.1 Primary Objective 10
2.1.2 Secondary Objectives 10
2.2 ENDPOINTS 10
2.2.1 Primary Endpoint 10
3 STUDY DESIGN 10
3.1 Methodology: 10
3.2 Observation Sites: 11
3.3 Type of Observations: 11
3.4 Data Collectors: 11
3.5 Recruitment of Disguised Patients' Caregiver and Conduction of Observations: 12
3.6 Project work-plan: 12
4 STUDY POPULATION 13
4.1 NUMBER OF PARTICIPANTS 13
4.2 INCLUSION CRITERIA 13
4.2.1 INCLUSION CRITERIA OF DISGUISED CAREGIVER: 13
4.2.2 INCLUSION CRITERIA OF HEALTHCARE PROFESSIONALS UNDER OBSERVATION 13
4.2.3 EXCLUSION CRITERIA 14
5 PARTICIPANT SELECTION AND ENROLMENT 14
5.1 IDENTIFYING PARTICIPANTS 14
5.2 CONSENTING PARTICIPANTS 14
5.2.1 Withdrawal of Study Participants 15
6 STUDY ASSESSMENTS 15
6.1 STUDY ASSESSMENTS 15
7 DATA COLLECTION 16
7.1 Source Data Documentation 17
7.2 Case Report Forms 17
8 STATISTICS AND DATA ANALYSIS 18
8.1 SAMPLE SIZE CALCULATION 18
8.2 PROPOSED ANALYSES 18
9 OVERSIGHT ARRANGEMENTS 19
9.1 INSPECTION OF RECORDS 19
9.2 RISK ASSESSMENT 19

9.3 STUDY MONITORING AND AUDIT 19
The ACCORD Sponsor Representative will assess the study to determine if an independent risk assessment is required. If required, the independent risk assessment will be carried out by the ACCORD Quality Assurance Group to determine if an audit should be performed before/during/after the study. 19
10 GOOD CLINICAL PRACTICE 19
10.1 ETHICAL CONDUCT 19
Before the study can commence, all required approvals will be obtained and any conditions of approvals will be met. 20
10.2 INVESTIGATOR RESPONSIBILITIES 20
10.2.1 Informed Consent 20
10.2.2 Study Site Staff 20
10.2.3 Data Recording 20
10.2.4 Investigator Documentation 20
10.2.5 Confidentiality 20
10.2.6 Data Protection 21
11 STUDY CONDUCT RESPONSIBILITIES 21
11.1 PROTOCOL AMENDMENTS 21
11.2 MANAGEMENT OF PROTOCOL NON COMPLIANCE 21
11.3 SERIOUS BREACH REQUIREMENTS 22
11.4 STUDY RECORD RETENTION 22
11.5 END OF STUDY 22
11.6 INSURANCE AND INDEMNITY 22
12 REPORTING, PUBLICATIONS AND NOTIFICATION OF RESULTS 23
12.1 AUTHORSHIP POLICY 23
13 REFERENCES 23

LIST OF ABBREVIATIONS

.

ACCORD	Academic and Clinical Central Office for Research & Development - Joint office for The University of Edinburgh and Lothian Health Board
AE	Adverse Event
AR	Adverse Reaction
CI	Chief Investigator
CRF	Case Report Form
GCP	Good Clinical Practice
ICH	International Conference on Harmonization
PI	Principal Investigator
QA	Quality Assurance
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction
HIV	Human Influenza Virus
LHWs	Lady Health Workers
BHU	Basic Health Unit
RHC	Rural Health Centre
GDP	Gross Domestic Product
WHO	World Health Organization
UNICEF	United Nations International Children's Emergency Fund
ARI	Acute Respiratory Illness
USAID	U.S. Agency for International Development
AKU	Agha Khan University
IMCI	Integrated Management of Childhood Illnesses

PAIMAN	Pakistan Initiative for Mothers and New-borns
MNCH	Maternal, Neonatal and Child Health
SP	Standardized Patients
KPK	Khyber Pakhtun Khwah
Y	Yes
N	No
eCRF	Electronic Case Report Forms
FLCF	First Level Care Facility
DFID	Department for International Development
ID	Identification
GPS	Global positioning system
ISF	Investigator Site File

1 INTRODUCTION

1.1 BACKGROUND

Pneumonia is an acute respiratory infection that affects the lungs [1]. In this disease, the alveoli (small sacs within lungs) get filled up with pus and fluid making it difficult to breathe [1]. In children under five, the most common presenting features of pneumonia are cough and /or difficult breathing/ lower chest in-drawing with or without fever [1]. Risk factors leading to pneumonia include lack of immunization, air pollution, overcrowding, parental smoking, under nutrition, non-hygienic practices, and pre-existing illnesses such as HIV and measles [2]. Early pneumonia identification and treatment saves lives as in severe cases, it can lead to death [3]. Initiating use of antibiotics upon onset of disease can hamper progression whereas absence of early intervention can have limited impacts even with intravenous antibiotics [4].

