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Effectiveness of an electronic clinical decision support system in improving the management of childhood illness in primary care in rural Nigeria: a prospective observational study

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Effectiveness of an electronic clinical decision support system in improving the management of childhood illness in primary care in rural Nigeria: a prospective observational study

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ABSTRACT

Introduction
Digital interventions can support health systems strengthening in resource-constrained settings. Clinical decision support systems (CDSS) provide evidence-based recommendations to health workers, tailored to individual patients, using clinical algorithms. Recent studies suggest that CDSS hold promise for the management of childhood illness in primary care, but evidence on effectiveness at scale is limited. We evaluated the impact of ‘ALMANACH’, a CDSS based on the Integrated Management of Childhood Illness (IMCI), on health and quality of care outcomes for children attending primary care facilities in north-eastern Nigeria.

Methods
In this prospective observational study, we compared caregiver-reported recovery of children (age 2-59 months) with acute illness in 45 facilities implementing ALMANACH with 44 facilities using paper-based IMCI. We collected sociodemographic and clinical information from caregivers and clinical records on Day 0, and recovery data from Day 7 phone follow-up. We calculated risk ratios and odds ratios for primary and secondary outcomes, and derived adjusted effect estimates using mixed-effects regressions.

Results
We recruited 1,929 children of which 1,021 (53%) attended facilities implementing ALMANACH, in March and between July-September 2020. Caregiver-reported recovery was significantly higher among children attending ALMANACH facilities (adjusted OR=2.63, 95% CI: 1.60-4.32). We observed an increase in parenteral antimicrobial prescriptions (adjusted OR=2.42 (1.00-5.85)), and a decrease in oral antimicrobials (adjusted OR=0.40 (0.22-0.73)) in ALMANACH facilities, as well as marked increases in referral, communication of diagnosis, and follow-up advice.

Conclusion
Implementation of digital CDSS in primary care can improve quality of care and recovery of sick children in resource-constrained settings. The effect is likely mediated by better guideline adherence by health workers supported step-by-step through evidence-based recommendations on clinical assessment, diagnosis, treatment and referral. These findings support the use of CDSS for health systems strengthening to progress towards universal health coverage.
ARTICLE SUMMARY

Strengths and limitations of this study

- To our knowledge, this is the first study to evaluate the impact of IMCI-related digital CDSS on health outcomes when implemented at scale in a programmatic context in resource-constrained settings

- Large prospective observational study, recruiting 1021 children from 45 intervention primary healthcare facilities and 908 children from 44 routine care facilities with high rates of follow-up completion at Day 7 for primary outcome assessment

- Though we adjusted for important potential confounders within the analysis, the nature of the evaluation in the context of large-scale implementation meant that it was not possible to randomise facilities, therefore contextual differences may have influenced our findings

- Despite the use of standardised tools and procedures, performance or detection bias could have occurred given that the intervention could not be blinded
INTRODUCTION

Global health initiatives place high expectations on digital technology to improve quality of care (QoC) in low- and middle-income countries (LMICs).[1,2] One promising approach is the implementation of digital Clinical Decision Support Systems (CDSS) for health care providers (HCPs) in remote regions and resource-constrained settings.[3,4] CDSS guide HCPs through clinical consultations with simple, structured, step-by-step decision logic, providing them with evidence-based diagnostic and treatment recommendations, displayed on a handheld digital device.

Effective, safe and person-centred QoC is essential to achieve universal health coverage.[5] To improve QoC for children under five years, WHO developed the Integrated Management of Childhood Illness (IMCI) guidelines,[6] now a standard for Primary Health Care (PHC) consultations in over 100 LMICs. It focuses on diagnosis, classification and treatment of conditions responsible for 70% of child mortality (malaria, pneumonia, diarrhoea, measles, and malnutrition). Evidence suggests that IMCI can improve QoC and reduce under-five mortality,[7–9] but its roll-out over the past two decades has not yielded the anticipated effect.[10] The reasons are manifold,[11–13] but non-adherence of HCPs to guidelines, possibly due to the difficulty of practical integration into the clinical workflow, plays a central role.[14–16]

While adherence to guidelines may be improved by providing them in a digital CDSS-format,[17–21] systematic reviews assessing the impact of such digital tools on health outcomes show heterogeneous results: some report improvements in certain QoC indicators,[3] others have shown little to no effect of CDSS use on morbidity and mortality.[22] Several IMCI-based CDSS are now available on smartphones or tablets.[23] Their efficacy has been demonstrated in clinical trial settings,[24,25] but evidence on effectiveness at larger scale, particularly in programmatic settings (i.e. under real-world conditions) is limited.[26]

In this study, we explore the impact of a digital IMCI-based CDSS, the ALgorithm for the MANAgement of CHildhood illness (ALMANACH), on clinical outcomes and QoC in the programmatic setting. ALMANACH was first developed and evaluated from 2010-2014 to address clinical management of febrile children (age two to 59 months) in Tanzania.[27] Controlled trials have demonstrated acceptance among end-users,[28] and clinical efficacy.[25,29]

ALMANACH was then further adapted for the programmatic setting of PHC clinics in Afghanistan and Nigeria, respecting national IMCI protocols, latest evidence, local epidemiology, and the daily work reality of the health facilities (Figure 1).[30] Evaluation of ALMANACH after one year of implementation showed good acceptance by HCPs, improved completeness of clinical assessment, better adherence to treatment recommendations, and reduced antibiotic prescription rates.[31]

The objective of this study was to evaluate the hypothesis that ALMANACH improves recovery of children from acute illness and QoC outcomes when implemented at scale in routine practice at primary care facilities.

METHODS

Study design and participants

We conducted a prospective observational study within the programmatic context of ALMANACH in Adamawa State, a conflict-torn region in North-Eastern Nigeria. Implementation, including the tablet-based CDSS, training and supportive supervision, began in the region in 2016. Government PHC facilities in four local government areas (LGAs) implementing ALMANACH and four LGAs implementing routine care (paper-based IMCI) were considered for inclusion. Facilities were excluded if they were: inaccessible (security or road issues); part of a larger facility (e.g. hospital outpatient departments); or involved in another major child health intervention.

Children 2-59 months of age who presented to a study facility during the data collection period with an acute illness were eligible for inclusion. Children attending for routine care only, physical trauma, or mental health problems were excluded as these consultations are not addressed by ALMANACH.

Patient and Public Involvement

Community engagement prior to and during the study was built on existing long-term relationships with community representatives from the LGAs and Ward Development Committees (WDCs). Representatives were consulted on the purpose and conduct of the study, with detailed consultation on the recruitment strategy, particularly in relation to
informed consent, though patients were not specifically involved in the study design. Planned dissemination activities include sharing of the findings with LGA and WDC representatives, and patients and the communities through an information campaign at the health facilities.

**Informed consent and ethical approval**

Caregivers of eligible children were recruited following informed consent. Verbal informed consent was obtained if the caregiver was willing to participate but not willing to provide written/thumbprint consent. This approach was taken as local community leaders advised that signing documents is regarded with suspicion both due to illiteracy and the high proportion of internally displaced people with identity protection concerns. No incentives were provided for participation. The study obtained ethical approval from the Health Research Ethics Committee of Adamawa, Nigeria (ADHREC 8/02/2020/003) and the Ethics Committee Northwest and Central Switzerland (Req-2020-00082).

**Procedures**

At each facility, trained non-clinical research assistants collected basic information about the facility amenities and services, and the training and experience of HCPs consulting children under five years of age (after informed consent).

Research assistants obtained basic sociodemographic details, main symptoms and information about prior care sought from caregivers whilst awaiting consultation. Brief exit interviews were conducted to record medication (prescription or medication in-hand), diagnosis and management advice as understood by the caregiver.

In ALMANACH facilities, consultation data (diagnosis, measurements, and investigations) were extracted from the CDSS database. In routine care facilities, consultation data were obtained from facility registries immediately after the consultation.

On day seven, research assistants conducted a standardised health outcome assessment by phone. If unsuccessful, further attempts were made on three consecutive days. If the caregiver was not reachable by phone, contact was attempted through a community representative. Children of caregivers not contactable by day ten were considered lost to follow-up. For follow-up occurring after day seven, caregivers were asked to reflect the status of the child on day seven.

Data collection was conducted in ALMANACH and routine care facilities in parallel, one LGA at a time within each group. All eligible facilities in the first three LGAs in each group were included; in the last LGAs (Hong and Song), the most accessible facilities out of those eligible were selected until the target sample size was reached. Data collection lasted three weeks per LGA, occurring from 3rd to 28th March and 17th July to 30th September 2020, with a forced interruption due to the SARS-CoV2 pandemic.

**Outcomes**

The primary outcome was day 7 caregiver-reported recovery, assessed at phone follow-up. Secondary outcomes were antibiotic and antimalarial prescription during the consultation, referral to hospital, and communication of diagnosis and follow-up advice to the caregiver, as assessed at exit interview.

**Statistical analysis**

The sample size to detect a difference in recovery from 60% in routine care to 70% in ALMANACH facilities was estimated with 85% power and 0.05 significance threshold, assuming a standard deviation of 10 percentage points of cure rates between facilities. To allow flexibility according to the fluctuating security situation, we calculated sample size for a range of cluster numbers, estimating that we would require between 48 and 42 facilities per study arm.

We examined imbalances in patients’ and HCPs’ characteristics between ALMANACH and routine care facilities using appropriate statistical tests. For each endpoint, we calculated its frequency in ALMANACH and routine care facilities separately. The ratio of these frequencies (risk ratio, RR) was used as the measure of the association between being treated in an ALMANACH facility and the endpoint. We also calculated the corresponding odds ratios (OR) as well as the 95%-confidence intervals (CI) for both measures.

Mixed logistic regressions were used to estimate adjusted odds ratios for each endpoint. The pre-specified set of adjustments for the analysis of the primary endpoint (recovery) consisted of child’s age, sex, the collection period (pre- and post-Covid-19 related restrictions), symptom duration, travel time to the facility, whether the child was
accompanied by their mother, presence or absence of five main symptoms, the qualification of the HCP and three facility-level variables: distance from a paved road and from the referral hospital (less or more than 30 minutes), and the average monthly number of consultations. Due to the observed imbalance between the study arms, we adjusted for whether care was sought in the two weeks preceding the consultation. The same set of variables was used to adjust the association of ALMANACH with the prescription of parenteral and oral antimicrobial treatment. Owing to the small number of cases, the analyses of referral to hospital, antibiotic, and antimalarial treatment were adjusted only for sex, age, collection period, HCP’s qualification and symptoms. Regressions included a random effect for the health worker nested in a random effect for the health facility.

Analyses of communication by the HCP to the child’s caregiver on diagnosis and follow-up were performed using negative binomial regression. The number of such consultations for every HCP was the dependent variable. The logarithm of the total number of consultations performed by the HCP during the study was included with its coefficient constrained to 1, thus the adjusted estimate can be interpreted as a rate ratio. All HCP and facility-level variables mentioned above were used to adjust.

To ensure that our estimates were not affected by loss to follow-up, we applied inverse probability weighting. The probability model to derive the weights was constructed using LASSO.[32] All reweighted estimates were virtually identical (within 0.05) to those from unweighted regressions, and thus we report only the latter.

Lastly, we conducted exploratory descriptive analysis of clinical records (from the ALMANACH database and from paper records in non-ALMANACH facilities) to further assess care processes. The decision logic of ALMANACH prompts direct referral when criteria for very severe disease are met, and differentiates certain assessments according to the presence or absence of fever and certain other symptoms and signs (Error! Reference source not found.). Subsequently, the denominators reported for variables in the analysis of care processes were considered as ‘indicated according to the algorithm’, whereas in routine care the denominator was considered as ‘indicated according to IMCI’.

All calculations were performed using Stata 16. We used the STROBE cohort checklist when writing our report.[33]

RESULTS

We recruited children from 89 PHC facilities (45 ALMANACH, 44 routine care). Out of 4148 children screened, we enrolled 1929 (46·5%), of whom 1021 (52·9%) were consulted in ALMANACH facilities and 908 (47·1%) in routine care facilities (figure 2).

About half of the enrolled children (48·4%) were under two years old, and 48·7% were female. The most commonly reported symptoms were fever (87·2%), cough/breathing problems (35·3%), diarrhoea (31·1%), and vomiting (30·8%). Children most frequently attended between two and seven days from symptom onset (41·2%). In both groups, children had commonly received medication for their illness within 2 weeks prior to the consultation (53·2% in ALMANACH and 57·4% in routine care facilities), mostly from patent medicine stores or pharmacies (43·1% vs 43·7% respectively). The majority of patients (76·0%) lived within 30 minutes travel of the health facility.

Provider cadre was most commonly Community Health Extension Workers (CHEWs) or Community Health Officers (CHOs) (49·3% ALMANACH vs 43·8% routine care) followed by Junior CHEWs (25·7% vs. 20·3% respectively). Over one third of HCPs (34·0% in ALMANACH and 39·2% in routine care facilities) had never received IMCI training. Participant, facility and HCP characteristics are shown in table 1, with additional detail in appendix 1.
| Children & care-seeking | ALMANACH | Routine care | p value | Total |
|-------------------------|----------|-------------|---------|-------|
|                         | n (%)    | n (%)       |         |       |
| Pre-SARS-CoV2 (March 2020) | 343 (61·4) | 216 (38·6) | < 0·001 * | 559 (100) |
| During SARS-CoV2 (Jul-Sep 2020) | 678 (49·5) | 692 (50·5) |         | 1370 (100) |

| Age in months |          |          |         |       |
|---------------|----------|----------|---------|-------|
| 2 to 5        | 105 (10·3) | 101 (11·1) | 206 (10·7) |
| 6 – 11        | 140 (13·7) | 118 (13·0) | 258 (13·4) |
| 12 – 23       | 256 (25·1) | 213 (23·5) | 469 (24·3) |
| 24 – 59       | 508 (49·8) | 453 (49·9) | 961 (49·8) |
| Unknown       | 12 (1·2)  | 23 (2·5)  | 35 (1·8)  |

| Sex |          |          |         |       |
|-----|----------|----------|---------|-------|
| Female | 483 (47·3) | 456 (50·2) | 939 (48·7) |
| Male | 526 (51·5) | 429 (47·3) | 955 (49·5) |
| Unknown | 12 (1·2)  | 23 (2·5)  | 35 (1·8)  |

| Presenting symptoms |          |          |         |       |
|---------------------|----------|----------|---------|-------|
| Fever | 899 (88·1) | 783 (86·2) | 1,682 (87·2) |
| Cough / difficulty breathing | 369 (36·1) | 312 (34·4) | 681 (35·3) |
| Diarrhoea | 317 (31·1) | 283 (31·2) | 600 (31·1) |
| Vomiting | 329 (32·2) | 264 (29·1) | 593 (30·8) |
| Skin | 41 (4·0) | 55 (6·1) | 96 (5·0) |
| Other | 333 (36·7) | 371 (36·5) | 704 (36·5) |

| Onset of symptoms prior to consultation |          |          |         |       |
|-----|----------|----------|---------|-------|
| Same or previous day | 265 (26·0) | 275 (30·3) | 540 (28·0) |
| 2 days to < 1 week | 439 (43·0) | 362 (39·9) | 801 (41·5) |
| 1 – 2 weeks | 230 (22·5) | 194 (21·4) | 424 (22·0) |
| ≥ 2 weeks | 76 (7·4) | 63 (6·9) | 139 (7·2) |
| Unknown | 11 (1·1)  | 14 (1·5)  | 25 (1·3)  |

| Treatment in last 2 weeks |          |          |         |       |
|---------------------------|----------|----------|---------|-------|
| Yes | 543 (53·2) | 521 (57·4) | 1,064 (55·2) |
| No | 474 (46·4) | 379 (41·7) | 853 (44·2) |
| Unknown | 4 (0·4)  | 8 (0·9)  | 12 (0·6)  |

| Reported travel time to facility |          |          |         |       |
|---------------------------------|----------|----------|---------|-------|
| < 30 minutes | 696 (68·2) | 770 (84·8) | 1,466 (76·0) |
| ≥ 30 minutes | 307 (30·1) | 128 (14·1) | 435 (22·6) |
| Unknown | 18 (1·8) | 10 (1·1) | 28 (1·5) |

| Health care providers |          |          |         |       |
|-----------------------|----------|----------|---------|-------|
| CHEW / CHO | 71 (49·3) | 67 (43·8) | 138 (46·5) |
| Junior CHEW | 37 (25·7) | 31 (20·3) | 68 (22·9) |
| Nurse / midwife | 2 (1·4) | 4 (2·6) | 6 (2·0) |
| Other | 34 (23·6) | 51 (33·4) | 85 (28·6) |

| Last IMCI training received (date) |          |          |         |       |
|-----------------------------------|----------|----------|---------|-------|
| <1 year ago (2020) | 1 (0·7) | 3 (2·0) | 4 (1·4) |
| 1 – 2 years ago (2018, 2019) | 55 (38·2) | 41 (26·8) | 96 (32·3) |
| 3 – 4 years ago (2016, 2017) | 17 (11·8) | 22 (14·4) | 39 (13·1) |
| ≥ 5 years ago (prior to 2016) | 9 (6·3) | 13 (8·5) | 22 (7·4) |
| Never | 49 (34·0) | 60 (39·2) | 109 (36·7) |
| Unknown | 13 (9·0) | 14 (9·2) | 27 (9·1) |

| Health facilities |          |          |         |       |
|-------------------|----------|----------|---------|-------|
| Distance from referral hospital |          |          |         |       |
| < 30 minutes | 16 (35·6) | 20 (45·5) | 36 (40·5) |
| ≥ 30 minutes | 29 (64·4) | 24 (54·6) | 53 (59·6) |

| No. consultations children (U5) at facility / month |          |          |         |       |
|-----------------------------------------------------|----------|----------|---------|-------|
| 0 – 99 | 15 (33·3) | 22 (50·0) | 37 (41·6) |
| 100 – 199 | 16 (35·6) | 15 (34·1) | 31 (34·8) |
| ≥ 200 | 11 (24·4) | 4 (9·1) | 15 (16·9) |
| Unknown | 3 (6·7) | 3 (6·8) | 6 (6·7) |

| Health facility power supply |          |          |         |       |
|------------------------------|----------|----------|---------|-------|
| All day (no interruptions) | 7 (15·6) | 4 (9·1) | 11 (12·4) |
| All day (interruptions) | 10 (22·2) | 15 (34·1) | 25 (28·1) |
| ≤ Half a day | 17 (37·8) | 16 (36·4) | 33 (37·1) |
Day 7 recovery rates differed markedly between ALMANACH and routine care. In ALMANACH facilities, 849 (85.4%) of 994 children with complete follow-up were reported to have fully recovered. In routine care facilities, 603 (71.4%) of 845 children were reported fully recovered. The odds ratio (OR) for day 7 recovery between groups was 2.34 (95% CI = 1.87-2.96) and 2.63 (1.60-4.32) after adjusting as described above.

