MINISTRY OF HEALTH UGANDA

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# October - December, 2022

Dear Reader,

We take great pleasure in welcoming you to Issue 4 Volume 7 of the Uganda National Institute of Public Health (UNIPH) Quarterly Epidemiological Bulletin.

We aim to inform the district, national, and global stakeholders on disease outbreak investigations, public health surveillance, and interventions undertaken in detecting, preventing, and responding to public health events in Uganda.

In this issue, we present a variety of articles including; methanol poisoning following alcohol consumption, factors associated with acute watery diarrhoea among under 5s, risk factors for death among children with severe malaria, trends and spatial-distribution of: pneumonia among under 5s, air quality in Kampala city, and cervical cancer in Uganda, COVID-19 impacts on: all cause mortality in Regional Referral Hospitals, and gender based violence among adolescent girls and young women, risk factors for death among hospitalized pregnant women with COVID-19, Lost to follow up among HIV+ patients on tuberculosis preventive treatment, and rapid ART initiation following rollout of Point of Care Early Infant Diagnosis testing.

Should you have any questions or require additional information related to articles in this bulletin please contact us on: jzalwango@musph.ac.ug, hnelly@musph.ac.ug, OR lbulage@musph.ac.ug

We hope you find this information valuable and we shall appreciate any feedback from you.



*Inside this issue:*

# Updates

## Uganda PHFP Shines at the 2nd International Conference on Public Health in Africa (CPHIA), Kigali Convention Center, Rwanda,13th – 15th December 2022

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From 2021, Africa Centers for Disease Control and Prevention (Africa CDC) has organized annual conferences to help further Africa CDC's mission to **"**strengthen Africa's public health institutions' capacities, capabilities, and partnerships to prevent, detect, and respond quickly and effectively to disease threats based on science, evidence-based policy, and data-driven interventions and programs**".**

In Dec 2022, the 2nd International Conference on Public Health in Africa was held in Kigali, Rwanda with the theme, *Preparedness for future Pandemic and Post-Pandemic Recovery: Africa at a Crossroad*. This offered a unique platform for African leaders, researchers, policymakers, and stakeholders to share scientific findings and public health perspectives and collaborate on research, innovation and public health across the continent.

The Uganda Public Health Fellowship Program (PHFP) participated in this knowledge sharing event where a number of oral and poster presentations were made. Marie Gorreti Zalwango, a fellow at the PHFP won the best oral presentation award for the presentation on "Risk factors for death among children with severe malaria in Namutumba District, Uganda, September 2021-February 2022".

Other presentations from the PHFP shared during the conference included: Investigation of human tungiasis cases, Sheema District, Uganda, November 2021 to February 2022; Increased all-cause mortality at regional referral hospitals in Uganda during the COVID-19 pandemic, 2020-2021 by Sherry Rita Ahirirwe; Trends and spatial distribution of neonatal sepsis in Uganda, 2016-2020,Deaths among pregnant women due to severe COVID 19 at admission- a case control study, Uganda June 2020-August 2021 by Stella Martha Migamba, and Preparedness and risk assessment for plague in West Nile Region-Uganda, August 2021 by Immaculate Atuhaire.

*PHFP Fellow Gorreti Marie Zalwango receives the best oral presentation award from the Africa CDC acting Director Dr. Ahmed Ogwell Ouma at the closing ceremony for the 2nd International conference on Public Health in Africa*

## Air Quality; The opportune sphere worth pursuit

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Are you aware about the air you breathe? Have you ever known that the air you breathe might have harmful effects on your health? Do you know that people are dying prematurely due to air pollution? Last but not least, do you even know that it is your responsibility to improve the air you breathe? Based on these rhetorical questions, a PHFP fellow (Mackline Ninsiima) decided to prioritize her attention to air quality during her deployment at Kampala Capital City Authority (KCCA); an opportunity that has been a great game-changer in her career world. Air quality is one of the outstanding health concerns today; a silent killer accounting for an estimated 6.7 million premature deaths worldwide.

The PHFP fellow at the KCCA host site was privileged to present the air quality operations and spatio-temporal trends of air quality in Kampala City during the East African stakeholder's conference organized by United Nations Environment Programme (UNEP) and at the Air Quality and Health Symposium organized by GEO Health Hub at the University of Nairobi and Columbia Global Centre, Nairobi. The majority of the roundtable discussions were centered on projects evaluating the effects of air quality on health across the East African Cities.

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Mackline Ninsiima (seated in the middle) among the delegates from Kampala, Nairobi, Addis Ababa, Kigali, and Burundi during the Air Quality stakeholder conference organized by UNEP

## Cohort 2022 Fellow's manuscript writing workshop, Jinja, 05th-09th December 2022

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A manuscript writing workshop was held during December 05-09, 2022 for all PHFP Cohort 2022 Advanced Field Epidemiology Fellows who had completed a public health project as evidenced by a report or a draft manuscript. The workshop was funded by the US-CDC Foundation under the Data for Health Initiative. Thirty participants attended and included fourteen fellows, five mentors, ten Uganda National Institute of Public Health (UNIPH) staff.

Training sessions were led by the US-CDC Resident Advisor for the Uganda Public Health Fellowship Program (PHFP), UNIPH staff including Uganda Public Health Fellowship Program (PHFP) supervisors, UNIPH Program Coordinators, and Scientific Communication mentors. During the workshop, short theoretical and hands-on writing sessions ere held with the goal of generating complete draft manuscripts by each fellow at the end of the 5-day workshop.

The mentorship continued post site as participants were required to continue developing their manuscripts under the guidance of mentors. The mentors will continue to support the fellows until publication of the manuscripts.

*Fellows cohort 2022, mentors, and PHFP staff during a manuscript presentation in the scientific writing workshop*

## Outbreak investigations responded to: Ebola virus disease outbreak response September-December, 2022

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On 20th September 2022, the Ministry of Health declared an outbreak of Sudan ebolavirus (SVD) after a case managed at Mubende Regional Referral Hospital (MRRH) in Mubende District was confirmed through testing at the Uganda Virus Research Institute (UVRI). This is the first time in more than a decade that Uganda reported an outbreak of Sudan ebolavirus. The largest Ebola outbreak in Uganda occurred in 2000–2001 with 425 cases and 224 deaths (*Sudan* strain). This Ebola outbreak is the second largest in Uganda with 142 total confirmed cumulative cases and 55 cumulative deaths from 10 districts.

The PHFP team and alumni were among the first teams to respond to this Ebola outbreak, primarily under the surveillance pillar. The PHFP team and the alumni were assigned head of case investigation, active case search, contact listing, tracing and follow up, developing epidemiological links, updating daily situation reports in all the nine districts and at the national level. The PHFP team diligently performed these roles throughout the response, from September to December 2022. Thanks to the entire PHFP family (mentors, supervisors, administrators, current fellows, and alumni) for swinging into action to put an end to the Ebola outbreak.

On the 11th, January 2023, Uganda was declared Ebola-free. We thank all the responders for the great work done to achieve this victory.

**PHFP supervisor and fellows conducting a phone interview with one of the confirmed case-patient in the ETU of Mubende regional referral hospital during the Ebola outbreak**

## Upcoming events

## International Health Days January-March 2023

**Authors and institutional affiliations:** Jane Frances Zalwango and Helen Nelly Naiga, Uganda Public Health Fellowship Program-Field Epidemiology Fellows, Cohort 2022

Every year, days referred to as international health days are set aside to commemorate different public health issues. This draws the public's attention to these public health issues, improving awareness and information dissemination to these areas of concern.

### January 29th, 2023: World Leprosy Day

Leprosy still exists! Approximately 200,000 people are diagnosed with leprosy every year, with millions more living with leprosy-related disabilities, primarily in Asia, Africa, and South America. Every year on the last Sunday of January, the world commemorates World Leprosy Day (WLD). This international day provides an opportunity to honor those who have suffered from leprosy, increase awareness of the disease, and advocate for an end to leprosy-related stigma and discrimination. The theme for this year is "Act Now. End Leprosy." Three key messages are being emphasized: elimination is possible, act now by prioritizing leprosy elimination, and reach the unreached.

**Fun fact:** The last Sunday of January was chosen as the WLD by French humanitarian, Raoul Follereau as a tribute to the life of Mahatma Gandhi, who did much work with persons affected by leprosy and died at the end of January in 1948.

### February 4th, 2023: World Cancer Day

World Cancer Day is observed worldwide on February 4th. The aim is to inform and encourage people on its prevention, early detection, and treatment. World Cancer Day 2023 is the second year of the three-year 'Close the Care Gap' campaign, which focuses on equity. The second year will be focused on bringing together individuals, groups, advocates, and decision-makers to push for change and take action. Real-world progress is highlighted alongside innovation and medical achievements. Even little efforts, such as encouraging neighbors to transport a neighbor to cancer treatment or ensuring that the neighborhood school provides a variety of healthy and affordable food options, can have a big impact.

**Fun fact:** World Cancer Day has become one of the most celebrated health awareness days around the world. Different colors and symbols are used to identify and promote the fight against different types of cancer. The pink ribbon represents breast cancer awareness, while the orange ribbon raises awareness of childhood cancer. The American Cancer Society uses the daffodil flower to symbolize hope for a world without cancer.

### March 24th, 2023: World Tuberculosis Day

Each year we commemorate World Tuberculosis (TB) Day to raise public awareness about the devastating health, social and economic consequences of TB and to step up efforts to end the global TB epidemic.
**Fun fact:** The date marks the day in 1882 when Dr. Robert Koch announced that he had discovered the bacterium that causes TB paving way for diagnosis and cure.

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## Methanol poisoning caused by adulteration of alcohol at production stage in a factory in North Western Uganda, August 2022

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### Summary

**Background:** Methanol is a toxic industrial solvent which, when ingested can cause vision loss, severe illness, and death. In August 2022, the Ugandan Ministry of Health was notified of a cluster of sudden deaths in Arua City and Madi-Okollo District in persons who had consumed gin (Gin X) produced from a local manufacturer (Manufacturer A). We investigated the outbreak to determine the scope of the problem, identify the risk factors for the sudden deaths, and recommend control and prevention measures.
**Methods:** We defined a suspected case as acute onset of blurred vision with abdominal pain, general body weakness, headache, or profuse sweating in a resident of Arua City or Madi-Okollo districts from 16–26 August 2022. A retrospective cohort study was carried out among the cases to identify risk factors for death. In collaboration with Uganda Police Force and the Uganda National Bureau of Standards, we collected samples of Gin X from manufacturer A for methanol toxicology analysis at the Government Analytical Laboratory in Kampala. Autopsies were carried out on all deceased case-patients.
**Results:** We identified 48 cases (47 males and 1 female); 18 (38%) died. The median age of cases was 32 years (IQR 26-46). Compared with cases who consumed one 200ml bottle or less of Gin X, the risk of dying was 4 times (RR=4.1, 95% CI: 0.49-34, p=0.19) higher (non-significant) among those who drank 2 bottles, and 10 times (RR=10.7, 95% CI: 1.5-75, p=0.02) higher among those who drank ≥3 bottles. The mean methanol content among the five samples which were collected from manufacturer A was 594,424 mg/L (range 259,263 - 809,193 mg/L), higher than the maximum recommended limit of 50mg/L. Eight autopsies all showed liver inflammation oedema, gastrointestinal bleeding, and pulmonary oedema which is consistent with methanol poisoning. We found out that manufacturer A was not licensed to produce gins but rather fruit wines only.
**Conclusion:** This outbreak was caused by consumption of Gin X manufactured by manufacturer A which was adulterated with methanol at the production stage. We recommend strict enforcement of the laws that govern alcohol production and distribution.

### Background

Methanol is a toxic industrial organic solvent which is used as a cleansing solution, pesticide, and an alternative bio-fuel [1, 2]. It is also sometimes mixed with ethanol in alcoholic beverages either by mistake or intentionally as a cheap substitute for ethanol. Methanol poisoning is an important public health problem because of its severe consequences. The maximum safe limit of methanol in drinking alcohol is 50mg/L [3]. Once ingested, it undergoes enzymatic oxidation and is converted to highly toxic formic acid which can lead to metabolic acidosis, neurotoxicity, optic nerve damage and death [4]. Symptoms usually appear 12-24 hours after ingestion but can be delayed if ethanol is ingested simultaneously [5].
Unregulated and unrecorded alcohol productions are responsible for most methanol poisoning outbreaks due to adulteration of alcoholic beverages. Low income countries are disproportionately affected due to poor capacity to regulate and monitor the sale of the unrecorded alcoholic beverages [6]. Delays in notification of the health system to respond to outbreaks, poor health seeking behavior of the victims, and unavailability of adequate resources to treat methanol toxicity can lead to severity of symptoms and high case fatality rates [7].
On 18th August 2022, the Uganda Ministry of Health (MoH) through the Public Health Emergency Operations Centre (PHEOC) received a report about a cluster of deaths in Arua City. This incident reportedly occurred after multiple persons consumed alcohol which was packed in plastic bottles from a local alcohol manufacturer. The victims presented with headache, backache, restlessness, difficulty in breathing, and loss of consciousness before they died. The same incident was also reported in the

neighboring district of Madi-Okollo after consumption of the same beverage. We investigated the outbreak to determine the scope of the problem, cause of sudden deaths, identify the risk factors for the sudden deaths in these clusters, and recommend control and prevention measures.

## Methods

### Outbreak area

The investigation was conducted in Arua City and Madi-Okollo District which are both located in North Western Uganda (Figure 1). This region is bordered by Democratic Republic of Congo in the west and South Sudan in the North. It is served by Arua Regional Referral Hospital (ARRH), which is the main referral treatment facility.

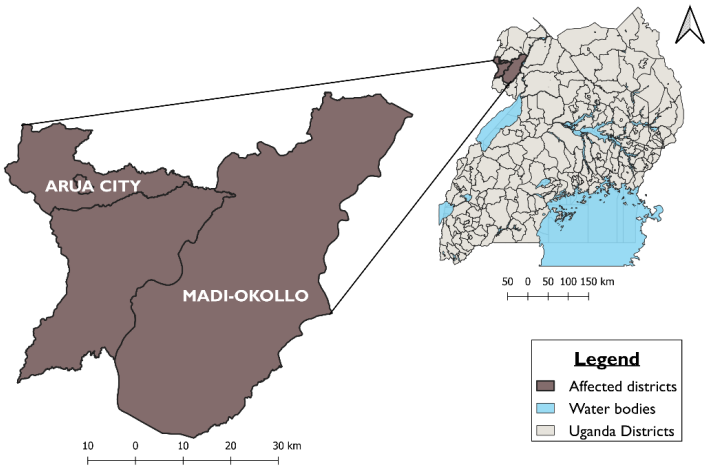


**Figure 1: Location of Arua City and Madi-Okollo Districts, Uganda**

### Case definition and finding

We defined a suspected case as; onset of blurred vision or abdominal pain with any of the following: general body weakness, headache, dizziness, profuse sweating, or loss of vision in a resident of Arua City or Madi-Okollo District from 16 to 26 August 2022.

We reviewed medical records from ARRH and other health facilities where the cases sought care from for the month of August 2022. With the help of community health workers who are also referred to as village health team members we conducted community case-finding in Arua City and Madi-Okollo District in the affected sub counties. We interviewed survivors and next-of-kin of the deceased to develop a line list of the suspected cases. We also conducted key informant interviews with the local community leaders to investigate the occurrence of similar cases in the communities.

### Descriptive epidemiology

We analyzed the line list data to characterize case-patients by their clinical presentations. We used attack rates to describe the distribution of cases by age and place of residence. The attack rates were calculated using population data from the Uganda National Bureau of Statistics (UBOS) population projections for Arua City and Madi-Okollo District.

### Laboratory and post mortem investigations

In collaboration with the Uganda Police Force and the Uganda National Bureau of Standards (UNBS) - the body responsible for licensing and certification of products in Uganda, eight samples of the suspected gin were collected and submitted to the Government Analytical Laboratory (GAL) in Kampala for toxicological analysis. Additionally, police carried out eight autopsies on the deceased from ARRH.

### Case management

We identified data on how the survivors and deceased were managed through visiting the heath facilities where they sought treatment, reviewing their medical records, and the type of treatment they received.

### Trace-back investigations and environmental assessment

We interviewed survivors, next of kin of the deceased, the owners of the factory, owners of bars and shops that were selling alcohol to identify the source of the implicated gin X, and the point at which and why it might have been adulterated.

### Hypothesis generation interviews

We used a structured questionnaire to interview survivors and next of kin of the deceased on the case-patients' alcohol exposures two days prior to their onset of symptoms.

### Retrospective cohort study

The initial investigation showed that all cases had consumed gin X from 16 to 26 August 2022, suggesting that gin X was implicated. We then conducted a retrospective cohort study and enrolled all cases in the two most affected sub-counties in Arua City and Madi-Okollo District to determine the risk of death after consuming gin X. We used a structured questionnaire to interview all cases. The questionnaire inquired whether they drunk gin X between 16 to 26 August 2022, the exposure dates, place where they drunk gin X from, and the quantity of gin X taken.

**Ethical considerations:** This outbreak investigation was in response to a public health emergency and was therefore determined to be non-research. The MoH gave a directive to in-

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vestigate this outbreak and the office of the Center for Global Health, US Center for Disease Control and Prevention determined that this activity was not human subject research and that its primary intent was for public health practice or disease control.

The authors sought permission to conduct the investigation from District Health authorities of Arua City and Madi-Okollo District. Permission was also sought from the administrators of the health facilities to access data about patients who had been admitted and those that had died. The authors sought verbal informed consent from the respondents who were survivors, next of kin of the deceased, local leaders, and police detectives. They were all informed that their participation was voluntary and their refusal would not attract any negative consequences. Data which was collected did not contain individual personal identifiers as a way of ensuring confidentiality.

## Results

### Descriptive epidemiology

A total of 48 suspected cases (47 male) were line listed, including 30 in Arua City (AR=8/100,000) and 18 in Madi-Okollo District (AR=10/100,000). The outbreak affected the 25-34-year age group (AR=27/100,000) more than other age groups (Table 1). Eighteen deaths were reported (case-fatality rate: 38%), including 12 in Arua City and 6 in Madi-Okollo District. The median age of cases was 32 years (IQR 26-46). Cases presented with blurred vision (79%), abdominal pain (77%), headache (70%), dizziness (69%), and other symptoms (Table 2).

**Table 1: Attack rates and case fatality rate of methanol poisoning by age group, sex, and district among 48 cases of methanol poisoning during an outbreak in Arua City and Madi-Okollo District, Uganda, August 2022**

| Characteristic | Population* | Total cases | Total deaths | Case fatality rate (%) | Attack rate per 100,000 people |
|---|---|---|---|---|---|
| **Total** | 255,889 | 48 | 18 | 38 | 19 |
| **Age (years)** | | | | | |
| 18-24 | 88,119 | 6 | 0 | 0 | 7 |
| 25-34 | 70,149 | 19 | 6 | 32 | 27 |
| 35-44 | 40,431 | 9 | 4 | 44 | 22 |
| ≥45 | 57,280 | 14 | 8 | 57 | 24 |
| **Sex** | | | | | |
| Male | 122,827 | 47 | 18 | 38 | 38 |
| Female | 133,062 | 1 | 0 | 0 | 1 |
| **District** | | | | | |
| Arua City | 172,945 | 30 | 12 | 40 | 17 |
| Madi-Okollo | 82,944 | 18 | 6 | 33 | 22 |

*Projected 2022 population based on the 2014 census

**Table 2: Distribution of clinical signs and symptoms among 48 cases of methanol poisoning during an outbreak in Arua City and Madi-Okollo District, Uganda, August 2022**

| Symptom | n | (%) |
|---|---|---|
| Blurred vision | 38 | 79 |
| Abdominal Pain | 37 | 77 |
| Headache | 34 | 70 |
| Dizziness | 33 | 69 |
| Profuse Sweating | 24 | 50 |
| Difficulty in breathing | 22 | 46 |
| Staggering movements | 20 | 42 |
| Chest pain | 20 | 42 |
| Shivering | 16 | 33 |
| Loss of vision | 15 | 31 |
| Fever | 14 | 29 |
| Loss of consciousness | 12 | 25 |
| Vomiting | 12 | 25 |
| Diarrhea | 7 | 14 |
| Confusion | 6 | 13 |
| Nausea | 2 | 4 |
| Others | 5 | 10 |

Cases were clustered around the bars which also acted as main distributors of gin X (Figure 2). This outbreak only affected one subcounty in each district. That is, Ayivu division in Arua City (AR=7/100,000) and Ogoko subcounty in Madi-Okollo District (AR=13/100,000).

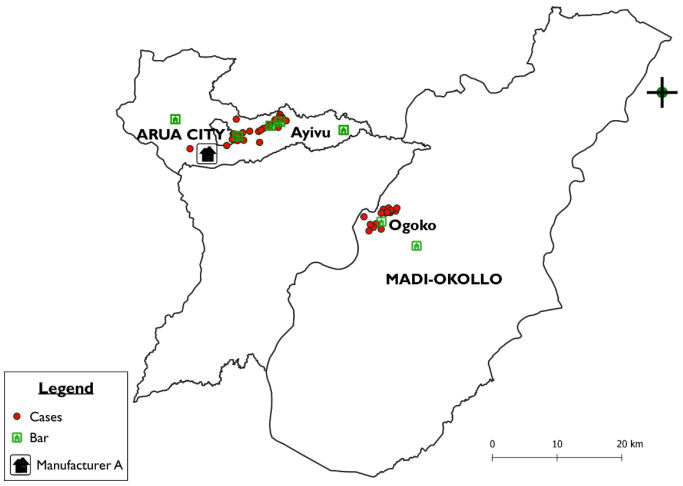


**Figure 2: Geographical distribution of methanol poisoning cases during an outbreak in Arua City and Madi-Okollo District, Uganda August 2022**

The index case first developed symptoms on 17 August and the last on 24 August 2022. The epidemic curve suggests a point source exposure lasting for 7 days (Figure 3). The number of cases reduced after police intervention on 21 August, 2022. This was done through closure of manufacturer A, seizure, and destruction of stock of the main distributors.

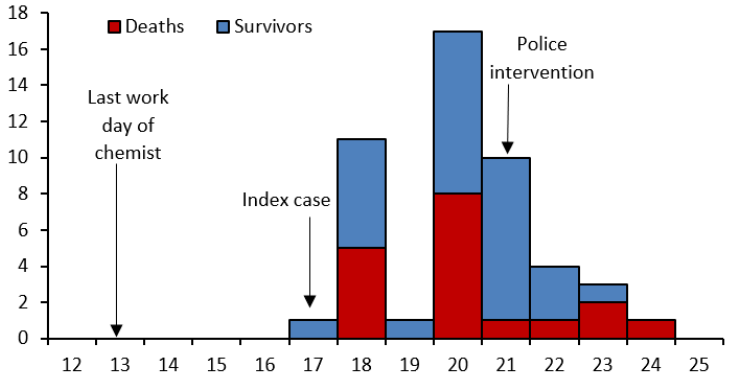


**Figure 3: Symptom onset and deaths during the methanol poisoning outbreak in Arua City and Madi-Okollo District, August 2022**

### Case management

All cases consumed gin X from 17 to 23 August 2022 before the onset of symptoms. The average time between the last ingestion of alcohol and onset of symptoms was 13 hours (SD±6) and the mean time between onset of symptoms and death was 20 hours (SD±16).

Among the 18 deaths, 14 (78%) occurred in the community without accessing any health facility while the rest died in health facilities. Fourteen survivors (11 from Madi-Okollo District and 3 from Arua City) were referred to ARRH for treatment. The rest of the survivors were managed at home. The average duration of stay in the hospital for those who were admitted was two days. Despite having a diagnosis of methanol poisoning, none of the case-patients who were admitted in ARRH received intravenous ethanol, which is the recommended treatment.

### Laboratory and autopsy investigation results

According to the UNBS report, among the eight samples picked from manufacturer A, five contained excessive concentrations of methanol above the maximum recommended limit of 50mg/L. Their mean methanol content was 594,424 mg/L (range 259,263-809,193 mg/L) [8]. All the eight autopsies that were conducted revealed liver inflammation, gastrointestinal bleeding and pulmonary oedema, all of which are consistent with methanol poisoning.

### Trace-back investigation findings

After interviewing the cases, four bars which were the possible source of the implicated gin X were identified, that is, three in Arua City and one in Madi-Okollo District. These bars also acted as the main distributors of gin X in the region. Interviews with the bar owners reveled that they all got their supply of gin X from Manufacturer A located in Arua City.

Manufacturer A was a small-scale alcohol-producing company run in a home setting with production capacity of less than 1,000 liters per day. It had been in existence since 2001 and

was fully licensed by UNBS to produce pineapple wine prior to this outbreak. Manufacturer A did not have an established storage, inventory, and warehouse management system. The bottles did not have serial numbers and the production batches lacked batch numbers.

In April 2022, manufacturer A started engaging in production of gin X and hired a chemist for this role. Production went on illegally without licensing from UNBS from April until August 2022.
At the beginning of August 2022, a disagreement ensued between the chemist and the proprietor of manufacture A which was concerning about the high cost of buying raw materials. It was alleged that the chemist would buy raw materials cheaply and then quote a higher figure to the proprietor. Despite this disagreement, the chemist continued to work until his last day of 13 August 2022. After the 13 August 2022 production, the chemist did not return back for work and all his known phone contacts were unreachable. Four days later, the index case appeared.

### Retrospective cohort study findings

The risk of death increased significantly with increasing number of gin X bottles consumed (Table 3).

**Table 3: Dose-response relationship among cases after consumption gin X in Arua City and Madi-Okollo District, Uganda during a methanol poisoning outbreak, August 2022**

| | Alive n (%) | Dead n (%) | RR | 95% CI | p-value |
|---|---|---|---|---|---|
| **Gin X quantity consumed** | | | | | |
| ≤ 1 bottle | 14 (46.7) | 1 (5.6) | Ref. | | |
| 2 bottles | 8 (26.6) | 3 (16.7) | 4.1 | (0.49 – 34.26) | 0.19 |
| 3 bottles | 3 (10.0) | 6 (33.3) | 10 | (1.42 – 70.22) | 0.02* |
| > 3 bottles | 2 (6.7) | 5 (27.8) | 10.7 | (1.52 – 75.35) | 0.02* |
| Not specified | 3(10.0) | 3(16.6) | 7.5 | (0.96-58.59) | 0.06 |

1 bottle (200ml size) contains 200mls of gin X

### Discussion

This was a methanol poisoning outbreak following adulteration of illicit alcohol at production stage from manufacture A. Almost entirely only males were affected. Four out of ten people died after consumption of the gin X. The risk of death increased with increasing quantity of gin X consumed. This investigation highlights the need for enhanced food poisoning community-based surveillance and public awareness about the dangers of illicit alcohol.
The adulterated alcohol was traced back to manufacturer A, which was illegally producing the gin.

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Unrecorded and unregulated alcohol has been linked to several methanol poisoning outbreaks [9, 10]. The proportion of unregulated alcohol as a percentage of total alcohol is high among low income countries with an estimated value of 42 percent in Uganda [11]. Unregulated alcohol production possess a health security threat because its produced without regulatory and market oversight and hence increasing the risk of safety, poor quality, and chances of adulteration [9].
During this investigation, tracing back the exact batch where the poisonous alcohol gin X was drawn from was difficult because of poor store keeping practices of manufacturer A. The packaging of gin X lacked serial numbers which made it difficult in identifying the possible points of adulteration along the supply chain beyond the production stage. This improper documentation is contradictory to best practices of labelling and coding alcoholic beverages[12]. In future, proper labeling and coding of alcoholic batches by manufactures could allow efficient trace-back.
Males were the only ones who were entirely affected by this outbreak. This is in line with other Ugandan studies which show a huge gender disparity in regard to alcohol consumption where men consume alcohol more than women [13, 14]. It is not surprising that the methanol alcohol poisoning outbreak affected more men than women.
This outbreak caused 18 deaths with a Case Fatality Rate (CFR) of 38 percent. This is high compared to what has been reported in some African studies. Retrospective studies done in Libya (2013) and Kenya (May and July 2014) indicate that among 1,000 patients who were poisoned in Libya, 101 died corresponding to CFR of 10% while among the 341 and 126 cases in Kenya, 100 and 26 people died corresponding to 29% and 21% CFR respectively[15]. The deaths in our study were likely associated with not seeking proper health care as many cases didn't go to health facilities and died at home. Wu X et al, 2022 note that early diagnosis and timely medical care are essential in reducing morbidity and mortality of methanol poisoning [7].
Although methanol is present in most alcoholic drinks and poses no harm at low levels, excesses above 50g/L can be lethal [3]. As with other toxic agents, methanol toxicity is dose dependent. There was a significant increased risk of death with increasing dose of methanol consumed. This is in agreement with findings from a systematic review which was done in 2017 and concluded that the concentration of biological exposure indices and clinical symptoms for methanol exposure have a dose response relationship[16].

**Study limitations**

We were unable to confirm presence of methanol in blood of case-patients since at the time of the investi-

methanol exposure have a dose response relationship[16].

**Study limitations**

We were unable to confirm presence of methanol in blood of case-patients since at the time of the investigation most survivors had already been discharged from hospital or were recovering. The blood samples which were earlier collected by police, were not properly stored and were submitted late to the GAL. This could not permit analysis. However, the patients' clinical presentations, epidemiologic data, laboratory toxicological findings, and post mortem results were all consistent with methanol poisoning.

**Conclusion**

We concluded that this outbreak was caused by consumption of gin X which was adulterated with high concentration of methanol at the production stage from manufacturer A. There could have been a possibility that this adulteration was intentional following the disagreement between the chemist and the proprietor. We recommend the enforcement of the laws that govern alcohol production and distribution in Uganda. The UNBS could carry out regular impromptu checks for methanol even on other previously certified alcoholic brands.

**Public health actions taken**

Immediately after the outbreak was detected the Ministry of Health instructed the investigation. With support from the Uganda Police Force and the UNBS, the implicated manufacturer was closed and stopped production on 21 August 2022. Two employees of manufacturer A and one of the main dealers of gin X in Arua city were apprehended on 21 August 2022 and prosecuted in courts of law. The chemist and the proprietor went on the run and were believed to have fled the country by the time of this investigation.
Stocks gin X were withdrawn from the major distributors and destroyed. Community sensitization was carried out with support from Arua City and Madi-Okollo District authorities on radio talk shows and community gatherings. Community event-based surveillance was strengthened where members of the community were encouraged to report any suspicious alcohol related symptoms and deaths to the local health authorities.

## Conflict of interest

The authors declare that they had no conflict of interest.


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## References


1. Joshi DR, Adhikari N: An overview on common organic solvents and their toxicity. *J Pharm Res Int* 2019, 28(3):1-18.
2. Ott J, Gronemann V, Pontzen F, Fiedler E, Grossmann G, Kersebohm DB, Weiss G, Witte C: Methanol. *Ullmann's encyclopedia of industrial chemistry* 2000.
3. Paine A, Davan AD: Defining a tolerable concentration of methanol in alcoholic drinks. *Human & experimental toxicology* 2001, 20(11):563-568.
4. Ashurst JV, Nappe TM: Methanol toxicity. 2018.
5. Barceloux DG, Bond GR, Krenzelok EP, Cooper H, Vale JA: American Academy of Clinical Toxicology practice guidelines on the treatment of methanol poisoning. *Journal of toxicology Clinical toxicology* 2002, 40(4):415-446.
6. Ssebunnya J, Kituyi C, Nabanoba J, Nakku J, Bhana A, Kigozi F: Social acceptance of alcohol use in Uganda. *BMC psychiatry* 2020, 20(1):1-7.
7. Wu X, Gu M, Wang W, Zhang H, Tang Z: Case Report: Early Recognition, Treatment, and Occupational Safety Protection are Crucial for Methanol Toxicity. *Frontiers in Medicine* 2022, 9.
8. UNBS: Uganda National Bureau of Standards (UNBS); Statement on Adulterated Gin (City5) and Death of Consumers in Arua City and Neighbouring Districts. In.; 2022.
9. Manning L, Kowalska A: Illicit Alcohol: Public Health Risk of Methanol Poisoning and Policy Mitigation Strategies. *Foods (Basel, Switzerland)* 2021, 10(7).
10. Rehm J, Kailasapillai S, Larsen E, Rehm MX, Samokhvalov AV, Shield KD, Roerecke M, Lachenmeier DW: A systematic review of the epidemiology of unrecorded alcohol consumption and the chemical composition of unrecorded alcohol. *Addiction (Abingdon, England)* 2014, 109 (6):880-893.
11. Probst C, Manthey J: Unrecorded alcohol use: a global modelling study based on nominal group assessments and survey data. 2018, 113 (7):1231-1241.
12. Vukatana K, Sevrani K, Hoxha E: Wine Traceability: A Data Model and Prototype in Albanian Context. *Foods (Basel, Switzerland)* 2016, 5 (1):11.
13. Kabwama SN, Ndyanabangi S, Mutungi G, Wesonga R, Bahendeka SK, Guwatudde D: Alcohol use among adults in Uganda: findings from the countrywide non-communicable diseases risk factor cross-sectional survey. *Global health action* 2016, 9:31302.
14. Wagman JA, Nabukalu D: Prevalence and correlates of men's and women's alcohol use in agrarian, trading and fishing communities in Rakai, Uganda. 2020, 15(10):e0240796.
15. Rostrup M, Edwards JK, Abukalish M, Ezzabi M, Some D, Ritter H, Menge T, Abdelrahman A, Rootwelt R, Janssens B: The methanol poisoning outbreaks in Libya 2013 and Kenya 2014. *PloS one* 2016, 11(3):e0152676.
16. Moon C-S: Estimations of the lethal and exposure doses for representative methanol symptoms in humans. *Annals of Occupational and Environmental Medicine* 2017, 29(1):44.

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## Factors Associated with Acute Watery Diarrhea among Children Aged 0–59 Months in Obongi District, Uganda, April 2022: A Case–Control Study

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### Summary

**Introduction**: Diarrheal diseases are a leading cause of morbidity in Ugandan children. Despite having a 2-dose rotavirus vaccination coverage of >95% from 2019 to 2021, Obongi District consistently reported the highest incidence of acute watery diarrhea (AWD) in the country during the period January 2017-April 2022. We assessed the factors associated with AWD among children aged 0-59 months in Obongi District in the month of April 2022.

**Methods**: We conducted a 1:2 unmatched case–control study. We defined a case of AWD as the passage of ≥3 loose/liquid stools per day with negative malaria and pneumonia tests in a child aged 0-59 months residing in Itula or Palorinya sub-counties from 1-30 April 2022. We reviewed medical records and interviewed case-persons' caregivers. A control was a child aged 0-59 months from a neighboring household with no AWD from 1-30 April. We used logistic regression to identify factors associated with AWD.

**Results**: Among 193 cases and 386 controls, 104 (54%) cases and 183 (47%) controls were male (p=0.14) and 58 (30%) cases and 127 (33%) controls were aged 12-23 months (p=0.56). In total, 187 (97%) cases and 369 (96%) controls had received at least one dose of rotavirus vaccine (p=0.45), and 58 (30%) cases and 120 (34%) controls (p=0.34) treated their drinking water by boiling/ using chlorine. Suffering from a comorbidity (undernutrition, diabetes mellitus, and/or HIV) (AOR=12; CI: 2.5-53), having a caregiver who did not wash hands with soap and water after visiting the toilet (AOR=3.9; CI: 1.2-13), and living in households that used borehole water versus piped water (AOR=4.0; CI: 1.7-9.6) were associated with AWD.

**Conclusion**: Comorbidities, failure of caregivers to wash their hands with soap after visiting toilets, and use of borehole water were associated with AWD. Community sensitization on handwashing at critical times, using clean water and soap, and expanded use of piped water could reduce AWD incidence in this area.

### Introduction

Acute watery diarrhea (AWD) is the second leading cause of mortality among children aged 0–59 months worldwide, causing an estimated 525,000 deaths and 1.7 billion child cases annually (1). In Uganda, acute watery diarrhea is among the top ten causes of morbidity in children aged 0–59 months, accounting for up to 8% of all outpatient visits (2). The trends and spatial distribution of acute watery diarrhea among children aged 0–59 months from 2016–2021 showed an average national incidence of 12 (±2.1) cases per 100 children (E.N., unpublished data).

Studies in Ethiopia and Zambia showed that the use of unprotected water sources, age of the child caregiver, child weaning time, family size, low maternal education, poor sanitation, contaminated water source, duration of breast feeding, failure to wash hands, absence of rotavirus vaccination, failure to dispose of feces hygienically, and adequate food hygiene were significant predictors of AWD among children aged 0–59 months (3-9). Other studies showed that child-related factors such as sex (10), age (11), and malnutrition (12) were associated with childhood diarrhea.

The World Health Organization (WHO) recommends the use of the rotavirus vaccine as part of a comprehensive strategy to control AWD in addition to treatment packages and preventive strategies such as oral rehydration salt (ORS) solution, zinc supplements, rehydration with intravenous fluids (in cases of severe dehydration or shock), promotion of early and exclusive breastfeeding, continuous breast feeding (breast milk is an excellent rehydration fluid), hand washing, supply of clean and safe water

and sanitation, and provision of nutrient-rich foods (13, 14). The majority of children (90%) who receive the rotavirus vaccine are protected from severe rotavirus diarrhea, and approximately 70% of them are completely protected from all forms (severe and mild) of rotavirus disease (15). Before the introduction of the rotavirus vaccine in 2018, rotavirus diarrhea was responsible for nearly 40% of all AWD cases and nearly 11,000 deaths among children under 5 years of age in Uganda annually (14, 16). In addition to the WHO recommended treatment packages and preventive strategies for AWD that were already in use (17), on 26 June 2018, the government of Uganda through the Ministry of Health (MoH) introduced the rotavirus vaccine into the Uganda National Expanded Program on Immunization (UNEPI) to protect children from AWD (14, 16). The rotavirus vaccine is free and available in health facilities and through community vaccination outreaches throughout the country (18). Uganda immunizes its children at 6 and 10 weeks of age with an interval of at least 4 weeks between doses (18).Acute watery diarrhea among children aged 0–59 months is a notifiable disease in Uganda (19). AWD surveillance is passive as part of the national integrated disease surveillance and response system (19). When an AWD case is diagnosed at a health facility, the information about that case is filled into the health facility outpatient register or inpatient register depending on whether the patient was treated as an outpatient or inpatient, respectively (19-21). At the end of every month, the total number of AWD cases at the health facility are added and reported to the district and the MoH through the health unit outpatient monthly report (HMIS 105) and the health unit inpatient monthly report (HMIS form 108) (19-21). These reports are then uploaded into the electronic district health information system version 2 (DHIS2), where they are easily accessed by MoH policy makers and other stakeholders (19, 22). Despite having a 2-dose rotavirus vaccination coverage of >95% from 2019–2022, Obongi District consistently reported the highest incidence rates of AWD in Uganda, with >45 cases/100 children aged 0–59 months each year from 2017–2021 (E.N., unpublished data). Identifying factors associated with AWD among children aged 0–59 months in Uganda would provide evidence to guide the Ministry of Health (MoH), Obongi District local government, and implementing partners to control AWD in this age group. To generate this evidence, we identified the factors associated with AWD among children aged 0–59 months in Obongi District in the month of April 2022.

## Methods

### Study setting

Obongi District is a refugee-hosting district in Uganda, primarily hosting refugees from South Sudan. Its refugee population was estimated at 128,500 persons (23), outnumbering the host community population, estimated at 50,000 people (24). It was estimated that 12% of refugees in Obongi District were children aged 0–59 months (23). Obongi District is in the West Nile Region of Uganda and is bordered by Moyo District in the north, Adjumani District in the east, Yumbe District in the west, and Madi-Okolo District in the south. It comprises six subcounties (Aliba, Ewafa, Gimara, Itula, Obongi Town Council, and Palorinya) (25), of which Itula and Palorinya contributed more than 75% of the AWD cases among children aged 0–59 months in the district (22). The current safe water coverage of Itula and Palorinya subcounties is 11,379 (95%), with only 73 (57%) of all water sources, 2 (60%) of the shallow wells, 52 (49%) of the deep boreholes, 6 (86%) of the rainwater tanks, and 13 (100%) of the tap stands in a functional state as of September 2022 (26). The household latrine coverage of Itula and Palorinya subcounties was 93.4% as of September 2022 (27).

