BHP

BOTSWANA HARVARD HEALTH PARTNERSHIP

ANNUAL REPORT 2024

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BOTSWANA HARVARD HEALTH PARTNERSHIP

2024 ANNUAL REPORT

Botswana Harvard Health Partnership
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2024 - Annual Report
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BHP Annual Report Task Team
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Strategic Foundations

VISION:
To be a World-Renowned Public Health Institute.

MISSION:
To Fight HIV/AIDS and Emerging Public Health Challenges Through Innovative Research, Education and Capacity Building That Impacts Policy and Practice.

CORE VALUES

• Excellence

To achieve our vision of being a "world renowned public health institute" we at BHP commit to quality driven research and training programmes and processes. We will be second to none in our drive to attain quality in our research and training.

• Innovation

BHP staff is committed to finding solutions to the evolving HIV /AIDS pandemic and other public health challenges. We shall endeavor to be continuously innovative and resourceful in our quest to understand and address public health challenges.

• Collaboration

BHP recognizes that the fight against HIV /AIDS and other public health challenges will not be won by one individual or one institution. We commit and emphasize the importance of teamwork and collaborative research in our activities.

• Botho

An encompassing Setswana word that means amongst other, integrity, respect, honesty, and compassion. We are committed to adhering to moral and ethical principles treating all our customers, including research participants, with respect, dignity and compassion. All information about studies will be handled with utmost confidentiality.

• Beneficence

All activities done at BHP shall be of relevance and benefit to those affected by HIV /AIDS and/or other public health challenges. The knowledge generated through our research shall be used to advise public health policy and shall be shared with the general public and scientific community for the benefit of mankind. We shall be guided by the principle of "Do Not Harm" in our Research and related activities.

2 BHP at a glance

ESTABLISHMENT

The Botswana Harvard Health Partnership (BHP) is a Not-for-Profit, limited liability organization, established through a partnership between the Government of Botswana, represented by the Ministry of Health (MoH), and Harvard University (HU), represented by the Harvard T.H. Chan School of Public Health (HSPH). It was established in 1996 and registered as a limited liability company in 2007 initially as The Botswana Harvard AIDS Institute and re-named The Botswana Harvard Health Partnership on the 2nd of November 2022 in recognition of the expansion of mandate and portfolio of research and programmes beyond HIV/AIDS.

BUSINESS

Knowledge generation and dissemination, advocacy, health policy transformation and systems strengthening through research, education and capacity building.

CONTACT DETAILS

Registered Office: Botswana Harvard HIV Reference Laboratory
Plot 1836 (Princess Marina Hospital premises)
North Ring Road, Gaborone, Botswana

MAILING ADDRESS

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Web: www.bhp.org.bw

Company Auditors: Baker Tilly Botswana (Pty) Ltd
Company Secretaries: DPS Consulting
Company Attorneys: Armstrong's Attorneys, Notaries & Conveyancers
Main Bankers: Standard Chartered Bank & Stanbic Bank

3. GOVERNANCE

a. Board Members

Dean Jane J. Kim
Chair: Dean for Academic Affairs at the Harvard T.H. Chan School of Public Health and K.T. Li Professor of Health Economics in the Department of Health Policy and Management and the Center for Health Decision Science.

Prof. Sarah Fortune
John LaPorte Given Professor of Immunology and Infectious Diseases at the Harvard TH Chan School of Public Health, Director of the TB Research Program at the Ragon Institute of MGH, Harvard and MIT and Chair of the Department of Immunology

Prof. Sheila Tlou
Co-Chair of the Global HIV Prevention, Former Minister of Health and Wellness Botswana

Prof. Mark Elliott
Mark Schwartz Professor of Chinese and Inner Asian History, and Vice Provost for International Affairs, Harvard University

Prof. Michael Hughes
Professor of Biostatistics, Director, Center for Biostatistics in AIDS Research Harvard TH Chan School of Public Health.

Mr. Mpaphi Blasis Mbulawa
Acting Coordinator - National Health Laboratory, Ministry of Health, Botswana

3. GOVERNANCE

b. Board of Directors

Prof. Roger Shapiro
Professor, Department of Immunology and Infectious Diseases, Harvard T.H. Chan School of Public Health.

Mr. Modise Modise
Economist & Former Permanent Secretary of Development, Office of the President

Ms. Kate Calvin
Executive Dean at the, Harvard T.H. Chan School of Public Health.

Dr. Shahin Lockman
Professor, Department of Immunology and Infectious Diseases, Harvard T.H. Chan School of Public Health.

Dr. Pamela Smith- Lawrence
Director of Health Services, Ministry of Health (MOH), Botswana

Mr. Christopher Hughes
Head of Group Business Transformation for the Letshego Group of Companies and the Founding Director of LEAD Consultancy.

Dr. Joseph Makhema
Chief Executive Officer BHP

Mr. Cornelius Gaetsaloe
Chief Operations Officer BHP - Ex Officio Member, non-voting Director

3. GOVERNANCE

c. Executive Management

Joseph Moeketsi Makhema
MB. ChB, FRCP (UK)
Chief Executive Officer

Gaerolwe Masheto
MD, PGDip FamMed
Deputy Chief Executive Officer

Cornelius Gaetsaloe
BCom, AHMP, AFP
Chief Operations officer

Dineo Thebe
BAcc
Director, Finance and Grants

Beauty M. Malumbela
Dip.HRM, BSc, MBA
Head of HR, Comms and Strategy

3. GOVERNANCE

d. Senior Management

Sikhulile Moyo
MSc, MPH, PhD
Laboratory Director

Ayotunde Omoz-Oarhe
MBBS, MPH
Gaborone Clinical Research Site Leader

Ponego Ponatshego
MD, DTMH
Molepolole Clinical Research Site Leader

Tumalano Sekoto
RN, MPH
Regulatory Manager

Terence Mohammed
BSc
Laboratory Operations Manager

Nyaladzi Maphorisa
BSc
Laboratory Clinical Manager

Tshepho T. Frank
BPharm
Pharmacy Manager

Tshenolo Ntalabgwe
BSc, MPH
Quality Assurance Manager

Coulson Kgathi
BSc
Software Development and Data Management Manager

Thuso Mokane
BSc
Information Technology Manager

Ronald Ruele
AAT, ACCA
Finance Manager

Kevin Moshoeshoe
AAT, CERM
Grants Manager

3. GOVERNANCE

e. Principal Investigators

Gbolahan Ajibola
MD, MPH

Motswedi Anderson
BSc, PhD

Ava Avalos
MD

Laura Bogart
PhD

Lisa Butler
MA, MPH, PhD

Ellen Caniglia
ScD

Adam R. Cassidy
PhD, LP, ABPP-CN

Bruce Chabner
MD

Scott Dryden-Peterson
MD, MSc (epi)

Jason A. Efstathiou
MD, DPhil

Tendani Gaolathe
BS, MD

Simani Gaseitsiwe
BSc, PhD

3. GOVERNANCE

e. Principal Investigators

Jennifer Jao
MD, MPH

Joseph Jarvis
MBBS, BSc, MSc, MRCP, PhD, DTMH

Sara Schwanke Khilji
MD, MPH, FACP

Catherine Koofhethile
BSc, MSc, PhD

David Lawrence
MD

Shahin Lockman
MD, MPH

Rebecca Luckett
MD, MPH

Doreen Ramogola-Masire

Richard Marlink,
MD

Chelsea Morroni
MBChB, DFSRH, MPH, PhD

Mosepele Mosepele
MD, MSc

Lucy Mupfumi
PhD

3. GOVERNANCE

e. Principal Investigators

Rosemary Musonda
PhD

Vladimir Novitsky
MD, PhD

Kathleen M. Powis
MD, MPH, MBA

Kaelo Seatla
MD, MPH, PhD

Roger L. Shapiro
MD, MPH

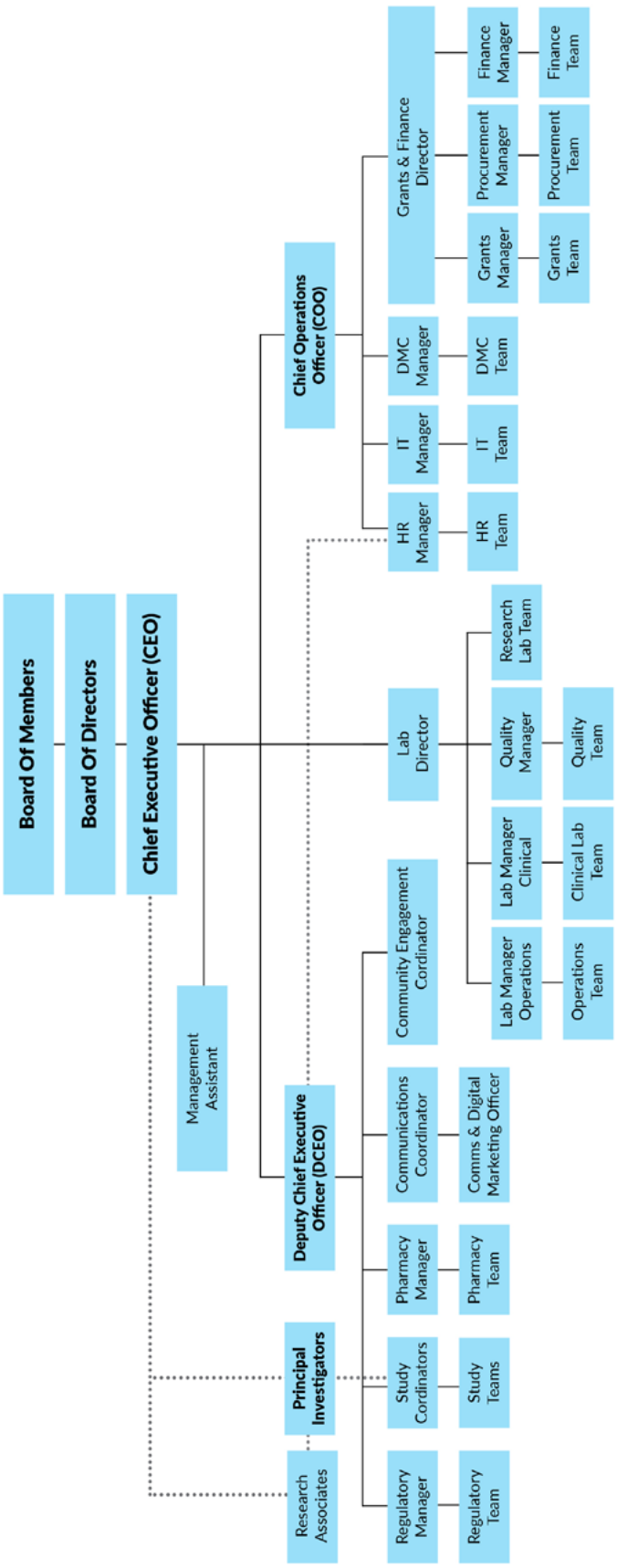
Emily Shava
MBChB, MSc

Nabila Youssouf
PhD

Neo M. Tapela
MD, MPH

Rebecca Zash
MD

4. ORGANISATIONAL STRUCTURE



5. ACRONYMS

AAAS	-African Academy of Sciences
ACTG	-Advancing Clinical Therapeutics Globally for HIV/AIDS and Other Infections
AIDS	-Acquired Immuno-Deficiency Syndrome
APTI	-African Postdoctoral Training Initiative
AREF	-Africa Research Excellence Fund
ART	-Antiretroviral Therapy
ARV	-Antiretroviral
BIDMC	-Beth Israel Deaconess Medical Center
BIUST	-Botswana International University of Science and Technology
BHHRL	-Botswana Harvard HIV Reference Laboratory
BHP	-Botswana Harvard Health Partnership
BHP CAB	-Botswana Harvard Partnership Community Advisory Board
BOMAID	-Botswana Medical Aid Society
BoMRA	-Botswana Medicines Regulatory Authority
bNAbs	-Broadly Neutralizing Antibodies
BOTSOGO	-Botswana Global Oncology Outreach
BSHRI	-Botswana Sexual and Reproductive Health Initiative
CAB-LA	-Long-Acting Cabotegravir
CAVD	-Collaboration for AIDS Vaccine Discovery
CDC	-Centers for Disease Control and Prevention
CD4	-Cluster of Differentiation 4 (immune cells)
CEYOHO	-Center for Youth of Hope
CI	-Confidence Interval
CM	-Cryptococcal Meningitis
CODA	-Contraceptives and Dolutegravir-based ART
COVID-19	-Coronavirus Disease 2019
CoVPN	-COVID-19 Prevention Trials Network
CT	-Chlamydia trachomatis
CROI	-Conference on Retroviruses and Opportunistic Infections
CTU	-Clinical Trials Unit
DHMT	-District Health Management Team
DTG	-Dolutegravir
DRST	-Department of Research, Science, and Technology
EBI	-Evidence-Based Interventions
EFV	-Efavirenz
EIT	-Early Infant Treatment
EMA	-European Medicines Agency
EQA	-External Quality Assurance
FY	-Financial Year
FTC	-Emtricitabine
GCLP	-Good Clinical Laboratory Practice
GETSA	-The Genomic Epidemiology of Treponema Pallidum in Southern Africa
GISAID	-Global Initiative on Sharing All Influenza Data
HEU	-HIV-Exposed Uninfected
HEP TSG	-Hepatitis Transformative Science Group
HIV/AIDS	-Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome
HIV	-Human Immunodeficiency Virus
HIV-1	-Human Immunodeficiency Virus Type 1
HPTN	-HIV Prevention Trials Network
HPV	-Human Papillomavirus
HR	-Human Resources
HSPH	-Harvard T.H. Chan School of Public Health
HU CFAR	-Center for HIV AIDS Research
HUU	-HIV-Unexposed Uninfected
IAS	-International AIDS Society
IDCC	-Infectious Diseases Care Clinic
IMPAACT	-International Maternal Pediatric Adolescent AIDS Clinical Trials Network
INSTI-N	-Integrase Strand Transfer Inhibitor-Naïve
ISO	-International Organization for Standardization

