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Provider skills, medications and diagnostic studies used to care for patients in a rural Ugandan Emergency Department

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Title: Provider skills, medications, and diagnostic studies used to care for patients in a rural Ugandan Emergency Department

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Abstract

Objectives: To determine the most commonly utilized resources (provider procedural skills, medications, laboratory studies and imaging) needed to care for patients

Setting: A single Emergency Department of a district level hospital in rural Uganda

Participants: 26,710 patient visits

Results: Procedures were performed for 65.6% of patients, predominantly intravenous cannulation, wound care, bladder catheterization, and orthopedic procedures. Medications were administered to 87.6% of patients, most often pain medications, antibiotics, IV fluids, anti-malarials, nutritional supplements, and vaccinations. Laboratory testing was utilized for 85% of patients, predominantly malaria smears, rapid glucose testing, HIV assays, blood counts, urinalyses, and blood type. Radiology testing was performed for 17.3% of patients, including plain films, point of care ultrasound and formal ultrasound.

Conclusion: This study describes the skills and resources needed to care for a large prospective cohort of patients seen in a district hospital ED in rural SSA. It demonstrates the vast majority of patients were treated with a small formulary of critical medications and limited access to labs and imaging, but providers require a broad set of decision-making and procedural skills.

Strengths and limitations of the study:

The study follows a large, multi-year cohort which accounts for seasonal variation in disease prevalence

Data reflects local resource limitations, additional tests and imaging may have been helpful to optimize patient outcomes

No assessment was made of the appropriateness of procedures and testing, or whether additional studies might have been indicated

Introduction:

Strengthening emergency and acute care infrastructure is a high priority for the World Health Organization,¹ and content experts have made important strides to develop a framework for emergency care development.² However, there are few longitudinal evaluations of facility level data that assess the epidemiology of patient presentations, the consumable and non-consumable resources used for care, and the clinical and procedural skills required to deliver emergency care in sub-Saharan Africa (SSA) on which to base these efforts.^{3 4 5 6} The limited data that do exist are largely from urban areas or describe presentations over a short time frame, introducing possibility of bias, given the seasonal nature of some diseases thought to be prevalent in this area. It is estimated that 62% of the population of SSA lives in rural areas,⁷ indicating that data from rural areas is essential to guide emergency care development.

The uncategorized burden of disease likely contributes to the lack of funding and slow progress of emergency medicine development in these countries.⁸ While several emergency medicine training programs have been developed over the past decade^{9 10 11 12 13 14} and the African Federation for Emergency Medicine has developed a Curriculum for Emergency Care training,¹⁵ the educational content of these efforts has largely been drawn from international guidelines and expert consensus of foreign emergency physicians and local physicians providing emergency care in these settings.

Lack of information regarding the most frequently utilized procedural skills and the resources required to care for acutely ill and injured patients hinders the development of emergency care

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3 delivery and training in low resource settings. This study describes the resources and clinical
4 skills utilized to care for a large, longitudinal cohort of patients presenting to a not-for-profit
5 district hospital in rural Uganda. It addresses some of the research gaps in service delivery,
6 resource utilization and training needs necessary to ensure effective emergency care as identified
7 in a recent consensus statement.¹⁶ This knowledge could inform required training and protocols,
8 as well as emergency care formulary development, and checklists of useful laboratory resources
9 and diagnostic imaging modalities to refine the proposed framework for emergency care
10 development in SSA.¹⁷
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24 **Methods**

25 *Study design*

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34 This is a retrospective analysis of a prospectively collected data from a quality assurance
35 database of patients seen at the Karoli Lwanga Hospital ED from November 2009 through
36 February 2015. The database includes demographic information, as well as diagnostic studies,
37 medications administered, and procedures performed during ED care. Labs, imaging and
38 procedures ordered in the ED but delayed until the patient was admitted to the ward were
39 included, so the numbers reflect the resources that providers felt were needed to care for the
40 patients, regardless of whether the resources were immediately available in the emergency
41 department.
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53 *Background and Study Setting*

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6 Karoli Lwanga Hospital is a private, not-for-profit district hospital located in the town of
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8 Nyakibale, in the Rukungiri district of rural southwest Uganda. The district covers 1445 square
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10 kilometers, and the 2012 census listed 321,300 persons. Life expectancy is 50 years, compared to
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12 a national figure of 58.7 years. The HIV prevalence rate is 8.7% compared to a national rate of
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14 7.2%. The maternal mortality rate is 474 per 100,000 live births, compared to a national rate of
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16 440 per 100,000. The infant mortality rate is 76 per 1000 live births, compared to national rate of
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18 45 per 1000. There are 2 district hospitals in the area, 63 health centers, and 17 private clinics.
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21 The nearest referral hospital is in Mbarara, some 110 km away from Nyakibale.^{18 19}
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27 Karoli Lwanga Hospital has a six-bed ED with an average census of 500 patients per month. The
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29 ED is located centrally in the hospital, adjacent to most wards. The outpatient department (OPD)
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31 operates 9 am to 5 pm Monday through Friday and from 8 am until noon on Saturday.
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34 Ambulatory patients are informally triaged, usually by a nurse or clinical officer, and may be
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36 referred to the ED based on chief complaint or concerning signs or symptoms noted on patient
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38 evaluation. Patients who are non-ambulatory, severely ill, or acutely injured are seen in the ER
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40 directly, as are those arriving during hours when OPD is closed. The ED hours varied during the
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42 time of the study, but always began at 8 am and extended until at least 10 pm. For the past
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44 several years, the ED sees patients between 8 am and 2 am.
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51 The ED is staffed by non-physician clinicians locally known as Emergency Care Practitioners
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53 (ECPs); these are nurses who are enrolled in or have completed a two-year training program in
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55 emergency care. During the period of the study, ECPs transitioned from full-time supervision by
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3 EM board-certified/board eligible physicians to more independent patient care with supervision
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5 by senior-level ECPs and intermittent supervision by EM physicians. This training program and
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7 care delivery model have been described elsewhere.^{20 21} Hospital-based Ugandan physicians
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9 were on call for consultation for severely ill patients being admitted and major acute surgical
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11 emergencies.
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14 15 16 17 *Data collection and Analysis* 18