### Study design and population

We conducted an unmatched case–control study in Itula and Palorinya subcounties to assess the factors associated with AWD among children aged 0–59 months. The study respondents were child caregivers living in Itula and Palorinya subcounties of Obongi District in Uganda. We defined a case of AWD as the passage of ≥3 loose or liquid stools per day with negative malaria and pneumonia tests in a child aged 0–59 months residing in Itula or Palorinya subcounties, Obongi District, from 1–30 April 2022. A control was a child aged 0–59 months who did not suffer from AWD from 1–30 April 2022 and was from households that had no case in them residing in Itula or Palorinya Subcounties, Obongi District, from 1–30 April 2022. Overall, we studied children aged 6–59 months residing in Itula and Palorinya subcounties, Obongi District, from 1–30 April 2022.

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### Sample size

The sample size was determined using the Fleiss formula, which is one of the double population proportion formulas. The required sample size was calculated using the Fleiss formula in Epi Info software version 7 with the following assumptions: the prevalence of childhood diarrhea derived from a study performed by Asfaha K.F. *et al* in Zana District of Ethiopia in 2015 (28) with 18% and 34% proportions of controls and cases, respectively, using untreated drinking water as one of the determinant factors of acute watery diarrhea morbidity, a ratio of case to control of 1:2, 95% confidence level, 5% margin of error and 80% power to generate a sample size of 549. The final sample size for this study after considering a nonresponse rate of 5% was 579 (193 cases and 386 controls).

### Case finding, sampling procedures, and exclusion criteria

We line listed 298 AWD cases among children aged 0–59 months documented in April 2022 in the 10 health facilities of Itula and Palorinya subcounties, which contributed more than 75% of the AWD cases in the district. Two hundred forty-one (81%) of the line listed case-patients were refugees from South Sudan. The line list included the child's name, nationality status, next of kin, age, date of visit to the health facility, diagnosis at discharge, laboratory investigations that were done and their results, village, and subcounty of residence. Once we listed all the cases from the outpatient and inpatient registers of the 10 health facilities, we selected the 193 cases from the line list by simple random sampling. Controls of the same age range as the cases were used. Controls were randomly selected from the Community Health Workers' list of households with children aged 0–59 months without any case during the study period (1–30 April 2022). One control was randomly selected from each control household. Cases and controls whose caregivers did not verbally consent to participate in the study and those whose caregivers were not available after two follow-up visits were excluded from the study.

### Study variables and data collection

Using a pretested structured electronic questionnaire, we interviewed the mothers or caregivers of the cases and controls. The questionnaire had inbuilt skips, validations, and mandatory fields that ensured high-quality data collection. Variables considered for the case control study were identified after conducting an extensive literature review (3-12, 28). These included child status (case/control), sociodemographic characteristics (nationality of household members; child's sex, age, birth order, and subcounty of residence; household location in a refugee settlement or not, child caregiver's category, age, marital status, and highest level of education attained; sex and occupation of the household head; number of household members and children 0–59 months in the household), child-caring practices (child received rotavirus vaccine, number of rotavirus vaccine doses received, child received measles vaccine, number of measles vaccine doses received, Vitamin A received in the 6 months, time the child spent on exclusive breastfeeding, child's weaning age, age at which the child stopped breastfeeding, caregiver's history of diarrhea, family member's history of diarrhea, and child comorbidity status), and water, sanitation, and hygiene/WASH characteristics (main source of water in the home, roundtrip distance to fetch water, home drinking water treatment, separate storage container for drinking water, toilet facility at home, method of handwashing, caregiver hand washing after visiting the toilet, before feeding the child, after cleaning the child's buttocks, after disposal of child's stool/urine, and before preparing food, hand washing facility at home, hand washing facility near toilet, child stool disposal method, presence of child stool in compound, and presence of refuse in compound).

### Data analysis

An Excel dataset from the electronic database server was exported to STATA version 14 for cleaning and subsequent descriptive and statistical analysis. The outcome variable was child status, which was dichotomized by assigning '1' for the cases and '2' for the controls. Descriptive statistics, such as frequencies with percentages, were computed for the different variables. Logistic regression analysis was used at both the bivariate and multivariate levels to generate crude odds ratios (CORs) and adjusted odds ratios (AORs) with 95% confidence intervals (CIs), respectively. Crude associations were determined at bivariate analysis, and a cutoff point of $p \leq 0.1$ was used to consider variables for the logistical regression model using a backward

stepwise method where confounders were controlled. If variables included in the multivariate model resulted in a loss of significance, they were removed. Covariates with $p<0.05$ were considered factors associated with the incidence of AWD among children aged 0–59 months in Obongi District. We tested the model using the Hosmer–Lemeshow goodness of fit test. We conducted additional common reference group analysis for the factors that were statistically significantly associated with AWD among children aged 0–59 months in Obongi District using MedCalc's software (29). We also conducted a supplementary analysis of the main source of water in the household and drinking water treatment in the household using a common reference group.

### Ethical considerations

The Ministry of Health of Uganda gave the directive and approval to carry out this investigation. In agreement with the International Guidelines for Ethical Review of Epidemiological Studies by the Council for International Organizations of Medical Sciences (1991) and the Office of the Associate Director for Science, CDC/Uganda, it was determined that this activity was not human subject research and that its primary intent was public health practice or disease control activity (specifically, epidemic or endemic disease control activity). This activity was reviewed by the CDC and was conducted consistent with applicable federal law and CDC policy. All experimental protocols were approved by the US CDC human subjects review board and the Uganda Ministry of Health and were performed in accordance with the Declaration of Helsinki. Parental/legal guardian verbal informed consent was obtained on behalf of all the children before the start of each interview since they were aged less than 5 years.

### Results

#### Sociodemographic characteristics of children aged 0–59 months, child caregivers, households, and household heads, Obongi District, Uganda, April 2022

A total of 193 cases and 386 controls with their respective mothers or caregivers were sampled for this study, with a response rate of 100% in both study groups. One hundred seventy-seven (91.7%) cases and 335 (86.8%) controls were refugees, 104 (53.9%) cases and 183 (47.4%) controls were male, 73 (37.8%) cases were aged 6–11 months and 127 (32.9%) controls were aged 24–35 months, 178 (92.2%) cases and 337 (87.3%) controls were living in refugee settlements, and 142 (73.6%) cases and 267 (69.2%) controls were from Itula Subcounty (Table 1).

Regarding child caregivers, 173 (89.6%) cases and 363 (94.0%) controls were cared for by their biological parents, 133 (68.9%) cases and 284 (73.6%) controls had caregivers aged 20–34 years, 142 (73.6%) cases, and 263 (68.1%) controls had caregivers who had attained primary education as their highest level of education (Table 1).

In this study, 117 (60.6%) cases and 243 (63.0%) controls were from households headed by males, and 133 (68.9%) cases and 243 (63.0%) controls were from households in which the households were mainly farmers. One hundred eight (56.0%) cases and 263 (68.1%) controls came from large households having 5–9 members, 128 (66.3%) cases and 240 (62.2%) controls came from households having 2–3 children aged 0–59 months, and 79 (40.9%) cases were second or third borne as 168 (43.5%) controls were fourth borne or more (Table 1).

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**Table 1: Socio-demographic characteristics of respondents in a study assessing the factors associated with acute watery diarrhea among children aged 0–59 months, Obongi District, Uganda, April 2022**

| Characteristic | Cases (N=193) | | Controls (N=386) | |
|---|---|---|---|---|
| | Frequency (n) | Percent (%) | n | % |
| **Nationality of household members** | | | | |
| Nationals | 16 | 8.3 | 51 | 13.2 |
| Refugee | 177 | 91.7 | 335 | 86.8 |
| **Child sex** | | | | |
| Female | 89 | 46.1 | 203 | 52.6 |
| Male | 104 | 53.9 | 183 | 47.4 |
| **Child age group (Months)** | | | | |
| 0-5 | 25 | 13.0 | 46 | 11.9 |
| 6–11 | 73 | 37.8 | 69 | 17.9 |
| 12–23 | 58 | 30.0 | 127 | 32.9 |
| 24–35 | 28 | 14.5 | 81 | 21.0 |
| 36–47 | 3 | 1.6 | 38 | 9.8 |
| 48–59 | 6 | 3.1 | 25 | 6.5 |
| **Household in settlement** | | | | |
| Yes | 178 | 92.2 | 337 | 87.3 |
| No | 15 | 7.8 | 49 | 12.7 |
| **Subcounty** | | | | |
| Itula | 142 | 73.6 | 267 | 69.2 |
| Palorinya | 51 | 26.4 | 119 | 30.8 |
| **Caregiver category** | | | | |
| Parent | 173 | 89.6 | 363 | 94.0 |
| Grandmother | 15 | 7.8 | 19 | 4.9 |
| Older siblings | 5 | 2.6 | 4 | 1.0 |
| **Marital status of caregiver** | | | | |
| Married/Cohabiting | 165 | 85.5 | 358 | 92.7 |
| Single | 14 | 7.3 | 19 | 4.9 |
| Divorced/Separated | 14 | 7.3 | 9 | 2.3 |
| **Caregiver age group (yrs)** | | | | |
| 16–19 | 27 | 14.0 | 22 | 5.7 |
| 20–34 | 133 | 68.9 | 284 | 73.6 |
| ≥35 | 33 | 17.1 | 80 | 20.7 |
| **Highest education level caregiver** | | | | |
| No formal education | 26 | 13.5 | 55 | 14.2 |
| Primary | 142 | 73.6 | 263 | 68.1 |
| Secondary | 22 | 11.4 | 63 | 16.3 |
| Tertiary/University | 3 | 1.6 | 5 | 1.3 |

**Table 1: Socio-demographic characteristics of respondents in a study assessing the factors associated with acute watery diarrhea among children aged 0–59 months, Obongi District, Uganda, April 2022**

| Characteristic | Cases (N=193) | | Controls (N=386) | |
|---|---|---|---|---|
| | Frequency (n) | Percent (%) | n | % |
| **Sex household head** | | | | |
| Male | 117 | 60.6 | 243 | 63.0 |
| Female | 76 | 39.4 | 143 | 37.0 |
| **Occupation household head** | | | | |
| Farmer | 133 | 68.9 | 243 | 63.0 |
| Unemployed | 38 | 19.7 | 61 | 15.8 |
| Business person | 16 | 8.3 | 54 | 14.0 |
| Others | 6 | 3.1 | 28 | 7.3 |
| **HH size** | | | | |
| Small (2–4) | 64 | 33.2 | 74 | 19.2 |
| Large (5–9) | 108 | 56.0 | 263 | 68.1 |
| Very Large (≥10) | 21 | 10.9 | 49 | 12.7 |
| **No. of children<5 years** | | | | |
| One | 40 | 20.7 | 130 | 33.7 |
| 2–3 | 128 | 66.3 | 240 | 62.2 |
| ≥4 | 25 | 13.0 | 16 | 4.1 |
| **Child's birth order** | | | | |
| 1st born | 44 | 22.8 | 70 | 18.1 |
| 2nd–3rd born | 79 | 40.9 | 148 | 38.3 |
| ≥4th born | 70 | 36.3 | 168 | 43.5 |

**Child caring practices of respondents in a study assessing the factors associated with acute watery diarrhea among children aged 0–59 months, Obongi District, Uganda, April 2022**

Among the children included in this study, 187 (96.9%) cases and 369 (95.6%) controls had received rotavirus vaccine, of which 159 (85%) cases and 311 (84.3%) controls had received two or more doses. One hundred seventeen (60.6%) cases and 287 (74.4%) controls had received measles vaccines, of which 96 (82.1%) cases and 222 (77.4%) controls had only received one measles vaccine dose. One hundred twenty-nine (66.8%) cases and 252 (65.3%) controls had received vitamin A supplementation in the six months before April 2022, 113 (58.5%) cases and 224 (58.0%) controls were exclusively breastfed for six months or more, 43 (22.3%) cases and 53 (13.7%) controls had caregivers who suffered from diarrhea during the study period, and 85 (44.0%) cases and 89 (23.1%) controls came from households that had another family member who suffered from diarrhea during the study period (Table 2).

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**Table 2: Child caring practices of respondents in a study assessing the factors associated with acute watery diarrhea among children aged 0–59 months, Obongi District, Uganda, April 2022**

| Characteristic | Cases (N=193) | | Controls (N=386) | |
|---|---|---|---|---|
| | Frequency (n) | Percent (%) | n | % |
| **Rotavirus vaccine** | | | | |
| Yes | 187 | 96.9 | 369 | 95.6 |
| No | 6 | 3.1 | 17 | 4.4 |
| **Doses of rotavirus vaccine*** | | | | |
| One | 28 | 15 | 58 | 15.7 |
| ≥Two | 159 | 85 | 311 | 84.3 |
| **Measles vaccine** | | | | |
| Yes | 117 | 60.6 | 287 | 74.4 |
| No | 66 | 34.2 | 89 | 23.1 |
| Don't know | 10 | 5.2 | 10 | 2.6 |
| **Doses of measles vaccine†** | | | | |
| One | 96 | 82.1 | 222 | 77.4 |
| ≥Two | 21 | 17.9 | 65 | 22.6 |
| **Vitamin in previous 6 months** | | | | |
| Yes | 129 | 66.8 | 252 | 65.3 |
| No | 53 | 27.5 | 121 | 31.3 |
| Don't know | 11 | 5.7 | 13 | 3.4 |
| **Time exclusively breastfed** | | | | |
| <6 months | 80 | 41.5 | 162 | 42.0 |
| ≥6 months | 113 | 58.5 | 224 | 58.0 |
| **Weaning age** | | | | |
| <6 months | 80 | 41.5 | 162 | 42.0 |
| At 6 months | 46 | 23.8 | 88 | 22.8 |
| >6 months | 67 | 34.7 | 136 | 35.2 |
| **Age stopped breastfeeding (month)** | | | | |
| 0–6 | 87 | 45.1 | 124 | 32.1 |
| 7–18 | 39 | 20.2 | 71 | 18.4 |
| ≥18 | 67 | 34.7 | 191 | 49.5 |
| **Caregiver suffered from Diarrhea** | | | | |
| Yes | 43 | 22.3 | 53 | 13.7 |
| No | 150 | 77.7 | 333 | 86.3 |
| **Family member suffered from Diarrhea** | | | | |
| Yes | 85 | 44.0 | 89 | 23.1 |
| No | 108 | 56.0 | 297 | 76.9 |
| **Child had a comorbidity** | | | | |
| Yes | 31 | 16.1 | 9 | 2.3 |
| No | 162 | 83.9 | 377 | 97.7 |
| **Child had malnutrition** | | | | |
| Yes | 28 | 14.5 | 8 | 2.1 |
| **Child had Diabetes Mellitus (DM)** | | | | |
| Yes | 4 | 2.1 | 1 | 0.3 |
| **Child had HIV** | | | | |
| Yes | 2 | 1.0 | 0 | 0 |

- *Among 187 cases and 369 controls that received rotavirus vaccine, †Among 117 cases and 287 controls that received measles vaccine

**Water, sanitation, and hygiene characteristics of respondents in Itula and Palorinya Sub-counties, Obongi District, Uganda, April 2022**

Concerning the water, 114 (59.1%) case and 160 (41.5%%) control households used pipped water as the main source of water, 135 (69.9%) case and 289 (74.9%) control households did not subject drinking water to any form of treatment, and 109 (56.5%) case and 251 (65.0%) control households had separate containers for drinking and domestic water. All case and control households had toilets, 24 (12.4%) case and 97 (25.1%) control caregivers used water and soap to wash their hands, 106 (54.9%) case and 245 (63.5%) control caregivers did not wash their hands after visiting the toilet, and 43 (22.3%) case and 56 (14.5%) control households had child stool in their compounds (Table 3).

**Table 3: Water, sanitation, and hygiene characteristics of respondents in Itula and Palorinya Subcounties, Obongi District, Uganda, April 2022**

| Characteristic | Cases (N=193) | | Controls (N=386) | |
|---|---|---|---|---|
| | Frequency (n) | Percent (%) | n | % |
| **Main source of water** | | | | |
| Pipped | 114 | 59.1 | 160 | 41.5 |
| Borehole | 79 | 40.9 | 226 | 58.5 |
| **Roundtrip distance to fetch water** | | | | |
| ≤30 minutes | 98 | 50.8 | 200 | 51.8 |
| >30 minutes | 95 | 49.2 | 186 | 48.2 |
| **Home water treatment*** | | | | |
| Yes | 58 | 30.1 | 120 | 34.1 |
| **Separate container for drinking water** | | | | |
| Yes | 109 | 56.5 | 251 | 65.0 |
| **Toilet facility at home (Yes)** | 193 | 100.0 | 386 | 100.0 |
| **Method of handwashing** | | | | |
| Water only | 129 | 66.8 | 218 | 56.5 |
| Water and soap | 24 | 12.4 | 97 | 25.1 |
| Don't wash hands | 40 | 20.7 | 71 | 18.4 |
| **Wash hands after visiting the toilet** | | | | |
| Yes | 87 | 45.1 | 141 | 36.5 |
| **Wash hands before feeding the child** | | | | |
| Yes | 161 | 83.4 | 317 | 82.1 |
| **Wash hands after cleaning child's buttock** | | | | |
| Yes | 143 | 74.1 | 301 | 78.0 |
| **Wash hands after disposal of child's stool/ urine** | | 0.0 | | 0.0 |
| Yes | 149 | 77.2 | 303 | 78.5 |
| **Wash hands before preparing food** | | | | |
| Yes | 146 | 75.6 | 289 | 74.9 |
| **Hand washing facility at home** | | | | |
| Yes | 45 | 23.3 | 131 | 33.9 |
| **Hand washing facility near toilet†** | | | | |
| Yes | 23 | 51.1 | 45 | 34.4 |
| **Child stool disposal method** | | | | |
| Toilet | 170 | 88.1 | 350 | 90.7 |
| Covered by soil | 18 | 9.3 | 28 | 7.3 |
| Open space | 5 | 2.6 | 8 | 2.1 |
| **Child stool in compound** | | | | |
| Yes | 43 | 22.3 | 56 | 14.5 |
| **Refuse in compound** | | | | |
| Yes | 61 | 31.6 | 90 | 23.3 |

*Among 352 controls that responded to home water treatment, †Among 45 cases and 131 controls that received rotavirus vaccine

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**Factors associated with acute watery diarrhea among children aged 0–59 months in Obongi District, Uganda, April 2022**

At the bivariate logistic regression analysis stage, children living in households with 5–9 people and more than 10 people had two times the odds of suffering from AWD than those from households with 1–4 people (COR: 2.1; CI: 1.4–3.2 and COR: 2 CI: 1.1–3.7, respectively). Children suffering from a comorbidity such as HIV, malnutrition, and diabetes mellitus (DM) had eight times the odds of suffering from acute watery diarrhea than those who did not have a comorbidity (COR: 8.0; CI: 3.7–17). Children living in households that had no hand washing facility near the toilet had two times the odds of suffering from acute watery diarrhea than those who lived in households that had a hand washing facility near the toilet (COR: 2.0; CI: 1.1–4). Children living in households that had caregivers who did not wash their hands with soap after visiting the toilet had 40 percent more odds of suffering from acute watery diarrhea than those who lived in households that had caregivers who washed their hands with soap after visiting the toilet (COR: 1.4; CI: 1.1–2.0). Children living in households that used borehole water had two times the odds of suffering from AWD than those who lived in households that used pipped water (COR: 2.1; CI: 1.4–2.9) (Table 4).

In the logistic regression model, after controlling for nationality of household members, child birth order, number of household occupants, child sex, household in settlement, and hand washing facility near the toilet, children suffering from a comorbidity such as diabetes and HIV had 12 times the odds of suffering from AWD than those who did not suffer from any comorbidity (AOR: 12; CI: 2.5–53), children whose caregivers did not wash hands with soap and water after visiting the toilet had four times the odds of suffering from acute watery diarrhea than those whose caregivers washed their hands after visiting the toilets (AOR: 3.9; CI: 1.2–13), and children living in households that used borehole water had four times the odds of suffering from acute watery diarrhea than those who lived in households that used pipped water (AOR: 4.0; CI: 1.7–9.6) (Table 4).

**Table 4: Bivariate and multivariate logistic regression analysis results of factors associated with acute watery diarrhea among children aged 0–59 months, Obongi District, Uganda, April 2022**

| Characteristic | Case (N=193) | | Control (N=386) | | COR (95% CI) | AOR (95% CI) |
|---|---|---|---|---|---|---|
| | n | % | n | % | | |
| **Nationality of HH members** | | | | | | |
| Nationals | 16 | 8.3 | 335 | 86.8 | 1.00 | 1.00 |
| Refugee | 177 | 91.7 | 51 | 13.2 | 0.6 (0.33–1.1) | 1.4 (0.23–7.9) |
| **Child's birth order** | | | | | | |
| 1st born | 44 | 22.8 | 70 | 18.1 | 1.00 | 1.00 |
| 2nd–3rd born | 79 | 40.9 | 148 | 38.3 | 1.2 (0.74–1.9) | 0.6 (0.17–1.9) |
| ≥4th born | 70 | 36.3 | 168 | 43.5 | 1.5 (0.94–2.4) | 0.9 (0.26–2.9) |
| **HH size** | | | | | | |
| Small (2–4) | 64 | 33.2 | 74 | 19.2 | 1.00 | 1.00 |
| Large (5–9) | 108 | 56.0 | 263 | 68.1 | 2.1 (1.4–3.2) | 1.3 (0.44–3.9) |
| Very large (≥10) | 21 | 10.9 | 49 | 12.7 | 2.0 (1.1–3.7) | 0.9 (0.18–4.6) |
| **Child sex** | | | | | | |
| Female | 89 | 46.1 | 203 | 52.6 | 1.00 | 1.00 |
| Male | 104 | 53.9 | 183 | 47.4 | 0.8 (0.55–1.1) | 0.5 (0.22–1.2) |
| **Child had a comorbidity** | | | | | | |
| No | 162 | 83.9 | 377 | 97.7 | 1.00 | 1.00 |
| Yes | 31 | 16.1 | 9 | 2.3 | 8.0 (3.7–17) | 12 (2.5–53) |
| **Household in settlement** | | | | | | |
| No | 15 | 7.8 | 49 | 12.7 | 1.00 | 1.00 |
| Yes | 178 | 92.2 | 337 | 87.3 | 0.6 (0.32–1.1) | 0.3 (0.04–2.1) |
| **Hand washing facility near toilet**† | | | | | | |
| Yes | 23 | 51.1 | 45 | 34.4 | 1.00 | 1.00 |
| No | 22 | 48.9 | 86 | 65.6 | 2.0 (1.1–4) | 1.1 (0.48–2.7) |
| **Wash hands with soap after visiting the toilet** | | | | | | |
| Yes | 87 | 45.1 | 141 | 36.5 | 1.00 | 1.00 |
| No | 106 | 54.9 | 245 | 63.5 | 1.4 (1.1–2.0) | 3.9 (1.2–13) |
| **Main source of water** | | | | | | |
| Pipped | 114 | 59.1 | 160 | 41.5 | 1.00 | 1.00 |
| Borehole | 79 | 40.9 | 226 | 58.5 | 2.1 (1.4–2.9) | 4.0 (1.7–9.6) |

*Significant association at *p* value < 0.05, †Among 45 cases and 131 controls that received rotavirus vaccine

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Additional analysis of the three factors associated with AWD in this study (suffering from comorbidities such as HIV, caregiver's failure to wash hands with soap after visiting the toilet and using borehole water) using a common reference group yielded the following: child comorbidity alone was associated with increased odds of AWD among children (OR: 10, CI: 1.4–93) (Table 5). The odds of AWD among children having a caregiver who did not wash their hands after visiting the toilet and belonging to households that used borehole water were reduced by absence of a comorbidity (OR: 0.3, CI: 0.16–0.54). The odds of AWD among children under the care of caregivers who did not wash their hands after visiting the toilet were increased by suffering from a comorbidity (OR: 4.6, CI: 1.2–18) (Table 5). The odds of AWD among children belonging to households that used borehole water were reduced if their caregivers washed their hands after visiting the toilet and absence of a comorbidity (OR: 0.5; CI: 0.27–0.89) (Table 5).

**Table 5: Common reference group analysis of factors associated with acute watery diarrhea among children aged 0–59 months, Obongi District, Uganda, April 2022**

| Main source of water | Washed hands with soap after visiting the toilet | Child had a comorbidity | Case (N=192) | | Control (N=386) | | OR (95% CI) |
|---|---|---|---|---|---|---|---|
| | | | n | % | n | % | |
| Pipped (-) | Yes (-) | No (-) | 36 | 44 | 45 | 56 | 1.0 |
| Borehole (+) | No (+) | Yes (+) | 6 | 55 | 5 | 45 | 1.5 (0.42–5.3) |
| + | + | - | 30 | 19 | 126 | 81 | 0.3 (0.16–0.54) |
| + | - | + | 6 | 100 | 0 | 0 | 16 (0.88–297) |
| - | + | + | 11 | 79 | 3 | 21 | 4.6 (1.2–18) |
| - | - | + | 8 | 89 | 1 | 11 | 11 (1.4–93) |
| - | + | - | 59 | 35 | 111 | 65 | 0.7 (0.39–1.1) |
| + | - | - | 37 | 28 | 95 | 72 | 0.5 (0.26–0.85) |

*Significant association at p value <0.05

## Discussion

Acute watery diarrhea has remained a major cause of morbidity and mortality among children 0–59 months in Uganda despite several interventions that have been put in place to address it. We set out to identify factors associated with AWD among children aged 0–59 months in Obongi District during April 2022. This study showed that suffering from comorbidities such as HIV, caregiver's failure to wash hands with soap after visiting the toilet and using borehole water were the factors associated with acute watery diarrhea among children aged 0–59 months in Obongi District.

In this study, children suffering from comorbidities such as HIV, malnutrition, and DM had higher odds of suffering from acute watery diarrhea than those who did not suffer from any comorbidity. These comorbidities lower the child's immunity, and as a result, the child is predisposed to frequent infections such as AWD from agents and sources from which they would not have been infected (30). Our findings are similar to findings from other studies in Zambia, Ethiopia, and Sudan that showed that comorbidities such as HIV and malnutrition were associated with recurrent AWD among children aged 0–59 months (9, 31, 32).

In this study, we also found that children whose caregivers did not wash their hands with clean water and soap after visiting the toilet had more odds of suffering from AWD than those whose caregivers washed their hands using clean water and soap after visiting the toilet. This is not surprising since

hand washing using clean water and soap kills diarrhea-causing organisms and hence reduces its transmission from one person to the other (33). Dirty hands serve as gateways for carrying infectious pathogens to the child's food during feeding of the child, thereby predisposing the child to diarrhea-causing agents (33). Similar findings were also reported in studies carried out in Ethiopia, Zambia, Botswana, Uganda, Tanzania, and Nepal, which also reported that caregivers' hand washing habits, especially of washing hands with clean water and soap at critical times, such as after visiting the toilet, were protective against AWD among children 0–59 months (8, 9, 34-39). However, a study carried out in Ethiopia among children aged 0–59 months did not find any significant association between washing hands at critical times, such as after visiting the toilet, and AWD (28). This might be because that study was carried out among nationals of a fairly stable socioeconomic status compared to the current study, which was conducted primarily among refugees of a low socioeconomic status.

This study showed that children living in households that used borehole water had higher odds of suffering from AWD than those who lived in households that mainly used pipped water that was chlorinated. The chlorine in pipped water disinfects (kills) or inactivates diarrhea-causing organisms, hence rendering it safe for home use (40). Itula and Palorinya subcounties of Obongi District are bounded by the River Nile and have high water tables, implying that toilets in the settlements could have easily contaminated the borehole water since the boreholes are not so deep. A study in Tanzania reported that borehole water was contaminated by fecal material attributed to the entry of sewage (human wastes) into underground water and recommended the treatment or boiling of borehole water before consumption (41). Although boreholes and other ground water sources are classified as improved and safe water sources (42), several microbiological studies of groundwater sources, including boreholes, have reported high rates of *Escherichia coli,* indicating fecal contamination of those sources (43-45). The high population densities in the settlements where these boreholes are located could have exposed them to contamination by children who touch the spouts (water outlets) when fetching water. A study conducted in Zimbabwe reported that although improved sources of water, such as boreholes, generally deliver 'safe' water, a proportion of those sources can easily be contaminated at the point of collection (46). Findings from our study are similar to findings in another study carried out in Nigeria that showed that protected groundwater sources such as boreholes were associated with a high risk of contracting diarrhea (47). However, our findings are contrary to findings in another study conducted in Uganda that showed that children from homes that mainly used borehole water were at reduced risk of AWD than those that mainly used piped water (48). The major difference between that study and the current study is that it was a cross-sectional study using the 2000/2001 Uganda Demographic and Health Survey dataset (48), yet ours is a case control study. That study never gave reasons why children aged 0–59 months from households that used borehole water were at a lower risk of contracting diarrhea compared to those who used pipped water.

**Study limitations**

This investigation had some limitations. Cases and controls were obtained for the month of April 2022; therefore, the seasonal variations in AWD during the year were not considered. Recall and social desirability bias might have influenced responses to some of the questions that were asked as they depended on the respondent's own memory, and findings from this study are based on self-reported data, although several measures, such as quality control and observation checks, were incorporated into the questionnaire to ensure the accuracy of the data collected.

**Conclusions and recommendations**

Suffering from a long-term illness such as HIV, malnutrition, and DM, caregivers' failure to wash their hands with soap after visiting toilets, and households using borehole water were associated with AWD among children aged 0–59 months in Obongi District. We recommended health facility management for all children with AWD. We also recommended education of communities on hand washing at critical times using clean water and

soap and expanded use of boreholes and piped water.

### Conflict of interest

The authors declare that they had no conflict of interest.

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### References

1. Diarrhoeal disease Fact Sheet [Internet]. World Health Organisation (WHO). 2017 [cited 3 October 2021]. Available from: https://www.who.int/news-room/fact-sheets/detail/diarrhoeal-disease.
2. MoH. Annual Health Sector Performance Report Financial Year 2020/21. www.health.go.ug: Ministry of Health (MoH), Uganda; 2022.
3. Gashaw TA, Walie YM. Prevalence and determinate factors of diarrhea morbidity among under five children in shake zone, Southwest Ethiopia, a community based cross-sectional study. Archives of Community Medicine and Public Health. 2019;5(1):008-14.
4. Getachew A, Guadu T, Tadie A, Gizaw Z, Gebrehiwot M, Cherkos DH, et al. Diarrhea prevalence and sociodemographic factors among under-five children in rural areas of North Gondar Zone, Northwest Ethiopia. International journal of pediatrics. 2018;2018.
5. Getachew B, Mengistie B, Mesfin F, Argaw R. Factors associated with acute diarrhea among children aged 0-59 months in Harar town, eastern Ethiopia. East African Journal of Health and Biomedical Sciences. 2018;2(1):26-35.
6. Gunsa GG, Rodamo KM, Dangiso DD. Determinants of Acute Diarrhoea among Children Aged 6-59 Months in Chiffre District, Southern Ethiopia: Unmatched Case-Control Study. J Gynecol Obstet. 2018;6(2):15-25.
7. Kasye DG, Garoma NH, Kassa MA. Assessment of the prevalence of diarrheal disease under-five children Serbo Town, Jimma Zone South West Ethiopia. Clin Mother Child Health. 2018;15(281):2.
8. Melese B, Paulos W, Astawesegn FH, Gelgelu TB. Prevalence of diarrheal diseases and associated factors among under-five children in Dale District, Sidama zone, Southern Ethiopia: a cross-sectional study. BMC Public Health. 2019;19(1):1-10.
9. Musonda C, Siziya S, Kwangu M, Mulenga D. Factors associated with diarrheal diseases in under-five children: a case control study at arthur davison children's hospital in Ndola, Zambia. Asian Pac J Health Sci. 2017;4(3):228-34.
10. Angesom T. Prevalence and Associated Factors of Diarrhea among Under-Five Children in Laelay-Maychew District, Tigray Region, Ethiopia: Addis Ababa University; 2015.
11. Sinmegn Mihrete T, Asres Alemie G, Shimeka Teferra A. Determinants of childhood diarrhea among underfive children in Benishangul Gumuz regional state, north West Ethiopia. BMC pediatrics. 2014;14(1):1-9.
12. Tamiso A, Yitayal M, Awoke A. Prevalence and determinants of childhood diarrhoea among graduated households, in rural area of Shebedino district, Southern Ethiopia, 2013. Science. 2014;2(3):243-51.
13. Information Sheet: Observed Rate of Vaccine Reactions: Rotavirus Vaccine [Internet]. World Health Organization (WHO). 2014 [cited 03 October 2021]. Available from: https://www.who.int/vaccine_safety/initiative/tools/Rotavirus_vaccine__rates_information_sheet.pdf?ua=1.
14. Government launches new Rotavirus vaccine to protect children in Uganda from diarrhea [Internet]. World Health Organisation (WHO).

2018 [cited 03 September 2021]. Available from: https://www.afro.who.int/news/government-launches-new-rotavirus-vaccine-protect-children-uganda-diarrhea.
15. Vaccines and Preventable Diseases: Rotavirus Vaccination [Internet]. Centres for Disease and Prevention (CDC). [cited 03 October 2021]. Available from: https://www.cdc.gov/vaccines/vpd/rotavirus/index.html.
16. Uganda Rolls out Rotavirus Vaccine into the Routine Immunization Schedule [Internet]. Ministry of Health, Uganda. 2018 [cited 03 September 2021]. Available from: https://www.health.go.ug/2019/12/02/uganda-rolls-out-rotavirus-vaccine-into-the-routine-immunization-schedule/.
17. Uganda Clinical Guidelines 2016: National Guidelines for Management of Common Conditions [Internet]. Ministry of Health, Government of Uganda. 2016. Available from: https://health.go.ug/sites/default/files/Uganda%20Clinical%20Guidelines%202016_FINAL.pdf.
18. MoH. Immunization in Practice and the New Routine Immunization Schedule: A Training Guide for Operational Level Health Workers. Ministry of Health (MoH), The Republic of Uganda; 2022.
19. MoH. National Technical Guidelines for Integrated Disease Surveillance and Response. Third ed: Ministry of Health; 2021.
20. Health Unit Outpatient Monthly Report (HMIS Form 105) [Internet]. Ministry of Health (MoH), Government of Uganda. 2019 [cited 20 October 2022]. Available from: https://www.malariaconsortium.org/gallery-file/06081045-69-hmis105healthunitoutpatientmonthlyreport.pdf.
21. MoH. Health Unit Inpatient Monthly Report (HMIS Form 108). Kampala, Uganda: Ministry of Health (MoH), Uganda; 2019.
22. Uganda eHMISUganda's Electronic Health Information System: DHIS2 [Internet]. Ministry of Health. Available from: https://hmis.health.go.ug/dhis-web-commons/security/login.action.
23. Uganda - Refugee Statistics January 2022 - Palorinya [Internet]. United Nations High Commission for Refugees (UNHCR). 2022. Available from: file:///C:/Users/HP/Downloads/Palorinya%20Settlement%20Profile_31Jan2022%20(1).pdf.
24. Population & Censuses: Census Population counts (2002 and 2014) by Region, District and Mid Year Population projections (2015-2021) [Internet]. Uganda Bureau of Statistics (UBOS). 2022 [cited 02 March 2022]. Available from: https://www.ubos.org/explore-statistics/20/.
25. Obongi District Investment Profile [Internet]. Ministry of Local Government, Obongi District. 2021. Available from: https://www.ugandainvest.go.ug/wp-content/uploads/2021/08/Obongi-2021.pdf.
26. Obongi District [Internet]. Directorate of Water Development, Ministry of Water and Environment (MWE), Republic of Uganda. 2022 [cited September 4, 2022]. Available from: http://wsdb.mwe.go.ug/index.php/reports/district/146.
27. UBOS. National Population and Housing Census 2014: Area Specific Profiles-Moyo District. Kampala: Uganda Bureau of Statistics (UBOS); 2017.
28. Asfaha KF, Tesfamichael FA, Fisseha GK, Misgina KH, Weldu MG, Welehaweria NB, et al. Determinants of childhood diarrhea in Medebay Zana District, Northwest Tigray, Ethiopia: a community based unmatched case–control study. BMC pediatrics. 2018;18(1):1-9.
29. Odds ratio calculator [Internet]. 2022. Available from: https://www.medcalc.org/calc/odds_ratio.php.
30. Mulholland K. Commentary: comorbidity as a factor in child health and child survival in developing countries. International Journal of Epidemiology. 2005;34(2):375-7.
31. Derseh B, Mruts K, Demie T, Gebremariam T. Co-morbidity, treatment outcomes and factors affecting the recovery rate of under -five children with severe acute malnutrition admitted in selected hospitals from Ethiopia: retrospective follow up study. Nutrition Journal. 2018;17(1):116.
32. Netsereab TB, Xenos P. Factors Associated with Diarrhea among Children Less Than 5 Years Old in Sudan. Journal of Health Research. 2017;31(Suppl. 2):S209-15.
33. Datta S, Singh Z, Boratne A, Senthilvel V, Bazroy J, Dimri D. Knowledge and practice of handwashing among mothers of under five children in rural coastal South India. International Journal of Medicine and public health. 2011;1(1).

Continued from page 24

34. Nantege R, Kajoba D, Ddamulira C, Ndoboli F, Ndungutse D. Prevalence and Factors Associated With Diarrheal Diseases Among Children Below Five Years in Selected Slum Settlements in Entebbe Municipality, Wakiso District, Uganda. 2022.
35. Arvelo W, Kim A, Creek T, Legwaila K, Puhr N, Johnston S, et al. Case–control study to determine risk factors for diarrhea among children during a large outbreak in a country with a high prevalence of HIV infection. International Journal of Infectious Diseases. 2010;14(11):e1002-e7.
36. Hashi A, Kumie A, Gasana J. Hand washing with soap and WASH educational intervention reduces under-five childhood diarrhoea incidence in Jigjiga District, Eastern Ethiopia: a community-based cluster randomized controlled trial. Preventive medicine reports. 2017;6:361-8.
37. Budhathoki SS, Bhattachan M, Yadav AK, Upadhyaya P, Pokharel PK. Eco-social and behavioural determinants of diarrhoea in under-five children of Nepal: a framework analysis of the existing literature. Tropical medicine and health. 2016;44(1):1-7.
38. Tesfaye TS, Magarsa AU, Zeleke TM. Moderate to severe diarrhea and associated factors among under-five children in Wonago District, South Ethiopia: A Cross-Sectional Study. Pediatric Health, Medicine and Therapeutics. 2020;11:437.
39. Kabhele S, New-Aaron M, Kibusi SM, Gesase AP. Prevalence and factors associated with diarrhoea among children between 6 and 59 months of age in mwanza city tanzania. Journal of Tropical Pediatrics. 2018;64 (6):523-30.
40. Water Disinfection with Chlorine and Chloramine: Chlorine and chloramine are the major disinfectants used in public water systems [Internet]. Centres for Disease Control and Prevention (CDC). 2020 [cited August 11, 2022]. Available from: https://www.cdc.gov/healthywater/drinking/public/water_disinfection.html.
41. Basamba TA, Sekabira K, Kayombo CM, Ssegawa P. Application of factor and cluster analyses in the assessment of sources of contaminants in borehole water in Tanzania. Polish Journal of Environmental Studies. 2013;22(2):337-46.
42. UN World Water Development Report 2022 'Groundwater: Making the invisible visible': New report : Is the solution to water crises hiding right under our feet? [Internet]. United Nations (UN). 2022 [cited 11 August, 2022]. Available from: https://www.unwater.org/un-world-water-development-report-2022/#:~:text=Groundwater%20presently%20provides%20half%20of,all%20water%20used%20for%20irrigation.
43. Richardson HY, Nichols G, Lane C, Lake IR, Hunter PR. Microbiological surveillance of private water supplies in England–The impact of environmental and climate factors on water quality. Water research. 2009;43(8):2159-68.
44. Kanyerere T, Levy J, Xu Y, Saka J. Assessment of microbial contamination of groundwater in upper Limphasa River catchment, located in a rural area of northern Malawi. Water SA. 2012;38 (4):581-96.
45. Howard G, Pedley S, Barrett M, Nalubega M, Johal K. Risk factors contributing to microbiological contamination of shallow groundwater in Kampala, Uganda. Water research. 2003;37 (14):3421-9.
46. Gundry SW, Wright JA, Conroy R, Du Preez M, Genthe B, Moyo S, et al. Contamination of drinking water between source and point-of-use in rural households of South Africa and Zimbabwe: implications for monitoring the Millennium Development Goal for water. Water Practice and Technology. 2006;1(2).
47. Hunter PR, Risebro H, Yen M, Lefebvre H, Lo C, Hartemann P, et al. Water source and diarrhoeal disease risk in children under 5 years old in Cambodia: a prospective diary based study. BMC Public Health. 2013;13(1):1-9.
48. Ssenyonga R, Muwonge R, Twebaze F, Mutyabule R. Determinants of acute diarrhoea in children aged 0–5 years in Uganda. East African Medical Journal. 2009;86(11):513-9.