For most secondary outcomes, we observed large differences between ALMANACH and routine care. HCPs referred patients to higher level of care over three times more often in the ALMANACH group (RR = 3.25 (2.12-4.96)). We saw an increase in parenteral antimicrobial prescription and a decrease in oral antimicrobial prescription in ALMANACH facilities, with adjusted odds ratios of 2.42 (1.00-5.85) and 0.40 (0.22-0.73), respectively. Differentiating antimicrobials into antibiotic and antimalarial treatment revealed that in ALMANACH facilities 120 (12.4%) of 966 children received parenteral antimalarials compared to 59 (6.9%) of 855 in routine care facilities; for parenteral antibiotics the respective difference was 56 (5.8%) of 966 vs 25 (2.9%) of 855. Oral antimalarial prescription rate was lower in ALMANACH facilities: 476 (49.3%) of 966 compared to 490 (57.3%) of 855 cases in routine care. There was no significant difference in oral antibiotic prescription between the groups (ALMANACH: 290 (30.0%) of 966 vs. routine care: 291 (34.0%) of 855).

The intervention affected the communication of diagnosis and follow-up advice to caregivers. In ALMANACH facilities 811 (84.0%) of 966 caregivers reported that HCPs explained the child’s diagnosis to them compared to only 557 (65.1%) of 855 in routine care facilities. The likelihood of receiving follow-up advice by the HCP was also much higher in ALMANACH facilities, with 596 (61.7%) of 966 families advised vs 179 (20.9%) of 855 in facilities without ALMANACH. Adjusted associations were very similar.

Lastly, we analysed differences in proportions of key diagnoses (according to IMCI protocols) made by HCPs in both groups. Pneumonia, diarrhoea, malnutrition, anaemia and suspected malaria were markedly more often diagnosed in ALMANACH facilities. Only the rates of diagnosis of malaria confirmed through rapid diagnostic tests were similar between ALMANACH and routine care groups. All estimates are summarised in Table 2.

### Table 1: Study sample characteristics: sociodemographic data, illness characteristics, information on health care providers, and health facilities

|                          | CHEW | CHO | U5 | Multiple answers possible | Chi-squared test | Fisher’s exact test |
|--------------------------|------|-----|----|---------------------------|------------------|---------------------|
| No electricity source    | 6 (13·3) | 8 (18·2) | 14 (15·7) |                           |                  |                     |
| Unknown                  | 5 (11·1) | 1 (2·3) | 6 (6·7) |                           |                  |                     |
| Health facility water supply |       |     |    |                           |                  |                     |
| Piped                    | 2 (4·4) | 2 (4·6) | 4 (4·5) |                           |                  |                     |
| Pump / well              | 33 (73·3) | 23 (52·3) | 56 (62·9) |                           |                  |                     |
| None                     | 7 (15·6) | 18 (40·9) | 25 (28·1) |                           |                  |                     |
| Unknown                  | 5 (11·1) | 1 (2·3) | 6 (6·7) |                           |                  |                     |
| Outages                  | 7 (15·6) | 10 (22·7) | 17 (19·1) |                           |                  |                     |

|                          | Parenteral antibiotics | Parenteral antimalarials |
|--------------------------|------------------------|--------------------------|
|                          | 10 (22·2) | 15 (34·1) | 25 (28·1) |
|                          | 15·6 | 31·8 | 23·6 |

Table 1: Study sample characteristics: sociodemographic data, illness characteristics, information on health care providers, and health facilities

CHEW = Community Health Extension Worker  CHO = Community Health Officer

U5 = Under five years of age

1 Multiple answers possible

# Chi-squared test

## Fisher’s exact test
Comparative analysis of ALMANACH and record data indicated further differences between the groups in care process outcomes. In ALMANACH facilities, 850 (8.3%) of 1021 consultations were conducted using ALMANACH. When ALMANACH was used, 850 (100%) children were screened for IMCI danger signs, 847 (99.6%) had a recorded weight, MUAC was recorded in 718 (99.9%) of 719 indicated, temperature recorded in 714 (95.1%) of 751 indicated, and pallor assessed in 745 (100%) of 745 indicated. In routine care facilities, we found no documentation of danger signs, 197 (21.7%) of 908 had a recorded weight, MUAC was recorded in 52 (6.6%) of 784 children 6 to 59 months old, and temperature in 469 (51.7%) of 908 cases. Using malaria assessment and treatment as an example of adherence to guidelines, we found lower effectiveness decay through the care pathway in ALMANACH compared to routine care facilities (Error! Reference source not found.).

**DISCUSSION**

This prospective observational study found significant improvements in caregiver-reported recovery of children seven days after primary care consultation associated with the implementation of the ALMANACH digital CDSS in a programmatic setting. This impact on health outcomes is likely mediated by better adherence to evidence-based guidelines, supported by demonstrated improvements in QoC process outcomes across assessment, diagnosis, and management.

**Table 2: Primary and secondary outcomes**

| Outcome                        | ALMANACH facilities cases | Routine care facilities cases | Unadjusted effect estimate | 95%-CI for unadjusted effect | Adjusted effect estimate | 95%-CI for adjusted effect |
|--------------------------------|---------------------------|-------------------------------|---------------------------|-------------------------------|--------------------------|----------------------------|
| Recovery after 7 days          | 849 994 85.4%             | 603 845 71.4%                 | RR 1.20                   | 1.14-1.26                     | RR 2.34                  | 1.87-2.96                  |
| Referral to hospital           | 96 1009 9.5%              | 26 861 3.0%                   | RR 3.25                   | 2.12-4.96                     | RR 3.48                  | 2.24-5.41                  |
| Diagnosis communicated to caregiver | 811 966 84.0%       | 557 855 65.1%                 | RR 1.29                   | 1.22-1.36                     | RR 1.27                  | 1.13-1.42                  |
| Follow-up advice given to caregiver | 596 966 61.7%      | 179 855 20.9%                 | RR 2.95                   | 2.56-3.39                     | RR 2.76                  | 2.12-3.58                  |
| Parenteral antimicrobial treatment | 164 966 17.0%        | 80 855 9.4%                   | RR 1.81                   | 1.42-2.33                     | RR 1.98                  | 1.41-2.63                  |
| Oral antimicrobial treatment   | 620 966 64.2%             | 636 855 74.4%                 | RR 0.62                   | 0.50-0.76                     | RR 0.86                  | 0.81-0.92                  |
| Parenteral antimalarial treatment | 120 966 12.4%        | 59 855 6.9%                   | RR 1.80                   | 1.34-2.42                     | N/A                      |                            |
| Oral antimalarial treatment    | 476 966 49.3%             | 490 855 57.3%                 | RR 0.86                   | 0.79-0.94                     | N/A                      |                            |
| Parenteral antibiotic treatment | 56 966 5.8%            | 25 855 2.9%                   | RR 1.98                   | 1.25-3.15                     | N/A                      |                            |
| Oral antibiotic treatment      | 290 966 30.0%             | 291 855 34.0%                 | RR 0.88                   | 0.77-1.01                     | N/A                      |                            |
| Suspected malaria              | 70 811 8.6%               | 77 557 13.8%                  | RR 0.62                   | 0.46-0.85                     | N/A                      |                            |
| Confirmed malaria              | 525 811 64.7%             | 363 557 65.2%                 | RR 0.99                   | 0.92-1.08                     | N/A                      |                            |
| Pneumonia                      | 59 811 7.3%               | 5 557 0.9%                    | RR 8.10                   | 3.27-20.06                    | N/A                      |                            |
| Diarrhea                       | 118 811 14.5%             | 46 557 8.3%                   | RR 1.76                   | 1.28-2.43                     | N/A                      |                            |
| Malnutrition                   | 57 811 7.0%               | 7 557 1.3%                    | RR 5.60                   | 2.57-12.17                    | N/A                      |                            |
| Anemia                         | 31 811 3.8%               | 3 557 0.5%                    | RR 7.10                   | 2.18-23.10                    | N/A                      |                            |

RR = Risk ratio; OR = Odds ratio; CI = confidence interval; N/A = not applicable

1 Adjusted rate ratio from negative binomial regression (see statistical analysis)
2 8 observations not used due to complete separation
In children for whom ALMANACH was used, we found almost complete adherence to key IMCI assessments. In contrast, in routine care facilities in this study, and other studies on IMCI-related quality of care, HCPs commonly complete assessments in fewer than 50% of consultations with sick children.[34,35] We posit that this adherence to IMCI assessments, guided by ALMANACH, led to an increase in severe illness detection, and of diagnoses that are important causes of morbidity and mortality, particularly pneumonia, anaemia, diarrhoea, and malnutrition.

In turn, we observed higher rates of referral and of treatment with parenteral antimicrobials, indicative of increased recognition and management of severe illness. Inadequate identification and treatment of severe disease are major barriers to reducing child mortality in LMICs.[36,37] Whilst the proportion of children with severe disease varies substantially between and within countries, with estimates varying from 5-21% in studies from comparable settings,[35,38] the 3.0% referral rate reported by caregivers in routine care facilities in this study is likely to be inappropriately low, and the 9-5% ALMANACH referral rate more consistent with the clinical need.

Further, ALMANACH significantly improved HCP communication with caregivers as evidenced by increased awareness of diagnosis and follow-up advice at exit interviews in ALMANACH facilities. Communication about a child’s illness and treatment are key standards set out by WHO for improving QoC for children at health facilities, and are associated with higher satisfaction with and intention to return to care.[5,39] In ALMANACH facilities, caregivers were made aware of diagnosis in 84.0% and given follow-up advice in 61-7% of consultations, substantially higher than in routine care facilities (65-1% and 20-9% respectively) and in multi-country IMCI studies in sub-Saharan African countries (43-70% and 20-57% respectively).[34,39]

These findings of increased adherence to key evidence-based practices are consistent with other studies of child health-related CDSS in resource-constrained settings, including ALMANACH.[19–21,29–31] Lack of training, and other knowledge gaps such as difficulty recalling specific criteria (e.g. respiratory rate cut-offs) contribute to low adherence to IMCI, as do low motivation and physical and cognitive overload associated with working in such challenging settings.[12] Qualitative feedback from HCPs suggests that IMCI-related CDSS can improve confidence in diagnoses and managements, strengthen motivation, and address the issue of cognitive overload through the step-by-step nature of the guidance tailored to individual patients, particularly for severity classification and drug dosing.[17,28]

But whilst increased adherence to guidelines has been consistently demonstrated, few studies have assessed the impact of IMCI-related CDSS on health outcomes and, to our knowledge, none in the context of a long-term, large-scale implementation. The ALMANACH controlled trial in Tanzania also found an increase in day seven recovery, though from a higher baseline of 92.0% in routine care to 97.3% in ALMANACH facilities.[25] This is relatively high compared to the day seven recovery rates we saw in this study (71.4% in routine care and 85.4% in ALMANACH facilities). The contextual differences in sociodemographic, epidemiological and health system factors are likely to account for this, though a more substantial Hawthorne effect may also have been in effect as data was collected inside the consultation room in the Tanzania study.

This study demonstrates that implementation of ALMANACH can deliver impact on health outcomes at scale in remote, resource-constrained PHC facilities, where drug stock-outs are common, many facilities lack basic amenities, and one third of HCPs have never received IMCI training. A recent systematic review and meta-analysis found only modest changes in health outcomes with CDSS implementation.[40] Most of the CDSS studies included in this review were implemented in high-income countries, where HCP’s access to resources is substantially higher than most PHCs implementing IMCI. This may indicate that CDSS can deliver most value when used to support HCPs with limited skills and resources, provided that they are appropriately contextualised and implemented.

In contrast with earlier ALMANACH studies,[29–31] we did not find a significant reduction in antibiotic prescription rates. Oral antibiotics were prescribed to 30.0% of children in ALMANACH and 34.0% in routine care facilities, slightly lower than the 43.1% (33.2–50.5) found in a recent meta-analysis of reported antibiotic use for sick children in LMICs. However, these may not reflect true antibiotic consumption rates given that most caregivers also reported treatment prior to consultation, most commonly from patent medicine stores or pharmacies. With increasing antibiotic prescription rates for children under five years of age, rising fastest in low-income countries, antimicrobial stewardship remains a global health priority to mitigate individual adverse events, rising antimicrobial resistance and resource waste.[41,42] Further gains in antimicrobial stewardship may be possible to achieve through integrating host biomarkers into IMCI-related CDSS.[24]
Our study has several limitations. Due to the nature of the evaluation in the programmatic setting, facilities were not randomised to ALMANACH or routine care. The presence of a large-scale child health intervention in some LGAs, combined with security- and weather-related accessibility issues, limited the number of suitable LGAs for the control group. Contextual differences including in epidemiology, health-seeking behaviour and the health system may therefore have influenced our data, though we adjusted for important potential confounders within the analysis.

Further, the intervention could not be blinded, so performance or detection bias could have occurred, despite the use of standardised tools and procedures. The Hawthorne effect may have influenced the data, which has been found to increase patient-reported quality of care by 13%. [43] The observer effect should be similar in both intervention and routine care facilities, although there is a possibility that a differential effect could occur if the tablet were used more than usual in ALMANACH facilities. To reduce the likelihood of influencing HCP performance, we avoided direct observation and only collected information from caregivers and records. This may have affected data quality due to the reliance on exit interviews potentially subject to recall or response bias caused by social desirability, gratitude or negative emotions, and the reliance on written clinical information, which may not reflect actual assessments or treatments. Lastly, given the complex nature of the intervention, incorporating the tablet-based CDSS along with training, mentorship and data feedback, we cannot determine the effect of the CDSS itself vs the entire intervention package. However, it is unlikely that training alone accounts for the difference in outcomes given that there was no major difference between groups in time since most recent IMCI training.

In conclusion, we found substantial impact of this IMCI-related CDSS on health and QoC outcomes, demonstrating that earlier findings in controlled or small-scale studies can be achieved at scale in a resource-constrained setting. Positive effects were seen across a range of process and outcome indicators, including assessment, diagnosis, treatment, and communication. These findings support the implementation of digital CDSS in resource-constrained settings as a means to strengthen progress towards universal health coverage.
AUTHOR CONTRIBUTIONS

Torsten Schmitz (TS), Fenella Beynon (FB), Capucine Musard (CM), Marek Kwiatkowski (MK), Marco Landi (ML), Daniel Ishaya (DI), Jeremiah Zira (JZ), Muazu Muazu (MM), Camille Renner (CR), Edwin Emmanuel (EE), Solomon Gideon Bulus (SB), Rodolfo Rossi (RR).

FB, TS, RR, MK, and ML conceived the study’s concept and designed its methodology. CM, CR, MM, FB, TS and DI designed and developed the data collection tools. ML, CM, CR, DI, EE, JZ, and MM realised the study implementation, training of data collectors, and monitored the data collection in the field. Statistical analyses were done by MK with contributions from RR and FB. CM and CR verified the underlying data. FB, TS, RR, CM and MK interpreted the results. The original manuscript was written by TS, FB, and CM with contributions from MK and RR, and the final version was reviewed and approved by all authors. The joint first authors FB and TS contributed equally to this paper.

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COMPETING INTERESTS

All authors declare no competing interest.

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DATA SHARING

Anonymised participant data can be made available from the publication date upon reasonable request to the corresponding author (TS), subject to completion of a data sharing agreement and approval from the Adamawa State Primary Health Care Development Agency.