Despite the availability of standard pneumonia management guidelines and multiple global efforts, pneumonia continues to be the leading killer of children under five, accounting to around 17% of the total under five deaths globally [5-8]. It has been estimated that annually there are around 120 million episodes of pneumonia among children with around 14 million progressing to severe episodes. Out of these cases, close to 1.3 million children die with 81% of these deaths occurring in children under 2 years of age [6]. 52% of these deaths occur in the Sub-Saharan region and South Asia with main contributions from India, Nigeria, Congo, Pakistan and Afghanistan [9]. In Pakistan, pneumonia contributes to 16% of under-five mortality in the country having a well-defined yet poorly functional healthcare system [10-12].

Healthcare in Pakistan is provided through two sectors; Public and private. The public sector includes community health workers, referred to as Lady Health Workers (LHWs) working under the National Program for Family planning and Primary Health Care. It also includes the First Level Care Facilities referred to as Basic Health Units (BHUs) and Rural Health Centres(RHCs) and district/tertiary care hospitals. The private sector includes the private clinic and private hospitals. The public sector provides healthcare free of cost or with minimal charges whereas the private sector is expensive as patients spend out-of-pocket for health service in this sector. This accounts to the wide difference of quality of care across both the sectors as the public sector is not funded adequately by the government to provide high quality services, due to only 2% of the GDP assigned to healthcare. Irrespective of the public and private sector, case management of pneumonia in children under five is supposed to be followed uniformly across all sectors as training of the healthcare providers is standard across all cadres of care under various programs in the country. Despite that fact, the mortality and morbidity rate due to pneumonia in children under five remains unchanged in the country.

1.2 1.2. RATIONALE FOR STUDY

WHO and UNICEF have developed multiple action/ intervention plans to curb pneumonia related morbidity and mortality in children under five and based on those plans Pakistan has launched multiple national programs. These programs include the National ARI control program which was launched in 1989 with the main objectives of reducing severity and mortality due to pneumonia and rationalize the use of

antimicrobials and other drugs for treatment of ARI [13]. It was supported by WHO, UNICEF and USAID. While the program was ongoing, in 1990, in a National workshop on policy related research action plan, organized by the Ministry of Health, the Ministry of Planning and Development and the Aga Khan University (AKU), ARI was ranked sixth of fifteen priority areas for national policy-linked research [13]. The National ARI Control program continued but WHO soon realized that this disease centric narrow approach has not been able to achieve its desired objectives. Therefore, it developed a more integrated approach and launched it globally as Integrated Management of Childhood Illnesses (IMCI) launched in Pakistan in 1998[14]. The approach in IMCI focused on improving case management skills of health workers, strengthening the health system, and addressing family and community practices. Concerns were raised that this is yet another attempt to launch a child health intervention vertically. Duplicity was very much evident from the fact that ARI existed as an independent program and was also part of the IMCI package. Between 2004-2010 PAIMAN, a USAID funded project was undertaken which focused on improving the status of maternal and newborn health in 10 districts (19% of the national population), which later expanded to 24 districts across the four provinces and Azad Jammu and Kashmir in Pakistan. ARI was an important component in that project [15]. The national Maternal, Neonatal and Child Health program (MNCH) was then launched in 2010 funded mainly by DFID implemented in 36 districts and ended after 5 years [16]. It was focused on strengthening of management and organization mechanism of healthcare delivery systems. Under all these programs, selected health care professionals, both community and facility based, were trained on WHO standard of ARI case management out of the 18,029 specialist doctors, 100,131 general physicians, 27,677 working nurses, 6,741 Lady Health Visitors and over 95,600 Lady Health Workers. Looking at the unchanged mortality statistics, there is a concern that these trainings might have failed to change the case management practices within the community. It is perhaps due to the fact that the monitoring and evaluation was not a strong point of these programs [15-18].

There is limited data within Pakistan which reflects the status of the quality of current pneumonia case management practices throughout the three tiered health system (primary health facilities, secondary care hospitals, and tertiary care hospitals) as well as the private sector. There are a number of approaches which can be used to assess standard case management including recall based patient surveys, questionnaire surveys of knowledge, prescription/chart analysis and use of standardized patients or disguised patients to assess actual practice[19]. Standardized patients (SP) are simulated patients who do not suffer from any disease per se but pretend to have those symptoms. They present in the designated clinics/hospitals and use a pre learnt script to provide a history of illness. The healthcare providers are unaware of the simulation of the cases. Upon taking the visit, the SP is then interviewed on the entire experience and in certain cases a recorder is used to audio record the visit. A disguised patient is one who although suffers from a particular disease but acts as a disguised observer as well and works the same way as a simulated patient. Considering the use of standardized patients (SPs) or disguised patients provides an actual picture of practice, therefore, it has been used extensively most recently [20]. This process provides an assessment of the practitioners' knowledge of appropriate care and the actual care delivered, i.e., adherence to standard treatment guidelines [21].

