Effect of Integrated Community Case Management on Access and Utilization of Maternal, Newborn and Child Health and Immunization Services in Hard-to-Reach Communities in Migori County, Kenya: A Quasi-Experimental Study

Duncan N. Shikuku (✉ dnshikuku@yahoo.com)

Save the Children <https://orcid.org/0000-0003-3580-7077>

Leakey K. Masavah

Save the Children

Maxwell Muganda

JHPIEGO

Felix Otieno

Department of Health, Migori County

George Magolo

Department of Health, Migori County

Lilian Njoki

Department of Health, Migori County

Tom Odhong

Department of Health, Migori County

Kenneth Sisimwo

Save the Children

Thomas Matete

Save the Children

Solomon Orero

JHPIEGO

Paul Kisia

Save the Children

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Abstract

Background

Integrated community case management (iCCM) improves access to management of leading causes of under 5 (U5) mortality. Evidence of iCCM on maternal and newborn health and immunization services is scanty. The objective of this study was to determine the additional effect of iCCM on antenatal, skilled birth attendance (SBA) and immunization coverage in hard-to-reach communities.

Methods

A quasi-experimental (nonequivalent control group pretest – posttest) design for iCCM in Migori county. The intervention was iCCM training, mentorship/coaching and supportive supervision of 20 community health volunteers (CHVs). Twelve months pre-post intervention Kenya Health Information System (KHIS) data between July 2017-Sept 2019 reviewed. Differences in proportions for MNCH indicators pre – post-training were tested through test of proportions and considered statistically significant at $P \leq 0.05$ values.

Results

Post-training, average monthly community cases identification increased from 1.3-5, 0-1.5, 8.9-11.8 for suspected pneumonia, malnutrition and malaria positive cases treated in the intervention sites respectively. Intervention communities reported significant increases in proportions of malaria positive cases treated (32.0% vs 47.8%), pregnant women referred for ANC (25.4% vs 45.8%), defaulters referred for ANC (9.8% vs 14.9%), newborns with danger signs referred (1.4% vs 7.3%), U5s referred for immunization (4% vs 7.5%) and defaulters referred for immunization (2.2% vs 3%) ($P \leq 0.05$). Control communities reported significant reductions in proportion of malaria positive cases treated (57.6% vs 41.6%) and U5s referred for immunization (10% vs 5%) ($P < 0.0001$) with no changes in MNH indicators ($P \geq 0.05$). Intervention facilities reported significant increases in 4th ANC coverage (39.4% vs 79.3%), SBA (24.5% vs 43%) and immunization coverage for U5s in all key expanded program on immunization antigens ($P \leq 0.05$) with no change in the control facilities.

Conclusion

iCCM improved access and utilization of ANC, SBA and immunization coverage in the hard-to-reach communities. Community level management of childhood illnesses using simple algorithms by CHVs as well as identification and referral of antenatal mothers for ANC, immunization defaulters, and newborns with danger signs for hospital management improved. Governments should strengthen community health systems so that CHVs are motivated and retained to carry out demand creation for maternal, newborn and child health and immunization services in hard-to-reach communities.

Background

In 2018, an estimated 5.3 million children died before reaching their fifth birthday, mostly in low- and middle-income countries (LMICs) with 2.8 million (52%) of these deaths occurring in sub-Saharan Africa and 1.5 million (29%) in Central and Southern Asia alone (1). Neonatal deaths accounted for 47 percent of the under-5 mortality. Pneumonia (15 percent), diarrhoea (8 per cent) and malaria (5per cent) remain among the leading causes of deaths among under-5 (U5) children globally – accounting for almost a third of global under-5 deaths (1, 2). Malnourished children, particularly those with severe acute malnutrition, have a higher risk of death from these common childhood illnesses (3).

The burden of child death is largest in sub-Saharan Africa (2). In 2018, 1 in 13 children died before his or her fifth birthday in sub-Saharan Africa – 16 times higher than the average ratio of 1 in 199 in high-income countries (1). Advances in ending deaths of children U5 from preventable diseases is critical. For instance, WHO and UNICEF in early 2000 developed an integrated community case management (iCCM), an equity-focused strategy aimed at improving access to and availability of essential community level treatment services. This is to be achieved through training, equipping, and supporting community health volunteers (CHVs) to manage – identify, assess, classify, and treat/refer – two or more illnesses together – including malaria, pneumonia, and diarrhoea – among children U5 in the community with limited access to health facility-based case management services (4, 5). In the hands of well trained, supplied and supervised CHVs, iCCM can increase access to healthcare in the underserved communities – due to geographical terrain, social, economic or natural barriers – receiving relatively inequitable public health services and contribute to prevention of U5 mortality and morbidity from easily preventable causes (6–12). In 2010, a total of 28 countries in sub-Saharan Africa through a national policy, memo or written guidelines for CCM implementation adopted and scaled-up implementation of iCCM for pneumonia, diarrhoea and malaria by deploying CHVs to areas where facility-based case management services are limited to improve the availability and geographic accessibility of integrated case management services closer to caregivers – parents/guardians (13–16). Community health volunteers are often relied upon by health facilities for creating demand for reproductive, maternal, newborn and child health and immunization services. Evidence has shown that community-based service delivery through community health workers can increase utilization of these services in rural, hard-to-reach or under-served areas (17, 18).

The WHO Rapid Access Expansion Programme (RAcE) program implemented in 5 African countries – Democratic Republic of Congo, Malawi, Mozambique, Niger and two States in Nigeria highlights key lessons learnt for successful implementation of iCCM. They include communities' trust and confidence in CHVs, CHV capacity and workload, community acceptability before introduction of a new intervention or delivery strategy, CHVs geographical coverage and their multi-purpose ability in curative, preventive and promotive activities demonstrating the limits of this cadre (19). This underscores the conceptualized enabling environment that promotes utilization of quality iCCM services including CHV deployment (availability and geographic distribution), quality of services (CHV training, supervision and adherence to protocols), enabling policy (supported by ministry of health, CHV motivation through monetary and non-monetary incentives, volunteer, treatment algorithms), demand creation (social mobilization, care seeking behaviour and availability of other health services) and availability of CHV supplies (medicines and diagnostics) for community-based treatments of childhood illnesses (12, 13).