PATIENT CONSENT AND ETHICAL APPROVAL

All caregivers of eligible children who participated in this study gave their informed consent before participating. The study obtained ethical approval from the Health Research Ethics Committee of Adamawa, Nigeria (ADHREC 8/02/2020/003) and the Ethics Committee Northwest and Central Switzerland (Req-2020-00082).
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ALMANACH LGAs: Lamurde, Jada, Gombi, Hong
Routine care LGAs: Numan, Guyuk, Shelleng, Song

ALMANACH PHC facilities
n = 45
Children screened
n = 2244
Children enrolled
n = 1021
Day 7 follow-up
n = 994

Routine care PHC facilities
n = 44*
Children screened
n = 1904
Children enrolled
n = 908
Day 7 follow-up
n = 845

Excluded
Age n = 211
Routine preventative care n = 744
Trauma n = 30
No consent n = 1
Other n = 10

Excluded
Age n = 314
Routine preventative care n = 858
Trauma n = 30
No consent n = 4
Other n = 17
Figure 3: Comparison of systems effectiveness decay for malaria assessment and treatment in ALMANACH and routine care facilities. Steps reflecting adherence to guidelines shown in blue, non-adherence shown in red, and not applicable in grey.
## ANNEX

### Annex 1: Patients and family sociodemographic data and care seeking information, health care provider and health facility characteristics

| Children & care-seeking | ALMANACH n (%) | Routine care n (%) | p value | Total n (%) |
|-------------------------|----------------|--------------------|---------|-------------|
| Pre-SARS-CoV2 (March 2020) | 343 (61·4) | 216 (38·6) | < 0·001 * | 559 (100) |
| During SARS-CoV2 (Jul-Sep 2020) | 678 (49·5) | 692 (50·5) | 0·02 * | 1370 (100) |

### Age in months

| Age in months | 2 to 5 | 6 – 11 | 12 – 23 | 24 – 59 | Unknown |
|---------------|--------|--------|---------|---------|---------|
| 105 (10·3) | 101 (11·1) | 213 (23·5) | 453 (49·9) | 23 (2·5) | 206 (10·7) |

### Sex

| Sex | Male | Female | Other |
|-----|------|--------|-------|
| 526 (51·5) | 483 (47·3) | 508 (49·8) | 939 (48·7) |

### Presenting symptoms

| Presenting symptoms | Fever | Cough / difficulty breathing | Diarrhoea | Vomiting | Skin | Other |
|---------------------|-------|-------------------------------|-----------|---------|------|-------|
| 899 (88·1) | 369 (36·1) | 317 (31·1) | 329 (32·2) | 41 (4·0) | 333 (36·7) | 1,682 (87·2) |

### Onset of symptoms prior to consultation

| Onset of symptoms prior to consultation | Same or previous day | 2 days to < 1 week | 1 – 2 weeks | ≥ 2 weeks | Unknown |
|----------------------------------------|---------------------|-------------------|-------------|-----------|---------|
| 265 (26·0) | 275 (30·3) | 783 (86·2) | 230 (22·5) | 76 (7·4) | 11 (1-1) | 540 (28·0) |

### Treatment in last 2 weeks

| Treatment in last 2 weeks | Yes | No | Unknown |
|---------------------------|-----|----|---------|
| 543 (53·2) | 474 (46·4) | 4 (0·4) | 1064 (55·2) |

### Source of previous treatment

| Source of previous treatment | Same facility | Other facility | Pharmacy / patent medicine store | Traditional healer | Informal (drug peddler / other) | Friend relatives/community | Unknown |
|------------------------------|---------------|---------------|---------------------------------|-------------------|---------------------------------|---------------------------|---------|
| 31 (3·0) | 56 (6·2) | 440 (43·1) | 22 (2·2) | 15 (1·5) | 4 (0·4) | 478 (46·8) | 87 (4·5) |

### Reported travel time to facility

| Reported travel time to facility | < 30 minutes | ≥ 30 minutes | Unknown |
|----------------------------------|--------------|--------------|---------|
| 696 (68·2) | 307 (30·1) | 18 (1·8) | 1,466 (76·0) |

### Accompanying caregiver

| Accompanying caregiver | Mother | Other |
|------------------------|--------|-------|
| 767 (75·1) | 254 (24·9) | 1,429 (74·1) |

### Mother’s educational level

| Mother’s educational level | No schooling | Primary | Secondary | Higher | Unknown |
|----------------------------|--------------|---------|-----------|--------|---------|
| 350 (34·3) | 124 (12·1) | 252 (24·7) | 38 (3·7) | 257 (25·2) | 631 (32·7) |

### No. children <5 in household

| No. children <5 in household | 1 – 2 | 3 – 4 | ≥ 5 | Unknown |
|------------------------------|------|------|-----|---------|
| 643 (63·0) | 211 (20·7) | 110 (10·8) | 57 (5·6) | 1260 (65·3) |

### Health care providers

| Health care providers | CHW / CHO | Other |
|-----------------------|-----------|-------|
| 144 (48·5) | 153 (51·5) | 297 (100) |
| Category                                      | CHEW  | Nurse / midwife | Other | Total |
|----------------------------------------------|-------|-----------------|-------|-------|
| Era                                         |       |                 |       |       |
| <1 year (2020)                              | 4     | 2 (2·8)         | 34    | 54    |
| 1 – 4 years (2016-2019)                     | 36    | (25·0)          | 44    | 80    |
| ≥ 5 years ago (prior to 2016)               | 91    | (63·2)          | 90    | 181   |
| Unknown                                     | 13    | (9·0)           | 14    | 27    |
| **Years of experience consulting children under 5 years (period)** |       |                 |       |       |
| <1 year (2020)                              | 1     | (0·7)           | 3     | 4     |
| 1 – 2 years ago (2018, 2019)                | 55    | (38·2)          | 41    | 96    |
| 3 – 4 years ago (2016, 2017)                | 17    | (11·8)          | 22    | 39    |
| ≥ 5 years ago (prior to 2016)               | 9     | (6·3)           | 13    | 22    |
| Never                                       | 49    | (34·0)          | 60    | 109   |
| Unknown                                     | 13    | (9·0)           | 14    | 27    |
| **HCPs’ last IMCI training (date)**         |       |                 |       |       |
| <1 year ago (2020)                          | 1     | (0·7)           | 3     | 4     |
| 1 – 2 years ago (2018, 2019)                | 55    | (38·2)          | 41    | 96    |
| 3 – 4 years ago (2016, 2017)                | 17    | (11·8)          | 22    | 39    |
| ≥ 5 years ago (prior to 2016)               | 9     | (6·3)           | 13    | 22    |
| Never                                       | 49    | (34·0)          | 60    | 109   |
| Unknown                                     | 13    | (9·0)           | 14    | 27    |
| **Date of ALMANACH training**               |       |                 |       |       |
| 2020                                        | 17    | (11·8)          | 2     | 19    |
| 2019                                        | 90    | (62·5)          | 1     | 91    |
| 2018                                        | 6     | (4·2)           | 0     | 6     |
| Never                                       | 31    | (21·5)          | 140   | 181   |
| **Health facilities**                       | 45    | (50·6)          | 44    | 89    |
| **Distance from main road**                 |       |                 |       |       |
| < 30 minutes                                | 32    | (71·1)          | 33    | 65    |
| ≥ 30 minutes                                | 13    | (28·9)          | 11    | 24    |
| **Distance from referral hospital**         |       |                 |       |       |
| < 30 minutes                                | 16    | (35·6)          | 20    | 36    |
| ≥ 30 minutes                                | 29    | (64·4)          | 24    | 53    |
| **No. consultations children (U5) at facility / month** |       |                 |       |       |
| 0 – 99                                       | 15    | (33·3)          | 22    | 37    |
| 100 – 199                                    | 16    | (35·6)          | 15    | 31    |
| ≥ 200                                       | 11    | (24·4)          | 4     | 15    |
| Unknown                                     | 3     | (6·7)           | 3     | 6     |
| **Health facility power supply**            |       |                 |       |       |
| All day (no interruptions)                  | 7     | (15·6)          | 4     | 11    |
| All day (interruptions)                     | 10    | (22·2)          | 15    | 25    |
| ≤ Half a day                                | 17    | (37·8)          | 16    | 33    |
| No electricity source                       | 6     | (13·3)          | 8     | 14    |
| Unknown                                     | 5     | (11·1)          | 1     | 6     |
| **Health facility water supply**            |       |                 |       |       |
| Piped                                       | 2     | (4·4)           | 2     | 4     |
| Pump / well                                  | 33    | (73·3)          | 23    | 56    |
| None                                         | 7     | (15·6)          | 18    | 25    |
| Unknown                                     | 5     | (11·1)          | 1     | 6     |
| Outages                                     | 7     | (15·6)          | 10    | 17    |
| **Stock-outs of medicines for severe illness** |       |                 |       |       |
| Parenteral antibiotics                       | 10    | (22·2)          | 15    | 25    |
| Parenteral antimarials                       | 7     | (15·6)          | 14    | 21    |

CHEW = Community Health Extension Worker  
CHO = Community Health Officer  
U5 = Under five years of age  
* Multiple answers possible  
## Chi-squared test  
## Fisher’s exact test
# Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

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| Reporting Item   | Page Number |
|------------------|-------------|
| **Title and abstract** |             |
| Title #1a        | 1           |
| Indicate the study's design with a commonly used term in the title or the abstract |
| Abstract #1b     | 3           |
| Provide in the abstract an informative and balanced summary of what was done and what was found |
| **Introduction** |             |
| Background / rationale #2 | 5 |
| Explain the scientific background and rationale for the investigation being reported |
| Objectives #3    | 5           |
| State specific objectives, including any prespecified hypotheses |
## Methods

| Study design #4 | Present key elements of study design early in the paper | 5 |
|-----------------|--------------------------------------------------------|---|
| Setting #5      | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 5-6 |
| Eligibility criteria #6a | Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. | 5-6 |
| Eligibility criteria #6b | For matched studies, give matching criteria and number of exposed and unexposed | |
| Variables #7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 6 |
| Data sources / measurement #8 | For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable. | 6-7 |
| Bias #9 | Describe any efforts to address potential sources of bias | 6,7,12 |
| Study size #10 | Explain how the study size was arrived at | 6 |
| Quantitative variables #11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why | 6-9 |
| Statistical methods #12a | Describe all statistical methods, including those used to control for confounding | 6-7 |
| Statistical methods #12b | Describe any methods used to examine subgroups and interactions | 6-7 |
| Statistical methods #12c | Explain how missing data were addressed | 6-7 |
| Statistical methods #12d | If applicable, explain how loss to follow-up was addressed | 6-7 |
Statistical methods

Describe any sensitivity analyses

n/a

Results

Participants

Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for exposed and unexposed groups if applicable.

Participants

Give reasons for non-participation at each stage

Participants

Consider use of a flow diagram

Descriptive data

Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.

Descriptive data

Indicate number of participants with missing data for each variable of interest

Descriptive data

Summarise follow-up time (e.g., average and total amount)

Outcome data

Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.

Main results

Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included.

Main results

Report category boundaries when continuous variables were categorized

Main results

If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses

Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses
Discussion

Key results #18 Summarise key results with reference to study objectives 10-11

Limitations #19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.

Interpretation #20 Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. 10-12

Generalisability #21 Discuss the generalisability (external validity) of the study results 11

Other Information

Funding #22 Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based 13

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Effectiveness of an electronic clinical decision support system in improving the management of childhood illness in primary care in rural Nigeria: an observational study

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Effectiveness of an electronic clinical decision support system in improving the management of childhood illness in primary care in rural Nigeria: an observational study

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ABSTRACT

Introduction
Digital interventions can support health systems strengthening in resource-constrained settings. Clinical decision support systems (CDSS) provide evidence-based recommendations to health workers, tailored to individual patients, using clinical algorithms. Recent studies suggest that CDSS hold promise for the management of childhood illness in primary care, but evidence on effectiveness at scale is limited. The objective of the study was to evaluate the impact of ‘ALMANACH’, a CDSS based on the Integrated Management of Childhood Illness (IMCI), on clinical recovery from acute illness and quality of care for children (age 2-59 months) attending primary care facilities in north-eastern Nigeria.

Methods
In this observational study, we compared caregiver-reported recovery of children with acute illness in 45 facilities implementing ALMANACH with 44 facilities using paper-based IMCI. We collected sociodemographic and clinical information from caregivers and clinical records on Day 0, and recovery data from Day 7 phone follow-up. We calculated risk ratios and odds ratios for primary and secondary outcomes, and derived adjusted effect estimates using mixed-effects regressions.

Results
We recruited 1,929 children of which 1,021 (53%) attended facilities implementing ALMANACH, in March and between July-September 2020. Caregiver-reported recovery was significantly higher among children attending ALMANACH facilities (adjusted OR=2·63, 95% CI: 1·60-4·32). We observed higher parenteral and lower oral antimicrobial prescription rates (adjusted OR=2·42 (1·00-5·85) and adj. OR=0·40 (0·22-0·73), respectively) in ALMANACH facilities, as well as marked higher rates for referral, communication of diagnosis, and follow-up advice.

Conclusion
Implementation of digital CDSS in primary care can improve quality of care and recovery of sick children in resource-constrained settings. The effect is likely mediated by better guideline adherence by health workers supported step-by-step through evidence-based recommendations on clinical assessment, diagnosis, treatment and referral. These findings support the use of CDSS for health systems strengthening to progress towards universal health coverage.
ARTICLE SUMMARY

Strengths and limitations of this study

- To our knowledge, this is the first study to evaluate the impact of IMCI-related digital CDSS on health outcomes when implemented at scale in a programmatic context in resource-constrained settings.
- Large observational study, recruiting 1021 children from 45 intervention primary healthcare facilities and 908 children from 44 routine care facilities with high rates of follow-up completion at Day 7 for primary outcome assessment.
- Though we adjusted for important potential confounders within the analysis, the nature of the evaluation in the context of large-scale implementation meant that it was not possible to randomise facilities, therefore contextual differences may have influenced our findings.
- Despite the use of standardised tools and procedures, performance or detection bias could have occurred given that the intervention could not be blinded.
INTRODUCTION

Global health initiatives place high expectations on digital technology to improve quality of care (QoC) in low- and middle-income countries (LMICs).[1,2] One promising approach is the implementation of digital Clinical Decision Support Systems (CDSS) for health care providers (HCPs) in remote regions and resource-constrained settings.[3,4] CDSS guide HCPs through clinical consultations with simple, structured, step-by-step decision logic, providing them with evidence-based diagnostic and treatment recommendations, displayed on a handheld digital device.

Effective, safe and person-centred QoC is essential to achieve universal health coverage.[5] To improve QoC for children under five years, WHO developed the Integrated Management of Childhood Illness (IMCI) guidelines,[6] now a standard for Primary Health Care (PHC) consultations in over 100 LMICs. It focuses on diagnosis, classification and treatment of conditions responsible for 70% of child mortality (malaria, pneumonia, diarrhoea, measles, and malnutrition). Evidence suggests that IMCI can improve QoC and reduce under-five mortality,[7–9] but its roll-out over the past two decades has not yielded the anticipated effect.[10] The reasons are manifold,[11–13] but non-adherence of HCPs to guidelines, possibly due to the difficulty of practical integration into the clinical workflow, plays a central role.[14–16]

While adherence to guidelines may be improved by providing them in a digital CDSS-format,[17–21] systematic reviews assessing the impact of such digital tools on health outcomes show heterogeneous results: some report improvements in certain QoC indicators,[3] others have shown little to no effect of CDSS use on morbidity and mortality.[22] Several IMCI-based CDSS are now available on smartphones or tablets.[23] Their efficacy has been demonstrated in clinical trial settings,[24,25] but evidence on effectiveness at larger scale, particularly in programmatic settings (i.e. under real-world conditions) is limited.[26]

In this study, we explore the impact of a digital IMCI-based CDSS, the ALgorithm for the MANAgement of CHildhood illness (ALMANACH), on clinical outcomes and QoC in the programmatic setting. ALMANACH was first developed and evaluated from 2010-2014 to address clinical management of febrile children (age two to 59 months) in Tanzania.[27] Controlled trials have demonstrated acceptance among end-users,[28] and clinical efficacy.[25,29]

ALMANACH was then further adapted for the programmatic setting of PHC clinics in Afghanistan and Nigeria, respecting national IMCI protocols, latest evidence, local epidemiology, and the daily work reality of the health facilities (Figure 1).[30] Evaluation of ALMANACH after one year of implementation showed good acceptance by HCPs, improved completeness of clinical assessment, better adherence to treatment recommendations, and reduced antibiotic prescription rates.[31]

The objective of this study was to evaluate the hypothesis that ALMANACH implementation improves clinical recovery of children (age two to 59 months) from acute illness and QoC outcomes when implemented at scale in routine practice at primary care facilities.

METHODS

Study design and participants

We conducted an observational study within the programmatic context of ALMANACH in Adamawa State, a conflict-torn region in North-Eastern Nigeria. In 2016, the International Committee of the Red Cross (ICRC) in partnership with the Adamawa State Primary Health Care Development Agency (ADSPHCDA) and technical support from the Swiss Tropical and Public Health Institute (Swiss TPH) initiated the step-wise roll out of ALMANACH to the State’s PHC facilities. One HCP per facility received a three day introduction training on how to use the tablet and a refresher on basic clinical concepts included in the CDSS. These HCPs were responsible for cascading their acquired knowledge to their colleagues. HCPs at all accessible ALMANACH facilities received a one day of start-up supervision, followed by supportive supervision and mentorship (checking correct use of the CDSS, technical trouble shooting, orientation for untrained HCPs) provided every 4-6 months by ICRC and ADSPHCDA staff. Additionally, all PHC facilities received the routine monthly supportive supervision by the government health agency, based on a national supervision protocol. Tablets were donated through the project, but
no additional support (e.g. drug or consumables supply) was provided. Further detailed description of the ALMANACH intervention is described elsewhere.[31]

The state’s PHC facilities are clustered into 21 local government areas (LGAs). At the time of the study, six LGAs had not yet implemented ALMANACH of which two were excluded due to security constraints. Control facilities were therefore selected from these LGAs. Four LGAs were selected for the intervention group that had a similar epidemiological and sociodemographic profile, after excluding those with security issues or that were implementing another major child health intervention.

Children 2-59 months of age who presented to a study facility during the data collection period with an acute illness were eligible for inclusion. Children attending for routine care only (e.g. immunization visit), physical trauma, or mental health problems were excluded as these consultations are not addressed by ALMANACH.

**Patient and Public Involvement**

Community engagement prior to and during the study was built on existing long-term relationships with community representatives from the LGAs and Ward Development Committees (WDCs). Representatives were consulted on the purpose and conduct of the study, with detailed consultation on the recruitment strategy, particularly in relation to informed consent, though patients were not specifically involved in the study design. Planned dissemination activities include sharing of the findings with LGA and WDC representatives, and patients and the communities through an information campaign at the health facilities.