IT	-Information Technology
KBFUS	-King Baudouin Foundation United States
LF-MRI	-Low-Field Magnetic Resonance Imaging
LIS	-Laboratory Information System
MAGUS	-Multi-Country Aetiology of Genital Ulcer Study
MCKT	-Ministry of Communications, Knowledge, and Technology
MDR-TB	-Multidrug-Resistant Tuberculosis
MIT	-Medical Internship Training
MMed	-Master of Medicine
MOH	-Ministry of Health
MPhil	-Master of Philosophy
MSc	-Master of Science
NCD	-Non-Communicable Disease
NGS	-Next-Generation Sequencing
NHL	-National Health Laboratory
NIAID	-National Institute of Allergy and Infectious Diseases
NIH	-National Institutes of Health
NIHR	-National Institute for Health Research
OHSU	-Oregon Health and Science University
PASC	-Post-Acute Sequelae of SARS-CoV-2
PCR	-Polymerase Chain Reaction
PI	-Principal Investigator
PhD	-Doctor of Philosophy
PHOENIx	-Protecting Households on Exposure to Newly Diagnosed Index Multidrug-Resistant Tuberculosis Patients
PK	-Pharmacokinetic
PLWH	-People Living with HIV
PMTCT	-Prevention of Mother-to-Child Transmission
PREPARE	-PRomoting Equity for Pregnant Adolescents in REsearch
PrEP	-Pre-Exposure Prophylaxis
POC	-Point of Care
POCUS	-Point-of-Care Ultrasound
QFT-Plus	-QuantiFERON-TB Gold Plus
RCR	-Responsible Conduct of Research
REVIVE	-(Study acronym not expanded in the text)
RPR	-Rapid Plasma Reagin (a test for syphilis)
SA AIDS	-South Africa AIDS Conference
SADCAS	-Southern African Development Community Accreditation Service
SANTHE	-Sub-Saharan African Network for TB/HIV Research Excellence
SARS-CoV-2	-Severe Acute Respiratory Syndrome Coronavirus 2
SE & DMC	-Software Engineering and Data Management Center
SGA	-Small-for-Gestational-Age
SLH	-Scottish Livingstone Hospital
SOP	-Standard Operating Procedures
sSCAN	-Sub-Saharan Congenital Abnormalities Network
STI	-Sexually Transmitted Infection
TAGENDI	-Addressing Gender and Diversity Regional Gaps in Clinical Research Capacity
TB	-Tuberculosis
TDF	-Tenofovir Disoproxil Fumarate
TESA	-Trials of Excellence in Southern Africa
TGF	-Transformative Science Group (ACTG)
TSG	-Cure Transformative Science Group
UB	-University of Botswana
UCT	-University of Cape Town
UKZN	-University of KwaZulu-Natal
US	-United States
VPN	-Virtual Private Network
WHO	-World Health Organization
WITS	-University of Witwatersrand
WLHIV	-Women Living with HIV
XTC	-Lamivudine (3TC)

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Foreword By Board Chairman

I am very happy to present the foreword to the Annual Report of the Botswana Harvard Health Partnership (BHP). This year marks yet another milestone in our journey to advance public health through groundbreaking research, capacity building, and impactful collaborations.

This year marks the start of a new five-year strategic plan for BHP, and a time for reflection on the accomplishments of the past five years. These accomplishments include the discovery of the Omicron virus (as part of our overall pivot to address critical needs during the COVID-19 pandemic); the promotion of several new Principal Investigators who are now based at BHP; the completion of PhDs for many young trainees; and an expanded research portfolio in genomic surveillance, tuberculosis, cancer, cardiovascular diseases, maternal and child health, HIV prevention, and HIV cure.

It is quite a list, and I could not be more proud of the entire research team at BHP. As we think ahead to the next five years, BHP is clearly positioned to remain a regional and global beacon of medical research excellence. The next five-year plan charts a vision for the future of BHP that prioritizes institutional growth, optimizing our programs, leveraging technology, and enhancing collaborations.

Our achievements are a testament to the unwavering dedication of our scientists, research teams, and collaborators. From publishing high-impact manuscripts to advancing clinical trials and mentoring the next generation of researchers, BHP continues to make strides in addressing public health threats. Notably, our laboratory remains at the forefront of innovation, maintaining its ISO accreditation and setting the standard for quality and excellence in the region.

The past year has seen political change in both Botswana and the United States, but BHP remains a constant and steady presence focused on improving health in Botswana. While we have faced challenges navigating financial constraints, BHP has demonstrated sound financial management. I commend the leadership and staff for their commitment to ensuring that the institution remains solvent and robust. I am particularly proud of the September Gala fundraising event, attended by President Masisi, that kicked off our in-country fundraising efforts. This event was a huge success and helped forge new relationships with businesses and institutions in Botswana, expanding both our revenue stream and community outreach. Bravo!

As we reflect on this year's accomplishments, I extend my deepest gratitude to my fellow Board members for their guidance and support, the BHP leadership for their visionary stewardship, and the entire BHP team for their dedication and hard work. I also thank our partners and donors for their continued trust and investment in our mission.

As we look ahead, I am confident that BHP will continue to thrive, innovating and breaking new ground in medical research. Together, we will ensure that BHP remains a pivotal force in addressing public health challenges and improving lives in Botswana, the region, and beyond.

With sincere gratitude,

Roger L Shapiro

Prof. Roger Shapiro
BHP Board Chairman

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Foreword By Chief Executive Officer

The year under review has been one of remarkable change and growth, marked by our continued pursuit of attainment of the BHP strategic objectives. This as we embark on a historic transition in Botswana's political landscape, the first change in government since independence in 1966. We draw inspiration from our nation's thriving democracy as we envision a future where BHP continues to flourish.

In line with this vision the new BHP 5- year strategic plan with its expanded institutional research and capacity building initiatives seeks to also harmonize with collaborative commitments in the memorandum of agreement with the Ministry of Health, to strengthen public health systems in Botswana.

This year marked remarkable progress for our team, with 95 manuscripts published in peer-reviewed journals, surpassing last year's total of 78. Among these, 21 appeared in journals with an impact factor exceeding 10, highlighting the high quality of our work.

Additionally, 35 publications featured local first authors, emphasizing our dedication to capacity building. Collectively, these publications garnered 242 citations (203 from clinical studies and 39 from laboratory-based research). The number of abstracts presented at local and international conferences slightly increased from 31 to 34.

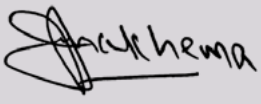
While Principal Investigator (PI)-initiated projects decreased from 37 to 28, Network Clinical Trials decreased to 10 studies last year's tally of 11. The financial year 2024 saw a 1.7% increase in revenue, a modest growth compared to last year's 6%. Revenue from new grant applications, however, rose significantly to $1.1 million, up from $0.586 million in FY2023. There were 24 grant applications in FY2024 seven of which were small grants up to $100K per year, 13 medium $100-500K per year and four large >$500K per year. Of these 18 were awarded four small and 14 medium. Those awarded were further categorized as 17 prime awards and seven subcontracts.

While we continue to face challenges such as declining revenue streams, our prudent financial management has ensured that we remain solvent with robust financial systems that have once more returned unqualified 2023/2024 annual financial and Generally Accepted Government Auditing Standards (GAGAS) audits. I commend the various BHP programmes for sound fiscal management and prioritizing capital and operating expenditures effectively.

I extend my heartfelt thanks to the BHP Board of Directors for their unwavering support and guidance during these challenging times. To our Principal Investigators, Research Associates, Scientists, Staff, and Collaborators, I express my profound gratitude for your dedication and selflessness in advancing BHP's mission.

With your collective efforts and our new strategic direction, BHP is well-positioned to continue breaking new ground in addressing pressing public health challenges. Together, we will remain at the forefront of scientific discovery and innovation.

Sincerely,



Dr. Joseph Makhema
BHP Chief Executive Officer

8 Executive Summary

The Botswana Harvard Health Partnership (BHP) has successfully concluded its 2023-2024 annual reporting period, showcasing impactful research and capacity building achievements aligned with its five strategic themes: Research Excellence, Capacity Building and Training, Operational Excellence, Public Policy and Advocacy, and Sustainability.

Research Excellence

Consistent with its mission to address HIV/AIDS and emerging public health challenges, BHP continues to expand and diversify its research portfolio. During this reporting period, 38 research projects were active, with 28 independent BHP Principal Investigators led, showcasing the institution's expertise in initiating and conducting research across various public health areas. This however represents a reduction from last year's total of 48 studies, attributed to the conclusion of several studies, including those focused on COVID-19.

The Clinical Trials Unit (CTU) conducted 10 studies across three Clinical Trials Networks: IMPAACT, ACTG, and HPTN. These included the following studies; PHOENIx, A5379, A5356, IMPAACT 2017, IMPAACT 2026, IMPAACT 2016, IMPAACT 2036, IMPAACT 2028, HPTN 084, and CoVPN 3008. These studies span diverse areas, including mother and child health, sexual reproductive health, tuberculosis, HIV and cardiovascular diseases, malignancies, human papillomavirus, pre-exposure prophylaxis, and drug-drug interactions.

BHP also achieved significant academic milestones during this period, publishing 95 manuscripts and presenting 34 abstracts at local and major international conferences, further solidifying its leadership in health research and innovation.

Capacity Building & Training

BHP has made significant strides in its mission to develop future scientists through various grants, including Trials of Excellence in Southern Africa (TESA), Sub-Saharan African Network for TB/HIV Research Excellence (SANTHE), and FOGARTY, aimed at supporting the next generation of local researchers.

During the reporting period, one fellow successfully obtained a PhD, and another completed an MSc degree. Currently, eight students are pursuing master's degrees, another eight are enrolled in PhD programs, and three are engaged in postdoctoral fellowships. These students are enrolled at partner academic institutions in Botswana and the region, co-supervised by BHP scientists and academics from these universities. Additionally, BHP continues to mentor early-career investigators, guiding them towards successful research careers and contributing to the growth of the scientific community.

In collaboration with its partners, BHP trains University of Botswana residents in Obstetrics and Gynaecology, Anaesthesia, Internal Medicine, and internship training at Scottish Livingstone Hospital through the BIDMC/OHSU program which also provides global health resident training of fellows from the Harvard affiliated Hospitals.

Operational Excellence

With a dedicated team of 273 staff members, BHP continues to advance its scientific agenda, solidifying its reputation as a globally recognized health research institution. The Grants and Finance Department plays a pivotal role in ensuring compliance, efficient resource management, and timely reporting. The division currently manages over 100 awards from various donors. In the 2024 financial year, revenue saw a modest increase of 1.7%. Notably, revenue from new grant applications rose significantly, reaching $1.1 million, up from $0.586 million in the 2023 financial year. This growth reflects the successful grant applications led by both local and international Principal Investigators (PIs).

The BHP Laboratory achieved a landmark milestone as the first medical laboratory accredited to the updated ISO 15189:2022 laboratory standard by the Southern African Development Community Accreditation Services (SADCAS). The lab has consistently upheld ISO accreditation since its initial certification in June 2019, demonstrating its commitment to excellence and quality in medical research.

Public Policy and Advocacy

BHP leverages its research to inform public health policy, guidelines development and programme implementation by actively engaging decision makers. BHP scientists contribute expert advice to national health teams and disseminate research findings to local and international audiences, enhancing evidence-based policymaking in Botswana and beyond.

Sustainability

To advance its long-term strategic objectives in research and training, BHP has partnered with the US branch of the Belgium-based King Baudouin Foundation (KBFUS) and their partner Every.org to accept donations from outside Botswana on BHP's behalf. Both KBFUS and Every.org are public charities in the United States. This fund development initiative allows BHP to receive philanthropic contributions from international donors, bolstering financial resilience to support its vital mission. Additionally, BHP held a successful fundraising event in the United States in March 2024 to further support its research efforts.

9 Introduction

The BHP is a non-profit, health research and capacity building institution founded in 1996 as a partnership between the Government of Botswana, represented by the Ministry of Health (MOH) and Harvard University, represented by the Harvard T.H Chan School of a public Health (HSPH). BHP's mission is to fight HIV/AIDS and other emerging public health challenges through research, education, and capacity building that impacts policy and practice.

BHP undertakes a broad research portfolio encompassing clinical trials, both network trials and BHP Principal Investigators initiated studies, implementation science, and laboratory-based research.

In addition to conducting cutting-edge research, BHP is committed to training future scientists through its capacity building and training initiative. Through collaborative initiatives with Harvard affiliated institutions and other US and European institutions, BHP offers mentorship and training to upcoming scientists. It also partners with local and regional universities who confer degrees for MSc, MPhil, and PhD candidates mentored and supervised by BHP researchers. BHP significantly contributes to the Ministry of Health's system-strengthening efforts, with its scientists providing technical expertise in various ministry committees and technical working groups.

