October 15, 2024

REVIVE Global Newsletter

From the Project Office

Message on behalf of the REVIVE Trial Steering Committee

The REVIVE trial addresses a critically important scientific question for HIV treatment programs in Africa and globally. There are still many people in these programs who enter care or return to care with advanced HIV disease and profound immunosuppression. These people have a high risk for mortality in the first 6 months after starting or restarting antiretroviral therapy, and we know that bacterial infections are an important contributor. Building on the findings of the REALITY trial, the REVIVE trial will answer the question as to whether azithromycin prophylaxis during the first 28 days of this vulnerable period, added to antiretroviral therapy and standard of care, reduces mortality. To definitively answer this question a very large study involving many countries across Africa is required.

The REVIVE trial commenced recruitment in May 2023, during a vanguard phase. The trial subsequently received funding from the Gates Foundation that will support the full enrolment of the planned 8000 participants. Currently enrolment is occurring at 27 active sites in 6 countries. Across these sites 983 participants have been enrolled – reflecting the hard work and dedication of all involved. There are additional sites in these countries preparing for activation and an additional 8 countries will join REVIVE once they have the necessary approvals in place and training has occurred. With the current sites continuing their excellent work and the new sites joining the trial, we need to increase recruitment across all sites from the current 100 to around 200 participants per month. This will allow the trial to achieve its target of completing enrolment by the end of 2027 and providing a definitive answer to this question – an answer that will have important implications for our HIV programs and our patients.

Finally, I wish to express sincere gratitude to all the REVIVE team members at each of the sites as well as the coordinating teams at PHRI and UCT for the work to date. We look forward to the continued REVIVE journey with you all and its successful completion.

Professor Graeme Meintjes

Chair of the REVIVE TSC

Worth the Read

This article discusses the issue of antiretroviral treatment interruption in the South African context - the magnitude of the problem, reasons for it, its consequences and interventions to address it.

Why people stop taking their HIV treatment and what we can do about it • Spotlight (spotlightnsp.co.za)

REVIVE Focus: Trial Population

We are delighted by the recruitment of all participating sites which is an enormous contribution to the successful completion of REVIVE. Currently around 25 sites are working hard everyday to screen, enroll, and follow-up participants; many more sites are in the pipeline to be activated within the next few months.

We would like to clarify the patient population that the REVIVE trial seeks to enrol. As per protocol, adults with confirmed HIV and CD4 count < 100 cells/mm^3 are potentially eligible. The intention of the REVIVE trial is to evaluate the effect of azithromycin prophylaxis together with antiretroviral therapy (and other components of AHD care) as a strategy to reduce mortality in advanced HIV. We therefore want to restrict the trial population to those who are entering or re-entering ART care or are switching to effective ART. Individuals who are already on effective ART for longer periods (>28 days) are not the focus of the trial and should not be enrolled, even if a recent CD4 count is less than 100 cells/mm^3.

Newsletter (Page 2)

REVIVE Featured: Introducing Verbal Autopsy

We are undertaking an initiative to assess the causes of death among participants with advanced HIV disease (AHD) in the REVIVE trial. We recognize the challenges associated with determining the exact cause of death in our study settings, particularly where access to diagnostic testing is limited or where participants may pass away at home. Furthermore, the variability in death registration across countries makes it difficult to gather consistent data.

To address this, we aim to better characterize the causes of death within the trial, as a significant number of deaths have so far been recorded with unknown or poorly defined causes. While several approaches exist for determining cause of death, many of these are logistically challenging and prohibitively expensive to implement, especially in low-resource settings.

Thus, we aim to perform an in depth cause of death analysis using available medical records and verbal autopsy interviews. A verbal autopsy involves collecting information from caregivers or family members of the deceased using a validated standardised tool to get comprehensive information on the events leading up to death. Our objective is to assess for a treatment effect between the two study arms while also contributing valuable knowledge to the broader understanding of mortality in individuals with AHD in Sub-Saharan Africa.

We will start by implementing this at sites with high reported mortality rates, with the plan to involve all REVIVE sites in due course. We look forward to your participation in this important aspect of our trial.

World AIDS Day 2024

A Tribute to Our Clinical Heroes in the Fight Against HIV/AIDS

As we look ahead to World AIDS Day on December 1st, 2024, we honour the incredible contributions of all clinical staff fighting against HIV/AIDS. Your commitment and compassion are the backbone of this battle, providing care, support, and hope to those affected. Day after day, you go beyond the call of duty, improving health outcomes and transforming lives. We celebrate your courage, resilience, and the profound impact you've made in communities worldwide. Thank you for breaking down stigma, advancing research, and helping to shape a future free of HIV/AIDS.

REVIVE Reminders

- **REVIVE Investigators Meeting**

December 6-9, 2024, in Victoria Falls, Zimbabwe. (Arrival 6 Dec, Meetings 7 & 8 Dec, Departure 9 Dec)

Please register by Friday, October 18, 2024 using the link on the invitation that you received, or advise if you are unable to attend.

