Innovative Management PRactices to Enhance hoSpital quality and Save lives in Malawi (IMPRESS)

A cluster randomised trial of the impact of a multi-faceted hospital management intervention on in-hospital mortality and the quality of clinical care for small and sick newborns

Study protocol

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Summary

Every year 2.5 million newborns die. Most of these deaths happen in hospital and could be prevented. Babies in their first 28 days of life represent some of the most vulnerable users of the health system, as they can die quickly. Malawi has made good progress in reducing neonatal deaths but mortality rates for small and sick neonates admitted to hospitals are persistently high. Now that most births happen in health facilities, there is an urgent need to improve hospital care for newborns and their families. There is strong evidence that health technologies are a necessary ingredient for improving survival of small and sick babies. However, in practice, babies do not always get these clinical interventions even when resources are available. Commonplace problems, such as poorly configured patient pathways, drug stockouts, staff shortages at critical times, and power outages, can be due to organisational failings rooted in poor management. Improving management practices – so that hospitals effectively manage and motivate staff, are data-driven in how they make decisions, and have in place systems to support quality improvement – offers the potential to turn the situation around.

We will undertake a cluster randomised trial to evaluate prospectively the impact of a multi-faceted management intervention on neonatal mortality, in collaboration with the Government of Malawi and Newborn Essential Solutions and Technologies (NEST360). The intervention is based on a co-design process that has incorporated formative research findings, a landscape review of quality improvement strategies, insights from implementation science, and intervention design workshops with hospital managers and health workers, and central level experts in Malawi. The multi-faceted intervention targets primarily middle management in the hospital and health staff in the neonatal unit. It will include the following core components: 1) identifying priority actions through a situation analysis; 2) monitoring the adoption of management practices; 3) facilitating the use of data for action by managers (including target setting and recognition awards); 4) implementing small tests of change; 5) hospital peer-to-peer learning; and 6) on-site management training. These core components will be accompanied by several support strategies: identifying champions, engaging the hospital leadership and facilitating better communication between managers and clinical staff.

The primary objective of the trial is to measure the impact of the intervention on all cause in-hospital mortality amongst small and sick newborns. Secondary outcomes include patient level measures of clinical quality, and hospital management performance. The trial will assess the effects of the intervention on the population of newborns admitted to the neonatal unit of study hospitals between month 9 and month 15 after the start of implementation. The study involves a comparison of 10 intervention and 20 control hospitals, with clinical outcomes measured using the Neonatal Inpatient Dataset, a routine patient level information system established by NEST360. Although not described in this trial protocol, the trial will be complemented by a process evaluation and an economic evaluation.

This research will generate novel evidence on hospital management practices, with two-way skills transfer between the UK and Malawi, strengthening capacity of health systems researchers and hospital staff. Through equitable partnership with government and global policy networks, the findings will likely be of great value to policymakers in Malawi, other countries in the region, and globally.

Introduction

Background

Every year 2.5 million newborns die within the first 28 days of life [1]. Since 1990, child mortality has dropped by half globally but neonatal mortality (death within the first 28 days of life) has declined much more slowly. Neonatal deaths during the first 28 days after birth now represent 45% of under-five deaths [2, 3], and complications of preterm birth are the world's leading killer of children. Most of the neonatal deaths happen in hospital and could be prevented. Babies in their first 28 days of life represent some of the most vulnerable users of the health system, as they can die quickly.

Sub-Saharan Africa has the highest rates of neonatal mortality worldwide, losing more than one million babies each year to preventable and treatable causes, such as prematurity, infections, and birth complications. The 2030 Sustainable Development Goals (SDG) deadline is only a decade away, and for the first time there is a global target for newborns - SDG target 3.2 committing to reduce neonatal mortality to 12 or fewer neonatal deaths per 1000 live births in every country. To reduce neonatal deaths requires large-scale implementation of care during labour, delivery, and the first week of life, and especially for small and sick babies [4, 5]. Reducing neonatal mortality below the SDG target of 12 (per 1000) specifically requires access to high quality of hospital care for small and sick babies.

Malawi was one of the fastest progressing countries in Africa for newborn survival, but progress has stalled. Now that most births happen in health facilities, there is an urgent need to improve hospital care for newborns and their families. Malawi is a founding member of WHO's Quality of Care Network and has committed to halving deaths for inpatient neonates in five years. There has been a long term focus on improving quality of care at birth and now there is a new focus on small and sick newborn care. The government package to address this target population is NEST360 which started in 2019 and seeks to implement a set of clinical interventions: provision of affordable technologies to keep babies warm, help them breath, treat jaundice and control infections; and training of technicians and clinicians.

Relevant literature

During the MDG era, global and national policy was focused primarily on access – increasing the coverage of essential health services. It is only in recent years that quality of care has risen high up on the policy agenda [6]. Malawi has embraced this agenda. The Health Sector Strategic Plan 2017-2022 gives utmost importance to quality of care [7]. The Ministry of Health (MoH) established a Quality Management Directorate to spearhead holistic quality improvement.

An analysis of seven African countries shows that Malawi has lower quality for primary care services than many of its peers [8]. Despite past progress, maternal (349 deaths per 100,000 live births) and neonatal mortality (23 deaths per 1,000 live births) remain high [9, 10]. Hospital data on neonates admitted with respiratory distress show high mortality rates in the region of 45% to 52% [11]. Regional data also point to a high burden of hospital-acquired neonatal infections and anti-microbial resistance (AMR) suggesting that patient safety and AMR stewardship are major quality challenges [12-14].

We conducted a systematic literature review to examine the global evidence on the relationship between the adoption of management practices and quality of care provided in hospitals. We searched for studies quantifying the relationship between levels of management scores and levels of quality of care with observational designs, and by looking at associations between changes in management scores and changes in quality of care in intervention studies.

We found 22 eligible studies that were evenly distributed between high-income and low- and middle-income settings, of which 20 were cross-sectional and two were before-and-after intervention studies. To investigate the management-quality relationship, we compared the proportion of significant positive associations with the proportion of null associations, stratified by type of outcome. We found some evidence of a relationship between hospital management and quality of care, with over half of associations being significantly positive at the five percent level for structural, process and health outcomes. The evidence was weaker for the relationship between management and patient satisfaction or experience with care. Due to potential confounding arising from the study designs, all studies had a moderate or serious risk of bias compared to the low risk of bias normally assigned to randomised trials.

To give a sense of the studies included in the systematic literature review, we briefly report the findings from two papers. One study collected primary data on hospital management practices in England using the World Management Survey methodology [15]. It found that a one standard deviation increase in the management score was associated with a reduction of 0.97 percentage points (6.2 percent) in mortality from acute myocardial infarction. A second study conducted in private health facilities in Tanzania found that a 10 percentage point increase in the management score was associated with a 2.9 percentage point improvement in correct treatment for outpatients [16].

The evidence from the review is consistent with the idea that the adoption of management practices can improve quality of care in hospitals. There remains a need to investigate the relationship using a study with a randomised design where potential confounders can be controlled for, and risk of bias is low. None of the studies on management had a focus on neonatal health and there were no studies in low-resources settings that were powered for mortality outcomes. Notable examples of qualitative research in this area include studies on the everyday resilience of district health systems [17] and the important role of hybrid clinical-managers [18].

Rationale

There is strong evidence from controlled studies on the effect of health technologies [19] and clinical interventions [20], such as medical training and clinical audits, on quality of care and mortality. By contrast, much less research attention has been given to broader, organisation-level factors, such as hospital management and other health system "software" that shape health service delivery [21-23]. Yet, clinical care in our setting depends critically on factors at the organisational level, as exemplified by common problems such as drug stock-outs, staff absenteeism, and power outages. Improving management practices – so that hospitals effectively manage staff, drugs and medical supplies, have sound financial management and are data-driven in their decisions – could plausibly improve quality of care. The evidence presented in the previous section on the association between management practices and quality of care from observational studies is consistent with this claim. The risk of bias in these studies, however, is such that the findings from the literature are merely hypothesis-

generating. They do not provide evidence of a causal relationship between hospital management and quality of care.