10+ Research Excellence

CLINICAL RESEARCH PROJECTS

PRINCIPAL INVESTIGATOR INITIATED RESEARCH PROJECTS

a) MOTHER AND CHILD STUDIES

1) Tsepamo: Birth Surveillance Outcomes

PI: Professor Roger L. Shapiro, MD, MPH

The Tsepamo study conducts surveillance of adverse birth outcomes and congenital abnormalities in infants (live and stillbirths) at or beyond 24 weeks gestation across 16 hospitals in Botswana, representing about 70% of all deliveries in the country. The study extracts maternal and infant data from obstetrical and outpatient records and actively monitors for all congenital malformations.

Out of 410,000 records that have been collected so far, 290,000 have been captured into the data set. Figure 1 and 2 below shows data and congenital abnormalities captured from July 2023 to June 2024.

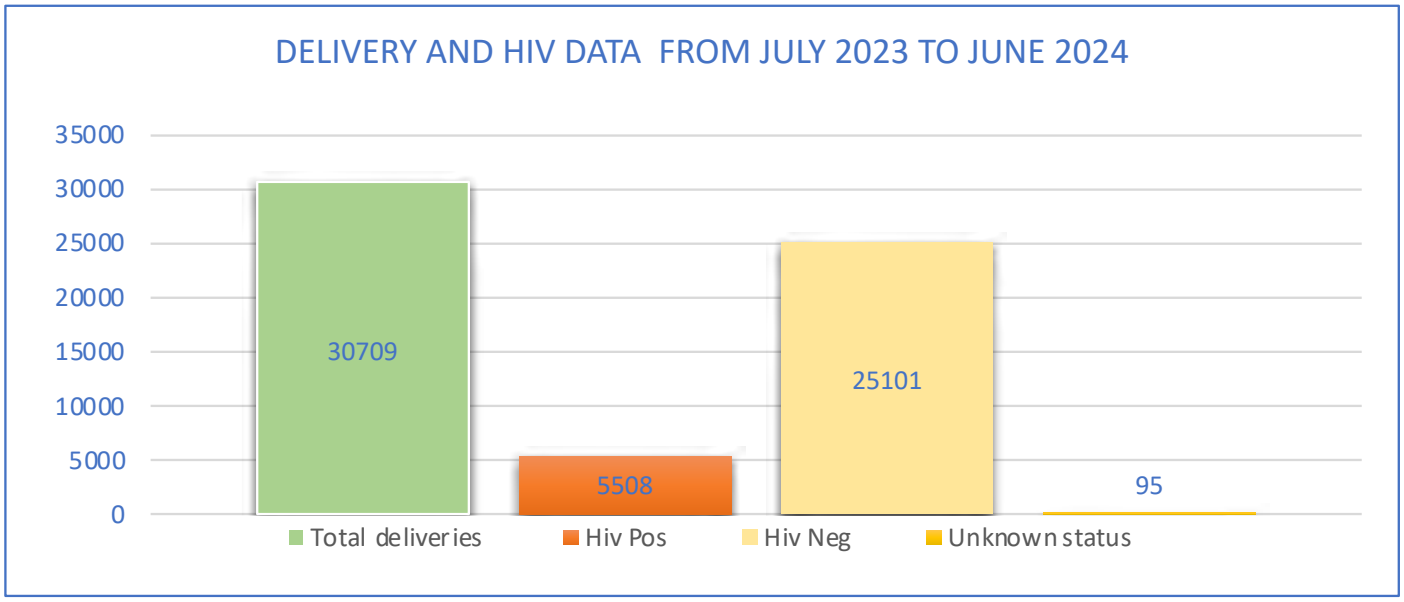


Figure 1:Delivery and HIV data

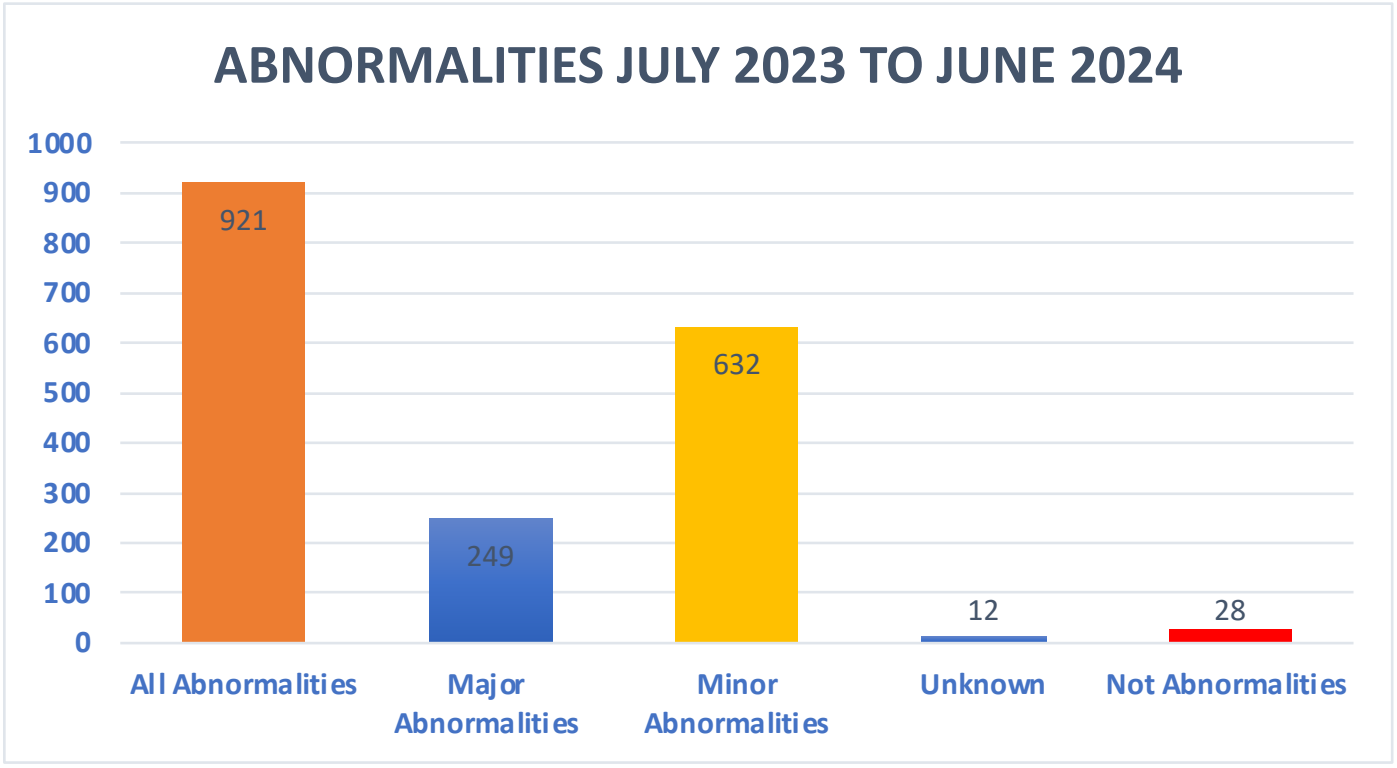


Figure 2: Birth Abnormalities

Sub-Studies within Tsepamo Study

- Safe Birth study is ongoing.
- Major abnormalities follow up study-approved and data collection and analysis started.
- Multiple Micronutrient Supplementation study has been approved and started the consent of the Clinics, awaiting to supply the clinics with the study drug.

Achievements

- The Congenital Abnormality review committee has been meeting successfully. Three geneticists from South Africa and two Clinicians from Botswana have been identified as key members who will continue training in reviewing congenital abnormalities. The group met twice this year.
- In August 2023, the study team hosted a stakeholder meeting to disseminate key scientific findings from Tsepamo study.
- Two manuscripts have been submitted to journals related to major congenital abnormalities and neural tube defects in Tsepamo (currently under review).
- Follow up of infants with major congenital abnormalities born to mothers with and without HIV have been conducted in the Tsepamo study to describe their health outcomes and to identify the clinical and social needs and utilization of health services for these children. Data collected have been accepted for oral presentation at a Neural Tube Conference and will be presented in August 2024.
- A manuscript for "Long-Term Outcomes of Children Born with Neural-Tube Defects in Botswana" has been submitted for publication.
- The study continues to present its findings at sSCAN (Sub-Saharan Congenital Abnormalities Network) on Quarterly basis

2) Early Infant Treatment Study: A Clinical Trial of HIV Positive Infants in Botswana

Principal Investigator: Professor Roger L. Shapiro, MD, MPH

The Early Infant Treatment (EIT) study is a single-arm, non-randomized clinical trial of early Antiretroviral Therapy (ART) in children who acquired HIV during the antepartum and peripartum period. Infants exposed to HIV were tested at birth, and if confirmed positive, they were immediately offered ART. The study sought to determine whether very early ART initiation in HIV-positive infants could limit the seeding of viral reservoirs and maintain immune response. The study met its initial recruitment aims and accrued 40 children at the Francistown and Gaborone Clinical research sites for longitudinal follow-up for up to 576 weeks. Longitudinal evaluation of viral reservoir is ongoing.

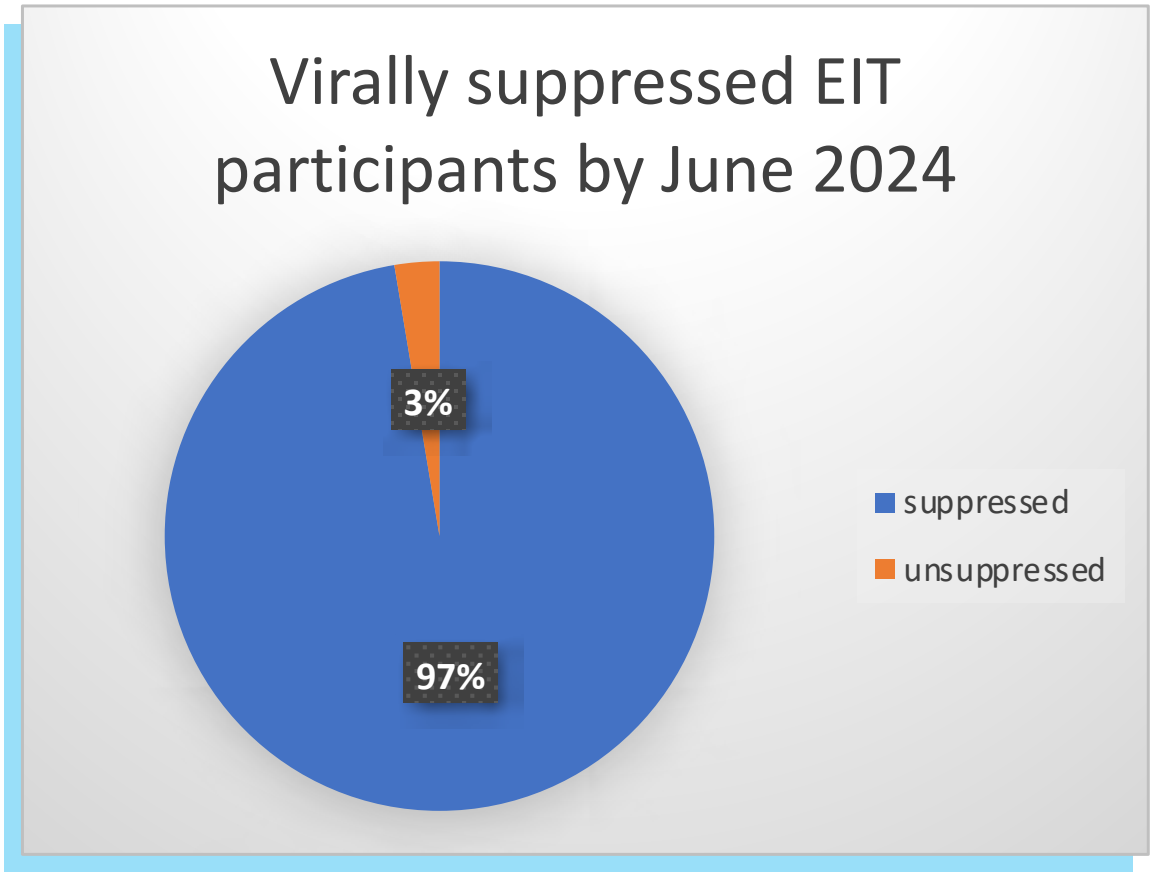


Figure 1: Virally suppressed EIT participants by June 2024

3) A Clinical Trial to Evaluate the Impact of Broadly Neutralizing Antibodies VRC01LS and 10-1074 on Maintenance of HIV Suppression in a Cohort of Early-Treated Children in Botswana (Dual bNAb Treatment in Children)/ Tatelo Study

PI: Professor Roger Shapiro, MD, MPH

The Tatelo Study is an interventional clinical trial of dual treatment with two broadly neutralizing monoclonal antibodies (bNAbs), VRC01LS and 10-1074, in HIV-1 positive children who are virally suppressed. The primary objectives of the study are to determine the safety, pharmacokinetics, dosing and antiviral efficacy of up to 24 weeks of VRC01LS and 10-1074 immunotherapy in these children. The trial also aims to evaluate effects of treatment with VRC01LS and 10-1074 on the size and cellular composition of residual viral reservoirs as well as the influence of VRC01LS and 10-1074 treatment on the magnitude and quality of antiviral innate and adaptive immune responses.