Challenges with access to health facilities, supply of commodities and trained staff, knowledge, confidence and incentives within communities to utilize services in a timely manner hinder quality of care despite availability of cost-effective treatment options (20). In SSA, only 31% of children with diarrhoea received treatment with oral rehydration salts, 37% with fever received any antimalarial (notwithstanding that not all of these children will have malaria), and medical care was sought for only 46% of children with symptoms of pneumonia (21). Just like other parts of Africa, local evidence in Kenya shows a similar sub-optimal picture in management of U5 illnesses. For instance, in 2014, 66% of children in Kenya with acute respiratory symptoms (cough and rapid breathing) – considered a proxy for pneumonia, were taken to a health facility or provided with medical advice or treatment, and 53% received antibiotics (22). Similarly, 58% of children with diarrhoea sought hospital care but only eight percent were given both ORS and Zinc as per the national policy guidelines on management of diarrhoea in U5s (23). Importantly, 74 percent of the children with diarrhoea were treated with some form of oral rehydration therapy, a marked increase from 2008-09 when only 39 percent of children with diarrhoea were treated with ORS.

Given the acceptance of iCCM as a delivery strategy to reach particularly those with limited access to health services, there has been much interest to add other interventions to the package such as maternal and newborn health through the introduction of home visits for newborn and pregnant women for community level service delivery (13, 16). This

promotes adoption of community newborn care practices as shown in the Malawi, Nepal, Bangladesh, and Uganda pilot that are key to reducing preventable neonatal mortalities (24).

Kenya is not on track for the attainment of U5 mortality rate to at least as low as the global target of 25 per 1000 live births by 2030 despite improvements in child mortality rates (25). Kenya's U5 mortality sharply declined from 115 to 52 deaths per 1,000 live births in 2014 (26). However, disparities persist in the management of the top 3 killers of U5 children in Kenya: pneumonia, diarrhoea and malaria and many children continue to die unnecessarily due to poor access to recommended treatment particularly pneumonia and diarrhoea. In 2013, Kenya developed the iCCM implementation framework anchored on the Ministry of Health (MOH) Community Health Strategy (MOH, 2007) and Child Survival and Development Strategy (MOPH, 2010) as well as the 'Policy Guidelines on Control and Management of Diarrhoeal Diseases in Children below Five Years'(27). Consequently MOH Malaria Control Unit, through funding from Global Fund round 10 and 11, facilitated trainings of CHVs in malaria case management in malaria endemic areas, including Migori County (28). The policy on use of antibiotics (Amoxicillin dispersible tablets for suspected pneumonia) by CHVs at the community level is under formulation (29). The iCCM strategy presented a platform for accelerating the control and management of childhood diarrhoea, malaria, pneumonia, neonatal causes and malnutrition at the community level and strengthen the health system, building upon the facility-level integrated management of newborn and childhood illness (IMNCI) activities thus contributing to the attainment of the SDG 3.2 by significantly reducing mortality attributed to the five conditions. These community case management frameworks provide a roadmap for CHVs implementation and monitoring at household and community levels.

Despite national improvements, Migori county compared poorly (vs national) in most maternal, newborn and child health indicators – key being diarrhoea management, nutrition, immunization and skilled birth attendance as reported in the 5-year (2010–2014) KDHS findings (26, 30). For instance, 59% vs 74% of U5 with diarrhoea received oral rehydration therapy, 3% vs 8% U5 with diarrhoea received ORS and Zinc, 69% vs 78% children received birth polio immunization, 47% vs 71% children were fully immunized at 12 months, 56% vs 58% women attended at least four antenatal care visits during pregnancy and 53% vs 61% of births were delivered in a health facility. In 2016 through donor support, it became the first county in Kenya to develop the county iCCM implementation plan (2016–2020) that focused on child survival envisioned “zero tolerance for preventable child deaths” (28). This was an innovative approach to accelerate reductions in incidence of the top childhood diseases in the county. Trainers of trainers in iCCM were developed in the county and trained CHVs in three hard-to-reach community units – Karapolo, Got Orango and Mobachi (implementation progress reports not available). Through support from the USAID funded AFYA Halisi project, the county trained CHVs from three facility-linked community units in hard-to-reach areas to implement community-based identification, management/referral of common childhood illnesses in under-5 s. This was an additional role to their other health preventive and promotive roles at the community and household level. These efforts aimed at improving the coverage of care in communities with poor access to health facilities for care.

Evidence around iCCM in Kenya has largely focused on the experiences of CHVs as agents of behavior change in the community, knowledge and skills assessment after training, coaching and after implementation (31, 32). This study examined the contribution of the iCCM strategy on the provision of a spectrum of quality maternal, newborn and child health services in hard-to-reach communities. Specifically, this study sought to determine the effect of iCCM implementation on diarrhea, pneumonia and malnutrition case identification and management; additive effect of iCCM implementation on maternal and newborn health (antenatal care coverage, skilled birth attendance and newborn/postnatal care) and immunization coverage in in the hard-to-reach communities of Migori county.

Methods

Study design

This was a nonequivalent control group pretest – posttest design, a quasi-experimental design that involves an intervention in an experimental/study group not randomly assigned and a control group, observed before and after its implementation (33). Data (from the Kenya Health Information System (KHIS), formerly the District Health Information System (DHIS2)) on community and health facility indicators for diarrhea (identified and treated) and pneumonia (identified and referred) at the community and antenatal, skilled birth attendance, newborn and immunization were reviewed. This was data for two intervention CUs (Komenya and Sagegi) and their link health facilities (Ongito and Kombe dispensaries respectively) and two control CUs (Misiwi and Gunga) – that only received basic CU training – and their link health facilities (Luciel and Nyamanga dispensaries respectively) of Migori county. The intervention was iCCM training conducted in June 2018 followed by other packages as summarized in Table 2 below. The pre-intervention period was between July 2017 – June 2018 and post-intervention period from Oct 2018 - Sept 2019. A 3-month ‘preparation’ interval between iCCM training and implementation was observed between the pre and post periods (July, August and September 2018). This period allowed preparation of the CHVs through issuance of recording/reporting tools, equipment (mid-upper arm circumference (MUAC) tapes, thermometers, respiratory timers) and the medications (Zinc and ORS) for iCCM implementation.

A “community health volunteer/worker” (CHV) was defined as a health worker delivering health care in the community, trained in some way in the context of the intervention, and having no formal health professional or paraprofessional certificate or tertiary education degree; regardless of whether or not they receive monetary payment (16). Importantly, the recruitment and management of CHVs is carried out by village and facility health committees.