Why is a *randomised* controlled trial needed? We have chosen an RCT because of the strong possibility that alternative designs would generate biased estimates of effect, thereby leading to misleading conclusions. The key concern is selection bias. Any non-random process of facility enrolment could potentially mean that those hospitals which decide, or are encouraged by the government, to participate are not the same as those not enrolled, for example in terms of motivation to improve quality. If such a factor is related to the study outcome, this can lead to bias and misleading results. Selection of this nature is very difficult to control for because the factors that lead facilities to be part of the programme are likely to be unobserved by the researcher. Assigning the intervention randomly ensures that the study arms are more likely to be balanced such that any difference, for example, in mortality can be attributed to the intervention and not to other factors.

Why is a *cluster* randomised trial needed? The Ottawa Statement on the Ethical Design and Conduct of Cluster Randomized Trials [Weijer et al 2012] recommends that the use of cluster as opposed to individual randomisation should be clearly justified. The reason for adopting the cluster randomised design is out of necessity. The multi-faceted hospital management intervention is best characterised as a health services or health systems intervention as it seeks to make changes in management practices at the hospital level. It is not a clinical intervention and, by its very nature, cannot be delivered at the level of an individual patient. This therefore precludes individual randomisation.

Our research builds on, and adds value to NEST360, providing a time-limited and cost-efficient opportunity to embark on a novel research agenda on hospital management practices. These links allow us to leverage rich data on mortality and processes of care, and facilitate access to the 36 largest hospitals in Malawi to collect further data on management. NEST360 was borne out of a needs assessment showing shortages in devices and trained staff. While addressing resource constraints at the clinical level is necessary for quality improvement, it may not be sufficient. We will test the idea that management practices affect quality.

Scope of study protocol

The IMPRESS project comprises two phases: a formative phase of research on hospital management followed by the co-design and evaluation of a hospital management intervention. The first phase has received ethics approval from LSHTM in the UK (ref: 22826) and KUHeS in Malawi (ref: P.02/21/3264). The second phase includes a trial, a process evaluation and an economic evaluation. This study protocol covers only the trial. A separate study protocol will be submitted for the process and economic evaluation.

This project builds on, and adds value to NEST360. Most pertinently, we will use a prospective de-identified individual level newborn admissions dataset generated by NEST360, which has received ethical approval from the National Health Sciences Research Committee in Malawi (ref: 1180) and the ethics committee at LSHTM (ref: 21892, dated 21/09/2020, version 1). The NEST360 study protocol covers in detail the ethical considerations related to these data and includes copies of the collaborative data sharing agreement and the data transfer agreement that govern the use of the data (see Appendix

1). Timothy Powell-Jackson (PI), Victor Mwapasa (PI) and Joy Lawn (co-I) are also named investigators on the NEST360 study protocol.

Overview of the trial design

IMPRESS will measure the impact of enhanced hospital management practices on neonatal mortality and the quality of clinical care for small and sick newborns by means of a cluster randomised controlled trial in Malawi. The trial will be carried out in 30 hospitals, with assessment of outcomes at the patient level. The study hospitals all participate in NEST360 – they receive a bundle of inputs and activities that include: the provision of affordable technologies to keep babies warm, help them breath, treat jaundice and control infections; the training of technicians and clinicians; enhanced data systems; and support for regular quality improvement visits.

There will be two study arms. Arm A hospitals will receive a multi-faceted management intervention in addition to the existing NEST360 activities (10 hospitals). Arm B hospitals will continue to receive the existing NEST360 activities (20 hospitals). The primary outcome, all cause in-hospital mortality, will be measured in the entire population of newborns admitted to the neonatal unit of the 30 study hospitals. This is through the Neonatal Inpatient Dataset, a routine patient level information system established by NEST360 that captures clinical data on all neonatal unit admissions.

The trial is anticipated to start in January 2023 and will end October 2024.

Aim and objectives

The study will address the research question: To what extent do management practices improve the quality of newborn care in hospitals in Malawi?

The aim of the research is to examine whether enhanced management practices can improve health outcomes and clinical quality for small and sick newborns in hospitals. A multi-disciplinary team from KUHeS and LSHTM will address the following interlinked objectives:

1. Evaluate effectiveness of the intervention on neonatal mortality through a cluster randomised trial;
2. Evaluate effectiveness of the intervention on the quality of clinical care and secondary outcomes through a cluster randomised trial;
3. Assess the intervention's acceptability, fidelity, and mechanisms through multi-methods research and estimate its cost-effectiveness.

The research builds on, and adds value to NEST360 that provides a bundle of novel devices and clinical training in neonatal units in hospitals but has identified hospital management as a key gap. It will generate novel evidence on hospital management, with two-way skills transfer between the UK and Malawi, and capacity strengthening of health systems researchers. The findings will likely be of great value to policymakers in Malawi, other countries in the region, and globally.

Methods: participants, interventions and outcomes

Study setting

Malawi is a low-income African country, with a GNI per capita of US$ 360 in 2018. On this metric, it is the third poorest country in the world according to the World Bank. The government is the dominant provider of healthcare, alongside a well-established faith-based health sector, providing over 85% of health services. Malawi has a district-based health system, with a hierarchy of health providers from the community level up to the tertiary level hospitals. Health spending is low ($32 per capita) and external donors are a significant source of finance (52%). There are shortages in health workers, with some estimates indicating that 45% of positions in the public sector are vacant.

Despite these challenges, Malawi made impressive progress in reducing child mortality during the MDG era, being one of few low-income African countries to meet the child survival target. There were increases in the coverage of essential health interventions, including skilled birth attendance, to the extent that more than 90% of women now deliver in a health facility. However, progress in neonatal mortality has been slower and now has major policy attention. Maternal (349 deaths per 100,000 live births) and neonatal mortality (23 deaths per 1,000 live births) remain high [9, 10].

Trial sites

Malawi is a small country with just over 100 hospitals. NEST360 has established a network of 36 hospitals to be part of it programme. These hospitals, selected by the Government of Malawi in partnership with NEST360, have more than 3,000 births per year and represent the vast majority of secondary and tertiary care provision in the country. There is a mix of levels, including all 4 central government hospitals, 24 of the 24 district hospitals, and 8 of the 38 largest Christian Health Association of Malawi (CHAM) hospitals. Hospitals excluded from NEST360 are mental health or small rural government hospitals, small CHAM hospitals and a few private for-profit hospitals.

Under IMPRESS, we will work with 30 of the 36 hospitals in NEST360 (defined as being part of the programme since 1st January 2022). In selecting the IMPRESS trial hospitals, we exclude the four central level hospitals, and two CHAM hospitals with the lowest in-hospital neonatal mortality (see Appendix 2 for list of study hospitals). The intervention is not designed to deal with the complexity of the management structure and the types of management problems found in the central hospitals. There are several reasons for working in hospitals that are already part of NEST360. First, the management intervention is designed to work alongside NEST360 activities in a synergistic manner. Careful attention has been taken to avoid unnecessary duplication or overlap, while some components are designed to reinforce and leverage existing NEST360 activities. Second, we seek to take advantage of the opportunity afforded by NEST360's Neonatal Inpatient Dataset to provide the first evaluation of a hospital management intervention on clinical outcomes.

The study hospitals had an average number of admissions to the neonatal unit of 1038 per year (range 164 to 4007) in the year between July 2021 and June 2022. The percentage of admissions by birthweight was: 2.5% (<1000g); 8.8% (1001g-1500g); 14.0% (1501g-2000g); 14.9% (2001g-2500g); and 51.0% (2501g +). The all cause in-hospital mortality rate was 155 per 1,000 neonatal unit admissions. The mortality by birthweight was: 750 per 1000 admissions (<1000g); 351 per 1000

admissions (1001g-1500g); 122 per 1000 admissions (1501g-2000g); 118 per 1000 admissions (2001g-2500g); 109 per 1000 admissions (2501g-4000g) and 51 per 1000 admissions (4001g +). In our baseline hospital management survey, the mean management score was 3.35 (range 2.44 to 4.24). This is measured on a scale of 1 to 5, based on evaluation of 28 management practices. Management performance was highest for "patient layout" (4.15) and lowest for "staff promotion" (2.23).

Participants

The target population of the study is all newborns admitted to the neonatal unit of the study hospitals. These patients comprise both babies born in the same hospital as the neonatal unit (inborn admission) and babies born elsewhere before being transferred to the study hospital neonatal unit (outborn admission). We will study the outcomes of approximately 15,200 newborns admitted to the neonatal unit of the study hospitals between month 9 and month 15 after the start of the intervention.