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22 The study population includes all ED patient visits from November 14, 2009 through February
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24 28, 2015. The start date reflects the initial day that data was collected on ED patients, which was
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26 approximately 4 months after the initial training of the ECPs began. Data were charted by ECPs
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28 on a structured written chart, which was entered into the quality assurance database by a trained
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30 research assistant at the time of ED disposition. Additionally, during most of the time period, the
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32 paper charts were scanned and securely saved as part of the QA processes. The QA database
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34 tracked 31 fields including demographics, vital signs, chief complaint, lab studies, imaging,
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36 medications administered, procedures performed, final diagnosis, disposition and condition on
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38 discharge. As this is the first program to utilize task-shifting for provision of emergency care in
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40 SSA, the QA database was created to monitor patient presentations and outcomes, to better
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42 characterize acute care needs, and to improve program operations and educational content.
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51 Data collection initially utilized Microsoft Excel (Microsoft, Redmond WA, USA) and was
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53 transitioned to Microsoft Access in March 2012. The database was de-identified prior to
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55 analysis. Data were merged and analyzed in Stata Statistical Software Version 13 (Stata
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3 Statistical Software: Release 13, College Station, TX: StataCorp LP). The data was formatted
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5 and cleaned, and the variables of interest were abstracted from the general database prior to
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7 analysis by a single researcher. Descriptive tables of the most common skills and resources were
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9 created.
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12 13 14 15 *Ethical review*

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20 This study was approved by the Mbarara University of Science and Technology Institutional
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22 Review Board, the Uganda National Council for Science and Technology, and University of
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24 Massachusetts Institutional Review Board (reference number HS 1405). Local approval was
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26 obtained from the medical superintendent of the hospital.
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31 **Results**

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36 The cohort includes a total of 26,710 patient visits. Males accounted for 14,720 (55.1%) visits.
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38 Pediatric patients under 5 years of age were 20.5% of total visits, and patients aged 5-17 were
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40 16.2% of visits. Adults 18-65 years accounted for 50.6% of visits, and elders over 65 accounted
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42 for 12.4% of visits. (Table 1)
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48 One or more procedures were performed during 17,509 (65.6%) patient visits, with a total of
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50 22,729 procedures performed. Multiple procedures were required for 3601 (14.8%) patient visits
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52 with a mean of 1.3 and a maximum of 7 procedures among those who required a procedure. The
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54 most common procedure performed was IV cannulation. Wound care procedures were next,
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3 followed by bladder catheterization, splinting and immobilization, procedural sedation, lumbar
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5 punctures, and incision and drainage of abscesses. (Table 2).
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10 A total of 73,317 doses of medications were administered. Medications were used for 23,401
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12 (87.6%) patient visits, with 20,705 (77.5%) receiving more than one medication. The most
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14 common class of medications used was analgesics, including acetaminophen, non-steroidal anti-
15
16 inflammatory, and opioid analgesics. The next most common class prescribed was antibiotics,
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18 followed by antimalarials, intravenous fluids, and nutritional supplements. Approximately 1800
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20 medications could not be classified due to misspellings or non-standard abbreviations.
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24 Medication categories are listed in Table 3, and examples of medications by category are listed
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26 in Table 4. Specific medications given to more than 0.5% of the patient cohort are listed in Table
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Laboratory tests were ordered for 22,708 (85.0%) patient visits, with a total of 38,378 studies
being performed. The most common study was malaria testing, done in 14,440 (54.0%) patient
visits. Bedside glucose was checked in 5666 (21.2%) patient visits. HIV testing was done in
5195 (19.4%) patient visits with CD4 testing for 465 (1.7%). Hemoglobin was run for 4108
(15.4%) patient visits. Urinalysis was performed for 3062 (11.5%) patient visits. Blood type was
checked for 1366 (5.1%) patient visits. (Table 6)

Radiology studies were performed for 4630 (17.3%) patient visits. Plain films were performed or
ordered on 1864 (7.0%) patient visits. The most common X-ray was a chest X-ray, done for
1071 patient visits (4.0% of the cohort, 45.6% of all plain films requested.) Other X-rays

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3 included 477 lower and 275 upper extremity films, 89 pelvis films, 88 skull films, and 73
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5 abdominal films. Plain film radiography was available only when a radiology technician was
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7 present, mostly weekday business hours, but with some call-in capacity on evenings and
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9 weekends. Point of care ultrasound (POCUS) was performed on 2194 (8.2%) patient visits
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11 including 417 FAST exams, 139 abdominal studies, 107 echocardiograms, and 73
12
13 transabdominal exams for obstetric or gynecological indications. Formal ultrasound imaging by
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15 the hospital radiology technician was requested for 998 (3.7%) patient visits. (Table 7)
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25 **Limitations**

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29 This is a single center study in rural Uganda with a unique training program that was developed
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31 after a needs assessment of the burden of disease,²² but which took into account resource
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33 limitations at Karoli Lwanga Hospital. Thus, it is possible our analysis failed to document
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35 potentially useful resources that were not available, thus were not part of the ECPs training.
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37 Other analyses of smaller portions of this data set looking at common diagnosis can help temper
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39 this limitation to some degree.²³ Practice patterns and proficiencies of the ECPs may not be
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41 representative of other clinicians. Increased availability of plain film radiography would likely
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43 have increased the number of patients with imaging in the ED. CT imaging could aid in
44
45 managing head trauma and some abdominal injuries but is not available at the site, however, this
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47 is true in most district hospitals in SSA. Likewise, there may be additional laboratory tests that
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49 would be useful but were not available routinely during study period or were subject to “stock-
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51 outs” of necessary reagents. While we did record tests ordered but not completed, if ECPs were
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3 aware of the stock-out, they may not have ordered a test even if they felt was indicated. Given
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5 the retrospective nature of this review, we do not have a way of controlling for this lack of
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7 ordering due to knowledge of stock-outs.
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12 Free text entry of data by non-medically trained research assistants resulted in a small amount of
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14 data being lost due to misspelling or incorrect transcription. Modifications to the data entry
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16 process have since reduced such errors. Additionally, there was no gold standard arbitration
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18 done to assess the true “need” for the interventions performed or to critique other interventions
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20 that might have been indicated. Nonetheless, this provides a pragmatic assessment of the real-
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22 world practice of emergency medicine at a district hospital in a rural area of SSA.
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29 **Discussion**