Such an approach in Pakistan can identify current pneumonia case management practices across the country because to-date no such study has been conducted in this field. The results of this study can help in informing design of future policies and

interventions that can in turn assist in reducing pneumonia related morbidity and mortality.

2 STUDY OBJECTIVES

2.1 OBJECTIVES

2.1.1 Primary Objective

To assess the standard practices of pneumonia case management at three levels of health care; community level, first level care facility and practitioner level, across Pakistan.

To assess the standard practices of pneumonia case management in the private sector across Pakistan.

2.1.2 Secondary Objectives

To determine the differences in pneumonia case management observed across the provinces of Pakistan in both public and private sector.

2.2 ENDPOINTS

2.2.1 Primary Endpoint

1. Correct history taking of case of pneumonia
2. Correct examination of case of pneumonia
3. Correct diagnosis of case of pneumonia
4. Correct treatment of case of pneumonia

3 STUDY DESIGN

3.1 Methodology:

This will be a qualitative study which will be conducted through participant observations over a period of 13 months across randomly selected sites in four provinces of Pakistan in addition to the federal capital. The provinces are Baluchistan, Khyber Pakhtun Khwah (KPK), Punjab and Sindh.

After obtaining ethical clearance, an observation tool will be developed based on standard WHO guidelines and input from field experts. This tool will be pretested upon finalization. At the same time an advisory committee will also be formulated composed of expert paediatricians and public health professionals who will provide their input into the implementation protocol and the tool. Once the tool is finalized trainings will be conducted on the tool and then observations will be conducted.

3.2 Observation Sites:

Observations sites will be randomly selected from each of the four provinces and the capital through our specialized sampling software. Upon site selection, observations will be made across the following levels of healthcare: community level, first level care facility (FLCF) and practitioner level both in the public and private sector. The community level observations will include observation of the pneumonia case management by the LHWs. LHWs are the primary care givers at the community level who cover around 60% of Pakistan. Their basic duties include education, counselling and basic management of the common maternal and child ailments. Each LHW covers around 100-120 household and visits each household once a month. The observations will be made either at the health house of the LHW or she will be requested to visit the household of the disguised patient.
The FLCF level will include observations made at the primary health care facilities which are the Basic Health Units (BHUs) and Rural Health Centres (RHCs). A basic health unit is located within a union council which is the smallest administrative unit in the Pakistani administrative system. Each basic health unit covers a catchment area of 25,000 households. Pakistan has around 5,290 BHUs although not all are functional. Services provided at BHU are promotive, preventive, curative and referral .LHWs refer patients usually to BHUs. RHCs provide in-patient service as compared to BHUs. They usually have 10-20 beds and cover a catchment area of 100,000 people. The RHC provides promotive, preventive, curative, diagnostics and referral services apart from the in-patient services. It also provides clinical, logistical and managerial support to the BHUs, LHWs, and dispensaries that fall within its geographical limits. RHC also provides medico-legal, basic surgical, dental and ambulance services. There are around 552 RHCs in Pakistan.
The practitioner level observations will include those of practitioners at both the private and public sector. The public sector will include observations made in outpatient departments of selected tertiary care hospitals across the study sites. Observations made at the private practitioner level will include selected solitary private clinics or clinics within private hospitals. The community and FLCF level will represent practices within the rural community and the practitioner level will represent practices within the semi urban/urban communities.

3.3 Type of Observations:

These will be participant, structured, disguised observations which will be done using a validated observation tool based on standard WHO pneumonia case management guidelines, developed in close collaboration with experts from University of Edinburgh. This tool will be pretested and translated into Urdu.

3.4 Data Collectors:

A team of data collectors, who will be healthcare professionals, will be trained on appropriate administration of the observation tool upon recruitment. The training will also include an introduction to pneumonia, its signs and symptoms, diagnosis and management according to WHO guidelines. A 3 day interactive training workshop will be conducted whereby mock excesses will also be conducted. A total of three trainings will be conducted whereby data collectors from Islamabad (capital), Punjab

and KPK will have one training as their participants can be managed to be brought in one location due to close proximity. Sindh and Baluchistan participants will have two separate trainings.

3.5 Recruitment of Disguised Patients' Caregiver and Conduction of Observations:

Each data collector will be provided a pre-defined list of addresses whereby the observations will be made. He/she will go to the location and will search the nearby community for cases of pneumonia in children under five. Once the cases have been identified, their caregivers will be sought. These caregivers are the primary individuals providing direct care to the child. Usually, these are the mothers, fathers, grandmothers or guardians of the child. They will explained the purpose of the study and will be requested to participate in the study by acting as disguised caregivers to accompany the data collector to the health facilities and upon agreement will sign a consent form. This means that they will disguise as an acquaintance of the data collector who will take them to the healthcare professional to be observed. They will take the ill child along, give the history of that child to the healthcare professional and answer any relevant questions which will be asked by him/her and get the child examined and treated. In the meantime, the data collector will make the relevant observations based on the observation tool which will be filled after the visit. The data collector will not reveal that he/she is a healthcare professional. Additionally, the data collector will also take an audio recorder along to record the entire conversation which will help in filling up the observation tool later and also validate the visit. Once the visit is completed, the data collector will take the caregiver back to their premises and fill up the observation tool in tablets within one hour of the visit.