Other study participants include clinicians and managers working in the study hospitals, and senior leadership team of the hospital.

Eligibility criteria of participants

The outcomes of the participants (small and sick newborns admitted to the neonatal unit of study hospitals) will be measured using the Neonatal Inpatient Dataset. We therefore lay out the eligibility criteria that determine which individuals are included and excluded from the Neonatal Inpatient Dataset and the subsequent analysis.

The inclusion criteria of participants are as follows:

- Baby admitted to the neonatal unit of a study hospital
- Baby alive at admission to the neonatal unit
- Admission to the neonatal unit is recorded

The exclusion criteria of participants are as follows:

- Birthweight of baby is 1000g or less

Babies with a birthweight of 1000g or less are excluded for several reasons. First, we do not expect the intervention to deliver benefits to this vulnerable group of babies because it is constrained by the clinical context in which we are working. The care system in Malawi does not provide much clinical support for babies in this birthweight category. To clarify, the multi-faceted management intervention is not a clinical intervention; it will not provide new clinical services. It intends to support better implementation of existing services for small and sick newborns. Babies under 1000g, who have much higher mortality and typically suffer multiple complications, generally require WHO level 3 care if they are to survive. Yet the study hospitals provide only WHO level 2 care, so however much the management intervention improves implementation of these clinical services, it is highly unlikely to affect mortality of babies under 1000g.

Second, there are concerns of missing data for babies with very low birthweight – in that some babies are not recorded as admitted into the neonatal unit – for reasons that are both complex and specific to the context in Malawi. We note that several other trials have excluded very low birthweight babies. A trial in Kenya and Uganda excluded babies with a birthweight of 1000g or less in the primary analysis

because they were considered previable [24]. A trial of kangaroo mother care in in Ghana, India, Malawi, Nigeria, and Tanzania excluded babies under 1000g [25].

Intervention

Co-design of the intervention

The development of the management intervention follows MRC guidance on complex interventions [26] and draws on practical, generic guidance on the importance of middle-level principles [27]. The co-design process is informed by the following inter-linked components: 1) a formative phase of research conducted over a 15-month period; 2) an externally-commissioned landscape review of different approaches that seek to improve the quality of clinical care in hospitals through better management practices; 3) insights from implementation science in applied health; and 4) a series of intervention design workshops with hospital managers and health workers, central level experts, and other stakeholders in Malawi.

Before describing these components in more detail, we note that intervention development is guided by a number of principles. First, the intervention should be multi-faceted – that is, it should comprise multiple components and activities, recognising that it is a health systems intervention addressing a complex set of issues. Second, the intervention should have a clearly articulated theory of change that has the buy-in of stakeholders and participants. Third, the intervention should be feasible to implement with the resources available to IMPRESS and it should be acceptable to all stakeholders involved. Fourth, the intervention should complement NEST360 activities to leverage synergies.

Formative phase of research

In-depth interviews and group model building with health workers and managers, conducted between September 2021 and February 2022 in four hospitals, have informed the design of the intervention in several respects. They have helped define the different domains of management relevant to hospitals in Malawi, and what government management systems and processes exist within each of these domains and to what extent they are implemented in practice. They have provided insights on sphere of control – to identify the management practices that fall under and those that fall outside of the decision-making authority of the hospital. Finally, through the development of causal loop diagrams they have enhanced understanding of how management practices hinder or facilitate quality of care, and the underlying causes of the weak management systems most important for quality.

Landscape review

The landscape review is an externally-commissioned piece of work that has provided a high-level view of different strategies that seek to improve the quality of clinical care in hospitals through better management. These include: external review and control of norms and standards; total quality management and excellence models; performance and quality reporting; and strategies to strengthen management and leadership. Within these broad strategies, it examined specific approaches that have been used (in terms of their historical roots, theoretical basis, pathways of impact, derailers, and evidence of effectiveness), and the tools (e.g. plan-do-study-act cycles) and activities (e.g. training) that are integral to their design and implementation. Country examples were used to illustrate some of the approaches, in terms of the objectives of the "intervention", where it was implemented, at what scale, and the tools and types of activities that were implemented.

Implementation science insights
Implementation strategies are defined as "methods or techniques used to enhance the adoption, implementation, and sustainability of a clinical program or practice". We draw on the conceptual development of such strategies by implementation scientists to inform the IMPRESS management intervention. Our starting point is the refined compilation of implementation strategies defined by the Expert Recommendations for Implementing Change (ERIC) study in Powell et al [28]. As a study team, we assessed the potential role of each strategy for IMPRESS on the basis of feasibility, acceptability and effectiveness. We consolidated and narrowed down these generic implementation strategies to a list of potential candidates that have been further "thickened" with specific ideas of activities and tools put forward by participants at district level workshops (see below).

Co-design workshops
The aforementioned components support the most important phase of the co-design process, which is a series of participatory workshops that bring together key stakeholders in Malawi to inform the development of the management intervention. The purpose of these workshops is to twofold: to generate a set of coherent ideas of specific tools and activities that could improve hospital management systems in support of clinical care in the neonatal unit; and to describe the causal principles at work, as well as support factors, derailers, and safeguards against derailers. Separate workshops with each of the 36 hospitals in NEST360 provided an opportunity for a large number of staff at all levels of the hospital to put forward ideas of activities and tools that they consider can address management problems identified during formative phase of the research. These ideas are carried over to a workshop involving participants from district and CHAM hospitals, the zonal health offices and the central level Ministry of Health to refine, prioritise and elaborate on the components of the intervention.

Intervention components

Core components of the intervention
The multi-faceted intervention will include a set of core components that are designed to work together over several phases of implementation. They include: 1) a situation analysis and management implementation plan; 2) monitoring adoption of management practices; 3) data for action; 4) small tests of change; 5) hospital peer-to-peer learning; and 6) management tools training.

The first component is an analysis of the current situation in each hospital. This draws on available data on managerial quality that have been generated from the baseline hospital management survey and data on clinical pathways from the Neonatal Inpatient Data. For each hospital, a detailed report of the current situation will be prepared, with the information reported in a user-friendly manner. This analysis will provide a foundation for discussions with hospital staff, culminating in a management implementation plan that sets out the recommendations for change.

The second component is the setting up of a monitoring system to measure a set of key management practices indicators at monthly intervals. The specific indicators linked to these management practices will be informed by the baseline record review tool and the discussions with hospital staff on the situation analysis report. The monitoring of the practices will be used to measure changes over time

resulting from the other components of the intervention. It therefore underpins and provides an important focus for the other activities.

The third component is about using data for action. This means improving the flow of information within the hospital, equipping staff with the skills to understand the data, and facilitating data review meetings. The focus will be on the existing Quality Improvement Support Team within each hospital and their use of two sources of data: clinical performance data from the Neonatal Inpatient Dataset and the adoption of management practices that will be monitored as part of the intervention. Feedback of these data will be through dashboards, showing changes over time with respect to targets set by the hospital and the relative performance of the hospital in comparison to other study hospitals. Recognition awards will be given each month to the best improvers.

The fourth component refers to an approach widely used in quality improvement globally. The idea is to implement changes in a cyclical fashion using small tests of change before taking changes system-wide. Tests of change will benefit from the systematic measurement of management practices and clinical quality, and results of the tests of change will be studied for insights on how to do better. The precise nature of this component will vary according to the priority problems agreed upon in the deliberation of the situation analysis findings.

The fifth component is peer-to-peer learning – providing hospitals with a platform to regularly share learning in improving management practices for the benefit of clinical quality. This will likely take the form of structured sessions over zoom and may involve site visits. Staff from two high performing hospitals (with low in-hospital mortality and good management scores) that are not part of the study will share best practice and act as coaches in the collaborative learning sessions.

The sixth component is management training. Rather than develop a generic management training course for all the study hospitals, a selection of training modules will be made available to respond flexibly to the needs of individual hospitals. The training will be problem-focused and delivered on site. It will aim to strengthen the skills of staff to use specific management tools or processes that can be of immediate practical use in the workplace.