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34 This is a longitudinal cohort of 26,710 acutely ill patient visits cared for in a rural emergency
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36 department in sub-Saharan Africa. The study builds on the work of previous authors in several
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38 important ways. First, to our knowledge, this is largest data set of emergencies presenting to a
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40 rural district hospital in a low-resource country. Additionally, we report detailed information on
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42 procedures performed and resources used for care in this large cohort over a five-year period. To
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44 deliver effective emergency care, ongoing research is required to further elucidate both training
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46 and resource needs in resource limited settings. By documenting current practice patterns of
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48 emergency care in a functional ED in rural Uganda, the data can inform training and resource
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50 allocation for providers in similar settings.
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3 In considering medical knowledge that should be included in emergency care training, the
4 spectrum of diseases presenting acutely must be understood. Data from the Global Burden of
5 Disease Study indicates an increasing contribution of non-communicable disease towards
6 worldwide mortality,²⁴ but it is unknown how much these diseases contribute to the burden of
7 emergencies in SSA. The data shows that ECPs cared for patients across all age ranges who
8 presented with diverse complaints. Commonly utilized medications and diagnostic tests indicate
9 that patients presented for emergency care with a broad array of communicable and non-
10 communicable diseases. Our data suggests that even in rural areas with high rates of
11 communicable diseases, non-communicable diseases contribute significantly to the need for
12 acute care. Additionally, given the fact that analgesics were given to 31.4% of patients and
13 approximately 2.5% of patients underwent procedural sedation, it can be inferred that the ECPs
14 managed a large burden of acutely painful conditions. High rates of splinting and
15 immobilization, as well as the number of FAST exams performed, indicate trauma care is a
16 prominent component of emergency care in this setting. This is consistent with Uzochina et al's
17 study from Nigeria and Wachira et al's data from Kenya.

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41 Skills such as x-ray interpretation and point of care ultrasound (POCUS) appear to be high yield,
42 given x-rays were performed on 7.0% and POCUS on 8.2% of patient visits. POCUS has been
43 shown in other studies to supplement limited radiography capacity and enhance safety of
44 invasive procedures in resource limited settings.^{25 26 27} The ECP training on POCUS has
45 increased over time and is described elsewhere.²⁸

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3 The variety of procedures performed indicates that providers in the setting likely require a broad
4 range of procedural skills. Peripheral IV access was the norm, but occasional patients required
5 intra-osseous access or cannulation of the external jugular vein. In addition to the common
6 procedures listed above, the ECPs are trained to perform paracenteses, thoracenteses, joint
7 aspirations, and nerve blocks. While these procedures are required relatively infrequently, they
8 are crucial for symptomatic relief, making the diagnosis, and guiding treatment for a significant
9 proportion of patients seen in rural EDs in SSA. The ability to perform these procedures in a
10 timely manner is required to deliver effective, quality emergency care.
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24 Resource allocation and preparation is the other essential component for effective emergency
25 care delivery. Based on the proposed framework by Calvello et al., Karoli Lwanga Hospital
26 should be an “intermediate facility”. In their framework, signal functions are defined as
27 “lifesaving saving clinical interventions” and a consensus-based list of these functions was
28 generated. While our study did not seek to specifically map which signal functions the ECPs
29 carried out, comparing their list of signal functions with medications administered, procedures
30 performed, and laboratory and diagnostic imaging testing used in our cohort, it is clear there is
31 significant overlap between their framework and the real-world practice of emergency care in
32 this setting.
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48 The medications most frequently used were pain medications, antibiotics, antimalarials, IV fluid
49 boluses, nutritional supplements, respiratory, and cardiac medications. These medications are on
50 the World Health Organization Model List of Essential Medications,²⁹ and are expected to be
51 widely available. Approximately 13% of patients received vaccinations as part of their
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3 emergency care, highlighting another health-systems strengthening role of emergency care, in
4 providing an additional venue for primary prevention. It is also encouraging to see some
5 evidence that patient's pain was addressed, as pain assessment and management has been
6 identified as a deficit in prior studies.³⁰
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15 There currently is no widely recognized list of essential emergency laboratory tests in low
16 resource settings, although the WHO is currently in the process of developing consensus-based
17 minimum package for this. From our data, it appears that point of care blood glucose testing,
18 malaria smears (or rapid diagnostic malaria tests), assessment of hemoglobin, blood typing, HIV
19 testing and fluid analysis (CSF, urine, pleural fluid, ascites, and joint aspirates) are all commonly
20 used. While used to a lesser extent, our database and clinical experience indicated pregnancy
21 testing is important in this setting as well. The ability to perform HIV screening is critical.
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Uganda adopted a national guideline recommending opt-out testing in 2005,³¹ but missed
opportunities for early diagnosis and initiation of antiretroviral treatment in difficult to reach
populations persist.^{32 33 34} Due to stock-outs and lack of point of care testing performed by ECPs,
this cohort of patients had a much lower rate of HIV testing than guidelines recommend. Testing
for HIV in the acute care setting offers patients a pathway to access the HIV continuum of care
and begin treatment at an earlier stage in the diagnosis, which in turn has been shown to make
management more effective reduce HIV transmission and the future burden of disease.^{35 36}
Future directions for research include comparing data at this facility with training needs and
resource allocation at other facilities in SSA. Additionally, formally assessing the use of signal
functions in this cohort could help refine the framework proposed to guide emergency care
implementation in SSA.