## Risk factors for death among children with severe malaria, Namutumba District, Eastern Uganda, September 2021 - February 2022

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**Summary**

**Background:** On February 17, 2022, a "strange disease', which was later confirmed as malaria, was reported to the Ministry of Health from Namutumba District, mainly affecting children and reportedly causing large numbers of child deaths since late 2021. We investigated to determine the scope of severe malaria deaths, identify factors associated, and recommend evidence-based control measures to inform proper programming for the prevention of malaria-associated deaths among children in Namutumba District.

**Methods:** We conducted an unmatched case-control study in March 2022 in Ivukula Subcounty. This subcounty had the highest attack rate per 1,000 population in the district. We defined a case as death with a history of fever AND any of the following: convulsions, difficulty in breathing, yellowing of eye or palms, tea-colored urine, anemia, loss of consciousness, or reduced urine output in a child ≤12 years from September 2021 to February 2022 in Ivukula Subcounty, Namutumba District. A control was defined as a severe malaria survivor. We actively searched for cases and controls with the help of VHTs in a ratio of 1:2 controls. A semi-structured interviewer-administered questionnaire was used to obtain demographic data and assess clinical, health-seeking, and health system risk factors. Drugs and bloodstock status information was obtained from health workers using semi-structured interviews. We identified risk factors for death using multivariate logistic regression and thematic analysis for qualitative data.

**Results:** We identified 46 cases and 77 controls. Among the 46 cases, 63% were <5 years, with 1:1 ratio for males and females. Death among children with severe malaria was significantly associated with treatment non-completion (aOR=9.7, 95%CI:1.8 – 52.9) and failure to receive blood transfusion for anemic patients (aOR=7.1, (95%CI: 1.4 – 36.2). Other findings that hindered access to effective care and treatment included failure to reach intended referral sites due to transport cost challenges, stockouts of antimalarials and blood products, and absence of integrated community case management of childhood illnesses (iCCM).

**Conclusion:** Failure to complete antimalarial treatment, not receiving blood transfusion for anemic patients, stockouts of malaria drugs, and failure to reach referral sites were major contributors to malaria mortality among children ≤12 years in Ivukula Subcounty, Namutumba District. We recommend a more accurate quantification of antimalarials for health facilities, offering transport support to severe patients referred to higher-level facilities, increasing access to blood products and activation of iCCM to avert numerous deaths among children in this area.

### Introduction

Globally, the scale-up of malaria prevention and control measures has made a significant contribution to the fight against malaria, with notable gains between 2000 and 2020 resulting in a 36% reduction in mortality[1]. Despite this decrease, the number of malaria-related deaths remains high, reaching 627,000 in 2020 as a result of the 241 million cases reported that year, with the World Health Organization (WHO) African Region bearing the highest burden[2].

In Uganda, malaria is still highly endemic in 95% of the country, with the remaining 5% prone to epidemics. The disease is one of the leading causes of morbidity and mortality in the country, responsible for 30-50% of outpatient visits and 15-20% of hospital admissions[3]. With such a heavy burden, the risk of death is high if not managed promptly and effectively. True to this, Uganda, which ranked third with a 5% contribu-

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tion of all global malaria cases in 2020, accounted for 3.5% of all reported deaths in the same year, ranking fifth in this regard[2].
We would expect Uganda's contribution to global deaths to be minimal with the current implementation of prompt and effective diagnosis and treatment of cases combined with other malaria control interventions such as the nationwide distribution of long-lasting insecticide-treated bed nets (LLINs) and indoor residual spraying (IRS). On the contrary, Uganda still registers approximately 20-30 deaths per week due to severe malaria according to the National Health Information System[4].
According to the Uganda National Malaria Control Program (NMCP), severe malaria is defined as malaria complicated by serious organ failures or abnormalities in the patient's blood or metabolism. The manifestations of severe malaria may include cerebral malaria (impairment of consciousness), severe anaemia, hemoglobinuria, acute respiratory distress syndrome, abnormalities in blood coagulation, low blood pressure caused by cardiovascular collapse, acute kidney injury, hyperparasitemia, and metabolic acidosis. Severe malaria is a medical emergency and should be treated urgently and aggressively using 3 doses of intravenous artesunate in 24 hours followed by a complete dose of artemether and lumefantrine (AL) for 3 days[5].
On February 17, 2022, a Member of Parliament in Busiki County, Namutumba District reported to the Uganda Ministry of Health (UMoH) about a 'strange disease', mainly affecting children. The condition was reportedly presenting as fever, anemia, urinating and coughing blood, and death, mostly among children 12 years of age and below and on investigation the disease was identified to be severe malaria. We investigated to determine the scope of severe malaria deaths, identify factors associated, and recommend evidence-based control measures.

## Methods

### Outbreak area

Namutumba District is located in the eastern part of Uganda, a region highly burdened with malaria. The district is made up of 2 constituencies and 20 sub-counties with a total population of approximately 320,000 people[6]. The population is served by 2 private hospitals, 1 Health center (H/C) IV, 7 H/C IIIs, and 25 H/C IIs. Only H/C IIIs are mandated to manage severe malaria while blood transfusion services are offered at the HC IV in the district; these products are received from Jinja Regional Referral Hospital on request and supply is not guaranteed. For further management beyond Nsinze H/C IV, referrals are made to Iganga Hospital, Jinja Regional Referral Hospital or Mbale Reginal Referral Hospital which are 31Km, 71Km and 79Km respectively away from Nsinze H/C IV.

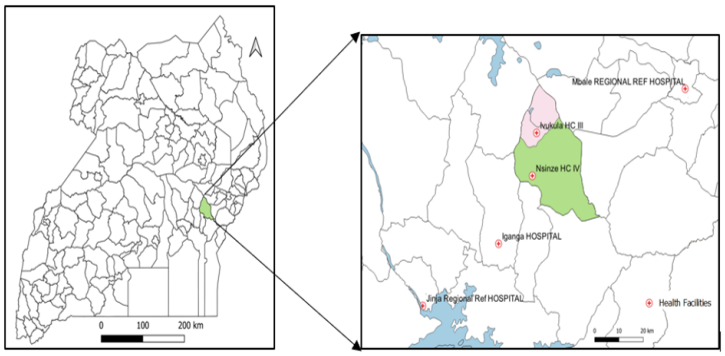


**Figure 1: Location of Namutumba District and Ivukula Subcounty on the map of Uganda and the relevant health facilities used in the referral network**

### Case definition and finding

We defined a case as fatal fever and any of the following: convulsions, difficulty in breathing, yellowing of eye or palms, tea-colored urine, anemia (subjective or clinically-identified), loss of consciousness, or reduced urine output child ≤12 years from September 2021 to February 2022 in Ivukula Subcounty. We chose to use clinical definitions and relied on the caretakers' memory to remember the child's presentation. For case-patients, majority of the caregivers had discarded the records immediately after the loss of their child or were not provided with the records at facilities

To find and ascertain the scope of severe malaria deaths in the district, we reviewed data on severe malaria and fatal malaria cases in the district health information system (DHIS2). This was followed by review of records from inpatient registers from all public and private health facilities in Namutumba District. Unfortunately, these data sources could not support the alleged increase in deaths among children (Figure 2).

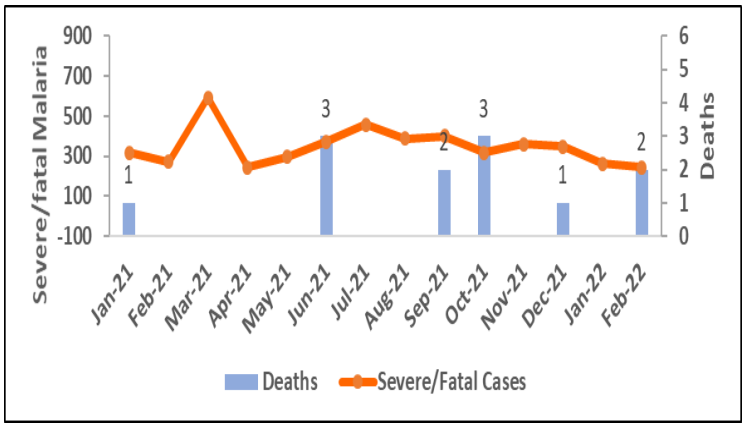


**Figure 2: Malaria deaths as per DHIS2, Namutumba District, September 2021 - February 2022**

We then hypothesized that the deaths could be happening in the community. We conducted semi-structured interviews with all Village Health Teams (VHTs) to ascertain the presence of community deaths. All VHTs from 640 villages of Namutumba District were contacted through phone call interviews to obtain the number of all deaths among children ≤12 years that occurred in the communities from September 2021 to February 2022, regardless of the cause. We calculated subcounty death rates among children ≤12 years using total population as a denominator, due to lack of age-specific population data (Figure 3).

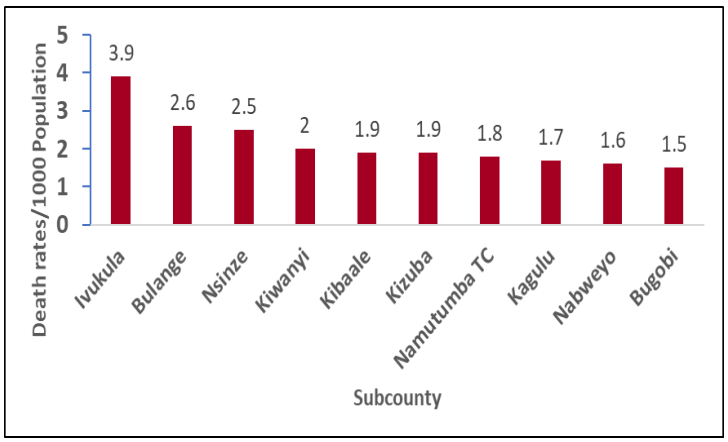


**Figure 3: Death attack rates/1,000 population for selected sub-counties, Namutumba District, September 2021 - February 2022**

We then focused our case finding based on the case definition to Ivukula Subcounty since it had the highest attack rates (Figure 3). We conducted active case search in the villages of Ivukula Subcounty and line listed the cases.

### Descriptive epidemiology

We calculated the median age, sex ratio, and made a geographical presentation of cases based on their homestead location. For the time factor, we constricted an epi curve to determine the period when the deaths increased.

### Hypothesis generation

On addition to the descriptive epidemiology from the line lists, we conducted key Informant interviews with the VHTs, health facility in charges, and health facility staff to identify factors that might be associated with malaria deaths to support hypothesis generation. Ten KII were conducted (2 health facility in charges, 4 health facility staff, and 4 VHTs. We also assessed stock details for facilities (2 H/C IIs and 1 H/C III) in Ivukula Subcounty from September 2021 to February 2022 to identify any antimalaria stock challenges if any.

### Case control study

We conducted an unmatched case-control study in Ivukula Subcounty, the most affected subcounty in the district to identify risk factors for deaths among children with severe malaria. Exposures assessed included child and caregiver demographic factors, child clinical factors, care-seeking practices, delays to care, care provided at facilities, adherence to care, and history of severe malaria. A control was non-fatal fever AND any of the following: convulsions, difficulty in breathing, yellowing of the eyes and palms, tea-colored urine, anaemia, loss of consciousness or reduced urine output in a child <12 years from September 2021 to February 2022 in Ivukula Sub-county. Controls were selected from the same parish as the cases in a ratio of 2:1. All children suffering from severe malaria at the time of the investigation were excluded since they still had the possibility of turning into cases. Furthermore, for homesteads with more than one case or control, only one case was considered to avoid collinearity. A semi-structured questionnaire was constructed in Epi-info 7 and administered using electronic forms or, when not available, paper-based forms which were entered into the database manually each evening. Data were cleaned and analyzed using Epi-info version 7.2.5.0 software. Univariant analysis and multivariant analysis using logistic regression was done to determine levels of association. First, crude odds ratios, 95% confidence interval (CI) and their respective p-values were obtained. All variables with p-values <0.05 were considered for multivariable analysis except for variables that were collinear. Multivariable logistic regression was conducted to obtain adjusted odds ratios with their respective 95% confidence interval (CI) and p-values. Variables with p-values <0.05 at multivariable analysis were considered to

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be significant and associated with the outcome.

### Ethical considerations

This investigation was in response to a public health emergency and was therefore determined to be non-research. The MoH gave the directive to investigate this outbreak. The Office of the Associate Director for Science, CDC/Uganda, also determined that this activity was not human subject research, and its primary intent was public health practice or a disease control activity (specifically, epidemic or endemic disease control activity). Written informed consent in English and the local language was sought from respondents or caretakers of diseased children. They were informed that their participation was voluntary and their refusal would not result in any negative consequences. To protect the confidentiality of the respondents, each was assigned a unique identifier which was used instead of their names.

## Results

### Descriptive epidemiology

We identified 61 deaths among children ≤12years of which 51 were due to severe malaria while 10 were from other causes (neonatal deaths (5), unknown cause (2), anaemia without fever (1), convulsions without fever (1) and severe pneumonia (1). Among the cases with severe malaria (51), 63% were below 5 years while 37% were older than 5 years. The median age was 4years, IQR (2-6) while 51% were male. Distribution of parishes with the highest number of deaths were: Nabitula (15; 29%), Kirongo (14; 27%), Kisewozi (9;18%), Budomero (7;14%), Kimenyulo (3;6%), Namukode (2; 4%) and Ivukula (1; 2%).

The highest number of child deaths in Ivukula Subcounty was recorded in September 2021 and January 2022 (Figure 4).

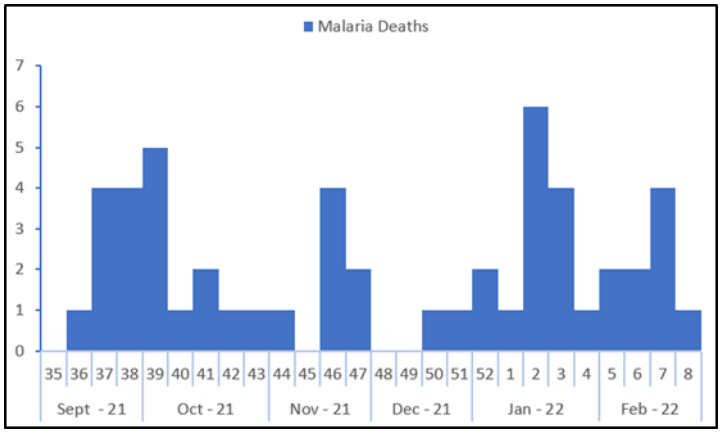


**Figure 4: Epidemiological curve for deaths among children, Ivukula Subcounty, Namutumba District, September 2021 - February 2022**

### Hypothesis generation findings

From the care giver interviews and KII from the health workers and VHTs, frequent drug stockouts were the most commonly-reported severe malaria deaths associated concern.

All health facilities assessed for stock status reported having received stock twice in the assessed 6 months (Table 1). The HCIII had received 200 doses of artesunate which was completely used up in 14 days. During periods of reduced stock of artesunate, patients are given the starter dose and advised to buy the rest. However, community members and healthcare workers noted that this often does not happen.

"During periods of reduced stock of artesunate, patients are given only the start dose and are advised to buy the rest but this does not happen to finance challenges…." A narration from one of the health workers at a HC III.

**Table 1: Antimalaria quantities delivered and their consumption period for facilities in Ivukula Subcounty, Namutumba District**

| Facility | Artemether-lumefantrine packs received per cycle (30 doses/ pack) | AL stock duration (days) | Artesunate doses received | Artesunate stock duration (days) |
|---|---|---|---|---|
| Lwatama H/C II | 34 | 21 | -- | -- |
| Namasita H/C II | 10 | 45 | -- | -- |
| Ivukula H/C III | 60 | 21 | 200 | 14 |

Other related factors included failure to receive blood products in severely anemic patients, failure to reach the high-level health facilities when referred due to economic constraints. One VHT revealed that; "caretakers often go home with very sick children and wait until transport money is acquired, hence children die from home or during transportation to the health facilities…."

Regarding blood products stock, the HC IV in-charge reported challenges in transport to pick blood products from Jinja regional referral hospital and on some occasions when transport is available, the stock at the regional referral is not available.

We hypothesized that either age and sex of the child, care giver status and education level, the duration to seek care, the health facility visited, availability of drugs and blood products and completeness of referral were contributing to the death of children below 12 years in Ivukula Subcounty, Namutumba District.

**Case control study findings**

A total of 46 cases and 77 controls were used for the case control study, 5 of the 51 cases were excluded from the case control study since they were from the same homestead as the other cases for collinearity concerns. Cases were not different from controls in age, 63% cases and 52% controls were below 5 years (p= 0.23). Similar proportions of cases (50%) and controls (53%) were females (p=0.73). Caregivers were older for cases than controls (median age 42 vs 35 years, p=0.01) and generally had lower levels of education (54% vs 35% with none or lower primary education, p=0.1) (Table 2).

Anemia was more common among cases than controls (85% vs 44%, p=0.002), as was jaundice (80% vs 58%, p=0.01), while convulsions were more common among controls than cases (53% vs 35%, p=0.06). Experiencing tea-colored urine was more common among cases than controls (61% vs 43%, p=0.05). Cases were more likely to need blood transfusion 58% compared to 32% among controls (p=<0.001) and were less likely to receive blood transfusion, cases 41% compared to 82% among controls (p=<0.001). Together, these suggest that cases might have been sicker than controls. (Table 2).

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**Table 2: Demographic characteristics for cases and controls during a study to assess for risk factors for death, Ivukula subcounty, Namutumba District, September 2021 - February 2022**

| Characteristic | Cases (N=46) n (%) | Controls (N=77) n (%) | COR (95% CI) | AOR (95% CI) |
|---|---|---|---|---|
| **Child characteristics** | | | | |
| Age in years | | | | |
| <5 | 29 (63) | 40 (52) | Ref | Ref |
| ≥5 | 17 (37) | 37 (48) | 0.6 (0.3 – 1.4) | 0.5 (0.1 -2.8) |
| Median age (years) | 3.5 | 4.5 | NA | |
| Sex | | | | |
| Female | 23 (50) | 41 (53) | Ref | Ref |
| Male | 23 (50) | 36 (47) | 1.1 (0.5-2.3) | 0.8 (0.2 – 3.9) |
| **Clinical Characteristics** | | | | |
| Anaemia (pale palms and eyes) | | | | |
| No | 7 (15) | 43 (56) | Ref | |
| Yes | 39 (85) | 34 (44) | 4.5 (1.8 – 11.3) *** | - |
| Convulsions | | | | |
| No | 30 (65) | 36 (47) | Ref | - |
| Yes | 16 (35) | 41 (53) | 0.5 (0.22 – 1.0) | |
| Difficulty in breathing | | | | |
| No | 22 (48) | 29 (38) | Ref | - |
| Yes | 24 (52) | 48 (62) | 0.6 (0.3 – 1.4) | |
| Jaundice | | | | |
| No | 9 (20) | 32 (42) | Ref | - |
| Yes | 37 (80) | 45 (58) | 2.9 (1.2 – 6.9) * | |
| Loss of consciousness | | | | |
| No | 33 (72) | 64 (83) | Ref | - |
| Yes | 13 (28) | 13 (17) | 1.9 (0.8 – 4.6) | |
| Tea colored Urine | | | | |
| No | 18 (39) | 44 (57) | Ref | |
| Yes | 28 (61) | 33 (43) | 2.1 (0.99 – 4.4) | |
| Needed blood transfusion | | | | |
| No | 16 (42) | 47 (68) | Ref | - |
| Yes | 22 (58) | 22 (32) | 2.9 (1.3 – 6.7) *** | |
| Received blood transfusion | | | | |
| Yes | 9 (41) | 18 (82) | Ref | Ref |
| No | 13 (59) | 4 (18) | 6.5 (1.6 – 25.8) ** | 7.1 (1.4 – 36.2) ** |

Note: COR= Crude Odds Ratio, AOR= Adjusted Odds Ratio, * p<0.05, ** p<0.01, *** p<0.001

**Factors associated with deaths among children with severe malaria, Ivukula Subcounty, Namutumba District, September 2021 - February 2022**

Community VHT consultations in Ivukula Subcounty were infrequent; neither cases (6%) nor controls (13%) had sought care from a VHT. We also noted that more cases (52%) than controls (35%) sought care in the first 24 hours.

The highest proportion of cases and controls attended a HCIII first, cases 43% and controls 49% (Table 2). While severe malaria is considered an emergency condition requiring urgent attention in clinical settings of level III and above, in Ivukula Subcounty 39% of the cases and 24% of the controls accessed their first level of care from small private clinics. Notably, completion of treatment given at the first facility was much lower among cases than controls (22% vs 61%, p=<0.001) (Table 3). The main reasons noted were death, drug and blood stockouts, referrals, inability to feed and lack of funds to purchase drugs.

Among those who went to a second facility following referral, the most common facility visited was a HCII (38% of cases and 43% of controls). This is in contrast to 11% of cases and 18% of controls who visited a HCII as their first facility an indication that clients did not go to the health facilities referred to since H/C II is not mandated to manage severe malaria cases. Among those given treatment, completion was again more frequent among controls than cases (89% vs 11%, p=<0.001) (Table 3).

Among the 123 cases and controls, 117 said they visited a second health facility without being referred. The most common reasons for visiting additional facilities without referral included: need for higher level of care (75% of cases and 84% of controls), need for blood products (16% cases and 3% controls), and drug stock outs at the first facility (9% cases and 13% controls). Important to note, still the most commonly visited facility was HC II which is not equipped to manage severe malaria cases (78% cases and 74% controls) (Table 3).

There was no difference among cases and controls regarding receipt of indoor residual spraying (IRS) during the last round of IRS in the district, 98% of cases and 96% of controls said their household had been sprayed.

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**Table 3: Factors associated with death among cases and controls with severe malaria in Ivukula subcounty, Namutumba District, September 2021 - February 2022**

| Characteristic | Cases (N=46) n (%) | Controls (N=77) n (%) | COR (95% CI) | AOR (95% CI) |
|---|---|---|---|---|
| **Caregiver characteristics** | | | | |
| Age in years | | | | |
| 18-24 | 4 (9) | 7 (9) | Ref | - |
| 25-44 | 20 (43) | 52 (68) | 0.67 (0.17 – 2.6) | |
| ≥45 | 22 (48) | 18 (23) | 2.14 (0.54 – 8.5) | |
| Median age | 42 | 35 | NA | |
| Type of caregiver | | | | |
| Father | 12 (26) | 17 (22) | Ref | - |
| Mother | 21 (46) | 52 (68) | 0.57 (1.23 – 1.4) | |
| Grandparent | 13 (28) | 8 (10) | 2.3 (0.73 – 2.3) | |
| Level of education | | | | |
| Secondary | 8 (17) | 17 (22) | Ref | - |
| Upper Primary | 13 (28) | 33 (43) | 0.8 (0.3 – 2.4) | |
| None-Lower Primary | 25 (54) | 27 (35) | 1.9 (0.7 – 5.4) | |
| **Health facility attended first for patients with severe malaria** | | | | |
| Health facility type | | | | |
| Health center II | 5 (11) | 13 (18) | | |
| Health center III | 20(43) | 35 (49) | | |
| Health center IV | 1 (2) | 3 (4) | | |
| Hospital | 2 (4) | 0 (0) | | |
| Private clinic | 18 (39) | 17(24) | | |
| Drug shop | 0 (0) | 3 (4) | | |
| Given antimalarial drugs at first facility | | | | - |
| Yes | 32 (69) | 50(70) | Ref | |
| No | 14 (31) | 21 (30) | 0.95 (0.4 – 2.2) | |
| Completed treatment given at first facility | | | | |
| Yes | 10 (22) | 47(61) | Ref | Ref |
| No | 36 (78) | 30 (39) | 5.6 (2.4 – 13.0) *** | 9.7 (1.8 – 52.9) ** |
| Reasons for not completing treatment (among those that could not) | | | - | - |
| Death | | | | |
| Failure to feed | 10 (28) | 0 (0) | | |
| Drug stock outs | 1 (3) | 0 (0) | | |
| Blood products stock out | 17 (47) | 22 (76) | | |
| Referred | 6 (17) | 2(7) | | |
| Failure to pay | 0 (0) | 1 (3) | | |
| | 2 (6) | 4 (14) | | |
| Time between illness onset to visiting first facility | | | | |
| ≤1 day | 24 (52) | 25(35) | Ref | Ref |
| >1 day | 22 (48) | 46 (65) | 0.5 (0.2 – 1.0) | 0.8 (0.2 –3.7) |
| **Facilities visited after first HF (only for referred patients)** | | | | |
| Health facility type | | | | |
| Health center II | 11 (38) | 16 (43) | | |
| Health center III | 3 (10) | 4 (11) | | |
| Health center IV | 9 (31) | 11 (30) | | |
| Hospital | 5 (17) | 4 (11) | | |
| Private clinic | 1 (3) | 2(5) | | |
| Given treatment at second facility | | | | |
| Yes | 9 (31) | 18 (48) | Ref | - |
| No | 20 (69) | 19 (51) | 0.5 (0.2 – 1.3) | |
| Completed treatment given at second facility | | | | - |
| Yes | 1 (11) | 16 (89) | Ref | |
| No | 8 (89) | 2 (11) | 42.5 (4.1 – 434.9) *** | |

In the bivariate analysis, five variables were found to be significantly associated with death among children with severe malaria (Table 2 & 3), only 2 were considered for multivariate analysis, need for blood transfusion, jaundice and having anaemia were excluded from the final model for collinearity with receiving blood transfusion.

From the multivariate analysis, following adjustment for child age, child sex and duration to seek care, two variables were found to be significantly associated with death among children with severe malaria. The odds of death among the children that did not completed their first treatment were 9.7 times higher than the odds among those who completed treatment (aOR=9.7, 95%CI:1.8 – 52.9), Additionally, the odds of deaths among anemic children who did not receive blood transfusion were 7.1 times higher than those who received blood transfusion (aOR=7.1, 95%CI:1.4 – 36.2) (Table 3).

**Discussion**

We assessed factors associated with death due to severe malaria among children ≤12 years following an alert of multiple deaths in the community. The analytic findings revealed that failing to complete antimalaria treatment and failure to receive blood transfusion among anemic patients requiring blood all increased risk of death. We also identified stockouts as a major challenge for health facilities and persons seeking care; care-seeking appeared to be less common during stockouts and low stock levels of antimalarials led to failure to disburse full courses of treatment. Inability to pay for the remaining course of treatment led to incomplete treatments, which were associated with death.

We found a strong association between failing to complete antimalarial treatment and deaths among children. According to WHO, poorly treated severe malaria can lead to high death rates, while effective treatment and supportive care reduces mortality to 10-20%. It is essential that full doses of parenteral antimalarial medication be given promptly in the initial treatment of severe malaria with a complete dose of intravenous or intramuscular artesunate for at least 24 hours and a continuation of artemisinin-based combination therapy (ACT) for 3 days[7]. However, in Ivukula Subcounty, parents reported that treatment completion was frequently challenged by drug stockouts or low stocks. We confirmed this finding by visiting facilities, where we found reports of antimalarials stockouts as a challenge.

Antimalarial drugs intended for 2 months were lasting a month or less, and artesunate, the required drug for treating severe malaria, lasted only two weeks at the facilities we visited. Additional reports from healthcare workers at facilities that they often gave only one dose to make the drugs last longer, forcing parents to purchase medication for their children sheds some light onto the reasons for non-completion. When parents are unable to purchase such medications, the child cannot complete treatment. Reassessment of the appropriate quantities of drugs to provide to health centers in the district, especially during upsurges, and emphasizing the importance of treatment completion is needed to ensure that this problem is addressed.

Beyond this, we found that referrals to higher-level facilities that could manage severe malaria were frequently not completed. Caretakers could only manage accessing lower-level facilities near them, yet these facilities are not equipped to manage severe malaria cases. This likely accounts for the high proportion of patients who accessed H/C IIs as their second level of health-seeking. Addressing this issue requires provision of transport support to enable all referred patients reach the intended referral hospitals, alternatively, upgrading some of the H/C II facilities to levels that can manage severe malaria could improve service access.

The need for blood transfusion and failure to receive it was a risk factor for deaths among children with severe malaria in our study. This is not surprising and likely reflects more severe illness among cases, which was also suggested in our comparison of cases and controls. Anaemia is one of the major complications of malaria infection, contributing directly or indirectly to hospitalization and deaths in young children. While malaria is responsible for anaemia due to hemolysis, anaemia in turn lowers the body's immunity leading to increased exposure to malaria infections and hence the repeated cycle[8]. Blood transfusions can be life-saving interventions for children with severe anaemia[9]. However, we found that blood transfusions were more often needed by cases, and less often received, compared to controls. Unfortunately, Ivukula Subcounty has no health facility equipped to provide blood transfusion services. Addressing this issue requires improving blood transfusion services closer to the communities by equipping HC IIIs with blood storage equipment and availing sufficient quantities of blood products.

In contrast to prior studies of severe malaria conducted elsewhere in sub-Saharan Africa[10-12],

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we did not find an association between age and mortality, perhaps explained by the overall low median age of our study population (< 5 years) relative to previously studied populations. Similar findings are seen in a study conducted in Zambia where age was not significant due to low median age of both cases and controls (<2yrs)[13].

### Study limitations

A limitation to this study was the absence of medical records for review. Because of this, we chose to use clinical definitions and relied on the caretakers' memory to remember the child's presentation. For case-patients, majority of the caregivers had discarded the records immediately after the loss of their child or were not provided with the records at facilities.

### Conclusion

The major contributors to malaria mortality among children ≤12 years in Ivukula Subcounty, Namutumba District were: not completing treatment for malaria, failure to receive blood transfusion among anemic patients that needed blood, stockouts of malaria drugs and blood products and failure to reach referral sites. These issues indicate both health system and individual challenges that need to be addressed. We therefore recommend, increasing access to blood products, accurate quantification of antimalarials for health facilities in upsurge districts, offering transport support to patients referred to higher-level facilities and activation of iCCM in the communities of Namutumba. Upgrade of the H/C IV to hospital status to enable proper management of cases in this area highly prevalent with malaria. Furthermore, an upgrade of health facilities for the district to have a general hospital and more H/C IIIs per subcounty to improved management of severe malaria with limited referrals. All this is hoped to avert numerous deaths among children in this area.

### Conflict of interest

The authors declare that they had no conflict of interest.

### Acknowledgments

We appreciate Namutumba District Local Government and the Village Health Teams for the guidance in the community during data collection.



### References

1. Organisation, W.H. *World Malaria Report*. 2021.
2. WHO, *World Malaria Report*2021.
3. Malaria, T. *Uganda Malaria Facts, Target Malaria. Severe Malaria Observatory*. 2022.
4. Uganda, M.o.H., *District health Information system. Division of Health Information*. 2022.
5. National Malaria Control Program, M.o.H.U., *Uganda National Malaria Control Policy.* . 2011. p. Pg 8.
6. District, N. *Namutumba District Local Government*. 2022; Available from: https://namutumba.go.ug/lg/district-location-and-its-neighbors.
7. WHO, *WHO Guidelines for malaria*. 2022, Global Malaria Programme: Geneva.
8. Health, C.G. *Division of Parasitic Diseases and Malaria* 2022.
9. Mutombo, A.M., et al., *Severe malaria and death risk factors among children under 5 years at Jason Sendwe Hospital in Democratic Republic of Congo.* Pan African Medical Journal, 2018. **29**(1): p. 1-8.
10. Carneiro, I., et al., *Age-patterns of malaria vary with severity, transmission intensity and seasonality in sub-Saharan Africa: a systematic review and pooled analysis.* PloS one, 2010. **5**(2): p. e8988.
11. Kamau, A., et al., *Malaria infection, disease and mortality among children and adults on the coast of Kenya.* Malaria journal, 2020. **19** (1): p. 1-12.
12. Kapesa, A., et al., *The current malaria morbidity and mortality in different transmission settings in Western Kenya.* PloS one, 2018. **13** (8): p. e0202031.
13. Ippolito, M.M., et al., *Risk factors for mortality in children hospitalized with severe malaria in northern Zambia: a retrospective case-control study.* The American Journal of Tropical Medicine and Hygiene, 2018. **98**(6): p. 1699.

## Sexual Gender-Based Violence among Adolescent Girls and Young Women 10-24 Years during COVID-19 Pandemic, Bukedi Region, Eastern Uganda

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### Summary

**Background**: Police reports of Sexual Gender-Based Violence (SGBV) in Uganda increased during the COVID-19 pandemic, primarily affecting adolescent girls and young women (AGYW) aged 10-24 years. In April 2022, we investigated factors associated with SGBV among AGYW during the COVID-19 pandemic in Bukedi Region, which reports the highest rates of SGBV among women (40% in 2016) in Uganda.

**Methods:** We use a mixed methods approach to examine data for SGBV cases among adolescent girls and young women (AGYW) aged 10-24 years at ten high-volume health facilities in Bukedi Region. The data were collected retrospectively for the period of March 2020 to December 2021, covering the highest-burden phases of the COVID-19 pandemic in Uganda. We conducted a neighbourhood-matched case-control study. A case was ≥1 SGBV episode (coerced sex) self-reported by an AGYW aged 10-24 years residing in Tororo and Busia Districts. Cases were identified from facility registers. For every case, we identified two neighbourhood-matched AGYW controls who reported no SGBV. We interviewed 108 randomly-selected cases from the health facility line list and 216 controls and asked about socio-demographics, economic changes they or their families experienced during COVID-19, and experiences with SGBV during COVID-19. We conducted key informant interviews with six health facility SGBV focal persons about possible factors associated with SGBV during the COVID-19 period. We used conditional logistic regression to obtain adjusted odds ratios and confidence intervals for the factors associated with SGBV. We analysed qualitative data using content analysis.
**Results:** Among 389 SGBV cases recorded in the facility registers, the mean age was 16.4 (SD±1.61: range 10-24) years, and 350 (90%) were 15-19 years of age. Two-thirds (214; 67%) were pregnant at the time their SGBV experience was recorded. Only eight (2%) received Post-Exposure Prophylaxis (PEP) for HIV. Among the 108 cases interviewed, 79 (73%) reported being physically forced into sex while 29 (27%) were pressured into sex through harassment and threats. Among those who mentioned the perpetrator (73; 68%), many reported it were a friend (29; 40%) or neighbour (17; 23%). In multivariate analysis, self-reports of sexual violence before the COVID-19 period [aOR=5.8, 95%CI: 2.8-12] and having older siblings [aOR=1.9, 95%:CI 1.1-3.4] were associated with SGBV during the COVID-19 period. Living with a family that provided all the basic needs was protective [aOR=0.42, 95%: CI 0.23-0.78]. The qualitative data reveal that poverty and being out of school for an extended period appeared to be associated with increased SGBV cases in the region during the COVID-19 period.
**Conclusion**: Previous SGBV and having families without the means to provide basic needs was associated with increased odds of SGBV during the COVID-19 pandemic in Uganda. Finding, supporting, and enacting protective interventions for potential and existing SGBV survivors and socioeconomically vulnerable AGYW could prevent SGBV during similar events in the future.

### Introduction

Sexual gender-based violence (SGBV) is defined as "any sexual act, attempt to obtain a sexual act, or other act directed against a person's sexuality using coercion, by any person regardless of their relationship to the survivor, in any setting" (1). Sexual gender-based violence predisposes survivors to HIV, unwanted teenage pregnancies, and mental illnesses like depression. Among adolescent girls and young women (AGYW), it may result in school dropouts, in-

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creased risk of mother-to-child HIV transmission, and socio-economic difficulties (2).

Uganda has a high prevalence of SGBV (22%) among women 15-49 years, according to the Uganda Population-based HIV Impact Assessment (UPHIA) 2016. Bukedi Region had the highest prevalence of SGBV among women at 40% and a teenage pregnancy rate of 22%, according to UPHIA 2016 (3). In Uganda, from March 2020 to January 2022, schools were closed as part of the COVID-19 pandemic response. Anecdotal reports from Uganda Police and an analysis of national SGBV program data suggested that SGBV cases had increased during the COVID-19 pandemic, especially during the two lockdown periods in 2020 and 2021 (4). Probable causes included prolonged out of school period and the implementation of multiple lockdowns, leading to girls exposure to perpetrators within homes and neighbourhoods during times they would otherwise have been elsewhere (5). While SGBV among AGYW does not necessarily lead to pregnancy, an analysis of District Health Information System (DHIS2) data showed a 33% increase in teenage pregnancies (among girls age 10-19 years) between 2020 and 2021 compared to 2019 in the Bukedi Region; which was believed to be linked to the increases in SGBV during this the COVID-19 pandemic period.
SGBV survivors receive Post Exposure Prophylaxis (PEP), emergency contraception, testing and treatment for STIs, and treatment of injuries or wounds (6). However, it was unclear how the health facilities addressed SGBV cases during the COVID-19 pandemic. In addition, there was limited information on factors associated with SGBV among adolescent girls and young women during the COVID-19 pandemic. We evaluated SGBV services and determined the factors associated with SGBV among AGYW during the COVID-19 pandemic in the Bukedi Region to inform areas of improvement and prevention measures for SGBV.

## Methods

### Study design and setting

We employed a mixed-methods approach, including a descriptive, qualitative, and case-control study among AGYW aged 10-24 years in Tororo and Busia districts, Bukedi Region. These two districts are in Eastern Uganda, bordering Kenya. Both have active trading activities and border points with many transit truck drivers. These districts reported the highest number of teenage pregnancies during COVID-19 period in Bukedi region (7).

### Case definition and finding

We defined a SGBV case as an AGYW aged 10-24 years who was recorded in the GBV register during March 2020 to December 2020. To find cases recorded during the pandemic period, we purposively selected ten high-volume health facilities providing SGBV care, including one District Hospital, one Health Center IV, and three high-volume Health Center IIIs from each of the two districts. In each facility, we created a line list of records of SGBV cases among AGYW aged 10-24 from the GBV HMIS 105 registers for the period of March 2020 to December 2021. Health care workers record information for GBV survivors who are identified through self-reporting or from routine screening for GBV, including in HIV care and treatment clinics and antenatal care clinics. Using a predesigned data abstraction form, we obtained patient information on the visit date, social demographic characteristics, management of SGBV cases, including HIV post-exposure prevention (PEP), family planning, outcome, and follow-up. Additional information on PEP provision was obtained from the PEP registers.

### Descriptive epidemiology

We analysed the line listed SGBV cases' data Using Epi-Info version 7.2.4.0. We described the SGBV cases by place and person and the quality of SGBV services received by the survivors. We used some of these analyses to identify the study site for the case control study.

## Case-control study to identify factors associated with sexual gender-based violence during the COVID pandemic period, Tororo and Busia District, Uganda

The SGBV incidence rates (IR) among subcounties ranged from 0.1% to 6%. Among the 11 subcounties with IR ≥3%, we randomly selected six (three from each district). These included Mukuju, Western division, and Usukuru subcounties from Tororo district and Masafu, Lumino, and Buyanga subcounties from Busia District (Figure 1). These six subcounties served as the sites for the case-control study.