Table 1
Intervention package for iCCM trained CUs

Intervention package	
1	iCCM training
2	Structured monthly and quarterly knowledge and skills checks visits
3	Coaching and mentorship of CHVs on diarrhoea, pneumonia, malnutrition case identification/detection (using appropriate equipment) and treatment skills to reinforce knowledge and skills
4	Supportive supervision of CHVs and facility HCWs including re-distribution/supply of basic drugs to CHVs from the link facilities
5	Data reviews and reporting for quality and decision-making
6	Identification of antenatal care and immunization defaulters from facility records

Study Setting

Migori County is found in the south western part of Kenya and borders Homa Bay County (North), Kisii County (North East), Narok (South East), Tanzania (West and South) and Lake Victoria to the West. The county also borders Uganda via Migingo islands in Lake Victoria. It has an area of 2,586.4 km² and divided into eight sub-counties: Nyatike, Uriri, Kuria West, Kuria East, Suna West, Suna East, Awendo and Awendo.

National demographic and health survey (2014) statistics showed that Migori county ranked top in diarrhoea (28%), second in fever/malaria (48%) and fifth (12.7%) in children with pneumonia prevalence in the country (26). Due to inter-subcounty differences in the prevalence rates of the top leading causes of childhood mortality in the county, two hard-to-reach community units (CUs) linked to health facilities with poor maternal, newborn and child health indicators were selected for iCCM training and implementation. These were Sagegi – attached to Kombe dispensary (Kuria West sub-county) and Komenya – attached to Ongito dispensary (Uriri sub-county). The population in the villages in the selected CUs were more than the WHO recommended 5 km away from their respective link health facilities. The third CU trained on iCCM (Kanying'ombe) was an urban community unit and close to the link facility and therefore not included in this study as it did not meet the criteria for a hard-to-reach community. 'Hard-to-reach' referred to populations who have little regular contact with skilled pregnancy and childbirth services including people living in areas 'too far' from the health services. 'Too far' not only refers to the physical distance but also logistics and human resource capacity as used in the 'reaching every district' strategy in immunization (34).

Two control CUs in the hard-to-reach areas attached to health facilities where the project did not support and/or facilitate enhanced defaulter tracing for immunization during the national immunization rapid response initiative between July and September 2019 were selected. The CUs did not receive any additional support from the project or other partner support in community health services (apart from the mandatory CU training). Besides, the CUs must have been reporting every month for selection. The selected control CUs (Misiwi – attached to Luciel dispensary in Kanyasa ward and Gunga – attached to Nyamanga dispensary in Kachieng ward), were both from the expansive Nyatike sub-county of Migori county. All the study/experimental and control CUs had less than 40 percent coverage for 4th ANC and skilled birth attendance before the intervention (Fig. 1).

Community Health Volunteers And Community Units In Kenya

In Kenya, all CHVs are trained to diagnose malaria with a malaria rapid diagnostic test (mRDT) and treat it with artemisinin-based combination therapy (ACT); treat under-5 children with diarrhoea using oral rehydration salts (ORS) and zinc; refer suspected pneumonia, mild to moderate malnutrition, and sick newborns to a health facility (27). Before being certified as CHVs, all candidates receive training in basic community health modules as defined by MOH which focuses on health and development, health promotion, and the Kenya community-based essential health package (Table 2) (35). Administratively, each CU serves about 5000 people. The CU is coordinated by a community health assistant (CHA), formerly the community health extension worker (CHEW), who supervises a maximum of 25 CHVs. Each CHV serves a maximum of 20 households or 100 people (35). However, due to cost implications in making a CU functional as well as supervisory efficiencies, reductions in number of CHVs per CU are experienced with some CHVs covering as high as 50–100 households depending on population density of a village.

Table 2
Kenya community-based essential health package

1	Disease prevention and control to reduce morbidity, disability and mortality
	<ul style="list-style-type: none"> • Communicable disease control: HIV/AIDS, STI, TB, malaria, epidemics • First aid and emergency preparedness/treatment of injuries/trauma • IEC for community health promotion and disease prevention
2	Family health services to expand family planning, maternal, child and youth services
	<ul style="list-style-type: none"> • MCH/FP, maternal care/obstetric care, immunization, nutrition, Community-Integrated Management of Childhood Illnesses (C-IMCI) • Adolescent reproductive health • Non-communicable disease control: Cardiovascular diseases, diabetes, neoplasms, anaemia, nutritional deficiencies, mental health • Other common diseases of local priorities within the district, e.g., eye disease, oral health, etc. • Community-based day-care centres • Community-based referral system, particularly in emergencies
3	Hygiene and environmental sanitation
	<ul style="list-style-type: none"> • IEC for water, hygiene, sanitation and school health • Excreta/solid waste disposal • Water supply and safety, including protection of springs • Food hygiene • Control of insects and rodents • Personal hygiene • Healthy home environment: environmental sanitation, development of kitchen gardens • Organizing community health days

Scope Of Iccm Training And Supportive Supervision

A total of 20 CHVs from the two CUs (each CU had 10 CHVs) received a 5-days' training on iCCM (using the iCCM Kenya curriculum (36)) with a key focus on the following components in under 5 children: identification of diarrhoea and treatment (using ORS and Zinc) and appropriate referral of complicated/chronic cases; identification of pneumonia/fast breathing using respiratory timers and referral for care; identification of mild, moderate and severe malnutrition using the MUAC tape and referral for care; identification of malaria using mRDT, treatment using ACTs and appropriate referral; assess the status of immunization, Vitamin A and deworming in under-5 children; assess for treatment at home and appropriate referral; correctly give home and pre-referral treatment; counsel caregivers on appropriate care for sick children, treatment compliance and follow up; provision of behavior change communication (BCC) messages at the household level and effectively manage medicines and other supplies in their kits.

Post iCCM training, the CHVs carried out the following package of interventions (Table 3).

