January 15, 2025

REVIVE Global Newsletter

From the Project Office

Message on behalf of the REVIVE Trial Steering Committee

Welcome to the first newsletter for 2025!

The end of 2024 saw us achieve two important milestones in the REVIVE trial. The first was the recruitment of the 1,000th patient by Dr. Vivian Kwaghe and the team. Congratulations to all the investigators and study staff who have contributed to this achievement. The second is that in late December we reached the threshold of recruiting 200 patients per month. This is important because we need to reach 200 to achieve our goals by the end of 2027. We now know that it is possible to reach and even surpass 200 per month and we look forward with great confidence to reaching our target.

New initiatives to be rolled out in 2025 include the Verbal Autopsy study which has already commenced piloting in several countries, and the Antimicrobial Resistance study which we hope to extend to all investigators who express an interest in participating.

There is still much work to be done and although we have a solid foundation in place we will need all investigators to help make this trial a success. By the time of the next newsletter, in about 3 months from now, we hope to be approaching the 2,000-mark in our recruitment.

Thanks to all for your wonderful efforts on this critically important trial.

Prof John Eikelboom
Co-PI REVIVE

Investigator's Meeting: Zimbabwe (December 2024)

A highly successful and productive Investigator Meeting was held December 6-8, 2024, in Victoria Falls, Zimbabwe. The meeting was attended by National Leaders, representatives from the trial sites, and members of the Project Office Teams at PHRI and UCT. In total there were 53 sites from 13 countries represented: a total of 65 attendees.

Attendees arrived on the 6th of December and a welcome dinner was held that evening, allowing colleagues to network and share experiences about the trial and clinical practice from across their different countries.

The 7th of December was a full day of presentations and discussion. This included an overview of trial progress including recruitment and baseline characteristics; discussions around enrolment projections, standard of care and retention; and CD4 testing plans. Breakout sessions were held in the afternoon involving 3-4 countries in each session sharing their on-the-ground experience around enrollment strategies, adherence and follow-up, the implementation of standard of care and other challenges. These sessions were extremely useful for the investigators, learning how others had addressed the challenges faced and put in place solutions. Sites that are yet to initiate enrolment were able to benefit from the experiences and lessons from established sites. This was followed by a wider group report- back and then presentations about sub-study plans (AMR and verbal autopsy), followed by the presentation of recognition awards for specific achievements (See Page 2).

The time available on 8th December was dedicated to individual meetings between each team of country investigators and the Project Office to address issues specific to those countries and answer their questions.

There was also time for informal networking and an opportunity to build a sense of a unified team and a common sense of purpose across the REVIVE trial network and for colleagues to get to know one another. The meeting provided an opportunity to reflect on the successes of 2024 (when trial enrolment passed 1000 participants, and many new sites were activated) but also to reflect and plan for the challenge ahead in reaching the enrolment target of 8000 participants.

Members of the REVIVE team left the meeting with a renewed commitment to ensure we arrive at a definitive answer to the key question for HIV programs across Africa that we are addressing in the trial.

Prof Graeme Meintjes
Chair of the REVIVE TSC

IM Awards

Fastest Regulatory Approval and Activation Time

Dr Albert Minga

Site 404 Cote d'Ivoire

1000th REVIVE Participant

Dr Vivian Kwaghe

Site 209 University of Abudja Teaching Hospital Nigeria

Going the Extra Mile to track LTFU Participants

Dr Leigh Wagner (PI) & Dr Shaheed Mathee (Co-PI)

Site 104 Site B Khayelitsha South Africa

Highest Recruitment Rate in Shortest Time since Activation in Sept 2024

Dr Ethel Kamuti

Site 702 (CIDRZ) Matero Clinical Research Site Zambia

Highest Rate of Recruitment

Dr Keneth Kananura

Site 301 Mbarara Regional Referral Hospital Uganda

From the REVIVE PI's & Steering Committee, to all National Leads, Investigators, Site Representatives and Service Providers who travelled from all corners of the globe to attend the Investigators Meeting, your time and effort underlines your commitment to the success of the REVIVE Trial.

Thank YOU!

REVIVE Featured: Anti-Microbial Sub-Study (AMR)

We are delighted to provide an update on the antimicrobial resistance (AMR) sub-study, which is nested in the REVIVE trial and separately funded. As presented at the Investigator Meeting at Victoria Falls, the aim of this sub-study is to understand the epidemiology of AMR in patients with advanced HIV and the possible impact of the azithromycin prophylaxis on the prevalence and patterns of AMR. In addition, biological samples collected as part of this study will improve our understanding of the burden of undetected bloodstream infections and sexual transmitted infections in this population.