The study is relevant for addressing the challenges of long-term antiretroviral treatment (ART) use in children, such as issues of adherence and toxicities associated with prolonged ART use. HIV positive children who were treated early may be the ideal candidates for use of broadly bNAbs as an alternative to ART because of their low HIV viral reservoir. The study has enrolled up to 40 HIV children from the Early Infant Treatment (EIT) Study who were at least 96 weeks of life and have maintained viral suppression (viral load <40 copies/mL) six months prior to enrollment. The study has had 100% retention and is now in long-term follow-up of all participants.

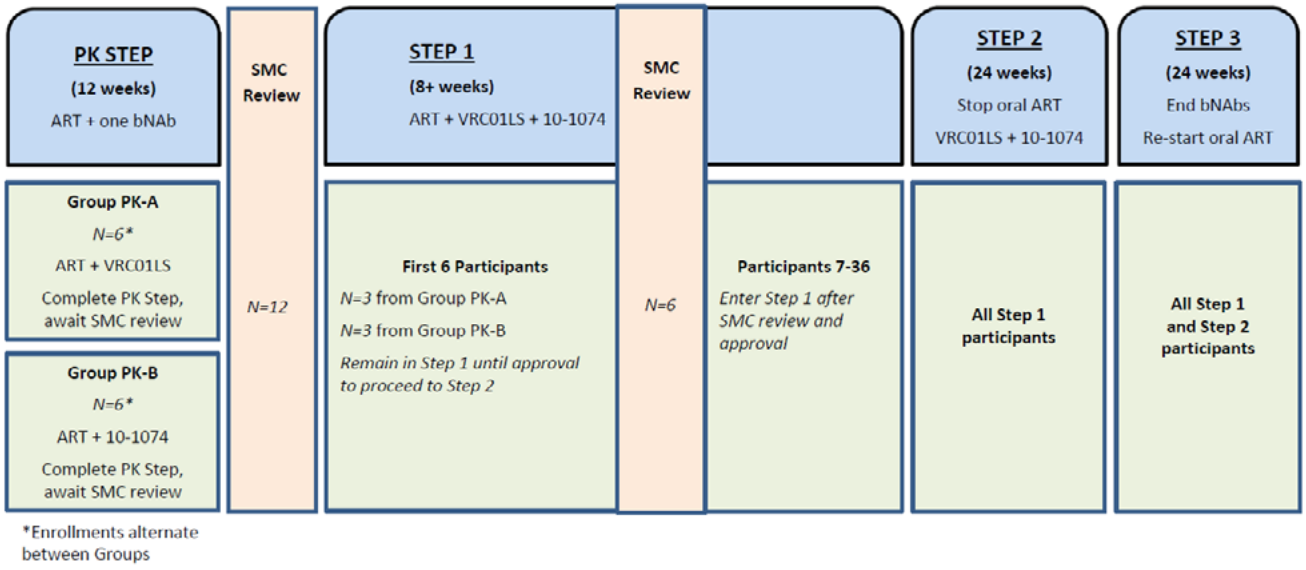


Figure 1: Study Schematic

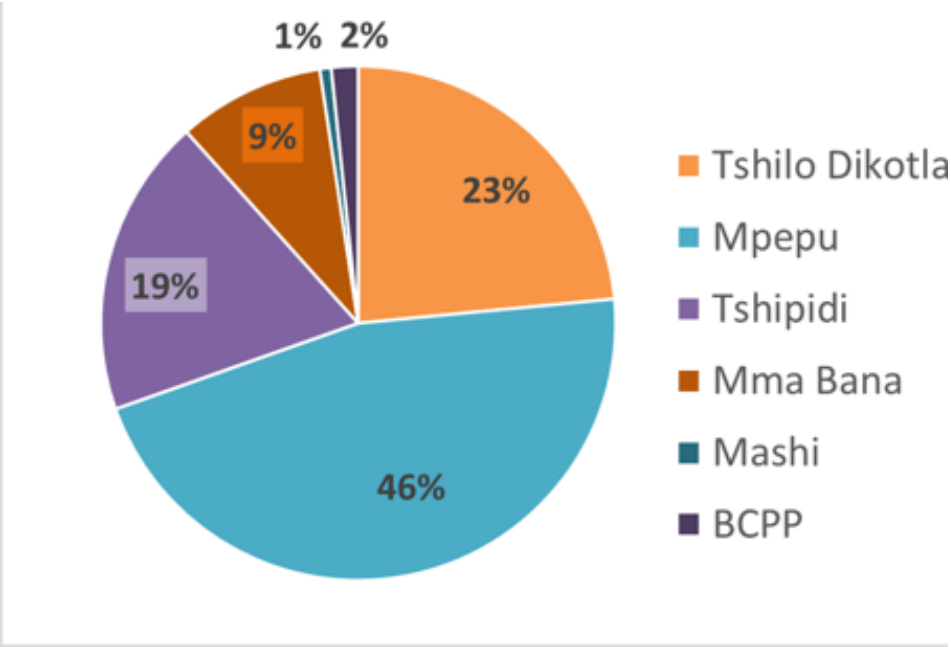
4) FLOURISH: Following Longitudinal Outcomes to Understand, Report, Intervene and Sustain Health for Infants, Children, Adolescents who are HIV Exposed Uninfected

PI: Kathleen M. Powis MD, MPH, MBA; Jennifer Jao, MD, MPH; Joseph Makhema, MB. ChB, FRCP

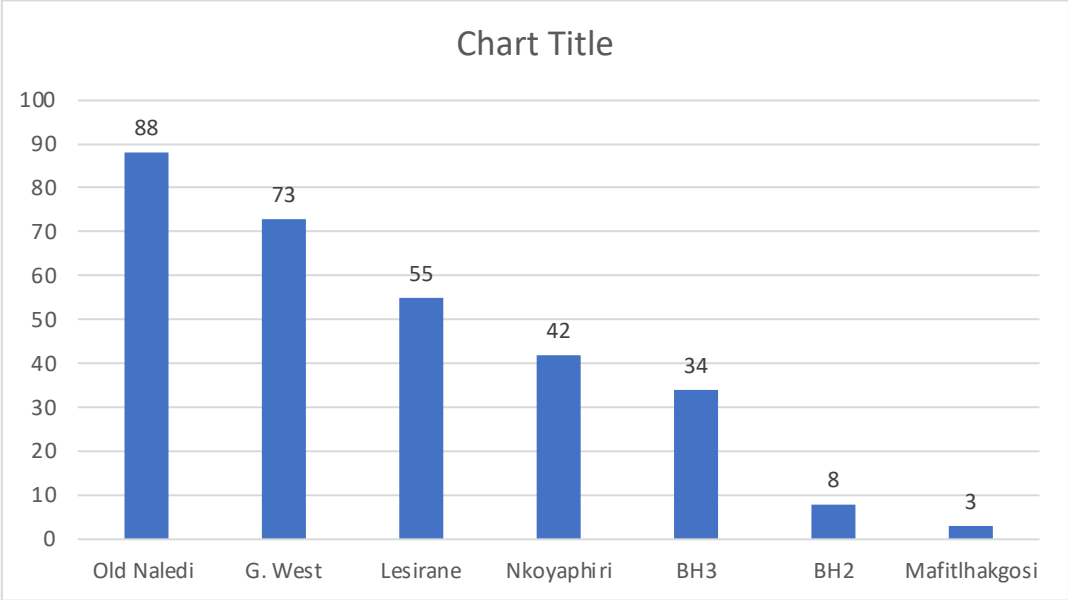
The FLOURISH study is a NIH funded prospective observational study [R33 HD103099] evaluating short- and long-term health and development outcomes of children and adolescents with fetal exposure to HIV but remained HIV-uninfected. The outcomes will be compared to children and adolescents who are born to women without HIV. The study is structured to identify possible biological, social, and structural mechanisms for identified differences between children who are HIV-exposed uninfected (HEU) and those born HIV-unexposed uninfected (HUU).

Study Recruitment and Retention

A total of 3,899 previous BHP participants were deemed eligible for recruitment into the FLOURISH study. Enrolment started in. . As of July 17,2024, the FLOURISH study has consented 2,581 participants, including 1,263 caregivers and 1,318 children (accounting for siblings and twins). Consented participants from previous BHP studies are shown in Figure 1. Of the participants enrolled, 365 mother-child pairs represent women newly enrolled in pregnancy and their infants. Antenatal clinic recruitment is shown in Figure 2. In total, the retention rate of previous BHP participants within the FLOURISH study is 98.1%, while newly enrolled pregnant women present a 96.6% retention rate.



Recruitment of Pregnant Women form Clinics



Interim Findings

Depression and Anxiety Among Caregivers

Caregivers participating in the FLOURISH study are screened for anxiety using the Generalizable Anxiety Disorder assessment tool (GAD-7), and for depression using the Patient Health Questionnaire (PHQ-9). Of 1,147 biological mothers participating in the FLOURISH study who were screened for depression and anxiety using the PHQ-9 and GAD-7, of whom 853 (74%) were living with HIV, the prevalence of the combined outcome of screening positive for depression or anxiety was higher among biological mothers living with HIV compared to biological mothers who were HIV sero-negative (12.5% versus 8.5%; p = 0.03). Among those who screened positive for depression, a significantly higher proportion of biological mothers with HIV experienced moderate to severe depression compared to biological mothers who were HIV sero-negative (65.7% versus 57.9%). Among 115 FLOURISH women referred for mental health who were reached after the referral, only 47% went to their local health clinical for care and 26% of the participants who did go to their local health clinic reported not receiving mental health care or support (Figure 3).

Figure 3: FLOURISH Participants' Self-Reported Experience Following Mental Health Referral

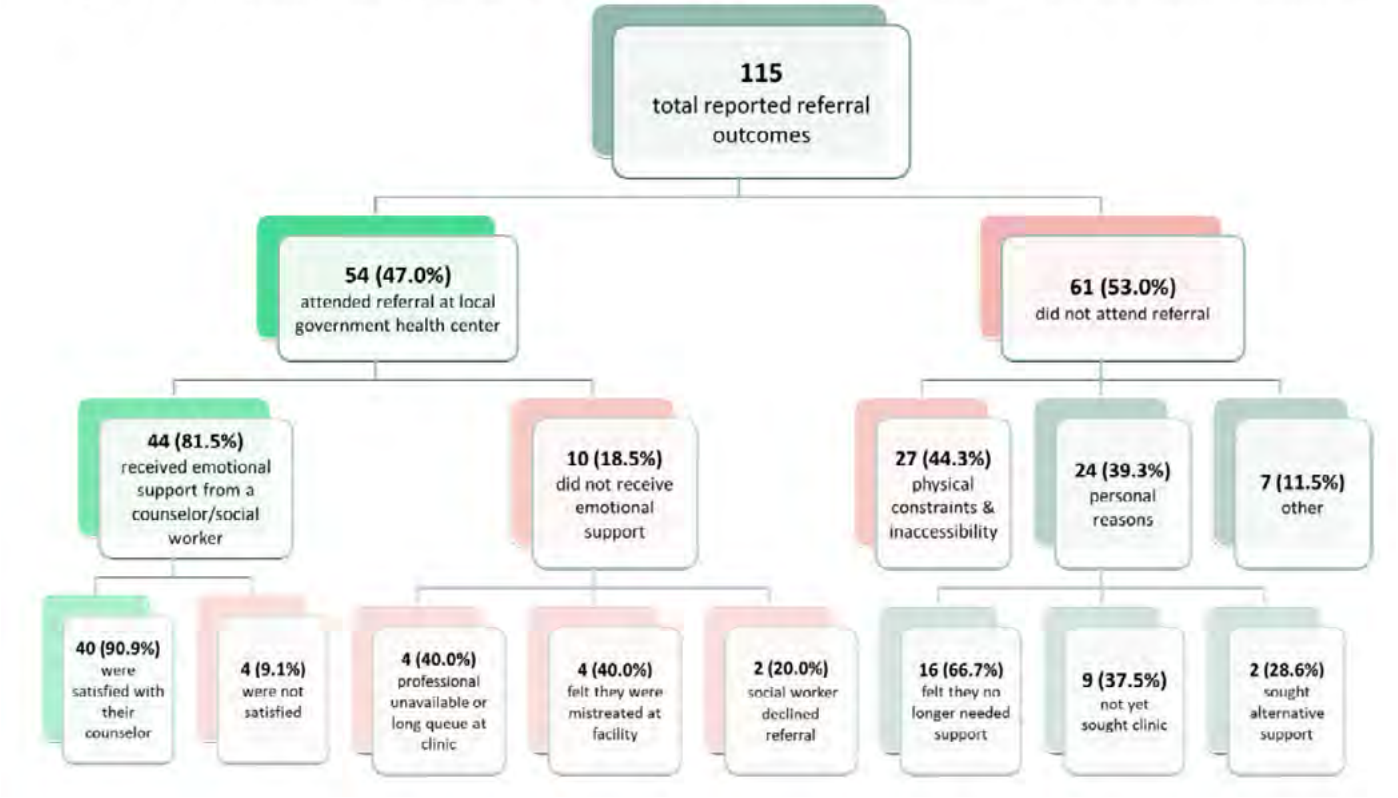


Table 1. Logistic Regression Model of Factors Associated with Lower Overall Academic Performance

Academic Achievement

Using caregiver reporting of child's school grades, academic performance in Mathematics, Science, English, Setswana and overall was compared by HIV exposure status among children attending standard 3-6 primary grades. In unadjusted analyses, children HEU are more likely to have lower overall academic performance compared to children HUU (Odds Ratio 77 [OR]: 2.05 [95% Confidence Interval (CI): 1.23, 3.44]) (Table 1), and lower performance in Mathematics, Science, and English.