Conclusions

This study tracks the resources utilized to diagnose, stabilize and treat a large cohort of consecutive patients seen in a not-for-profit, rural district ED in SSA. Analysis of the resources used and knowledge and skills applied to care for this patient cohort provide a rare glimpse of what emergency care delivery entails in rural SSA. The results of this study coupled with the previously developed framework to guide emergency care implementation will enable benchmarking and data-driven policy making for improvement of facility-based emergency care delivery in low resources settings within sub-Saharan Africa.

Author Contributions: CB, BR and UP performed data cleaning, statistical analysis and submission of this work. HH, SC, and MB inputted the data into the database. UP and SC conceived and designed the study and supervised all portions of the study. CB, SC and UP drafted the manuscript and all authors revised it. All authors take responsibility for the paper as a whole.

Competing Interests: The authors have no conflicts of interest to report

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Data Sharing: unpublished data is not be available to persons not affiliated with GEC

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Table 1
Demographics

	number	percent
Sex		
Male	14,720	55.1
Female	11,934	44.7
Unspecified	56	0.2
Age		
Children under 5 years	5,478	20.5
Pediatric 5-17 years	4,337	16.2
Adult 18-65 years	13,510	50.6
Elderly >65 years	3,305	12.4

Table 2
Procedures

Procedure	Number	Percent of procedures	Percent of cohort
IV	9,161	40.3	34.2
Wound care	7,246	31.9	27.1
Catheter	1,523	6.7	5.7
Splint & immobilization	743	3.3	2.8
Procedural sedation	663	2.9	2.5
Lumbar puncture	513	2.3	2.0
I & D	511	2.2	1.9

Table 3
Medications by Category

Medication class	Doses	Percent of medications given
Analgesics	22,981	31.4
Antibiotics	14,486	19.8
Antimalarials	5,495	7.5
IV fluids	5,445	7.4
Nutritional	4,785	6.5
Respiratory	3,394	4.6
GI	2,584	3.5
CNS/Neuro	2,495	3.4
Cardiac	2,489	3.4
Vaccines	1,984	2.7

Table 4

Most Common Medications by Category

Class	examples			
Analgesics	paracetamol/ acetaminophen	diclofenac	tramadol	Pethidine/ meperidine
Antibiotics	ceftriaxone	cloxacillin	gentamicin	metronidazole
Antimalarials	artemether/ lumefantrine	quinine	artesunate	sulfadoxine/ pyrimethamine
Nutritional supplements	dextrose	ORT	multivitamin	ready-to-use therapeutic food
Respiratory	oxygen	salbutamol	cough suppressant	nebulized magnesium
GI	omeprazole	metoclopramide	ranitidine	bisacodyl
CNS	diazepam	haloperidol	mannitol	amitriptyline
Cardiac	furosemide	nifedipine	aspirin	digoxin

Table 5

Most Common Medications by Number of Doses

Medication	Doses	Percent of medications
Paracetamol	14,697	20.0
Ceftriaxone	4,697	6.41
Diclofenac	4,508	6.2
Normal saline	3,672	5.0
Coartem	3,542	4.8
Tetanus vaccine	1,862	2.5
Tramadol	1,842	2.5
Quinine	1,775	2.4
Cloxacillin	1,686	2.3
Gentamicin	1,602	2.2
Ringers' lactate	1,446	2.0

Table 6
Laboratory Testing

Test	Number	Percent of cohort
Malaria	14,473	54.2
Capillary blood glucose	5,703	21.4
HIV test	5,213	19.5
Hemoglobin	4,070	15.2
Urinalysis	3,062	11.5
Blood group	1,366	5.1

Table 7
Imaging

	Number of Studies	Percent of Imaging
X-ray	2441	
Chest	1071	43.9
Arm	477	19.5
Leg	275	11.3
Unspecified	150	6.1
Pelvis	89	3.6
Skull	88	3.6
Abdomen	73	3.0
POCUS	2289	
Unspecified	1465	64.0
FAST	417	18.2
Abdominal	139	6.1
Cardiac Echo	107	4.7
Formal US	1006	
Unspecified	695	69.1
Abdominal	146	14.5
Pelvic/OB	130	12.9

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3 Legend of tables
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7 Table 1. Demographics
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9 Table 2. Procedures
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11 Table 3. Medication classes
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13 Table 4. Most Common Medications by Category
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15 Table 5. Most Common Medications by Total Doses
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17 Table 6. Laboratory studies
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19 Table 7. Imaging
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What resources are utilized in Emergency Departments in rural sub-Saharan Africa? A retrospective analysis of patient care in a district-level hospital in Uganda

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2
3 1 **Title:** What resources are utilized in Emergency Departments in rural sub-Saharan Africa? A
4 2 retrospective analysis of patient care in a district-level hospital in Uganda

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37 35
38 36 **Keywords:** procedural skills, medication formulary, radiology services, point-of-care ultrasound,
39 37 sub-Saharan Africa, acute care

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1
2 **Abstract**

3 Objectives: To determine the most commonly utilized resources (provider procedural skills,
4 medications, laboratory studies and imaging) needed to care for patients

5 Setting: A single Emergency Department (ED) of a district level hospital in rural Uganda

6 Participants: 26,710 patient visits

7 Results: Procedures were performed for 65.6% of patients, predominantly intravenous
8 cannulation, wound care, bladder catheterization, and orthopaedic procedures. Medications were
9 administered to 87.6% of patients, most often pain medications, antibiotics, IV fluids, anti-
10 malarians, nutritional supplements, and vaccinations. Laboratory testing was utilized for 85% of
11 patients, predominantly malaria smears, rapid glucose testing, HIV assays, blood counts,
12 urinalyses, and blood type. Radiology testing was performed for 17.3% of patients, including X-
13 rays, point of care ultrasound and formal ultrasound.

14 Conclusion: This study describes the skills and resources needed to care for a large prospective
15 cohort of patients seen in a district hospital ED in rural sub-Saharan Africa (SSA). It
16 demonstrates the vast majority of patients were treated with a small formulary of critical
17 medications and limited access to labs and imaging, but providers require a broad set of decision-
18 making and procedural skills.