Table 3
Scope of iCCM trained CHVs

CHVs post-iCCM tasks	
1	Household visits – assessment/screening and classification of the child's condition(s) using a simplified IMNCI-adapted algorithm (suspected pneumonia/fast breathing using respiratory timers); diarrhea; fever/malaria using thermometer & rapid diagnostic tests); malnutrition using MUAC tapes)
2	Referral of cases with general danger signs and other complicated cases (fast breathing/pneumonia, chronic diarrhea, bloody diarrhea, neonatal danger signs)*
3	Provision of treatment for the following conditions: <ul style="list-style-type: none"> • non-severe diarrhoea with oral rehydration salts and zinc; • non-severe malaria with artemisinin-based combination therapy
4	Assessment and referral of newborn danger signs
5	Assessment, classification and referral of uncomplicated severe acute malnutrition (SAM)
6	Follow-up of cases on treatment, follow-up of immunization and antenatal care defaulters and postnatal mothers/newborn household visitation within 48 hours of birth
7	Monthly data review meetings for quality performance and reporting
*Additional focus strengthened during supportive supervision and coaching visits included: identification of immunization and antenatal care defaulters from facility records (emphasis on full immunization coverage and every pregnant woman receiving antenatal and maternity care services); strengthening the care seeking and compliance with treatment of care givers	

Deworming and Vitamin A administration in under 5 s was not studied as there existed other national and county-led forums and rapid results initiatives at key points in the calendar year where they were conducted at scale in all communities to reach the eligible children.

Data Collection

Routine monthly reporting of community health indicators was conducted by CHVs using the standard community MOH primary reporting tools and the summaries from the primary tools were compiled in the community MOH secondary reporting tools by CHAs. Copies of verified MOH secondary reporting tools completed by CHAs were submitted to the Afya Halisi project team for monitoring.

Data was collected on key maternal, newborn and child health and immunization indicators in the facility and community. This included identification and treatment of diarrhoea with ORS and Zinc (2–59 months), identification and referral of children (2–59 months) with fast breathing/suspected pneumonia, identification and referral of malnourished children, visitation of newborns at home within 48 hours of birth and referral of sick newborns or those with danger signs to a health facility and identification and referral of immunization defaulters. Others included pregnant women seeking antenatal care services (first antenatal care visit and fourth visit) and skilled births in facilities.

Standard MOH reporting tools for community health services by CHVs were used for collecting routine service utilization data. They were: MOH 100 – Community Referral Form – reporting of all maternal, newborn and child health and immunization referred cases at the community to the health facility by CHVs; MOH 514 – Community Health Service

Delivery Log Book – reporting for all the service delivery data by the CHVs; MOH 515 – Community Health Extension Worker Summary, summarised by the Community Health Extension Worker all the data reported in MOH 514. Community Health Extension Worker and the health facility care provider verified the data reported in MOH 514 during the CHVs monthly data review meetings before eventual transfer into the MOH 515 summary tool. Monthly data verification of MOH 100, MOH 514 and MOH 515 reporting tools/records by the CHVs, CHA and facility healthcare worker in-charge during the monthly data review meetings at the end of every reporting month were conducted before submission of the summary reports to the sub-county community health strategy focal person and the sub-county HRIO for reporting. This aimed to ensure timely, complete, and accurate data reporting.

Healthcare workers verified and reported facility service utilization data on antenatal, maternity/delivery and postnatal care, immunization and nutrition in the primary service delivery registers. The respective reporting registers are: MOH 405 – antenatal care register, MOH 333 – maternity register, MOH 510 – immunization permanent register, MOH 511 – Child Welfare Clinic register, MOH 406 – postnatal care register, MOH 702 – immunization tall sheet and MOH 704 – Child Health and Nutrition Information System (CHANIS) tally sheet. The summarized data was later reported in the secondary reporting tools: MOH 711 for antenatal, maternity/delivery and postnatal care and MOH 711 for immunization and nutrition.

Project staffs and facility healthcare worker in-charge verified summarized facility and community level data of interest before submitting to the sub-county HRIO for reporting/uploading in the DHIS2/KHIS. DHIS2 is a protected open source public access system where all monthly MOH reporting is done and requires registration credentials to access. Final study data was accessed from the DHIS2/KHIS on 25th March 2020 (37).

Data analysis

Data was extracted from the DHIS2 in Ms Excel, cleaned and exported to STATA version 13 for data analysis. Means and/or proportions of community and health facilities' maternal, newborn and child health and immunization indicators of interest were computed. Child health cases computed were diarrhoea (identified and treated), pneumonia (identified and referred), malaria (identified and treated) and undernutrition (identified and referred). The community health data elements of interest (referrals) on maternal health – antenatal care, skilled birth attendance; newborn health – postnatal visits and neonatal danger signs identification/management; immunization and nutrition from the two time periods were compared using a two-sample test of proportions for differences post-ICCM training. The overall effect and differences of the community health data elements on health facilities' maternal (antenatal and skilled birth attendance coverage), newborn and child health and immunization coverage indicators were compared between the two periods through the two-sample t-tests. It is important to note that for the pre-intervention period, data was analysed for 8 months from Nov 2017 to June 2018 as operations in public/government health facilities were paralyzed by a protracted nationwide nurses/midwives' strike that lasted for five months from June 2017 to October 2017 (38, 39). P-values were reported to show the significance of the change due to the intervention where $P \leq 0.05$ values were considered statistically significant.

Results

1. Community Health Volunteers Reporting

At least 86% of the households were visited by CHVs and over 95% of the CHVs reported during the two periods in the intervention sites with no differences in the proportion of households visited and the CHVs reporting in the pre and post-ICCM training in the two CUs. However, there was a significant difference in the proportion of households visited in the control sites with no differences in CHVs reporting between the two periods (Table 4).

Table 4
Pre-post community household visitation and reporting in the two community units in Migori

	Intervention CUs			Control CUs		
	Pre-Mean (SD (±))	Post-Mean (SD (±))	P-value	Pre-Mean (SD (±))	Post-Mean (SD (±))	P-value
Proportion of households visited	86.2 (15.3)	88.7 (13)	0.2934	34.4 (23.2)	49.1 (25.4)	0.0353*
Proportion of CHV's reporting	97.1 (15.9)	95.8 (8.8)	0.37782	85 (33.7)	83 (38.3)	0.4334
Source: DHIS2						
*P ≤ 0.05 statistically significant						

2. Maternal, Newborn And Child Community Case Identification And Management

Post-training, a monthly average of 15 cases of diarrhoea in U5 children were identified with 11 (76%) of the cases correctly treated with the recommended Zinc and ORS. In comparison, a monthly average of 0.2 cases were identified in the control CUs (no treatment with Zinc and ORS). For suspected pneumonia, a total of 60 cases of children were diagnosed with fast breathing, a monthly increase from 1 to 5 children identified between the two periods in the intervention CUs. During the same period, there was a double increase in cases of malnutrition identified (0.8 to 1.5 per month) in U5 children (using the MUAC tapes) in the community and referred to the health facilities for appropriate treatment between the control CUs to intervention CUs. Cases of malaria tested positive on RDT and treated with ACT increased from 9 to 12 cases per month in the intervention CUs. There was a double reduction in the cases of malaria who tested positive on RDT (35 to 19.6) in the control CUs. In maternal health, there was a triple increase in the cases of ANC client defaulters who were identified and referred to the health facilities (2.5 to 6.5) for care with a double increase (6.6 to 10.1) in the cases referred for skilled delivery in the intervention CUs with no change in the control CUs. A 10-fold increase was observed in the number of newborns identified with danger signs and referred to the health facility for care in the intervention CUs with no change in the control CUs. A double increase from 10.3 to 20.6 was observed in the cases of children 0–11 months referred from the community to the health facilities for immunization services (Table 5).