Support components

These core components will be accompanied by several support strategies. The first is identifying champions. This will involve identifying individuals who dedicate themselves to supporting and driving through implementation, helping to overcome indifference or resistance. The second is engaging the hospital leadership. This involves meetings with the hospital leadership and encouraging it to show commitment to quality improvement in the neonatal ward. The third is facilitating better communication. This involves supporting teams of clinicians and managers who are implementing the changes to management processes and giving them protected time to reflect on the implementation effort, share lessons learned, and support one another's learning.

Target of intervention

The intervention will target middle managers in the hospital and health staff in the neonatal unit, as well as the hospital leadership. A secondary target of the intervention is the hospital leadership. In terms of institutional structures within the hospital, the primary focus is the Quality Improvement Support Team at the hospital level and Work Improvement Team at the neonatal unit level.

Duration of implementation
The intervention will be implemented in each intervention hospital for 12 months. See Timeline.

Phases of implementation
The management intervention will be delivered over three phases. The first is a diagnostic phase (1 month) comprising the first two components of the intervention. The second is an implementation phase involving the third and fourth component (month 2 to month 12). The third is a skills and learning phase involving the fifth and sixth component (month 7 to month 12).

Outcomes

The primary outcome is all cause in-hospital mortality of patients admitted to the neonatal unit of the study hospitals, measured over a six month period between month 9 and month 15 after the start of the management intervention.

The wide range of secondary clinical outcomes include:

- All cause in-hospital mortality over each of the third, fourth and fifth quarter-years of follow-up to track if the effect on mortality changes over time
- All cause in-hospital mortality in each birthweight category (1001g-1500g, 1501g-2000g, 2001g-2500g, 2501g+), measured between month 9 and month 15 after the start of the management intervention
- Proportion of newborns receiving pulse oximetry at admission, measured between month 9 and month 15 after the start of the management intervention
- Proportion of newborns with their temperature taken at admission, measured between month 9 and month 15 after the start of the management intervention
- Proportion of newborns with a glucose test taken at admission, measured between month 9 and month 15 after the start of the management intervention
- Proportion of newborns that has all three diagnostics at admission assessment (pulse oximetry, temperature taken, glucose test completed), measured between month 9 and month 15 after the start of the management intervention
- Proportion of newborns exclusively breastfed on discharge from the neonatal unit, measured between month 9 and month 15 after the start of the management intervention
- Proportion of newborns in need[1] receiving Continuous Positive Airway Pressure (CPAP) during admission to neonatal unit, measured between month 9 and month 15 after the start of the management intervention
- Proportion of newborns with clinical sepsis diagnosis given antibiotics during admission to neonatal unit, measured between month 9 and month 15 after the start of the management intervention
- Proportion of newborns with clinical sepsis diagnosis that have a blood culture done, measured between month 9 and month 15 after the start of the management intervention
- Proportion of newborns that have a blood culture done amongst those given antibiotics during admission to neonatal unit, measured between month 9 and month 15 after the start of the management intervention

[1] Those in need include two groups of babies: 1) those with birthweight 1000g-1499g; 2) those with birthweight 1500g-1999g and respiratory distress syndrome and hypoxia

- Proportion of newborns that have a birthweight of <2500g receiving kangaroo mother care (KMC) during admission to neonatal unit, measured between month 9 and month 15 after the start of the management intervention
- Proportion of newborns receiving a bilirubin test during admission amongst those showing jaundice at admission, measured between month 9 and month 15 after the start of the management intervention
- Proportion of newborns with a clinical jaundice diagnosis or bilirubin test who received phototherapy at any time during their neonatal unit stay, measured between month 9 and month 15 after the start of the management intervention
- Proportion of inborn newborns that had hypothermia (<36.5°C) at admission to neonatal unit, measured between month 9 and month 15 after the start of the management intervention
- Proportion of inborn newborns <2500g that had hypothermia (<36.5°C) at admission to neonatal unit, measured between month 9 and month 15 after the start of the management intervention

The management-related and other secondary outcomes include:

- Hospital management quality score, measured at month 15 after the start of the management intervention. This is an overall measure of the quality of management based on the Hospital Management Tool developed during the formative phase of research
- Hospital management records score, measured at month 15 after the start of the management intervention. This is an overall measure of the adoption of management practices based on the Record Review Tool developed during the formative phase of research
- Mean number of neonatal unit admissions per month, measured between month 9 and month 15 after the start of the management intervention
- Experience of care index, measured at month 15 after the start of the management intervention. This is an overall measure of experience of care based on responses to the individual items in the Experience of Care Survey, calculated as a percentage of the maximum score

Sample size

The sample size calculations are based on 10 intervention hospitals and 20 control hospitals, and incorporate the methods used in the randomisation, namely matching on baseline mortality. We also performed sample size calculations for a study of 10 intervention hospitals and 10 control hospitals but the results showed that it would be underpowered. See Appendix 10 for more details.

We estimate the study power via a design effect calculation [29]. The design effect corresponds to the factor by which the sample size must be inflated to achieve the same power as in an individually randomised study. Our calculation of the design effect accounts for three features of the study that impact on power: 1) cluster randomisation 2) variable cluster sizes and 3) matching. In practice, we first calculate a design effect for a simple cluster randomised trial without matching and with constant cluster size (DE1), then we multiply this effect by an effect to account for variable cluster size (DE2) and an effect to account for matching (DE3). The former increases the design effect, and the latter decreases it.

Once the design effect has been calculated, power can be calculated by translating the study sample size into an effective sample size for the equivalent individually randomised trial and using an off-the-shelf power calculator. We use the pwr.2p2n.test() function in R (package = "pwr").

Table 1. Parameter values

	Symbol	Value
Proportion of deaths among admission in control arm		0.13
Relative risk	RR	0.80
Mean cluster size (no. neonatal admissions)	m	450
Coefficient of variation of cluster sizes	CV	0.7
Intra cluster correlation	ρ	0.01
Correlation within matched triplets	ρ_x	0.4

The parameter values for the sample size calculation are estimated from data on neonatal admissions and mortality in study hospitals between June 2021 and June 2022. Admissions <1000g are excluded. The intra-cluster correlation, ρ, is calculated from an estimate of between-hospital variance obtained by fitting a random effects logistic regression. The correlation within matched triplets, ρ_x, is estimated by splitting the data into two six-month periods. Data from the first period are used to generate matched triplets and data from the second period are used to estimate the correlation between randomly selected pairs. Since the estimate depends on random selection, the process is repeated multiple times (n=100) and the average correlation is computed.

Table 2. Sample size calculations

p0	p1	RR	ρ	ρ_x	CV	m	DE1	DE2	DE3	DE	power
Panel A. 6 months of follow-up											
0.13	0.098	0.75	0.007	0.4	0.7	450	4.14	1.1	0.6	2.73	0.93
0.13	0.104	0.8	0.007	0.4	0.7	450	4.14	1.1	0.6	2.73	0.77
0.13	0.111	0.85	0.007	0.4	0.7	450	4.14	1.1	0.6	2.73	0.51
Panel B. 12 months of follow-up											
0.13	0.098	0.75	0.007	0.4	0.7	900	7.29	1.06	0.6	4.64	0.96
0.13	0.104	0.8	0.007	0.4	0.7	900	7.29	1.06	0.6	4.64	0.83
0.13	0.111	0.85	0.007	0.4	0.7	900	7.29	1.06	0.6	4.64	0.58

Assuming 450 admissions per hospital, which equates to six months of follow up, and 13% mortality in control clusters, the study has 77% power to detect a 20% reduction in morality in the intervention clusters and 93% power to detect a 25% reduction. Under an alternative scenario where follow up is for 1 year (i.e. 900 admissions per hospital), there is a slight increase in power (83% power for a 20% reduction and 96% power for 25% reduction).

Recruitment

Since the management intervention will be delivered at the level of the hospital and the collection of data on patient outcomes is done routinely through the established Neonatal Inpatient Dataset, there is no active recruitment of participants in this trial. As explained below, we are seeking a waiver of individual consent to access data from the Neonatal Inpatient Dataset.