19 **Strengths and limitations of the study:**

20 The study follows a large, multi-year cohort which accounts for seasonal variation in disease
21 prevalence

22 Data reflect local resource limitations; additional tests and imaging may have been helpful to
23 optimize patient outcomes

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3 1 No assessment was made of the appropriateness of procedures and testing, or whether additional
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5 2 studies might have been indicated
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10 4 **Introduction:**
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12 5 Improving the delivery of acute care services has been proposed as a means strengthen overall
13 6 health infrastructure by supplementing primary care and reducing fragmentation caused by
14 7 targeting markers of specific disease processes for improvement.¹ Global research in
15 8 development of systems for acute and emergency care is hampered by the variety of settings in
16 9 which emergency care takes place in different parts of the world, poor understanding of the
17 10 reasons patients seek emergency care, poor standardization of reporting measures, and lack of
18 11 consensus on the essential services that should be provided.² The African Federation of
19 12 Emergency Medicine (AFEM) has proposed a framework for emergency care development in the
20 13 region.³ However, there are few longitudinal evaluations of facility level data that assess the
21 14 epidemiology of patient presentations, the consumable and non-consumable resources used for
22 15 care, and the clinical and procedural skills required to deliver emergency care in sub-Saharan
23 16 Africa (SSA) on which to base these efforts.^{4 5 6 7} The limited data that exist are largely from
24 17 urban areas or describe presentations over a short time frame, introducing possibility of bias,
25 18 given the seasonal nature of some diseases thought to be prevalent in this area. It is estimated
26 19 that 62% of the population of SSA lives in rural areas,⁸ indicating that data from rural areas are
27 20 essential to guide emergency care development.
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53 22 The uncategorized burden of disease likely contributes to the lack of funding and slow progress
54 23 of development of emergency care in these countries.⁹ While several emergency medicine
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1 training programmes have been developed over the past decade^{10 11 12 13 14 15} and the African
2 Federation for Emergency Medicine has developed a Curriculum for Emergency Care training,¹⁶
3 the educational content of these efforts has largely been drawn from international guidelines and
4 expert consensus of foreign emergency physicians and local physicians providing emergency
5 care in these settings.

6
7 Lack of information regarding the most frequently utilized procedural skills and the resources
8 required to care for acutely ill and injured patients hinders the development of emergency care
9 delivery and training in low resource settings. This study describes the resources and clinical
10 skills utilized to care for a large, longitudinal cohort of patients presenting to a not-for-profit
11 district hospital in rural Uganda. It addresses some of the research gaps in service delivery,
12 resource utilization and training needs necessary to ensure effective emergency care as identified
13 in a recent consensus statement.¹⁷ This knowledge could inform required training and protocols,
14 emergency care formulary development, and checklists of useful laboratory resources and
15 diagnostic imaging modalities to refine the proposed framework for emergency care
16 development in SSA.¹⁸

17 18 **Methods**

19 20 *Study design*

21
22 This is a retrospective analysis of a prospectively collected data from a quality assurance
23 database of patients seen at the Karoli Lwanga Hospital Emergency Department (ED) from

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3 1 November 2009 through February 2015. The database includes demographic information
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5
6 2 obtained upon arrival in the ED, as well as diagnostic studies, medications administered, and
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8 3 procedures performed during ED care. Labs, imaging and procedures ordered in the ED but
9
10 4 delayed until the patient was admitted to the ward were included, so the numbers reflect the
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12 5 resources that providers felt were needed to care for the patients, regardless of whether the
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14 6 resources were immediately available in the Emergency Department.
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19 8 *Background and Study Setting*

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24 10 Karoli Lwanga Hospital is a private, not-for-profit district hospital located in the town of
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27 11 Nyakibale, in the Rukungiri district of rural southwest Uganda. The district covers 1445 square
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29 12 kilometers, and the 2012 census listed 321,300 persons. Life expectancy is 50 years, compared to
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31 13 a national figure of 58.7 years. The HIV prevalence rate is 8.7% compared to a national rate of
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33 14 7.2%. The maternal mortality rate is 474 per 100,000 live births, compared to a national rate of
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35 15 440 per 100,000. The infant mortality rate is 76 per 1000 live births, compared to national rate of
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37 16 45 per 1000. There are 2 district hospitals in the area, 63 health centers, and 17 private clinics.
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39 17 The nearest referral hospital is in Mbarara, some 110 km away from Nyakibale.^{19 20}
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46 19 Karoli Lwanga Hospital has a six-bed ED with an average census of 500 patients per month. The
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48 20 ED is located centrally in the hospital, adjacent to most wards. The outpatient department (OPD)
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50 21 operates from 9 am to 5 pm Monday through Friday and from 8 am until noon on Saturday.
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52 22 Ambulatory patients are informally triaged, usually by a nurse or clinical officer, and may be
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54 23 referred to the ED based on chief complaint or concerning signs or symptoms noted on patient
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1 evaluation. All patients thought to require hospital admission are sent from the OPD to the ED.
2 In addition, patients who are non-ambulatory, severely ill, or acutely injured are seen in the ED
3 directly, as are those arriving during hours when OPD is closed. The ED hours varied during the
4 time of the study, but always began at 8 am and extended until at least 10 pm. For the past
5 several years, the ED sees patients between 8 am and 2 am. For emergency patients arriving
6 during overnight hours when the ED is closed, hospital security would phone the on-call
7 physician or clinical officer. These patients are not included in this study; however, during a six
8 month period when the ED was open 24 hours a day, only two patients on average arrived
9 between the hours of 2 and 8 am per day.