Participation in the sub-study is optional for sites and should not affect recruitment for the main trial. The additional work required to participate in the AMR study will be acknowledged by a per-participant fee.

The primary focus of the sub-study is on the assessment of AMR in the gut and upper respiratory tract, which will be assessed through nasopharyngeal and rectal swabs. Investigators who agree to participate in the AMR study can opt out of additional blood and urine collection but are encouraged to participate if possible since these samples will provide important information about other areas of emerging resistance, which is a potential harm of the study intervention.

As of the time of this newsletter, investigators at >40 sites have expressed their interest in participating in the AMR sub-study, which will ensure that we can include enough participants to reliably answer our questions. We will set up calls with all National Leader and Site PIs who expressed their interest in the next weeks. This facilitates discussions about required infrastructure, study specific processes and assessment of site feasibility in detail. Afterwards we provide all relevant documents for ethical approval and support the submission process. This ensures timely activation of sites to contribute to this sub-study.

We are very excited to be moving forward with this important sub-study and look forward to working with many of our investigators. We would be happy to address any questions

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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.

- February 25th, *TB Meningitis: Diagnosis and Management,* presented by Prof Sean Wasserman — REVIVE Co-PI & St George's University of London
- March 25th, *Sample Size Considerations in Clinical Trials,* presented by Prof Shrikant Bangdiwala — Health Research Methods, Evidence and Impact, McMaster University
- April 29th, *CROI Update,* presented by Prof Graeme Meintjes— REVIVE Chair & Deputy Head of the UCT Department of Medicine & Infectious Diseases Physician
- May 27th, *Key concepts in modern clinical trials, covering non-inferiority and adaptive designs and platform trials,* presented by Prof Lehana Thabane, Faculty of Health Sciences, McMaster University

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.

Worth the Watch: Insights That Matter

WHO Launches New Clinical Trials Guidance

The Global Health Network recently hosted a comprehensive webinar titled **"WHO Launches New Clinical Trials Guidance – What Do I Need to Know?"**, shedding light on the World Health Organization's (WHO) updated guidelines for clinical trial design and implementation.

This guidance aims to ensure that clinical trials are ethical, inclusive, and aligned with global health priorities, particularly in resource-constrained settings.

Key discussions revolved around the importance of adapting trial methodologies to meet the unique challenges of diverse populations while maintaining scientific rigor. The updated guidance emphasizes collaboration among researchers, sponsors, and policymakers to enhance trial efficiency and ensure results are relevant to the needs of underrepresented communities.

Additionally, it addresses the integration of digital tools and innovative approaches to streamline trial processes. For researchers, this guidance serves as a critical resource to navigate evolving regulatory landscapes and ensure compliance with international best practices. By fostering equitable and robust research practices, the WHO aims to accelerate advancements in global health outcomes.

This webinar provided invaluable insights for professionals seeking to align their research with the latest standards and to contribute to more impactful clinical trials worldwide.

https://www.youtube.com/live/SkF_YlZQeR8?si=JI6XYz5tLPidnzB0

Worth the Read: Insights That Matter

Global Trends in CD4 Count Measurement and Distribution at First Antiretroviral Treatment Initiation

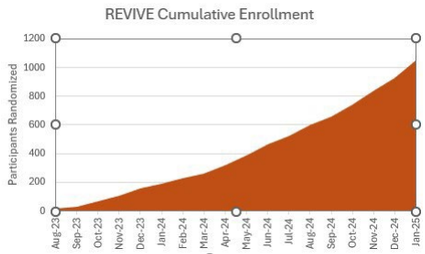
A recent study titled "Global Trends in CD4 Count Measurement and Distribution at First Antiretroviral Treatment Initiation" examines the evolution of CD4 count assessments in people with HIV (PWH) starting antiretroviral therapy (ART) world-wide. The research highlights significant shifts in CD4 measurement practices and the prevalence of advanced HIV disease at treatment initiation over time. Understanding these trends is crucial for optimizing HIV care and treatment strategies. For those interested in a comprehensive analysis of these global patterns, the full article is available here:

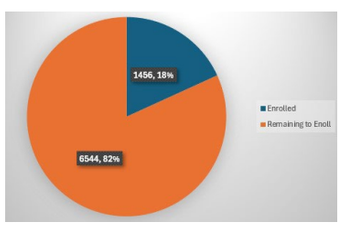
https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciae548/7877232?login=false

Please look out for the next edition on 15 April 2025

Newsletter (Page 4)

Country	Regulatory Status	Sites			Randomizations	
		Planned	Activated	Enrolling	Last 30 Days	Total
South Africa	Approved	21	14	13	5	367
Sierra Leone	Approved	3	2	2	14	345
Uganda	Approved	4	4	4	33	325
Nigeria	Approved	11	11	11	38	301
Ivory Coast	Approved	3	3	3	5	24
Zambia	Approved	3	3	3	35	91
Malawi	Approved	3	1	1	3	3
Ghana	Approved	3	0	0	0	0
Republic of Congo	Approved	1	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
Kenya	Pending	TBC				
Total		**61**	**38**	**37**	**133**	**1456**





Spotlight on Excellence

Celebrating Dr. Olukemi (Kemi) Adekanmbi

In this edition of the REVIVE newsletter, we celebrate the remarkable contributions of **Dr. Olukemi (Kemi) Adekanmbi**, a national lead who exemplifies dedication, expertise, and leadership in the fight against infectious diseases.

Dr. Adekanmbi is a distinguished physician and infectious disease specialist whose academic and professional journey reflects her unwavering commitment to advancing global health. She holds an **MBBS degree from the University of Ibadan, Nigeria**, and a **Master of Public Health with a concentration in global health from the Harvard School of Public Health**. Her rigorous training includes an **internal medicine residency at Abington Memorial Hospital, Pennsylvania, USA**, and an **infectious disease fellowship at the University of Maryland Medical Center, Baltimore, USA**. As a testament to her expertise, she is **board-certified by the American Board of Internal Medicine** in Internal Medicine and Infectious Disease and is a **fellow of the American College of Physicians**.

Currently, Dr. Adekanmbi serves as a **senior lecturer at the University of Ibadan** and an **honorary consultant at the University College Hospital (UCH), Ibadan**. At UCH, she holds multiple vital roles, including **head of the infectious disease department**, **clinical lead for infectious disease outbreak response**, and **overseer of the infectious disease isolation centers**. Further cementing her leadership in the field, she is the **Acting Director of the Infectious Disease Institute, University of Ibadan**.

Her research interests span critical areas, including **antimicrobial resistance and stewardship, HIV/AIDS, emerging infections, and neglected tropical diseases**, reflecting her dedication to addressing both current and emerging global health challenges.

In the REVIVE clinical trial, Dr. Adekanmbi plays a pivotal role as the National Lead for **Nigeria**, where she coordinates activities across **11 diverse sites**, including her own institution's ART clinic. Representing nearly all geo-political regions of Nigeria, the trial ensures a **truly representative sample of the country's diverse population**. Beyond her role in patient recruitment and site management, Dr. Adekanmbi views the trial as a platform for **capacity building**, as many participating site investigators are gaining their first clinical trial experience. Her leadership is instrumental in fostering a culture of excellence and empowering future clinical researchers in Nigeria.

Outside her professional commitments, Dr. Adekanmbi finds joy in **nature walks**, **spending time with her family**, and **providing leadership training to teenagers at her local church**. Her holistic approach to life and work serves as an inspiration to all who have the privilege of working with her.

We extend our heartfelt gratitude to Dr. Adekanmbi for her extraordinary contributions to the REVIVE trial and her unwavering dedication to improving health outcomes in Nigeria and beyond. Her leadership and passion exemplify the very best of the REVIVE mission.

While she very rarely writes poems, she wrote this while traveling back from the last Investigator meeting in Zimbabwe.

"It was an unlikely pairing…. a cardiologist and an ID doc
They needed to answer a question, but it would cost much more than a buck
They thought long and hard about WHO would foot the bill….
Then the answer came to them: who better than Melinda and Bill!
So, from Cape Town to Cairo and Freetown to Addis,
They built up a vast army of devoted REVIVE-alists
From protocols, approvals and knotty inclusion criteria……
To CRFs, sub-studies and even more talk about inclusion criteria
They forged ahead, one randomization at a time"
The goal, to enroll eight thousand and to spend every dime."

Dec 9, 2024, en-route to Addis Ababa