# HIV-1 Drug Resistance Surveillance in Tanzania

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- ✤ New infections have been reduced to a still high number of 54,000 new HIV infections in 2021
- $\clubsuit$  1.7 million people living with HIV,  ${\sim}86\%$  are under antiretroviral treatment



#### Tanzania HIV Impact Survey (2016-2017)

The switch to WHO-recommended dolutegravir (DGT) based ART

Increase of pretreatment NNRTI resistance in SSA.

Integrase based therapy-  $\rangle$  faster viral suppression, higher barrier to resistance and less side effects compared to NNRTI-based therapy

Since 2017, tenofovir/lamivudine/dolutegravir (TLD) available for 75USD/patient/year in low and middle income countries

 $\rightarrow$  WHO: Programmatic shift to integrase-based therapy

TLD is predicted to curb the number of new HIV infections and the spread of resistance

Antiretroviral Therapy in Tanzania, Treatment naive patients



# There is notable increase in prevalence of pre-ART HIV Drug Resistance to NRTIs, particularly in Eastern Africa



### Gupta et al.,2018

## The presence of inactive NRTI "backbone"

- Available data from RCT indicates that virologic efficacy of dolutegravir monotherapy has a sub-optimal potency, with virologic failures increasing significantly over time
- Certainly, surveillance of pre-existing resistance to the co-administered NRTIs remains particularly important, in resource-limited settings.
- Also, the distribution and dynamics of HIV-1 viral subtypes, matched to drug resistance mutations or changing ART regimens over time has not been described in Tanzania and in many other SSA countries

### **HIV Drug Resistance Surveillance at IHI SINCE 2013**

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AIDS Research and Human Retroviruses

Prevalence of Drug Resistance Mutations and HIV Type 1 Subtypes in an HIV Type 1-Infected Cohort in Rural Tanzania

Pax Masimba, Elimsaada Kituma, [...], and Ingrid Felg



JOURNAL ARTICLE Strengthening HIV therapy and care in rural Tanzania affects rates of viral suppression Alex J. Ntamatungiro Alex J. Ntamatungiro , Lukas Muri, Tracy R. Glass, Stefan Erb, Manuel Batte Hansjakob Furrer, Christoph Hatz, Marcel Tanner, Ingrid Felger, Thomas Kliml

Pre-treatment HIV-1 drug resistance in

Alex J Ntamatungiro X, Juliana Kagura, Maja Weisser, Joel M Francis

Journal of Antimicrobial Chemotherapy, dkac338,

antiretroviral therapy-naive adults in Eastern Africa: a systematic review and meta-analysis

Volume 72, Issue 7

PLOS ONE

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#### BRIEF REPORT

A Case Series of Acquired Drug Resistance-Associated Mutations in Human Immunodeficiency Virus-Infected Children: An Emerging Public Health Concern in Rural Africa

Anna Gamell,<sup>1,2,3</sup> Lukas Muri,<sup>1,2</sup> Alex Ntamatungiro,<sup>3</sup> Daniel Nyogea,<sup>3</sup> Lameck B. Luwanda,<sup>3</sup> Christoph Hatz,<sup>1,2</sup> Manuel Battegay,<sup>2,4</sup> Ingrid Felger,<sup>1,2</sup> Marcel Tanner,<sup>1,2</sup> Thomas Klimkait,<sup>5,a</sup> and Emilio Letang<sup>1,2,3,6,a</sup>

AIDS (London, England) Wolters Kluwer Her

Development of HIV drug resistance and therapeutic failure in children and adolescents in rural Tanzania: an emerging public health concern

Lukas Muri, Anna Gamell, [...], and Emilio Letang

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OPEN ACCESS PEER-REVIEWED BESEABCH ARTICLE

### High failure rates of protease inhibitor-based antiretroviral treatment in rural Tanzania – A prospective cohort study

Rahel E. Bircher 🔯, Alex J. Ntamatungiro 🔯, Tracy R. Glass, Dorcas Mnzava, Amina Nyuri, Herry Mapesi, Daniel H. Paris, Manuel Battegay, Thomas Klimkait 🗱, Maja Weisser 🔛 🖬, on behalf of the KIULARCO study group

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HIV Resistance Test Results for above studies have been used to Guide Therapy for most of the Study Participants The planned Next Generation Sequencing (NGS) platform establishment at IHI (2022), along with capacity building to perform NGS and analysis of NGS HIV sequence data will provide more insights as NGS platform offers greater power and comprehensive genomic coverage to detect novel or rare variants with deep sequencing.





Illumina MiSeq System

## HIV NGS starting research questions..,

<u>Approach</u>: To generate significant number of whole genome sequences of HIV isolates from ART-naive patients.

Transmitted HIV-1 Drug Resistance Dynamics	Biobanked KIULARCO ART-naive patients samples	Use the sequences as background to construct a phylogenetic	<i>Q1.</i> What is the rate change of transmitted HIV-1 drug resistance mutations for over a decade of ART-rollout in Tanzania? and impact of new ART regimen, (e.g. Intergrase inhibitors).
	Country-wide sampling of	tree, and to answer the	<i>Q2.</i> What are the source(s) of new HIV-1 resistant variants- infections in Kilombero and Ulanga antiretroviral Cohort?
	ART-niave	following	
	patients.	questions…	Q3. What is the the relative contribution of Lost of Follow-up
			HIV infected individuals?

# Strength

4 Ongoing prospective HIV cohort with biobank, clinical & demographic data

- **4** Skills to perform HIV NGS and associated bioinformatics
- Almost available NGS platform Ilumina Miseq System
- Exiting collaboration between IHI & the National AIDS Control Program

Ongoing Swiss TPH & IHI collaboration

# Opportunities for Improvement

- Bioinformatic data processing pipelines in support of next-generation sequencing-based HIV drug resistance testing.
- Lelays of Reagents & Consumables, also might be more expensive
- High-performance computing capacity capable of analyzing large NGS data

## Thank you for you attention