3.6 Project work-plan:

PROJECT ACTIVITIES	YEAR 1(Months)												YEAR 2
	1	2	3	4	5	6	7	8	9	10	11	12	1
Ethical Clearance	X	X											
Staff Recruitment		X											
Tool Development			X										
Inception Meetings for development of implementation strategies			X										
Pretesting and Finalization of the tool			X	X									
Data Collections (Trainings, identification of study site/centers, observations)				X	X	X	X	X	X				
Data Analysis & Reporting										X	X	X	X

4 STUDY POPULATION

4.1 NUMBER OF PARTICIPANTS

Two data collectors per province will be recruited to make the observations making a total of 10 data collectors for all the locations. Additionally, one caregiver per observation will be recruited by the data collectors to accompany them. Meaning 160 caregivers will be recruited. This is to avoid inconvenience to the caregiver and their affected under five children. In case, a community is encountered whereby the cases of pneumonia are very few, then the same caregiver will be accompanied for observation of an LHW, BHU and RHC of that locality as these facilities are closely located. If despite this practice, number of observations are not achievable per site than an additional site will be provided to the data collector to visit.

4.2 INCLUSION CRITERIA

4.2.1 INCLUSION CRITERIA OF DISGUISED CAREGIVERS:

- Caregivers of children under five years of age. These are those individuals who provide direct care to the child. These could either be a mother, father, grandmother or guardian.
- The child under five under that caregiver's household must have symptoms of pneumonia/severe pneumonia as indicated in section 6.1
- Caregivers consenting to be a part of the study.

4.2.2 INCLUSION CRITERIA OF HEALTHCARE PROFESSIONALS UNDER OBSERVATION

4.2.2.1 LHWs:

- Those who have been practicing as LHWs for more than one year as identified by talking to the community.
- Those who belong to the catchment area of the selected study sites

4.2.2.2 BHUs:

Functional BHUs with at least one licensed healthcare provider.

4.2.2.3 RHC:

Functional RHCs with at least one licensed healthcare provider.

4.2.2.4 Public Practitioners:

Paediatricians working in a government tertiary healthcare facility as a full time employee.

In case the facility/location does not have specialist paediatricians, then general physicians working full time within that facility.

4.2.2.5

4.2.2.6 Private Practitioners:

Full time/part time private paediatric practitioners working in either their private clinics or in private hospitals.

In case the facility/location does not have specialist paediatricians, then general physicians working within that facility.

4.2.3 EXCLUSION CRITERIA

4.2.3.1 EXCLUSION CRITERIA FOR DISGUISED CAREGIVERS:
Caregivers of children under five suffering from comorbidity with pneumonia.

4.2.3.2 EXCLSUIONCRITERIA FOR HEALTHCARE PROFESSIONALS UNDER OBSERVATION

BHUs or RHCs run by non -licensed healthcare professionals as there are certain locations whereby due to lack of licensed healthcare professional's facility technicians tend to attend to the patients based on their experience.

5 PARTICIPANT SELECTION AND ENROLMENT

5.1 IDENTIFYING PARTICIPANTS

Data collectors will be licensed healthcare professionals (doctors or nurses) with at least one 6-12 months of experience working in the field of paediatrics. They will be recruited after interviews with the selection team (Investigators and project manager) upon giving advertisements for posts of data collectors.

For selection of the LHWs to observe them, a randomly selected rural community through our computerized system will be generated from where the caregivers will be selected to act as disguised ones. Additionally, a complete list of functional RHCs and BHUs will be obtained from the corresponding district health office (DHO) which is the administrative authority for these centres. From that list, four BHUs and four RHCs per province will be randomly selected using a lottery method. For sampling of the practitioners, a list of tertiary care facilities will be obtained from the health department of each province and a list of private clinic and private hospitals from their corresponding directories. These lists will be used to randomly select five practitioners each from public and private sector. Once the BHU, RHC, private and public practitioner sites have been selected, disguised caregiver will be recruited and observations made. In case a healthcare provider is not available or if a facility has been closed down, the caregiver will be provided an alternate address.