Methods: assignment of intervention

Randomisation

Hospitals are assigned to intervention or control in a ratio of 1:2 using stratified randomisation. Stratification ensures that the number of hospital receiving intervention or control is well balanced within each stratum. The stratification variable is baseline all cause in-hospital mortality of patients admitted to the neonatal unit (10 strata). Hospitals are allocated to intervention or control using a computer generated randomisation list done by the trial statistician. Study hospitals will be informed of intervention assignment through in-person site visits. Specifically, the list will be used to prepare randomisation cards that are sealed in opaque envelopes. A member of the study team will explain how the randomisation was done and then open the envelope to reveal the randomisation card and treatment group assignment. Sealed envelopes provide a pragmatic, confidential and transparent method of implementing randomisation in the field.

Blinding

Due to the nature of the intervention, it is not possible to blind study hospitals to the intervention after assignment. Given that outcomes are assessed largely through the Neonatal Inpatient Dataset, whose functioning rests on health care providers and data clerks based within hospitals, it is not possible to blind the assessment of outcomes. Although no intentional effort will be taken to blind participants and their caretakers, we expect the vast majority will not be aware of intervention assignment even if such information were to alter their health care seeking behaviour. This is because the management intervention acts on the supply-side, targeting hospital managers and health workers. Moreover, there are enough "projects" happening in Malawi that a single trial in hospitals is unlikely to catch the attention of communities such that it changes the health care seeking behaviour of the families of small and sick newborns.

Methods: data collection and analysis

Data

The impact evaluation relies on data from three sources. First, we will use data from the Neonatal Inpatient Dataset to measure outcomes, including the primary outcome, during follow-up and at baseline. Second, we will conduct hospital management surveys based on methods that have been developed and refined during the formative phase of the research. Third, we will draw on data measuring availability of inputs and other characteristics of the hospital, collected routinely by NEST360.

Neonatal Inpatient Dataset

The Neonatal Inpatient Dataset has been developed and implemented through NEST360. It captures prospectively information on the population of admissions to the neonatal unit of the NEST360 hospitals. The IMPRESS study team will have access to de-identified patient level data in the Neonatal Inpatient Dataset, as formalised in a data sharing agreement between the Ministry of Health and KUHeS (see Appendix 3).

The Neonatal Inpatient Dataset tool is one of the first parsimonious core datasets to measure impact, coverage, and quality of care for inpatient small and sick newborn care. It was developed in a systematic manner through a three step process. First, global and national tools were identified and reviewed. Second, through co-design and implementation learning, variables were assessed for inclusion based on considerations set by policymakers from four African governments. These included electronic data entry, a parsimonious variable list, and prioritising data capture on outcomes and clinical care pathways. Third, the tool was reviewed and refined by >150 global experts during a multi-stakeholder workshop and online review process.

The Neonatal Inpatient Dataset tool includes 63 core variables across six discrete modules: birth details and maternal history; admission details and identifiers; complications and observations; interventions (including microbiology); discharge outcomes; and diagnosis or cause of death (see Appendix 4 for the data collection form). A standardised data dictionary has been formatted with consistent variable naming, module structure, variable formats, and reduced free text to aid user-friendly data collection, support data quality assessments, assist targeted mentorship and sustainable adaption in the future. These data provide the basis to generate the patient level outcomes to be assessed in the study. The data also contain information on patient case-mix (e.g. sex of baby and birthweight) with which to carry out adjusted analyses.

Data are entered electronically using REDCap in the neonatal unit of each hospital, which benefits from a dedicated onsite data collector. The Ministry of Health now provides direct financial support to each health facility to make data collection sustainable. Furthermore, it has adapted and deployed a new, improved national-level Critical Care Pathway (CCP) and Neonatal Admission Form (NAP) to align with Neonatal Inpatient Dataset variables highlighted during the co-design process. In hospitals where online connectivity is inconsistent, there are associated paper forms to enable timely data entry and onward processing at external locations where internet access is improved.

Prospectively collected data are available for all the NEST360 hospitals for admissions from at least 1st July 2021. This means we have data that cover an extensive baseline period, before the planned implementation of the management intervention in early 2023. As an illustration, data for the year from July 2021 to June 2022 cover 30,414 admissions of small and sick newborns in the study hospitals.

Hospital Management Survey

We will administer a Hospital Management Survey in month 6 and month 15 after the start of implementation of the management intervention. The data collection methods and those used to construct measures of managerial quality were developed during the formative phase of research. Indeed, the data collection conducted during the formative phase provides baseline measures of management for the study hospitals. The tools were informed by: a literature review identifying quantitative tools that have previously been used to measure management in a health care setting; a review of relevant Government of Malawi policies and guidelines; in-depth interviews with hospital managers exploring government systems in different domains of management; a four-day tool development workshop; and iterative piloting of tools.

The hospital management survey involves two main components, each corresponding to a tool: a hospital record review to observe evidence of management practices and an individual interview on management practices with hospital staff. The survey team makes a three day visit to each study hospital, during which they will conduct up to five interviews with hospital staff and complete the record review. Hospital staff in the following five categories are invited for interview: Sister In-Charge of Neonatal Unit; Unit Matron; Administrator; Chief Nurse Manager; and Chief Medical Manager. Because of variation in roles and responsibilities, some respondents are not required to answer questions in certain management domains

The hospital record review contain 25 items, across five management domains: delivery of care in the neonatal unit; human resources; quality and safety; finance; and leadership and governance (see Appendix 5). The presence of each item is mostly recorded as a binary response option. We score each response on a 0 to 1 scale, with the best response receiving 1 and the worst response 0. To generate the summary measure for a hospital, we take the mean across the 25 items, which is interpreted as the proportion of the maximum score obtainable. The potential advantage of this measure is that the presence of items in a hospital is relatively easy to assess in an objective manner, even if the measure lacks in-depth exploration of management within the hospital.

The tool for the interview on management practices with hospital staff is based on the World Management Survey approach, with extensive adaptation to our context (see Appendix 6). It measures adoption of 28 management practices across five management domains: delivery of clinical care in the neonatal unit; human resource management for health workers; target setting and monitoring; financial management; and leadership and governance. For each management practice, the respondent is asked a close-ended question, followed by several open-ended questions. The answer to the close-ended question is recorded using categorical response options. The responses to the open-ended questions are used as the basis for the survey team to evaluate the management practice on a 1 to 5 scale, using objective criteria that are provided in the interview guide. There are also some background questions on the characteristics of the respondent and some post-interview questions for the survey team to record their evaluation of the quality of the interview.

The survey team evaluation of the 28 management practices from the interviews is used to generate an overall score of management for a hospital. We proceed in two steps. First, for each management practice, we take the mean across the respondents who were scored within each hospital. Second, we take the mean across the 28 management practices to produce a summary score of management that is a continuous measure with a range of 1 (lowest possible) to 5 (highest possible). The implication of this method is that each management practice receives equal weight in the overall summary score.

Other hospital data

Data on the availability of hospital inputs within the neonatal unit are routinely collected by NEST360 during quarterly quality improvement visits. They include information on the availability of human resources by cadre, bed capacity and occupancy, device availability and functionality, and major events such as interruption of power. Baseline data on these measures provide an opportunity to assess baseline balance between intervention and control and to adjust estimates of effect in the analysis of impact.

In the course of the Hospital Management Survey, we will collect additional information from hospitals to assess exposure to each component of the management intervention, both in the intervention hospitals to assess implementation strength, and in control facilities to assess contamination. We will also assess whether hospitals are exposed to other interventions that could plausibly affect study outcomes (with a particular interest in any imbalance between intervention and control in exposure to other interventions). We will ask hospital managers and staff in the neonatal unit whether any new projects focusing on hospital management or clinical care for small and sick newborns have started in the previous two years and the nature of the support within each project. This will be further described in the process evaluation study protocol.

Experience of care survey

We will administer an Experience of Care Survey in month 15 after the start of implementation of the management intervention. In the course of the project, clients' experience of care has come to the fore. Our own Community Engagement and Involvement activities with mothers of babies who were admitted to a neonatal unit show that experience of care matters enormously to families. Participants gave striking examples of negative experiences concerning communication with health workers and the dignity, respect and support they had been given. Experience of care has been one of key priority features in the hospital management implementation plans drawn up by each hospital at the beginning of the intervention. In the field of quality of care more broadly, increasing emphasis is being given to experience of care, as exemplified by a recent Lancet series on maternal health in the perinatal period. The funder of the research project, NIHR, has approved through a formal process this experience of care survey has an additional component to the cluster RCT.