10
11 The ED is staffed by non-physician clinicians locally known as Emergency Care Practitioners
12 (ECPs); these are nurses who are enrolled in or have completed a two-year training programme
13 in emergency care. The training program was developed by a U.S.-based non-profit organization,
14 Global Emergency Care, that has been working to expand emergency care services in Uganda
15 since 2008, in collaboration with Karoli Lwanga Hospital, Mbarara University of Science and
16 Technology, and the Ugandan Ministry of Health. During the period of the study, ECPs
17 transitioned from full-time supervision by EM board-certified/board eligible physicians to more
18 independent patient care with supervision by senior-level ECPs and intermittent supervision by
19 EM physicians. This training programme and care delivery model have been described in more
20 depth elsewhere.^{21 22} Hospital-based Ugandan physicians were on call for consultation for acute
21 surgical emergencies and severely ill patients requiring admission.

22
23 *Data collection and Analysis*

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5 2 The study population includes all ED patient visits from November 14, 2009 through February
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7 3 28, 2015. The start date reflects the initial day that data were collected on ED patients, which
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9 4 was approximately 4 months after the initial training of the ECPs began. Orders were placed by
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11 5 ECPs on a structured hand-written chart; this information was prospectively entered into the
12
13 6 quality assurance database by a trained research assistant at the time of ED disposition.
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15 7 Additionally, during most of the time period, the paper charts were scanned and securely saved
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17 8 as part of the QA processes. The QA database tracked 31 fields including demographics, vital
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19 9 signs, chief complaint, lab studies, imaging, medications administered, procedures performed,
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21 10 final diagnosis, disposition and condition on discharge. As this is the first programme to utilize
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23 11 task-shifting for provision of emergency care in SSA, the QA database was created to monitor
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25 12 patient presentations and outcomes, to better characterize acute care needs, and to improve
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27 13 programme operations and educational content.
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36 15 Data collection initially utilized Microsoft Excel (Microsoft, Redmond WA, USA) and was
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38 16 transitioned to Microsoft Access in March 2012. The database was de-identified prior to
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40 17 analysis. Data were merged and analyzed in Stata Statistical Software Version 13 (Stata
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42 18 Statistical Software: Release 13, College Station, TX: StataCorp LP). The data were formatted
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44 19 and cleaned, and the variables of interest were abstracted from the general database prior to
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46 20 analysis by a single researcher. Descriptive tables of the most common skills and resources were
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48 21 created.
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55 23 *Ethical review*
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This study was approved by the Mbarara University of Science and Technology Institutional Review Board, the Uganda National Council for Science and Technology, and University of Massachusetts Institutional Review Board (reference number HS 1405). Local approval was obtained from the medical superintendent of the hospital.

Results

The cohort includes a total of 26,710 patient visits. Males accounted for 14,720 (55.1%) visits. Paediatric patients under 5 years of age were 20.5% of total visits, and patients aged 5-17 were 16.2% of visits. Adults 18-65 years accounted for 50.6% of visits, and elders over 65 accounted for 12.4% of visits (Table 1).

Table 1 Demographics		
	number	percent
Sex		
Male	14,720	55.1
Female	11,934	44.7
Unspecified	56	0.2
Age		
Children under 5 years	5,478	20.5
Paediatric 5-17 years	4,337	16.2
Adult 18-65 years	13,510	50.6
Elderly >65 years	3,305	12.4

1 One or more procedures were performed during 17,509 (65.6%) patient visits, with a total of
 2 22,729 procedures performed. Multiple procedures were required for 3601 (14.8%) patient visits
 3 with a mean of 1.3 and a maximum of 7 procedures among those who required a procedure. The
 4 most common procedure performed was IV cannulation. Wound care procedures were next,
 5 followed by bladder catheterization, splinting and immobilization, procedural sedation, lumbar
 6 punctures, and incision and drainage of abscesses. (Table 2).

Table 2
Procedures

Procedure	Number	Percent of procedures	Percent of cohort
IV	9,161	40.3	34.2
Wound care	7,246	31.9	27.1
Catheter	1,523	6.7	5.7
Splint & immobilization	743	3.3	2.8
Procedural sedation	663	2.9	2.5
Lumbar puncture	513	2.3	2.0
I & D	511	2.2	1.9

12 A total of 73,317 doses of medications were administered. Medications were used for 23,401
 13 (87.6%) patient visits, with 20,705 (77.5%) receiving more than one medication. The most
 14 common class of medications used was analgesics, including acetaminophen, non-steroidal anti-
 15 inflammatory, and opioid analgesics. The next most common class prescribed was antibiotics,
 16 followed by antimalarials, intravenous fluids, and nutritional supplements. Approximately 1800
 17 medications could not be classified due to misspellings or non-standard abbreviations.
 18 Medication categories are listed in Table 3, and the most commonly used medications from each

1 category are listed in Table 4. Specific medications given to more than 0.5% of the patient cohort
2 are listed in Table 5.

Table 3
Medications by Category

Medication class	Doses	Percent of medications given
Analgesics	22,981	31.4
Antibiotics	14,486	19.8
Antimalarials	5,495	7.5
IV fluids	5,445	7.4
Nutritional	4,785	6.5
Respiratory	3,394	4.6
GI	2,584	3.5
CNS/Neuro	2,495	3.4
Cardiac	2,489	3.4
Vaccines	1,984	2.7

Table 4
Most Common Medications by Category

Class	examples			
Analgesics	paracetamol/ acetaminophen	diclofenac	tramadol	Pethidine/ meperidine
Antibiotics	ceftriaxone	cloxacillin	gentamicin	metronidazole
Antimalarials	artemether/ lumefantrine	quinine	artesunate	sulfadoxine/ pyrimethamine
Nutritional supplements	dextrose	ORT	multivitamin	ready-to-use therapeutic food
Respiratory	oxygen	salbutamol	cough suppressant	nebulized magnesium
GI	omeprazole	metoclopramide	ranitidine	bisacodyl
CNS	diazepam	haloperidol	mannitol	amitriptyline
Cardiac	furosemide	nifedipine	aspirin	digoxin