**Informed consent and ethical approval**

Caregivers of eligible children were recruited following informed consent. Verbal informed consent was obtained if the caregiver was willing to participate but not willing to provide written / thumbprint consent. This approach was taken as local community leaders advised that signing documents is regarded with suspicion both due to illiteracy and the high proportion of internally displaced people with identity protection concerns. No incentives were provided for participation, neither to participants nor to HCPs. The study obtained ethical approval from the Health Research Ethics Committee of Adamawa, Nigeria (ADHREC 8/02/2020/003) and the Ethics Committee Northwest and Central Switzerland (Req-2020-00082).

**Procedures**

At each facility, trained non-clinical research assistants collected from the facility manager basic information about the facility amenities and services, and the training and experience of HCPs consulting children under five years of age (after informed consent).

For both groups, research assistants obtained basic sociodemographic details, main symptoms and information about prior care sought from caregivers whilst awaiting consultation. Brief exit interviews were conducted to record medication (prescription or medication in-hand), diagnosis and management advice as understood by the caregiver.

In ALMANACH facilities, consultation data (diagnosis, measurements, and investigations) were extracted from the CDSS database. In routine care facilities, consultation data were obtained from facility registries immediately after the consultation.

On day seven, research assistants conducted a standardised health outcome assessment by phone. If unsuccessful, further attempts were made on three consecutive days. If the caregiver was not reachable by phone, contact was attempted through a community representative. Children of caregivers not contactable by day ten were considered lost to follow-up. For follow-up occurring after day seven, caregivers were asked to reflect the status of the child on day seven.

Data collection was conducted in ALMANACH and routine care facilities in parallel, one LGA at a time within each group. All eligible facilities in the first three LGAs in each group were included; in the last LGAs (Hong and Song), the most accessible facilities out of those eligible were selected until the target sample size was reached. Data collection lasted three to four weeks per LGA, occurring from 3rd to 28th March and 17th July to 30th September 2020, with a forced interruption due to the SARS-CoV2 pandemic.
Outcomes

The primary outcome was day 7 caregiver-reported recovery, assessed at phone follow-up. Secondary outcomes were antibiotic and antimalarial prescription during the consultation, referral to hospital, and communication of diagnosis and follow-up advice to the caregiver, as assessed at exit interview.

Statistical analysis

The sample size to detect a difference in recovery from 60% in routine care to 70% in ALMANACH facilities was estimated with 85% power and 0.05 significance threshold, assuming a standard deviation of 10 percentage points of cure rates between facilities. To allow flexibility according to the fluctuating security situation, we calculated sample size for a range of cluster numbers, estimating that we would require between 48 and 42 facilities per study arm.

We examined imbalances in patients’ and HCPs’ characteristics between ALMANACH and routine care facilities using appropriate statistical tests. For each endpoint, we calculated its frequency in ALMANACH and routine care facilities separately. The ratio of these frequencies (risk ratio, RR) was used as the measure of the association between being treated in an ALMANACH facility and the endpoint. We also calculated the corresponding odds ratios (OR) as well as the 95%-confidence intervals (CI) for both measures.

Mixed logistic regressions were used to estimate adjusted odds ratios for each endpoint. The pre-specified set of adjustments for the analysis of the primary endpoint (recovery) consisted of child’s age, sex, the collection period (pre- and post-Covid-19 related restrictions), symptom duration, travel time to the facility, whether the child was accompanied by their mother, presence or absence of five main symptoms, the qualification of the HCP and three facility-level variables: distance from a paved road and from the referral hospital (less or more than 30 minutes), and the average monthly number of consultations. Due to the observed imbalance between the study arms, we adjusted for whether care was sought in the two weeks preceding the consultation. The same set of variables was used to adjust the association of ALMANACH with the prescription of parenteral and oral antimicrobial treatment. Owing to the small number of cases, the analyses of referral to hospital, antibiotic, and antimalarial treatment were adjusted only for sex, age, collection period, HCP’s qualification and symptoms. Regressions included a random effect for the health worker nested in a random effect for the health facility.

Analyses of communication by the HCP to the child’s caregiver on diagnosis and follow-up were performed using negative binomial regression. The number of such consultations for every HCP was the dependent variable. The logarithm of the total number of consultations performed by the HCP during the study was included with its coefficient constrained to 1, thus the adjusted estimate can be interpreted as a rate ratio. All HCP and facility-level variables mentioned above were used to adjust.

To ensure that our estimates were not affected by loss to follow-up, we applied inverse probability weighting. The probability model to derive the weights was constructed using LASSO.[32] All reweighted estimates were virtually identical (within 0.05) to those from unweighted regressions, and thus we report only the latter.

Lastly, we conducted exploratory descriptive analysis of clinical records (from the ALMANACH database and from paper records in non-ALMANACH facilities) to further assess care processes. The decision logic of ALMANACH prompts direct referral when criteria for very severe disease are met, and differentiates certain assessments according to the presence or absence of fever and certain other symptoms and signs (Figure 1). Subsequently, the denominators reported for variables in the analysis of care processes were considered as ‘indicated according to the algorithm’, whereas in routine care the denominator was considered as ‘indicated according to IMCI’.

All calculations were performed using Stata 16. We used the STROBE cohort checklist when writing our report.[33]
About half of the enrolled children (48.4%) were under two years old, and 48.7% were female. The most commonly reported symptoms were fever (87.2%), cough/breathing problems (35.3%), diarrhoea (31.1%), and vomiting (30.8%). Children most frequently attended between two and seven days from symptom onset (41.2%). In both groups, children had commonly received medication for their illness within 2 weeks prior to the consultation (53.2% in ALMANACH and 57.4% in routine care facilities), mostly from patent medicine stores or pharmacies (43.1% vs 43.7% respectively). The majority of patients (76.0%) lived within 30 minutes travel of the health facility.

Provider cadre was most commonly Community Health Extension Workers (CHEWs) or Community Health Officers (CHOs) (49.3% ALMANACH vs 43.8% routine care) followed by Junior CHEWs (25.7% vs. 20.3% respectively). Over one third of HCPs (34.0% in ALMANACH and 39.2% in routine care facilities) had never received IMCI training. Participant, facility and HCP characteristics are shown in table 1, with additional detail in appendix 1.
### ALMANACH

#### Children & care-seeking

|                          | Pre-SARS-CoV2 (March 2020) | Routine care | p value | Total          |
|--------------------------|----------------------------|--------------|---------|----------------|
|                          | n (%)                      | n (%)        |         | n (%)          |
| **During SARS-CoV2 (Jul-Sep 2020)** | 678 (49.5)                | 692 (50.5)   | < 0.001* | 1370 (100)     |

#### Age in months

| Age in months | n (%) | n (%) | p value | Total |
|---------------|-------|-------|---------|-------|
| 2 to 5        | 105 (10.3) | 101 (11.1) | 266 (10.7) | 559 (100) |
| 6 – 11         | 140 (13.7) | 118 (13.0) | 258 (13.4) | 498 (24.3) |
| 12 – 23        | 256 (25.1) | 213 (23.5) | 469 (24.3) | 928 (48.7) |
| 24 – 59        | 508 (49.8) | 453 (49.9) | 961 (49.8) | 1929 (100) |
| Unknown        | 12 (1.2)  | 23 (2.5)  | 35 (1.8)  | 117 (6.8)  |

#### Sex

| Sex      | n (%) | n (%) | p value | Total |
|----------|-------|-------|---------|-------|
| Female   | 483 (47.3) | 456 (50.2) | 939 (48.7) | 1818 (100) |
| Male     | 526 (51.5) | 429 (47.3) | 955 (49.5) | 1981 (100) |
| Unknown  | 12 (1.2)  | 23 (2.5)  | 35 (1.8)  | 117 (6.8)  |

#### Presenting symptoms

| Presenting symptoms | n (%) | n (%) | p value | Total |
|---------------------|-------|-------|---------|-------|
| Fever               | 899 (88.1) | 783 (86.2) | 1,682 (87.2) | 3,682 (100) |
| Cough / difficulty breathing | 369 (36.1) | 312 (34.4) | 681 (35.3) | 1,341 (100) |
| Diarrhoea           | 317 (31.1) | 283 (31.2) | 600 (31.1) | 1,200 (100) |
| Vomiting            | 329 (32.2) | 264 (29.1) | 593 (30.8) | 1,122 (100) |
| Skin                | 41 (4.0)   | 55 (6.1)  | 96 (5.0)  | 192 (100)  |
| Other               | 333 (32.7) | 371 (36.3) | 704 (36.5) | 1,308 (100) |

#### Onset of symptoms prior to consultation

| Onset of symptoms prior to consultation | n (%) | n (%) | p value | Total |
|----------------------------------------|-------|-------|---------|-------|
| Same or previous day                   | 265 (26.0) | 275 (30.3) | 540 (28.0) | 1,080 (100) |
| 2 days to < 1 week                     | 439 (43.0) | 362 (39.9) | 801 (41.5) | 1,641 (100) |
| 1 – 2 weeks                            | 230 (22.5) | 194 (21.4) | 424 (22.0) | 854 (100)  |
| ≥ 2 weeks                              | 76 (7.4)   | 63 (6.9)  | 139 (7.2)  | 275 (100)  |
| Unknown                                | 11 (1.1)   | 14 (1.5)  | 25 (1.3)   | 50 (100)   |

#### Treatment in last 2 weeks

| Treatment in last 2 weeks | n (%) | n (%) | p value | Total |
|---------------------------|-------|-------|---------|-------|
| Yes                       | 543 (53.2) | 521 (57.4) | 1,064 (55.2) | 2,107 (100) |
| No                        | 474 (46.4) | 379 (41.7) | 853 (44.2) | 1,327 (100) |
| Unknown                   | 4 (0.4)   | 8 (0.9)  | 12 (0.6)  | 24 (100)   |

#### Reported travel time to facility

| Reported travel time to facility | n (%) | n (%) | p value | Total |
|----------------------------------|-------|-------|---------|-------|
| < 30 minutes                     | 696 (68.2) | 770 (84.8) | 1,466 (76.0) | 2,862 (100) |
| ≥ 30 minutes                     | 307 (30.1) | 128 (14.1) | 435 (22.6) | 742 (100)  |
| Unknown                          | 18 (1.8)   | 10 (1.1)  | 28 (1.5)   | 56 (100)   |

#### Health care providers

| Health care providers | n (%) | n (%) | Total |
|----------------------|-------|-------|-------|
| CHEW / CHO           | 71 (49.3) | 67 (43.8) | 138 (46.5) |
| Junior CHEW          | 37 (25.7) | 31 (20.3) | 68 (22.9)  |
| Nurse / midwife      | 2 (1.4)   | 4 (2.6)  | 6 (2.0)   |
| Other                | 34 (23.6) | 51 (33.4) | 85 (28.6)  |

#### Last IMCI training received (date)

| Last IMCI training received (date) | n (%) | n (%) | p value | Total |
|------------------------------------|-------|-------|---------|-------|
| <1 year ago (2020)                 | 1 (0.7)   | 3 (2.0)   | 4 (1.4)   | 8 (100) |
| 1 – 2 years ago (2018, 2019)       | 55 (38.2) | 41 (26.8) | 96 (32.3) | 146 (100) |
| 3 – 4 years ago (2016, 2017)       | 17 (11.8) | 22 (14.4) | 39 (13.1) | 76 (100)  |
| ≥ 5 years ago (prior to 2016)      | 9 (6.3)   | 13 (8.5)  | 22 (7.4)  |
| Never                              | 49 (34.0) | 60 (39.2) | 109 (36.7) |
| Unknown                            | 13 (9.0)  | 14 (9.2)  | 27 (9.1)  |

#### Health facilities

| Health facilities | n (%) | n (%) | Total |
|-------------------|-------|-------|-------|
| Distance from referral hospital | 45 (50.6) | 44 (49.4) | 89 (100) |

#### Distance from referral hospital

| Distance from referral hospital | n (%) | n (%) | p value | Total |
|---------------------------------|-------|-------|---------|-------|
| < 30 minutes                    | 16 (35.6) | 20 (45.5) | 36 (40.5) | 72 (100) |
| ≥ 30 minutes                    | 29 (64.4) | 24 (54.6) | 53 (59.6) | 102 (100) |

#### No. consultations children (US) at facility / month

| No. consultations children (US) at facility / month | n (%) | n (%) | p value | Total |
|-----------------------------------------------------|-------|-------|---------|-------|
| 0 – 99                                              | 15 (33.3) | 22 (50.0) | 37 (41.6) | 72 (100) |
| 100 – 199                                           | 16 (35.6) | 15 (34.1) | 31 (34.8) | 61 (100)  |
| ≥ 200                                               | 11 (24.4) | 4 (9.1)  | 15 (16.9) | 30 (100)  |
| Unknown                                             | 3 (6.7)   | 3 (6.8)  | 6 (6.7)  |

#### Health facility power supply

| Health facility power supply | n (%) | n (%) | p value | Total |
|------------------------------|-------|-------|---------|-------|
| All day (no interruptions)   | 7 (15.6) | 4 (9.1)  | 11 (12.4) | 18 (100) |
| All day (interruptions)      | 10 (22.2) | 15 (34.1) | 25 (28.1) | 45 (100)  |
| ≤ Half a day                 | 17 (37.8) | 16 (36.4) | 33 (37.1) | 50 (100)  |
Day 7 recovery rates differed markedly between ALMANACH and routine care. In ALMANACH facilities, 849 (85.4%) of 994 children with complete follow-up were reported to have fully recovered. In routine care facilities, 603 (71.4%) of 845 children were reported fully recovered. The odds ratio (OR) for day 7 recovery between groups was 2.34 (95% CI = 1.87–2.96) and 2.63 (1.60–4.32) after adjusting as described above.

For most secondary outcomes, we observed large differences between ALMANACH and routine care. HCPs referred patients to higher level of care over three times more often in the ALMANACH group (RR = 3.25 (2.12–4.96)). We saw more parenteral antimicrobial prescription and a less oral antimicrobial prescription in ALMANACH facilities, with adjusted odds ratios of 2.42 (1.00–5.85) and 0.40 (0.22–0.73), respectively. Differentiating antimicrobials into antibiotic and antimalarial treatment revealed that in ALMANACH facilities 120 (12.4%) of 966 children received parenteral antimalarials compared to 59 (6.9%) of 855 in routine care facilities; for parenteral antibiotics the respective difference was 56 (5.8%) of 966 vs 25 (2.9%) of 855. Oral antimalarial prescription rate was lower in ALMANACH facilities: 476 (49.3%) of 966 compared to 490 (57.3%) of 855 cases in routine care. There was no significant difference in oral antibiotic prescription between the groups (ALMANACH: 290 (30.0%) of 966 vs. routine care: 291 (34.0%) of 855).

The intervention affected the communication of diagnosis and follow-up advice to caregivers. In ALMANACH facilities 811 (84.0%) of 966 caregivers reported that HCPs explained the child’s diagnosis to them compared to only 557 (65.1%) of 855 in routine care facilities. The likelihood of receiving follow-up advice by the HCP was also much higher in ALMANACH facilities, with 596 (61.7%) of 966 families advised vs 179 (20.9%) of 855 cases in routine care. There was no significant difference in oral antibiotic prescription between the groups (ALMANACH: 290 (30.0%) of 966 vs. routine care: 291 (34.0%) of 855).

Lastly, we analysed differences in proportions of key diagnoses (according to IMCI protocols) made by HCPs in both groups. Pneumonia, diarrhoea, malnutrition, anaemia were markedly more often, and suspected malaria markedly less often, diagnosed in ALMANACH facilities. Only the rates of diagnosis of malaria confirmed through rapid diagnostic tests were similar between ALMANACH and routine care groups. All estimates are summarised in Table 2.
Comparative analysis of ALMANACH and record data indicated further differences between the groups in care process outcomes. In ALMANACH facilities, 850 (83·3%) of 1021 consultations were conducted using ALMANACH. When ALMANACH was used, 850 (100%) children were screened for IMCI danger signs, 847 (99·6%) had a recorded weight, MUAC was recorded in 718 (99·9%) of 719 indicated, temperature recorded in 714 (95·1%) of 751 indicated, and pallor assessed in 745 (100%) of 745 indicated. In routine care facilities, we found no documentation of danger signs, 197 (21·7%) of 908 had a recorded weight, MUAC was recorded in 52 (6·6%) of 784 children 6 to 59 months old, and temperature in 469 (51·7%) of 908 cases. Using malaria assessment and treatment as an example of adherence to guidelines, we found lower effectiveness decay through the care pathway in ALMANACH compared to routine care facilities (Figure 3).