There is no single standardised tool for assessing experience of care, although this has been recognised as major priority for maternal and newborn health by WHO and others. There have been two recent reviews of relevant tools that seek to provide quantitative measures of experience of care in neonatal health [30, 31]. These reviews included a large set of candidate tools [32-43]. Many of them are well grounded in frameworks on people-centred care that emphasise various established domains of user experience: 1) effective communication; 2) respect and dignity; 3) support; and 4) user-centred [44-46]. We have developed a draft survey tool adapted from the previously used tools to the context in Malawi, expanding on the domains of people-centered care described above (see Appendix 12). Each experience of care item is a statement and respondents are asked whether they agree, disagree or are neutral. For example, one statement is "I was worried that my baby would pick up an infection while staying in the neonatal unit". The tool also includes common questions about the sociodemographic characteristics of the respondent.

The survey will comprise a structured interview with the mother or guardian of patients admitted to the neonatal unit of the study hospitals. We will exclude mothers or guardians under 18 years of age. The interview will be conducted by trained fieldworkers employed by KUHeS. For newborns who are discharged from the neonatal unit, the interview with the mother or guardian will be conducted face-to-face at the point of discharge. For newborns who die at hospital, we will ask permission from the mother or guardian to follow-up with them in two weeks' time to conduct an interview by phone. The interview – whether face-to-face or by phone – is expected to last 45 minutes, which includes information and consent procedures. The potential for distress amongst participants is fully recognised by the IMPRESS research team (we note that two of the KUHeS research team have experience of

conducting interviews with mothers of sick newborns). We will take steps to mitigate the distress and provide support to mothers or guardians, as outlined in "Ethical considerations".

To ensure mothers or guardians are able to talk freely without concerns of being overhead by health workers or us feeding information back to health workers, several steps will be taken. First, we will ensure the privacy of the respondents during interview. The interviews will be conducted in a quiet place, away from where staff in the neonatal unit work. Second, rigorous information and consent procedures will be undertaken, emphasising the confidentiality of the data, secure management of the data, and pseudonymisation. Third, fieldworkers will be trained to develop a rapport with respondents so they feel comfortable disclosing negative as well as positive experiences.

We will conduct interviews during a three-day visit to each hospital. Based on admission numbers from the Neonatal Inpatient Dataset, we anticipate interviewing on average 25 mothers or guardians per hospital (with a range of 20 to 30 interviews per hospital, depending on size of hospital, of which 2 to 3 will be deaths). This represents an anticipated total number of observations of 750.

Statistical analysis

The effect of the intervention will be estimated through a cluster-level analysis. This approach is commonly used to analyse cluster-randomised trials and is considered preferable to an individual-level analysis when the number of clusters is small [47]. Although a cluster-level analysis will result in some loss of efficiency due to the variation in cluster size, we anticipate that this loss will be small (see power calculation).

We will calculate cluster (hospital) summaries for each outcome. For binary outcomes the cluster summaries will be proportions and for continuous outcomes they will be means. For example, the primary outcome will be the proportion of deaths among neonatal admissions. The cluster summaries will be analysed using linear regression. We will account for the matched design by including the matching variable in the regression model as a fixed effect. Prior to inclusion in the regression model, cluster summaries will be log-transformed so that exponentiated regression coefficients can be interpreted as ratios.

In a secondary analysis of the primary outcome, we will adjust for case mix by subtracting predictions of log-scale mortality risk from the cluster summaries [47]. The resulting residuals will be analysed via linear regression as in the primary analysis. Mortality risk will be predicted by fitting an individual-level logistic regression model to the morality data. The model will include age, birthweigth and other individual-level risk factors (but not study group) as predictor variables.

A detailed analysis plan will be written prior to analysing the data.

Ethics

Ethical and other approvals

Ethical approval for this trial is being sought from the ethical review committees of LSHTM in the UK and KUHeS in Malawi. An overarching study protocol for IMPRESS was approved by the ethical

review committee of LSHTM (ref: 22826) on the basis that the approval did not cover the trial. Funding for the research is provided by the National Institute of Health Research which reviewed the research plans over two rounds involving numerous external peer reviewers.

Ethical considerations

We have chosen to use a cluster randomised controlled trial because of the strong possibility that alternative designs would generate biased estimates of effect due to a lack of balance between study arms in terms of initial characteristics and/or exposure to other interventions. Withholding the intervention from the control group is considered justified as there is genuine equipoise in whether the intervention is effective, and funding it not available to cover all eligible facilities within the timeframe of the research project.

There are a number of potential benefits of the research. Observational studies raise the prospect that enhanced hospital management practices could result in improvements in the quality of clinical care. It is also possible that certain management practices may promote greater health worker satisfaction. In the context of this trial, the management intervention has been designed to improve the quality of clinical care given to small and sick newborns, with a view to reducing in-hospital mortality. Any reductions in mortality could translate into a large increase in years of life gained. In addition, if the trial shows that the intervention is effective and cost-effective, leading to wider scale roll-out of the intervention, efforts will be made to ensure that the control hospitals are among the first to benefit from this wider implementation.

The study is unlikely to pose a significant risk to individuals involved in the study because the research requires no invasive procedures or examinations. Nevertheless, there are a number of risks which the study team will seek to minimise. First, there is a risk that the management intervention places an additional work burden on health care providers and mangers within the hospital. This could plausibly affect the motivation of staff and impinge on the time available to care for patients. Implementation staff making regular visits to hospitals will be trained to make a qualitative assessment of how the intervention is affecting staff allocation of time and the likelihood this is negatively impacting on the care given to patients. They will be required to provide regular monitoring reports to the IMPRESS study team in Blantyre. The data and safety monitoring committee will have the opportunity to monitor the outcomes on a continuous basis to detect possible unintended consequences of this nature.

Second, the management intervention may increase accountability, highlighting deficiencies in managerial performance which is traced back to the performance of individuals and not just management systems within a hospital. This may pose a risk to some health workers and managers. If poor performance is for reasons outside the control of an individual or comes from a failure of the hospital to support staff, this could be deemed unfair. Implementing staff will be trained to ensure that detailed root cause analyses are conducted in a constructive manner to identify solutions rather than apportion blame, with as much focus as possible on management practices rather than managers.

Third, the trial will use the prospective individual level newborn admissions dataset generated by NEST360. No individual consent is taken for these data since they are part of routine health information systems data and as such will be kept at each hospital, managed locally, and only de-

identified data will be shared with LSHTM following the collaborative data sharing agreement and data transfer agreement – both contained in the NEST360 study protocol. Given that implementation of NEST360 is being led by the Government of Malawi in collaboration with the NEST360 team, the necessary support for parents in the event of the loss of a newborn is coordinated by the government following locally approved structures and processes.

Fourth, the collection of data through the management survey imposes a time cost on interviewees and may result in some feelings of discomfort because they are being asked to be honest about how systems function in the hospital. These interviews will be conducted at the convenience of the interviewee and in a place that provides for confidentiality to be maintained. Interviews will be arranged so as to minimise disruption to care provision. Only trained research staff with previous experience in collection of data and appropriate local language skills will conduct the interviews. Informed written consent will be obtained from all those participating in the research. All participants will be informed about the objectives of the research and will be told that they are free to choose to participate or not, with no adverse consequences arising from their decision. We further note that by leveraging the existing Neonatal Inpatient Dataset we are minimising the time burden imposed by data collection.

Fifth, the hospital management interviews may yield information that is potentially sensitive. To prevent harms, we will ensure that all data are confidential and anonymised and we will avoid identification of particular facilities in the presentation of results.

Finally, we recognise the risk that the study has the potential to cause distress for respondents of the Experience of Care Survey. We will take a number of steps to mitigate the distress and provide support to mothers or guardians. Fieldworkers will be appropriately trained to recognise when respondents may be in distress and provide support to them during the interview process. There is no standard of care for referring parents in distress in Malawi. We will therefore explore the possibility of linking parents in distress to HIV counsellors working with families in relation to PMTCT. As described previously, we will not interview at the hospital mothers of babies who died but instead follow-up through phone interviews at a later date to reduce the potential for distress.

Informed consent

In a cluster randomised trial such as this one, consent takes place at various levels ranging from consent from the government authorities, to hospital consent, and finally to individual consent. However obtaining individual consent from the individual caretaker of every neonate involved in this study is not feasible. As described above, much of the routine data on outcomes come from the Neonatal Inpatient Dataset, which collects information without individual informed consent. These data will available to IMPRESS researchers only in a de-identified form and will be managed securely at all times.