5.2 CONSENTING PARTICIPANTS

A written and signed consent form will be obtained from the recruited disguised caregivers of children under five. A detailed consent form will be developed and will

be translated into Urdu. It will include statements on voluntary participation with refusal to continue at any point of the study with no penalty to the participants .Any queries of the caregivers regarding the study will be resolved prior to signing the

consent form. Those caregivers who will be able to read will be given the opportunity to do so and sign the form and those who will not be able to read will have the consent form read out to them by the data collector in the presence of a witness and thereafter have their thumb impression on the form. The witness will be any other household member over the age of 18 years. The witness will also be asked to sign the form in such a case. In case a caregiver accepts to be a part of the study but refuses to sign the document, he/she will be requested to have a decision maker of the household to sign the form.

No consent will be taken from the observed LHWs and healthcare providers of BHUs, RHCs, private and public healthcare facilities as we shall be conducting disguised observations. This is because if they are taken consent from, prior to the study, they will become cautious and chances are that the observations will not reflect their actual practice as they will change their practices. And considering there will be no harm generated on the part of the researchers and recruited caregivers therefore the benefit of not taking the consent outweighs the risk of taking consent.

5.2.1 Withdrawal of Study Participants

Caregivers will be free to withdraw from the study at any point in time or he/she can be withdrawn from the study by the investigator in case it is felt that the caregiver is not able to contribute to the observation making effectively. In any case, if a withdrawal occurs, the reason will be mentioned in the case report form. Efforts will however be made to ensure maximum retention of participants by providing them financial incentives (that will also cover the transportation and consultation costs).

6 STUDY ASSESSMENTS

6.1 STUDY ASSESSMENTS

The following assessments will be done while doing one time observations using the observation tool (Annex A):

1. History taking: (Did the healthcare provider inquire about the presenting complaints and the predisposing factors which might have led to the complaints)
    - ✓ Cough (presenting complaint)
    - ✓ Fast breathing (presenting complaint)
    - ✓ Laboured breathing (presenting complaint)
    - ✓ Fever (presenting complaint)
    - ✓ Immunization history (Predisposing factor)
    - ✓ Breastfeeding history (Predisposing factor)
    - ✓ Overcrowding (Predisposing factor)
    - ✓ Parental smoking (Predisposing factor)

- ✓ Air pollution (Predisposing factor)
- ✓ Nutritional history (Predisposing factor)
- ✓ Hygienic practices (Predisposing factor)
- ✓ Family history of HIV (Predisposing factor)

2. Examination:
   - ✓ Temperature (For fever)
   - ✓ Respiratory rate for 1 minute (For fast breathing)
   - ✓ Pallor (for anemia indicating malnutrition)
   - ✓ Skin rash (for measles)
   - ✓ Lower chest indrawing
   - ✓ Ausculation for wheeze and/or crepts
3. Diagnosis:
   - ✓ Cough with no fast breathing/chest in drawing: No pneumonia
   - ✓ With fast breathing and/or chest in drawing : Pneumonia
   - ✓ Pneumonia with any danger signs : Severe Pneumonia
4. Management:
   - ✓ No Pneumonia: Symptomatic treatment
   - ✓ Pneumonia: Oral amoxicillin 40mg/kg/dose twice daily for three days
   - ✓ Severe Pneumonia: For LHWs: First dose of oral antibiotic (amoxicillin) and referral to health facility and for health facilities , parenteral ampicillin 50mg/kg IV 6 hourly for five days along with gentamicin 7.5mg/kg/ IM or IV for five days.

7 DATA COLLECTION

Data will be collected in the form of observations and then entered upon leaving the facility within one hour of the observation. For the purpose of ensuring accurate data entry, the data collector will use the audio recording and the prescription, the copy of which will be kept with them.

A detailed checklist will be used to assess the adherence of the healthcare providers to standard guidelines. This checklist will include all aspects covered in section 6.1:

- ✓ History taking
- ✓ Examination
- ✓ Diagnosis
- ✓ Treatment/management

These areas encompass the guidelines of essential care for pneumonia. Here essential care refers to the questions providers must ask the caregiver and examinations provider must conduct to accomplish correct diagnosis.

7.1 Source Data Documentation

The checklist will be developed in the form of a structured Urdu questionnaire which will be pretested. It will then be transformed into a soft version using our online questionnaire development dashboard. The questionnaire will then be installed into tablets.

Data will be collected in tablets to avoid errors of skips and logic. It will have an essential component of not accepting incomplete forms which will ensure that complete data is being collected on site. This data will be sent to our headquarters from all over the country via online server. This will ensure rapid access to data and data confidentiality as it will only be accessed by our data manager located in the headquarters through a password restricted data dashboard.

Each data collector will be provided a tablet, its charging cable and a power-bank to ensure that the tablet is charged all the time. In case any technical error is faced in any of the tablets, he/she will inform the supervisor who will arrange an alternate tablet to enter data. Additionally, the data collector will also have extra hard copies of the questionnaires to enter data in case a technical error occurs in the tablet and if there is a delay in delivery of an alternate one. These hard copies will be sent to the project manager via courier on the same of completion of data collection to avoid delay in data entry. The data collector will also maintain a contact sheet which will include information on the location, date and time of the observation, name of the child and caregiver, phone number, observed health professional's name and level of health facility/care.