Table 2: Primary and secondary outcomes

| Outcome                          | ALMANACH facilities | Routine care facilities | Unadjusted effect estimate | 95%-CI for unadjusted effect | Adjusted effect estimate | 95%-CI for adjusted effect |
|----------------------------------|---------------------|------------------------|---------------------------|-------------------------------|--------------------------|-----------------------------|
| Recovery after 7 days            | 849 994 85·4%      | 603 845 71·4%          | RR 1·20                   | 1·14-1·26                    | OR 2·34                   | 1·87-2·96                   |
| Referral to hospital             | 96 1009 9·5%       | 26 861 3·0%            | RR 3·25                   | 2·12-4·96                    | OR 3·48                   | 2·24-5·41                   |
| Diagnosis communicated to caregiver | 811 966 84·0%  | 557 855 65·1%          | RR 1·29                   | 1·22-1·36                    | OR 3·93                   | 1·89-8·14                   |
| Follow-up advice given to caregiver | 596 966 61·7%  | 179 855 20·9%          | RR 2·95                   | 2·56-3·39                    | OR 2·67                   | 1·13-1·42                   |
| Parenteral antimicrobial treatment | 164 966 17·0%   | 80 855 9·4%            | RR 1·81                   | 1·42-2·33                    | OR 1·98                   | 1·41-2·63                   |
| Oral antimicrobial treatment     | 620 966 64·2%     | 636 855 74·4%          | RR 0·86                   | 0·81-0·92                    | OR 0·62                   | 0·50-0·76                   |
| Any antimicrobial treatment      | 745 966 77·1%     | 690 855 80·1%          | RR 0·96                   | 0·91-1·00                    | OR 0·81                   | 0·64-1·01                   |
| Parenteral antimalarial treatment | 120 966 12·4%    | 59 855 6·9%            | RR 1·80                   | 1·34-2·42                    | OR 0·86                   | 0·79-0·94                   |
| Oral antimalarial treatment      | 476 966 49·3%     | 490 855 57·3%          | RR 0·86                   | 0·79-0·94                    | OR 0·86                   | 0·77-1·01                   |
| Parenteral antibiotic treatment  | 56 966 5·8%       | 25 855 2·9%            | RR 1·98                   | 1·25-3·15                    | OR 0·88                   | 0·77-1·01                   |
| Oral antibiotic treatment        | 290 966 30·0%     | 291 855 34·0%          | RR 0·88                   | 0·77-1·01                    | OR 0·88                   | 0·77-1·01                   |
| Antibiotic and antimalarial treatment | 189 966 19·6% | 168 687 19·6%          | RR 1·00                   | 0·83-1·20                    | OR 0·99                   | 0·79-1·25                   |
| Suspected malaria                | 70 811 8·6%       | 77 557 13·8%           | RR 0·62                   | 0·46-0·85                    | OR 0·62                   | 0·46-0·85                   |
| Confirmed malaria                | 525 811 64·7%     | 363 557 65·2%          | RR 0·99                   | 0·92-1·08                    | OR 0·99                   | 0·92-1·08                   |
| Pneumonia                        | 59 811 7·3%       | 5 557 0·9%             | RR 8·10                   | 3·27-20·06                   | OR 8·09                   | 3·26-20·06                   |
| Diarrhea                         | 118 811 14·5%     | 46 557 8·3%            | RR 1·76                   | 1·28-2·43                    | OR 1·76                   | 1·28-2·43                   |
| Malnutrition                     | 57 811 7·0%       | 7 557 1·3%             | RR 5·60                   | 2·57-12·17                   | OR 5·60                   | 2·57-12·17                   |
| Anemia                           | 31 811 3·8%       | 3 557 0·5%             | RR 7·10                   | 2·18-23·10                   | OR 7·10                   | 2·18-23·10                   |

RR = Risk ratio  OR = Odds ratio  CI = confidence interval  N/A = not applicable

1 Adjusted rate ratio from negative binomial regression (see statistical analysis)

2 8 observations not used due to separation (combinations of covariates predicting the outcome perfectly)
DISCUSSION

This observational study found significant improvements in caregiver-reported recovery of children seven days after primary care consultation associated with the implementation of the ALMANACH digital CDSS in a programmatic setting. This impact on health outcomes is likely mediated by better adherence to evidence-based guidelines, supported by demonstrated improvements in QoC process outcomes across assessment, diagnosis, and management.

In children for whom ALMANACH was used, we found almost complete adherence to key IMCI assessments. In contrast, in routine care facilities in this study, and other studies on IMCI-related quality of care, HCPs commonly complete assessments in fewer than 50% of consultations with sick children.[34,35] We posit that this adherence to IMCI assessments, guided by ALMANACH, led to higher detection of severe illness and of diagnoses that are important causes of morbidity and mortality, particularly pneumonia, anaemia, diarrhoea, and malnutrition. The significantly higher rate of these IMCI diagnoses (and lower rate of ‘suspected’ malaria diagnosis) made in ALMANACH facilities supports this assumption, which may also have contributed to more accurate antimicrobial prescription.

In turn, we observed higher rates of referral and of treatment with parenteral antimicrobials, indicative of increased recognition and management of severe illness. Inadequate identification and treatment of severe disease are major barriers to reducing child mortality in LMICs.[36,37] Whilst the proportion of children with severe disease varies substantially between and within countries, with estimates varying from 5-21% in studies from comparable settings,[35,38] the 3.0% referral rate reported by caregivers in routine care facilities in this study is likely to be inappropriately low, and the 9.5% ALMANACH referral rate more consistent with the clinical need.

Further, ALMANACH showed significantly better HCP communication with caregivers as evidenced by higher rates of awareness of diagnosis and follow-up advice at exit interviews in ALMANACH facilities. Communication about a child’s illness and treatment are key standards set out by WHO for improving QoC for children at health facilities, and are associated with higher satisfaction with and intention to return to care.[5,39] In ALMANACH facilities, caregivers were made aware of diagnosis in 84.0% and given follow-up advice in 61.7% of consultations, substantially higher than in routine care facilities (65.1% and 20.9% respectively) and in multi-country IMCI studies in sub-Saharan African countries (43.70% and 20.57% respectively).[34,39]

These findings of better adherence to key evidence-based practices are consistent with other studies of child health-related CDSS in resource-constrained settings, including ALMANACH.[19–21,29–31] Lack of training, and other knowledge gaps such as difficulty recalling specific criteria (e.g. respiratory rate cut-offs) contribute to low adherence to IMCI, as do low motivation and physical and cognitive overload associated with working in such challenging settings.[12] Qualitative feedback from HCPs suggests that IMCI-related CDSS can improve confidence in diagnoses and managements, strengthen motivation, and address the issue of cognitive overload through the step-by-step nature of the guidance tailored to individual patients, particularly for severity classification and drug dosing.[17,28]

But whilst increased adherence to guidelines has been consistently demonstrated, few studies have assessed the impact of IMCI-related CDSS on health outcomes and, to our knowledge, none in the context of a long-term, large-scale implementation. The ALMANACH controlled trial in Tanzania also found higher day seven recovery rates, though also in the control recovery was higher (92.0% in routine care to 97.3% in ALMANACH facilities).[25] This is relatively high compared to the day seven recovery rates we saw in this study (71.4% in routine care and 85.4% in ALMANACH facilities). The contextual differences in sociodemographic, epidemiological and health system factors are likely to account for this, though a more substantial Hawthorne effect may also have been in effect as data was collected inside the consultation room in the Tanzania study.

This study demonstrates that implementation of ALMANACH can deliver impact on health outcomes at scale in remote, resource-constrained PHC facilities, where drug stock-outs are common, many facilities lack basic amenities, and one third of HCPs have never received IMCI training. A recent systematic review and meta-analysis found only modest changes in health outcomes with CDSS implementation.[40] Most of the CDSS studies included in this review were implemented in high-income countries, where HCP’s access to resources is substantially higher than most PHCs implementing IMCI. This may indicate that CDSS can deliver most value when used to support HCPs with limited skills and resources, provided that they are appropriately contextualised and implemented.
In contrast with earlier ALMANACH studies,[29–31] we did not find significant lower antibiotic prescription rates. Oral antibiotics were prescribed to 30·0% of children in ALMANACH and 34·0% in routine care facilities, slightly lower than the 43·1% (33·2–50·5) found in a recent meta-analysis of reported antibiotic use for sick children in LMICs. However, these may not reflect true antibiotic consumption rates given that most caregivers also reported treatment prior to consultation, most commonly from patent medicine stores or pharmacies. With increasing antibiotic prescription rates for children under five years of age, rising fastest in low-income countries, antimicrobial stewardship remains a global health priority to mitigate individual adverse events, rising antimicrobial resistance and resource waste.[41,42] Further gains in antimicrobial stewardship may be possible to achieve through integrating host biomarkers into IMCI-related CDSS.[24]

Our study has several limitations. Due to the nature of the evaluation in the programmatic setting, facilities were not randomised to ALMANACH or routine care. The presence of a large-scale child health intervention in some LGAs, combined with security- and weather-related accessibility issues, limited the number of suitable LGAs for the control group. Contextual differences including epidemiology, health-seeking behaviour and the health system may therefore have influenced our data, though we adjusted for important potential confounders within the analysis. Further, the intervention could not be blinded, so performance or detection bias could have occurred, despite the use of standardised tools and procedures. The Hawthorne effect may have influenced the data, which has been found to increase patient-reported quality of care by 13%.[43] The observer effect should be similar in both intervention and routine care facilities, although there is a possibility that a differential effect could occur if the tablet were used more than usual in ALMANACH facilities. To reduce the likelihood of influencing HCP performance, we avoided direct observation and only collected information from caregivers and records. We did not conduct repeat clinical assessments after consultations due to the potential need to modify treatment, which could have influenced the primary outcome. It was therefore not possible to have complete certainty about the content of clinical consultations, not to conduct a thorough analysis of correct assessment, classification and treatment (including of antimicrobial appropriateness) of all IMCI diagnoses, and thus we were only able to provide some insights into the differences in routinely documented quality of care indicators. Lastly, given the complex nature of the intervention, incorporating the tablet-based CDSS along with training, mentorship and data feedback, we cannot determine the effect of the CDSS itself vs the entire intervention package. However, it is unlikely that training alone accounts for the difference in outcomes given that there was no major difference between groups in time since most recent IMCI training.

In conclusion, we found substantial impact of this IMCI-related CDSS on health and QoC outcomes, demonstrating that earlier findings in controlled or small-scale studies can be achieved at scale in a resource-constrained setting. Positive effects were seen across a range of process and outcome indicators, including assessment, diagnosis, treatment, and communication. These findings support the implementation of digital CDSS in resource-constrained settings as a means to strengthen progress towards universal health coverage.
FIGURE LEDGENDS / CAPTION

Figure 1: Clinical consultation flow logic in ALMANACH Nigeria CDSS

Figure 2: Study flow. *45 facilities included, but no participants attended eligible for screening or recruitment at one facility in the routine care arm.

Figure 3: Comparison of systems effectiveness decay for malaria assessment and treatment in ALMANACH and routine care facilities. Steps reflecting adherence to guidelines shown in blue, non-adherence shown in red, and not applicable in grey.

AUTHOR CONTRIBUTIONS
Torsten Schmitz (TS), Fenella Beynon (FB), Capucine Musard (CM), Marek Kwiatkowski (MK), Marco Landi (ML), Daniel Ishaya (DI), Jeremiah Zira (JZ), Muazu Muazu (MM), Camille Renner (CR), Edwin Emmanuel (EE), Solomon Gideon Bulus (SB), Rodolfo Rossi (RR).

FB, TS, RR, MK, and ML conceived the study’s concept and designed its methodology. CM, CR, MM, FB, TS and DI designed and developed the data collection tools. ML, CM, CR, DI, EE, JZ, and MM realised the study implementation, training of data collectors, and monitored the data collection in the field. Statistical analyses were done by MK with contributions from RR and FB. CM and CR verified the underlying data. FB, TS, RR, CM and MK interpreted the results. The original manuscript was written by TS, FB, and CM with contributions from MK and RR, and the final version was reviewed and approved by all authors. The joint first authors FB and TS contributed equally to this paper.

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COMPETING INTERESTS
All authors declare no competing interest.

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DATA SHARING
Anonymised participant data can be made available from the publication date upon reasonable request to the corresponding author (TS), subject to completion of a data sharing agreement and approval from the Adamawa State Primary Health Care Development Agency.

PATIENT CONSENT AND ETHICAL APPROVAL
All caregivers of eligible children who participated in this study gave their informed consent before participating. The study obtained ethical approval from the Health Research Ethics Committee of Adamawa, Nigeria (ADHREC 8/02/2020/003) and the Ethics Committee Northwest and Central Switzerland (Req-2020-00082).
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Start of consultation

- Patient registration
- Danger signs screening
- Malnutrition screening
- Jaundice/anemia screening

Fever screening

- Malaria/Severe febrile disease
- Cough/Coryza/Difficulty breathing
- Measles
- Diarrhoea
- Dehydration
- Ear problem
- Sore throat
- No identified cause of fever

Severe disease

- Urgent referral

Fever

- Cough/Coryza/Difficulty breathing
- Diarrhoea
- Dehydration
- Ear problem

Skin problem

- HIV screening
- Vitamin A & anthelmintic prevention

Immunization check

- Classification(s)
- Treatment recommendations

General feeding recommendations

End of consultation
ALMANACH LGAs: Lamurde, Jada, Gombi, Hong
Routine care LGAs: Numan, Guyuk, Shelleng, Song

ALMANACH PHC facilities
n = 45

Children screened
n = 2244

Children enrolled
n = 1021

Day 7 follow-up
n = 994

Routine care PHC facilities
n = 44*

Children screened
n = 1904

Children enrolled
n = 908

Day 7 follow-up
n = 845

Excluded
Age n = 314
Routine preventative care n = 858
Trauma n = 30
No consent n = 4
Other n = 17

Excluded
Age n = 211
Routine preventative care n = 744
Trauma n = 30
No consent n = 1
Other n = 10
Figure 3: Comparison of systems effectiveness decay for malaria assessment and treatment in ALMANACH and routine care facilities. Steps reflecting adherence to guidelines shown in blue, non-adherence shown in red, and not applicable in grey.
## ANNEX

### Annex 1: Patients and family sociodemographic data and care seeking information, health care provider and health facility characteristics

| Children & care-seeking | ALMANACH | Routine care | p value | Total |
|--------------------------|----------|--------------|---------|-------|
|                         | n (%)    | n (%)        |         | n (%) |
| Pre-SARS-CoV2 (March 2020) | 343 (61·4) | 216 (38·6) | < 0·001 * | 559 (100) |
| During SARS-CoV2 (Jul-Sep 2020) | 678 (49·5) | 692 (50·5) |         | 1370 (100) |

### Age in months

| Age in months | ALMANACH | Routine care | p value | Total |
|---------------|----------|--------------|---------|-------|
| 2 to 5        | 105 (10·3) | 101 (11·1)   | 0·02 *  | 206 (10·7) |
| 6 – 11        | 140 (13·7) | 118 (13·0)   |         | 258 (13·4) |
| 12 – 23       | 256 (25·1) | 213 (23·5)   |         | 469 (24·3) |
| 24 – 59       | 508 (49·8) | 453 (49·9)   |         | 961 (49·8) |
| Unknown       | 12 (1·2)   | 23 (2·5)     |         | 35 (1·8)   |

### Sex

| Sex | ALMANACH | Routine care | Total |
|-----|----------|--------------|-------|
| Female | 483 (47·3) | 456 (50·2) | 939 (48·7) |
| Male   | 526 (51·5) | 429 (47·3) | 955 (49·5) |
| Unknown | 12 (1·2)  | 23 (2·5)   | 35 (1·8)   |

### Presenting symptoms

| Presenting symptoms | ALMANACH | Routine care | p value | Total |
|---------------------|----------|--------------|---------|-------|
| Fever               | 899 (88·1) | 783 (86·2)  | 0·23 *  | 1,682 (87·2) |
| Cough / difficulty breathing | 369 (36·1) | 312 (34·4)  | 0·41 *  | 681 (35·3) |
| Diarrhoea           | 317 (31·1) | 283 (31·2)  | 0·96 *  | 600 (31·1) |
| Vomiting            | 329 (32·2) | 264 (29·1)  | 0·14 *  | 593 (30·8) |
| Skin                | 41 (4·0)   | 55 (6·1)    | 0·04 *  | 96 (5·0)   |
| Other               | 333 (36·7) | 371 (36·3)  | 0·88 *  | 704 (36·5) |

### Onset of symptoms prior to consultation

| Onset of symptoms prior to consultation | ALMANACH | Routine care | p value | Total |
|----------------------------------------|----------|--------------|---------|-------|
| Same or previous day                    | 265 (26·0) | 275 (30·3)  |         | 540 (28·0) |
| 2 days to < 1 week                      | 439 (43·0) | 362 (39·9)  |         | 801 (41·5) |
| 1 – 2 weeks                             | 230 (22·5) | 194 (21·4)  |         | 424 (22·0) |
| ≥ 2 weeks                               | 76 (7·4)   | 63 (6·9)    | 0·27 *  | 139 (7·2)  |
| Unknown                                | 11 (1·1)   | 14 (1·5)    |         | 25 (1·3)   |

### Treatment in last 2 weeks

| Treatment in last 2 weeks | ALMANACH | Routine care | p value | Total |
|---------------------------|----------|--------------|---------|-------|
| Yes                       | 543 (53·2) | 521 (57·4)  |         | 1,064 (55·2) |
| No                        | 474 (46·4) | 379 (41·7)  | 0·05 *  | 853 (44·2) |
| Unknown                   | 4 (0·4)   | 8 (0·9)     |         | 12 (0·6)   |

### Source of previous treatment

| Source of previous treatment | ALMANACH | Routine care | p value | Total |
|------------------------------|----------|--------------|---------|-------|
| Same facility                | 31 (3·0)  | 56 (6·2)     |         | 87 (4·5) |
| Other facility               | 31 (3·0)  | 21 (2·3)     |         | 52 (2·7) |
| Pharmacy / patent medicine store | 440 (43·1) | 397 (43·7)  |         | 837 (43·4) |
| Traditional healer           | 22 (2·2)  | 27 (3·0)     | 0·05 *  | 49 (4·5) |
| Informal (drug peddler / other) | 15 (1·5)  | 13 (1·4)    |         | 28 (1·5) |
| Friend relatives/community   | 4 (0·4)   | 7 (0·8)      |         | 11 (1·0) |
| Unknown                      | 478 (46·8) | 387 (42·6)  |         | 865 (44·8) |