Consent of hospitals to participate in the trial

Hospitals have already been sensitised to the overall aim and objectives of the IMPRESS project through multiple visits and in-person engagement with the management team and the research committee of each hospital. We will carry out further sensitisation with hospital managers at each sitel to explain more details about the trial – including its objective and what activities will be implemented

under the management intervention. Consent to participate in the trial will be obtained from hospitals prior to the start of implementation of the intervention. A representative of the hospital will be asked to give consent. We expect this to be the Hospital Director or a designated person such as the Chief Medical Manager.

For the consent process, an information form will be read and given to participants on the purpose of the study, the risks and benefits of the study, the broad content of the management intervention, the confidentiality of data collected, the voluntary nature of participation in the study, the possibility of withdrawing the hospital from the study at any time without reason, and the contact details of the principal investigators (see Appendix 7). The information and consent form will be professionally translated from English into Chichewa and made available in both languages.

Consent of hospital managers for data collection

Consent of hospital staff will be sought prior to interviews for the hospital management survey. For the consent process, an information form will be read and given to participants on the purpose of the study, the risks and benefits of the study, the broad content of the interview, the confidentiality of the data, the sharing of anonymised data, the voluntary nature of the interview, the possibility of stopping the interview at any time without reason, and the contact details of the principal investigators (see Appendix 8). The information and consent form will be professionally translated into Chichewa. Since these study participants will be over the age of 18 years, there will be no proxy consent required.

Consent of mothers or guardians for data collection

Consent of mothers or guardians will be sought prior to interviews for the Experience of Care Survey. For the consent process, an information form will be read and given to participants on the purpose of the study, the risks and benefits of the study, the broad content of the interview, the confidentiality of the data, the sharing of anonymised data, the voluntary nature of the interview, the possibility of stopping the interview at any time without reason, and the contact details of the principal investigators (see Appendix 13). The information and consent form will be professionally translated into Chichewa. Since these study participants will be over the age of 18 years, there will be no proxy consent required.

Waiver of individual consent to access NID data

A waiver of individual patient consent is requested to access the data from the Neonatal Inpatient Dataset for the purpose of the evaluation of the IMPRESS hospital management intervention. This request is justified by the following considerations:

i. The use of the data for the research purposes set out in this study protocol involves no more than minimal risk to participants as the data will be de-identified and accessed securely by the researchers within IMPRESS doing the analysis;
ii. The rights and welfare of research participants will not be adversely affected by the sharing of these data with the IMPRESS study team as the data are stored confidentially and shared in de-identified form;
iii. The research could not practicably be carried out without the waiver, as attempting to obtain written informed consent from all caretakers of patients admitted to the neonatal unit in a study of this scale would not be feasible;
iv. The data being collected by the Neonatal Inpatient Dataset are part of the Ministry of Health's national information system and are covered by previous ethical approvals obtained by

NEST360 from the National Health Sciences Research Committee in Malawi and LSHTM in the UK.

Data management

An important ethical risk of the study pertains to breaches of confidentiality. The study will make every effort to minimise the risk of breaches of confidentiality, particularly in relation to data management and the linking of datasets. The research intends to link data from different sources. Refer to the data management plan in Appendix 8 for details.

Neonatal Inpatient Dataset

We provide here an overview of how the Neonatal Inpatient Dataset is managed. For further details, see the NEST360 study protocol in Appendix 1. The data are collected and managed through REDCap, chosen due to the enhanced accessibility, security, ease of use, flexibility, linkage and the ability to formulate in-built validation fields. Data are stored on servers of the designated country partner and backed up regularly to hard drives and to cloud-based storage or as per existing institutional policy. The server is maintained by the NEST360 designated country partner and backed up regularly during the whole period of data collection.

Data cleaning and data completeness checks take place in multiple stages. Data teams in Malawi review data and quality check data weekly. Each tool contains built-in quality checks, including forced fields and forced ranges. These quality checks standardise and validate the data at the point of entry, so that it is difficult to enter data in the incorrect format or outside the appropriate range. Radio button and dropdown fields are used whenever possible to improve data quality. Data quality is assessed using an automated data report and query list highlighting critical inconsistencies or erroneous entries. The report reviews variable completeness, skip pattern inconsistencies, out-of-range values, and examines records for clinical data gaps where "not recorded", or missing date is selected. The country data team uses these reports to manually correct entries utilising source documentation. Query list responses are used to enhance subsequent reports to ensure irremediable errors are not repetitively featured. Data timeliness is analysed using the time between the date of admission and the date of form entry. Associated graphics are colour coded to enable monitoring of data entry backlogs.

The data systems are further supported using a data flow scheme, a data sharing agreement covering all NEST360 partners, and a set of standard operating procedures. Removal of identifiable information (e.g., names, phone numbers and address notes/directions) happens prior to the automated flow of data such that the pooled data from hospitals are de-identified to ensure that no data provided will compromise the privacy and protection of participants' confidentiality. The Neonatal Inpatient Dataset and operating procedures support all appropriate General Data Protection Regulations (GDPR) and WHO data principles [48].

Hospital Management Survey

Data from the hospital management survey will be entered into ODK at the point of interview. Data will be transmitted directly to a secure KUHeS server, where the data can be accessed only by the IMPRESS data manager. Only de-identified data from the interviews with hospital managers will be shared with other IMPRESS researchers. Hospital management data will contain hospital identifiers to

allow them to be linked with data from other sources, such as the Neonatal Inpatient Dataset. However, data will only be presented in aggregate form in the dissemination of findings such that individual hospitals are not identified.

Experience of Care Survey

Data from the Experience of Care Survey will be entered into tablets using ODK at the point of interview. Data will be transmitted directly to a secure KUHeS server, where the data can be accessed only by the IMPRESS data manager. To minimise the risk of re-identification of participants, we will employ a number of strategies.

Only pseudonymized data from the interviews will be shared by the data manager with other IMPRESS researchers. Specifically, the data manager will convert age into age categories and years of education into educational attainment categories. To be clear, the dataset will not contain the names or date of birth of respondents.

The individual level data will contain hospital identifiers to allow them to be linked at the hospital level with other data collected within this study protocol, such as the intervention assignment arm or hospital management score. The hospital identifier is a numerical code corresponding to a study hospital. The codebook containing the hospital identifier and the hospital name will be kept separate from any other datasets. Only specified persons in the IMPRESS team (KUHeS data manager, the two statisticians, LSHTM research fellow, PI) will have access to this codebook. There will be no other hospital level variables within the Experience of Care dataset that can help identify the hospital (e.g. hospital name, district).

Data will only be presented in aggregate form and by subgroups in the dissemination of findings such that individual respondents cannot be identified. Specifically, we will not present data by hospital (even by hospital code) or by baby status on discharge (i.e. alive or dead). Nor will be present data in which the number of participants in a cell is less than 10. This will be further help to reduce the risk of identification of individual participants due to small numbers.

The information containing the phone number of carers' whose baby died (and therefore will be interviewed by phone) will be held by the data manager as a separate dataset and will not be linked to any other dataset.

In sharing the dataset beyond the IMPRESS study team, we will randomly generate (scramble) a new hospital level identifier that cannot be linked to the hospital name even in possession of the hospital codebook. It is important to note that a hospital identifier is required for replication of the trial analysis which is why we cannot strip the dataset of this variable altogether.

The Experience of Care survey dataset that contains a hospital identifier will be retained for 10 years.

Hospital characteristics

Data on the availability of hospital inputs, captured during NEST360 quarterly quality improvement visits, will be managed in accordance with the data management plan.

Trial management and oversight

Registering the trial

The trial will be registered prospectively prior to the start of implementation with ISRCTN Registry. It is the preferred partner of the Department of Health and Social Care and is supported by NIHR, amongst other organisations.

