

# Building a sickle cell disease screening program in the Republic of Uganda: The Uganda Sickle Surveillance Study (US3) with three years of follow-up screening results

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## BACKGROUND

- ❖ The prevalence of sickle cell disease in the Republic of Uganda is higher than in the United States, but no accurate country-wide data exist and no newborn screening program has been established.
- ❖ The Early Infant Diagnosis (EID) program is well-established to analyze dried blood spots (DBS) collected from HIV-exposed infants, i.e., those born to HIV+ mothers. HIV+ infants are identified and placed into specialty care.
- ❖ At the request of the Uganda Ministry of Health, a partnership was developed between Cincinnati Children's Hospital, Makerere University, and the Uganda Central Public Health Laboratories (CHPL) to build local laboratory capacity for testing DBS for sickle cell trait and disease.
- ❖ The Uganda Sickle Surveillance Study (US3) was designed to identify sickle trait or disease in DBS collected throughout the national EID program. After US3, screening commenced in high-burden districts with local capacity built to provide clinical care for affected infants.

## OBJECTIVES

- ❖ To build local capacity for laboratory skills with the following specific objectives:
  - Establish a national sickle cell laboratory with appropriate equipment and reagents;
  - Train local technologists to test all DBS received by the EID program;
  - Analyze the data to determine the country-wide burden and create a geospatial map of sickle trait and disease.
- ❖ To build local capacity to improve clinical management of sickle cell disease with the following specific objectives:
  - Perform educational training workshops in high-burden districts;
  - Teach local healthcare providers about the rationale and benefits of testing at-risk children for sickle cell disease;
  - Initiate public awareness through health fairs and radio announcements to increase screening efforts.

## FORMING THE PARTNERSHIP

- ❖ **Uganda Ministry of Health**
  - Commissioned up-to-date data across the country regarding the sickle cell burden;
  - Prioritized high-burden districts to provide limited resources for sickle cell interventions and improvements through primary care;
  - Offered to leverage health policy agendas and mobilize funding for sustainable sickle cell services.
- ❖ **Uganda Central Public Health Laboratories**
  - Identified local laboratory technologists for training;
  - Procured all reagents with in-country vendors;
  - Launched the US3 study and the follow-on sickle cell testing campaign.



- ❖ **Cincinnati Children's Hospital**
  - Purchased all required laboratory equipment and reagents to launch the US3 project;
  - Provided technical expertise in sickle cell testing methodologies and training, including weekly Skype calls with quality assessments;
  - Conducted remote monitoring and analysis of results to curate data in real-time.
- ❖ **Makerere Univ. College of Health Sciences**
  - Provided an academic home for the sickle screening efforts including local IRB approvals;
  - Facilitated announcement and discussion of the main results at the end of the US3 study;



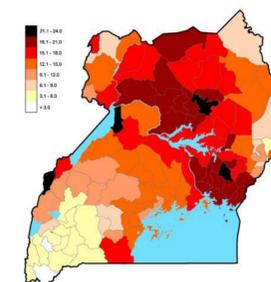
- Performed educational training at high-burden districts to increase screening and to establish local sickle cell clinics at the district hospitals.

## INITIAL US3 SCREENING RESULTS

- ❖ **Uganda Sickle Surveillance Study (US3)**
  - 97,631 samples were tested from 2014-2015;
  - The overall trait prevalence was 13.3% and the disease prevalence was 0.7%;
  - Non-uniform distribution was noted across Uganda with highest burden in central regions.



Ndeezi et al, Lancet Global Health 2016



### ❖ Screening and Training Efforts

- Initiation in selected districts with the highest prevalence of sickle trait and disease;
- Wave 1 (Oct 2014) included Gulu and Lira districts with high populations;
- Wave 2 (April/May 2015) included Dokolo, Jinja, Kampala, Kitgum, Oyam, and Tororo;
- Wave 3 (July/August 2016) included Alebtong, Agago, Amolatar, Apac, Bundibugyo, Lamwo, Luwero, Mityana, Mubende, and Pader.

### ❖ Education and Community Outreach

- Sickle cell education and training was provided for healthcare providers about diagnostic testing and the new CPHL screening program;
- Affected infants and children identified were referred to local district hospitals for specialized care, using teaching guidelines provided by national healthcare experts;
- Program fundraising efforts included an annual Bugando Kingdom Fun Run;



- Outreach screening events;
- World Sickle Cell Day celebration, June 19.

## POST-US3 SCREENING RESULTS

- ❖ **Targeted screening of high burden districts**
  - 112,352 samples were tested from 2015-2018;
  - Prevalence of trait (15.5%) and disease (1.3%) was higher than in the original US3 study.

Regions of Uganda	US3 (1 year) 97,631 samples		Post-US3 (3 years) 112,352 samples	
	Trait (%)	Disease (%)	Trait (%)	Disease (%)
Central 1	1896 (12.9)	69 (0.5)	2497 (13.1)	144 (0.8)
Central 2	1566 (14.1)	94 (0.8)	1646 (14.4)	128 (1.1)
East Central	1306 (19.9)	96 (1.5)	2128 (19.2)	225 (2.0)
Kampala	1835 (13.6)	90 (0.7)	3533 (13.7)	235 (0.9)
Mid Eastern	752 (15.5)	60 (1.2)	1004 (17.4)	115 (2.0)
Mid Northern	2445 (19.2)	160 (1.3)	4067 (18.5)	394 (1.8)
Mid Western	1431 (11.1)	64 (0.5)	848 (14.5)	59 (1.0)
North East	702 (15.8)	46 (1.0)	1100 (16.4)	100 (1.5)
South Western	631 (4.6)	23 (0.2)	135 (6.4)	3 (0.1)
West Nile	415 (13.8)	14 (0.5)	422 (16.5)	19 (0.7)
<b>TOTAL</b>	<b>12979 (13.3)</b>	<b>716 (0.7)</b>	<b>17380 (15.5)</b>	<b>1422 (1.3)</b>

Table 1. Sickle cell screening in US3 and the post-US3 period, with samples collected using targeted screening from the highest burden districts. Results confirm the high burden of sickle trait and disease in Uganda, especially in the East Central and Mid Northern regions.

### ❖ Uganda National Sickle Cell Laboratory

- After local laboratory capacity was achieved, the new Central Public Health Laboratories was expanded to include a large sickle cell lab.
- This lab offers free sickle cell testing to babies, toddlers, and adults.



### ❖ Upcoming Research Objectives

- To obtain follow-up data on babies identified with sickle cell disease;
- To explore the observed co-morbidity between sickle cell disease and HIV;
- To characterize hemoglobin variants identified during sickle surveillance efforts;
- To characterize genetic modifiers of sickle cell disease such as alpha-thalassemia trait or G6PD deficiency, using DNA-based technology;
- To investigate isolated districts with high/low trait prevalence, to determine the influence of environmental, social, and genetic factors.