Table 5
Pre-post community case identification and management in the select community units in Migori

Indicator	Intervention		Control	
	Pre (mean)	Post (mean)	Pre (mean)	Post (mean)
Diarrhoea				
CHEW Number of cases of diarrhoea identified in children 0–59 months (A)	3 (0.4)	180 (15)	0 (0)	2 (0.2)
CHEW Number of children of 2–59 months with diarrhoea treated with Zinc and ORS (B)	0 (0)	137 (11)	N/A	N/A
Proportion of children 2–59 months with diarrhoea correctly treated with Zinc and ORS (B/A*100)	0 (0)	76.1 (6)	N/A	N/A
Fast breathing/suspected pneumonia				
CHEW Number of children 0–59 months age presenting with fast breathing and referred for treatment	10 (1.3)	60 (5)	0 (0)	1 (0.1)
Malnutrition				
CHEW Moderate Malnutrition	0 (0)	18 (1.5)	0 (0)	10 (0.8)
CHEW Severe Malnutrition	0 (0)	4 (0.3)	0 (0)	1 (0.1)
Fever/malaria				
CHEW Number of fever cases managed	354 (44.3)	498 (41.5)	158* (19.8)	428* (35.7)
CHEW Number of fever cases < 7 days with RDT done	354 (44.3)	480 (40)	486 (60.8)	565 (47.1)
CHEW Number of fever cases < 7 days with RDT + ve	222 (27.8)	297 (24.8)	280 (35)	235 (19.6)
CHEW Number of under 5 years Malaria cases (RDT + ve) treated with ACT	71 (8.9)	142 (11.8)	95 (11.9)	97 (8.1)
Maternal health				
CHEW Referred for ANC	52 (6.5)	239 (19.9)	66 (8.3)	162 (13.5)
CHEW Defaulters referred for ANC	20 (2.5)	78 (6.5)	0 (0)	1 (0.1)
CHEW Referred for skilled delivery	53 (6.6)	121 (10.1)	54 (6.8)	79 (6.6)
Newborn health				
CHEW Number of newborns visited at home within 48 hours of birth	72 (9)	165 (13.8)	61 (7.6)	100 (8.3)

Source: DHIS2

*data missing in some months

CHEW – Community Health Extension Worker; ORS – Oral Rehydration Salts, RDT – Rapid Diagnostic Test, ACT – Artemisinin-based Combination Therapy, ANC – antenatal care

	Intervention		Control	
CHEW Referred newborns with danger signs	1 (0.1)	12 (1)	0 (0)	0 (0)
Immunization				
CHEW Children of 0–11 months referred for immunization	82 (10.3)	247 (20.6)	90 (11.3)	126 (10.5)
CHEW Defaulters referred for immunization	45 (5.6)	99 (8.3)	14 (1.8)	32 (2.7)
Source: DHIS2				
*data missing in some months				
CHEW – Community Health Extension Worker; ORS – Oral Rehydration Salts, RDT – Rapid Diagnostic Test, ACT – Artemisinin-based Combination Therapy, ANC – antenatal care				

3. Community Health Indicators Performance

Maternal health

There was a double increase in the proportion of pregnant women referred from the community to the health facility for antenatal care (25.4% vs 45.8%, $P < 0.0001$) and pregnant women defaulters referred for antenatal care (9.8% vs 14.9%, $P = 0.0327$) in the intervention CUs. Consequently, there was a significant increase in the proportion of pregnant women referred from the community for antenatal care in the control CUs. However, there were no differences in the referrals from the community to health facilities for skilled births in both intervention and control CUs (Table 6).

Newborn health

There was a five-times increase (1.4% vs 7.3%, $P = 0.0337$) in the newborns identified with danger signs and referred to the health facility for appropriate care in the intervention CUs. Even though there was a significant increase (43.9 vs 68.5%, $P < 0.0001$) in the proportion of newborns visited at home within 48 hours of birth in the control CUs, there were no newborns identified with danger signs referred for hospital care (Table 6).

Immunization

There were significant increases in proportions of children 0–11 months referred for immunization (4% vs 7.5%, $P < 0.0001$) and defaulters referred for immunization (2.2% vs 3%, $P = 0.0366$) in the intervention CUs. Conversely, there was a double reduction (10% vs 5%, $P < 0.0001$) in the children 0–11 months referred for immunization with no change in the proportion of identified defaulters referred for immunization in the control CUs (Table 6).

Malaria case management

Interestingly, a significant 16% decrease (57.6% vs 41.6%, $P < 0.0001$) in the number of fever cases who tested positive for malaria (RDT) in the control CUs with no change in the intervention CUs was observed. A 16% increase in the intervention CUs (32.0% vs 47.8%, $P = 0.0001$) and 7% increase in the control CUs (41.3% vs 33.9%, $P = 0.0409$) were observed in the cases of fever who tested positive for malaria and were treated with ACT as recommended (Table 6).