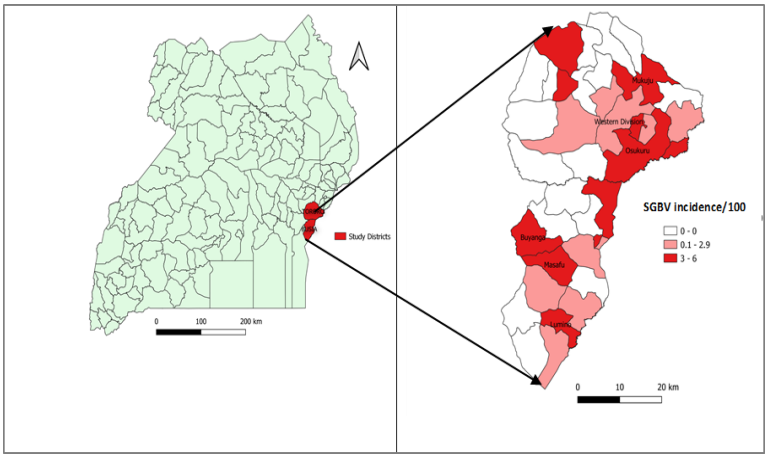


**Figure 1. Sexual gender-based violence incidence rate among adolescent girls and young women in Busia and Tororo Districts, March 2020 -December 2021**

We conducted a neighbourhood-matched case-control study to determine factors associated with SGBV among AGYW during COVID-19 (March 2020 to December 2021), covering the highest-burden phases of the COVID-19 pandemic in Uganda. We defined a case as an AGYW aged 10-24 years who reported at least one episode of SGBV to any of 10 high-volume health facilities in Tororo and Busia Districts during this time. For every case, we identified two neighbourhood-matched AGYW controls who reported no SGBV. A control was an AGYW aged 10 -24 years who did not experience an episode of SGBV during COVID-19 period.

We assumed a reduction in family income during the pandemic was a significant risk factor for SGBV with an odds ratio of 2 and 40% of the controls exposed. At a ratio of 1:2 cases to controls and 80% power, we obtained a sample size of 324 (108 cases and 216 controls). Using a line list of SGBV cases from the ten health facilities, we randomly selected SGBV cases for interviews. We traced the cases for interviews in the community with the help of the social workers and village health teams and consecutively interviewed them until we reached 108 cases. We identified two neighbourhood-matched control AGYW who reported no SGBV during the COVID-19 period for every case; controls were asked to confirm that they never experienced SGBV during COVID-19 (March 2020 to December 2021). The controls were identified from a randomly selected neighbour households of cases that had an AGYW living with them. For each household, we interviewed one control. If controls were >1 in a house hold, we used a random number to select a participant for interviews.

Using a predesigned questionnaire, we interviewed cases and controls to obtain information on socio-demographics, risk factors for SGBV, care and services received, economic activities undertaken during COVID-19 by the participant and their immediate family place of residence before and during COVID-19, school attendance before and during COVID-19, household size, household members living in the house, household members' occupation, day and night-time activities of the case, parental supervision, and others. We adopted the recent Uganda's Violence Against Children (VAC) Survey (2018) questionnaire, (8) and tailored it to our study. To determine the factors associated with SGBV, we conducted conditional logistic regression analysis.

## Key informant interviews to identify factors associated with SGBV during the pandemic

We attempted to interview all GBV focal persons who manage SGBV cases as key informants at the ten facilities; however, only six facilities had the GBV focal person present during data collection. Using a predesigned key informant guide that had open ended questions. We asked about possible root causes of increased SGBV cases in the region and explored challenges related to high rates of teenage pregnancies, management of SGBV during the pandemic, and availability of drugs such as emergency contraceptives and PEP. The interviews were recorded and transcribed into word document. We proof read the transcripts, identified the common codes. These were then developed into broader themes. Results were summarised into short texts and quoted verbatim and were used to support the quantitative findings.

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### Ethical considerations

This was the Ministry of Health (MoH) directive to evaluate the factors associated with the increased numbers of Sexual Gender-based Violence during COVID-29. However, we also sought permission from the district health officials and heads of the health facilities before conducting the study. A non-research determination form was submitted to US CDC for clearance before the commencement of the assessment as a requirement. The Office of the Associate Director for Science, U.S. Centers for Disease Control and Prevention, determined that this activity was in response to a public health issue with the primary intent of public health practice (epidemic disease control activity). It was determined, therefore, to not be human subjects research. All protocols were approved by the Ministry of Health and US CDC and performed in accordance with the declaration of Helsinki.
We obtained verbal consent from respondents before the interviews. During data collection, we assigned respondents unique identifiers instead of names to protect their confidentiality; no unique identifier information was recorded.

### Results

### Description of sexual Gender-based Violence cases

We found 389 SGBV cases of AGYW recorded at the ten selected health facilities in Tororo and Busia Districts from March 2020 to December 2021. Their mean age was 16.4 years (SD± 1.61: range, 10-24 years) and most (350; 90%) were 15-19 years of age. The majority (214; 67%) were pregnant at the time their SGBV event was recorded in the facility register. Many (180; 46%) presented to the facility at time points beyond 72 hours. Among the 209 who presented within 72 hours, only 8 received PEP (Table 1).

**Table 1: Characteristics of sexual gender-based violence cases managed at health facilities during the COVID-19 period in Bukedi sub-region, 2020-2021**

| Variable | Frequency n=389 | (%) |
|---|---|---|
| **Age** | | |
| 10-14 | 25 | (6.4) |
| 15-19 | 350 | (90) |
| 20-24 | 14 | (3.6) |
| **Marital status** | | |
| Married | 198 | (51) |
| Not married | 191 | (49) |
| **HIV test done** | | |
| Yes | 321 | (83) |
| No | 65 | (17) |
| **Followed up by HCW after initial visit at least once** | | |
| Yes | 16 | (4.1) |
| No | 373 | (96) |
| **Followed up by HCW after initial visit at least 4 times (as recommended)** | | |
| Yes | 0 | (0) |
| No | 389 | (100) |
| **Pregnant** | | |
| Yes | 214 | (67) |
| No | 107 | (33) |
| **Time between event and presentation for care** | | |
| <24 hours | 97 | (25) |
| 24-72 hours | 112 | (29) |
| >72 hours | 180 | (46) |
| **PEP among person who presented <72 hrs (n=209)** | | |
| Yes | 8 | (3.8) |
| No | 209 | (96) |

HCW- Health care worker

Findings from analysis of the health facility data were confirmed by responses from the key informant interviews. Most GBV focal persons reported that AGYW experiencing SGBV reported too late to the health facility to be eligible for post-exposure prophylaxis. Many of these cases were only identified as SGBV survivors during their antenatal care visits, often for pregnancies that resulted from the SGBV event or events. As a result, they were not eligible for emergency oral contraceptives despite the fact that medicines were available.

*"The management of the SGBV cases was a big challenge during the COVID-19 period. Most girls presented here very late, some already pregnant and whenever you asked them why they never came early, they reported they feared the perpetrators. You had nothing to do for them apart from counselling" Key informant II*

### Description of sexual gender-based violence cases considered for the case-control study

Of the 108 cases interviewed, 79 (73%) reported being physically forced into sex while 29 (27%) reported that they were pressured into sex through harassment and threats. Most (88; 82%) reported that the episode was their first SGBV experience during COVID-19 period. Among 73 (68%) who agreed to share information about the perpetrator, 29 (40%) reported it was a friend and 17 (23%) said it was the neighbour. The majority (71; 67%) reported to the health facility after 72 hours or more; of these, 42 (58%) said that they delayed reporting due to feelings of social stigma about their SGBV experience. The most reported adverse outcome from the episode was unwanted pregnancy (38; 35%) (Table 2).

**Table 2: Characteristics of sexual gender-based violence cases considered for the case control study during the COVID-19 period in Bukedi sub-region, 2020-2021**

| | N=108 | (%) |
|---|---|---|
| **Type of SGBV** | | |
| Physically forced sex | 79 | (73) |
| Pressured into sex through harassment | 29 | (27) |
| **First time experience of SGBV during COVID-19** | 88 | (82) |
| **Time of Sexual event** | | |
| Day | 23 | (21) |
| Evening | 21 | (19) |
| Night | 44 | (40) |
| Declined to answer | 20 | (19) |
| **Type of perpetrator (among 73 providing information)** | | |
| Friend | 29 | (40) |
| Neighbour | 17 | (23) |
| Relative | 9 | (12) |
| Others | 18 | (25) |
| **Where the incident occurred** | | |
| On the way somewhere | 25 | (21) |
| Friends place | 25 | (23) |
| Home | 26 | (24) |
| Relative home | 11 | (10) |
| Workplace | 2 | (1.9) |
| Not comfortable to mention the place | 20 | (19) |
| **Adverse outcomes** | | |
| Unwanted pregnancy | 38 | (35) |
| Depression | 20 | (19) |
| Anxiety | 12 | (11) |
| STI | 7 | (6.5) |
| Others | 14 | (13) |
| **Reported they received emergency contraception** | 35 | (32) |
| **Time from SGBV event to presentation to health facility** | | |
| Immediately | 18 | (27) |
| 1-3 days | 18 | (27) |
| >3 days | 72 | (67) |
| **Self-reported they received PEP from health facility or other site (among 102 who provided a response)** | 35 | (34) |
| **Self-reported they received PEP from health facility or other site (among 36 who presented <3 days after event)** | 20 | (56) |
| **Reasons for reporting to the health facilityy > 3 days (n=72)** | | |
| Social stigma | 42 | (58) |
| Fear of retaliation | 13 | (18) |
| ack of awareness | 13 | (18) |
| Others | 4 | (5.6) |

*PEP; Post Exposure Prophylaxis, STI: Sexually Transmitted Infection

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**Factors associated with sexual gender-based violence among adolescent girls and young women during COVID-19, Tororo and Busia districts, Uganda**

In bivariate analysis, having older siblings [cOR=1.7, 95% CI: 1.04-2.8], ever being pregnant before the COVID-19 period [cOR=2.5, 95%CI: 1.6-4.0], ever being sexually violated before the COVID-19 period [cOR=8.1, 95% CI: 4.1-16], ever being involved in sex work [cOR=3.4,95% CI: 2.1-5.6] were associated with SGBV during COVID-19. In contrast, having a family being able to provide all basic needs was protective [cOR=0.33, 95% CI: 0.20-0.56] (Table 3). Age, being in school before COVID-19 period, level of education, ever having had children, knowledge and use of family planning, and family change in economic status during the COVID-19 period were not significantly associated with SGBV. In multivariable analysis, experiencing sexual violence before COVID-19 [aOR=5.8, 95% CI: 2.8-12] and having older siblings [aOR=1.9, 95%CI: 1.1-3.4] remained significantly associated with SGBV during COVID-19 period. The family's ability to provide all basic needs [aOR=0.42, 95%:CI 0.23-0.78] was protective. While the odds of SGBV decreased with increasing age, the association was not significant (Table 3).

**Table 3: Characteristics of cases and controls and their association with Sexual Gender Based Violence during the COVID-19 period in Bukedi sub-region, 2020-2021**

| Characteristic | Cases (n=108) | | Controls (n=216) | | Bivariate Analysis | | Multivariate Analysis | |
|---|---|---|---|---|---|---|---|---|
| | n | (%) | n | (%) | cOR | 95% CI | aOR | 95% CI |
| **Age in years** | | | | | | | | |
| 10–14 | 16 | (15) | 47 | (22) | Ref | | | |
| 15-19 | 67 | (62) | 107 | (50) | 1.8 | (0.97-3.5) | 0.94 | (0.44-2.03) |
| 20-24 | 26 | (24) | 61 | (28) | 1.3 | (0.60-2.6) | 0.52 | (0.20-1.3) |
| **Has older sibling(s)** | 77 | (71) | 126 | (58) | 1.7 | (1.04-2.8) | 1.9 | (1.1-3.4) |
| **Ever pregnant before COVID-19 period** | 63 | (58) | 76 | (35) | 2.5 | (1.6-4.0) | 1.7 | (0.86-3.2) |
| **Sexually violated before COVID-19 period** | 40 | (37) | 8 | (3.7) | 8.1 | (4.1-16) | 5.8 | (2.8-12) |
| **Ever involved in sex work** | 54 | (50) | 47 | (22) | 3.4 | (2.1-5.6) | 1.7 | (0.9-3.2) |
| **Family provides all basic needs** | 63 | (58) | 172 | (80) | 0.33 | (0.20-0.56) | 0.42 | (0.23-0.78) |
| **Knows about family planning** | 58 | (54) | 110 | (51) | 1.06 | (0.67-1.7) | - | - |
| **Ever used family planning** | 29 | (27) | 51 | (24) | 1.1 | (0.66-1.9) | - | - |
| **Ever had children** | 44 | (41) | 56 | (26) | 0.83 | (0.39-1.7) | - | - |
| **Stayed with during COVID-19** | | | | | | | | |
| Parent | 69 | (64) | 151 | (70) | Ref | - | - | - |
| Friends/relatives | 40 | (37) | 64 | (30) | 1.3 | (1.04-1.6) | - | - |
| **Highest education level** | | | | | | | | |
| None | 3 | (2.8) | 2 | (0.9) | Ref | - | - | - |
| Primary | 73 | (68) | 130 | (60) | 0.37 | (0.06-2.2) | - | - |
| Secondary | 32 | (30) | 69 | (32) | 0.31 | (0.05-1.9) | - | - |
| Tertiary | 0 | (0.0) | 6 | (2.8) | 1 | - | - | - |
| **In school before COVID-19** | 86 | (80) | 182 | (84) | 0.64 | (0.35-1.2) | - | - |
| **Family economic status changed during COVID-19** | 87 | (80) | 154 | (77) | 1.2 | (0.68-2.1) | - | - |

Results from the informant interviews supported these findings. Five out of six GBV focal persons pointed out that families of their clients were unable to provide basic needs to their families, including the girls exposed to SGBV.

"*During COVID 19, there was a lot of poverty as a result of disrupted businesses and closure of schools. As a result, most parents were unable to support their children. Girls were idle, and such could have forced them to look for necessities from elsewhere*" Key informant IV

**Discussion**

Adolescent girls and young women in the Bukedi region experienced high rates of sexual gender-based violence during the COVID-19 period. Many reported cases were pregnant at the time their SGBV experience was recognized and recorded. Close to half delayed at least three days to report their experience, making them ineligible for PEP; however, even among those that reported earlier, few received PEP. Previous experiences of sexual violence and having older siblings increased the odds of SGBV, while having sufficient resources within the family to cater to the needs of the AGYW was protective.

Sexual violence exposes AGYW to HIV acquisition; Uganda reports a national HIV prevalence of 4.3% among adult men ≥15 years, a concern for public health (9). This poses a high risk of HIV transmission to survivors of SGBV. PEP is an important intervention to reduce the risk of contracting HIV after an unprotected sexual encounter, and in Uganda, it is available in public and private health facilities (10). Care provided after SGBV includes psychosocial support, PEP to prevent HIV, and emergency contraception to prevent pregnancy. However, both emergency contraceptives and PEP must be given within 72 hours of the event to be effective (11). We identified many missed opportunities for preventing HIV infection and pregnancy among AGYW who experienced SGBV in Bukedi Region. Interviews with the GBV focal persons, as well as the high rate of pregnancy among AGYW identified as SGBV survivors from the clinic registers, suggested that many AGYW presented because of their pregnancy rather than the SGBV event itself. AGYW cited fears of the perpetrator and stigma as reasons they did not present immediately. Given that many SGBV events will not result in pregnancy, the high frequency of pregnancy among SGBV survivors who report suggests that the reports described in this paper are the tip of the iceberg. Many women who do not become pregnant because of the SGBV likely simply do not report. Fear of public stigma is a well-documented factor that hinders patients from accessing health care services (9,10). Unfortunately, social stigma related to SGBV is known to worsen physical and psychological health impacts (13) and may increase the risk of additional violence (14). Efforts are needed to support AGYW to report SGBV and enable adequate and timely care to prevent HIV and unwanted pregnancies. The Uganda Child Help Line (UCHL) 116 was found to be more acceptable channel to report sexual violence compared to others such as health facilities (15). UCHL was implemented by Ministry of Gender Labour and Social Development (MGLSD) to improve reporting of child abuse and sexual violence but there is still low awareness and a need for more advocacy. In addition, active case finding for SGBV survivors may be necessary to ensure appropriate care and support to the affected persons.

Even among the AGYW who presented early, few received PEP. However, even among those who received PEP, it appears it was often inappropriately given, highlighting a knowledge gap on PEP use among the health care workers and the users. Due to data gaps in the SGBV healthy facility registers, we could not verify the appropriateness of PEP use for all reported incidents. Similar findings were noted in a study done in Uganda to compare post-rape care before and during COVID-19 using national Health Management Information System (HMIS) and UCHL data. In this study, 50% of the cases received PEP beyond the recommended 72 hours during the first six month of COVID-19 (16). This highlights the need for flexible methods of service delivery to increase timely access and utilisation of PEP among SGBV survivors. These might include community based approaches such as “off-facility PEP medication delivery” and “PEP hotlines” (16). These community-based approaches

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were piloted in rural populations in Kenya and Uganda; results showed increased uptake and completion of PEP in the population. In addition, there is need to train health care workers on PEP eligibility so that it is only given when it will be effective, and not when it is not appropriate.

Having experienced SGBV before the COVID-19 period and having older siblings were both associated with SGBV during COVID-19. Repeated sexual violence during COVID-19 suggests that affected girls may be continually exposed to the same perpetrator(s). Other studies have also found that individuals who are sexually victimised were likely to be re-victimised (15, 16,17). Therefore, psychosocial support and ways to protect the once identified survivors are necessary to prevent repeated SGBV experiences. In addition, there is need to strengthen the 'parents/guardians' daughter relationship to enable the girl's open up to parents in case of SGBV through evidence based interventions such as community parenting programs (19). It is not clear why having older siblings was associated with increased risk of SGBV. However, it may simply reflect a younger age of the SGBV victim compared to non-SGBV survivors; age was found to be negatively associated with SGBV in our study.

We found that having a family providing all the basic needs to AGYW was protective against SGBV during COVID-19. Unfortunately, as a result of COVID-19 measures like the closure of bars, shops, saloons, and markets and movement restrictions (20) many families were unable to provide basic needs for their children (21, 22). Efforts to support vulnerable AGYW with basic needs like food, clothing, and shelter among others may be necessary during future pandemics or similar situations to prevent SGBV.

## Study limitations

Our study was subject to several limitations. Firstly, health facility data were incomplete, and this could have resulted in inconclusive information on the health care services. We found irregularities with documentation of health facility registers, especially information on dates of incidence and follow-up services, and data on repeated episodes of SGBV. We could not tell from the data if the persons who were offered PEP accepted or completed the dosage. In addition, information on the first point of care was missing, hence we could not establish if the cases who were recorded as pregnant were identified due to pregnancy through the antenatal clinics. We used the health facility data to identify the cases, and thus our data certainly represent an underestimate of the problem as well as reflecting possible bias if the survivors who did not present to the facility differ from those who do. Also, given the sensitivity of the subject and self-reporting of the data, some cases did not respond to questions related to the perpetrator resulting into potential bias.

## Conclusion

Sexual gender-based violence negatively affected the lives of many adolescent girls and women during the COVID-19 pandemic. Most survivors did not present in time for HIV exposure prophylaxis and therefore efforts to improve access to services through community education and engagement with AGYW is key for PEP uptake when needed. Public health programs in the future may need to focus on identifying or supporting known survivors of SGBV and those who are socioeconomically vulnerable and identifying approaches to protect them, especially during school closures or other events that leave them close to home.

## Conflict of interest

The authors declare that they had no conflict of interest.

## Acknowledgments

We appreciate the health facilities and the data collection teams, especially the health facility GBV focal persons, for the support rendered to interview the cases. We commend the AGYW who participated and shared their experiences to inform the factors associated with SGBV during the COVID-19 period.

published. If cited as a reprint, it should be referenced in the original form.

**References**


1. Violence against women [Internet]. [cited 2021 Dec 20]. Available from: https://www.who.int/westernpacific/health-topics/violence-against-women
2. WHO | Gender-based violence in health emergencies [Internet]. WHO. World Health Organization; [cited 2022 Jan 6]. Available from: http://www.who.int/health-cluster/about/work/task-teams/genderbasedviolence/en/
3. udhs - Bing [Internet]. [cited 2022 Jan 6]. Available from: https://www.bing.com/search?q=udhs&form=WNSGPH&qs=MT&cvid=f94bf64014b146fab0c9de60c5c77ec6&pq=UDHS&cc=UG&setlang=en-UG&nclid=AC7F2871CA2810F4E3ACF4DC56F34B94&ts=1641451817090&wsso=Moderate
4. Sexual violence against women and girls in Uganda increased during the COVID-19 pandemic [Internet]. aidsmap.com. [cited 2022 Jan 6]. Available from: https://www.aidsmap.com/news/jul-2021/sexual-violence-against-women-and-girls-uganda-increased-during-covid-19-pandemic
5. Covid reveals flaws in the protection of girls in Uganda : Recommendations on how to tackle sexual and gender-based violence - Uganda [Internet]. ReliefWeb. [cited 2022 Jan 6]. Available from: https://reliefweb.int/report/uganda/covid-reveals-flaws-protection-girls-uganda-recommendations-how-tackle-sexual-and
6. Interagency-GBV-Case-Management-Guidelines_Final_2017.pdf [Internet]. [cited 2022 Jan 21]. Available from: http://www.gbvims.com/wp/wp-content/uploads/Interagency-GBV-Case-Management-Guidelines_Final_2017.pdf
7. Independent T. Over 47,000 girls impregnated in Bukedi during COVID [Internet]. The Independent Uganda: 2021 [cited 2022 Aug 23]. Available from: https://www.independent.co.ug/over-47000-girls-impregnated-in-bukedi-during-covid/
8. Ministry fo Gender, Uganda. Violence Against Children Survey 2018. 2018.
9. MOH, Uganda U. Preliminary results of 2020 the Uganda Population Population-based HIV Impact assessment [Internet]. 2022 [cited 2022 Jul 21]. Available from: www.mediacentre.go.ug/media/release-preliminary-results-2020-uganda-population-based-hiv-impact-assessment
10. Ministry of Health, Uganda. The National policy guidelines on Post Exposure Prophylaxis for HIV, Hepatitis B and Hepatitis C. 2007.
11. World Health Organization, Organization IL. Post-exposure prophylaxis to prevent HIV infection : joint WHO/ILO guidelines on post-exposure prophylaxis (PEP) to prevent HIV infection [Internet]. World Health Organization; 2007 [cited 2022 Jul 21]. Available from: https://apps.who.int/iris/handle/10665/43838
12. Subu MA, Wati DF, Netrida N, Priscilla V, Dias JM, Abraham MS, et al. Types of stigma experienced by patients with mental illness and mental health nurses in Indonesia: a qualitative content analysis. International Journal of Mental Health Systems. 2021 Oct 18;15(1):77.
13. Schmitt S, Robjant K, Elbert T, Koebach A. To add insult to injury: Stigmatization reinforces the trauma of rape survivors – Findings from the DR Congo. SSM - Population Health. 2021 Mar 1;13:100719.
14. Barnett JP, Maticka-Tyndale E, Kenya T. Stigma as Social Control: Gender-Based Violence Stigma, Life Chances, and Moral Order in Kenya. Social Problems. 2016;63(3):447–62.
15. Gumbie, et, al. Child Abuse — Research: Sauti 116 Uganda Child Helpline, A rapid assessment of the gaps in the reporting system and public's knowledge and awareness of the service [Internet]. GLI. 2020 [cited 2022 Jul 19]. Available

Continued from page 44

from: https://www.globallivingston.org/dir/research/tag/Child+Abuse
16. Apondi R, Awor A, Nelson L, Cheptoris J, Ngabirano F, Egbulem CD, et al. Gender-based violence shadows COVID-19: Increased sexual violence, HIV exposure and teen pregnancy among girls and women in Uganda. Journal of the International AIDS Society. 2021 Jul 1;24(S4):53–5.
17. Ayieko J, Petersen ML, Kabami J, Mwangwa F, Opel F, Nyabuti M, et al. Uptake and outcomes of a novel community-based HIV post-exposure prophylaxis (PEP) programme in rural Kenya and Uganda. Journal of the International AIDS Society. 2021;24(6):e25670.
18. Mohammed F. The Repetition Compulsion: Why Rape Victims Are More Likely To Be Assaulted Again [Internet]. Girls' Globe. 2015 [cited 2022 Jun 13]. Available from: https://www.girlsglobe.org/2015/08/04/the-repetition-compulsion-why-rape-victims-are-more-likely-to-be-assaulted-again/
19. Daniel et al. A Ugandan Parenting Programme to Prevent Gender-Based Violence: Description and Formative Evaluation [Internet]. [cited 2022 Sep 9]. Available from: https://journals.sagepub.com/doi/full/10.1177/10497315211056246
20. AfricaNews. Uganda imposes another lockdown: What are the restrictions? [Internet]. Africanews. 2021 [cited 2022 May 21]. Available from: https://www.africanews.com/2021/06/07/uganda-imposes-another-lockdown-what-are-the-restrictions/
21. Danish Refugee Council. Uganda Cash Consortium stories: Basic needs approach implementation in Imvepi, Rhino Camp & Nakivale refugee settlements - Uganda | ReliefWeb [Internet]. [cited 2022 May 21]. Available from: https://reliefweb.int/report/uganda/uganda-cash-consortium-stories-basic-needs-approach-implementation-imvepi-rhino-camp

## Trends and spatial distribution of pneumonia admissions and deaths among children under five years in Uganda, 2013-2021

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**Summary**

**Background:** Pneumonia is the second leading cause of hospital admissions and deaths among children <5 years in Uganda. While the pneumococcal conjugate vaccine was introduced to the routine immunisation schedule in 2013, little is known about the country's progress in reducing pneumonia admissions and deaths since then. We described the trends and spatial distribution of pneumonia hospital admissions and mortality among children <5 years in Uganda during 2013–2021.

**Methods:** We analysed aggregate secondary data on pneumonia admissions and deaths from the District Health Information System 2, 2013–2021. Pneumonia admissions and mortality rates were calculated per 100,000 children <5 years at national, regional, and district levels. Logistic regression was used to assess the significance of the trend. To contextualize the findings, we also collected data on reporting rates, defined as the percentage of complete submitted monthly reports over the study period divided by the number of expected reports.

**Results:** There were 753,978 pneumonia admissions and 13,632 deaths during 2013–2021 among children <5 years. Reporting rates for admissions and death during this period increased from 78% to 92%. Annual admissions decreased by 4% (OR=0.96, 95% CI: 0.96-0.96) from 2013 to 2021. Northern Region had the smallest decline (OR=0.99, 95% CI: 0.99-0.99) while Central Region had the largest (OR=0.92, 95% CI: 0.92-0.92). Admission rates were highest (1,900 to 14,209 /100,000) in Kotido and Gulu districts over all 9 years. Annual mortality rates decreased by 6% (OR=0.94, 95% CI: 0.93-0.95) over the study

period, with the smallest decline in Eastern Region (OR=0.95, 95% CI: 0.94-0.96) and the largest in Central Region (OR=0.93, 95% CI: 0.92-0.94). Gulu District had the highest mortality rates (40 to 110/100,000) over all 9 years.

**Conclusion:** Both hospital admissions and mortality from pneumonia among children <5 years declined during 2013-2021 in Uganda despite increases in reporting. Existing interventions should be intensified to further accelerate the declines.

## Background

Pneumonia, a largely preventable disease persists as a major public health problem among children <5 years of age. By 2019, pneumonia was the leading infectious cause of death among children <5 years accounting for 14% of all deaths with one child dying of pneumonia every 39 seconds(1). Fifty percent of the pneumonia cases and deaths are reported in Sub-Saharan Africa with an annual incidence of 10,493 and mortality of 253 per 100,000 children <5 years of age(2).

Even with marked reductions in pneumonia globally (from 178 to 138 million cases annually), reductions in Sub-Saharan Africa have been much slower(2,3). By 2020, the prevalence of pneumonia among children <5 years in Eastern Africa was 34,000 per 100,000 children <5 years of age(4). Furthermore, although pneumonia incidence and mortality reduced, there was a three-fold increase in pneumonia admissions in Sub-Saharan Africa in this age group(3). Particulary in Uganda pneumonia remains the second leading cause of all hospital admissions among children <5 years of age(5). This places a substantial burden on the health system as pneumonia accounts for a significant proportion of paediatric admissions. An economic burden is also placed on the already impoverished families. On average Ugandan households spend 62 US dollars per hospitalised episode of pneumonia(6).

To avert this burden, Uganda joined the rest of the world in 2013 to implement various global initiatives such as the integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD)(7). This initiative led to the introduction of pneumococcal conjugate vaccine introduced to the routine immunisation schedule. This was to be complimented by other low-cost interventions including exclusive breastfeeding for the first six months and continued breastfeeding with appropriate complementary feeding thereafter, use of simple, standardized guidelines for the identification and treatment of pneumonia in the community through integrated community case management of childhood illnesses and reduction of household air pollution with improved stoves. With these interventions, Uganda like the rest of the world targeted to reduce the incidence of pneumonia requiring admission by 75% in children <5 years of age compared to 2010 levels and reduce mortality from pneumonia in children <5 years of age to fewer than 3 per 1000 live births by 2025(7).

Little is documented on Uganda's progress towards these goals. Previous studies(8,9) conducted in Uganda assessed prevalence of pneumonia at specific time points hence less informative about the progress over time. Additionally, these studies were conducted in particular regions and may not be generalisable to the entire country or show any spatial differences if any exist. We assessed the trends and spatial distribution of pneumonia admissions and mortality rate among children <5 Uganda, 2013-2021.

## Methods

We conducted a secondary analysis of pneumonia surveillance data generated from the entire Uganda and stored in the District Health Information System 2 (DHIS-2). Uganda is a low-income country located in Eastern Africa with

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20% of its population aged <5 years.

The DHIS-2 system collects data on priority diseases, conditions, and events of public health importance like pneumonia based on the Integrated Disease Surveillance and response guidelines(10). We specifically abstracted aggregate data of both pneumonia admissions and deaths from the inpatient monthly reports (Health Management Information System forms (HMIS) 108) from 2013 to 2021 into excel and imported into Epi info 7 software for analysis.

Using the aggregate data on pneumonia admissions and deaths we calculated the annual incidence of pneumonia admissions and mortality rate using population data from the Uganda Bureau of Statistics as a denominator. Facility based mortality rates were calculated as the proportion of pneumonia cases who died following admission. Pneumonia admissions were defined as hospital stay due to pneumonia based on the ICD-10 framework as a primary diagnosis. Pneumonia deaths were defined as in-patient deaths with pneumonia as the main cause of death.

We calculated annual incidence of pneumonia admissions, overall mortality, and facility-based mortality rates at national, regional, and facility levels. We used line graphs to describe national and regional trends. Additionally, logistic regression analysis was conducted to evaluate the overall trend using Epi info 7 software. Choropleth maps drawn using QGIS software were used to show the spatial distribution of pneumonia admissions and mortality in the country. To further contextualize the findings, we also abstracted data on reporting rates, calculated as the percentage of complete submitted monthly reports over the study period divided by the number of expected reports.

Our study utilized routinely generated aggregated surveillance data with no personal identifiers in health facility in-patient monthly reports, Ministry of Health (MoH) through the DHIS-2. The MoH of Uganda through the office of the Director General Health Services gave approval to access data for pneumonia admissions and death from the DHIS-2. We stored the abstracted data set in a password-protected computer and only shared it with the investigation team. In addition, The Office of the Associate Director for Science, U.S. Centers for Disease Control and Prevention, determined that this study was not a human subjects research with the primary intent of improving use of surveillance data to guide public health planning and practice.

## Results

### National incidence of pneumonia admissions among children under 5 years, Uganda, 2013-2021

Over the study period, there was a total of 753,978 admitted pneumonia cases. The PCV vaccine coverage increased from 60% to 92% (Figure 1). The national average incidence of pneumonia admissions was 1,127 (Range:750 to 1,319) admitted cases per 100,000 children <5 years, with the highest in 2019 (1,319 cases per 100,000). Overall, there was a 4% decline in the incidence of pneumonia admissions among children <5 years (OR= 0.96,95% CI: 0.956-0.957), p=<0.001 (Figure 1)

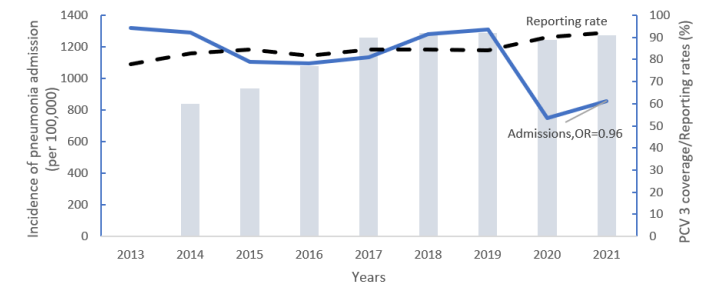


**Figure 1: Incidence of pneumonia admissions among children <5 years, Uganda, 2013-2021**

### Overall trends in the overall pneumonia mortality, among children under 5 years, Uganda, 2013-2021

During the study period, there were 13,632 deaths occurred among children <5 years admitted with pneumonia. The PCV vaccine coverage increased

from 60% to 92% (Figure 1). The national average overall pneumonia mortality rate was 21 (Range: 26 to 14) deaths per 100,000 children <5 years with the highest in 2013(26). Overall, there was a 6% decline in the overall pneumonia mortality among children <5 years (OR= 0.93,95% CI: 0.93-0.95), p=<0.001(Figure 2).

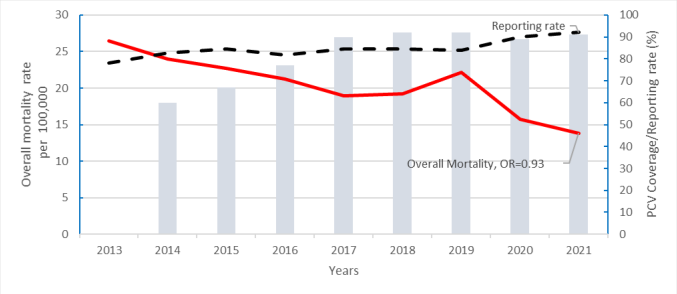


**Figure 2: National trends in the overall mortality among children under 5 years, Uganda, 2013-2021**

## Pneumonia facility-based mortality rate among children under 5 years, Uganda, 2013 -2021

The average national pneumonia facility-based mortality rate was 1,805 (Range: (Range:1, 612 to 2,097) per 100,000 children <5 years, with the highest in 2020 (2,097 per 100,000 children). Overall, the pneumonia facility-based mortality rate declined by 2% (OR:0.98,95% CI:0.97-0.99). Changes in pneumonia facility-based mortality rate varied with no changes observed at health centre IV (OR:0.97,95% CI:0.95-1.00), p=0.058 and general hospital level (OR:1.00,95% CI:0.99-1.02), p=0.288. At health centre III level, pneumonia facility-based mortality rate declined (OR:0.95,95% CI:0.93-0.99), while it increased at the regional referral level (OR:1.05,95% CI:1.02-1.08) (Figure 3).

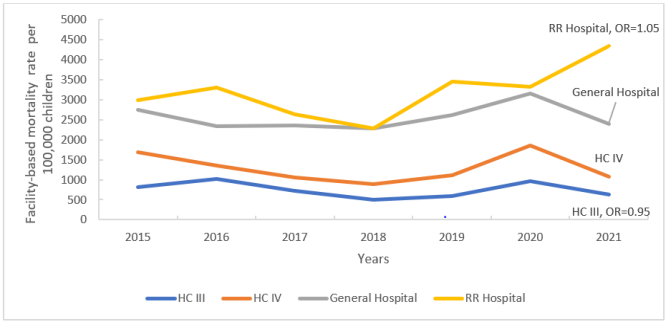


**Figure 3: Trends in pneumonia facility-based mortality rate across levels among children under 5 years, Uganda, 2013-2021**

## Regional trends of incidence of pneumonia admissions, overall mortality rate, and facility -based mortality rate among children under 5 years, Uganda, 2013-2021

Pneumonia admissions significantly declined across all regions (Table 1). The greatest decline in the incidence of pneumonia admissions was in the central region (OR:0.92, CI: 0.920-0.924, P<0.001) while the smallest decline was in the northern region (OR:0.99,95% CI:0.99-0.99, P<0.001). Unlike pneumonia admissions, facility-based mortality rate only declined in the northern region, 7% (0R=0.93,95% CI:0.919-0.943). Overall, pneumonia mortality significantly declined across all regions. The greatest decline in pneumonia mortality was in the central region (OR:0.92, CI: 0.912-0.943, P<0.001) while the smallest decline was in the eastern region (OR:0.95,95% CI:0.936-0.963, P<0.001) (Table 1).

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**Table 1: Regional trends of incidence pneumonia admissions, overall mortality rate, and facility -based mortality, among children under 5 years, Uganda, 2013-2021**

| | Incidence of pneumonia admissions | | | Facility based mortality rate | | | Overall mortality | | |
|---|---|---|---|---|---|---|---|---|---|
| **Region** | ***OR*** | ***95% CI*** | ***P-value*** | ***OR*** | ***95% CI*** | ***P-value*** | ***OR*** | ***95% CI*** | ***P-value*** |
| Central | 0.92 | 0.92 - 0.92 | <0.001 | 1.00 | 0.99-1.020 | 0.332 | 0.93 | 0.91-0.94 | <0.001 |
| Eastern | 0.95 | 0.94-0.95 | <0.001 | 1.00 | 0.99-1.019 | 0.603 | 0.95 | 0.94-0.96 | <0.001 |
| Northern | 0.99 | 0.99-0.99 | <0.001 | 0.93 | 0.92-0.94 | <0.001 | 0.93 | 0.92-0.94 | <0.001 |
| Western | 0.95 | 0.95-0.95 | <0.001 | 0.99 | 0.98-1.00 | 0.264 | 0.94 | 0.93-0.96 | <0.001 |

**Spatial distribution of incidence of pneumonia admissions and overall mortality among children under 5 years, Uganda, 2013-2021**

Incidence of pneumonia admissions among children < 5 years were highest (1,900 to 14,209 /100,000) in Kotido and Gulu districts over all 9 years (Figure 4). Gulu district had the highest mortality rates (40 to 110/100,000) over all 9 years. Kasese district had consistently high incidence of pneumonia admissions and overall mortality rates.