	Unadjusted Models		Adjusted Model	
Covariates of Interest	Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value
HEU versus HUU	2.05 (1.23, 3.44)	<0.01	1.96 (0.85, 4.51)	0.11
Low Maternal Education[1]	2.46 (1.06, 5.74)	0.04	2.13 (0.89, 5.09)	0.09
Caregiver Depression/Anxiety at Enrollment[2]	1.10 (0.50, 2.38)	0.82		
Absence of Household Electricity	1.52 (0.72, 3.22)	0.27		
Household Food Insecurity in the Last Year[3]	0.86 (0.52, 1.40)	0.54		
Male Child	1.66 (1.04, 2.64)	0.03	1.81 (1.12, 2.94)	0.02
Preterm Birth[4]	1.46 (0.69, 3.11)	0.32		
Low Birthweight (<2500 grams)	1.81 (0.89, 3.69)	0.10	1.71 (0.83, 3.56)	0.15
Never Breastfed	1.48 (0.93, 2.37)	0.10	0.88 (0.41, 1.88)	0.75

[1]Low maternal education defined as no or primary education only
[2]Maternal Depression was evaluated using the PHQ9 screening tool and anxiety via the GAD7 screening tool.
[3]Household food insecurity was defined as being present if a caregiver reported that in the last 12 months that the household ever had to cut the size of meals or skip meals because there was not enough food in the household.
[4]Preterm birth was defined as a gestational age < 37.0 week completed gestational age.
Abbreviations: HEU: HIV-exposed uninfected; HUU: HIV-unexposed uninfected; P=Pula
NB: Covariates in unadjusted analyses with a p-value ≤ 0.20 were included in the adjusted model.

Collaborations and Sub-studies

A total of five FLOURISH sub-studies have opened in the past four years (Figure 4). Three of which have since closed, and data analysis is underway. Dr. Roxanna Haghighat, a medical student at HMS who graduated from Oxford University with a PhD in Social Intervention and Policy Evaluation, under the mentorship of Dr. Powis, has completed her mixed-methods study entitled "Experiences of Infant Feeding Decision-Making among Mothers Living with and without HIV in Botswana" which is embedded in the FLOURISH study. Infant feeding practices data routinely collected during quarterly calls from 198 FLOURISH postpartum study participants between July 2022 and December 2023 showed a low prevalence of 6-month of exclusive breastfed at 29.8%, without significant difference noted by participant HIV status (30.8% for persons HIV sero-negative versus28.7% for persons living with HIV). Returning to work or school without adequate support in these locations for continued breastfeeding was the single biggest reason why exclusive breastfeeding was discontinued prior to the infant reaching six-months of age, highlighting the need for structural interventions to improve duration of exclusive breastfeeding.

Another ongoing sub-study is the Infant Brain Ultrasound sub-study lead by Pediatric Radiologist, Dr. Hansel Otero, which involves brain ultrasounds conducted in infants to evaluate associations between in utero exposure to HIV and maternal antiretroviral (ARV) drugs and brain volume and structure for infants HIV-exposed uninfected in FLOURISH infants. This study is continuing to enroll and follow mother-infant pairs. As of 15-July-24, a total of 169 scans have been completed, including 90 infants with a brain ultrasound at birth, with 24 infants born preterm undergoing a follow-up ultrasound at 2 months of life, per the study protocol, and 55 brain ultrasounds as infants age to 6 months of life. This study has yielded three presentations, thus far.

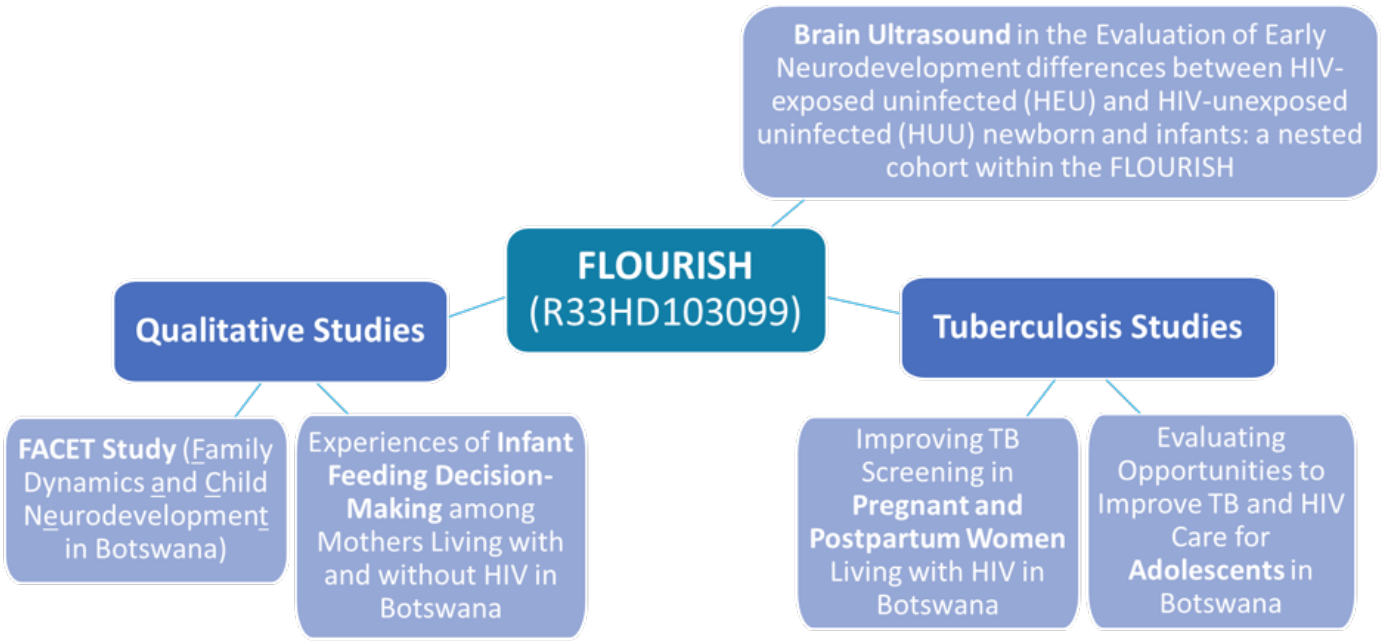


Figure 4. Sub-studies within FLOURISH

5) Point-of-Care HIV Testing and Early Dolutegravir Use for Infants "Moso study"

PIs: Roger Shapiro MD, MPH, Gbolahan Ajibola MD, MPH

The Moso Study offers targeted point-of-care HIV testing to high-risk neonates and enrolls HIV-positive neonates into a longitudinal cohort for early treatment with dolutegravir (DTG)-based ART. Infants diagnosed with HIV will are started on treatment at 7 days of life. Neonates at high risk of acquiring HIV in-utero are tested immediately post-delivery and ART is started within 7 days of HIV diagnosis. The rationale for the Moso study is to implement birth testing in a cost-effective manner (reducing costs associated with HIV testing at birth while still identifying over 95% of neonates acquiring HIV in-utero) and to optimize clinical, immunological and virologic outcomes in infected children through early initiation of a DTG-based regimen.

Study Progress

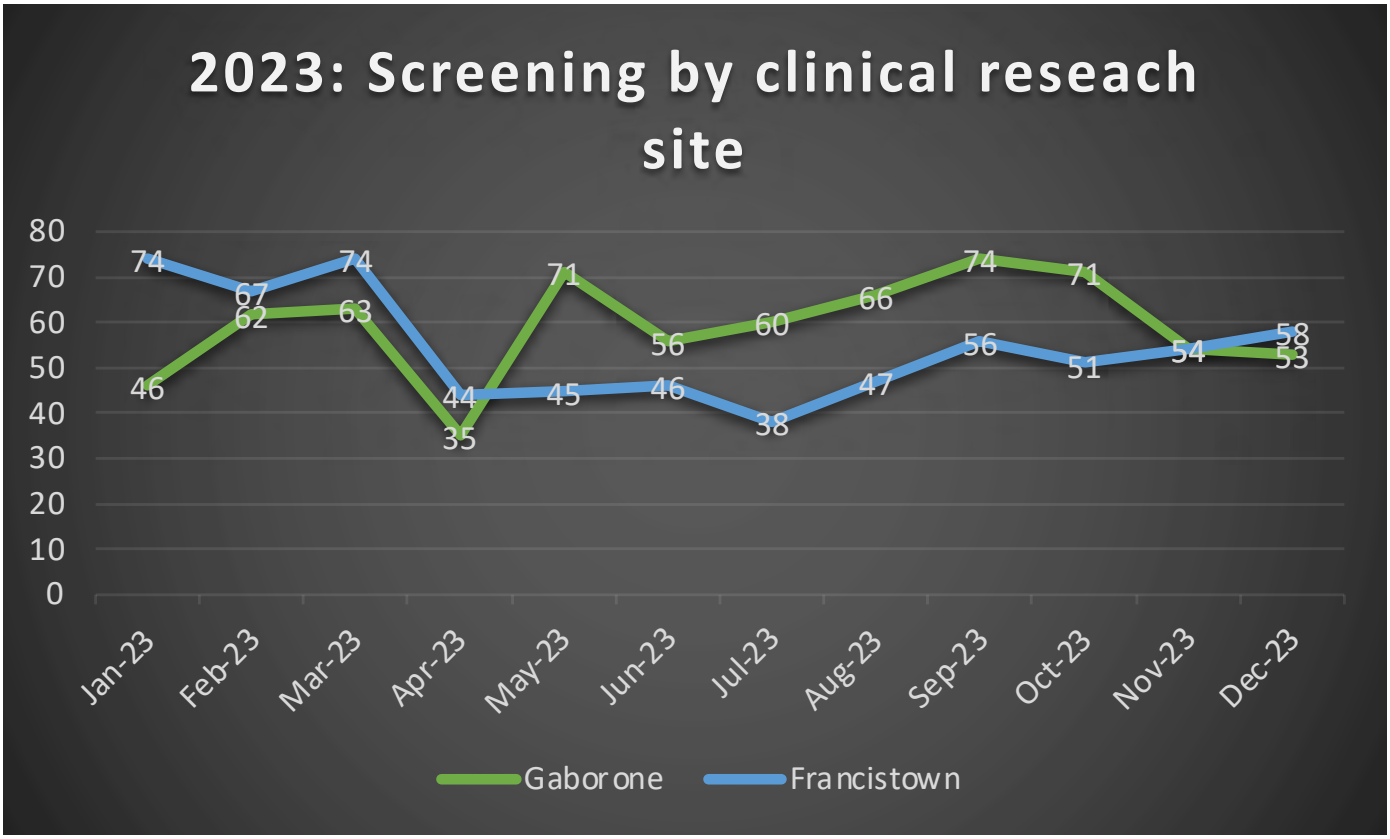


Figure 1. Screening by site from July 2022 to December 2023

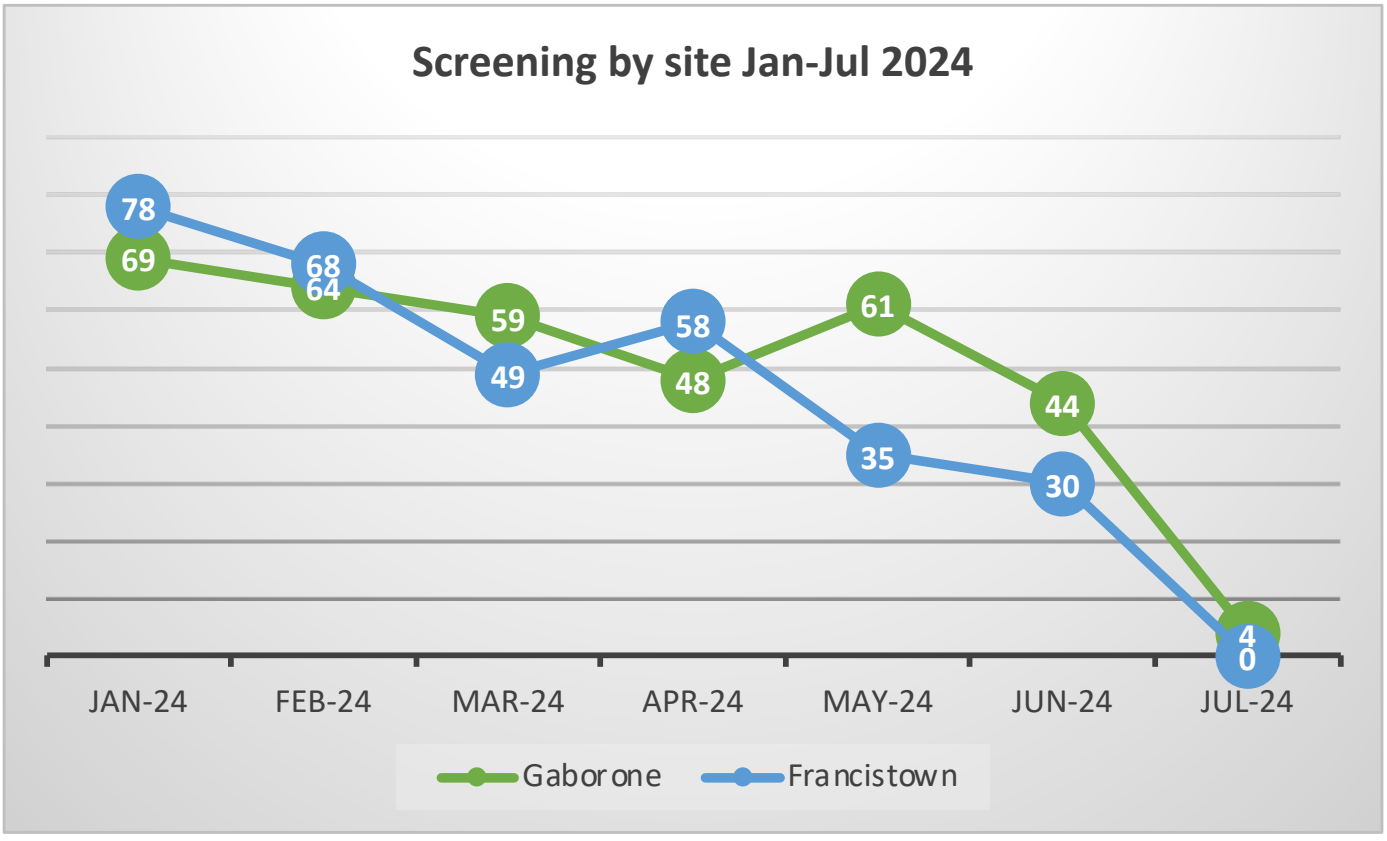


Figure 2: Screening by site January 2024 - July 2024

A total of 2627 infants, of 2627 were screened,2338 were eligible for testing at six weeks (aged 4-8 weeks). Among the 2338 eligible infants, 1335 were tested and have results available, 1003 reported to have tested with pending results, or had not yet been tested while 121 have not reached 6 -8 weeks of age. From those with results, 1333 remained negative and 2 had tested positive. The two infants who tested positive were promptly linked to care.
The longitudinal aspect of the study enrolled 14 study participants across both sites in the DTG cohort. Unfortunately, one death occurred in the Gaborone site at 2 weeks of age, due to events unrelated to study participation. There has been 100% retention of all 13 study participants.