### Reported travel time to facility

| Reported travel time to facility | ALMANACH | Routine care | p value | Total |
|---------------------------------|----------|--------------|---------|-------|
| < 30 minutes                    | 696 (68·2) | 770 (84·8)  | < 0·001 * | 1,466 (76·0) |
| ≥ 30 minutes                    | 307 (30·1) | 128 (14·1)  |         | 435 (22·6) |
| Unknown                         | 18 (1·8)  | 10 (1·1)    |         | 28 (1·5)  |

### Accompanying caregiver

| Accompanying caregiver | ALMANACH | Routine care | Total |
|------------------------|----------|--------------|-------|
| Mother                 | 767 (75·1) | 662 (72·9)   | 1,429 (74·1) |
| Other                  | 254 (24·9) | 246 (27·1)   | 500 (25·9) |

### Mother’s educational level

| Mother’s educational level | ALMANACH | Routine care | Total |
|----------------------------|----------|--------------|-------|
| No schooling               | 350 (34·3) | 281 (31·0)   | 631 (32·7) |
| Primary                    | 124 (12·1) | 134 (14·8)   | 258 (13·4) |
| Secondary                  | 252 (24·7) | 212 (23·4)   | 464 (24·1) |
| Higher                     | 38 (3·7)   | 34 (3·7)     | 72 (3·7)   |
| Unknown                    | 257 (25·2) | 247 (27·2)   | 504 (26·1) |

### No. children <5 in household

| No. children <5 in household | ALMANACH | Routine care | Total |
|-------------------------------|----------|--------------|-------|
| 1 – 2                         | 643 (63·0) | 617 (68·0)   | 1,260 (65·3) |
| 3 – 4                         | 211 (20·7) | 211 (23·2)   | 422 (21·9) |
| ≥ 5                           | 110 (10·8) | 77 (8·5)     | 187 (9·7)  |
| Unknown                       | 57 (5·6)  | 3 (0·3)      | 60 (3·1)   |

### Health care providers

| Health care providers | ALMANACH | Routine care | Total |
|----------------------|----------|--------------|-------|
|                       | 144 (48·5) | 153 (51·5)   | 297 (100) |

### Qualification

| Qualification | ALMANACH | Routine care | Total |
|---------------|----------|--------------|-------|
| CHW / CHO     | 776 (75·6) | 800 (79·4)  | 1,576 (78·3) |
### Chi-squared test

3  Other qualifications: Lab technician; EHO; medical doctor (n=1); other;

2  Other symptoms: Child is feeling very weak/not drinking/not eating; child has an ear problem; belly problem; pain; painful urination; runny nose; blood in the stool; sore throat, I don’t know; other;

1  Multiple answers possible

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Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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In your methods section, say that you used the STROBE cohort reporting guidelines, and cite them as:

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| Reporting Item | Page Number |
|----------------|-------------|
| **Title and abstract** | |
| Title | #1a | Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| Abstract | #1b | Provide in the abstract an informative and balanced summary of what was done and what was found | 3 |
| **Introduction** | |
| Background / rationale | #2 | Explain the scientific background and rationale for the investigation being reported | 5 |
| Objectives | #3 | State specific objectives, including any prespecified hypotheses | 5 |
# Methods

| Study design | Present key elements of study design early in the paper | 5 |
|-------------|--------------------------------------------------------|---|
| Setting     | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 5-6 |
| Eligibility criteria | Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. | 5-6 |
| Eligibility criteria | For matched studies, give matching criteria and number of exposed and unexposed | |
| Variables   | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 6 |
| Data sources / measurement | For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for exposed and unexposed groups if applicable. | 6-7 |
| Bias        | Describe any efforts to address potential sources of bias | 6,7,12 |
| Study size  | Explain how the study size was arrived at | 6 |
| Quantitative variables | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why | 6-9 |
| Statistical methods | Describe all statistical methods, including those used to control for confounding | 6-7 |
| Statistical methods | Describe any methods used to examine subgroups and interactions | 6-7 |
| Statistical methods | Explain how missing data were addressed | 6-7 |
| Statistical methods | If applicable, explain how loss to follow-up was addressed | 6-7 |
Statistical methods

Describe any sensitivity analyses

n/a

Results

Participants

Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.

Give reasons for non-participation at each stage

Consider use of a flow diagram

Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.

Indicate number of participants with missing data for each variable of interest

Summarise follow-up time (eg, average and total amount)

Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.

Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included

Report category boundaries when continuous variables were categorized

If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion

Key results #18 Summarise key results with reference to study objectives 10-11

Limitations #19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.

Interpretation #20 Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.

Generalisability #21 Discuss the generalisability (external validity) of the study results

Other Information

Funding #22 Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

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Effectiveness of an electronic clinical decision support system in improving the management of childhood illness in primary care in rural Nigeria: an observational study

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Effectiveness of an electronic clinical decision support system in improving the management of childhood illness in primary care in rural Nigeria: an observational study

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ABSTRACT

Objectives
To evaluate the impact of ‘ALMANACH’, a digital clinical decision support system (CDSS) based on the Integrated Management of Childhood Illness (IMCI), on health and quality of care outcomes for sick children attending primary healthcare (PHC) facilities.

Design
Observational study, comparing outcomes of children attending facilities implementing ALMANACH with control facilities not yet implementing ALMANACH.

Setting
PHC facilities in Adamawa State, North-Eastern Nigeria.

Participants
Children 2-59 months presenting with an acute illness. Children attending for well child or nutrition visits (e.g. immunization, growth monitoring), physical trauma, or mental health problems were excluded.

Interventions
The ALMANACH package (the CDSS with training, mentorship and data feedback) was rolled-out across Adamawa’s PHC facilities by the Adamawa State Primary Health Care Development Agency, in partnership with ICRC and Swiss TPH. Tablets were donated, but no additional support or incentives were provided. Control facilities received supportive supervision based on the national supervision protocol.

Primary and secondary outcome measures
The primary outcome was caregiver-reported recovery at day 7 phone follow-up. Secondary outcomes were antibiotic and antimalarial prescription, referral, and diagnosis and follow-up communication, assessed at day 0 exit interview.

Results
We recruited 1,929 children, of which 1,021 (53%) attended ALMANACH facilities, between March and September 2020. Caregiver-reported recovery was significantly higher among children attending ALMANACH facilities (adjusted OR=2·63, 95% CI: 1·60-4·32). We observed higher parenteral and lower oral antimicrobial prescription rates (adjusted OR=2·42 (1·00-5·85) and adj. OR=0·40 (0·22-0·73), respectively) in ALMANACH facilities, as well as markedly higher rates for referral, communication of diagnosis, and follow-up advice.

Conclusion
Implementation of digital CDSS with training, mentorship and feedback in primary care can improve quality of care and recovery of sick children in resource-constrained settings, likely mediated by better guideline adherence. These findings support the use of CDSS for health systems strengthening to progress towards universal health coverage.
ARTICLE SUMMARY

Strengths and limitations of this study

- To our knowledge, this is the first study to evaluate the impact of IMCI-related digital CDSS on health outcomes when implemented at scale in a programmatic context in resource-constrained settings.
- Large observational study, recruiting 1021 children from 45 intervention primary healthcare facilities and 908 children from 44 control facilities with high rates of follow-up completion at Day 7 for primary outcome assessment.
- Though we adjusted for important potential confounders within the analysis, the nature of the evaluation in the context of large-scale implementation meant that it was not possible to randomise facilities, therefore contextual differences may have influenced our findings.
- Despite the use of standardised tools and procedures, performance or detection bias could have occurred given that the intervention could not be blinded.
INTRODUCTION

Global health initiatives place high expectations on digital technology to improve quality of care (QoC) in low- and middle-income countries (LMICs).[1,2] One promising approach is the implementation of digital Clinical Decision Support Systems (CDSS) for health care providers (HCPs) in remote regions and resource-constrained settings.[3,4] CDSS guide HCPs through clinical consultations with simple, structured, step-by-step decision logic, providing them with evidence-based diagnostic and treatment recommendations, displayed on a handheld digital device.

Effective, safe and person-centred QoC is essential to achieve universal health coverage.[5] To improve QoC for children under five years, WHO developed the Integrated Management of Childhood Illness (IMCI) guidelines,[6] now a standard for Primary Health Care (PHC) consultations in over 100 LMICs. It focuses on diagnosis, classification and treatment of conditions responsible for 70% of child mortality (malaria, pneumonia, diarrhoea, measles, and malnutrition). Evidence suggests that IMCI can improve QoC and reduce under-five mortality,[7–9] but its roll-out over the past two decades has not yielded the anticipated effect.[10] The reasons are manifold,[11–13] but non-adherence of HCPs to guidelines, possibly due to the difficulty of practical integration into the clinical workflow, plays a central role.[14–16]

While adherence to guidelines may be improved by providing them in a digital CDSS-format,[17–21] systematic reviews assessing the impact of such digital tools on health outcomes show heterogeneous results: some report improvements in certain QoC indicators;[3] others have shown little to no effect of CDSS use on morbidity and mortality.[22] Several IMCI-based CDSS are now available on smartphones or tablets.[23] Their efficacy has been demonstrated in clinical trial settings,[24,25] but evidence on effectiveness at larger scale, particularly in programmatic settings (i.e. under real-world conditions) is limited.[26]

In this study, we explore the impact of a digital IMCI-based CDSS, the ALgorithm for the MANAgement of CHildhood illness (ALMANACH), on clinical outcomes and QoC in the programmatic setting. ALMANACH was first developed and evaluated from 2010-2014 to address clinical management of febrile children (age two to 59 months) in Tanzania.[27] Controlled trials have demonstrated acceptance among end-users,[28] and clinical efficacy.[25,29]

ALMANACH was then further adapted for the programmatic setting of PHC clinics in Afghanistan and Nigeria, respecting national IMCI protocols, latest evidence, local epidemiology, and the daily work reality of the health facilities (Figure 1).[30] Evaluation of ALMANACH after one year of implementation showed good acceptance by HCPs, improved completeness of clinical assessment, better adherence to treatment recommendations, and reduced antibiotic prescription rates.[31]

The objective of this study was to evaluate the hypothesis that ALMANACH implementation improves clinical recovery of children (age two to 59 months) from acute illness and QoC outcomes when implemented at scale in routine practice at primary care facilities.

METHODS

Study design and participants

We conducted an observational study within the programmatic context of ALMANACH in Adamawa State, a conflict-torn region in North-Eastern Nigeria. In 2016, the International Committee of the Red Cross (ICRC) in partnership with the Adamawa State Primary Health Care Development Agency and technical support from the Swiss Tropical and Public Health Institute (Swiss TPH) initiated the step-wise roll-out of ALMANACH to the State’s PHC facilities. One HCP per facility received a three day introduction training on how to use the tablet and a refresher on basic clinical concepts included in the CDSS. These HCPs were responsible for cascading their acquired knowledge to their colleagues. HCPs at all accessible ALMANACH facilities received a one day of start-up supervision, followed by supportive supervision and mentorship (checking correct use of the CDSS, technical trouble shooting, orientation for untrained HCPs) provided every 4-6 months by ICRC and Agency staff. Additionally, all PHC facilities received the routine monthly supportive supervision by the government health agency, based on a national supervision protocol. Tablets were donated through the project, but no additional support (e.g. drug or
consumables supply, or financial incentives) was provided. Further detailed description of the ALMANACH intervention is described elsewhere. [31]

The State’s PHC facilities are clustered into 21 local government areas (LGAs). At the time of the study, 6 LGAs had not yet implemented ALMANACH of which two were excluded due to security constraints. Control facilities were therefore selected from the remaining four LGAs. Four LGAs were selected for the intervention group that had a similar epidemiological and sociodemographic profile, after excluding those with security issues or that were implementing another major child health intervention.

Children 2-59 months of age who presented to a study facility during the data collection period with an acute illness were eligible for inclusion. Children attending for ‘well child’ or nutrition visits (e.g. immunization, growth monitoring), physical trauma, or mental health problems were excluded as these consultations are not addressed by ALMANACH.

Patient and Public Involvement

Community engagement prior to and during the study was built on existing long-term relationships with community representatives from the LGAs and Ward Development Committees (WDCs). Representatives were consulted on the purpose and conduct of the study, with detailed consultation on the recruitment strategy, particularly in relation to informed consent, though patients were not specifically involved in the study design. Planned dissemination activities include sharing of the findings with LGA and WDC representatives, and patients and the communities through an information campaign at the health facilities.

Informed consent and ethical approval

Caregivers of eligible children were recruited following informed consent. Verbal informed consent was obtained if the caregiver was willing to participate but not willing to provide written / thumbprint consent. This approach was taken as local community leaders advised that signing documents is regarded with suspicion both due to illiteracy and the high proportion of internally displaced people with identity protection concerns. No incentives were provided for participation, neither to participants nor to HCPs. The study obtained ethical approval from the Health Research Ethics Committee of Adamawa, Nigeria (ADHREC 8/02/2020/003) and the Ethics Committee Northwest and Central Switzerland (Req-2020-00082).

Procedures

At each facility, trained non-clinical research assistants collected from the facility manager basic information about the facility amenities and services, and the training and experience of HCPs consulting children under five years of age (after informed consent).

For both groups, research assistants obtained basic sociodemographic details, main symptoms and information about prior care sought from caregivers whilst awaiting consultation. Brief exit interviews were conducted to record medication (prescription or medication in-hand), diagnosis and management advice as understood by the caregiver.

In ALMANACH facilities, consultation data (diagnosis, measurements, and investigations) were extracted from the CDSS database. In control facilities, consultation data were obtained from facility registries immediately after the consultation.

On day seven, research assistants conducted a standardised health outcome assessment by phone. If unsuccessful, further attempts were made on three consecutive days. If the caregiver was not reachable by phone, contact was attempted through a community representative. Children of caregivers not contactable by day ten were considered lost to follow-up. For follow-up occurring after day seven, caregivers were asked to reflect the status of the child on day seven.

Data collection was conducted in ALMANACH and control facilities in parallel, one LGA at a time within each group. All eligible facilities in the first three LGAs in each group were included; in the last LGAs (Hong and Song, last due being the least accessible at the time of the study), the most accessible facilities out of those eligible were selected until the target sample size was reached. Data collection lasted three weeks per LGA, occurring from 3rd to 28th March and 17th July to 30th September 2020, with a forced interruption due to the SARS-CoV2 pandemic.
Outcomes
The primary outcome was day 7 caregiver-reported recovery, assessed at phone follow-up. Secondary outcomes were antibiotic and antimalarial prescription during the consultation, referral to hospital, and communication of diagnosis and follow-up advice to the caregiver, as assessed at exit interview.

Statistical analysis
The sample size to detect a difference in recovery from 60% in control to 70% in ALMANACH facilities was estimated with 85% power and 0.05 significance threshold, assuming a standard deviation of 10 percentage points of cure rates between facilities. To allow flexibility according to the fluctuating security situation, we calculated sample size for a range of cluster numbers, estimating that we would require between 48 and 42 facilities per study arm.

We examined imbalances in patients’ and HCPs’ characteristics between ALMANACH and control facilities using appropriate statistical tests. For each endpoint, we calculated its frequency in ALMANACH and control facilities separately. The ratio of these frequencies (risk ratio, RR) was used as the measure of the association between being treated in an ALMANACH facility and the endpoint. We also calculated the corresponding odds ratios (OR) as well as the 95%-confidence intervals (CI) for both measures.

Mixed logistic regressions were used to estimate adjusted odds ratios for each endpoint. The pre-specified set of adjustments for the analysis of the primary endpoint (recovery) consisted of child’s age, sex, the collection period (pre- and post-Covid-19 related restrictions), symptom duration, travel time to the facility, whether the child was accompanied by their mother, presence or absence of five main symptoms, the qualification of the HCP and three facility-level variables: distance from a paved road and from the referral hospital (less or more than 30 minutes), and the average monthly number of consultations. Due to the observed imbalance between the study arms, we adjusted for whether care was sought in the two weeks preceding the consultation. The same set of variables was used to adjust the association of ALMANACH with the prescription of parenteral and oral antimicrobial treatment. Owing to the small number of cases, the analyses of referral to hospital, antibiotic, and antimalarial treatment were adjusted only for sex, age, collection period, HCP’s qualification and symptoms. Regressions included a random effect for the health worker nested in a random effect for the health facility.

Analyses of communication by the HCP to the child’s caregiver on diagnosis and follow-up were performed using negative binomial regression. The number of such consultations for every HCP was the dependent variable. The logarithm of the total number of consultations performed by the HCP during the study was included with its coefficient constrained to 1, thus the adjusted estimate can be interpreted as a rate ratio. All HCP and facility-level variables mentioned above were used to adjust.

To ensure that our estimates were not affected by loss to follow-up, we applied inverse probability weighting. The probability model to derive the weights was constructed using LASSO.[32] All reweighted estimates were virtually identical (within 0.05) to those from unweighted regressions, and thus we report only the latter.

Lastly, we conducted exploratory descriptive analysis of clinical records (from the ALMANACH database and from paper records in non-ALMANACH facilities) to further assess care processes. The decision logic of ALMANACH prompts direct referral when criteria for very severe disease are met, and differentiates certain assessments according to the presence or absence of fever and certain other symptoms and signs (Error! Reference source not found.). Subsequently, the denominators reported for variables in the analysis of care processes were considered as ‘indicated according to the algorithm’, whereas in control facilities the denominator was considered as ‘indicated according to IMCI’.