In order to ensure that data is provided timely, the data collector will be asserted on sending the entered data as soon as the form in the tablet is filled. Therefore, each tablet will have a network enabled sim with an internet connectivity which will ensure that the data is transferred timely. In case there is decreased network coverage, the data collector will send the form as soon as an area of strong connectivity is reached. Additionally, if he/she reaches a location which has Wi-Fi connectivity then it will be used to send the forms. In case a tablet gets lost as soon as the observation is made, then the data collector will inform the supervisor who will arrange an alternate tablet and will check whether all data has reached the server or not. In case partial data is obtained, then those cases will be identified and the data collector will be asked to fill another observation form (using the recordings and recall) in the replaced tablet and ensure that data has been obtained by the supervisor. Tablets will be password enabled such that no one can gain access into the data except for the data collector. Considering all data will be sent to the server immediately after collection and will not be saved within the tablets, therefore even on being lost no one will be able to access the data.

7.2 Case Report Forms

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Electronic CRFS (eCRFs) will be used for improved data quality, avoidance of manual data entry errors and confidentiality etc. It will include the following key points:

- ✓ Protocol ID
- ✓ Site code
- ✓ Subject ID

- ✓ Respondent Initials
- ✓ Respondent demographics (age, gender, educational level)
- ✓ Age of the youngest child
- ✓ Phone number
- ✓ Alternate phone number
- ✓ Prescription picture
- ✓ GPS location
- ✓ Date of visit
- ✓ Place of visit (LHW/BHU/RHC/Private clinic/Public tertiary hospital)
- ✓ Name of the healthcare provider
- ✓ Data collector initials/ID
- ✓ Time spent in consultation
- ✓ Visit checklist (as indicated by section 6.1)
- ✓ Reason of withdrawal from the study

8 STATISTICS AND DATA ANALYSIS

8.1 SAMPLE SIZE CALCULATION

Considering this is a qualitative study therefore an approximate estimate of the sample will be provided. Event sampling will be employed whereby a pre-defined checklist of behaviours will be developed to record all occurrences. The sample size is based on point of theoretical saturation although we plan to conduct at least 32 observations from each of the four provinces and the federal capital (LHWS; 6, BHU Medical officer; 4, RHC medical officer; 4, private practitioner; 9, and public practitioner; 9). Thus a minimum of 160 observations will be conducted. Data will be collected over a period of six months.

8.2 PROPOSED ANALYSES

Behavioural coding will be employed to prepare the data for analysis. This means that a predetermined code will be given to each variable against each category of observations (History, examination, diagnosis and treatment). Each variable will be answered as “Y’ meaning yes, the task was accomplished and “N” meaning no, the task was not accomplished (section 6.1). Additionally, the responses will be labelled as correct, partially correct and incorrect for history taking and examination. If on history taking, the healthcare provider asks questions on all variables, then the responses will be labelled as correct and if any one variable is missed then the response is indicated as partially correct and in case less than 50% of the variables are asked about, then the responses will be labelled as incorrect. The same labels will be specified for the examination. In case of diagnosis and treatment, the labels will be specified as correct and incorrect only as there is no partially correct diagnosis and treatment regimens. The overall frequencies and percentages of these responses will be calculated and cross tabulated across the provinces.

9 OVERSIGHT ARRANGEMENTS

9.1 INSPECTION OF RECORDS

Investigators and institutions involved in the study permit trial related monitoring and audits on behalf of the sponsor, REC review, and regulatory inspection(s). In the event of audit or monitoring, the Investigator agrees to allow the representatives of the sponsor direct access to all study records and source documentation. In the event of regulatory inspection, the Investigator agrees to allow inspectors direct access to all study records and source documentation.

9.2 RISK ASSESSMENT

A study specific risk assessment will be performed by representatives of the co-sponsors, ACCORD monitors and the QA group, in accordance with ACCORD governance and sponsorship SOPs. Input will be sought from the Chief Investigator or designee. The outcomes of the risk assessment will form the basis of the monitoring plans and audit plans. The risk assessment outcomes will also indicate which risk adaptions (delete if no adaptations were possible) could be incorporated into to trial design.

9.3 STUDY MONITORING AND AUDIT

The ACCORD Sponsor Representative will assess the study to determine if an independent risk assessment is required. If required, the independent risk assessment will be carried out by the ACCORD Quality Assurance Group to determine if an audit should be performed before/during/after the study.

Risk assessment, if required, will determine if audit by the ACCORD QA group is required. Should audit be required, details will be captured in an audit plan. Audit of Investigator sites, study management activities and study collaborative units, facilities and 3rd parties may be performed.

10 GOOD CLINICAL PRACTICE

10.1 ETHICAL CONDUCT

The study will be conducted in accordance with the principles of the International Conference on Harmonisation Tripartite Guideline for Good Clinical Practice (ICH GCP).