Oversight

Independent advisory group

The research programme is overseen by an Independent Advisory Group that meets at least annually. Meetings are organised to coincide with visits by the UK research team to Malawi and a modest amount has been budgeted for these meetings. International members of the Advisory Group join by Zoom. In advance of each meeting, the Project Management Team prepares a report detailing progress, project risks and planned activities. The members include:

- Co-Chairs: Charles Mwansambo (Principal Secretary, Ministry of Health, Malawi) and Professor Sassy Molyneux (Oxford University);
- Members are: Frank Wafula (Senior Lecturer, Strathmore University Business School), Katherine Semraux (Associate Professor, Harvard University), Jishnu Das (Professor, Georgetown University, Alison Morgan (Global Financing Facility, World Bank), Solome Nampewo (Health Systems Coordinator, WHO Malawi), Juliana Lunguzi (SRHR Coordinator, UNFPA Malawi), Ajib Phiri (Paeditrician, Kamuzu University of Health Sciences), and a NIHR representative;

The two Leads, the Collaborators, and members of the IMPRESS study team, as available, also participate in Independent Advisory Groups meetings

Data and safety monitoring

An independent data and safety monitoring committee with at least three members (a child or neonatal health expert, a public health specialist or epidemiologist, and statistician) will be established before any field activity starts. The data and safety monitoring committee will provide independent advice on the effectiveness data of the intervention tested, so contributing to safeguarding the interests of the trial participants. The data and safety monitoring committee will have the possibility to monitor the outcomes on a continuous basis and possibly recommend to stop the study if any major safety concern appears. A data and safety monitoring committee charter, where the relevant terms of reference are clearly defined, will be signed by each member of the Committee before starting the trial (see draft in Appendix 11).

Sponsor and indemnity

London School of Hygiene & Tropical Medicine is the main research sponsor for this study. For further information regarding the sponsorship conditions, please contact the Research Governance and Integrity Office: London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT. Tel: +44 207 927 2626. Email: RGIO@lshtm.ac.uk. London School of Hygiene & Tropical

Medicine holds Public Liability ("negligent harm") and Clinical Trial ("non-negligent harm") insurance policies which apply to this trial.

Funding

The National Institute of Health Research under its Global Health Policy and Systems Research Programme is funding the research project.

Audit and inspections

The study may be subject to audit by the London School of Hygiene & Tropical Medicine under their remit as sponsor, the Study Coordination Centre and other regulatory bodies to ensure adherence to GCP.

Community engagement and involvement

We have been engaging with key stakeholders during the formative phase of research and the co-design of the intervention, and this will continue through to the final synthesis of findings and dissemination. We have developed a community engagement and involvement strategy and this guides our approach.

To work with hospitals requires building a trusting relationship supported by good communication. The first phase of the IMPRESS project was devoted to in-depth formative research, which involved considerable stakeholder engagement at the hospital level. In particular, we have presented the project research plans to the research committees and the senior management of each hospital. We have provided feedback on the results of the formative phase to each hospital individually, discussed what the findings mean to them, and sought their input in the co-design phase of the management intervention. Engagement with stakeholders will be an ongoing process through regular contact by the research team. Hospital managers will be involved in another co-design workshop and there will be further sensitization on the trial itself. Willingness to participate in the trial will be sought from a hospital representative – typically the head of the hospital – will be requested to provide informed consent. Needless to say, such a study would not be feasible without close engagement with the Ministry of Health. The Principal Secretary is the Chair of the Independent Advisory Group, and the Director of Health Services is a named Collaborator. We have engaged closely with the Quality Management Directorate, with senior civil servants in this department joining the study team on site visits during the formative phase and providing input into the co-design of the management intervention.

The other key community stakeholders relevant to this research are: parent representatives, community leaders (particularly senior women who are custodians of culture), hospital advisory committee members and healthcare professional associations. Community engagement and involvement (CEI) with these stakeholders is facilitated through the following budgeted activities:

- Co-production and intepretation. In the course of the project, we will organise workshops at the district level with members of the Hospital Advisory Committees (community members and representatives) and Community Health Action Groups (representatives of religious leaders, women's groups, village health committee members, less privileged vulnerable

groups, and youth). The first of these are to engage community members in the co-design of the research. The last two workshops will be timed to coincide with key deliverables in Year 4. These workshops will seek to engage community members with the findings, elicit their interpretations, and help find the most appropriate language and framing for the research findings.

- Advisory committee meetings. In the course of the project, we plan to hold at least one advisory committee meeting each year. We will seek ways to involve two parent representatives and two community leaders (from hospital advisory committees) in the functioning of the committee. This may not be in the meetings themselves as they may feel intimidated and less willing to speak up. The advisory committee will provide one forum for community representatives to contribute to the research design, strategic decisions during the course of the research programme, and the dissemination of findings. The co-chair of the advisory committee, Dr Charles Mwansambo, has had extensive experience leading research on using participatory approaches for community engagement and invovlement in Malawi.
- Active involvement in the co-design of the hospital management intervention. As described above, we have been engaging with the key stakeholders in the co-design of the intervention through in-person workshops at the study sites and a central level co-design workshop.
- Leveraging the field visits for data collection, the research staff at KUHeS are engaging with hospital advisory committees at regular points throughout the research cycle. These opportunities will also be used to engage with parent representatives (serving on the hospital advisory committees) on an individual basis to provide a more private forum.

Outputs and dissemination

Ensuring that the study findings have maximum impact is given high priority by all partners in our research team. It is also an area of strength for this project, given the extent of our current engagement in networks involving potential research users.

Outputs

The planned outputs from the IMPRESS project include:

- A set of validated tools to measure management practices at the hospital and district level.
- Novel data on the extent to which hospitals adopt management practices and evidence on which practices matter for quality.
- A co-designed hospital management intervention based on a well-articulated theory of change and developed with scalability in mind.
- The first rigorous evidence in a low-income setting on the effectiveness of a hospital intervention to improve management practices, quality of care and patient outcomes.
- Process findings on implementation, mechanisms, context and costs, to inform scale-up and generalisability to other countries.
- Cross-cutting: capacity strengthening of a cadre of management trainers with capability to scale up intervention, hospital clinicians and managers, and health system researchers in KUHeS.

Key groups of users

We have identified four key groups of users. In addition, as these groups act on the research findings, there is clear potential for neonates to benefit from improved quality of care in hospitals across the whole of Malawi.

i) National stakeholders. They include national and district government bodies, professional associations and NGOs. We will ensure the research findings are taken up by making extensive use of well-established, trusted relationships. Likaka (Collaborator), Director in MoH and Chair of Technical Working Group (TWG) on Quality Management, is a vital partner in ensuring that the research findings inform policy. KUHeS has long-standing links with the Ministry of Health, and is deeply embedded in the structures of decision making. Nyondo-Mipando (co-I) is member of the TWGs on Quality Management and Human Resources for Health. Dube (Collaborator) is on the Government's influential Newborn Steering Committee. We will make presentations with these TWGs at each stage of the research and organise policy dialogue meetings at the bi-annual National Conference on Quality Management. We will have a national dissemination meeting to initiate high level policy discussion of the findings.

ii) Hospital managers and clinicians. We will engage early with this key group of users through three zonal sensitisation workshops to maximise ownership and input into the design. There will then be continuous engagement through both the data collection and implementation of the hospital management intervention. Finally, there are three zonal dissemination meetings with study hospital staff.

iii) International funders. We will leverage our long-standing relationships with stakeholders such as WHO, FCDO and Gates to ensure maximum reach. We will coordinate closely with NEST360 in communicating findings through its network in Kenya, Tanzania, and Nigeria. In addition to regular contact through these networks, we will target international stakeholders through presentations at conferences (Health Systems Global, iHEA, ISQua). We will also summarise our findings in a range of media including public webinars, policy briefs and animations.

iv) Academic community. We aim to publish in a range of prestigious academic journals and are committed to ensuring open access. We will make study tools and data publicly available on LSHTM Data Compass.

Publications

Our publications plan is regularly updated and this guides what publications we plan to submit to journals. It includes timelines and equitable principles, promoting first authorship for more junior academic team members. The main trial paper will be submitted to an international medical journal. Other outputs will accompany academic publications, including policy briefs, infographics, slide packs, and short videos.

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Appendix

1. NEST360 study protocol
2. List of study hospitals
3. Data sharing agreement
4. Neonatal inpatient dataset form
5. Hospital management record review tool
6. Hospital consent to participate in trial
7. Hospital manager consent for survey
8. Hospital management interview tool
9. Data management plan
10. Power calculations
11. DSMC charter