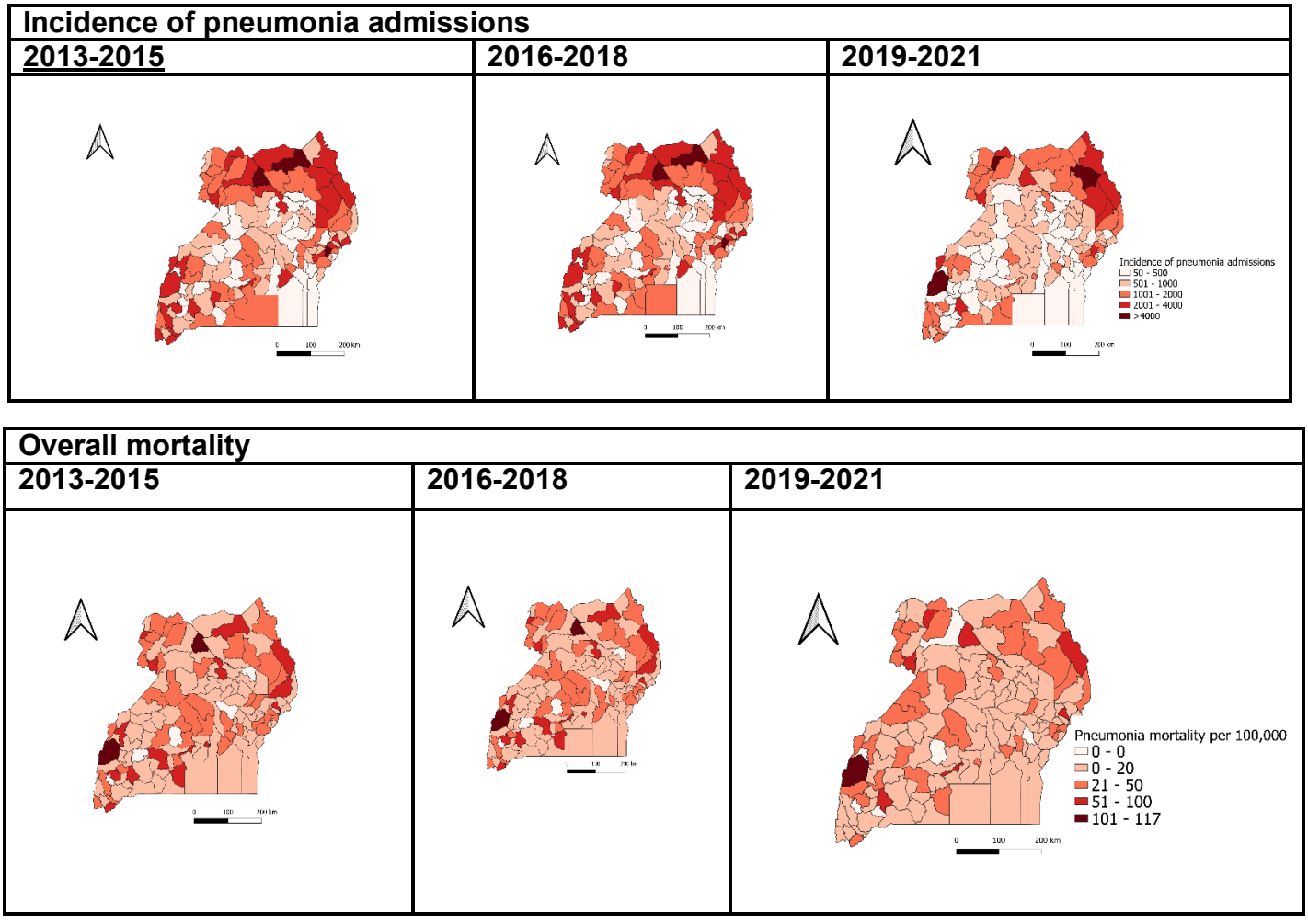


**Figure 4: Spatial distribution of incidence of pneumonia admissions and overall mortality among children <5 years, Uganda, 2013-2021**

## Discussion

We described the trends and spatial distribution of pneumonia hospital admissions and mortality among children <5 years in Uganda during 2013–2021.Our findings indicate declines (<10%) in the incidence of pneumonia admissions, overall mortality, and facility-based mortality rates over the 9-year period. These declines differed across region, with the lowest decline in the incidence of pneumonia admissions and mortality observed in the northern region and eastern regions respectively. Declines in the pneumonia facility-based mortality rate were only observed at the health centre III level and in northern region. Pneumonia facility-based mortality rate increased at regional referral hospital level.

Like the global trend, our findings indicate a reduction in pneumonia admissions over the 9-year period(3). However, declines in the incidence in pneumonia admissions reported in this study were below those previously observed in other studies in African Countries where the Pneumococcal Vaccine(PCV) vaccine was introduced(11,12). A study in Burkina Faso(12) indicated 34% reduction in pneumonia admissions among children <5, five years following the introduction of PCV. In another study in Zambia(11) pneumonia admissions declined by 37.8% and 28.8% among children aged <1 year and 1–4 years, respectively. Previous studies conducted among children<5 years with severe pneumonia(13,14) indicated the presence of other pneumonia-causing organisms that the PCV vaccine does not protect against such as the Klebsiella species and other viral pneumonia-causing organisms. These could contribute to slower declines in pneumonia admissions despite the high PCV coverage. Additionally, the observed declines in pneumonia admissions in 2020 could be attributed to the limited access to healthcare during the COVID-19 lockdown leading to fewer documented pneumonia admissions and not actual declines in pneumonia requiring admission(15).

Pneumonia mortality declines in both overall and facility-based mortality reported in this study were below those observed in other studies in Africa where the pneumonia vaccine was introduced. A study in South Africa(16) indicated a 33% and 26% reduction in pneumonia mortality among children aged 1 to 11 months and 1 to 4 years respectively. Anticipated gains in reduction of hospital pneumonia mortality could be prevented by the presence of overlapping risk factors previously documented in Uganda. These include undernutrition, delayed health care seeking, comorbidities such as HIV, limited access to oxygen, and stock out of essential treatments (17–21). Additionally, declines in pneumonia mortality may vary across countries due to differences in coding of the cause of death (22).

Notably, the decline in the facility-based mortality rate were far below (less than half) the decline in the overall mortality rate. This indicates a slower progress in the health care system's capacity to reduce pneumonia mortality among children <5 years(23). Existing gaps in timely seeking of appropriate treatment and access to parenteral antibiotics and oxygen (where necessary) and treatment failure resulting from anti-microbial resistance in developing countries like Uganda may contribute to slower declines in the facility-based mortality rate(24). In Uganda, critical children are more likely to complete the referral process,(25) it is therefore not surprising that the facility based mortality rate at regional referral hospital level increased overtime.

Regional differences in the trend of incidence of pneumonia admissions, pneumonia overall mortality, and facility-based mortality rate were observed. The lowest declines in the incidence of pneumonia incidence and mortality were observed in the northern and eastern regions. These regions are characterised with poverty and poor housing, all of which

are associated with an increased likelihood of pneumonia requiring admission and mortality(26,27).

### Limitations

Our findings should be interpreted with the following limitation. We used in-patient data which could lead to underestimation of the true pneumonia mortality due to the exclusion of community deaths. Secondly, we used aggregate secondary data which lacked key variables to further explore trends across sub categories within this age group.

### Conclusion

We highlight declines in the incidence of pneumonia admissions, overall mortality rate, and facility-based rate over the nine years following the introduction of the PCV vaccine in Uganda. Existing interventions should be intensified to further accelerate the decline in order to achieve set targets.

### Conflict of interest

The authors declare that they had no conflict of interest.

### Acknowledgments

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### References

1. Perin J, Mulick A, Yeung D, Villavicencio F, Lopez G, Strong KL, et al. Global, regional, and national causes of under-5 mortality in 2000-19: an updated systematic analysis with implications for the Sustainable Development Goals. Lancet Child Adolesc Heal. 2022 Feb;6(2):106–15.
2. Troeger CE, Khalil IA, Blacker BF, Biehl MH, Albertson SB, Zimsen SRM, et al. Quantifying risks and interventions that have affected the burden of lower respiratory infections among children younger than 5 years: an analysis for the Global Burden of Disease Study 2017. Lancet Infect Dis [Internet]. 2020 Jan 1;20(1):60–79. Available from: https://doi.org/10.1016/S1473-3099(19)30410-4
3. McAllister DA, Liu L, Shi T, Chu Y, Reed C, Burrows J, et al. Global, regional, and national estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: a systematic analysis. Lancet Glob Heal. 2019 Jan;7(1):e47–57.
4. Beletew B, Bimerew M, Mengesha A, Wudu M, Azmeraw M. Prevalence of pneumonia and its associated factors among under-five children in East Africa: a systematic review and meta-analysis. BMC Pediatr. 2020 May;20(1):254.
5. MoH M of HU. Ministry of Health Annual Sector Performance Report 2020/2021 [Internet]. Kampala, Uganda; 2021. Available from: http://library.health.go.ug/publications/performance-management/annual-health-sector-performance-report-financial-year-202021
6. Ekirapa-Kiracho E, De Broucker G, Ssebagereka A, Mutebi A, Apolot RR, Patenaude B, et al. The economic burden of pneumonia in children under five in Uganda. Vaccine X. 2021 Aug;8:100095.
7. WHO (World Health Organisation). Ending preventable child deaths from pneumonia and diarrhoea by 2025: the integrated global action plan for pneumonia and diarrhoea (GAPPD). 2013;
8. Kiconco G, Turyasiima M, Ndamira A, Yamile OA, Egesa WI, Ndiwimana M, et al. Prevalence and associated factors of pneu-

monia among under-fives with acute respiratory symptoms: a cross sectional study at a Teaching Hospital in Bushenyi District, Western Uganda. Afr Health Sci. 2021 Dec;21(4):1701–10.
9. Ma C, Gunaratnam LC, Ericson A, Conroy AL, Namasopo S, Opoka RO, et al. Handheld Point-of-Care Lactate Measurement at Admission Predicts Mortality in Ugandan Children Hospitalized with Pneumonia: A Prospective Cohort Study. Am J Trop Med Hyg. 2019 Jan;100(1):37–42.
10. MoH (Minstry of Health Uganda). National Technical Guidelines for Integrated Disease Surveillance and Response Third Edition [Internet]. 2021. Available from: https://www.afro.who.int/sites/default/files/2021-09/2_Uganda 3rd IDSR Tech Guideline_PrintVersion_10Sep2021.pdf
11. Mpabalwani EM, Lukwesa-Musyani C, Imamba A, Nakazwe R, Matapo B, Muzongwe CM, et al. Declines in Pneumonia and Meningitis Hospitalizations in Children Under 5 Years of Age After Introduction of 10-Valent Pneumococcal Conjugate Vaccine in Zambia, 2010–2016. Clin Infect Dis [Internet]. 2019 Sep 5;69 (Supplement_2):S58–65. Available from: https://doi.org/10.1093/cid/ciz456
12. Kaboré L, Ouattara S, Sawadogo F, Gervaix A, Galetto-Lacour A, Karama R, et al. Impact of 13-valent pneumococcal conjugate vaccine on the incidence of hospitalizations for all-cause pneumonia among children aged less than 5 years in Burkina Faso: An interrupted time-series analysis. Int J Infect Dis [Internet]. 2020 Jul 1;96:31–8. Available from: https://doi.org/10.1016/j.ijid.2020.03.051
13. Nantanda R, Hildenwall H, Peterson S, Kaddu-Mulindwa D, Kalyesubula I, Tumwine JK. Bacterial aetiology and outcome in children with severe pneumonia in Uganda. Ann Trop Paediatr. 2008 Dec;28(4):253–60.
14. Nantanda R, Tumwine JK, Ndeezi G, Ostergaard MS. Asthma and Pneumonia among Children Less Than Five Years with Acute Respiratory Symptoms in Mulago Hospital, Uganda: Evidence of Under-Diagnosis of Asthma. PLoS One [Internet]. 2013 Nov 29;8(11):e81562. Available from: https://doi.org/10.1371/journal.pone.0081562
15. Burt JF, Ouma J, Lubyayi L, Amone A, Aol L, Sekikubo M, et al. Indirect effects of COVID-19 on maternal, neonatal, child, sexual and reproductive health services in Kampala, Uganda. BMJ Glob Heal [Internet]. 2021;6(8). Available from: https://gh.bmj.com/content/6/8/e006102
16. Kleynhans J, Tempia S, Shioda K, von Gottberg A, Weinberger DM, Cohen C. Estimated impact of the pneumococcal conjugate vaccine on pneumonia mortality in South Africa, 1999 through 2016: An ecological modelling study. PLOS Med [Internet]. 2021 Feb 16;18 (2):e1003537. Available from: https://doi.org/10.1371/journal.pmed.1003537
17. Iroh Tam P-Y, Wiens MO, Kabakyenga J, Kiwanuka J, Kumbakumba E, Moschovis PP. Pneumonia in HIV-exposed and Infected Children and Association With Malnutrition. Pediatr Infect Dis J [Internet]. 2018;37(10):1011–3. Available from: http://europepmc.org/abstract/MED/29505479
18. Banga D, Baren M, Ssonko NV, Sikakulya FK, Tibamwenda Y, Banga C, et al. Comorbidities and Factors Associated with Mortality among Children under Five Years Admitted with Severe Acute Malnutrition in the Nutritional Unit of Jinja Regional Referral Hospital, Eastern Uganda. Int J Pediatr. 2020;2020:7809412.
19. Källander K, Hildenwall H, Waiswa P, Galiwango E, Peterson S, Pariyo G. Delayed care seeking for fatal pneumonia in children aged under five years in Uganda: a case-series study. Bull World Health Organ. 2008 May;86 (5):332–8.
20. Nabwire J, Namasopo S, Hawkes M. Oxygen Availability and Nursing Capacity for Oxygen Therapy in Ugandan Paediatric Wards. J Trop Pediatr [Internet]. 2018 Apr 1;64(2):97–103. Available from: https://doi.org/10.1093/tropej/fmx033
21. Masters SH, Burstein R, DeCenso B, Moore K, Haakenstad A, Ikilezi G, et al. Pharmaceutical Availability across Levels of Care: Evidence from Facility Surveys in Ghana, Kenya, and Uganda. PLoS One [Internet]. 2014 Dec

Continued from page 52

11;9(12):e114762. Available from: https://doi.org/10.1371/journal.pone.0114762
22. de Oliveira LH, Shioda K, Valenzuela MT, Janusz CB, Rearte A, Sbarra AN, et al. Declines in Pneumonia Mortality Following the Introduction of Pneumococcal Conjugate Vaccines in Latin American and Caribbean Countries. Clin Infect Dis an Off Publ Infect Dis Soc Am. 2021 Jul;73(2):306–13.
23. Souris M, Gonzalez J-P. COVID-19: Spatial analysis of hospital case-fatality rate in France. PLoS One [Internet]. 2020 Dec 15;15(12):e0243606. Available from: https://doi.org/10.1371/journal.pone.0243606
24. Graham SM, English M, Hazir T, Enarson P, Duke T. Challenges to improving case management of childhood pneumonia at health facilities in resource-limited settings. Bull World Health Organ. 2008 May;86(5):349–55.
25. Nanyonjo A, Bagorogoza B, Kasteng F, Ayebale G, Makumbi F, Tomson G, et al. Estimating the cost of referral and willingness to pay for referral to higher-level health facilities: a case series study from an integrated community case management programme in Uganda. BMC Health Serv Res [Internet]. 2015;15(1):347. Available from: https://doi.org/10.1186/s12913-015-1019-5
26. Atamanov A, Malasquez Carbonel EA, Masaki T, Myers CA, Granguillhome Ochoa R, Sinha N. Uganda Poverty Assessment: Strengthening Resilience to Accelerate Poverty Reduction. 2022;
27. Azab SFAH, Sherief LM, Saleh SH, Elsaeed WF, Elshafie MA, Abdelsalam SM. Impact of the socioeconomic status on the severity and outcome of community-acquired pneumonia among Egyptian children: a cohort study. Infect Dis Poverty [Internet]. 2014;3(1):14. Available from: https://doi.org/10.1186/2049-9957-3-14

## Loss to Follow-up among People Living with HIV on Tuberculosis Preventive Treatment at Four Regional Referral Hospitals, Uganda, 2019–2021

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### Summary

**Introduction:** Tuberculosis (TB) remains the leading cause of death among people living with HIV (PLHIV). TB prevention among PLHIV can be achieved with TB preventive treatment (TPT) for many years. The six-month course (isoniazid) was the most readily available in Uganda during 2019-2021. While the national TPT completion target is 95%, program data indicated a substantial loss to follow-up (LTFU) of 12% in the period 2019-2021. We determined the factors associated with TPT LTFU among PLHIV in four regional referral hospitals (RRHs) in Uganda from 2019-2021 to inform mitigation measures.

**Methods:** We abstracted program data from the TPT registers on patient LTFU at Masaka, Mbale, Mubende, and Jinja RRHs. Additional data collected included client demographics, duration of HIV antiretroviral therapy (ART), year of TPT initiation, adherence, and point of entry. We conducted bivariate analysis using the chi-square test. Variables with $p<0.05$ in bivariate analysis were included in the logistical regression model using a backward stepwise method to establish factors associated with LTFU.

**Results:** Among 24,206 clients who started on TPT in the four RRHs with a median age of 40 years (range, 1-90 years), 15,962 (66%) were female, and 22,260 (92%) had TPT adherence >95%. Factors associated with LTFU included being on ART for <3 months (AOR: 3.1, 95% CI: 2.1-4.5) and 20-24 years (AOR: 4.7, 95% CI: 1.9-12) or 25-29 years (AOR: 3.3, 95% CI: 1.3-8.2) compared to 15-19 years.

**Conclusions:** Close follow-up of PLHIV aged 20-29 years and those newly initiated on ART could improve TPT completion.

## Introduction

Tuberculosis (TB) is the leading cause of death among people living with human immunodeficiency virus (PLHIV) infection (1). Of the global TB deaths in 2019, 208,000 (33%) were living with HIV (1). To reduce the TB burden in this population, the World Health Organization (WHO) recommends tuberculosis preventive treatment (TPT) for PLHIV without active TB, including children living with HIV aged ≥12 months as well as pregnant and breastfeeding mothers (2-6). From 2019–2021, Uganda implemented a six-month course with isoniazid and pyridoxine for TPT (2, 3). Alternative recommended regimens of TPT were a 6-month daily equivalent of a rifamycin-based regimen, 1-month daily rifapentine, and isoniazid regimen as well as a 4-month daily rifampicin regimen (3). TPT can stop the development of TB disease effectively for many years, but reinfection with TB bacilli after completing treatment may reverse this protection (7, 8). Studies on the benefit of repeated TPT are ongoing, and PLHIV who have completed TB treatment may also receive a TPT course (7, 8).

The TPT care cascade includes TB symptom screening to exclude active TB, determining those eligible, enrolling them, and treatment monitoring to ensure completion of TPT (2, 3). Although Uganda rolled out Isoniazid Preventive Therapy (IPT) in June 2014, by July 2019, only 16% of all eligible PLHIV without active TB in Uganda had received TPT. During the period July–October 2019, the Ministry of Health (MoH) in Uganda implemented a 100-day accelerated scale-up of TPT with a target of enrolling 300,000 PLHIV in 100 days and achieving 100% coverage by the end of 2022 in this population (9, 10). Program data in Uganda show that of the 916,345 PLHIV initiated on TPT from January 2019–December 2021, 808,653 (88%) completed, and 107,692 (12%) were lost to follow-up (11). However, contributory factors to this level of loss to follow-up from treatment have not been systematically analyzed. We determined the factors associated with TPT loss to follow-up (LTFU) among PLHIV in four regional referral hospitals (RRHs) in Uganda to inform program improvements in Uganda and beyond.

## Methods

### Study design and data source

We conducted a secondary analysis of routinely collected program surveillance data in the national TPT registers to determine the magnitude of LTFU and associated factors among PLHIV attending Masaka, Mbale, Mubende, and Jinja RRHs in Uganda. These facilities contributed 63,908 (3.5%) of the cumulative number of PLHIV clients ever enrolled in ART care across the country as of December 31, 2021 (11).

### Study population

Our study population included all PLHIV in Uganda who received HIV/ART services from the highlighted four health facilities from January 1, 2019–31 December 2021.

### Data abstraction

We abstracted data on the factors associated with TPT LTFU among PLHIV from the TPT registers of Mbale, Jinja, Mubende, and Masaka RRHs. No personal identification information was collected from the TPT registers.

### Study variables

***Outcome variable:*** This was the outcome at the end of six months after TPT initiation, which was indicated by either completion or loss to follow-up. Other outcomes (still on TPT, died, referred to another health facility, and deliberately stopped by health workers) were also collected. However, they were not included in determining factors associated with LTFU after TPT initiation.

***Exposure variables:*** These included the patient's age, sex, regional referral hospital, year of TPT initiation (either 2019, 2020, or 2021), ART status at TPT initiation (being on ART for <3 months), being on ART for ≥3 months, and not indicated), point of entry (either HIV/ART clinic or OPD), TPT regimen (either isoniazid/INH or Q-TIB/cotrimoxazole plus isoniazid plus vitamin B 6), and average adherence levels (either good (>95%), fair (≥85–95%), or poor (<85)).

### Data analysis

We used STATA Version 14.0 for the analysis

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of TPT outcomes, levels, and factors associated with loss to follow-up. At the bivariate level, we used the chi-square test ($Chi^2$) to determine factors associated with loss to follow-up, while at the multivariate analysis level, we used logistic regression to generate adjusted odds ratios (AORs) with 95% confidence intervals (CIs). Variables with $p<0.05$ in bivariate analysis were included in the model. At the multivariate analysis level, $p<0.05$ showed statistically significant associations between the outcome and the independent variables. AORs were used instead of prevalence ratios because the prevalence of loss to follow-up was less than 10% (12). We tested the model using the Hosmer–Lemeshow goodness of fit test.

### Ethical considerations

The Office of the Associate Director for Science, U.S. CDC/Uganda, and the U.S. CDC human subjects review determined that this activity was not human subjects research. Its primary intent was public health response and tuberculosis control. This activity was reviewed by the U.S. CDC and was conducted consistent with applicable federal law and CDC policy. All experimental protocols were approved by the US CDC human subjects review board and the Uganda Ministry of Health and were performed in accordance with the Declaration of Helsinki. We used routinely collected aggregate surveillance data that did not have any personal identifiers. No personal identification information was collected from any of the records sources.

## Results

### Demographic and clinical characteristics

A total of 24,206 records of PLHIV were abstracted. Of these 10,047 (42%) PLHIV were from Masaka RRH, 15,962 (66%) were female, and 20,740 (86%) had been on ART for more than three months. A total of 4,986 (21%) were aged more than 50 years, 24,204 (99.99%) were enrolled in the ART clinic, and 23,677 (98%) were on isoniazid and pyridoxine. TPT outcomes included 23,592 (97%) completed, of which 22,260 (92%) had good adherence. Other outcomes included 76 (0.3%) who died, 31 (0.1%) who were stopped, 96 (0.4%) who were transferred to other facilities, 141 (0.6%) still on TPT, 36 (0.2%) not evaluated, and 234 (1.0%) lost to follow-up (Table 1).

**Table 1: Characteristics of people living with HIV who were initiated on tuberculosis preventive treatment, Uganda, 2019–2021**

| Characteristic | Frequency (n=24,206) | % |
|---|---|---|
| **Regional Referral Hospital** | | |
| Masaka | 10,047 | 42 |
| Mbale | 5,653 | 23 |
| Mubende | 4,902 | 20 |
| Jinja | 3,604 | 15 |
| **Sex** | | |
| Female | 15,962 | 66 |
| **Year of TPT initiation** | | |
| 2019 | 17,671 | 73 |
| 2020 | 3,755 | 16 |
| 2021 | 2,780 | 12 |
| **ART Status at TPT Initiation** | | |
| Being on ART for ≥3 months | 20,740 | 86 |
| Being on ART for <3 months | 1,531 | 6 |
| Not indicated | 1,935 | 8 |
| **Age group** | Median (40 years) | Range (1, 90) |
| 1–4 | 76 | 0.3 |
| 5–9 | 292 | 1 |
| 10–14 | 523 | 2 |
| 15–19 | 657 | 3 |
| 20–24 | 1,127 | 5 |
| 25–29 | 2,306 | 10 |
| 30–34 | 3,510 | 15 |
| 35–39 | 4,086 | 17 |
| 40–44 | 3,617 | 15 |
| 45–49 | 3,026 | 13 |
| ≥50 | 4,986 | 21 |
| **Point of entry** | | |
| HIV/ART Clinic | 24,204 | 99.99 |
| **TPT Regimen** | | |
| INH | 23,677 | 98 |
| Q-TIB (CTX+ INH+ Vit B6) | 529 | 2 |
| **Outcome at end of 6 months** | | |
| Completed | 23,592 | 97 |
| Loss to follow-up | 234 | 1 |
| Still on TPT | 141 | 0.6 |
| Died | 76 | 0.3 |
| Transferred to another facility | 96 | 0.4 |
| Not evaluated | 36 | 0.2 |
| Stopped by health workers | 31 | 0.1 |
| **Reason for stopping TPT *** | | |
| Side effects | 14 | 45 |
| Developed active TB | 7 | 23 |
| Treatment Interaction | 2 | 7 |
| Others | 8 | 26 |
| **Average adherence levels** | | |
| Good (>95%) | 22,260 | 92 |
| Fair (≥85–95%) | 255 | 1 |
| Poor (<85) | 5 | 0.02 |
| Not indicated | 1,686 | 7 |

*Deliberately stopped by health workers (31)

### Factors associated with loss to follow-up after TPT initiation among PLHIV in Uganda, 2019–2021

In the bivariate analysis, sex ($p$=0.009), age group ($p$<0.001), TPT regimen ($p$=0.019), regional referral hospitals ($p$<0.001), average adherence levels ($p$<0.001), and ART status at TPT initiation ($p$<0.001) were significantly different between those who completed the six-month course of TPT and those who were lost to follow-up (Table 2).

**Table 2: Bivariate analysis of factors associated with loss to follow-up after tuberculosis preventive treatment initiation among people living with HIV, Uganda, 2019–2021**

| Characteristics | TPT Status at the end of treatment | | | | Chi$^2$ | *p*-value |
|---|---|---|---|---|---|---|
| | Completed | | LTFU† | | | |
| | n=22,723 | % | n=232 | % | | |
| **Sex** | | | | | 6.9 | 0.009 * |
| Female | 15,090 | 99 | 173 | 1 | | |
| Male | 7,633 | 99 | 59 | 1 | | |
| **Age group** | | | | | 241 | <0.001 * |
| 15–19 | 645 | 99 | 5 | 1 | | |
| 20–24 | 1,034 | 96 | 48 | 4 | | |
| 25–29 | 2,182 | 97 | 65 | 3 | | |
| 30–34 | 3,428 | 99 | 18 | 1 | | |
| 35–39 | 4,011 | 99 | 20 | 1 | | |
| 40–44 | 3,540 | 99 | 28 | 1 | | |
| 45–49 | 2,977 | 99 | 20 | 1 | | |
| ≥50 | 4,906 | 99 | 28 | 1 | | |
| **TPT Regimen** | | | | | 5.5 | 0.019 * |
| INH | 22,199 | 99 | 232 | 1 | | |
| Q-TIB (CTX+ INH+ Vit B6) | 524 | 100 | 0 | 0 | | |
| **Regional Referral Hospital** | | | | | 766 | <0.001 * |
| Masaka | 9,639 | 100 | 0 | 0 | | |
| Mbale | 5,265 | 99 | 51 | 1 | | |
| Mubende | 4,559 | 100 | 0 | 0 | | |
| Jinja | 3,260 | 95 | 181 | 5 | | |
| **Average adherence levels ‡** | | | | | 2.6 | <0.001 * |
| Good (>95%) | 21,293 | 99.8 | 34 | 0.2 | | |
| Fair (≥85–95%) | 249 | 99 | 2 | 1 | | |
| Poor (<85) | 5 | 100 | 0 | 0 | | |
| **Year of TPT initiation** | | | | | 3.5 | 0.172 |
| 2019 | 16,638 | 99 | 176 | 1 | | |
| 2020 | 3,541 | 99 | 39 | 1 | | |
| 2021 | 2,544 | 99 | 17 | 1 | | |
| **ART Status at TPT Initiation** | | | | | 196 | <0.001 * |
| Being on ART for ≥3 months | 19,587 | 99 | 126 | 1 | | |
| Being on ART for <3 months | 1,371 | 97 | 41 | 3 | | |
| Not indicated | 1,765 | 96 | 65 | 4 | | |

†Loss to follow-up, * Significant association at $p$<0.05, ‡ Among 21,547 that completed and 36 who were lost to follow-up

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After adjusting for all statistically significant variables in the bivariate analysis (Table 2), new patients on HIV/ART care during the quarter (AOR: 3.1, 95% CI: 2.1–4.5), ages 20–24 years (AOR: 4.7, 95% CI: 1.9–12) and 25–29 years (AOR: 3.3, 95% CI: 1.3–8.2) were more likely to be lost from TPT (Table 3).

**Table 3: Multivariate analysis of factors associated with loss to follow-up after tuberculosis preventive treatment initiation among people living with HIV, Uganda, 2019–2021**

| Characteristics | TPT Status at the end | | | | AOR (95% CI) | *p*-value |
|---|---|---|---|---|---|---|
| | Completed | | LTFU† | | | |
| | n | % | n | % | | |
| **Sex** | | | | | | |
| Female | 15,090 | 99 | 173 | 1 | 1.0 | |
| Male | 7,633 | 99 | 59 | 1 | 0.9 (0.6–1.2) | 0.381 |
| **Age group** | | | | | | |
| 15–19 | 645 | 99 | 5 | 1 | 1.0 | |
| 20–24 | 1,034 | 96 | 48 | 4 | 4.7 (1.9–12) | 0.001* |
| 25–29 | 2,182 | 97 | 65 | 3 | 3.3 (1.3–8.2) | 0.012* |
| 30–34 | 3,428 | 99 | 18 | 1 | 0.6 (0.2–1.6) | 0.317 |
| 35–39 | 4,011 | 99 | 20 | 1 | 0.6 (0.2–1.7) | 0.337 |
| 40–44 | 3,540 | 99 | 28 | 1 | 1.0 (0.4–2.7) | 0.921 |
| 45–49 | 2,977 | 99 | 20 | 1 | 0.9 (0.3–2.5) | 0.882 |
| ≥50 | 4,906 | 99 | 28 | 1 | 0.9 (0.3–2.3) | 0.780 |
| **ART Status at TPT Initiation** | | | | | | |
| Being on ART for ≥3 months | 19,587 | 99 | 126 | 1 | 1.0 | |
| Being on ART for <3 months | 1,371 | 97 | 41 | 3 | 3.1 (2.1–4.5) | <0.001* |

†Loss to follow-up, * Significant association at $p<0.05$

## Discussion

In this study, we analyzed outcomes of TPT among PLHIV in regional referral hospitals and factors associated with LTFU, which contributes the most among the unsuccessful outcomes. This study showed that having been newly started on ART (being on ART for less than 3 months) during the quarter, ages of 20–24 years and 25–29 years were associated with increased odds of LTFU after initiation on TPT among PLHIV.

Our findings are similar to findings from other settings in the Democratic Republic of Congo, Zimbabwe, Tanzania, Ethiopia, Malawi, and Botswana that showed that patients who were already on ART at the time of TPT initiation had increased TPT completion rates compared to the new ones on ART or those not yet enrolled on ART (13-18). This occurrence could be attributed to stigma (19-21), poor adherence (22), and a lack of understanding of the role of TB prevention in the absence of symptoms (23). It is also plausible that the pill burden among PLHIV newly starting ART and TPT at the same time presents a larger challenge than in ART-experienced patients (14). However, a study in Nigeria suggested otherwise, which may be attributed to the very low number of PLHIV who were newly on ART compared to the number of those who were already on ART included in that study (24).

We found patients in the 20–24 years and 25–29-year age groups with increased odds of loss to follow-up after initiation on TPT, similar to findings from other studies in Zimbabwe, Malawi, Italy, and the United States. (14, 25-27). We could attribute this to the high stigma among younger PLHIV aged 20–29 years compared to the older population, as reported elsewhere (28). Older PLHIV have developed coping mechanisms and hence have low levels of negative self-image (29-32). On the other hand, this could be attributed to migration or movement of the young population in search of employment opportunities as previously reported (33), hence the higher likelihood of loss to follow-up among them.

## Study limitations

The secondary data that we used were limited by the number of possi-

ble variables we could use in determining factors associated with LTFU after TPT initiation. Nonetheless, the data we used provided a good reflection of the factors associated with LTFU after TPT initiation in Masaka, Mbale, Mubende, and Jinja RRHs in Uganda during the study period. Since we only collected data on regional referral hospitals, our results might have been less representative if the loss of follow-up in lower-level health facilities differed along with associated factors.

## Conclusions and recommendations

Although our study had limited coverage, the findings concur with what has been established in other settings. Patients newly initiated on ART and those in the 20–29 age group are more likely to be lost from TPT before completion. MoH could prioritize these patient categories for close follow-up to improve TPT outcomes and reduce the burden of TB among PLHIV. Given that some patients may be lost due to migration while on longer TPT regimens, MOH could expedite the scale-up of shorter WHO-recommended regimens as one of the mitigation measures.

## Conflict of interest

The authors declare that they had no conflict of interest.


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## References


1. WHO. Global tuberculosis report 2020. Geneva: World Health Organization; 2020.
2. WHO. Operational handbook on tuberculosis. Module 1: prevention - tuberculosis preventive treatment. Geneva: World Health Organization; 2020.
3. WHO. Consolidated guidelines on tuberculosis: Module 1: Tuberculosis preventive treatment. Geneva: World Health Organisation; 2020.
4. Badje A, Moh R, Gabillard D, Guéhi C, Kabran M, Ntakpé J-B, et al. Effect of isoniazid preventive therapy on risk of death in west African, HIV-infected adults with high CD4 cell counts: long-term follow-up of the Temprano ANRS 12136 trial. The Lancet global health. 2017;5(11):e1080-e9.
5. Rangaka MX, Wilkinson RJ, Boulle A, Glynn JR, Fielding K, Van Cutsem G, et al. Isoniazid plus antiretroviral therapy to prevent tuberculosis: a randomised double-blind, placebo-controlled trial. The Lancet. 2014;384(9944):682-90.
6. Group TAS. A trial of early antiretrovirals and isoniazid preventive therapy in Africa. New England Journal of Medicine. 2015;373(9):808-22.
7. Answers to Frequently Asked Questions on TB preventive treatment (TPT) associated with the 2020 WHO TPT guidance [Internet]. World Health Organization (WHO). 2020 [cited September 28, 2022]. Available from: https://www.who.int/docs/default-source/campaigns-and-initiatives/world-tb-day-2020/5-faqs-tb-preventive-treatment.pdf?sfvrsn=d633097e_2#:~:text=TPT%20can%20halt%20progression%20to,months%20is%20recommended%20for%20PLHIV.
8. WHO consolidated guidelines on tuberculosis: tuberculosis preventive treatment [Internet]. World Health Organization (WHO). 2020. Available from: https://apps.who.int/iris/bitstream/handle/10665/331170/9789240001503-eng.pdf.
9. WHO. Uganda Launches Scale-up Plan for Tuberculosis Preventive Treatment WHO Website: World Health Organisation; 2019 [updated 04 July 2019; cited 2021 18/07/2021]. Available from: https://www.afro.who.int/news/uganda-launches-scale-plan-tuberculosis-preventive-treatment.
10. Ministry of Health Launches 100-day plan to scale up Tuberculosis Treatment among People Living With HIV/AIDS [Internet]. Ministry of Health. 2019 [cited 18/07/2021]. Available from: https://www.health.go.ug/2019/12/02/ministry-of-health-launches-100-day-plan-to-scale-up-tuberculosis-treatment-among-people-living-with-hiv-aids/.

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11. Uganda eHMISUganda's Electronic Health Information System: DHIS2 [Internet]. Ministry of Health. Available from: https://hmis.health.go.ug/dhis-web-commons/security/login.action.
12. Viera AJ. Odds ratios and risk ratios: what's the difference and why does it matter? Southern medical journal. 2008;101 (7):730-4.
13. Thindwa D, MacPherson P, Choko A, Khundi M, Sambakunsi R, Ngwira L, et al. Completion of isoniazid preventive therapy among human immunodeficiency virus positive adults in urban Malawi. The international journal of tuberculosis and lung disease. 2018;22(3):273-9.
14. Gust DA, Mosimaneotsile B, Mathebula U, Chingapane B, Gaul Z, Pals SL, et al. Risk factors for non-adherence and loss to follow-up in a three-year clinical trial in Botswana. PloS one. 2011;6(4):e18435.
15. Alfred A. Determinants of isoniazid preventive therapy uptake among children living with HIV in Njombe, Tanzania 2021.
16. Takarinda K, Choto R, Harries A, Mutasa-Apollo T, Chakanyuka-Musanhu C. Routine implementation of isoniazid preventive therapy in HIV-infected patients in seven pilot sites in Zimbabwe. Public Health Action. 2017;7(1):55-60.
17. Ayele H, Van Mourik M, Bonten M. Predictors of adherence to isoniazid preventive therapy in people living with HIV in Ethiopia. The International Journal of Tuberculosis and Lung Disease. 2016;20(10):1342-7.
18. Yotebieng M, Edmonds A, Patricia L, Wenzi LK, Ndjibu PT, Lusiama J, et al. High completion of isoniazid preventive therapy among HIV-infected children and adults in Kinshasa, Democratic Republic of Congo. AIDS (London, England). 2015;29(15):2055.
19. Tsai AC, Bangsberg DR, Bwana M, Haberer JE, Frongillo EA, Muzoora C, et al. How does antiretroviral treatment attenuate the stigma of HIV? Evidence from a cohort study in rural Uganda. AIDS and Behavior. 2013;17(8):2725-31.
20. Li Z, Morano JP, Khoshnood K, Hsieh E, Sheng Y. HIV-related stigma among people living with HIV/AIDS in rural Central China. BMC health services research. 2018;18(1):1-7.
21. Munseri P, Talbot E, Mtei L, Fordham von Reyn C. Completion of isoniazid preventive therapy among HIV-infected patients in Tanzania. The International Journal of Tuberculosis and Lung Disease. 2008;12(9):1037-41.
22. Shayo GA, Moshiro C, Aboud S, Bakari M, Mugusi FM. Acceptability and adherence to Isoniazid preventive therapy in HIV-infected patients clinically screened for latent tuberculosis in Dar es Salaam, Tanzania. BMC infectious diseases. 2015;15(1):1-8.
23. Jacobson KB, Niccolai L, Mtungwa N, Moll AP, Shenoi SV. “It’s about my life”: facilitators of and barriers to isoniazid preventive therapy completion among people living with HIV in rural South Africa. AIDS care. 2017;29(7):936-42.
24. Olajide O, Okonkwo P, Ajayi O, Adetoye D, Ogunsola O, Ibiloye O, et al. Determinants of Isoniazid Preventive Therapy Completion among People Living with HIV in Oyo and Ogun States, Southwest Nigeria. Journal of Community Medicine and Primary Health Care. 2022;34(1):23-37.
25. Matyanga C, Takarinda K, Owiti P, Mutasa-Apollo T, Mugurungi O, Buruwe L, et al. Outcomes of antiretroviral therapy among younger versus older adolescents and adults in an urban clinic, Zimbabwe. Public Health Action. 2016;6 (2):97-104.
26. Ammassari A, Murri R, Pezzotti P, Trotta MP, Ravasio L, De Longis P, et al. Self-reported symptoms and medication side effects influence adherence to highly active antiretroviral therapy in persons with HIV infection. Journal of acquired immune deficiency syndromes (1999). 2001;28 (5):445-9.
27. Kleeberger CA, Buechner J, Palella F, Detels R, Riddler S, Godfrey R, et al. Changes in adherence to highly active antiretroviral therapy medications in the Multicenter AIDS Cohort Study. Aids. 2004;18(4):683-8.
28. Subedi B, Timilsina BD, Tamrakar N. Perceived stigma among people living with HIV/ AIDS in Pokhara, Nepal. HIV/AIDS (Auckland, NZ). 2019;11:93-103.
29. Steward WT, Herek GM, Ramakrishna J, Bharat S, Chandy S, Wrubel J, et al. HIV-related stigma: adapting a theoretical framework for use in India. Social science & medicine. 2008;67 (8):1225-35.

30. Emlet CA, Brennan DJ, Brennenstuhl S, Rueda S, Hart TA, Rourke SB. The impact of HIV-related stigma on older and younger adults living with HIV disease: does age matter? AIDS care. 2015;27(4):520-8.
31. Kerrigan D, Vazzano A, Bertoni N, Malta M, Bastos FI. Stigma, discrimination and HIV outcomes among people living with HIV in Rio de Janeiro, Brazil: the intersection of multiple social inequalities. Global Public Health. 2017;12(2):185-99.
32. Radcliffe S, Neaigus A, Bernard MA, Shepard C. HIV-related stigma in a New York City sample of adults in outpatient care for HIV infection: a short report. AIDS care. 2015;27(9):1156-61.
33. Fatti G, Mothibi E, Meintjes G, Grimwood A. Antiretroviral treatment outcomes amongst older adults in a large multicentre cohort in South Africa. PloS one. 2014;9(6):e100273.