Before the study can commence, all
required approvals will be obtained and any conditions of approvals will be met.

10.2 INVESTIGATOR RESPONSIBILITIES

The Investigator is responsible for the overall conduct of the study at the site and compliance with the protocol and any protocol amendments. In accordance with the principles of ICH GCP, the following areas listed in this section are also the responsibility of the Investigator. Responsibilities may be delegated to an appropriate member of study site staff.

10.2.1 Informed Consent

The Investigator is responsible for ensuring informed consent is obtained before any protocol specific procedures are carried out.

Participant Information and Informed Consent Forms will be provided. The oral explanation to the participant will be performed by the Investigator or qualified delegated person, and will cover all the elements specified in the Participant Information Sheet and Consent Form.

The participant will be given every opportunity to clarify any points they do not understand and, if necessary, ask for more information. The participant will be given sufficient time to consider the information provided. It will be emphasized that the participant may withdraw their consent to participate at any time without loss of benefits to which they otherwise would be entitled.

The participant will be informed and agree to their records being inspected by regulatory authorities and representatives of the sponsor(s).

The Investigator or delegated member of the trial team and the participant will sign and date the Informed Consent Form(s) to confirm that consent has been obtained.

The participant will receive a copy of this document and a copy filed in the Investigator Site File (ISF).

10.2.2 Study Site Staff

The Investigator is familiar with the protocol and the study requirements. It will be the Investigator's responsibility to ensure that all staff assisting with the study is adequately informed about the protocol and their trial related duties.

10.2.3 Data Recording

The Principal Investigator is responsible for the quality of the data recorded in the CRF at each Investigator Site.

10.2.4 Investigator Documentation

The Principal Investigator will ensure that the required documentation is available in local Investigator Site files ISFs.

10.2.5 Confidentiality

All evaluation forms, reports, and other records will be identified in a manner designed to maintain participant confidentiality. All records will be kept in a secure storage area with limited access. Clinical information will not be released without the

written permission of the participant. The Investigator and study site staff involved with this study will not disclose or use for any purpose other than performance of the study, any data, record, or other unpublished, confidential information disclosed to those individuals for the purpose of the study. Prior written agreement from the sponsor or its designee must be obtained for the disclosure of any said confidential information to other parties.

10.2.6 Data Protection

All Investigators and study site staff involved with this study will comply with the requirements of the Data Protection Act 1998 with regard to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles. Access to collated participant data will be restricted to individuals from the research team treating the participants, representatives of the sponsor(s) and representatives of regulatory authorities.

Computers used to collate the data will have limited access measures via user names and passwords.

Published results will not contain any personal data that could allow identification of individual participants.

11 STUDY CONDUCT RESPONSIBILITIES

11.1 PROTOCOL AMENDMENTS

Any changes in research activity, except those necessary to remove an apparent, immediate hazard to the participant in the case of an urgent safety measure, will be reviewed and approved by the Chief Investigator.

Amendments will be submitted to a sponsor representative for review and authorisation before being submitted in writing to the appropriate REC, and local R&D for approval prior to participants being enrolled into an amended protocol.

11.2 MANAGEMENT OF PROTOCOL NON COMPLIANCE

Prospective protocol deviations, i.e. protocol waivers, will not be approved by the sponsors and therefore will not be implemented, except where necessary to eliminate an immediate hazard to study participants. If this necessitates a subsequent protocol amendment, this should be submitted to the REC, and local R&D for review and approval if appropriate.

Protocol deviations will be recorded in a protocol deviation log and logs will be submitted to the sponsors every 3 months. Each protocol violation will be reported to the sponsor within 3 days of becoming aware of the violation. All protocol deviation logs and violation forms should be emailed to QA@accord.scot

Deviations and violations are non-compliance events discovered after the event has occurred. Deviation logs will be maintained for each site in multi-centre studies. An alternative frequency of deviation log submission to the sponsors may be agreed in writing with the sponsors.

11.3 SERIOUS BREACH REQUIREMENTS

A serious breach is a breach which is likely to effect to a significant degree:

(a) the safety or physical or mental integrity of the participants of the trial; or

(b) the scientific value of the trial.

If a potential serious breach is identified by the Chief investigator, Principal Investigator or delegates, the co-sponsors (seriousbreach@accord.scot) will be notified within 24 hours. It is the responsibility of the co-sponsors to assess the impact of the breach on the scientific value of the trial, to determine whether the incident constitutes a serious breach and report to research ethics committees as necessary.

11.4 STUDY RECORD RETENTION

All study documentation will be kept for a minimum of 3 years from the protocol defined end of study point. When the minimum retention period has elapsed, study documentation will not be destroyed without permission from the sponsor. All data will be stored in both hard and soft files. Hard files will include audio recording DVDs, any notes, consent forms and incentive acceptance sheets. This data will be saved in locked cupboards in the office premises with the key kept safe with the project manager. Soft files will include audio recordings, exel sheet observation data, analysis results and report. These files will be saved in password enables computer system with limited access.