Table 6
Pre-post community maternal, newborn and immunization indicators for intervention and control community units in Migori

Indicator	Intervention					Control				
	Pre		Post		P-value	Pre		Post		P-value
Maternal health (N= CHEW Total pregnant women)	N = 205	%	N = 522	%		N = 324	%	N = 482	%	
CHEW Referred for ANC	52	25.4	239	45.8	< 0.0001*	66	20.4	162	33.6	< 0.0001*
CHEW Defaulter referred for ANC	20	9.8	78	14.9	0.0327*	0	0	1	0.2	0.206
CHEW Referred for Skilled Delivery	53	25.9	121	23.2	0.2236	54	16.7	79	16.4	0.4587
Newborn health (N= CHEW Total children 0–28 days)	N = 106		N = 243			N = 139	%	N = 146	%	
CHEW Number of newborns visited at home within 48 hours of birth	72	67.9	165	67.9	0.4983	61	43.9	100	68.5	< 0.0001*
CHEW Referred newborns with danger signs ^a	1	1.4	12	7.3	0.0337*	0	0	0	0	-
Immunization (N = CHEW total children 0–12 months)	N = 2056	%	N = 3296	%		N = 899	%	N = 2534	%	
CHEW Children of 0–11 months referred for immunization	82	4	247	7.5	< 0.0001*	90	10	126	5	< 0.0001*
CHEW Defaulter referred for Immunization	45	2.2	99	3	0.0366*	14	1.6	32	1.3	0.2547
Malaria management (N = CHEW Number of fever cases < 7 days with RDT done)	N = 354	%	N = 480	%		N = 486	%	N = 565	%	
CHEW Number of fever cases < 7 days with RDT + ve	222	62.7	297	61.9	0.4027	280	57.6	235	41.6	< 0.0001*
CHEW Number of under 5 years Malaria cases (RDT + ve) treated with ACT ^b	71	32.0	142	47.8	0.0001*	95	33.9	97	41.3	0.0409*
Source: DHIS2										
ANC – antenatal care; CHEW – Community Health Extension Worker; RDT – rapid diagnostic test; ACT – artemisinin combination therapy										
^a Denominator for the intervention (pre – 72, post – 165) and control (pre – 61, post – 100)										
^b Denominator for the intervention (pre – 222, post – 297) and control (pre – 280, post – 235)										
*P ≤ 0.05 statistically significant										

4. Overall facility maternal, child health and immunization coverage indicators performance

Maternal health

There was an overall significant increase on all the maternal health indicators at the health facilities in the intervention sites: proportion of pregnant women who attended at least one ANC visit during pregnancy (103.5% vs 142.5%, $P = 0.048$), proportion of pregnant women who completed four ANC visits doubled (39.4% vs 79.3%, $P < 0.0001$), and the proportion of births conducted by skilled birth attendants doubled (24.5% vs 43%, $P = 0.002$). Conversely, there was a significant reduction in the proportion of women who attended at least one ANC visit during pregnancy (38.2% vs 23.1%, $P = 0.0402$) with no change in fourth ANC attendance and skilled birth attendance coverage in the control sites (Table 7).

Child health

There were no significant changes in the proportions of children U5 treated for diarrhoea and pneumonia at the health facilities in both the intervention and control sites ($P \geq 0.05$) (Table 7). Malaria case management has not been included since there were marked disproportionate errors in data reporting quality in the DHIS2 at the facility level for both intervention and control sites.

Immunization

There were significant increases in all the key antigens as per the Kenya Expanded Program of Immunization (KEPI) in the intervention sites. The antigens below the recommended averages of at least 90% coverage in the pre-intervention phase all improved to above 90% coverage for BCG (62.7% vs 102.6%, $P = 0.0097$), birth polio (58.7% vs 92.8%, $P = 0.01$) and Pentavalent 1 (82.4% vs 140.5%, $P = 0.0008$) in the intervention sites. The immunization coverages (pre and post) for all antigens in the control sites were lower than the recommended 90% for all antigens with no differences reported between the pre and post intervention periods ($P > 0.05$). The proportion of children under one year who are fully immunized (described as children who received BCG, three doses of Pentavalent, Polio and Pneumococcal vaccine each, Measles/Rubella 1 with a dose of Vitamin A) by their first birthday significantly increased in the intervention sites (96.2% vs 130.8%, $P = 0.0371$) with no change observed in the control sites (53.7% vs 60.4%, $P > 0.05$), which had lower than the minimum expected 90% coverage. Even though the Measles/Rubella 2 coverage administered to children under 5 years at 18 months or at 24 months significantly increased from 55–87.5% ($P = 0.0471$) in the intervention sites, this was still lower than the expected 90% coverage in high-risk populations. The coverage for Measles/Rubella 2 in the control sites was lower than the expected 90% (21.7% vs 30.1%) with no differences between the two periods ($P > 0.05$) (Table 7).

Table 7
Pre and post facility maternal and child health indicators in the two community units

Pre and post facility maternal and child health indicators in the two community units										
	Intervention					Control				
	Pre		Post		P-Value	Pre		Post		P-Value
	Mean	SD±	Mean	SD±		Mean	SD±	Mean	SD±	
Maternal health										
Proportion of pregnant women who attended at least one ANC visit during pregnancy	103.5	42.5	142.5	84.4	0.048*	38.2	30.9	23.1	22	0.0402*
4th ANC coverage	39.4	28.9	79.3	22.7	< 0.0001*	16.7	13	21.6	23.1	0.2214
Proportion of deliveries conducted by skilled birth attendants	24.5	9.4	43	22.8	0.002*	27.1	31	22.5	23.6	0.3024
Child Health										
Children U5 treated for diarrhoea	0.02	0.02	0.02	0.03	0.4501	0	0	0	0	0.4207
Children U5 treated for pneumonia	1.1	1.7	1.3	2.3	0.3787	0.2	0.3	0.2	0.4	0.4863
Immunization										
BCG Coverage	62.7	24.4	102.6	62.1	0.0097*	38.1	26.4	29.4	25.7	0.1516
OPV birth dose coverage	58.7	24.7	92.8	52.2	0.01*	23.8	22.4	28.4	26	0.2815
PENTA 1 coverage	82.4	26.5	140.5	64.5	0.0008*	52.8	28.2	53.1	28	0.4873
PENTA 2 coverage	91.5	24.3	140.4	70	0.0055*	46.4	28.8	50.9	29.9	0.31
PENTA 3 coverage	91.9	32.1	135	63.1	0.0081*	57.8	27.1	59.4	26.5	0.4287
Proportion of under ones vaccinated against MR1	95.6	45	135.6	67.1	0.0218*	58.7	26.3	60.8	30.8	0.4144
Proportion of children under one year who are fully immunized	96.2	45.4	130.8	65.5	0.0371*	53.7	22.9	60.4	28.5	0.2158
Proportion of under ones vaccinated against MR2	55	43.5	87.5	66.7	0.0471*	21.7	20.3	30.1	30.1	0.1661
Penta 3 drop-out rate	-18.7	45.3	-1.8	34.9	0.0953	-18.2	57.1	-37.7	90	0.2232
MR1 drop-out rate	-21.1	44.8	-4.1	48.3	0.1346	-27.5	68	-50.8	171.4	0.3044
Source: DHIS2										
SD – standard deviation; ANC – antenatal care; U5 – under 5 years; BCG – <i>Bacillus Calmette–Guérin</i> ; PENTA – <i>Pentavalent containing 5 antigens namely – Diphtheria, Pertussis, Tetanus, Hemophilus influenza type b and Hepatitis B</i> ; MR – Measles/Rubella; *p ≤ 0.05 statistically significant										