## Spatio-temporal trends of air quality in Kampala City, 2020–2022

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### Summary

**Background:** Fine particulate matter ($PM_{2.5}$) is among the health damaging air pollutants that pose adverse health risks to humans, with levels >15 µg/m$^3$ being associated with serious health effects. $PM_{2.5}$ has been recommended as the best measure of air quality due to its prevalence in the environment and broad range of health effects. We aassessed the spatio-temporal trends of air quality based on the $PM_{2.5}$ concentrations in Kampala City, January 2020 – June 2022.

**Methods:** $PM_{2.5}$ concentrations generated by Clarity Node Solar-Powered monitors were abstracted from the Clarity dashboard. We computed the 24-hour average $PM_{2.5}$ from January 1, 2020–June 30, 2022 at the city and division levels. Average $PM_{2.5}$ concentrations per hour were compared by hour of the day (midnight – 11pm) to understand the variations in air quality. Seasonal Mann-Kendall statistical test was applied to assess the significance of the observed trends based on Kendall's tau correlation coefficient (r) and p-values.

**Results:** The 24-hour average $PM_{2.5}$ was 59 µg/m$^3$ (24-hourly average range: 18-182 µg/m$^3$ from January 1, 2020–June 30, 2022). High $PM_{2.5}$ concentrations were observed in Kawempe and Central compared to the other divisions. Two $PM_{2.5}$ concentration peaks were observed from 10am–midday (73.2 – 72.9 µg/m$^3$) and 8pm–9pm (73.3–77 µg/m$^3$). Generally, there was a negligible but significant decreasing trend in air quality from January 2020 to June 2022 ($r = -0.27$, $p < 0.001$). Of note, $PM_{2.5}$ increased during April–June quarter throughout all evaluation years [2020 ($r=0.56$, $p=0.006$), 2021 ($r=0.26$, $p=0.030$), and 2022 ($r=0.37$, $p=0.030$)].

**Conclusion:** $PM_{2.5}$ air concentrations in Kampala City exceeded the maximum WHO-recommended levels even in times without vehicle traffic. Studies are needed to identify sources of pollution in Kampala City to develop interventions to improve air quality.

### Introduction

Air pollution, the contamination of air with substances that are harmful to human health, is one of the outstanding health concerns today [1]. It is a silent killer accounting for an estimated 6.67 million premature deaths worldwide [2]. Evidence links air pollution to varied conditions includes ischemic heart disease, stroke, lung cancer, chronic obstructive pulmonary disease, pneumonia, type 2 diabetes, and neonatal disorders. Air pollution has also been associated with many disastrous, but less evidence-based health impacts such as infant mortality, low birth weight, pre-term delivery, mental health conditions, and neurological impairment [3]. Sources of air pollution may be categorized as domestic solid biomass energy uses, exhaust and non-exhaust emissions from vehicles, industrial emissions, and burning of solid waste. According to World Health Organization (WHO) and United States Environmental Protection Agency (EPA), the major health-damaging measurable air pollutants are: particulate matter, ozone, nitrogen dioxide, sulfur dioxide,

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lead, and carbon monoxide.

Particulate Matter (PM) is formed in the atmosphere as a result of chemical reactions between different pollutants, and contains tiny liquid or solid droplets that can be inhaled dependent on their size and cause serious health effects [4]. Particulate matter pollution includes $PM_{2.5}$, extremely fine particles with diameters that are generally 2.5 micrometers or smaller and $PM_{10}$, particles with diameters of 10 micrometers and smaller. Fine particulate matter ($PM_{2.5}$) is among the health damaging air pollutants that pose adverse risks to humans due to its small size and diameter: which easily permit penetration into invasive systems [5]. $PM_{2.5}$ has been recommended as the best measure of air quality due to its prevalence in the environment and broad range of health effects. According to the 2021 World Health Organization Air Quality Guidelines, the 24–hour average targeted safe level of $PM_{2.5}$ is less than or equal to 15 µg/$m^3$ whereas the annual targeted safe level is less than or equal to 5 µg/$m^3$. Long term exposure to unsafe levels of PM2.5 increases the risk of excess mortality from aggravated asthma, chronic obstructive pulmonary disease, lung cancer, stroke, diabetes mellitus, and incidence of maternal and fetal complications among others [6]. According to the Global Burden of Disease report, $PM_{2.5}$ has been greatly attributed to occurrence of 6.4 million premature deaths [2, 3].

Cities are more prone to poor air quality compared to non-urban areas. This is attributed to high population density, exhaust emissions from vehicles and industries, infrastructure construction, open fuel and solid waste burning. Based on the 2021 World Air Quality Report, Kampala was ranked among the cities with polluted air 5 to 7 times higher than the WHO annual targeted “safe” level [7, 8]. Limited evidence has been presented about how $PM_{2.5}$ concentrations is spatially and temporally distributed across Kampala City. Understanding the spatial and temporal distributions of $PM_{2.5}$ concentrations is critical to act as a foundation for Kampala Capital City Authority and other government agencies to implement strategic evidence-based decisions to improve air quality in the city. We assessed the spatio-temporal trends of air quality based on the $PM_{2.5}$ concentrations in Kampala City from January 2020 – June 2022.

## Methods

In December 2019, Kampala Capital City Authority installed Clarity Node Solar-Powered Monitors for outdoor air quality monitoring in all the divisions of Kampala City; Kawempe, Nakawa, Central, Makindye and Rubaga. We conducted a secondary analysis of air quality surveillance data generated by Clarity Node Solar-Powered monitors. We abstracted hourly $PM_{2.5}$ concentrations generated by calibrated clarity node solar powered monitors from January, 2020 – June, 2022 from the Clarity Dashboard.

For spatial distribution, 24-hourly average $PM_{2.5}$ concentrations from January 1, 2020 – June 30, 2022 was computed at the city and division levels. We then used choropleth maps to show the distribution of 24-hour average $PM_{2.5}$ concentrations across the divisions of Kampala City. We used a line graph to show the trend of the hourly average $PM_{2.5}$ concentrations by hour of the day (midnight–11pm) to understand the variations of air quality by hour of the day. We also used a line graph to show the trend of the 24-hour average $PM_{2.5}$ concentrations in Kampala City from January 1, 2020 – June 30, 2022. Seasonal Mann-Kendall (MK) statistical test was applied to assess the significance of the observed trends by quarterly periods. Statistical significance was set at a p-value <0.05.

Approval to conduct this project under the Non-Research Determination criteria was obtained from the U. S. Centers of Disease Control and Prevention (CDC). Administrative clearance to extract $PM_{2.5}$ concentration data from the Clarity Dashboard was obtained from Kampala Capital City Authority (KCCA). All methods were performed in accordance with the Approval and Administrative Clearance.

## Results

### Variations of $PM_{2.5}$ concentrations by hour of the week, January 2020–June 2022

Two $PM_{2.5}$ concentration peaks were observed throughout the day (Figure 1). The first peak was observed between 10am and midday (73.2 – 72.9 µg/$m^3$) whereas the

second peak was observed between 8pm and 9pm (73.3–77 µg/m$^3$).

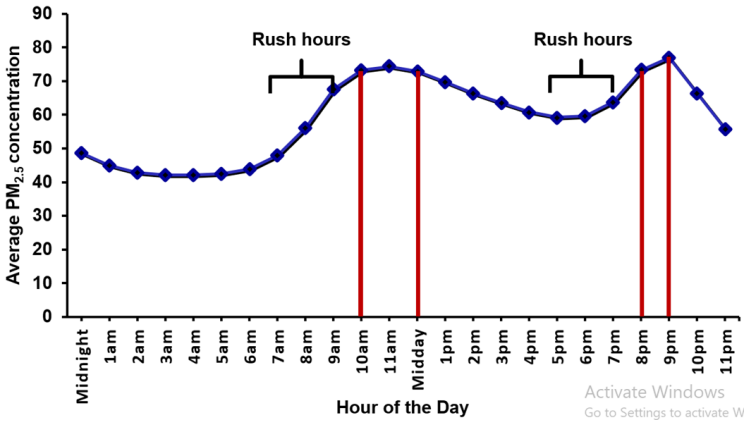


**Figure 1: Average $PM_{2.5}$ concentrations by hour of the day, January 2020–June 2022**

### Spatial distribution of $PM_{2.5}$ in Kampala City, January, 2020–June, 2022

Overall, the 24-hour average $PM_{2.5}$ concentrations was 59 µg/m$^3$ in Kampala City from January, 2020–June, 2022. Despite the general decreasing trend in $PM_{2.5}$ across the biannual periods, high $PM_{2.5}$ concentrations were observed in Kawempe and Central compared to the other divisions (Figure 2).

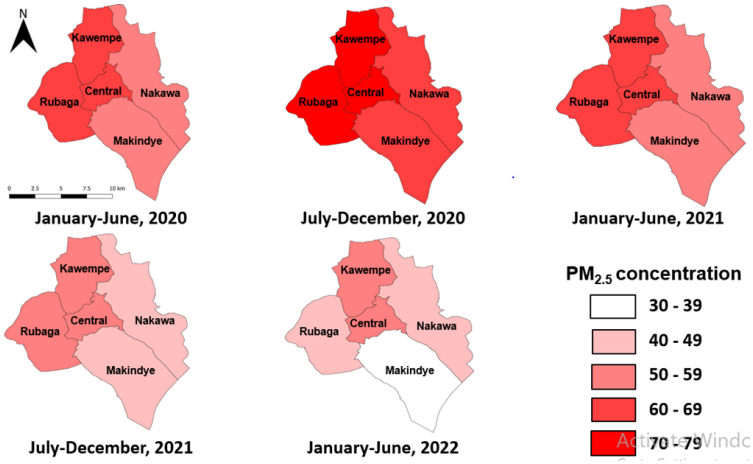


**Figure 2: Spatial distribution of $PM_{2.5}$ in Kampala City, January 2020–June 2022**

### Trends of $PM_{2.5}$ in Kampala City, January, 2020–June, 2022

There are cyclical variations of $PM_{2.5}$ concentration alternating between 18 µg/m$^3$ and 182 µg/m$^3$ (Figure 3). Based on the correlation coefficient and p-value (r = -0.27, p<0.001), there is a negligible but significant decreasing trend in $PM_{2.5}$ concentrations from January 2020–June 2022. $PM_{2.5}$ increased during April–June throughout all evaluation years [2020 (r=0.56, p=0.006), 2021 (r=0.26, p=0.030), and 2022 (r=0.37, p=0.030)] (Table 1). Another increasing significant trend was observed in October–December, 2020 (r=0.32, p=0.032) (Figure 3).

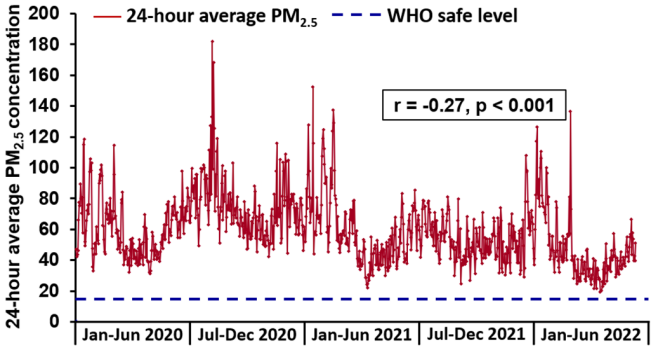


**Figure 3: Trend of $PM_{2.5}$ in Kampala City, January 2020–June 2022**

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**Table 1: Trends of $PM_{2.5}$ concentrations in Kampala City, January 2020–June 2022**

| Quarterly periods | $PM_{2.5}$ concentration range (Minimum – Maximum) | Seasonal Mann-Kendall test statistic (S') | Kendall's tau correlation coefficient | p-value |
|---|---|---|---|---|
| Jan – March 2020 | 32.0 – 118.5 | -68 | -0.27 | 0.051 |
| April – June 2020 | 31.5 – 97.8 | 142 | 0.56 | 0.006 |
| July – Sept 2020 | 49.3 – 106.2 | -48 | -0.19 | 0.054 |
| Oct – Dec 2020 | 42.5 – 116.0 | 80 | 0.32 | 0.032 |
| Jan – March 2021 | 43.7 – 152.1 | -48 | -0.19 | 0.138 |
| April – June 2021 | 22.0 – 82.6 | 66 | 0.26 | 0.030 |
| July – Sept 2021 | 24.7 – 85.2 | -108 | -0.43 | 0.008 |
| Oct – Dec 2021 | 27.1 – 73.0 | -2 | -0.01 | 0.967 |
| Jan – March 2022 | 24.1 – 134.8 | -104 | -0.41 | 0.011 |
| April – June 2022 | 18.8 – 66.1 | 94 | 0.37 | 0.030 |

## Discussion

In this study, we assessed the spatio-temporal trends of air quality based on $PM_{2.5}$ concentrations in Kampala City from January 2020—June 2022. We found that the 24-hour average $PM_{2.5}$ concentration level was 59 µg/$m^3$ (Range = 18-152 µg/$m^3$ from January 2020-June 2022); exceeding the WHO targeted safe level at 15 µg/$m^3$. Two peak hours with high levels of hourly average $PM_{2.5}$ concentrations; (73.2–72.9) and (73.3–77) were observed during morning (10am–midday) and evening (8pm—9pm) hours of the day respectively. We also observed a general decreasing trend in the $PM_{2.5}$ concentration indicating slight improvement in air quality in Kampala City.

High $PM_{2.5}$ concentrations reported in this study coincide with a longitudinal study which reported relatively high levels of 24-hourly average $PM_{2.5}$ at 47 µg/$m^3$ (±29) [9]. Another longitudinal study across selected urban centers in Southern, Eastern, and Central Uganda showed that the 24-hourly average $PM_{2.5}$ varied widely between 34 and 107 µg/$m^3$ [10]. A pilot cross sectional spatial assessment conducted in Kampala City reported 24-hourly average $PM_{2.5}$ concentration at 138.6 µg/$m^3$ [11]. Ground assessments revealed that poorer air quality was observed in Kampala compared to Nairobi and Addis Ababa [12]. Regardless of the varying levels of the 24-hour average $PM_{2.5}$ concentrations, there is unhealthy air quality evidenced by $PM_{2.5}$ concentration exceeding the targeted safe level.

An observation of two $PM_{2.5}$ concentration peaks at specified times of the day coincides with study findings from 3,110 sites across the world which showed that $PM_{2.5}$ concentrations are higher in the morning (7:00-10:00 hrs) and evening (21:00-23:00 hrs) [13]. Air quality monitoring data generated by the Beta Attenuation Monitor (BAM) 1022 showed two $PM_{2.5}$ peaks correspondingly registered at 08:00 hrs (61.3µg/$m^3$) and 23:00 hrs (71.2 µg/$m^3$) in the morning and evening hours in Kampala City [14]. Average circadian variations also showed twice-daily $PM_{2.5}$ peaks early in the morning (06:00 to 08:00) and later in the evening (18:00 to 19:00) across 11 cities in Sub-Saharan Africa [9]. The morning and evening peak $PM_{2.5}$ concentrations are highly attributed to thermal inversion and automobile traffic hours. $PM_{2.5}$ concentrations during these traffic rush hours indicating that traffic emissions could be speculated among the biggest contributors of air pollution. The second peak in the evening is also impacted by the decrease in the planetary boundary layer, which increases the dispersion of $PM_{2.5}$ concentrations to the ground level [12].

Despite the observed decreasing trend, the high $PM_{2.5}$ concentrations observed in Kawempe and Central divisions could be attributed to divisions having many informal settlements, food businesses

which use biomass fuel for cooking and small-scale industries which may not be complying to the emission inventory regulatory guidelines. However, the reasons for the general observed decreasing trend are unknown. It is possible that there could have been behavioral changes and less traffic on the roads that led to improved air quality over time, which may or may not be related to the COVID – 19 pandemic. Furthermore, the difference observed across the quarterly periods could also be attributed to meteorological parameters of rainfall density, humidity, temperature, wind speed, and atmospheric mixing layer height.

### Study limitations

Three out of the 25 air quality monitors were non-functional for 4 months implying missing $PM_{2.5}$ concentration data during the affected period. This could have led to underestimation or overestimation of the air quality levels during the affected months and overall assessment period.

Conclusion

We found unhealthy air quality evidenced by $PM_{2.5}$ concentration exceeding the WHO targeted safe level even during times of less traffic and economic activities in Kampala City. Furthermore, there was a slight improvement in air quality evidenced by the decreasing $PM_{2.5}$ concentration trend from January 2020 to June 2022. However, the reasons for the observed decreasing trend are unknown. It is possible that there could have been behavioral changes and less traffic on the roads that led to improved air quality over time. Ultimately, there is need to prioritize the implementation of interventions aimed at improving air quality in Kampala city. Based on this evidence, the Kampala Capital City Clean Air Action Plan with interventions spanning from individual responsibility to roles of different stakeholders towards improving air quality in the city was developed. Initiatives to improve air quality cannot be confined to only Kampala Capital City Authority; hence the need for multi-sectoral collaboration to achieve the mandate of the Kampala Capital City Clean Air Action Plan. It is also important to conduct studies to understand the major contributing factors to poor air quality in this city.

### Conflict of interest

The authors declare that they had no conflict of interest.


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### References


1. IHME, HEI, and UBC, Institute for Health Metrics and Evaluation, Health Effects Institute, University of British Columbia. State of Global Air; Global Health Impacts of Air Pollution. Available from: https://www.stateofglobalair.org/health/global. Accessed on: 28th May 2022. 2020.
2. Murray, C.J., et al., Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet, 2020. 396(10258): p. 1223-1249.
3. World_Bank, The Global Health Cost of PM2. 5 Air Pollution: A Case for Action Beyond 2021. 2022, The World Bank.

Continued from page 64

4. Manisalidis, I., et al., Environmental and health impacts of air pollution: a review. Frontiers in public health, 2020: p. 14.
5. Zhang, L., et al., Short-term and long-term effects of PM2. 5 on acute nasopharyngitis in 10 communities of Guangdong, China. Science of the Total Environment, 2019. 688: p. 136-142.
6. Sang, S., et al., The global burden of disease attributable to ambient fine particulate matter in 204 countries and territories, 1990–2019: A systematic analysis of the Global Burden of Disease Study 2019. Ecotoxicology and Environmental Safety, 2022. 238: p. 113588.
7. IQAir, 2021 World Air Quality Report: Region & City PM2.5 Ranking. Available from: file:///C:/Users/HP/Downloads/world-air-quality-report-2021-en%20(1).pdf. Accessed on: 9th June 2022. 2021.
8. Petkova, E.P., et al., Particulate matter pollution in African cities. Air Quality, Atmosphere & Health, 2013. 6(3): p. 603-614.
9. Awokola, B., et al., Longitudinal Ambient PM2. 5 Measurement at Fifteen Locations in Eight Sub-Saharan African Countries Using Low-Cost Sensors. Atmosphere, 2022. 13(10): p. 1593.
10. Okure, D., et al., Characterization of Ambient Air Quality in Selected Urban Areas in Uganda Using Low-Cost Sensing and Measurement Technologies. Environmental Science & Technology, 2022. 56(6): p. 3324-3339.
11. Kirenga, B.J., et al., The state of ambient air quality in two Ugandan cities: a pilot cross-sectional spatial assessment. International journal of environmental research and public health, 2015. 12(7): p. 8075-8091.
12. Singh, A., et al., Air quality assessment in three East African cities using calibrated low-cost sensors with a focus on road-based hotspots. Environmental Research Communications, 2021. 3(7): p. 075007.
13. Manning, M.I., et al., Diurnal patterns in global fine particulate matter concentration. Environmental Science & Technology Letters, 2018. 5(11): p. 687-691.
14. Atuyambe, L., et al. The status of air quality in Kampala city, Uganda 2017-2019: Results from the Eastern Africa GEO-Health Hub using a high-tech reference monitor (Beta Attenuation Monitor 1022). in ISEE Conference Abstracts. 2020.

## Increasing trend in all–cause mortality at Regional Referral Hospitals in Uganda during the COVID–19 pandemic (2020–2021)

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**Summary**
**Background:** Testing limitations and inadequate mortality surveillance systems complicate the analysis of data on the true burden of deaths associated with pandemics. One solution is to calculate excess mortality (EM). We described temporal trends in all–cause mortality at regional referral hospitals (RRHs) in Uganda and estimated EM during two years of the COVID19 pandemic compared with five years of historical data (2015–2019).
**Methods:** Monthly aggregate deaths, admissions, and reporting rates data were abstracted for 15 RRHs from the Ministry of Health (MOH) District Health Information System (DHIS2), 2015–2021. We used logistic regression to model temporal trends in all–cause mortality from 2015–2021. We estimated EM, calculated in–hospital deaths/10,000 admissions in 2020 and 2021 and compared them to expected levels using the upper bound of the 95%confidence interval of historical average (2015–2019). Excess deaths were divided by expected

deaths threshold to calculate EM percentage.
**Results:** With reference to 2015, there was a significant increase in all–cause mortality at RRHs that more than doubled in 2021 (AOR=1.46, 95% CI = (1.42–1.50), $p$<0.001) compared to 2020 (AOR=1.20, 95%CI = (1.16–1.23), $p$<0.001). EM at RRHs exceeded expected levels for six months in 2020: April (7%), May (2%), June (25%), August (10%), October (4%), and November (4%). From June to November 2021, EM exceeded expected levels consecutively (57%, 25%, 22%, 1%, 10%, 6%). The highest EM peaks were recorded in both years in June, but the peak in 2021 was double that of 2020. EM exceeded expected levels at 13 (86%) of the 15 RRHs in 2021 and 11 (73%) in 2020.
**Conclusion:** There was a significantly increasing trend in all–cause mortality at RRHs during the study period. EM at RRHs exceeded expected levels during the pandemic period when compared to historical data. MOH can track the progression of epidemics in various regions using EM to inform targeted control measures that avert preventable deaths caused by health system shocks.

## Introduction

When the first case of Coronavirus Disease (COVID–19) was detected in Uganda, the government instituted control measures that comprised strong restrictions on movement (1). These stringent measures have been praised for the slow community transmission of COVID–19 at the beginning of the pandemic in Uganda (2). However, they led to lower utilisation of health services (3) including at Regional Referral Hospitals (RRHs) which were designated as COVID–19 treatment units (CTUs) (4).
Two main indicators were utilised for tracking the COVID–19 pandemic in countries, namely: the number of confirmed cases and the number of deaths (5) as these data are easy to measure and are readily available. However, identifying COVID –19 cases and deaths in Africa was a challenge due to limitations in testing (6) especially at the beginning of the pandemic. In Uganda, testing capacity increased over one year later, in June 2021 when Rapid Diagnostic Test kits (RDTs) became widely available (7). Tracking trends in illness and deaths caused by the virus was complicated by testing that was typically limited to priority groups such as healthcare workers, truck drivers, symptomatic and hospitalised cases as well as their contacts (7). Thus, monitoring the pandemic's trajectory requires the use of alternative analyses to complement available information. The World Health Organization (WHO) recommends monitoring the evolution of the pandemic using the total number of deaths irrespective of cause in order to overcome this challenge (8). Since this method includes not only confirmed deaths by COVID–19, it can help illustrate the direct and indirect impact of the COVID–19 pandemic. During the first wave of COVID-19 in Uganda, cases started peaking in August 2020 with a small peak recorded in September and the highest peak recorded in December 2020. The second wave seen in 2021 peaked in the month of June and with the third wave starting to peak in December 2021. The strain on health systems caused by overwhelming cases of COVID-19 (9) may have contributed to higher overall mortality rates due to a lack of timely and adequate care for other health conditions at healthcare facilities. It is likely that we failed to capture deaths that occurred in the community as a result of patients' fear of getting medical care owing to restrictions in movement (4). Excess deaths (ED) measures the difference in the reported number of deaths in the present year in comparison to historical data from previous years in a given population (8, 10). This can enable planners at Ministry of Health (MOH) to monitor the evolution of the pandemic at various hospitals and the impact of the pandemic control measures (8).
Morbidity and mortality data generated at healthcare facilities are collected and reported continuously through health management information system (HMIS) (11). Mortality data are readily available as they are aggregated on paper forms and entered into an online repository, namely: District Health Information System (DHIS2) (12, 13). Analysing all–cause mortality data can be the first step in detecting monthly excess deaths above normal expected levels (EL). We described temporal trends in all-cause mortality and the magnitude of excess deaths during two years of the COVID–19 pandemic to help quantify the burden of the pandemic in Uganda.

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## Methods

### Study setting

We conducted the study at 15 out of 17 RRHs in Uganda which were mandated to treat COVID-19 patients at the time. The other two hospitals were commissioned as regional referral hospitals in 2021 and 2022 but were excluded from this study since they did not offer regional referral services at the beginning of the pandemic in 2020. According to Uganda's health system, RRHs are regionally located in sub-health zones and presumed to serve a population of 2 million people. They provide referral services as well as specialised medical and surgical care that may not be available at the district level hospitals they supervise (14). At the onset of the pandemic in Uganda, RRHs were mandated to treat and manage COVID–19 patients because of their capacity and availability of services such as intensive care units (ICUs) or high dependency units (HDUs) that were lacking at other health facility levels. The 15 RRHs in this study included: Arua, Naguru, Entebbe, Fort Portal, Gulu, Hoima, Jinja, Kabale, Lira, Masaka, Mbale, Mbarara, Moroto, Mubende and Soroti (Figure 1).

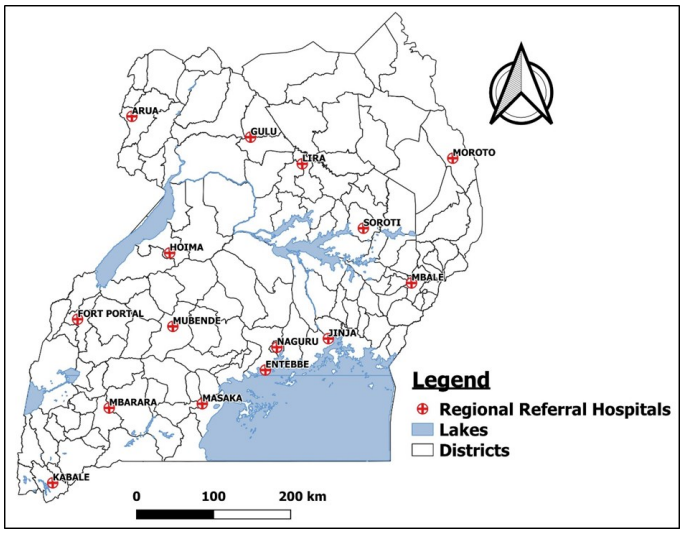


**Figure 1: Location of regional referral hospitals, Uganda, considered for the study**

### Study design and data source

We conducted a descriptive study using routinely collected HMIS data submitted to Ministry of Health electronic database: DHIS2, from 2015 to 2021. It is structured by organisation units with individual health facilities assigned to over 2000 sub–counties and 146 districts in Uganda. Health facilities report monthly data on diseases, commodities, and service delivery through DHIS2. Data are collected through a paper–based system of registers, tally sheets, and monthly data HMIS reporting forms at each health facility. Due to good internet connectivity and availability of infrastructure at RRHs, the collated monthly data are directly entered into the web–based DHIS2 (13). The software captures and remotely stores facility–level data by month and can generate quarterly or yearly reports by different administrative levels (health facility, district, region). The data entered and stored into the system are available to registered users and other stakeholders through a password protected log–in system (Figure 2).

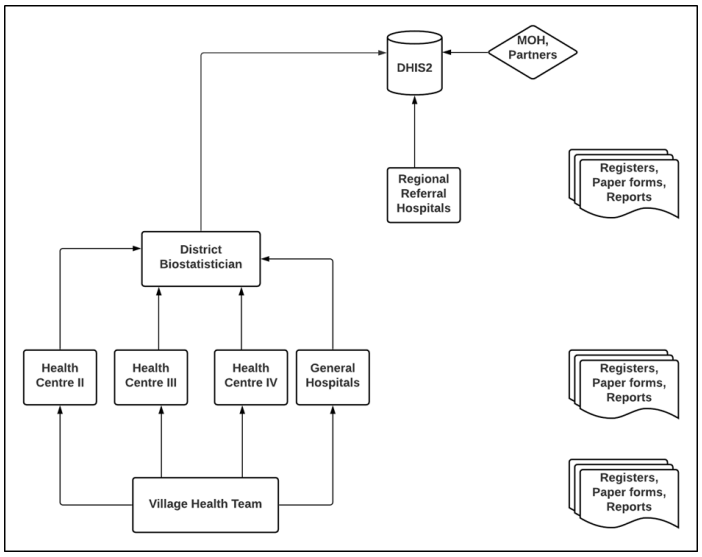


**Figure 2: Data flow to the district health information system (DHIS2)**

### Study variables, data abstraction, and analysis

All–cause mortality data were abstracted from the MOH DHIS2 from 2015 to 2021. In–patient department (IPD) deaths and admissions data are reported on a monthly basis as aggregate numbers using HMIS–108 reporting form. Monthly IPD deaths and admissions data were abstracted for 15 RRHs using the variables total number of deaths and total number of admissions. Reporting rates for the monthly IPD report were also abstracted for the period 2015–2021. Reporting rate refers to the number of reports submitted divided by the number of expected

reports. In Uganda, health facilities are expected to submit one IPD report on a monthly basis. We used logistic regression to model temporal trends in all–cause mortality data from 2015 to 2021 using EpiInfo version 7.2.5.0. We calculated overall death rates as a fraction of IPD admissions per year using data from the 15 RRHs. In this study, death rates were calculated in relation to IPD admissions because these were the patients at risk of dying from healthcare facilities. We used R statistical computing language (15) to visualise average annual deaths, admissions and reporting rates per RRH. We calculated excess deaths in 2020 and 2021 using the five–year historical deaths data (2015–2019) with a Microsoft Excel excess mortality calculator (16) to display lower and upper thresholds for what would be the expected range of deaths over the study period. Excess deaths were calculated by deriving the average of historical deaths data and using the standard error function for confidence intervals. The confidence interval for the average was calculated using the sample standard deviations. Graphs showing the upper and lower limits of historical deaths, admissions, and death rates/10,000 admissions (95% CI) were drawn. Since number of deaths can be affected by changes in admissions for deaths reported in healthcare facilities, we addressed this by calculating excess deaths for in–hospital deaths per 10,000 admissions. In–hospital 2020 and 2021 death rates per 10,000 admissions were compared to the expected level of deaths using the upper bound of the 95% confidence interval of historical average over the 5–years (2015–2019). Excess deaths (ED) percent is expressed as ED count divided by expected deaths threshold.

### Ethical Consideration

We utilized secondary aggregate data reported through Uganda's Ministry of Health DHIS2. Permission to analyse the data was sought from Ministry of Health through the office of the Director General. The study was exempted from IRB approval since this was non–patient level data routinely collected and aggregated in a central database. The office of the CDC director for science determined that this was a non-research project.

## Results

### Temporal trends in death rates at regional referral hospitals in Uganda during the COVID–19 pandemic (2020–2021)

Taking 2015 as the reference year, there was a 2% non–significant increase in death rates at RRHs in 2016 (AOR=1.02, 95%CI = (0.99–1.05), $p$=0.142) which significantly increased in 2017 (AOR=1.24, 95%CI = (1.21–1.27), $p$<0.001) and 2018 (AOR=1.26, 95%CI = (1.23–1.29), $p$<0.001). It then slightly decreased in 2019 (AOR=1.21, 95%CI = (1.18–1.24), $p$<0.001) and 2020 (AOR=1.20, 95%CI = (1.16–1.23), $p$<0.001), and increased again in 2021 (AOR=1.46, 95%CI = (1.42–1.50), $p$<0.001). Overall, there was an increasing trend in death rates at RRHs that more than doubled in 2021 (46%) from levels seen between 2017–2020. This trend was statistically significant from 2017 to 2021 (Figure 3).

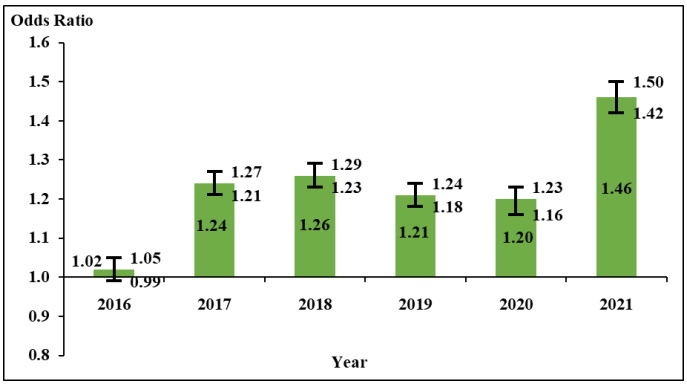


**Figure 3: Temporal trends in death rates at regional referral hospitals in Uganda during the COVID–19 pandemic (2020–2021)**

### Reporting rates for in-patient HMIS form at regional referral hospitals, 2015-2021

With the exception of Entebbe and Fort Portal RRHs, all other 13 hospitals maintained 100% reporting rates during the pandemic period in 2020 and 2021. Overall, reporting rates at RRHs ranged from 93 to 100%.

### Excess mortality during the COVID-19 pandemic (2020-2021)

Overall, in 2020, the number of deaths per 10,000 admissions at RRHs exceeded expected levels for six months: April 7% (n=25/360), May 2% (n=6/364), June 25% (n=86/345), August

Continued from page 68

10% (n=34/341), October 4% (n=15/343), and November 4% (n=13/357). The highest peak in 2020 was observed in June. In 2021, the number of deaths per 10,000 admissions at RRHs exceeded expected levels for six consecutive months: June 57% (n=198/345), July 25% (n=87/355), August 22% (n=75/341), September 1% (n=3/355), October 10% (n=33/343) to November 6% (n=22/357). The month of June had the highest peak in 2021 (57%) which is more than double that observed in 2020 (25%) for the same month (Figure 4).

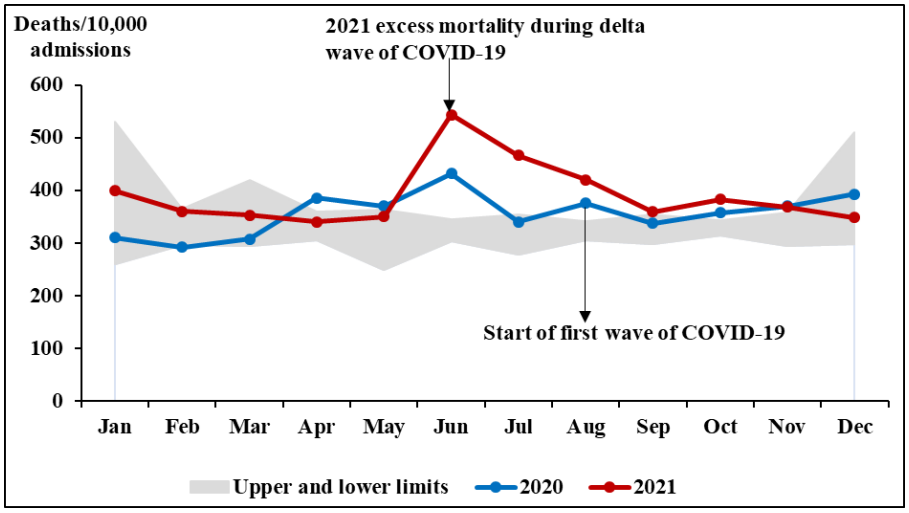


**Figure 4: Overall 2020 and 2021 deaths per 10,000 admissions at RRHs in Uganda by month compared to the upper and lower limits (95% CI) of historical average**

**Excess mortality at regional referral hospitals in Uganda during the COVID–19 pandemic (2020–2021)**

Out of 15 hospitals, death rates exceeded expected levels at 13 (86%) hospitals in 2021 and 11 (73%) hospitals in 2020 compared to pre–pandemic levels (Figure 5a & 5b).

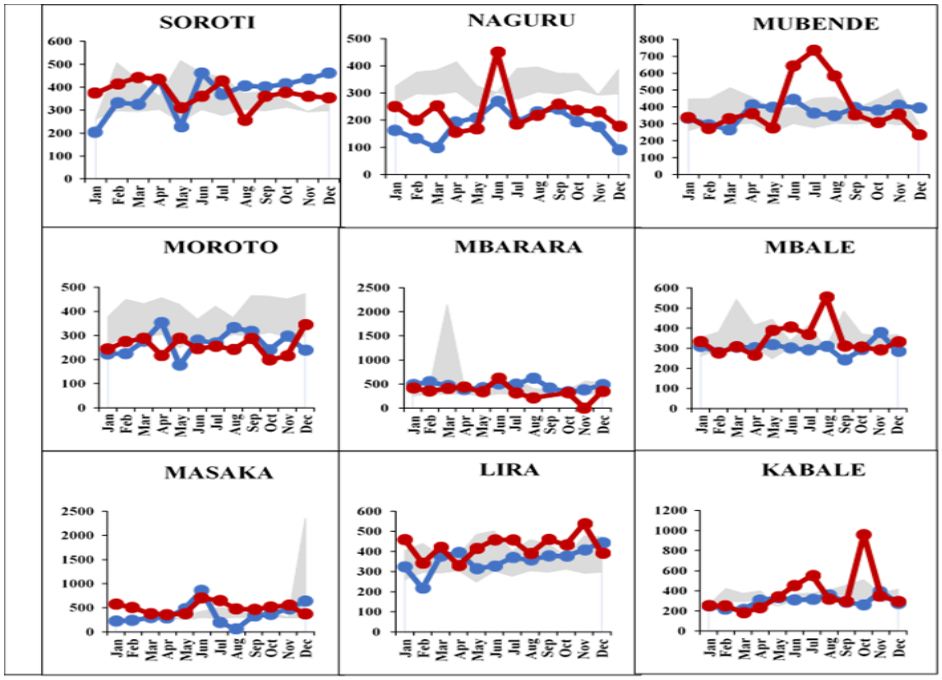


**Figure 5a:2020 and 2021 deaths per 10,000 admissions per regional referral hospital in Uganda by month compared to the upper and lower limits (95% CI) of historical average (2015–2019)**

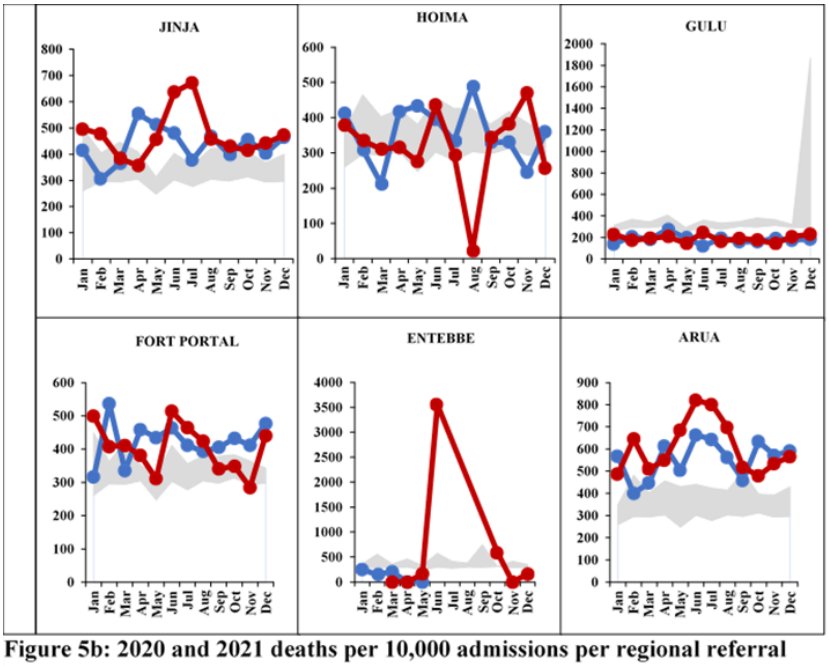


**Figure 5b: 2020 and 2021 deaths per 10,000 admissions per regional referral hospital in Uganda by month compared to the upper and lower limits (95% CI) of historical average (2015–2019)**

## Discussion

We described temporal trends in all-cause mortality and established the magnitude of excess deaths at RRHs during two years of the COVID–19 pandemic to help quantify its burden in Uganda. We found an increasing trend in mortality rates at regional referral hospitals and observed excess mortality during the pandemic period, 2020-2021.