11.5 END OF STUDY

The end of study is defined as the submission of the study report.

The Investigators or the co-sponsor(s) have the right at any time to terminate the study for clinical or administrative reasons.

The end of the study will be reported to the REC, and R+D Office(s) and co-sponsors within 90 days, or 15 days if the study is terminated prematurely. The Investigators will inform participants of the premature study closure and ensure that the appropriate follow up is arranged for all participants involved. End of study notification will be reported to the co-sponsors via email to resgov@accord.scot.

A summary report of the study will be provided to the REC within 1 year of the end of the study.

11.6 INSURANCE AND INDEMNITY

The co-sponsors are responsible for ensuring proper provision has been made for insurance or indemnity to cover their liability and the liability of the Chief Investigator and staff.

The following arrangements are in place to fulfil the co-sponsors' responsibilities:

- The Protocol has been designed by the Chief Investigator and researchers employed by the University and collaborators. The University has insurance in place (which includes no-fault compensation) for negligent harm caused

by poor protocol design by the Chief Investigator and researchers employed by the University.

- Sites participating in the study will be liable for clinical negligence and other negligent harm to individuals taking part in the study and covered by the duty of care owed to them by the sites concerned. The co-sponsors require individual sites participating in the study to arrange for their own insurance or indemnity in respect of these liabilities.
- Sites which are part of the United Kingdom's National Health Service will have the benefit of NHS Indemnity.
- Sites out with the United Kingdom will be responsible for arranging their own indemnity or insurance for their participation in the study, as well as for compliance with local law applicable to their participation in the study.

12 REPORTING, PUBLICATIONS AND NOTIFICATION OF RESULTS

12.1 AUTHORSHIP POLICY

Ownership of the data arising from this study resides with the study team.

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ANNEX B- PARTICIPANT INFORMATION SHEET/CONTACT SHEET

Sr. No	LOCATION	Name of Child under five	Age of child	Name of caregiver	Address of child	Phone number of caregiver	Consented/ Did not consent	Professional observed (Enter code)*	Name of the facility	Contact Result (observation accomplished/not acched

***"Professional observed" code:**

LHW = 1

BHU = 2

RHC = 3

Public practitioner = 4

Private practitioner = 5

ANNEX C- OBSERVATION TOOL

CLINICAL OBSERVATIONS (were the following parameters followed)	
1. History taking	Y/N
Cough	
Fast breathing	
Laboured breathing	
Fever	
Immunization	
Breastfeeding history	
Overcrowding	
Parental smoking/Household member smoking	
Air pollution (indoor cooking stove)	
Nutritional history	
Hygienic practices	
Family history of HIV	
2. Examination (Did the healthcare provider make the following necessary examinations apart from others)	
Temperature	
Respiratory rate counting for 1 minute	
Pallor	
Skin rash	
Examine lower chest in drawing	
Auscultate for wheeze or crepts	
3. Diagnosis (Did the healthcare provider make the correct diagnosis based on WHO guidelines)	
Cough with no fast breathing/chest in drawing: No pneumonia	
With fast breathing and/or chest in drawing : Pneumonia	
Pneumonia with any danger signs : Severe Pneumonia	
4. Management (Did the healthcare provider manage the case per the guidelines)	

No Pneumonia: Symptomatic treatment	
Pneumonia: Oral amoxicillin 40mg/kg/dose twice daily for three days	
Severe Pneumonia: *For LHWs:* First dose of oral antibiotic (amoxicillin) and referral to health facility and *For BHUs:* First dose of oral antibiotic (amoxicillin) and referral to rural health centre or tertiary care hospital *For health facilities (public and private) :* Parenteral ampicillin 50mg/kg IV 6 hourly for five days along with gentamicin 7.5mg/kg/ IM or IV for five days.	

SCORE: (Count the total number of Y and enter the value in the table below)

ACTIVITY OBSERVED	" Y" SCORED	TOTAL
History Taking		12
Examination		6
Diagnosis		1
Management		1

OBSERVATION RESULT*:

ACTIVITY OBSERVED	SELECT THE APPRORIATE RESPONSE
History Taking	Correct/partially correct/ incorrect
Examination	Correct/partially correct/ incorrect
Diagnosis	Correct/ Incorrect
Management	Correct/ Incorrect

***RESULT CRITERIA:**

For history taking:

Correct: Score of 12

Partially correct: Score of <12 but >6

Incorrect: Score of <6

For Examination:

Correct: Score of 6

Partially correct: Score of <6 but >3

Incorrect: Score of <3

For Diagnosis:

Correct: 1

Incorrect: 0

For Management:

Correct: 1

Incorrect: 0

Any other pertinent information:

_____
_____
_____
_____