Achievements

• Botswana Guidelines adopted birth testing for HIV in high-risk neonates.
• As part of its capacity-building initiative, Moso study team conducted a Point of Care HIV testing training for healthcare personnel from the study recruitment facilities and the District Health Management Teams (DHMTs). Trained a Total of 62 health care workers, this includes Midwives, PMTCT coordinators, heath care auxiliaries, counsellors and health educators.

6) Motheo Study: Neurodevelopment in Children Exposed in Utero to Dolutegravir of Efavirenzeoint-of-Care HIV Testing and Early Dolutegravir Use for Infants

PIs: Dr Shahin Lockman MD MSc, Dr Adam Cassidy PhD, LP, ABPP

The Motheo Study, which began enrollment in March 2021 seeks to compare developmental outcomes (neurodevelopment and psychosocial) at two years of age in HIV HIV-negative children born to HIV positive mothers who were exposed in utero to DTG/TDF/XTC (N=200); EFV/TDF/XTC (N=200); and children born to women without HIV. The study will also compare the outcomes at five years of age and evaluate symptoms of depression, anxiety, sleep problems and weight in the mothers of participating children. The study has reached its enrollment target of 560 child-mother pairs. The 5-year assessments started in March 2024 and 29 of the 560 total participants have been assessed to date. Data analysis is ongoing.

An additional aim has been added to include a low-field magnetic resonance (LF-MRI) brain scans in a subset of up to 50 children to assess feasibility of pediatric LF-MRI in Botswana and to explore whether in utero exposure to HIV and to DTG/FTC/TDV or EFV/FTC/TDF is associated with differences in brain structure at ~3-4 years of age. The study has so far enrolled 37 participants with complete head scans, with 16 exposed to DTG, 14 to EFV, and seven unexposed to HIV or ART.

Motheo Study Team with BHP Chief Executive Officer, Dr Joseph Makhema

7) The Doris Duke Study: Adverse cardiometabolic impact of antiretroviral treatment regimens among pregnant and postpartum women and their infants

PI: Dr Rebecca Zash, MD

The Doris Duke study is a prospective cohort study that assesses the cardiometabolic impact of antiretroviral treatment in pregnant and postpartum women. The study aims to enroll and prospectively follow 900 woman-infant pairs immediately after delivery to 18 months post-partum using both phone calls and in-person visits. The 900 women and their newborn infants enrolled are divided into two arms: 450 women on DTG and 450 without HIV. The primary objectives of the study are to compare weight gain, dietary intake, blood pressure, and hyperglycemia in pregnancy and through 18 months post-partum among women living with HIV on DTG, those on EFV and women without HIV. It also aims to evaluate the impact of weight gain and dietary intake on adverse birth outcomes such as preterm delivery, small-for-gestational-age (SGA), and neonatal death, and child growth through 18 months of age.

The study opened to accrual in June 2023. A total of 2832 postpartum mothers have been screened in Gaborone and Molepolole. Of those, 1129 women were found to be eligible, and 892 (79%) consented to participate in the study. The study is ongoing.

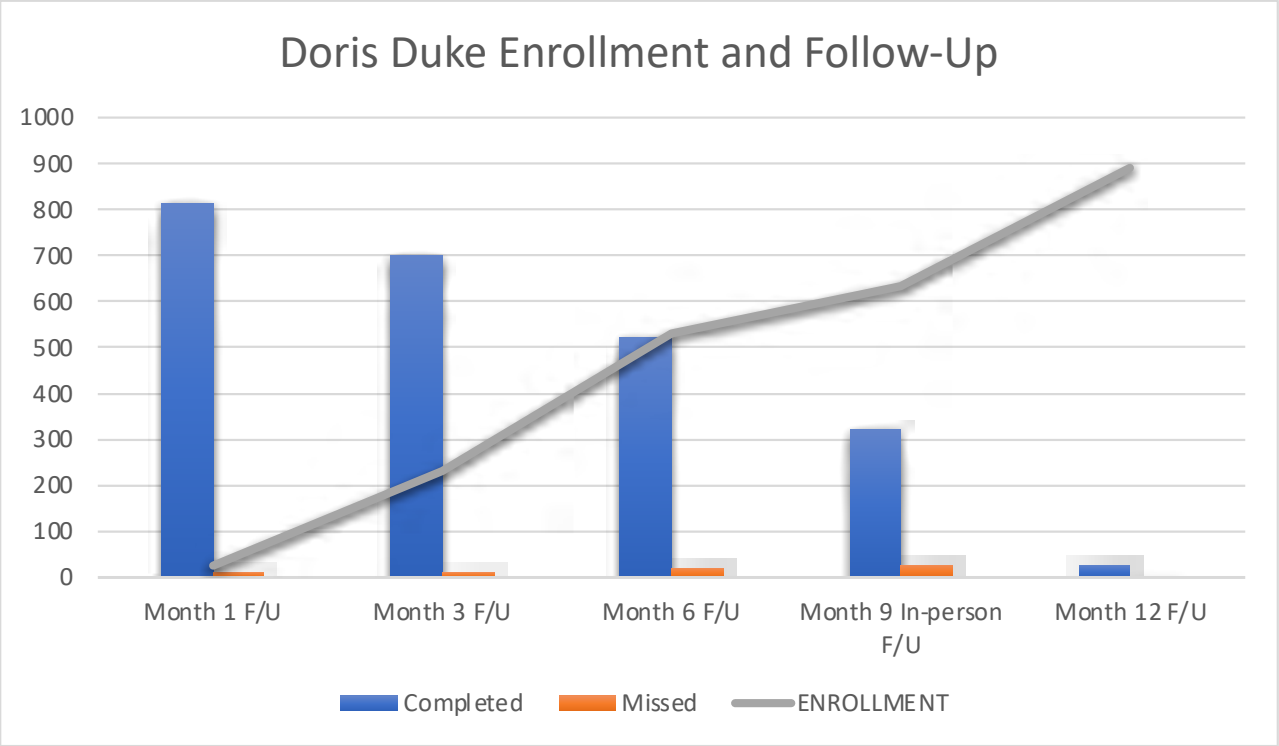


Figure 1: Study Schematic

8) Tshireletso Study: Linking HIV Prevention and Postpartum Care: Safety, Efficacy and Feasibility of Cabotegravir-LA PrEP in a High-Risk Breastfeeding Population in Botswana

PI: Dr Rebecca Zash, MD

The Tshireletso study is a hybrid implementation/safety study of long-acting cabotegravir (CAB-LA) as pre-exposure prophylaxis (PrEP) to prevent HIV infection in a post-partum cohort in Botswana. The study seeks to evaluate the uptake, adherence, acceptability, and effectiveness of CAB-LA PrEP program for women at high risk of HIV immediately postpartum, with follow-up co-located with routine postpartum. The study aims to enroll 500 women at high risk for HIV while they are admitted to the postpartum maternity ward after delivery. Recruitment is currently taking place in up to four government-run healthcare facilities in Gaborone and Molepolole. The mothers will be followed up for 24 months.

The study opened to accrual on the 30th of November 2023. A total of 1292 postpartum mothers were screened in Gaborone and Molepolole, with 414 mothers (32%) found eligible for study participation. Subsequently, 198 mothers were enrolled across both sites. The study has completed 176 follow-ups at month one, 109 at month three, 45 at month five, and six at month seven. There has been a 97.4% retention of study participants (5 participants are now off study).

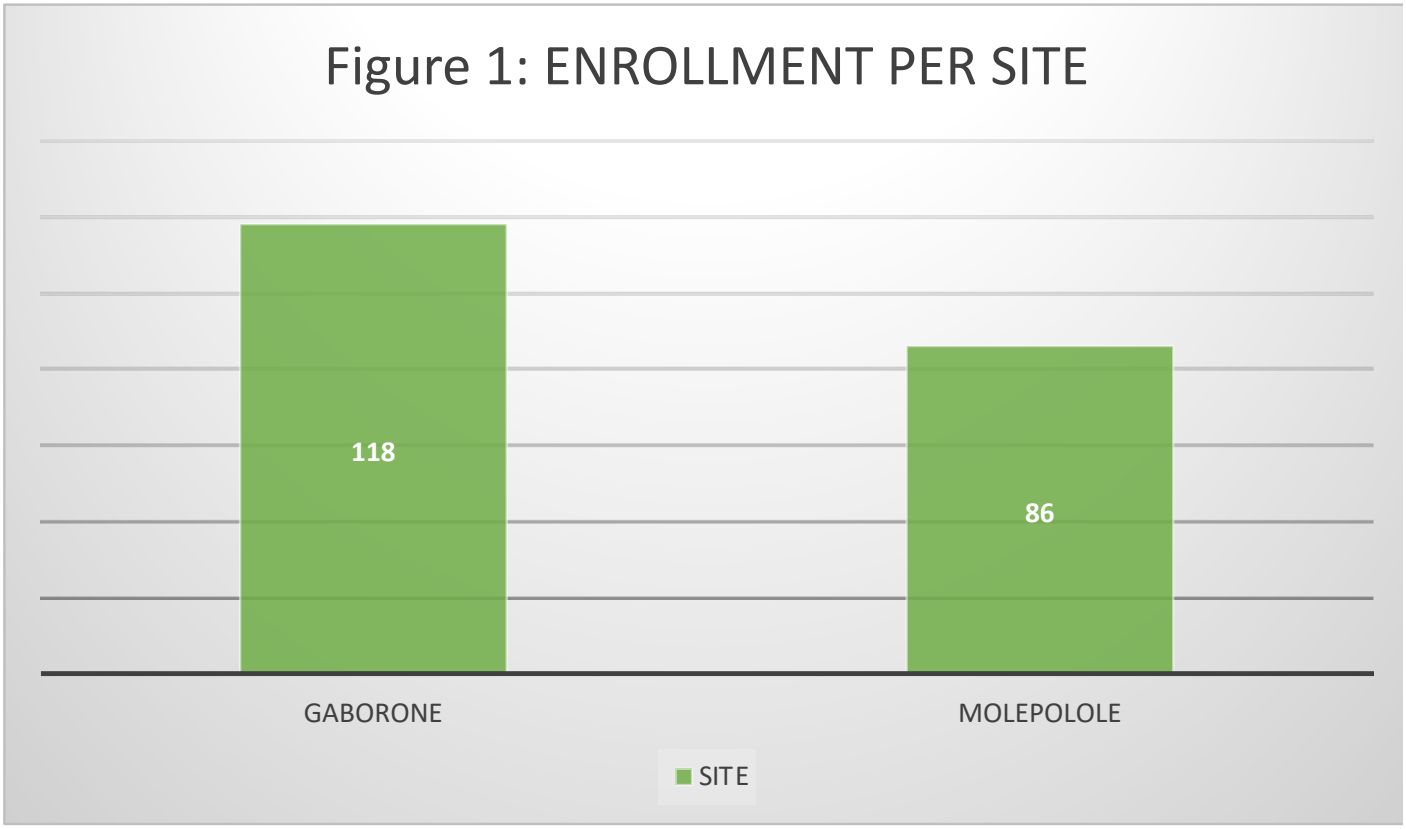


Figure 1: Study Schematic

PK Sub-study (30 participants)

A pharmacokinetic (PK) sub-study will occur among 30 breastfeeding women and their infants who are a part of the main study. A total of twenty-six (26) mothers have been enrolled on the PK sub-study. Three mothers are now off study before completing all four PK visits.

Mixed Method Qualitative Sub-Study

A total of 40 Mothers have been enrolled on the mixed method qualitative sub study. Twenty mothers declined CAB-LA as a method of PrEP and twenty agreed to join the study and take CAB-LA. The sub-study is now in its analysis period.