Discussion

This study set to demonstrate that apart from increased case detection and treatment and/or referral for diarrhoea and suspected pneumonia, iCCM had the potential to contribute to additional improvements in antenatal care, skilled births and immunization coverage and nutritional screening for undernutrition in the hard-to-reach communities. Through this community health platform, previously low service uptake and utilization in antenatal care, skilled births, community case (diarrhoea, malaria, suspected pneumonia and undernutrition) identification and management and immunization services improved in the catchment hard-to-reach communities in Migori. This finding is consistent with other studies in low and middle resourced countries in SSA where iCCM has been implemented (8, 10, 19, 32, 40, 41).

Household visitation by CHVs is an integral part of their responsibilities. The significantly low households visited in the control sites could be attributed to weak community-facility linkages, low supervision, erosion of skills/ knowledge, and lack of review of performance and targeted strategies to improve community health services in rural hard-to-reach areas. As community “gatekeepers,” CHVs can be proactive in household visitations when supported with the basic community health diagnostic equipment (e.g. MUAC tapes, thermometers and respiratory timers) and basic drugs like ORS and Zinc that may help build trust between the community and the CHVs who are seen as community ‘doctors.’ Evidence in Uganda among CHVs showed that putting health-related knowledge into community action was among the important motivators for CHVs to conduct household visitations (42). However, there is also evidence from a peri-urban setting in Kenya among CHVs that lack of material resources necessary for CHVs’ work and lack of motivation are demotivating factors contributing to low household visitations (31).

This study demonstrated that CHVs diagnosed uncomplicated diarrhoea cases and correctly treated 3 of every 4 cases identified post-training with the nationally recommended ORS and Zinc (23). Commodity stock-outs in the link health facilities that re-supply CHVs contribute to some cases missing treatment as per the recommended guidelines. Supply chain management is part of the health system bottleneck yet a key cornerstone for planning and sustainability of iCCM services that is likely to affect overall performance of CHVs trained on iCCM in poor and rural hard-to-reach areas (10, 43–45).

This finding is similar to a cross-sectional study conducted in rural Ethiopia and a multi-country study in SSA on implementation strength and quality of care provided by community health workers (46, 47). Our findings also demonstrated improvement in the identification of childhood illnesses through simple diagnostic equipment. The improvement observed in the cases of suspected pneumonia detected by use of respiratory timers in taking respiratory rates and undernutrition cases by use of MUAC tapes is testament that through provision of diagnostic tools, high quality treatment for sick children can be achieved thereby contributing to quality interventions and health outcomes (40). Quarterly supportive supervision and mentorship conducted on regular basis ensured that knowledge and skills are maintained to promote quality community health care service utilization (32). These findings support evidence from other studies that when well trained and mentored, CHVs can correctly manage multiple childhood illnesses (8, 9, 15, 19, 32, 41, 46, 48, 49).

Community malaria case management improved at the intervention sites compared to the controls. First, the fever cases diagnosed as positive for malaria through RDT improved while there was a significant reduction in the same at the controls. Secondly, there was a marked increase in the proportion of cases correctly diagnosed and treated with the recommended ACT by CHVs both at the intervention and controls. These findings are consistent with another study by Oresanya et al in Nigeria and Zalisk et al in Malawi (10, 41). This can be explained by the fact that Migori is a malaria endemic zone where through the national malaria program, community units received prior training in malaria testing using RDTs and treatment using ACTs. This study underscores the fact that iCCM training and coaching/mentorship received reinforced the CHVs’ knowledge and skills in managing common childhood illnesses by following the iCCM prescribed algorithm for decision-making on management /treatment of illnesses as evidenced by another Kenyan study (32).

There was overall improvement in the proportion of pregnant women who attended at least one ANC visit during pregnancy and those that completed the four focused ANC visits in the intervention sites. This is recommended towards identification of danger signs in pregnancy and planning for individual birth plan that contributes to maternal health monitoring, early identification maternal and fetal complication, and eliminating preventable maternal and perinatal morbidities and mortalities (50). World Health Organization recommends community-based health systems interventions with specific focus on packages of interventions that include household and community mobilization and antenatal home visits (51). These recommendations aim to improve antenatal care utilization, women's experience of care and perinatal health outcomes, particularly in rural settings with low access to health services. This study demonstrated that referral of pregnant women for antenatal care alone is not enough. Follow up on defaulters referred for ANC helps to ensure that the pregnant women access skilled antenatal care attendance, a feature well illustrated in the intervention CUs and health facilities with eventual improvement on antenatal care coverage. Health messages on the need for ANC attendance by the trusted CHVs in the community plays an integral role in improving antenatal care coverage in these hard-to-reach communities.

The proportion of deliveries conducted by skilled birth attendants, now known as skilled health personnel, in the intervention sites doubled. This can be attributed to the focused demand creation activities to improve access to quality lifesaving interventions from frontline community providers. Through community mobilization and advocacy for skilled birth attendance by the CHVs during their household visits and sensitizations, it can be acknowledged that the community becomes responsive to the benefits associated with skilled birth attendance as highlighted by a multi-country study on newborn care practices in Malawi, Nepal, Bangladesh and Uganda. In that study, women from Malawi, Nepal and Bangladesh who were visited by a CHV three or more times during pregnancy were more likely to report use of selected life-saving newborn care practice (24). Implementation of iCCM in addition to the MNH package with focused demand creation activities can improve access to quality lifesaving interventions anchored on the community health strategy (24, 41).

Newborn visitation in the community in the early days of life is crucial in screening for life-threatening neonatal danger signs. Despite improvements in newborns visited at home within 48 hours of birth in the control community units, there was no change in the numbers with danger signs referred to health facilities for appropriate care. However, in the intervention sites, there was a significant increase in the numbers of newborns identified with danger signs and referred to health facilities for appropriate care although no change in the newborns visited within the same period. Community health volunteers trained in iCCM are equipped with knowledge and skills to identify danger signs that could be life-threatening in U5s including the neonatal period and referred them to health facilities for appropriate care. It must be acknowledged that children face the highest risk of dying in their first month of life, at a global rate of 18 deaths per 1,000 live births. A third of all neonatal deaths tend to occur on the day of birth and close to three quarters die in the first week of life (52, 53). Therefore, this evidence suggests that focusing on the critical periods immediately following birth is essential to saving more newborn lives for realization of SDG 3 target by 2030.