A significantly increasing trend in death rates at RRHs from 2016 to 2021 was identified, implying that even before the pandemic, death rates at RRHs increased but remained steady until 2020 when the pandemic hit. The low rate observed in 2020 may be explained by the low utilisation of health services during the pandemic as evidenced by Uganda's first wave (4, 17) which has been attributed to stringent lockdown measures. The double increase observed in 2021 may be explained by the huge drop in the number of admissions at RRHs. Other studies have shown low healthcare utilisation when pandemic control measures were instituted that may have largely been facilitated by mobility restrictions (3, 4, 18). Even though admissions and deaths relatively declined, the mortality rate greatly increased in 2021. This probably points to a stronger disruption in healthcare services as staff had to be reassigned to CTUs which may have caused delays in providing services to patients admitted in other wards at RRHs (4). MOH should continue to prioritise prompt funding for surge capacity at healthcare facilities to enable health systems manage shocks like those caused by the COVID–19 pandemic.

We found that the number of deaths in 2021 were higher than those in 2020 in the first half of the year taking on an almost similar trend for the last half of the year where they remained below the monthly expected number of deaths in both years. The number of deaths at RRHs fell below expected levels in April and May 2020 which coincides with the period of the first lockdown measures (1). In 2021, the number of deaths at RRHs steadily increased from January to May remaining within expected levels until they exceeded the threshold in June. The second total lockdown measures were instituted on 17 June 2021 (1) which might explain the subsequent drop in number of deaths to within expected levels that was observed for the remainder of the year.

There was a huge drop in IPD admissions in April 2020 and June 2021 which coincide with the first and second lockdowns (1) that caused huge disruptions in movement. Overall, admissions were lower than expected during the two years of the pandemic, more so in 2021. Many people stayed away from healthcare facilities due to lack of transport as well as other factors such as perceived risk of COIVD–19 (4). Even with increase in ambulatory services as mandated by MOH, restrictions on movement had the unintended consequence of reducing access to specialised medical services provided at RRHs. In future, MOH should advise government to institute less mobility restrictive measures so that patients can continue having access to healthcare facilities.

Death rates at RRHs exceeded expected levels for six months in both 2020 (non–consecutive) and 2021 (consecutively). The month of June had the highest peak in both years. However, the peak in 2021 was more than double that observed in 2020 for the same month. This finding points to the first and

second waves of the pandemic in Uganda which peaked in August–September 2020 and June 2021 (17). During the first wave of the pandemic, Uganda had registered only thousands in cases of COVID–19 and few deaths. Most cases were among truck drivers and community transmission was still low. The excess death rate may be explained by the disruption in service utilisation where the number of deaths did not match the decline in admissions. These findings are supported by a study which found that patients were reluctant seeking care due to mobility restrictions and fear of getting COVID–19 from health facilities (4).

The excess deaths observed in this study provide evidence of the gravity of the COVID –19 pandemic in Uganda through its direct and indirect impacts on mortality. Although stringent pandemic control measures reduced the transmission of COVID–19, MOH should be cognisant of strong measures that do not avert preventable deaths. For instance, the guidelines for the continuity of essential health services (19) should be quickly implemented in case of such a contagious outbreak in future.

## Study limitations

We utilized secondary data aggregated on paper reporting forms before being entered into DHIS2, one drawback could be human errors made during tallying of data from health facility registers or during data entry. Similarly, within DHIS2, currently the only dimension of data quality we can utilise is reporting rates. However, this does not directly point to completeness of reporting. Some of the RRHs did not submit reports for some of the months and we cannot with certainty attribute blanks to zero reporting which would be more informative. Lastly, it is possible that patients might have had repeated hospitalizations.

## Conclusion

There was an increasing trend in all-cause mortality at RRHs from 2016 to 2021. Compared to historical data, RRHs recorded excess mortality for six months in both 2020 and 2021. Expanding mortality surveillance to use excess mortality as an indicator can help MOH monitor the mortality burden during epidemics to guide targeted control measures that avert preventable deaths.

## Conflict of interest

The authors declare that they had no conflict of interest.

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## References

1. Ministry of Health. Timeline COVID-19 response Info hub: Ministry of Health 2020 [cited 2022 28/02/2022]. Available from: https://covid19.gou.go.ug/timeline.html.
2. Uganda Radio Network (URN). Parliament makes U-turn, praises Museveni in COVID fight: The Observer,; 2020 [30/03/2022]. Available from: https://observer.ug/news/headlines/64749-parliament-makes-u-turn-praises-museveni-in-covid-fight.
3. Tumwesigye NM, Denis O, Kaakyo M, Biribawa C. Effects of the COVID-19 pandemic on health services and mitigation measures in Uganda: Center for Global Development Washington; 2021.
4. Steven NK, Suzanne NK, Fred M, Rawlance N, Susan K, Rhoda KW. Essential Health Services:Uganda: Exemplars in Global Health; 2022 [05/04/2022]. Available from: https://www.exemplars.health/emerging-topics/epidemic-preparedness-and-response/essential-health-services/uganda.
5. World Health Organisation. COVID□19 Strategic Preparedness and Response (SPRP):Monitoring and Evaluation Framework Ge-

neva: WHO; 2020 [Available from: https://www.who.int/docs/default-source/coronaviruse/who-ncov-me-framework-web.pdf?sfvrsn=656e430f_1&download=true.
6. Colombo S, Scuccato R, Fadda A, Cumbi AJ. COVID-19 in Africa: the little we know and the lot we ignore. Epidemiologia e Prevenzione. 2020;44(5-6 Suppl 2):408-22.
7. Alice N, Suzanne NK, Fred M, Rawlance N, Susan K, Rhoda KW. Testing & Surveillance: Uganda: Exemplars in Global Health
2022 [27/04/2022]. Available from: https://www.exemplars.health/emerging-topics/epidemic-preparedness-and-response/testing-and-surveillance/uganda.
8. World Health Organisation. The true death toll of COVID-19: estimating global excess mortality: WHO; 2022 [Available from: https://www.who.int/data/stories/the-true-death-toll-of-covid-19-estimating-global-excess-mortality.
9. World Health Organisation. Risk of COVID-19 surge threatens Africa's health facilities 2021 [Available from: https://www.afro.who.int/news/risk-covid-19-surge-threatens-africas-health-facilities.
10. Eurostat. Glossary:Excess mortality - Statistics Explained 2020 [Available from: https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Glossary:Excess_mortality.
11. World Health Organisation. Assessment of health facility data quality: Data quality report card – Uganda, 2010–2011. WHO, Department of Health Statistics and Information Systems (HSI) WHO Geneva, Resource Centre and Quality Assurance Department of the Uganda Ministry of Health, Uganda WHO country office; 2011 December 2011.
12. UiO:University of Oslo. DHIS2 Software Overview: University of Oslo; 2022 [28/03/2022]. Available from: https://dhis2.org/overview/.
13. Kiberu VM, Matovu JK, Makumbi F, Kyozira C, Mukooyo E, Wanyenze RK. Strengthening district-based health reporting through the district health management information software system: the Ugandan experience. BMC medical informatics and decision making. 2014;14(1):1-9.
14. Ministry of Health. Uganda Hospital and Health Centre IV Census Survey 2014 2014 [15/07/2021]. Available from: http://library.health.go.ug/publications/health-infrastructure/uganda-hospital-and-health-centre-iv-census-survey.
15. R Core Team (2022). R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria https://www.R-project.org
16. Vital Strategies. Excess mortality calculator for monthly analysis. : NY: Vital Strategies; 2020 [Available from: https://preventepidemics.org/covid19/resources/excess-mortality/.
17. Johns Hopkins University & Medicine. Coronavirus Resource Center: Johns Hopkins University & Medicine; 2022 [28/04/2022]. Available from: https://coronavirus.jhu.edu/region/uganda.
18. Burt JF, Ouma J, Lubyayi L, Amone A, Aol L, Sekikubo M, et al. Indirect effects of COVID-19 on maternal, neonatal, child, sexual and reproductive health services in Kampala, Uganda. BMJ global health. 2021;6(8):e006102.
19. Ministry of Health (MOH). Guidance on Continuity of Essential Health Services during the COVID-19 outbreak Kampala: MOH; 2020 [Available from: https://tciurbanhealth.org/wp-content/uploads/2020/05/MOH-GUIDANCE-ON-BUSINESS-CONTINUITY-000.docx3_.pdf

## Risk factors associated with deaths among hospitalized pregnant women with COVID-19 in Uganda, June 2020-August 2021

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### Summary

**Background:** Pregnant women are at higher risk than other COVID-19 patients for severe COVID-19 disease. Few studies have been done to understand risk factors for death among COVID-19-infected pregnant women in Africa. We investigated risk factors for death among hospitalized pregnant women with COVID-19 in Uganda.

**Methods:** We abstracted demographic and clinical characteristics from files of pregnant women admitted during any trimester with confirmed SARS-CoV-2 infection at eleven hospitals in Uganda. We conducted an unmatched case-control study among hospitalized pregnant women with COVID-19 during June 2020-August 2021; cases were those who died while controls were those who

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recovered and were discharged during the same period. We enrolled 33 cases and 109 controls. We analysed risk factors for death using multivariable logistic regression adjusted for age, trimester, parity, and presence of comorbidities because these factors have previously been associated with COVID death or maternal death.

**Results:** Of 33 cases and 109 controls, 32 (97%) cases and 73 (67%) controls were hospitalised in 2021 (p=0.01). Thirty-two (97%) cases and 85 (78%) controls had COVID-19 symptoms at admission (p=0.04). Nineteen (58%) cases and nine (8%) controls had severe or critical COVID-19 disease at admission (p<0.001). The median length of hospitalisation for cases was 3 days (IQR: 1-6) while that for controls was 7 days (IQR: 4-11) (p<0.001). Odds of seeking care from another medical facility before admission were higher among cases than controls (OR unadjusted= 3.0, 95% CI: 1.1-7.9). Having severe disease at admission increased odds of death ($OR_{adj}$= 16, 95% CI: 3.9 -69), while admission for ≥ 6 days was protective ($OR_{adj}$= 0.2, 95% CI: 0.1- 0.8).

**Conclusion:** Pregnant women with COVID -19 who died had higher odds of being admitted with symptomatic, severe disease compared with those who survived. Earlier facilities cases visited could have delayed referral to the hospitals where they died few days after hospitalisation. Orienting facilities on referral of pregnant women with COVID-19 could improve their clinical outcomes.

## Background

Uganda registered its first case of COVID-19 on 21 March, 2020. By the end of August 2021, nearly 100,000 cases of COVID-19 had been confirmed, with almost 3,000 deaths (1). During the first wave of COVID-19, which lasted from August to December 2020, several healthcare services, including maternal health, were affected; this negatively impacted pregnancy and neonatal outcomes in Uganda (2).

Pregnant women are at high-risk for developing severe COVID-19 due to immune changes that result from pregnancy (3). Studies outside of Uganda have shown that pregnant women with COVID-19 are at greater risk of maternal mortality, hypertensive disorders of pregnancy, severe infections, and intensive care admission compared to those without COVID-19 infection (4).

Other studies have shown risk factors for deaths among hospitalized pregnant women with COVID-19 infection to include smoking, cardiovascular disease, age group under 19 or over 38 years, diabetes, and increased body mass index(5).The above studies have been conducted in high resource countries or outside Africa. However, few studies have been done to understand risk factors for COVID-19 mortality among pregnant women in Africa. The identification of such factors would enable design of interventions to reduce mortality risk when a pregnant woman is found to be infected, such as targeted risk messaging. The total number of pregnant women with COVID-19 in Uganda as of September 2021 was unknown; however, deaths among women with COVID-19 were notified and investigated as part of maternal death surveillance. We investigated risk factors for deaths among pregnant women infected with COVID-19 in Uganda who were hospitalized in the period June 2020- August 2021to inform optimal quality of care hence reduce excess mortality from COVID-19.

## Methods

### Study setting

We conducted the study at eleven hospitals with COVID-19 treatment units in Uganda. The hospitals included included Arua Regional Referral Hospital (RRH), Fort Portal RRH, Hoima RRH, Jinja RRH, Mbale RRH, Mbarara RRH, Mubende RRH, Masaka RRH, St. Mary's Lacor Hospital, Naguru Hospital, and Entebbe Hospital. According to District Health Information Systems 2 (DHIS2) data, these hospitals notified and reviewed deaths of pregnant women with confirmed COVID-19 between June 2020 and August 2021. The DHIS2 is an electronic version of data from the Health Management Information System (HMIS). The HMIS is a paper-based reporting system in which integrated health facility data on several conditions are reported on a weekly and monthly basis. DHIS2 data on maternal deaths notification and review provides summaries of events surrounding deaths among pregnant women including investigations done, comorbidities, interventions, and possible cause(s) of death (6).

### Study design

We conducted an unmatched case-control study and retrospectively extracted hospital data from files of pregnant women admitted with COVID-19 at the eleven hospitals. We defined a case as a pregnant woman who tested positive for COVID-19 by rapid diagnostic testing (RDT) or polymerase chain reaction (PCR) and was hospitalized between June 2020 and August 2021, and died at the health facility. Controls were pregnant women who had a positive COVID-19 test and were admitted during the study period but recovered (were discharged).

The outcome variables in this study were death or discharge from hospital. The independent variables included socio- demographic variables, clinical characteristics, data on seeking care elsewhere, and period of current admission. Socio-demographic variables were age, gestational age, and parity. Clinical characteristics were presence and number of COVID-19 symptoms, disease severity (clinical state at admission), presence of underlying comorbidities including hypertension, delivery status while hospitalised. Gestational age was classified according to the Ministry of Health grouping of trimesters (7). Hypertension was defined as a systolic blood pressure (BP) of ≥140 mmHg and/or diastolic blood pressure of 90 mmHg, pre-hypertension as systolic BP between 120 and 140 mmHg and/or diastolic BP between 80 and 90 mmHg. Length of hospital stay for cases was defined as the number of days from admission date to date of death, while for controls, it was defined as days from admission to discharge dates. Length of hospital stay was dichotomised at the median value with one category being days below the median score and the other being days from the median upwards. Year of admission was used as a proxy for the first and second waves of COVID-19 in Uganda which periods were November-December 2020, and April-June 2021 respectively.

We used a standard questionnaire to retrieve data from patient files at the health facilities for both cases and controls.

### Data analysis

We analysed data using Stata software version 14. We presented data on age groups, gestational age, parity, COVID-19 symptoms, clinical state at admission, presence of comorbidities, delivery status, and period of admission using frequencies and percentages. Age and gestational age were also presented using mean and standard deviation, as well as number of pregnancies carried and number of children. In bivariate analysis, llogistic regression was done for each independent variable and the outcome of variable of death.

Multivariable binary logistic regression was done to assess the association between variables that had a p-value of $p<0.2$ at bivariate analysis and the dependent variable of death. If two variables were highly correlated, only one was included in the final model. Age and gestational age were included in the final model to control for confounding as they are potential confounding factors. A p value cut off of $<0.05$ was used for statistical significance.

### Ethical considerations

A non-research determination form was submitted to US CDC for clearance before the commencement of the study. The Office of the Associate Director for Science, U.S. Centers for Disease Control and Prevention cleared the study. In the districts, we sought permission from the District Health Officers and the executive directors of the health facilities to retrieve data. We obtained verbal consent from hospital records department, COVID-19 treatment unit heads, and maternity unit In charges before retrieving data. During data collection, we used patient identification numbers and initials to protect their confidentiality. We stored the data in password-protected computers.

### Results

#### Socio-demographic and clinical characteristics of hospitalized pregnant women with COVID-19, Uganda, June 2020- August 2021

This study compared pregnant women who were admitted with COVID-19 in ten hospitals and died with those who were discharged. A total of 143 patient's data were reviewed. We identified 33 cases and 109 controls. The mean age of pregnant women in the study was 29 years (± 7) while mean gestational age was 31 weeks (± 7). The average number of times each woman had been pregnant was 3(± 2) and the mean number of children per woman was 2 (±2). The median length of hospitalisation for cases was 3 days (IQR: 1-6) while that for controls was 7 days (IQR: 4-11) ($p<0.001$).

Thirty-two (97%) cases and 73 (67%) controls were hospitalised in 2021. Among 31 case-patients and 105 controls with trimester data, 22 (70%) case-patients and 71 (68%) controls were in the third trimester of pregnancy.

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Thirty-two (97%) case-patients and 85 (78%) controls had symptoms of COVID-19 (p= 0.04). Nineteen (58%) case-patients and nine (8%) controls had severe or critical COVID-19 disease at admission (Table 1).

**Table 1: Socio-demographic and clinical characteristics of hospitalized pregnant women with COVID-19, Uganda, June 2020- August 2021**

| Variable | Total | Cases (died) | Controls (discharged) |
|---|---|---|---|
| | Frequency (%) | Frequency (%) | Frequency (%) |
| **Age group (years) (n=142)** | | | |
| 15-34 | 106 (75) | 27 (82) | 79 (72) |
| 35-42 | 36 (25) | 6 (18) | 30 (28) |
| **Gestational age (weeks) (n=136)** | | | |
| 7 _21 | 43 (32) | 9 (29) | 34 (32) |
| 29-40 | 93 (68) | 22 (71) | 71 (68) |
| **COVID-19 symptoms (n=142)** | | | |
| No | 25 (18) | 1 (3) | 24 (22) |
| Yes | 117 (82) | 32 (97) | 85 (78) |
| **Number of COVID-19 symptoms** | | | |
| 0-1 | 37 (26) | 3 (9) | 34 (31) |
| 2 to 8 | 106 (74) | 30 (91) | 76 (69) |
| **Clinical state (n=142)** | | | |
| Mild-moderate disease | 114 (80) | 14 (42) | 100 (92) |
| Severe and critical disease | 28 (20) | 19 (58) | 9 (8) |
| **Mother delivered (n=142)** | | | |
| No | 97 (68) | 17 (52) | 80 (73) |
| Yes | 45 (32) | 16 (48) | 29 (27) |
| **Year of admission** | | | |
| 2020 | 37 (26) | 1 (3) | 36 (33) |
| 2021 | 105 (74) | 32 (97) | 73 (67) |
| **Systolic blood pressure (n=132)** | | | |
| <120 | 79 (60) | 14 (45) | 65 (64) |
| 120-139 | 42 (32) | 12 (39) | 30 (30) |
| ≥140 | 11 (8) | 5 (16) | 6 (6) |
| **Diastolic blood pressure (n=132)** | | | |
| <80 | 93 (71) | 21 (68) | 72 (71) |
| 80-89 | 27 (20) | 6 (19) | 21 (21) |
| ≥90 | 12 (9) | 4 (13) | 8 (8) |

**Distribution of symptoms of COVID-19 among hospitalized pregnant women at 19 hospitals, Uganda, June 2020-August 2021**

Cough was the most common symptom among both cases (81%) and controls (84%) whereas difficulty in breathing was more than twice as common among cases than controls (81% versus 35%). An equal proportion of cases and controls (38%) had fever (Table 2).

**Table 2: Distribution of symptoms of COVID-19 among hospitalized pregnant women at 19 hospitals, Uganda, June 2020-August 2021**

| Symptom | Total (n=117) | | Cases (n= 32) | | Controls (n=85) | |
|---|---|---|---|---|---|---|
| | Frequency | % | Frequency | % | Frequency | % |
| Cough | 98 | 83 | 26 | 81 | 72 | 84 |
| Difficulty in breathing | 55 | 47 | 26 | 81 | 29 | 34 |
| Fever | 45 | 38 | 13 | 41 | 34 | 40 |
| Chest pain | 40 | 34 | 12 | 38 | 28 | 33 |
| Runny nose | 28 | 24 | 3 | 9 | 25 | 29 |
| Body weakness | 26 | 22 | 2 | 6 | 24 | 28 |
| Headache | 23 | 19 | 4 | 13 | 19 | 22 |
| Sore throat | 18 | 15 | 6 | 19 | 12 | 14 |
| Poor appetite | 12 | 10 | 2 | 6 | 10 | 12 |
| Shortness of breath | 7 | 6 | 4 | 13 | 3 | 3 |
| Chills/ rigors | 6 | 5 | 1 | 3 | 5 | 6 |
| Loss of smell | 6 | 5 | 1 | 3 | 5 | 6 |
| Loss of taste | 5 | 4 | 1 | 3 | 4 | 5 |

### Factors associated with deaths among pregnant women with COVID-19

At bivariate analysis, several factors were associated with deaths among pregnant women. However, after adjusting for maternal age, weeks of gestation, parity, and having comorbidities in the multivariable model, clinical state at admission and length of hospital stay were the factors independently associated with deaths. Nineteen case-patients (58%) and 9 controls (8%) had severe or critical disease at admission ($OR_{adj}$= 16, 95% CI: 3.9 -69). Ten case-patients (30%) were admitted at the hospital for 6 or more days compared to 70 controls (64%) ($OR_{adj}$= 0.2, 95% CI: 0.1- 0.8). Having severe disease at admission increased odds of death, while admission for 6 or more days was protective (Table 3).

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**Table 3: Risk factors for deaths among hospitalised pregnant women with COVID-19, Uganda, June 2020- August 2021**

| Variable | Cases (%) | Controls (%) | uOR (95% CI) | aOR (95% CI) |
|---|---|---|---|---|
| **Clinical state (n=142)** | | | | |
| Mild-moderate disease | 14 (42) | 100 (92) | 1 | 1 |
| Severe and critical disease | 19 (58) | 9 (8) | 15(5.7-40) | 16 (3.9-69) |
| **Length of hospital stay (days) (n=142)** | | | | |
| 0-5 | 23 (70) | 39 (36) | 1 | 1 |
| 6- 149 | 10 (30) | 70 (64) | 0.2(0.1-0.6) | 0.2(0.1-0.8) |
| **Year of admission (n=142)** | | | | |
| 2020 | 1 (3) | 36 (33) | 1 | 1 |
| 2021 | 32 (97) | 73 (67) | 16(2.1-120) | 6.2(0.1-439) |
| **Number of comorbidities(n=142)** | | | | |
| 0 | 28 (85) | 101 (93) | 1 | 1 |
| 1 to 2 | 5 (15) | 8 (7) | 2.3(0.7-7.4) | 2.5(0.2-28) |
| **Age group (years) (n=142)** | | | | |
| 15-34 | 27 (82) | 79 (72) | 1 | 1 |
| 35-42 | 6 (18) | 30 (28) | 0.6(0.2-1.6) | 0.1(0.004-2) |
| **Gestational age (weeks) (n=136)** | | | | |
| 7_28 | 9 (29) | 34 (32) | 1 | 1 |
| 29-40 | 22 (71) | 71 (68) | 1.2(0.5-2.8) | 3.1(0.3-28) |
| **Parity (n=125)** | | | | |
| 0 | 7 (23) | 19 (20) | 1 | 1 |
| 1 to 9 | 23 (77) | 76 (80) | 0.8(0.3-2.2) | 1.2(0.1-10) |
| **Care from other health facility before admission (n=105)** | | | | |
| No | 7 (26) | 40 | 1 | 1 |
| Yes | 20 (74) | 38 | 3.0(1.1-7.9) | 0.1 (0.01-0.8) |
| **COVID-19 symptoms (n=142)** | 1 (3) | 24 (22) | 1 | |
| Yes | 32 (97) | 85 (78) | 9.0(1.2-70) | |
| **Difficulty in breathing (n=117)** | | | | |
| No | 6 (19) | 56 (66) | 1 | |
| Yes | 26 (81) | 29 (34) | 8.4(3.1-23) | |
| **Runny nose (n=117)** | | | | |
| No | 29 (91) | 60 (71) | 1 | |
| Yes | 3 (9) | 25 (29) | 0.2(0.1-0.9) | |
| **General malaise (n=117)** | | | | |
| No | 30 (94) | 61 (72) | 1 | |
| Yes | 2 (6) | 24 (28) | 0.2(0.04-0.8) | |
| **Mechanical ventilation(n=124)** | | | | |
| **Yes** | 2 (11) | 1 (1) | 1 | |
| No | 17 (89) | 104 (99) | 0.1(0.01-1.0) | |
| **Systolic blood pressure (n=131)** | | | | |
| < 140 | 26 (84) | 94 (94) | 1 | |
| ≥140 | 5 (16) | 6 (6) | 3.0(0.9-11) | |
| **Diastolic blood pressure (n=131)** | | | | |
| <90 | 27 (87) | 92 (92) | 1 | |
| ≥90 | 4 (13) | 8 (8) | 1.7(0.5-6.1) | |

## Discussion

This study revealed that pregnant women with COVID-19 who died (cases) were more likely to be admitted with symptomatic, severe disease, and died few days after hospitalization. On the other hand, few pregnant women who survived had severe COVID-19 disease at admission although they spent more days in hospital on average than cases. Having severe disease at admission increased odds of

death, while admission for 6 or more days was protective. However, the admission time is likely to be related to death before that time period. That is, survivors survived for at least 6 days while those who died did not.

A study conducted in Uganda in the Kampala Metropolitan area revealed that 94% of the reported deaths among all persons with confirmed COVID-19 occurred among people who had advanced disease at hospital admission (3). Hantoushzadehet al. (4) studied nine women seven of whom died, and reported a potential for maternal death due to COVID-19 in the second and third trimester; all these women presented with severe COVID-19 at admission, similar to the pregnant women who died in this study.

The finding in this study of difficulty in breathing being a risk factor for death is similar to what was found in Ethiopia where shortness of breath was a significant predictor of death among patients with severe COVID-19 (5). A study in France and Belgium revealed that pregnant women were at higher risk for hospital admission than non-pregnant women because of respiratory distress (6). Pregnancy results in compression of the diaphragm upwards and hormonal changes alter the upper airway tract; additionally, during the third trimester, there is limited expansion of the chest wall and total respiratory compliance reduces (7). Pregnant women diagnosed with COVID-19 should be therefore monitored closely for signs of respiratory distress so that appropriate interventions are promptly instituted.

Age in this study was not a risk factor for death among hospitalised pregnant women. This finding differs from that of Laopaiboonet al. (8) that advanced maternal age above 35 years increases the risk of maternal death and from what Liet al. (9) found that older age was associated with death among patients with COVID -19. In this study, 8% of women had systolic blood pressure ≥ 140 mmHg while 9% had diastolic blood pressure ≥ 90 mmHg which are indicative of hypertension. The prevalence of hypertension in this study is lower than that of 27 % that was found among hospitalised patients in Uganda byElayeeteet al. (10) in an earlier study. Although prevalence of hypertension in this study was similar between cases and controls, in Brazil, hypertension was higher among pregnant women who died than those who had COVID-19 and recovered (11).

## Study limitations

Our findings should be interpreted in line with the following limitations. We could note evaluate clinical characteristics fully because of missing information in patient files such as laboratory reports, weight and height measurements, and information on comorbidities. Although we included patients from eleven hospitals, the sample size of 143 was still small and could have affected the direction of the study outcomes in either direction.

## Conclusion

Women who died were also more likely to have sought care at another medical facility before reaching the admitting hospital for care. This suggests that the earlier facilities these women visited could have delayed to refer them to the hospitals where they eventually died a few days after admission. This possibly explains why they presented with severe disease. This study demonstrates the importance of prompt referral of pregnant women with COVID-19 before disease advances to severe stage. Even amidst lockdown, there should be a strategy that encourages pregnant women to utilise advanced health care services at the earliest opportunity. This optimises the utility of therapeutic interventions.

## Conflict of interest

The authors declare that they had no competing interests.


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## References


1. MOH. Corona Virus Disease (COVID-19) case confirmed Uganda: Ministry of Health; 2021 [Available from: https://www.health.go.ug/covid/category/press-release/page/2/.

Continued from page 78

2. Burt JF, Ouma J, Amone A, Aol L, Sekikubo M, Nakimuli A, et al. Indirect Effects of COVID-19 on Maternal, Neonatal, Child, Sexual and Reproductive Health Services in Kampala, Uganda. medRxiv. 2021.
3. Phoswa WN, Khaliq OP. Is pregnancy a risk factor of COVID-19? European Journal of Obstetrics & Gynecology and Reproductive Biology. 2020;252:605-9.
4. Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, et al. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: the INTERCOVID multinational cohort study. JAMA pediatrics. 2021.
5. Mendez-Dominguez N, Santos-Zaldívar K, Gomez-Carro S, Datta-Banik S, Carrillo G. Maternal mortality during the COVID-19 pandemic in Mexico: a preliminary analysis during the first year. BMC Public Health. 2021;21(1):1-9.
6. MOH. National Technical Guidelines for Integrated Disease Surveillance and Response. Third ed2021.
7. MOH. Goal Oriented Antenatal Care Protocol Uganda: Ministry of Health, Uganda; 2018 [Available from: https://platform.who.int/docs/default-source/mca-documents/policy-documents/operational-guidance/UGA-MN-21-02-OPERATIONAL-GUIDANCE-2018-eng-Goal-Oriented-ANC.pdf.

## Spatial and Temporal Trends of Cervical Cancer, Uganda, 2012-2021: Analysis of Surveillance Data

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### Summary

**Background:** Cervical cancer is the commonest cancer and the leading cause of cancer-related deaths among women in Uganda. The Uganda Ministry of Health (MoH) has adopted a number of strategies to address the burden of cervical cancer, including cervical cancer screening in public health facilities, family planning services and human papillomavirus vaccination for girls aged 9-13 years. However, the impact of these interventions on cervical cancer incidence is not documented. We described the spatial and temporal trends of cervical cancer screening and incidence among women attending health facilities in Uganda from 2012 to 2021 to inform programming by relevant institutions.
**Methods:** We extracted surveillance data for screening and incident cervical cancer cases per month during 2012-2021 by district, region and country. We calculated the screening and incidence rate by district, region and country level using the Uganda Bureau of Statistics population projections of total female population aged 15+ as the denominator. We calculated significance of the trends over time using logistic regression.
**Results**: A total of 439,230 women were screened for cervical cancer from 2017 to 2021. The highest screening rate was in 2020 (1,420/100,000) and the lowest was in 2019 (10/100,000). There was a 378% increase in the screening rate over the years. Nationwide, 14,257 newly diagnosed cervical cancer cases were observed from 2012 to 2021.The peak incidence of cervical cancer was 2,020 (20/100,000) in 2016 and the lowest incidence was 1,143 (5/100,000) recorded in 2021. There was a 32% decrease in the incidence of cervical cancer from 12/100,000 in 2012 to 5/100,000 in 2021 ($p<0.001$). Regionally, there was a significant decrease in the incidence of cervical cancer over the years except in Northern Uganda which had a 2% increase over the years. Central Uganda had the biggest decrease of 8% over the years.
**Conclusions:** Despite the significant increase in cervical cancer screening, fewer cases of cervical cancer were registered in Uganda over the years. Only Northern Uganda had an increase in incidence of cervical cancer over the years. We recommend expansion of screening to cover all eligible female populations and strengthening of strategies to sustain the decline in cervical cancer cases. Further investigations are needed to understand the reasons for the increasing incidence in Northern Uganda.

### Background

In 2020, cervical cancer was the fourth commonest cancer worldwide with 604,000 new cases and 342,000 deaths; the Low and Middle Income Countries (LMICs) bearing the brunt at 84% of new cases and 90% of deaths (1) East Africa had the highest age standardized cervical cancer mortality of 30 per 100,000 and second highest incidence rate of 40/100,000 in 2018 (2). In Uganda, cervical cancer was the commonest cancer among women with an age standardized rate (ASR) incidence of 56.2 per 100,000 and cancer related death rate of 41.4 per 100,000 in 2020 (3).

Most of the cervical cancer cases (at least 95%) are due to infection with human papillomaviruses (HPV) that are transmitted through sexual intercourse (4). Majority of sexually active women are infected with HPV in their lifetime but nearly all clear the infection in a year (5). Unfortunately, 12% of acute HPV infections become persistent and may progress to precancerous lesions or invasive cervical cancer over decades (6). This known cause plus the long natural history of HPV infection allows an opportunity for effective interventions to manage cervical cancer (7). Cervical cancer can be prevented by HPV vaccination. Additionally, screening for cervical cancer aids timely intervention to treat precancerous lesions (8).

Papanicolaou (PAP) smear testing has been used as a screening tool for cervical cancer for more than 50 years in Uganda (9). The Uganda Ministry of Health (MoH) recommends screening with Visual Inspection with Acetic acid (VIA) for all women aged 25-49 years. The screening is scheduled every year for HIV positive women and every 3 years for HIV-negative women (9). However, screening uptake has been low due to limited resources or unwillingness to commit financial resources (10). HPV vaccination was scaled up in Uganda in 2015 after 2 successful pilot studies in 2008 and in 2012, and is now part of the national routine immunisation program (11).

Despite these measures, the incidence of cervical cancer is still unacceptably high. There is limited documentation of trends and geographical distribution of cervical cancer in Uganda. We describe the spatial and temporal trends of cervical cancer screening and incidence among women attending health facilities in Uganda, 2012-2021 to inform programming by relevant institutions including MoH.

## Methods

### Study design, data source, and study population

We analyzed surveillance data on screening and newly diagnosed cervical cancer among women attending health facilities in Uganda, 2012-2021 from the District Health Information System version 2 (DHIS2). DHIS2 is a platform for reporting, analysis, and dissemination of health data reported through the health management information system (12). Cervical cancer screening and diagnosis in Uganda is routinely carried out in family planning clinics in health facilities from Health Centre III (HC III) upwards. However, since 2020, cervical cancer screening is also being carried out in HIV clinics. At the healthy facilities, cervical cancer individual level patient data on screening and diagnosis is recorded in outpatient department registers. The individual level patient data is then summarised in the outpatient department monthly report among other parameters in the report. The reports from HC III facilities are then submitted to the HC IV and then to the district level.
At the district, data for health facility levels III and IV are entered into the DHIS2 by the district biostatistician. Regional and national referral hospitals send data directly to DHIS2. At the MoH headquarters, data from all health facilities are collated and the national performance on each indicator is determined.

The DHIS2 specifically contains data regarding cervical cancer screening, total cases, and newly diagnosed cases. We considered all records of women who tested positive for cervical cancer from 2012–2021 and all women who screened for cervical cancer from 2017–2021 as reflected in the DHIS2. Data for cervical cancer screening was not available before 2017 because it was not being reported at the time.

### Study variables, data abstraction, and analysis

We extracted district, regional, and national data from the DHIS2 on: Newly diagnosed cancer of the cervix cases from the HMIS 108-GC01a in the new DHIS2 (2020-2021) and HMIS 108-6 in the old DHIS2 (2012-2019) and cases of cervical cancer screening done from HMIS 105-MC11a in the new DHIS2 (2020-2021) and LMIS in the old DHIS2 (2012-2019). We also abstracted data

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on outpatient reporting rates from the HMIS 105:01 from the new DHIS2 (2020-2021) and HMIS 105:1 in the old DHIS2 (2012-2019) to show accuracy of the trend. We abstracted data on adult women aged 15+ from the Uganda National Bureau of Standards from 2014–2021. For the years 2013 and 2014, the population was calculated using the national yearly growth rates.

We extracted surveillance data for screening and incident cervical cancer cases per month during 2012-2021 regionally, nationally, and per district. We calculated the screening and incidence rate at the national, regional, and district level. The screening and incidence of cervical cancer was calculated using the population projections of total female population as the denominator for the country, region, or district by the Uganda Bureau of Statistics. We calculated significance of the cervical cancer trends over time using logistic regression in Epi-info version 7. We interpreted the odds ratios as the odds of increase or decrease in the incidence of cervical cancer or cervical cancer screening per 100,000 women per year. Choropleth maps were drawn using QGIS version 3.6.3 to show the regional and district-level distribution of cervical cancer.

## Ethics considerations

Our study utilized routinely collected aggregated program surveillance data that did not have any personal identifiers. We obtained permission to use the HMIS data from the Ministry of Health Resource Centre which has the overall mandate to collect and store health related information. Additionally, the U.S. Centers for Disease Control and Prevention (CDC) Center for Global Health determined our study was non-research whose primary intention was to address public health problems. We stored data in password-protected computers and data was not shared with anyone outside the investigation team.

## Results

### Trends of incidence, screening rate, and outpatient reporting rate of cervical cancer, Uganda, 2012 –2021

Overall, a total of 439,230 women were screened for cervical cancer from 2017 to 2021. The highest screening rate was in 2020 (1,420/100,000) and the lowest was in 2019 (10/100,000). Nationwide, 14,257 newly diagnosed cervical cancer cases were registered from 2012 to 2021. The peak incidence of cervical cancer was 2,020 (20/100,00) in 2016 and the lowest incidence was 1,143 (5/100,000) in 2021. There was a 378% general increase in the screening rate over the years and the outpatient reporting rates also increased across the years. There was an overall decrease in incidence of cervical cancer despite the increase in outpatient reporting rates and screening rates (Figure 1 and Table 2).

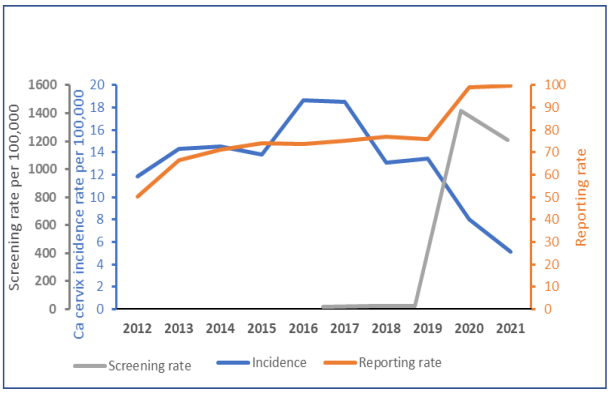


**Figure 1: Trends of incidence, screening rate of cervical cancer, and outpatient reporting rate, Uganda, 2012 –2021**

**Table 1: Significance of the trends of cervical cancer incidence, Uganda,2012 to 2020**

| Year | Incidence | OR | 95% CI | P-Value |
|---|---|---|---|---|
| 2012 | 12 | 1 | | |
| 2013 | 14 | 1.1 | 1.1 - 1.3 | < 0.001 |
| 2014 | 15 | 1.2 | 1.1 - 1.3 | < 0.001 |
| 2015 | 14 | 1.2 | 1.07 - 1.2 | < 0.001 |
| 2016 | 20 | 1.6 | 1.5 - 1.7 | < 0.001 |
| 2017 | 17 | 1.6 | 1.4 - 1.7 | < 0.001 |
| 2018 | 13 | 1.1 | 1.02 - 1.2 | 0.016 |
| 2019 | 13 | 1.1 | 1.05 - 1.2 | < 0.001 |
| 2020 | 8 | 0.7 | 0.62 - 0.74 | < 0.001 |
| 2021 | 5 | 0.4 | 0.4 - 0.5 | < 0.001 |

Regionally, Western region had the highest overall incidence (15.6/100,00) while the Eastern region had the lowest overall incidence (12/100,000). There was a general increase in reporting rate across all regions from 2012 to 2021 (Figure 2).