Tshireletso Study Team

b) HIV/TB STUDIES

1) Improving TB Screening in Pregnant and Postpartum Women Living with HIV in Botswana

PIs: Melanie M. Dubois, MD, MPH; Joseph Makhema, MBChB, FRCP

The maternal tuberculosis (TB) study is a sub-study of the FLOURISH study evaluated the extent to which TB screening occurred during the antenatal and postpartum periods among women living with HIV (WLHIV). Participants were screened for TB symptoms or contact with a household member with TB disease at two months postpartum, with those screening positive referred for further TB evaluation.

This study was conducted between October 2022 and November 2023 and has 95 recruited WLHIV, with 93 completing the two-month postpartum visit. Of the 93, nine (10%) participants screened positive for TB symptoms. Individual semi-structured interviews were conducted with eight (8) of these participants at the six-month postpartum visit, and nine (9) medical staff members at the local government clinics in Gaborone to evaluate barriers and facilitators to TB diagnosis and care for pregnant and postpartum WLHIV. Data analyses and thematic coding of the interviews is ongoing.

2) Evaluating Opportunities to Improve TB and HIV Care for Adolescents in Botswana

PIs: Melanie M. Dubois, MD, MPH; Sikhulile Moyo, MSc, MPH, PhD

The adolescent tuberculosis (TB) study is a sub-study of the FLOURISH study designed to quantify the prevalence of HIV and TB among 50 adolescents aged 10 to 17 enrolled in the FLOURISH study. These included 25 who were HIV-exposed at birth but did not acquire HIV through vertical transmission and 25 who were born to women without HIV. The study explored barriers to care engagement and delivery among adolescents referred by the study team for further evaluation to government health centers following positive TB testing or screening.

This study was conducted between February 2023 to May 2024 and enrolled 50 adolescents, with 25 adolescents HIV-exposed uninfected (HEU) and 25 adolescents HIV-unexposed uninfected (HUU). Three of the 25 (12%) adolescents HEU tested positive quantiFERON-TB Gold Plus (QFT-Plus), while none of the adolescents HUU tested positive. Six adolescents were referred for further TB evaluation due to QFT-Plus testing and/or positive TB symptom screening. None of the participants had positive HIV testing or a recent household TB contact. Individual semi-structured interviews were performed with four adolescents and five medical staff members from clinics in Greater Gaborone to evaluate barriers and facilitators for TB diagnosis and care for adolescents. Data analyses and thematic coding of the interviews is ongoing.

c) HIV WITH OR WITHOUT NON-COMMUNICABLE DISEASES

1) Integrating Hypertension and Cardiovascular Diseases Care into Existing HIV Services Package in Botswana (InterCARE Study)

PIs: Prof. Mosepele Mosepele MD, MSc, Tendani Gaolathe BS, MD, Kathleen Wirth Hurwitz

The InterCARE trial aims to assess the effectiveness of a multi-component strategy to improve the adoption of evidence-based interventions (EBIs) and increase treatment success rates for hypertension among adults with both HIV and hypertension. The study is structured in two phases: an initial pilot phase and the main trial.

The pilot phase demonstrated promising results, with early analyses indicating higher rates of achieving normal blood pressure at six- and twelve-month follow-up visits. The main phase, a cluster-randomized clinical trial, is now underway, enrolling adult participants with dual diagnoses of HIV and hypertension across 14 infectious diseases care clinics (IDCCs) in Botswana.

A total of 4,655 participants have been enrolled in the randomized trial, divided almost equally between the intervention group (2,327) and control group (2,328), achieving a high retention rate of 97% at the six-month follow-up. The twelve-month follow-up is currently in progress, with plans to continue tracking participants for up to 24 months.

In addition to its primary objectives, the InterCARE study includes several sub-studies that further explore various aspects of intervention uptake and health outcomes, providing a comprehensive understanding of factors influencing the effectiveness of hypertension management among individuals with a dual diagnosis.

2) IMPRINT NIHR Global Health Research Group

PIs: Prof Joe Jarvis MBBS, BSc, MSc, MRCP, PhD, DTMH, Prof. Mosepele Mosepele MD, MSc

The group aims to improve the diagnosis and treatment of the four major HIV-associated fungal infections of public health importance and to ensure that these improvements are made widely available to populations most affected in Africa (Botswana, Democratic Republic of Congo, Mozambique, Guinea, Malawi, South Africa), and South-East Asia (Vietnam). The group brings together leading academic researchers, clinical and public health leaders, non-governmental organisations including Médecins Sans Frontières and the Drugs for Neglected Diseases initiative, and community and patient representatives. Focused on people living with advanced HIV disease (or AIDS), the group's objectives include;

1. Treatment: Implementing new, short-course treatments for cryptococcal meningitis (CM).
2. Prevention: Improving the screen-and-treat strategy to identify and treat early cryptococcal disease.
3. Health Economics: Generating essential economic data to support the different screening and treatment approaches and policy changes.
4. Diagnostics: Developing new diagnostics tests for PCP which is difficult to diagnose.
5. Training: Training healthcare workers and researchers in clinical epidemiology, health economics and/or public health, and laboratory research.
6. Community Engagement: Engaging people living with advanced HIV disease and community representatives to ensure that their voices are heard and integrated.

The project has made significant progress with a National situational analysis having found that at least 50% of the patients are receiving the Liposomal amphotericin- B regimen as the 1st line treatment of CM. Stakeholder that includes Civil Society Organisations, implementing partners, and regulators (Botswana Medicines Regulatory Authority-BOMRA) have been engaged. The group supported the integration of the AMBITION-cm regimen into HIV Treatment guidelines. The liposomal amphotericin and flucytosine are available for use routine care and Flucytosine which was previously not registered in Botswana is now registered with BOMRA.

Community Engagement Workshops and patient materials have been developed to raise awareness, and over 100 healthcare workers have been trained on the use of the short course regimens for CM treatment. Data collection on treatment outcomes at 13 hospitals is complete, with analysis underway.

Group Photo of SHARE-CM participants with the study team during the April 2024 Meeting at BHP.

3) Single, high-dose AmBisome to reduce excess mortality from cryptococcal meningitis (SHARE-CM)

PIs: Prof Joe Jarvis MBBS, BSc, MSc, MRCP, PhD, DTMH, Prof. Mosepele Mosepele MD, MSC and David Lawrence

This is a five-year (2021-2026) non-research grant funded by the CDC to facilitate implementation of the short course regimen for treating HIV-associated cryptococcal meningitis. Building on the success of the AMBITION-cm phase III study, the project aims to reduce CM-related mortality by leverage individual and institutional experience in delivering the ACTA and AMBITION-cm short-course regimens to facilitate widespread implementation across Botswana.

The objectives of the project are to:
1. Perform a comprehensive baseline situational analysis to ascertain the status of cryptococcal meningitis management guidelines, national policy, and resource access in Botswana, map the landscape with regards to local and external implementing partners involved in delivering advanced HIV disease and CM interventions, and develop collaborative, country-specific strategies.
2. Engage stakeholders to integrate short-course regimens into national treatment guidelines and facilitate access to essential antifungals.
3. Train healthcare workers to deliver high quality care for HIV-associated cryptococcal meningitis including screening, diagnosis, and treatment using the short-course regimens and other nationally recommended CM treatment regimens.
4. Increase patient and community awareness of HIV-associated cryptococcal meningitis and encourage health-seeking behaviours and to ensure that the voices of people living with advanced HIV disease and community representatives are meaningfully included and heard across the entire scope of work, the group will develop strategies and tools to increase patient health literacy around HIV-associated fungal infections, collect qualitative data to learn from the experience of patients with HIV-associated fungal infections and facilitate meaningful engagement through a community advisory board.
5. Monitor and evaluate the progress and impact of implementing short-course regimens to support routine HIV programming goals.

4) Loneliness, Sleep Quality, Quality of Life, and Hypertension Among People Living with HIV

PI: Professor Mosepele Mosepele, MD, MSc

This is a one-year study at Princess Marina Hospital IDCC involving 200 individuals aged 40 and older who are living with HIV (PLWH). The study includes two equally sized groups: 100 participants with hypertension and 100 without. The research seeks to survey aging PLWH in Botswana on key factors such as loneliness, social isolation, sleep quality, and quality of life, alongside relevant health outcomes, including hypertension status. By understanding the relationships among these factors, the study aims to provide insights to guide health interventions that could improve the well-being and quality of life of aging PLWH.

The primary objective is to examine how loneliness and sleep quality correlate with quality of life, health behaviors, and health outcomes in this population. The hypothesis is that PLWH who report greater loneliness, higher social isolation, and poorer sleep quality will exhibit lower quality of life, poorer mental and physical health, and higher rates of chronic conditions. These individuals may engage in fewer health-promoting behaviors, such as physical activity, and show a greater likelihood of engaging in riskier behaviors, such as alcohol consumption and smoking. To date, the study has recruited 70 participants, comprising 40 individuals with hypertension and 30 without.

d) DRUG-DRUG INTERACTIONS

1) Contraceptives and Dolutegravir-based ART (CODA) Study

PIs: Dr Chelsea Moroni, MD, MPH, PhD

The Contraceptives and Dolutegravir-based ART (CODA) Study is a Phase IV, open label, non-randomized, parallel-arm, pharmacokinetic study. It investigates whether drug-drug interactions occur when the subdermal contraceptive implant (levonorgestrel) or the depot medroxyprogesterone acetate (DMPA) injectable are concurrently used with dolutegravir (DTG)-based ART.

In HIV prevalence settings, provision of contraception is challenging due to proven drug-drug interactions between certain ART agents and hormonal methods. While DTG, a WHO-recommended first-line treatment for HIV, is highly effective in managing HIV, there is little data on its effect on hormonal contraception.

The fill this gap, the CODA study aims to provide rigorous and complete evidence on the risk of drug-drug interactions between hormonal contraceptives and DTG, which is urgently needed to inform local and international health guidelines. Recruitment for the study began in October 2021 and enrolment, and follow-up were completed in February 2023. Pharmacokinetic analysis is ongoing at the University of Liverpool.

2)The Botswana Epidemiological ART Treatment Cohort Study 2 (2TheBEAT)

PI: Ava Avalos, MD

The Botswana Epidemiological ART Treatment Cohort Study 2 (2TheBEAT) is an observational, non-interventional retrospective study documenting the clinical outcomes and efficacy of dolutegravir (DTG)-based regimens in adults and adolescents. Covering data from 2016 to 2023, the study evaluates the impact of Botswana's Treat All Strategy on patients within the National ART Programme.

The study tracks two specific cohorts. Cohort 1 includes 1,500 ART treatment-naïve adults who began DTG-based regimens and 1,500 who started on efavirenz (EFV)-based regimens. This group focuses on assessing the effectiveness of the TDF/3TC (or FTC) combination with DTG compared to the TDF/3TC (or FTC) and EFV regimen in ART-naïve patients, measuring factors such as rates of virological suppression, time to suppression, rebound, and non-response.

Cohort 2 consists of ART-experienced but integrase inhibitor-naïve (INSTI-N) adults (1,000) and adolescents (500) who were transitioned to DTG-based regimens. This cohort will evaluate DTG's effectiveness in patients switching from first- or second-line ART treatments, assessing similar virological outcomes as in Cohort 1.

The study successfully reached its enrolment target of 4,500 participants. Data cleaning and analysis are currently underway to provide insights into the efficacy of DTG regimens and to inform future HIV treatment strategies in Botswana.

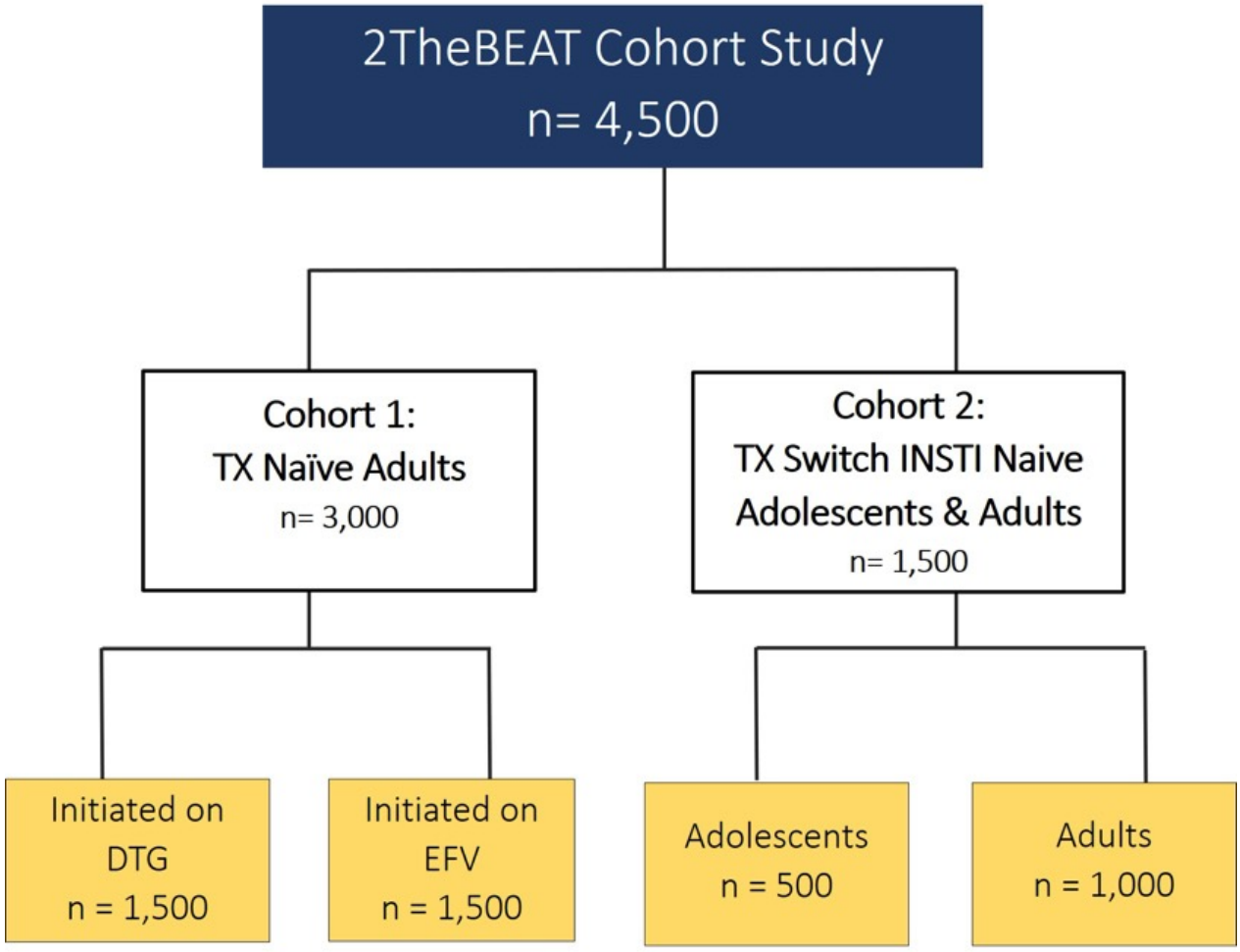


Figure 1: Study Schematic

e) SEXUAL REPRODUCTIVE HEALTH

BSRHI Team: Dedicated to advancing Sexual and Reproductive Health research

1) The diagnosis and treatment of Chlamydia Trachomatis and Neisseria Gonorrhea in Woman to prevent adverse neonatal consequences (Maduo/STI Study).