All calculations were performed using Stata 16. We used the STROBE cohort checklist when writing our report.[33]

RESULTS
We recruited children from 89 PHC facilities (45 ALMANACH, 44 control). Out of 4148 children screened, 525 (12.7%) children were excluded due to their age, 1602 (38.6%) because attending for well child or nutrition visits, 60 (1.4%) for trauma. 5 caregivers did not consent for their child to participate in the study and 27 (0.7%) were excluded for other reasons. Of 1929 children enrolled, 1021 (52.9%) were consulted in ALMANACH facilities and 908 (47.1%) in control facilities (figure 2).
About half of the enrolled children (48.4%) were under two years old, and 48.7% were female. The most commonly reported symptoms were fever (87.2%), cough/breathing problems (35.3%), diarrhoea (31.1%), and vomiting (30.8%). Children most frequently attended between two and seven days from symptom onset (41.2%). In both groups, children had commonly received medication for their illness within 2 weeks prior to the consultation (53.2% in ALMANACH and 57.4% in control facilities), mostly from patent medicine stores or pharmacies (43.1% vs 43.7% respectively). The majority of patients (76.0%) lived within 30 minutes travel of the health facility.

Provider cadre was most commonly Community Health Extension Workers (CHEWs) or Community Health Officers (CHOs) (49.3% ALMANACH vs 43.8% control) followed by Junior CHEWs (25.7% vs. 20.3% respectively). Over one third of HCPs (34.0% in ALMANACH and 39.2% in control facilities) had never received IMCI training. Participant, facility and HCP characteristics are shown in table 1, with additional detail in appendix 1.
| Children & care-seeking                          | ALMANACH n  | Control n  | p value | Total n  |
|------------------------------------------------|-------------|------------|---------|----------|
|                                                | (%)         | (%)        |         | (%)      |
| Pre-SARS-CoV2 (March 2020)                     | 343 (61.4)  | 216 (38.6) | < 0.001* | 559 (100) |
| During SARS-CoV2 (Jul-Sep 2020)                | 678 (49.5)  | 692 (50.5) |         | 1370 (100) |
| **Age in months**                              |             |            |         |          |
| 2 to 5                                         | 105 (10.3)  | 101 (11.1) |         | 206 (10.7) |
| 6 – 11                                         | 140 (13.7)  | 118 (13.0) |         | 258 (13.4) |
| 12 – 23                                        | 256 (25.1)  | 213 (23.5) |         | 469 (24.3) |
| 24 – 59                                        | 508 (49.8)  | 453 (49.9) | 0.02*   | 961 (49.8) |
| Unknown                                        | 12 (1.2)    | 23 (2.5)   |         | 35 (1.8)  |
| **Sex**                                        |             |            |         |          |
| Female                                         | 483 (47.3)  | 456 (50.2) |         | 939 (48.7) |
| Male                                           | 526 (51.5)  | 429 (47.3) | 0.02*   | 955 (49.5) |
| Unknown                                        | 12 (1.2)    | 23 (2.5)   |         | 35 (1.8)  |
| **Presenting symptoms**                        |             |            |         |          |
| Fever                                          | 899 (88.1)  | 783 (86.2) | 0.23*   | 1,682 (87.2) |
| Cough / difficulty breathing                   | 369 (36.1)  | 312 (34.4) | 0.41*   | 681 (35.3) |
| Diarrhoea                                      | 317 (31.1)  | 283 (31.2) | 0.96*   | 600 (31.1) |
| Vomiting                                       | 329 (32.2)  | 264 (29.1) | 0.14*   | 593 (30.8) |
| Skin                                           | 41 (4.0)    | 55 (6.1)   | 0.04*   | 96 (5.0)  |
| Other                                          | 333 (36.7)  | 371 (36.3) | 0.88*   | 704 (36.5) |
| **Onset of symptoms prior to consultation**    |             |            |         |          |
| Same or previous day                           | 265 (26.0)  | 275 (30.3) |         | 540 (28.0) |
| 2 days to < 1 week                             | 439 (43.0)  | 362 (39.9) |         | 801 (41.5) |
| 1 – 2 weeks                                    | 230 (22.5)  | 194 (21.4) | 0.27*   | 424 (22.0) |
| ≥ 2 weeks                                      | 76 (7.4)    | 63 (6.9)   |         | 139 (7.2) |
| Unknown                                        | 11 (1.1)    | 14 (1.5)   |         | 25 (1.3)  |
| **Treatment in last 2 weeks**                  |             |            |         |          |
| Yes                                            | 543 (53.2)  | 521 (57.4) |         | 1,064 (55.2) |
| No                                             | 474 (46.4)  | 379 (41.7) | 0.05*   | 853 (44.2) |
| Unknown                                        | 4 (0.4)     | 8 (0.9)    |         | 12 (0.6)  |
| **Reported travel time to facility**           |             |            |         |          |
| < 30 minutes                                   | 696 (68.2)  | 770 (84.8) | < 0.001* | 1,466 (76.0) |
| ≥ 30 minutes                                   | 307 (30.1)  | 128 (14.1) |         | 435 (22.6) |
| Unknown                                        | 18 (1.8)    | 10 (1.1)   |         | 28 (1.5)  |
| **Health care providers**                      | 144 (48.5)  | 153 (51.5) |         | 297 (100) |
| **Qualification**                              |             |            |         |          |
| CHEW / CHO                                     | 71 (49.3)   | 67 (43.8)  |         | 138 (46.5) |
| Junior CHEW                                    | 37 (25.7)   | 31 (20.3)  |         | 68 (22.9) |
| Nurse / midwife                                | 2 (1.4)     | 4 (2.6)    | 0.35*   | 6 (2.0)  |
| Other†                                         | 34 (23.6)   | 51 (33.4)  |         | 85 (28.6) |
| **Last IMCI training received (date)**         |             |            |         |          |
| <1 year ago (2020)                             | 1 (0.7)     | 3 (2.0)    |         | 4 (1.4)  |
| 1 – 2 years ago (2018, 2019)                   | 55 (38.2)   | 41 (26.8)  |         | 96 (32.3) |
| 3 – 4 years ago (2016, 2017)                   | 17 (11.8)   | 22 (14.4)  |         | 39 (13.1) |
| ≥ 5 years ago (prior to 2016)                  | 9 (6.3)     | 13 (8.5)   | 0.45*   | 22 (7.4) |
| Never                                          | 49 (34.0)   | 60 (39.2)  |         | 109 (36.7) |
| Unknown                                        | 13 (9.0)    | 14 (9.2)   |         | 27 (9.1) |
| **Health facilities**                          | 45 (50.6)   | 44 (49.4)  |         | 89 (100)  |
| **Distance from referral hospital**            |             |            |         |          |
| < 30 minutes                                   | 16 (35.6)   | 20 (45.5)  | 0.39*   | 36 (40.5) |
| ≥ 30 minutes                                   | 29 (64.4)   | 24 (54.6)  |         | 53 (59.6) |
| **No. consultations children (US) at facility / month** |          |            |         |          |
| 0 – 99                                         | 15 (33.3)   | 22 (50.0)  |         | 37 (41.6) |
| 100 – 199                                      | 16 (35.6)   | 15 (34.1)  |         | 31 (34.8) |
| ≥ 200                                          | 11 (24.4)   | 4 (9.1)    | 0.19*   | 15 (16.9) |
| Unknown                                        | 3 (6.7)     | 3 (6.8)    |         | 6 (6.7)  |
| **Health facility power supply**               |             |            |         |          |
| All day (no interruptions)                     | 7 (15.6)    | 4 (9.1)    |         | 11 (12.4) |
| All day (interruptions)                        | 10 (22.2)   | 15 (34.1)  |         | 25 (28.1) |
| ≤ Half a day                                   | 17 (37.8)   | 16 (36.4)  | 0.82*   | 33 (37.1) |
Day 7 recovery rates differed markedly between ALMANACH and control facilities. In ALMANACH facilities, 849 (85.4%) of 994 children with complete follow-up were reported to have fully recovered. In control facilities, 603 (71.4%) of 845 children were reported fully recovered. The odds ratio (OR) for day 7 recovery was 2.34 (95% CI = 1.87-2.96) in ALMANACH compared to control facilities, and 2.63 (1.60-4.32) after adjusting as described above.

For most secondary outcomes, we observed large differences between ALMANACH and control facilities. HCPs referred patients to higher level of care over three times more often in the ALMANACH group (RR = 3.25 (2.12-4.96)). We saw an more parenteral antimicrobial prescription and a less oral antimicrobial prescription in ALMANACH facilities, with adjusted odds ratios of 2.42 (1.00-5.85) and 0.40 (0.22-0.73), respectively. Differentiating antimicrobials into antibiotic and antimalarial treatment revealed that in ALMANACH facilities 120 (12.4%) of 966 children received parenteral antimalarials compared to 59 (6.9%) of 855 in control facilities; for parenteral antibiotics the respective difference was 56 (5.8%) of 966 vs 25 (2.9%) of 855. Oral antimalarial prescription rate was lower in ALMANACH facilities: 476 (49.3%) of 966 compared to 490 (57.3%) of 855 cases in control facilities. There was no significant difference in oral antibiotic prescription between the groups (ALMANACH: 290 (30.0%) of 966 vs. control: 291 (34.0%) of 855).

The intervention affected the communication of diagnosis and follow-up advice to caregivers. In ALMANACH facilities 811 (84.0%) of 966 caregivers reported that HCPs explained the child’s diagnosis to them compared to only 557 (65.1%) of 855 in control facilities. The likelihood of receiving follow-up advice by the HCP was also much higher in ALMANACH facilities, with 596 (61.7%) of 966 families advised vs 179 (20.9%) of 855 in facilities without ALMANACH. Adjusted associations were very similar.

Lastly, we analysed differences in proportions of key diagnoses (according to IMCI protocols) made by HCPs in both groups. Pneumonia, diarrhoea, malnutrition, anaemia were markedly more often, and suspected malaria markedly less often, diagnosed in ALMANACH facilities. Only the rates of diagnosis of malaria confirmed through rapid diagnostic tests were similar between ALMANACH and control groups. All estimates are summarised in Table 2.

Table 1: Study sample characteristics: sociodemographic data, illness characteristics, information on health care providers, and health facilities

CHEW = Community Health Extension Worker  CHO = Community Health Officer
U5 = Under five years of age

1 Multiple answers possible
2 Other symptoms: Child is feeling very weak/not drinking/not eating; Child has an ear problem; Belly problem; Pain; Painful urination; Runny nose; Blood in the stool; Sore throat, I don’t know; Other;
3 Other qualifications: Lab technician; EHO; Medical doctor (n=1); Other;
* Chi-squared test
+ Fisher’s exact test

| Stock-outs of medicines for severe illness | Parenteral antibiotics | Parenteral antimalarials |
|------------------------------------------|------------------------|-------------------------|
| No electricity source                    | 6 (13.3)               | 10 (22.2)               |
| Unknown                                  | 5 (11.1)               | 7 (15.6)                |
| Health facility water supply*            |                        |                         |
| Piped                                    | 2 (4.4)                | 2 (4.4)                 |
| Pump / well                              | 33 (73.3)              | 15 (34.1)               |
| None                                     | 7 (15.6)               | 15 (34.1)               |
| Outages                                  | 7 (15.6)               | 10 (22.7)               |
| Stock-outs of medicines for severe illness |                        |                         |
| Parenteral antibiotics                    | 10 (22.2)              | 25 (56.9)               |
| Parenteral antimalarials                 | 7 (15.6)               | 21 (46.7)               |

Day 7 recovery rates differed markedly between ALMANACH and control facilities. In ALMANACH facilities, 849 (85.4%) of 994 children with complete follow-up were reported to have fully recovered. In control facilities, 603 (71.4%) of 845 children were reported fully recovered. The odds ratio (OR) for day 7 recovery was 2.34 (95% CI = 1.87-2.96) in ALMANACH compared to control facilities, and 2.63 (1.60-4.32) after adjusting as described above.
Comparative analysis of ALMANACH and record data indicated further differences between the groups in care process outcomes. In ALMANACH facilities, 850 (83·3%) of 1021 consultations were conducted using ALMANACH. When ALMANACH was used, 850 (100%) children were screened for IMCI danger signs, 847 (99·6%) had a recorded weight, MUAC was recorded in 718 (99·9%) of 719 indicated, temperature recorded in 714 (95·1%) of 751 indicated, pallor assessed in 745 (100%) of 745 indicated, and respiratory rate recorded in 192 (100%) of 192 indicated. In control facilities, we found no documentation of danger signs or respiratory rate, 197 (21·7%) of 908 had a recorded weight, MUAC was recorded in 52 (6·6%) of 784 children 6 to 59 months old, and temperature in 469 (51·7%) of 908 cases. Using malaria assessment and treatment as an example of adherence to guidelines, we found lower effectiveness decay through the care pathway in ALMANACH compared to control facilities (Error! Reference source not found.).

### Table 2: Primary and secondary outcomes

| Outcome                  | ALMANACH facilities cases | Control facilities cases | Unadjusted effect estimate | 95%-CI for unadjusted effect | Adjusted effect estimate | 95%-CI for adjusted effect |
|--------------------------|---------------------------|--------------------------|---------------------------|------------------------------|--------------------------|------------------------------|
| Recovery after 7 days    | 849 994 85·4%            | 603 845 71·4%           | RR 1·20                   | 1·14-1·26                   | OR 2·34                   | 1·87-2·96                   |
| Referral to hospital     | 96 1009 9·5%             | 26 861 3·0%             | RR 3·25                   | 2·12-4·96                   | OR 3·48                   | 2·24-5·41                   |
| Diagnosis communicated to caregiver | 811 966 84·0%          | 557 855 65·1%           | RR 1·29                   | 1·22-1·36                   | RR 1·27                   | 1·13-1·42                   |
| Follow-up advice given to caregiver | 596 966 61·7%        | 179 855 20·9%           | RR 2·95                   | 2·56-3·39                   | RR 2·76                   | 2·12-3·58                   |
| Parenteral antimicrobial treatment | 164 966 17·0%      | 80 855 9·4%             | RR 1·81                   | 1·42-2·33                   | OR 0·86                   | 0·81-0·92                   |
| Oral antimicrobial treatment | 620 966 64·2%         | 636 855 74·4%           | OR 0·62                   | 0·50-0·76                   | OR 0·40                   | 0·22-0·73                   |
| Any antimicrobial treatment | 745 966 77·1%         | 690 855 80·1%           | OR 0·96                   | 0·91-1·00                   | OR 0·98                   | 0·91-1·01                   |
| Parenteral antimalarial treatment | 120 966 12·4%        | 59 855 6·9%             | RR 1·80                   | 1·34-2·42                   | N/A                      | N/A                         |
| Oral antimalarial treatment | 476 966 49·3%         | 490 855 57·3%           | RR 0·86                   | 0·79-0·94                   | N/A                      | N/A                         |
| Parenteral antibiotic treatment | 56 966 5·8%          | 25 855 2·9%             | RR 1·98                   | 1·25-3·15                   | N/A                      | N/A                         |
| Oral antibiotic treatment | 290 966 30·0%          | 291 855 34·0%           | RR 0·88                   | 0·77-1·01                   | N/A                      | N/A                         |
| Antibiotic and antimalarial treatment | 189 966 19·6%     | 168 687 19·6%           | RR 1·00                   | 0·83-1·20                   | OR 0·99                   | 0·79-1·25                   |
| Suspected malaria        | 70 811 8·6%             | 77 557 13·8%            | RR 0·62                   | 0·46-0·85                   | OR 0·87                   | 0·41-1·85                   |
| Confirmed malaria        | 525 811 64·7%           | 363 557 65·2%           | RR 0·99                   | 0·92-1·08                   | N/A                      | N/A                         |
| Pneumonia                | 59 811 7·3%             | 5 557 0·9%              | RR 8·10                   | 3·27-20·06                  | N/A                      | N/A                         |
| Diarrhea                 | 118 811 14·5%           | 46 557 8·3%             | RR 1·76                   | 1·28-2·43                   | N/A                      | N/A                         |
| Malnutrition             | 57 811 7·0%             | 7 557 1·3%              | RR 5·60                   | 2·57-12·17                  | N/A                      | N/A                         |
| Anemia                   | 31 811 3·8%             | 3 557 0·5%              | RR 7·10                   | 2·18-23·10                  | N/A                      | N/A                         |

**RR = Risk ratio OR = Odds ratio CI = confidence interval N/A = not applicable**

1. Adjusted rate ratio from negative binomial regression (see statistical analysis)
2. 8 observations not used due to separation (combinations of covariates predicting the outcome perfectly)
DISCUSSION

This observational study found significant improvements in caregiver-reported recovery of children seven days after primary care consultation associated with the implementation of the ALMANACH digital CDSS with training, mentorship and data feedback in a programmatic setting. This impact on health outcomes is likely mediated by better adherence to evidence-based guidelines, supported by demonstrated improvements in QoC process outcomes across assessment, diagnosis, and management.

In children for whom ALMANACH was used, we found almost complete adherence to key IMCI assessments. In contrast, in control facilities in this study, and other studies on IMCI-related quality of care, HCPs commonly complete assessments in fewer than 50% of consultations with sick children.\[34,35\] We posit that this adherence to IMCI assessments, guided by ALMANACH, led to higher detection of severe illness and of diagnoses that are important causes of morbidity and mortality, particularly pneumonia, anaemia, diarrhoea, and malnutrition. The significantly higher rate of these IMCI diagnoses (and lower rate of ‘suspected’ malaria diagnosis) made in ALMANACH facilities supports this assumption, which may also have contributed to more accurate antimicrobial prescription.

In turn, we observed higher rates of referral and of treatment with parenteral antimicrobials, indicative of increased recognition and management of severe illness. Inadequate identification and treatment of severe disease are major barriers to reducing child mortality in LMICs.\[36,37\] Whilst the proportion of children with severe disease varies substantially between and within countries, with estimates varying from 5-21% in studies from comparable settings,\[35,38\] the 3·0% referral rate reported by caregivers in control facilities in this study is likely to be inappropriately low, and the 9·5% ALMANACH referral rate more consistent with the clinical need.