Immunization coverage increased significantly in all antigens at the intervention health facilities with no change at the control health facilities. This study demonstrated that despite a significant improvement in the number of immunization referrals made by the CHVs, it is the overall improvement in defaulter tracking to identify immunization defaulters and referral to the health facilities that is key in these hard-to-reach communities. This finding is similar to the study findings evaluating the effect of enhanced defaulter tracing in the hard-to-reach communities in Migori county (54). This therefore means that efforts should be made to strengthen defaulter tracking mechanisms in the communities to improve immunization coverage and utilization in rural hard-to-reach populations. This is in line with the WHO's reaching every child/district (RED/REC) strategy that advocates for partnering with communities to promote and deliver immunization services which best fit local needs and reach all eligible populations (11). Through integration of community health

services, there is an opportunity to reduce inequities in immunization coverage, key areas for immunization programs in Africa underscored by the Global Vaccines Action Plan 2011–2020 (55).

Service utilization at both intervention and control sites is optimal based on the Pentavalent 3 and Measles/Rubella 1 drop-out rates of less than 10%. However, access to the services is suboptimal at the control sites (52.8% coverage for Pentavalent 1 vaccine), lower than the expected minimum of at least 80% as recommended by WHO (11). This implies that demand creation strategies must be intensified through the community health platforms and iCCM provides the earliest opportunity to achieve the expected coverages. However, it should be noted that there were over 100% immunization coverages in the post-intervention phase in the intervention health facilities for most antigens. It should be acknowledged that the facility expanded program on immunization (EPI) targets assigned by the MOH departments are usually mere estimates based on available demographic data that may not be very accurate hence performance as per the results may be over 100% for some of the antigens.

This study has strengths and weaknesses. To the best of our knowledge, this is the first published study in Kenya on the effect of iCCM on maternal and newborn health. The choice to have a comparison group with similar characteristics as the intervention sites makes the findings credible and change observed in the intervention sites is not just part of a secular trend – similar changes occurring in those kinds of facilities because of other contextual factors. This is also supported by the fact that all the study CUs had less than 40 percent coverage for 4th ANC and skilled birth attendance before the intervention. There were no changes in the proportion of CHVs reporting before and after the intervention in both sites. This therefore means that the selected intervention and control CUs had equal chances of over 80% of the CHVs reporting monthly. Besides, the fact that no stipends were provided by the project for the CHVs to carry out their community health responsibilities strengthens the sustainability of the model in hard-to-reach communities. Data quality challenges (timeliness, accuracy and completeness) are common with the use of DHIS2 data. The project team supported the subcounty teams conduct data verifications with individual health facilities and CUs before reporting in the health information system. The small samples of intervention mean that these findings should be interpreted within the local context.

Conclusion

Training and implementation of iCCM to build the knowledge and skills of CHVs in community case management using simple algorithms can lead to improved identification and treatment of malaria, diarrhoea, suspected pneumonia and malnutrition in the hard-to-reach communities. Beyond strengthening knowledge and skills in common childhood illnesses identification and management, iCCM broadly improved competencies and motivation of the CHVs which essentially contributed to improved access and utilization of skilled birth attendance (antenatal care, skilled births in health facilities, early neonatal care danger signs identification and referral for treatment) and childhood immunization. The CHVs are further involved in demand creation for maternal child health services, though delivery of targeted health messages at household level for improved health seeking behavior. Routine mentorship, coaching and support supervision of CHVs reinforced their knowledge and skills in identification of antenatal and immunization defaulters and referral to health facilities in hard-to-reach communities. Enhanced defaulter tracking by CHVs for antenatal and immunization care provides the platform under which facility utilization of health services can be strengthened.

Recommendations

Key recommendations from the findings of this quasi-experimental study are: governments (national and county) should invest more resources in strengthening the community health systems so that CHVs are motivated and retained to carry out demand creation for maternal, newborn and child health and immunization services in hard-to-reach communities. This can be achieved through formulation of community health sensitive policies that will ensure funding, CHV

motivation and provision of essential supplies. Regular mentorship and coaching should be integrated in community health interventions to reinforce the knowledge and skills acquired for realization of improved performance in community maternal, newborn and child case identification and management. In addition, community-facility linkages should be strengthened through data demand and information use to identify service gaps, coverage inequities and prioritization of strategies to improve community maternal, newborn and child health and immunization services utilization.

Abbreviations

ANC - Antenatal care

CHA - Community Health Assistant

CHEW - Community Health Extension Worker

CHV - Community Health Volunteer

CU - Community Unit

DHIS - District Health Information System

FIC - Fully Immunized Child

HRIO - Health Information and Records Officer

iCCM - Integrated Community Case Management of Childhood Illnesses

KEPI - Kenya Expanded Programme on Immunization

MOH - Ministry of Health

MUAC - Mid-Upper Arm Circumference

ORS - Oral Rehydration Salts

SBA - Skilled Birth Attendance

SD - Standard Deviation

SDG - Sustainable Development Goals

U5 - Under 5

Declarations

Ethics approval and consent to participate

No institutional review board determination was sought for the study because the Kenya DHIS2 data are publicly available (37), and the use of program reports in aggregate form was not human subjects' research (56).

Consent for publication

Not applicable

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. The data was extracted from the Kenya Health Information System (KHIS), formerly the District Health Information System 2 (DHIS2), an open source public access system where all MOH reporting is done and requires registration credentials to access. The link to the databases used is <https://hiskenya.org/dhis-web-pivot/>.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

DNS: conceived the idea, designed the procedures, provided technical support for the intervention and data collection at the facility and community level, performed data curation, data analysis and interpretation of results and drafted the manuscript; LKM, MM, FO, GM, LN, TO, KS and SO participated in the design, provided the technical support to the intervention and substantively reviewed and validated the manuscript; KS, TM, SO and PK participated in the design of the intervention, provided the overall technical guidance to implementation, interpreted the analysis results and substantively reviewed and validated the manuscript. All authors read and approved the final manuscript.

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Figures

Figure 1

Map showing the iCCM intervention and control health facilities in Migori County. Map is author's own generated using the QGIS software. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.