If you have any questions, please contact us at REVIVE@phri.ca

- **CD4 Redcap Survey—CD 4 Support**

To best support the ever changing CD4 testing landscape, a Redcap survey was circulated to all PI's at REVIVE sites. The survey till take approximately 5 minutes to complete.

October 15, 2024

Site Spotlight
Dr. Keneth Kananura (PI, Site 301)
Mbarara Regional Referral Hospital, Uganda

A Pillar of Excellence in Clinical Practice, Education, and Research

Dr Keneth Kananura is a highly respected physician currently making a significant impact at Mbarara Regional Referral Hospital, where his expertise and dedication to patient care are evident in both outpatient and inpatient settings. His journey in medicine began at Uganda's premier institution, Makerere University, where he graduated with a Bachelor of Medicine and Bachelor of Surgery (MBChB) in 2014. With a passion for continuous learning and professional growth, Dr. Kananura returned to Makerere to earn his Master of Medicine degree in Internal Medicine in 2022, solidifying his position as a specialist in the field.

Beyond his clinical commitments, Dr Kananura has made substantial contributions to the academic community. He serves as an educator and mentor at Mbarara University of Science and Technology (MUST), where he guides and nurtures the talents of both undergraduate and postgraduate students. His approach to teaching goes beyond textbooks, as he shares real-world insights and encourages critical thinking, preparing his students to excel in the complex and demanding world of medicine.

Dr Kananura's influence extends beyond the hospital and lecture halls. He is currently the site principal investigator for the REVIVE Trial at Mbarara, where he leads a dedicated team in an ambitious research initiative aimed at improving healthcare outcomes. His leadership in this role reflects his dedication to advancing medical knowledge and ensuring that research findings translate into better health practices and policies.

Colleagues and students alike admire Dr. Kananura for his unwavering commitment to excellence, compassionate patient care, and passion for teaching. His multifaceted contributions have not only elevated the standards of care at Mbarara Regional Referral Hospital but have also enriched the medical community through his research and mentorship.

Dr Keneth Kananura's work exemplifies the ideal blend of clinician, educator, and researcher. His dedication to healthcare and passion for improving community health outcomes make him a beacon of inspiration and a role model for aspiring medical professionals across Uganda and beyond.

REVIVE Monthly Seminars

The UCT Project Office is proud to present the last webinars for 2024, addressing subjects of interest to the REVIVE study network.

- October 30th, *Pneumococcal colonization dynamics in health and disease: Tales from an African birth cohort,* presented by Dr Felix Dube— Dept of Molecular and Cell Biology at the University of Cape Town

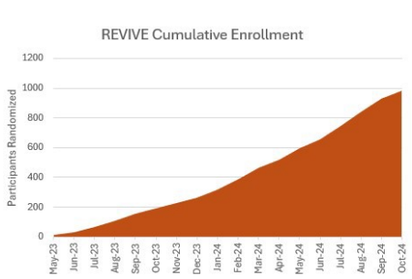
- November 19th, *TB diagnostics in HIV-associated TB,* presented by Dr Bianca Sossen— Research Medical Officer at the University of Cape Town

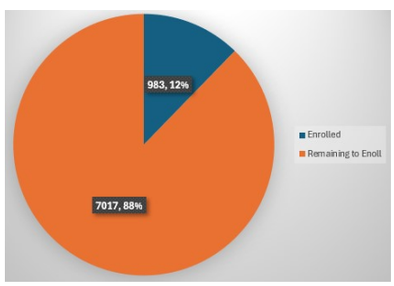
We are inviting you to please e-mail *reviveteam@uct.co.za* would you like to contribute to the library of presenters for 2025, including your suggested topic.

Please look out for the next edition on 15 January 2025

Newsletter (Page 4)

Country	Regulatory Status	Sites			Randomizations	
		Planned	Activated	Enrolling	Last 30 Days	Total
South Africa	Approved	21	6	5	24	299
Sierra Leone	Approved	3	2	2	15	294
Uganda	Approved	4	4	3	20	194
Nigeria	Approved	11	11	8	30	181
Ivory Coast	Approved	3	1	1	1	8
Zambia	Approved	3	3	1	7	7
Republic of Congo	Approved	1	0	0	0	0
Malawi	Pending	3	0	0	0	0
Ghana	Pending	3	0	0	0	0
Ethiopia	Pending	4	0	0	0	0
Mozambique	Pending	1	0	0	0	0
Rwanda	Pending	1	0	0	0	0
Tanzania	Pending	3	0	0	0	0
Total		**61**	**27**	**20**	**97**	**983**





Participating Countries: 14
Participating sites: 61
Enrolling countries: 6
Activated sites: 27
Participant enrollment: 983