Table 5
Most Common Medications by Number of Doses

Medication	Doses	Percent of medications
Paracetamol	14,697	20.0
Ceftriaxone	4,697	6.41
Diclofenac	4,508	6.2
Normal saline	3,672	5.0
Coartem	3,542	4.8
Tetanus vaccine	1,862	2.5
Tramadol	1,842	2.5
Quinine	1,775	2.4
Cloxacillin	1,686	2.3
Gentamicin	1,602	2.2
Ringers' lactate	1,446	2.0

Laboratory tests were ordered for 22,708 (85.0%) patient visits, with a total of 38,378 studies being performed. The most common study was malaria testing, done in 14,440 (54.0%) patient visits. Bedside glucose was checked in 5666 (21.2%) patient visits. HIV testing was done in 5195 (19.4%) patient visits with CD4 testing for 465 (1.7%). Haemoglobin was run for 4108 (15.4%) patient visits. Urinalysis was performed for 3062 (11.5%) patient visits. Blood type was checked for 1366 (5.1%) patient visits. (Table 6)

Table 6
Laboratory Testing

Medication	Doses	Percent of medications
Paracetamol	14,697	20.0
Ceftriaxone	4,697	6.41
Diclofenac	4,508	6.2
Normal saline	3,672	5.0
Coartem	3,542	4.8

Tetanus vaccine	1,862	2.5
Tramadol	1,842	2.5
Quinine	1,775	2.4
Cloxacillin	1,686	2.3
Gentamicin	1,602	2.2
Ringers' lactate	1,446	2.0

Radiology studies were performed for 4630 (17.3%) patient visits. X-rays were performed or ordered on 1864 (7.0%) patient visits. The most common X-ray was a chest X-ray, done for 1071 patient visits (4.0% of the cohort, 45.6% of all X-rays requested.) Other X-rays included 477 lower and 275 upper extremity films, 89 pelvis films, 88 skull films, and 73 abdominal films. X-rays were available only when a radiology technician was present, mostly weekday business hours, but with some call-in capacity on evenings and weekends. Point of care ultrasound (POCUS) was performed on 2194 (8.2%) patient visits including 417 focused assessment with sonography in trauma (FAST) exams, 139 abdominal studies, 107 echocardiograms, and 73 transabdominal exams for obstetric or gynecological indications. Formal ultrasound imaging by the hospital radiology technician was requested for 998 (3.7%) patient visits. (Table 7)

Table 7
Imaging

	Number of Studies	Percent of Imaging
X-ray	2441	
Chest	1071	43.9
Arm	477	19.5
Leg	275	11.3
Unspecified	150	6.1
Pelvis	89	3.6
Skull	88	3.6
Abdomen	73	3.0
POCUS	2289	
Unspecified	1465	64.0

FAST	417	18.2
Abdominal	139	6.1
Cardiac Echo	107	4.7
Formal US	1006	
Unspecified	695	69.1
Abdominal	146	14.5
Pelvic/OB	130	12.9

14 **Limitations**

19 4 This is a single center study in rural Uganda with a unique training programme that was
 20
 21 5 developed after a needs assessment of the burden of disease,²³ but which took into account
 22
 23 6 resource limitations at Karoli Lwanga Hospital. Thus, it is possible our analysis failed to
 24
 25 7 document potentially useful resources that were not available, thus were not part of the ECPs
 26
 27 8 training. Other analyses of smaller portions of this data set looking at common diagnoses can
 28
 29 9 help temper this limitation to some degree.²⁴ Practice patterns and proficiencies of the ECPs
 30
 31 10 may not be representative of other clinicians. Increased availability of the X-ray technician
 32
 33 11 would likely have increased the number of patients undergoing imaging in the ED. CT imaging
 34
 35 12 could aid in managing head trauma and some abdominal injuries but is not available at the site;
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 37 13 however, this is true in most district hospitals in SSA. Likewise, there may be additional
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 39 14 laboratory tests that would be useful but were not available routinely during study period or were
 40
 41 15 subject to “stock-outs” of necessary reagents. While we did record tests ordered but not
 42
 43 16 completed, if ECPs were aware of the stock-out, they may not have ordered a test even if they
 44
 45 17 felt was indicated. Given the retrospective nature of this review, we do not have a way of
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 47 18 controlling for this lack of ordering due to knowledge of stock-outs.
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1 Free text entry of data by non-medically trained research assistants resulted in a small amount of
2 data being lost due to misspelling or incorrect transcription. Modifications to the data entry
3 process have since reduced such errors. Additionally, patients arriving in the overnight hours
4 when the ED was closed were not included in this analysis. Finally, there was no gold standard
5 arbitration done to assess the true “need” for the interventions performed or to critique other
6 interventions that might have been indicated. Nonetheless, this provides a pragmatic assessment
7 of the real-world practice of emergency care at a district hospital in a rural area of SSA.

9 Discussion

10
11 This is a longitudinal cohort of 26,710 acutely ill patient visits cared for in a rural emergency
12 department in sub-Saharan Africa. The study builds on the work of previous authors in several
13 important ways. First, to our knowledge, this is largest data set of emergencies presenting to a
14 rural district hospital in a low-resource country. Additionally, we report detailed information on
15 procedures performed and resources used for care in this large cohort over a five-year period. To
16 deliver effective emergency care, ongoing research is required to further elucidate both training
17 and resource needs in resource-limited settings. By documenting current practice patterns of
18 emergency care in a functional ED in rural Uganda, the data could inform training and resource
19 allocation for providers in similar settings.

20
21 In considering medical knowledge that should be included in emergency care training, the
22 spectrum of diseases presenting acutely must be understood. Data from the Global Burden of
23 Disease Study indicate an increasing contribution of non-communicable disease towards

1 worldwide mortality,²⁵ but it is unknown how much these diseases contribute to the burden of
2 emergencies in SSA. The data show that ECPs cared for patients across all age ranges who
3 presented with diverse complaints. Commonly utilized medications and diagnostic tests indicate
4 that patients presented for emergency care with a broad array of communicable and non-
5 communicable diseases. Our data suggest that even in rural areas with high rates of
6 communicable diseases, non-communicable diseases contribute significantly to the need for
7 acute care. Additionally, given the fact that analgesics were given to 31.4% of patients and
8 approximately 2.5% of patients underwent procedural sedation, it can be inferred that the ECPs
9 managed a large burden of acutely painful conditions. High rates of splinting and
10 immobilization, as well as the number of FAST exams performed, indicate trauma care is a
11 prominent component of emergency care in this setting. This is consistent with Uzoechina et al.'s
12 study from Nigeria and Wachira et al.'s data from Kenya.