Further, ALMANACH showed significantly better HCP communication with caregivers as evidenced by higher rates of awareness of diagnosis and follow-up advice at exit interviews in ALMANACH facilities. Communication about a child’s illness and treatment are key standards set out by WHO for improving QoC for children at health facilities, and are associated with higher satisfaction with and intention to return to care.\[5,39\] In ALMANACH facilities, caregivers were made aware of diagnosis in 84·0% and given follow-up advice in 61·7% of consultations, substantially higher than in control facilities (65·1% and 20·9% respectively) and in multi-country IMCI studies in sub-Saharan African countries (43·70% and 20·57% respectively).\[34,39\]

These findings of better adherence to key evidence-based practices are consistent with other studies of child health-related CDSS in resource-constrained settings, including ALMANACH.\[19–21,29–31\] Lack of training, and other knowledge gaps such as difficulty recalling specific criteria (e.g. respiratory rate cut-offs) contribute to low adherence to IMCI, as do low motivation and physical and cognitive overload associated with working in such challenging settings.\[12\] Qualitative feedback from HCPs in Burkina Faso and Tanzania suggests that IMCI-related CDSS can improve confidence in diagnoses and managements, strengthen motivation, and address the issue of cognitive overload through the step-by-step nature of the guidance tailored to individual patients, particularly for severity classification and drug dosing.\[17,28\] Though we did not collect qualitative data as part of this study, it is possible that similar factors were mediators of effectiveness in Adamawa. However more research is needed to understand the relative importance of context and different components of the intervention package as enablers (including those mentioned above and others such as general investment in staff and commitment of the ADSPHCDA) and barriers (such as staff turnover and consultation length) to adoption and guideline adherence.

Whilst increased adherence to guidelines has been consistently demonstrated, few studies have assessed the impact of IMCI-related CDSS on health outcomes and, to our knowledge, none in the context of a long-term, large-scale implementation. The ALMANACH controlled trial in Tanzania also found higher day seven recovery rates, though also in the control recovery was higher (92·0% in control to 97·3% in ALMANACH facilities).\[25\] This is relatively high compared to the day seven recovery rates we saw in this study (71·4% in control and 85·4% in ALMANACH facilities). The contextual differences in sociodemographic, epidemiological and health system factors are likely to account for this, though a more substantial Hawthorne effect may also have been in effect as data was collected inside the consultation room in the Tanzania study.

This study demonstrates that implementation of ALMANACH can deliver impact on health outcomes at scale in remote, resource-constrained PHC facilities, where drug stock-outs are common, many facilities lack basic amenities, and one third of HCPs have never received IMCI training. A recent systematic review and meta-analysis found only modest changes in health outcomes with CDSS implementation.\[40\] Most of the CDSS studies included...
In this review were implemented in high-income countries, where HCP’s access to resources is substantially higher than most PHCs implementing IMCI. This may indicate that CDSS can deliver most value when used to support HCPs with limited skills and resources, provided that they are appropriately contextualised and implemented. In contrast with earlier ALMANACH studies,[29–31] we did not find significant lower antibiotic prescription rates.

Oral antibiotics were prescribed to 30·0% of children in ALMANACH and 34·0% in control facilities, slightly lower than the 43·1% (33·2–50·5) found in a recent meta-analysis of reported antibiotic use for sick children in LMICs. However, these may not reflect true antibiotic consumption rates given that most caregivers also reported treatment prior to consultation, most commonly from patent medicine stores or pharmacies. With increasing antibiotic prescription rates for children under five years of age, rising fastest in low-income countries, antimicrobial stewardship remains a global health priority to mitigate individual adverse events, rising antimicrobial resistance and resource waste.[41,42] Further gains in antimicrobial stewardship may be possible to achieve through integrating host biomarkers into IMCI-related CDSS.[24]

Our study has several limitations. Due to the nature of the evaluation in the programmatic setting, facilities were not randomised to ALMANACH or control. The presence of a large-scale child health intervention in some LGAs, combined with security- and weather-related accessibility issues, limited the number of suitable LGAs for the control group. Contextual differences including in epidemiology, health-seeking behaviour and the health system may therefore have influenced our data, though we adjusted for important potential confounders within the analysis. Further, the intervention could not be blinded, so performance or detection bias could have occurred, despite the use of standardised tools and procedures. The Hawthorne effect may have influenced the data, which has been found to increase patient-reported quality of care by 13%. [43] The observer effect should be similar in both intervention and control facilities, although there is a possibility that a differential effect could occur if the tablet were used more than usual in ALMANACH facilities. To reduce the likelihood of influencing HCP performance, we avoided direct observation and only collected information from caregivers and records. We did not conduct repeat clinical assessments after consultations due to the potential need to modify treatment, which could have influenced the primary outcome. It was therefore not possible to have complete certainty about the content of clinical consultations, not to conduct a thorough analysis of correct assessment, classification and treatment (including of antimicrobial appropriateness and referral appropriateness) of all IMCI diagnoses, and thus we were only able to provide some insights into the differences in routinely documented quality of care indicators. Lastly, given the complex nature of the intervention, incorporating the tablet-based CDSS along with training, mentorship and data feedback, we cannot determine the effect of the CDSS itself vs the entire intervention package. However, it is unlikely that training alone accounts for the difference in outcomes given that there was no major difference between groups in time since most recent IMCI training.

In conclusion, we found substantial impact of this IMCI-related CDSS on health and QoC outcomes, demonstrating that earlier findings in controlled or small-scale studies can be achieved at scale in a resource-constrained setting. Positive effects were seen across a range of process and outcome indicators, including assessment, diagnosis, treatment, and communication. These findings support the implementation of digital CDSS, with training, mentorship and data feedback, in resource-constrained settings as a means to strengthen progress towards universal health coverage.

Figure captions

Figure 1: Clinical decision support algorithm flow in the ALMANACH Nigeria

Figure 2: Study flow. *45 facilities included, but no participants attended eligible for screening or recruitment at 1 facility in the routine care arm.

Figure 3: Comparison of systems effectiveness decay for malaria assessment and treatment in ALMANACH and routine care facilities. Steps reflecting adherence to guidelines shown in blue, non-adherence shown in red, and not applicable in grey.
AUTHOR CONTRIBUTIONS
Torsten Schmitz (TS), Fenella Beynon (FB), Capucine Musard (CM), Marek Kwiatkowski (MK), Marco Landi (ML), Daniel Ishaya (DI), Jeremiah Zira (JZ), Muazu Muazu (MM), Camille Renner (CR), Edwin Emmanuel (EE), Solomon Gideon Bulus (SB), Rodolfo Rossi (RR).

FB, TS, RR, MK, and ML conceived the study’s concept and designed its methodology. CM, CR, MM, FB, TS and DI designed and developed the data collection tools. ML, CM, CR, DI, EE, JZ, and MM realised the study implementation, training of data collectors, and monitored the data collection in the field. Statistical analyses were done by MK with contributions from RR and FB. CM and CR verified the underlying data. FB, TS, RR, CM and MK interpreted the results. The original manuscript was written by TS, FB, and CM with contributions from MK and RR, and the final version was reviewed and approved by all authors. The joint first authors FB and TS contributed equally to this paper.

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COMPETING INTERESTS
All authors declare no competing interest.

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DATA SHARING
Anonymised participant data can be made available from the publication date upon reasonable request to the corresponding author (TS), subject to completion of a data sharing agreement and approval from the Adamawa State Primary Health Care Development Agency.

PATIENT CONSENT AND ETHICAL APPROVAL
All caregivers of eligible children who participated in this study gave their informed consent before participating. The study obtained ethical approval from the Health Research Ethics Committee of Adamawa, Nigeria (ADHREC 8/02/2020/003) and the Ethics Committee Northwest and Central Switzerland (Req-2020-00082).
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ALMANACH LGAs: Lamurde, Jada, Gombi, Hong
Routine care LGAs: Numan, Guyuk, Shelleng, Song

ALMANACH PHC facilities
n = 45
Children screened
n = 2244
Children enrolled
n = 1021
Day 7 follow-up
n = 994

Routine care PHC facilities
n = 44*
Children screened
n = 1904
Children enrolled
n = 908
Day 7 follow-up
n = 845

Excluded
Age n = 211
Routine preventative care n = 744
Trauma n = 30
No consent n = 4
Other n = 10

Routine preventative care n = 858
Trauma n = 30
No consent n = 4
Other n = 17
Figure 3: Comparison of systems effectiveness decay for malaria assessment and treatment in ALMANACH and routine care facilities. Steps reflecting adherence to guidelines shown in blue, non-adherence shown in red, and non-applicable in grey.
ANNEX

Annex 1: Patients and family sociodemographic data and care seeking information, health care provider and health facility characteristics

| Children & care-seeking | ALMANACH n (%), Routine n (%), p value, Total n (%) |
|-------------------------|-----------------------------------------------------|
| Pre-SARS-CoV2 (March 2020) | 343 (61.4), 216 (38.6), < 0.001 *, 559 (100) |
| During SARS-CoV2 (Jul-Sep 2020) | 678 (49.5), 692 (50.5), 1,370 (100) |

**Age in months**
- 2 to 5: 105 (10.3), 101 (11.1), 206 (10.7)
- 6 to 11: 140 (13.7), 118 (13.0), 258 (13.4)
- 12 to 23: 256 (25.1), 213 (23.5), 469 (24.3)
- 24 to 59: 508 (49.8), 453 (49.9), 961 (49.8)
- Unknown: 12 (1.2), 23 (2.5), 35 (1.8)

**Sex**
- Female: 483 (47.3), 456 (50.2), 939 (48.7)
- Male: 526 (51.5), 429 (47.3), 955 (49.5)
- Unknown: 12 (1.2), 23 (2.5), 35 (1.8)

**Presenting symptoms**
- Fever: 899 (88.1), 783 (86.2), 1,682 (87.2)
- Cough / difficulty breathing: 369 (36.1), 312 (34.4), 681 (35.3)
- Diarrhoea: 317 (31.1), 283 (31.2), 600 (31.1)
- Vomiting: 329 (32.2), 264 (29.1), 593 (30.8)
- Skin: 41 (4.0), 55 (6.1), 96 (5.0)
- Other: 333 (32.7), 371 (36.3), 704 (36.5)

**Onset of symptoms prior to consultation**
- Same or previous day: 265 (26.0), 275 (30.3), 540 (28.0)
- 2 days to < 1 week: 439 (43.0), 362 (39.9), 801 (41.5)
- 1 to 2 weeks: 230 (22.5), 194 (21.4), 424 (22.0)
- ≥ 2 weeks: 76 (7.4), 63 (6.9), 139 (7.2)
- Unknown: 11 (1.1), 14 (1.5), 25 (1.3)

**Treatment in last 2 weeks**
- Yes: 543 (53.2), 521 (57.4), 1,064 (55.2)
- No: 474 (46.4), 379 (41.7), 853 (44.2)
- Unknown: 4 (0.4), 8 (0.9), 12 (0.6)

**Source of previous treatment**
- Same facility: 31 (3.0), 56 (6.2), 87 (4.5)
- Other facility: 31 (3.0), 21 (2.3), 52 (2.7)
- Pharmacy / patent medicine store: 440 (43.1), 397 (43.7), 837 (43.4)
- Traditional healer: 22 (2.2), 27 (3.0), 49 (4.5)
- Informal (drug peddler / other): 15 (1.5), 13 (1.4), 28 (1.5)
- Friend relatives/community: 4 (0.4), 7 (0.8), 11 (1.0)
- Unknown: 478 (46.8), 387 (42.6), 865 (44.8)

**Reported travel time to facility**
- < 30 minutes: 696 (68.2), 770 (84.8), < 0.001 *, 1,466 (76.0)
- ≥ 30 minutes: 307 (30.1), 128 (14.1), 435 (22.6)
- Unknown: 18 (1.8), 10 (1.1), 28 (1.5)

**Accompanying caregiver**
- Mother: 767 (75.1), 662 (72.9), 1,429 (74.1)
- Other: 254 (24.9), 246 (27.1), 500 (25.9)

**Mother's educational level**
- No schooling: 350 (34.3), 281 (31.0), 631 (32.7)
- Primary: 124 (12.1), 134 (14.8), 258 (13.4)
- Secondary: 252 (24.7), 212 (23.4), 464 (24.1)
- Higher: 38 (3.7), 34 (3.7), 72 (3.7)
- Unknown: 257 (25.2), 247 (27.2), 504 (26.1)

**No. children <5 in household**
- 1 to 2: 643 (63.0), 617 (68.0), 1,260 (65.3)
- 3 to 4: 211 (20.7), 211 (23.2), 424 (21.9)
- ≥ 5: 110 (10.8), 77 (8.5), < 0.001 *, 187 (9.7)
- Unknown: 57 (5.6), 3 (0.3), 60 (3.1)

**Health care providers**
- 144 (48.5), 153 (51.5), 297 (100)

Qualification
- CHW / CHO
### Chi-squared test

3 Other qualifications: Lab technician; EHO; medical doctor (n=1); other;

1 Other symptoms: Child is feeling very weak/not drinking/not eating; child has an ear problem; belly problem; pain; painful urination; runny nose; blood in the stool; sore throat, I don’t know; other;

3 Other qualifications: Lab technician; EHO; medical doctor (n=1); other;

8 Chi-squared test

95 Fisher’s exact test

#### Health facilities

| Distance from main road | < 30 minutes | 30 – 60 minutes | ≥ 60 minutes |
|-------------------------|--------------|-----------------|--------------|
| 0 – 99                  | 15 (33·3)    | 22 (50·0)       | 37 (41·6)    |
| 100 – 199               | 16 (35·6)    | 15 (34·1)       | 31 (34·8)    |
| ≥ 200                   | 11 (24·4)    | 4 (9·1)         | 15 (16·9)    |
| Unknown                 | 3 (6·7)      | 3 (6·8)         | 6 (6·7)      |

### Health facility power supply

| All day (no interruptions) | 7 (15·6) | 4 (9·1) | 11 (12·4) |
| All day (interruptions)    | 10 (22·2) | 15 (34·1) | 25 (28·1) |
| ≤ Half a day               | 17 (37·8) | 16 (36·4) | 33 (37·1) |
| No electricity source      | 6 (13·3) | 8 (18·2) | 14 (15·7) |
| Unknown                    | 5 (11·1) | 1 (2·3) | 6 (6·7) |

### Health facility water supply

| Piped                    | 2 (4·4) | 2 (4·6) | 1·0 ** | 4 (4·5) |
| Pump / well              | 33 (73·3) | 23 (52·3) | 0·01 ** | 56 (62·9) |
| None                     | 7 (15·6) | 18 (40·9) | 0·01 ** | 25 (28·1) |
| Unknown                  | 5 (11·1) | 1 (2·3) | 0·20 ** | 6 (6·7) |
| Outages                  | 7 (15·6) | 10 (22·7) | 0·43 ** | 17 (19·1) |

### Stock-outs of medicines for severe illness

| Parenteral antibiotics   | 10 (22·2) | 15 (34·1) | 0·15 ** | 25 (28·1) |
| Parenteral antimarials    | 7 (15·6) | 14 (31·8) | 0·13 ** | 21 (23·6) |

**CHEW = Community Health Extension Worker**  **CHO = Community Health Officer**  
**U5 = Under five years of age**

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1 Multiple answers possible

2 Other symptoms: Child is feeling very weak/not drinking/not eating; child has an ear problem; belly problem; pain; painful urination; runny nose; blood in the stool; sore throat, I don’t know; other;

3 Other qualifications: Lab technician; EHO; medical doctor (n=1); other;

8 Chi-squared test

95 Fisher’s exact test
Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cohort reporting guidelines, and cite them as:

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| Reporting Item       | Page Number |
|----------------------|-------------|
| **Title and abstract** |             |
| Title                | #1a         | Indicate the study’s design with a commonly used term in the title or the abstract | 1 |
| Abstract             | #1b         | Provide in the abstract an informative and balanced summary of what was done and what was found | 3 |
| **Introduction**     |             |                                           |   |
| Background / rationale | #2         | Explain the scientific background and rationale for the investigation being reported | 5 |
| Objectives           | #3         | State specific objectives, including any prespecified hypotheses | 5 |

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### Methods

| Study design #4 | Present key elements of study design early in the paper | 5 |
| Setting #5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 5-6 |
| Eligibility criteria #6a | Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. | 5-6 |
| Eligibility criteria #6b | For matched studies, give matching criteria and number of exposed and unexposed | |
| Variables #7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 6 |
| Data sources / measurement #8 | For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable | 6-7 |
| Bias #9 | Describe any efforts to address potential sources of bias | 6,7,12 |
| Study size #10 | Explain how the study size was arrived at | 6 |
| Quantitative variables #11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why | 6-9 |
| Statistical methods #12a | Describe all statistical methods, including those used to control for confounding | 6-7 |
| Statistical methods #12b | Describe any methods used to examine subgroups and interactions | 6-7 |
| Statistical methods #12c | Explain how missing data were addressed | 6-7 |
| Statistical methods #12d | If applicable, explain how loss to follow-up was addressed | 6-7 |
**Statistical methods**

Describe any sensitivity analyses

n/a

**Results**

**Participants**

Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.

Give reasons for non-participation at each stage 7, Fig.2

Consider use of a flow diagram Fig.2

Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.

Indicate number of participants with missing data for each variable of interest 7-9

Summarise follow-up time (eg, average and total amount)

Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.

Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included 6-7, 9-10

Report category boundaries when continuous variables were categorized 8-9

If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses 9-10
Discussion

Key results #18 Summarise key results with reference to study objectives 10-11

Limitations #19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.

Interpretation #20 Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. 10-12

Generalisability #21 Discuss the generalisability (external validity) of the study results 11

Other Information

Funding #22 Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based 13

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