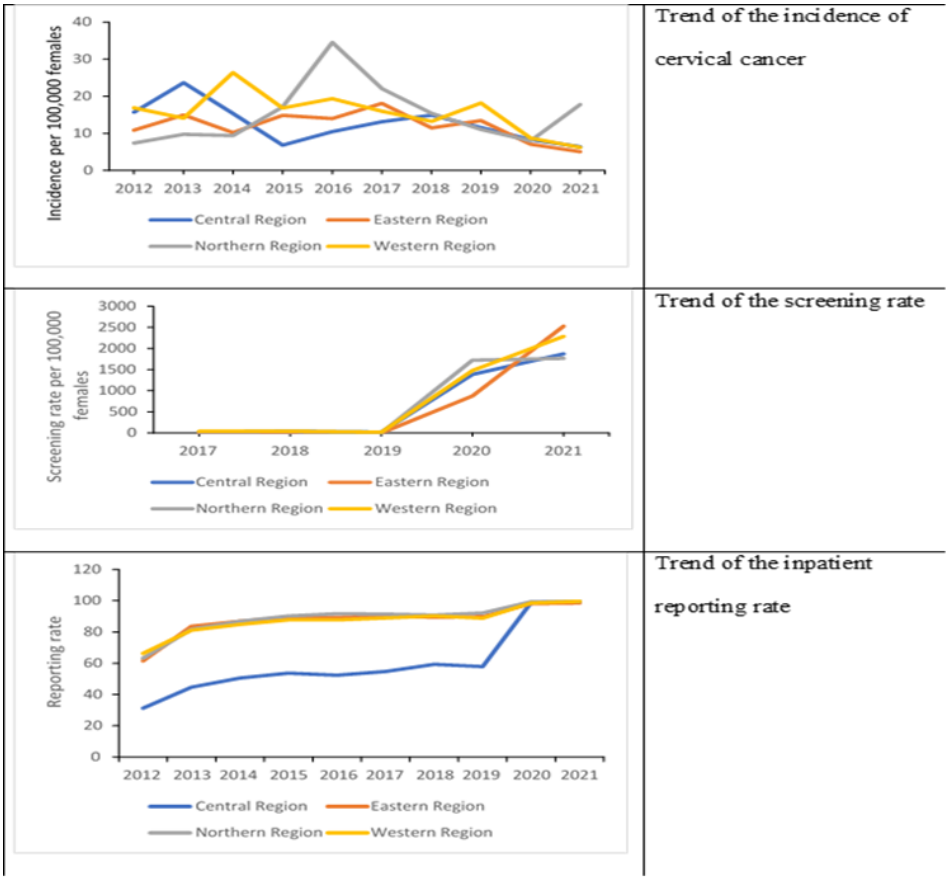


**Figure 2: Trend of incidence, screening for cervical cancer, and inpatient reporting rates by region, Uganda, 2012–2021**

Continued from page 82

Regional trends analysis shows that the incidence in Northern Uganda increased by 2% over the 10 years while the incidence in the other regions of Uganda decreased over time with Central Uganda having the biggest decrease of 8% (Table 2).

**Table 2: Significance of the trends of cervical cancer incidence from 2017 to 2020 at regional level in Uganda**

| Region | Odds Ratio | 95% CI | P-Value |
|---|---|---|---|
| Central Region 2012/2021 | 0.916 | 0.928 – 0.905 | < 0.001 |
| Eastern Region 2012/2021 | 0.945 | 0.957 – 0.934 | < 0.001 |
| Northern Region 2012/2021 | 1.020 | 1.032 – 1.008 | < 0.001 |
| Western region 2012/2021 | 0.924 | 0.934 – 0.914 | < 0.001 |

**Spatial distribution of cervical cancer in Uganda, 2012-2014**

The incidence of cervical cancer was highest in Northern Uganda except for the years 2012 and 2014 where it was highest in Western Uganda. Similarly, Western Uganda had some districts with high incidence of cervical cancer over the years (Figure 3). There were variations of incidence rates over the years by districts nationwide (Figure 3).

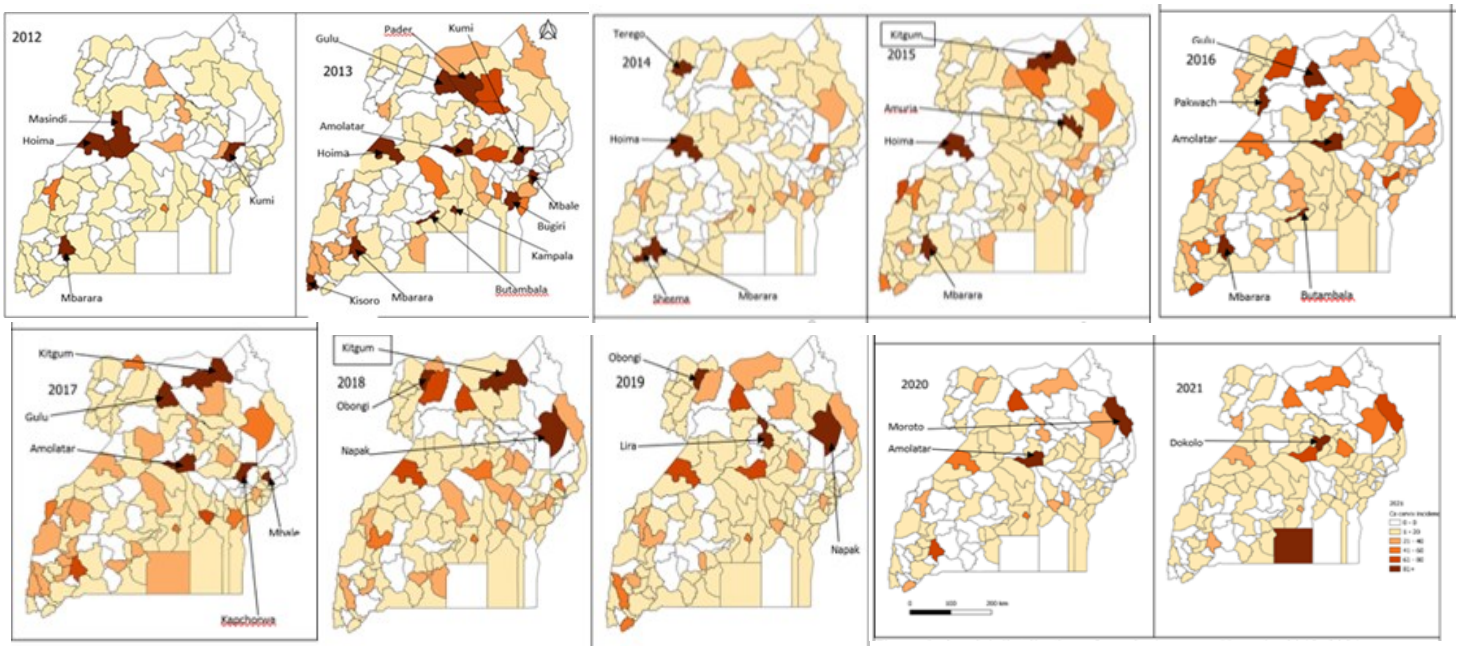


**Figure 3: Spatial distribution of cervical cancer Uganda, 2012-2021**

## Discussion

Our findings showed overall decreasing incidence of cervical cancer in the country from 2012 to 2020. They also showed a significant increase in incidence of cervical cancer from 2012 to 2019 and then a decrease during 2020 and 2021. Regionally, only the Northern region had an increase in the incidence of cervical cancer over the years. The Central region had the most significant decrease in incidence of cervical cancer over time. The trends are similar to many other studies done globally for the past 2 decades that have shown decreasing incidence of cervical cancer (13, 14). However, a study in Kampala by Jedy-Agba et al., showed an increase in incidence of cervical cancer from 1991 to 2015 (15). The reasons for the decreasing trend in Uganda could be due to implementation of safe male circumcision policy since 2010 which encourages all males to be circumcised (16). Although, safe male circumcision was initially introduced as a means of reducing HIV transmission. However, many studies have demonstrated that uncircumcised men have an increased risk of HPV infection which is localised at the glans penis or corona decreasing the risk of HPV infection (17, 18). Furthermore, in 2015, the Government of Uganda under Ministry of Health upscaled HPV vaccination in the whole country as a way of helping to reduce cervical cancer and it can be done in different health facilities for girls aged 9 – 14 years (11).

The initial increase in the incidence of cervical cancer could have been due to increased cervical cancer screening. The initial decline that follows could have been be due to low screening rates: however, the incidence in 2020 and 2021 declines even further despite the increase in screening rates. This could be because of the decline in reporting rates and the lock down and other restrictions on transport and increase in transport charges in 2020 and 2021 may have prevented women who really needed screening services from accessing them. The increase in screening noted in 2020 and 2021 was due to an increase in screening for cervical cancer among eligible women living with HIV (19).

Despite the national decrease in cervical cancer incidence over the years, the Northern region had an increase in the incidence of cervical cancer over time. This is could be because Northern Uganda had the highest reporting rate over time compared to other regions. In addition, Northern Uganda has a high prevalence of childhood marriages (20) which exposes the young girls to sexual intercourse at an early age which increases their risk of cervical cancer. This supports the need for HPV vaccination for eligible girls especially while they are still in school and the need to address childhood marriages as a means of preventing cervical cancer in addition to the existing ways of preventing cervical cancer in the country.

The central region had the most decrease in the incidence of cervical cancer over time. This is contrary to what is expected since the Central region has the highest prevalence for HIV (21) which increases the risk of cervical cancer. However, this could be because of the improvement in Antiretroviral treatment in Uganda which could have led to a decrease in cervical cancer (22). Thus, despite the decrease in the incidence cervical cancer, there is still need to strengthen cervical cancer screening services in the region.

The low incidence of cervical cancer in Eastern Uganda could be due to practice of male circumcision. Studies have showed that women whose male patterners are circumcised are less likely to get infected with HPV. In Eastern Uganda, there is a practice of male circumcision in the Bugishu region. In addition, a study on the impact of safe male circumcision done in Uganda showed that Eastern Uganda had the highest uptake of safe male circumcision (23, 24). Despite the lower incidence in Eastern Uganda, efforts are still needed to reduce cervical cancer.

Despite the current decreasing prevalence of cervical cancer, Uganda still has a long way to reach the WHO target of eliminating cervical cancer by the next generation. Therefore, there is need to strengthen cervical cancer screening in the entire population especially in Northern Uganda. There is also need to emphasize community education about cervical cancer screening to improve detection of cases especially in central Uganda where the incidence is expected to be higher.

### Study limitations

Because DHIS2 data is aggregated and does not represent patient-level data like age, we could not describe the individual characteristics to show the change in cervical cancer incidence with age; yet based on literature, older age has been documented to be associated with cervical cancer. There is poor uptake of screening in Uganda as low as 4.8% in rural areas (9), hence a likely underestimation of the incidence in the country. Eastern Uganda had 0 reporting for cervical cancer screening for the years 2018 and 2019, something unlikely to be true, hence a possible underestimation of the magnitude of cervical cancer in the region and the entire country.

### Conclusions

Despite the significant increase in cervical cancer screening, fewer cases of cervical cancer were registered in Uganda over the years. Only Northern Uganda had an increase in incidence of cervical cancer over the years. We recommend expansion of screening to cover all eligible female populations and strengthening of strategies to sustain the decline in cervical cancer cases. Further investigations are needed to understand the reasons for the increasing incidence in Northern Uganda.

### Conflict of interest

The authors declare that they had no conflict of interest.

### Acknowledgements

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### References

1. Isabirye A, Mbonye MK, Kwagala B. Predictors of cervical cancer screening uptake in two districts of Central Uganda. PLOS ONE. 2020;15 (12):e0243281.
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424.
3. International WCRF. Cervical cancer statistics. 2022.
4. WHO. Cervical cancer. 2020. Available at: https://www.who.int/news-room/fact-sheets/detail/cervical-cancer// [Accessed on 23 Septermber 2022].
5. WHO. Comprehensive cervical cancer control: a guide to essential practice. Geneva. 2014.
6. Adebamowo SN, Olawande O, Famooto A, Dareng EO, Offiong R, Adebamowo CA. Persistent Low-Risk and High-Risk Human Papillomavirus Infections of the Uterine Cervix in HIV-Negative and HIV-Positive Women. Front Public Health. 2017;5:178.
7. Nakisige C, Trawin J, Mitchell-Foster S, Payne BA, Rawat A, Mithani N, et al. Integrated cervical cancer screening in Mayuge District Uganda (ASPIRE Mayuge): a pragmatic sequential cluster randomized trial protocol. BMC Public Health. 2020;20(1):142.

8. WHO. Cervical Cancer: Eliminating cervical cancer. 2020.
9. Nakisige C, Schwartz M, Ndira AO. Cervical cancer screening and treatment in Uganda. Gynecologic oncology reports. 2017;20:37-40.
10. Ndejjo R, Mukama T, Musabyimana A, Musoke D. Uptake of Cervical Cancer Screening and Associated Factors among Women in Rural Uganda: A Cross Sectional Study. PloS one. 2016;11(2):e0149696.
11. Kisaakye E, Namakula J, Kihembo C, Kisakye A, Nsubuga P, Babirye JN. Level and factors associated with uptake of human papillomavirus infection vaccine among female adolescents in Lira District, Uganda. Pan Afr Med J. 2018;31:184.
12. Claire Biribawa RN, Frederick Oporia, Ezekiel Baguma, Lilian Bulage, Denis Okethwangu, Alex Riolexus Ario, Olive Kobusingye. Trends of Injuries due to Gender Based Violence, Uganda, 2012 - 2016, a retrospective descriptive analysis. JIEPH. 2020;3.
13. Zhang X, Zeng Q, Cai W, Ruan W. Trends of cervical cancer at global, regional, and national level: data from the Global Burden of Disease study 2019. BMC Public Health. 2021;21(1):894.
14. Shujuan Lin KG, Simeng Gu, Liuqing You, Sangni Qian, Mengling Tang, Jianbing Wang, Kun Chen, and Mingjuan Jin. Worldwide trends in cervical cancer incidence and mortality, with predictions for the next 15 years. 2021.
15. Jedy-Agba E, Joko WY, Liu B, Buziba NG, Borok M, Korir A, et al. Trends in cervical cancer incidence in sub-Saharan Africa. British journal of cancer. 2020;123(1):148-54.
16. Health Mo. Safe male circumsicion policy. 2010.
17. Hernandez BY, Wilkens LR, Zhu X, McDuffie K, Thompson P, Shvetsov YB, et al. Circumcision and human papillomavirus infection in men: a site-specific comparison. The Journal of infectious diseases. 2008;197(6):787-94.
18. Vanbuskirk K, Winer RL, Hughes JP, Feng Q, Arima Y, Lee SK, et al. Circumcision and acquisition of human papillomavirus infection in young men. Sexually transmitted diseases. 2011;38(11):1074-81.
19. Josephine Connie Ninsiima IL, Evelyn Akello, Tamara Nsubuga- Nyombi, Charity Nuwagaba Kyomugisha, Steven Baveewo, Mina Nakawuka, Simon Muhumuza, Julius Kalamya Namonyo, Rhodah Wanyenze. Roll out of cervical cancer screening and treatment program for HIV-infected women in Uganda: Implications for national scale up. 8th National Quality Improvement Conference2021.
20. UNICEF. Ending Child Marriage and Teenage Pregnancy in Uganda. A Formative Research to Guide the Implemenetation of the National Strategy on Ending Child Marriage and Teenage Pregnancy in Uganda. 2015.
21. MoH. Uganda Population-Based HIV Impact Assessment UPHIA 2016-2017. 2019.
22. Kelly H, Weiss HA, Benavente Y, de Sanjose S, Mayaud P. Association of antiretroviral therapy with high-risk human papillomavirus, cervical intraepithelial neoplasia, and invasive cervical cancer in women living with HIV: a systematic review and meta-analysis. Lancet HIV. 2018;5(1):e45-e58.
23. Svare EI, Kjaer SK, Worm AM, Osterlind A, Meijer CJ, van den Brule AJ. Risk factors for genital HPV DNA in men resemble those found in women: a study of male attendees at a Danish STD clinic. Sex Transm Infect. 2002;78(3):215-8.
24.Morris BJ, Hankins CA, Banerjee J, Lumbers ER, Mindel A, Klausner JD, et al. Does Male Circumcision Reduce Women's Risk of Sexually Transmitted Infections, Cervical Cancer, and Associated Conditions? Front Public Health. 2019;7:4.

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## Rapid Antiretroviral Therapy Initiation following roll out of Point-of-Care Early Infant Diagnosis Testing, Uganda, 2018- 2021

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**Summary**

**Background**: Uganda Ministry of Health recommends a first HIV DNA-PCR test at 4-6 weeks for early infant diagnosis (EID) of HIV-exposed infants (HEIs), immediate results return and initiation of antiretroviral therapy (ART) for HIV-positive infants. In 2019, MOH introduced point-of-care (POC) whole-blood EID testing in 33 health facilities and scaled up to 133 in 2020. We assessed turnaround time for test results and ART linkage before and after implementation of POC testing.

**Methods**: We evaluated EID register data for HEIs at 10 health facilities with POC and high-volume EID testing minimum EID testing volume of 12 infants per month from 2018-2021. At each facility, we abstracted data for 12 months before and after POC rollout. We compared time to sample collection, results receipt, and ART initiation between periods using medians, Wilcoxon rank-sum, and log-rank tests.

**Results**: Data for 4,004 HEIs were extracted, including 1,688 (42%) pre-POC and 2,316 (58%) during POC. Overall, ninety-four percent of infants (3,762/4,004) had a first EID test. Median age at sample collection was 44 (IQR 38-52) days pre-POC and 42 (IQR 38-52) days during POC (p<0.001). Overall 3,762 HEIs tested, 3,667 (97%) had test results. HIV-positive infants' (n=69) median age at sample collection was 92 (IQR 45-120) days pre-POC and 127 (IQR 74-206) days during POC (p=0.03). HIV positivity rate was 1.7% (27/1,610) pre-POC and 2.0% (42/2,057) during POC (p=0.09). For all infants, median days from sample collection to results receipt by infants' caregivers were 29 (IQR 16-54) pre-POC and 1 (IQR 0-28) during POC (p<0.001); among HIV-positive infants, median days were 22 (IQR 4-30) pre-POC and 0 (0-3) during POC (p<0.001). Pre-POC, 0% (0/23) HIV-positive infants started ART on the sample collection day compared to 40% (17/42) during POC; ART linkage by 60 days after sample collection was 91% (21/23) pre-POC and 100% (42/42) during POC (p<0.001).

**Conclusion**: POC testing improved EID results turnaround time and ART initiation for HIV positive infants. Later age at testing among infants who turn HIV-positive suggests missed opportunities in identifying HIV-exposed infants.

While POC expansion could further improve ART linkage and loss to follow-up, there's need to examine barriers surrounding the POC target of initiating ART on the sample collection day.

## Background

Global estimates in 2020 showed that Early Infant Diagnosis (EID) of HIV coverage is still low. Only 68% of HIV- exposed infants (HEIs) were tested within 2 months of age in 2020 (1). Despite this indicator, countries continue to scale up interventions to eliminate mother to child transmission (MTCT) of HIV. Uganda is one of the countries on track towards eMTCT and is being considered for World Health Organization (WHO) certification of pre-elimination status (2).

The standard of care for EID of HIV involves collecting dried blood spots (DBS) from HEIs at health facilities and conducting Polymerase Chain Reaction (PCR) tests on these samples at a specialized reference laboratory. The Uganda Ministry of Health (MOH) standard on EID testing, adopted from the WHO 2015 guidelines, recommends that infants born to HIV positive mothers should have their first PCR test done at 4-6 weeks of age or as soon as the infant is identified thereafter as being born to an HIV-positive mother (3). Also, infants aged <18 months suspected to have HIV or with unknown exposure status should be screened for exposure, tested if exposed, and immediately initiated on anti-retroviral therapy (ART) if HIV-positive (4). This initiation is known as linkage to ART. Providing rapid results decreases loss to follow-up and reduces mortality in HIV-infected children (4).

Although 69,207 (70.8%) HEIs in Uganda were tested for HIV before 18 months of age; only 44% of these got their 1$^{st}$ PCR test within 6 weeks of age between July 2017 and June 2018(2). To facilitate rapid turnaround time for HIV results in infants, in 2019 the Uganda Ministry of Health rolled out point-of-care (POC) EID testing in 33 health facilities across the country and scaled it up to 133 health facilities in 2020. POC testing is a convenient medical testing at the site of client PMTCT & HEI/EID service delivery to increase chances that the mother-infant pairs and clinical team will promptly receive results, thus enabling

Studies in Malawi and Mozambique showed that > 98% of infants that received POC testing got their results and >70% of them were started on ART on the same day they received their results (8, 9). The impact of point-of-care testing on EID turnaround time and linkage to ART among HIV-positive infants in Uganda is unknown. We assessed turnaround time and ART linkage before and after implementation of POC testing.

## Methods

### Study setting

We conducted the study for the period of February 2018- September 2021 at ten health facilities with POC EID testing. These included three regional referral hospitals (RRH) (Fort Portal RRH, Mubende RRH, and Kawempe RRH), four general hospitals (Kiboga Hospital, Lyantonde Hospital, Mityana Hospital, and Kyenjojo Hospital), and 3 health centre IVs (Kyegegwa HC IV, Mpigi HC IV, and Ssembabule HC IV). The health facilities were considered because they reported the highest numbers of HIV exposed infants (HEIs) tested for HIV in 2020, and had a minimum EID testing volume of 12 infants per month according to the District Health Information System version 2 (DHIS 2), the national online health database.

### Study design and data source

We conducted a retrospective evaluation of data for HIV exposed infants at the ten health facilities before and after the implementation of POC EID testing. At each facility, we abstracted data from EID registers for 12 months following the roll out of POC testing at the facility. For comparison, we also abstracted data for 12 months before POC roll out (pre-POC period) when centralized testing at a reference laboratory was the standard of care. According to national guidelines, three DNA PCR tests are conducted for HIV exposed infants. The study utilized results for the first DNA PCR test.

### Study variables and data collection

We used a questionnaire programmed into Kobo collect on tablet computers to collect demographic information including infant's identification number, sex, date of birth, date of registration at the facility, date of

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collection and dispatch of first PCR test, dates results received, dates results given to care giver, ART enrollment status and date, and final EID outcome (discharged negative, referred for ART, lost, died negative, died positive). We used the date of registration of the infant to determine whether they were in the pre-POC period or in the POC period. DNA PCR results turnaround times were defined as the number of days from sample collection to return of results to the clinic and to the caregiver. For turnaround time from sample collection to results receipt at clinic, we used dates of results received at the clinic or date of last clinic visit for censored observations. For turnaround time from sample collection to results receipt by caregiver, we used dates of caregiver results receipt.

A sub-group analysis was conducted among infants that tested positive for HIV to assess turnaround times and the effect of POC testing on time to ART initiation. The primary outcome in this study was time to ART initiation of HIV positive infants. Time to ART initiation was defined as the number of days between dates of sample collection and initiation on ART whereas same day ART initiation was starting ART on the same day of sample collection and results receipt. Positivity rate was defined as the proportion of infants that tested HIV positive out of the number tested and had valid results. The secondary study outcome was time to first DNA PCR sample collection from birth. Only HEIs who had date of result returned to caregiver were included in the analysis for proportion of those with HIV test results or were considered to have received an HIV test result.

**Data management**

Trained research assistants working in the EID clinics at the health facilities completed the questionnaire in Kobo collect app on tablet computers. Data was transferred from the tablet computers to the Kobo server on a daily basis. We downloaded this data from the server into Excel sheets, cleaned and imported it into Stata version 14 for analysis. Duplicate entries were removed in Stata using the exposed infant number and health facility name. HEIs missing dates for a step in the care cascade were excluded in the analysis for that particular step.

**Data analysis**

In univariable analysis, we presented summary statistics for all variables. Categorical variables were presented as frequencies and proportions whereas continuous variables were described using medians and interquartile ranges.

We compared time-to-sample collection, results receipt at the clinic and by the care giver and ART initiation between pre-POC and post-POC periods using the Wilcoxon rank-sum test and Kaplan-Meier curves. The log rank test was used to test for differences in time to ART initiation between the pre-POC period and the POC period as displayed in Kaplan Meier curves.

**Ethical considerations**

A non-research determination form was submitted to US CDC for clearance before the commencement of the evaluation as a requirement. The Office of the Associate Director for Science, U.S. Centers for Disease Control and Prevention cleared this evaluation as non-research. In the districts, we sought permission from the District Health Officers and the executive directors of the health facilities to retrieve data. We obtained verbal consent from health facility EID clinic In-charges before retrieving data. During data collection, we used infant identification numbers and initials to protect their confidentiality. We stored the data in password-protected computers.

## Results

### Testing characteristics of the HIV-exposed infants

This study assessed turnaround time from sample collection to receipt of results by the clinic and care giver, as well as ART linkage before and after the implementation of POC EID testing.

A total of 4,004 HIV exposed infants' data were extracted, 1,688 (42%) from the pre-POC period and 2,316 (58%) from the POC period. Of these, 94% (3,762/4,004) had a first DNA PCR test done and 97% of these (3,667/3,762) had results. Sixty-nine infants tested positive for HIV giving an overall HIV positivity rate of 1.9 % (69/3,667) and was similar in the pre- and post- POC periods. Nine (9/65, 14%) HIV positive infants died while on ART. Sixty-five (94%) HIV positive infants in this study were initiated on ART (Figure 1).

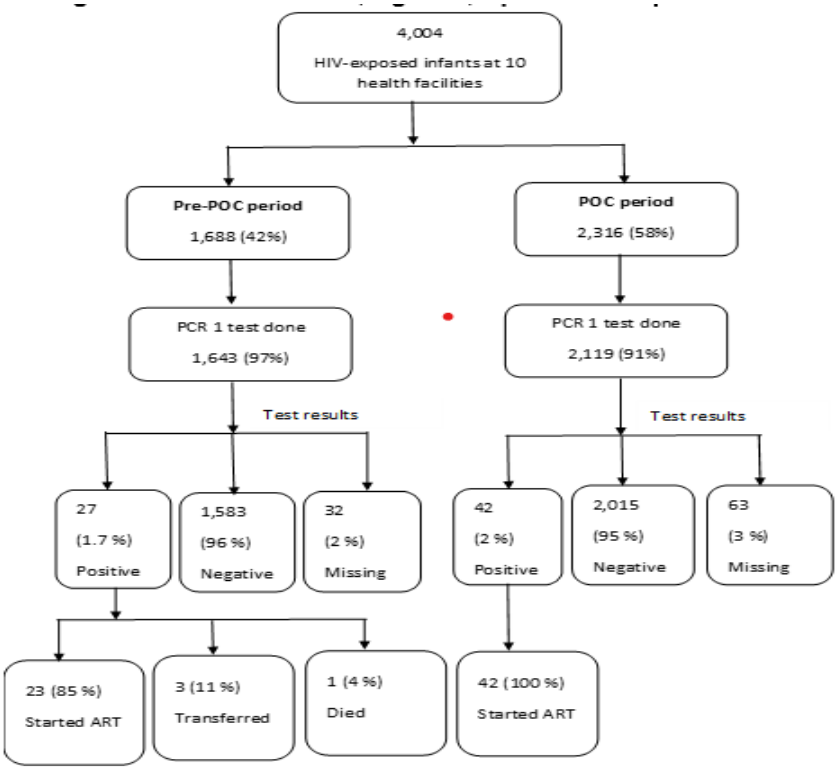


**Figure 1: Flow chart for HEIs' cohorts before and after rollout of point-of-care testing at ten health facilities, Uganda, April 2018- September 2021**

Overall, there was an almost equal proportion of males and females (47% vs 48%) with 83% (3,118/ 3,762) of HEIs being aged less than 60 days (2 months) at the time of sample collection. Thirty percent (1,081/3,615) of the HEIs received their results at the clinic on the same day of sample collection; in the POC period, 44% (924/2,057) of results were returned to the clinic on the same day of sample collection while for the pre-POC period, this proportion was 10% (157/1,610) ($p<0.001$). The proportion of infants' caregivers who received results on the same day of sample collection was 40% in the POC period versus 6% in the pre-POC period ($p<0.001$). The proportion of HEIs caregivers who received their first DNA PCR test results within 28 days of sample collection increased from 50 % in the pre-POC period to 79% in the POC period ($p<0.001$) (Table 1).

The sub-group analysis showed that pre-POC, 0% (0/23) of HIV-positive infants started ART on the sample collection day compared to 40% (17/42) during POC; ART linkage by 60 days after sample collection was 91% (21/23) pre-POC and 100% (42/42) during POC ($p<0.001$) (Table 1).

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**Table 1: Socio-demographic and testing characteristics of HIV exposed infants at ten health facilities pre and post-point of care initiation, Uganda, April 2018-Sep 2021**

| Characteristic | Total Frequency (%) | Pre-POC Frequency (%) | POC Frequency (%) | p-value |
|---|---|---|---|---|
| **Sex (n= 4,004)** | | | | |
| Male | 1,894 (47) | 853 (51) | 1,041 (45) | <0.001 |
| Female | 1,918 (48) | 810 (48) | 1,108 (48) | |
| Missing | 183 (5) | 25 (1) | 167 (7) | |
| **Health facility level (n=4,004)** | | | | |
| Health centre IV | 763(19) | 346(21) | 417(18) | 0.080 |
| Hospital | 1,698(42) | 688(41) | 1,010(44) | |
| Regional referral hospital | 1,543(39) | 654(39) | 889(38) | |
| **Age at sample collection(days) (n=3,762)** | | | | |
| Less than 60 | 3,118(83) | 1,355(82) | 1,763(83) | <0.001 |
| 60-180 | 516(13) | 257(15.6) | 259(12) | |
| 181-365 | 105(3) | 25(2) | 80(4) | |
| >365 | 23(1) | 6(0.4) | 17(1) | |
| **Age** | | | | |
| Median (IQR) | 43(34-51) | 44(38-52) | 42(33-50) | <0.001 |
| **Time from sample collection to result receipt at clinic (days) (n= 3,615)** | | | | |
| same day (0) | 1,081 (30) | 157 (10) | 924 (46) | <0.001 |
| 1 to 7 | 598 (17) | 192 (12) | 406 (20) | |
| 8 to 28 | 1,242 (34) | 789 (50) | 453 (22) | |
| 29 to 60 | 547 (15) | 370 (23) | 177 (9) | |
| > 60 | 147 (4) | 84 (5) | 63 (3) | |
| **Time from sample collection to result receipt by care giver (days) (n= 3,503)** | | | | |
| same day (0) | 865 (25) | 89 (6) | 776 (40) | <0.001 |
| 1 to 7 | 618 (18) | 188 (12) | 430 (22) | |
| 8 to 28 | 835 (24) | 500 (32) | 335 (17) | |
| 29 to 60 | 749 (21) | 496 (32) | 253 (13) | |
| > 60 | 436 (12) | 284 (18) | 152 (8) | |
| **HIV positive infants** | | | | |
| **Age at sample collection(days) (n=69)** | | | | |
| Less than 60 | 18 (26) | 9 (32) | 9 (22) | 0.240 |
| 60-180 | 35 (51) | 16 (57) | 19 (46) | |
| 181-365 | 11 (16) | 2 (7) | 9 (22) | |
| >365 | 5 (7) | 1 (4) | 4 (8) | |
| **Age** | | | | |
| Median (IQR) | 100(58-166) | 92(45-120) | 127(74-206) | 0.030 |
| **Time from sample collection to ART initiation (days) (n=65)** | | | | |
| same day (0) | 17 (26) | 0 (0) | 17 (40) | <0.001 |
| 1 to7 | 15 (23) | 2 (9) | 13 (31) | |
| 8 to 28 | 22 (34) | 13 (57) | 9 (21) | |
| 29 to 60 | 9 (14) | 6 (26) | 3 (7) | |
| > 60 | 2 (3) | 2 (9) | 0 (0) | |
| **Time from result receipt by caregiver to ART initiation (days) (n=65)** | | | | |
| same day (0) | 50 (77) | 19 (83) | 31 (74) | 0.720 |
| 1 to7 | 11 (17) | 3 (13) | 8 (19) | |
| 8 to 28 | 4 (6) | 1 (4) | 3 (7) | |

The overall median time from births to sample collection was 43 days (IQR 34-51) (p<0.001). Median time from sample collection to results receipt by the caregiver decreased from 29 days (IQR 16-54) in the pre-POC period to 1 day (IQR 0-28) during the POC period (p <0.001). The median number of days from birth to sample collection for HIV positive infants was 92 (IQR 45-120) in the pre-POC period while in the POC period, it was 127 (IQR 74-206) days (p=0.03). The median time from sample collection to ART initiation decreased from 23 days (IQR 8-33) in the pre-POC period to 1 day (IQR 0-12) in the POC period (p<0.001) (Table 2).

**Table 2: Turnaround times (days) from sample collection to clinic and caregiver receipt of results before and after roll out of point of care early infant diagnostic testing, Uganda, April 2018- September 2021**

| | n | Median (IQR) days | | | p value |
|---|---|---|---|---|---|
| **All HIV exposed infants** | | **Total** | **Pre-POC** | **POC** | |
| Sample collection to results receipt at clinic | 3,615 | 12(0-26) | 20(11-31) | 1(0-18) | <0.001 |
| Sample collection to results receipt by caregiver | 3,510 | 18(1-35) | 29(16-54) | 1(0-28) | <0.001 |
| Age at result receipt by caregiver | 3,510 | 66(45-93) | 74(57-104) | 50(40-81) | <0.001 |
| **HIV positive infants** | | | | | |
| Sample collection to results receipt at clinic | 69 | 1(0-19) | 18(4-29) | 0(0-3) | <0.001 |
| Sample collection to results receipt by caregiver | 69 | 1(0-23) | 22(4-30) | 0(0-3) | <0.001 |
| Sample collection to ART initiation | 65 | 6(0-25) | 23(8-33) | 1(0-12) | 0.001 |
| Age at result receipt by caregiver | 69 | 117(74-184) | 106(73-157) | 133(75-212) | 0.340 |
| Age at ART initiation | 65 | 135(77-206) | 135(74-178) | 133(77-224) | 0.260 |

The time from sample collection to results receipt at the clinic in the POC period was statistically different from that in the pre-POC period (log rank p<0.001). The time from sample collection to results receipt by care giver in the POC period was statistically different from that in the pre-POC period (log rank p<0.001). The difference between time from sample collection to ART initiation for HIV positive infants before and after introduction of POC at health facilities is statistically significant (log rank p< 0.001) (Figure 2).

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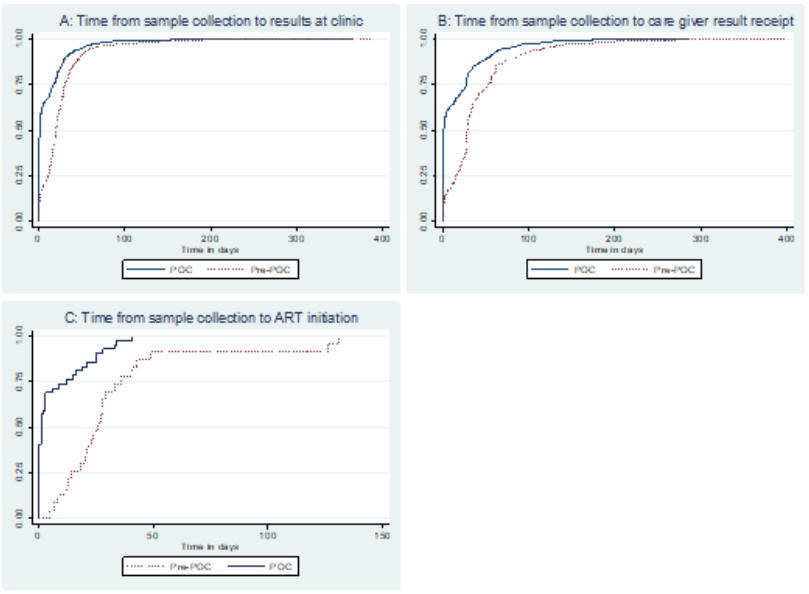


**Figure 2: Kaplan Meier curves showing turn around times from sample collection to clinic receipt of results (A), care giver receipt of results (B), and ART initiation (C) for HIV exposed infants at ten health facilities, Uganda, April 2018- September 2021**

## Discussion

In this evaluation, the novel point-of-care EID technology improved turnaround times from sample collection to results return to the clinic and caregiver, as well as linkage to ART for HIV positive infants. Of all HEIs, 83% had their first DNA PCR test done within 2 months of age. The median test turnaround time from sample collection to results at the clinic decreased from 20 days in the pre-POC period to 1 day in the POC period. The proportion of HIV infected infants was 1.9 % all of whom were linked to ART. All HIV positive infants in the POC period were initiated on art within 60 days after sample collection compared to 91% in the pre-POC period and the difference was statistically significant. This study provides information on performance of point-of-care EID testing technology at public health facilities following it's roll out.

The findings from this study of faster turnaround times and ART initiation rates following the introduction of POC testing are consistent with those from previous studies in other African countries (8-10). We found that 94% of HEIs had a first DNA PCR test done and 83% of them received testing within 2 months of age.

These proportions are greater than the 88% of HEIs that had an EID test and 74% who had their first DNA PCR within 2 months of age reported in the national annual joint AIDs review in 2021(11). This suggests EID program improvement towards attainment of the 95-95-95 2030 UNAIDS fast track target of having 95% of all people living with HIV knowing their status, 95% of all people diagnosed with HIV receiving antiretroviral therapy (ART), and 95% of all people on ART achieving viral suppression.

Notably, infants that tested positive for HIV had their first DNA PCR sample collected at a higher median age of 100 days compared to that of negative infants with a median age of 43 days at sample collection. Later age at testing among infants who turn HIV-positive suggests missed opportunities in identifying HIV-exposed infants.

The proportion of HEIs results returned at the clinic and given to care giver on the same day of sample collection was lower in this study compared to studies elsewhere. This was due to early programmatic challenges reported at the health facilities reported that included stock outs of cartridges and breakdown of the machines, which caused facilities to revert to conventional EID testing during such times.

HIV prevalence in this study of 1.9% is similar to the positivity rate of 1.7% documented in the 2021 Uganda annual AIDS review (11). HIV positivity in the POC period was slightly higher than in the pre-POC period at 2% versus 1.7% respectively. It differs from what Mwenda, Fong (9) found in Malawi where HIV positivity was 5.7% in the POC arm and 3.2% in the baseline arm. 91% in the pre-POC period.

In this study, all HIV positive infants after POC roll out were initiated on ART within 60 days after sample collection compared to 91% in the pre-POC period. This demonstrates progress in ART linkage of HEIs given that in 2021, children aged 0-9 years had the lowest ART coverage of 60% compared to other age groups (11).

In contrast, in Mozambique, 90% of HIV positive infants were initiated on ART by 60 days during POC compared to 13% under conventional testing(8). In Malawi, twice as many HIV positive infants were initiated on ART in the POC arm compared with the baseline arm (9). While POC expansion in Uganda could further improve ART linkage and loss to follow-up, there's need to examine barriers surrounding the POC target of initiating ART on the sample collection day.

## Limitations

This study used secondary data. Some data points were missing due to lack of documentation at some of the health facilities. This could have led to under estimation of the magnitude of the outcomes. In addition, some health facilities reported stock out of cartridge for POC testing and breakdowns of the machines sometimes. During such periods, they reverted to conventional EID testing. This might have led to misrepresentation of the turnaround times in this study.

## Conflict of interest

The authors declare that they had no conflict of interest.


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## References


1. UNAIDS. UNAIDS Data 2020 2020 [Available from: https://www.unaids.org/sites/default/files/media_asset/2020_aids-data-book_en.pdf.
2. UAC. Uganda AIDS Country Progress Report July 2017 to June 2018. Uganda: Uganda AIDS Commission; 2018.
3. MOH. Consolidated Guidelines for Prevention and Treatment of HIV in Uganda. Uganda: Ministry of Health; 2016.
4. WHO. WHO Recommendations on the diagnosis of HIV infection in infants and children. Geneva, Switzerland: World Health Organization; 2010.
5. WHO. HIV diagnosis and ARV use in HIV-exposed infants: a programmatic update. Geneva, Switzerland: World Health Organization; 2018.
6. WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva, Switzerland World Health Organization; 2016.
7. WHO. Updated recommendations on HIV prevention, infant diagnosis, Antiretroviral initiation and monitoring. 2021.
8. Jani IV, Meggi B, Loquiha O, Tobaiwa O, Mudenyanga C, Zitha A, et al. Effect of point-of-care early infant diagnosis on antiretroviral therapy initiation and retention of patients. Aids. 2018;32 (11):1453-63.
9. Mwenda R, Fong Y, Magombo T, Saka E, Midiani D, Mwase C, et al. Significant patient impact observed upon implementation of point-of-care early infant diagnosis technologies in an observational study in Malawi. Clinical Infectious Diseases. 2018;67(5):701-7.
10. Boeke CE, Joseph J, Wang M, Abate ZM, Atem C, Coulibaly KD, et al. Point-of-care testing can achieve same-day diagnosis for infants and rapid ART initiation: results from government programmes across six African countries. Journal of the International AIDS Society. 2021;24(3):e25677.