13
14 Skills such as X-ray interpretation and point of care ultrasound (POCUS) appear to be high yield,
15 given X-rays were performed on 7.0% and POCUS on 8.2% of patient visits. POCUS has been
16 shown in other studies to supplement limited radiography capacity and enhance safety of
17 invasive procedures in resource limited settings.^{26 27 28} The ECP training on POCUS has
18 increased over time and is described elsewhere.²⁹

19
20 The variety of procedures performed indicates that providers in the setting likely require a broad
21 range of procedural skills. Peripheral IV access was the norm, but occasional patients required
22 intra-osseous access or cannulation of the external jugular vein. In addition to the common
23 procedures listed above, the ECPs are trained to perform paracenteses, thoracenteses, joint

1 aspirations, and nerve blocks. While these procedures are required relatively infrequently, they
2 are crucial for symptomatic relief, making the diagnosis, and guiding treatment for a significant
3 proportion of patients seen in rural EDs in SSA. The ability to perform these procedures in a
4 timely manner is required to deliver effective, quality emergency care.

5
6 Resource allocation and preparation is the other essential component for effective emergency
7 care delivery. Based on the AFEM framework, Karoli Lwanga Hospital should be an
8 “intermediate facility”. In the framework, signal functions are defined as “lifesaving saving
9 clinical interventions,” and a consensus-based list of these functions was generated. While our
10 study did not seek to specifically map which signal functions the ECPs carried out, comparing
11 the list of signal functions with medications administered, procedures performed, and laboratory
12 and diagnostic imaging testing used in our cohort, it is clear there is significant overlap between
13 the framework and the real-world practice of emergency care in this setting.

14
15 The medications most frequently used were pain medications, antibiotics, antimalarials, IV
16 fluids, nutritional supplements, respiratory medications, and cardiac medications. These
17 medications are on the World Health Organization Model List of Essential Medications³⁰ and are
18 expected to be widely available. Approximately 13% of patients received vaccinations as part of
19 their emergency care, highlighting another health-systems strengthening role of emergency care,
20 in providing an additional venue for primary prevention. It is also encouraging to see some
21 evidence that patients’ pain was addressed, as pain assessment and management has been
22 identified as a deficit in prior studies.³¹

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3 1 There currently is no widely recognized list of essential emergency laboratory tests in low
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5 2 resource settings, although the WHO is currently in the process of developing a consensus-based
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7 3 minimum package for this. From our data, it appears that point of care blood glucose testing,
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9 4 malaria smears (or rapid diagnostic malaria tests), assessment of haemoglobin, blood typing,
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11 5 HIV testing and fluid analysis (CSF, urine, pleural fluid, ascites, and joint aspirates) are all
12
13 6 commonly used. While used to a lesser extent, our database and clinical experience indicated
14
15 7 pregnancy testing is important in this setting as well. The ability to perform HIV screening is
16
17 8 critical. Uganda adopted a national guideline recommending opt-out testing in 2005,³² but missed
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19 9 opportunities for early diagnosis and initiation of antiretroviral treatment in difficult to reach
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21 10 populations persist.^{33 34 35} Due to stock-outs and lack of point of care testing performed by ECPs,
22
23 11 this cohort of patients had a much lower rate of HIV testing than guidelines recommend. Testing
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25 12 for HIV in the acute care setting offers patients a pathway to access the HIV continuum of care
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27 13 and begin treatment at an earlier stage in the diagnosis, which in turn has been shown to make
28
29 14 management more effective and to reduce HIV transmission and the future burden of disease.³⁶
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31 15 ³⁷
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33 16 Future directions for research include comparing data from this facility with training needs and
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35 17 resource allocation at other facilities in SSA. Additionally, formally assessing the use of signal
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37 18 functions in this cohort could help refine the framework proposed to guide emergency care
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39 19 implementation in SSA.
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21 **Conclusions**

1 This study tracks the resources utilized to diagnose, stabilize and treat a large cohort of
2 consecutive patients seen in a not-for-profit, rural district ED in SSA. Analysis of the resources
3 used and knowledge and skills applied to care for this patient cohort provides a rare glimpse of
4 what emergency care delivery entails in rural SSA. The results of this study coupled with the
5 previously developed framework to guide emergency care implementation will enable bench-
6 marking and data-driven policy making for improvement of facility-based emergency care
7 delivery in low resources settings within sub-Saharan Africa.

8 **Author Contributions:** CB, BR and UP performed data cleaning, statistical analysis and
9 submission of this work. HH, SC, and MB inputted the data into the database. UP and SC
10 conceived and designed the study and supervised all portions of the study. CB, SC and UP
11 drafted the manuscript and all authors revised it. SM provided program support for ECP
12 curriculum development and contributed to study design. All authors take responsibility for the
13 paper as a whole.

15 **Competing Interests:** The authors have no conflicts of interest to report

16 **Funding:** GEC is a non-profit organization and operates largely on private donations and small
17 family foundation grants. The authors did not receive funding for this study.

19 **Data Sharing:** files will not be available for sharing

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	2	
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4	
Objectives	3	State specific objectives, including any prespecified hypotheses		
Methods				
Study design	4	Present key elements of study design early in the paper	4-5	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5	
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7	
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls		
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants		
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed		
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	n/a	
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	8-10	
Bias	9	Describe any efforts to address potential sources of bias	10-11	
Study size	10	Explain how the study size was arrived at	4-5	

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-10
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	n/a
		(c) Explain how missing data were addressed	10
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	(a) 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	n/a
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	8-10
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) 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	8-10
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-12
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	10-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-14
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	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.