PI: Dr Chelsea Moroni, MD, MPH, PhD

Maduo, meaning "Results" in Setswana, is an NIH-funded study which aims to determine the burden of Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG) among asymptomatic pregnant women and to examine how testing of these infections affects post-delivery CT/NG prevalence and vertical CT/NG transmission to infants. The study also to accesses the acceptability, feasibility and cost-effectiveness of CT and NG testing and treating during antenatal care, as well as exploring partner notification preferences and experiences.

As in most sub-Saharan African countries, the syndromic management approach is used for management of STIs in Botswana which often misses asymptomatic cases and can lead to overtreatment for infections that are not present. While new diagnostic technologies for STI screening such as the Cepheid GeneXpert are increasingly becoming more affordable and available, However, there is a lack of data from Botswana to inform roll-out and scale up of chlamydia and gonorrhoea screening during pregnancy. This study aims to collect critical data to inform policymakers and enhance management of STIs during antenatal care and improve maternal and neonatal outcomes.

The study has completed recruitment of 500 participants from four clinics in the greater and follow-up of all participants have also been completed. To date, six papers have been published in peer reviewed journals, with data analysis ongoing for several more publications. Study findings were presented at the South Africa AIDS (SA AIDS) Conference in June 2023 and the 2023 STI and HIV World Congress in Chicago, USA in July 2023. The next steps include working with the Ministry of Health to explore the relevance of these findings for policy and practice change in Botswana.

Key results to date:

- Chlamydia and gonorrhoea prevalence among 251 asymptomatic pregnant women screened at the first antenatal care (ANC) visit was 23% and 1%, respectively.
- The highest prevalence of chlamydia was in the 15-24 age group (31%) (Figure 2).
- Chlamydia and gonorrhoea screening was highly acceptable; 96% of eligible women accepted testing.
- Chlamydia and gonorrhoea screening and treatment was feasible; 100% of participants enrolled were successfully screened and notified of results and 98% of participants were treated.
- At test-of-cure which took place approximately four weeks post-treatment, all participants were cured.

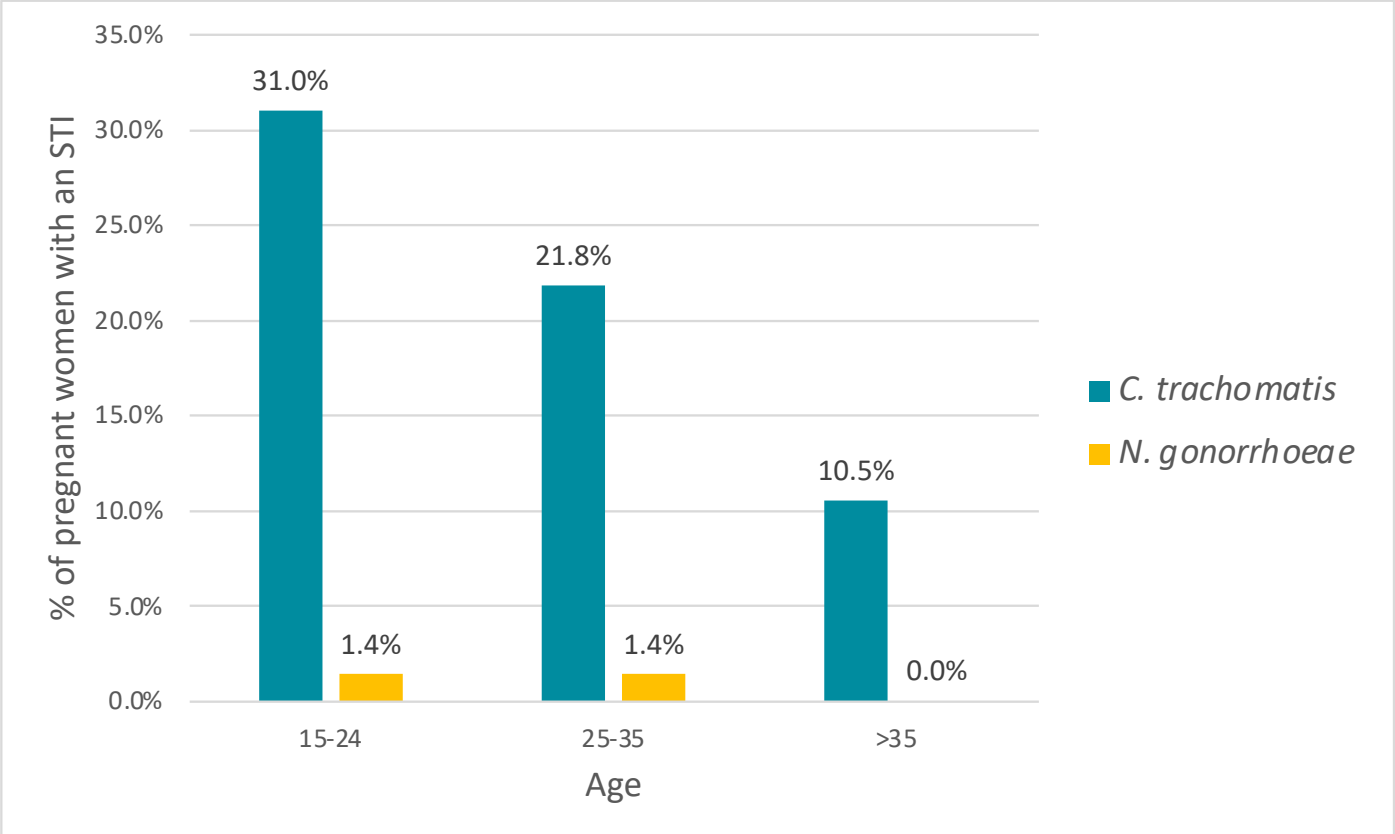


Figure 1. STI prevalence by age in pregnant women screened at first antenatal care visit in the Maduo Study, Botswana (2021-2022). STIs included Chlamydia trachomatis (C. trachomatis) and Neisseria gonorrhoeae (N. gonorrhoeae).

2) Maduo Syphilis Study: Dual HIV/syphilis point-of-care testing to improve identification and treatment of syphilis among pregnant women in Gaborone, Botswana.

PI: Dr Chelsea Moroni, MD, MPH, PhD

Maduo Syphilis is a Centers for AIDS Research (CFAR)-funded study which aims to assess the acceptability and feasibility of implementing point-of-care syphilis testing and treatment among pregnant women by providing. The study provides dual HIV and syphilis point-of-care testing for pregnant women who are HIV uninfected or undiagnosed, and point-of-care syphilis testing for HIV positive pregnant women with same-day treatment.

Botswana, which has the third-highest HIV prevalence in the world, has successfully scaled up rapid antenatal HIV testing coverage. However, antenatal syphilis testing and treatment is insufficient and thus women living with HIV continue to experience adverse pregnancy and neonatal outcomes. One strategy for improving syphilis testing and treatment coverage and reaching the World Health Organization's dual elimination goals is to integrate dual point-of-care HIV and syphilis testing. This strategy could increase syphilis testing by leveraging the success of the HIV testing program.

The study began in October 2023 and 400 participants were recruited from two clinics in Gaborone and completed follow-up in August 2023. Data analysis and manuscript preparation are ongoing.

3) Partner Notification Study: Use of expedited partner therapy in the treatment of sex partners of pregnant women with STIs.

PI: Dr Chelsea Moroni, MD, MPH, PhD

The Partner Notification Study is a sub-study of the Maduo Study which explores sex partner treatment strategies of sex partners of pregnant women to prevent adverse pregnancy outcomes in a high HIV prevalence setting. The study focuses on the experiences and attitudes of index patients, their sex partners, and local stakeholders regarding expedited partner therapy, where the index patient delivers treatment directly to the partner as a partner treatment strategy. The study aims to better understand social and

structural factors affecting partner treatment and provide insights to improve health services to this population.

The study has conducted qualitative in-depth semi-structured interviews with 30 participants who tested positive for chlamydia and/or gonorrhoea, 20 sex partners of participants testing positive for chlamydia and/or gonorrhoea, 20 stakeholders which includes clinicians, programme managers and policy makers providing or working in antenatal or sexual and reproductive healthcare in Botswana.

The study started in October 2022 and enrolled 28 participants testing positive for STIs, 10 sex partners and 15 stakeholders. Enrolment was completed in October 2023. Coding and analysis for the project is underway.

4) MAGUS Study: Multi-Country Aetiology of Genital Ulcer Study (MAGUS)

PI: Dr Chelsea Moroni, MD, MPH, PhD

The study which is being conducted in collaboration with the London School of Hygiene and Tropical Medicine and the Wellcome Sanger Institutes, aims to understand the causes of genital ulcer disease. Syphilis remains a significant cause of morbidity and mortality globally, with increased incidence rates observed in many populations. Most low and middle-income countries, including Botswana, rely solely on syndromic management of STIs which resulted in limited diagnostic surveillance data to inform treatment guidelines. The Multi-Country Aetiology of Genital Ulcer (MAGUS) Study seeks to address the gaps understanding of the genomic epidemiology of organisms associated with genital ulcer disease and hopes to help inform treatment guidelines.

The study began in October 2022 and completed participant enrolment in December 2023, with a total of 186 participants. PCR testing has been completed at the BHP laboratory and samples have been shipped to the Sanger Institute in the UK for genome sequencing. The findings were presented at the IUSTI 2024 conference in Sydney, Australia in September 2024.

5) PREPARE Study: PRomoting Equity for Pregnant Adolescents in REsearch (PREPARE)

PI: Dr Chelsea Moroni, MD, MPH, PhD

The PRomoting Equity for Pregnant Adolescents in REsearch (PREPARE) is a multi-country study aimed at addressing ethical concerns regarding the inclusion of pregnant adolescents in HIV and co-infections research. The study is being conducted in collaboration with the University of Northern California at Chapel Hill and Botswana-Baylor Children's Clinical Centre of Excellence.

Pregnant adolescents are often excluded from HIV prevention and treatment studies, which has led to significant gaps in the evidence base for policy and care decisions. The study interviews adolescents who have been pregnant and are living with or at risk of HIV to understand their views on research participation. The study also engages a diverse group of HIV research stakeholders on the inclusion of pregnant and lactating adolescents in the HIV and co-infections research agenda and participation in clinical trials.

The study completed enrolment in October 2023, with 40 adolescents and 17 stakeholders enrolled. The study established a youth advisory board to ensure that the research is relevant and reflects of the needs of pregnant adolescents living with HIV. Analysis is ongoing.

6) PrEP DCE Study: Evaluation of pregnant and breastfeeding women's preferences and attitudes towards long-acting pre-exposure prophylaxis: A discrete choice experiment (DCE)

PI: Dr Chelsea Moroni, MD, MPH, PhD

The PrEP DCE Study aims to evaluate the preferences and attitudes of pregnant and breastfeeding women towards long-acting pre-exposure prophylaxis (PrEP) using a discrete choice experiment.

Novel longer-acting PrEP agents in the pipeline are promising for increased HIV prevention options, improved adherence, and better coverage. These include dapivirine vaginal rings, long acting injectables, and newer oral ARVs, such as Islatravir, now being studied as PrEP. While answers to questions on efficacy and safety of these agents are pertinent, evidence shows that uptake of and adherence to new products by target populations is even more important to effective HIV prevention. Therefore, this study seeks to understand the values, needs, practices and preferences of the target population, to inform customized health recommendations, future research, implementation, and sustainability of HIV prevention.

The study started in May 2023 and was completed in December 2023. Ten (10) participants were enrolled for in-depth interviews in Botswana and 150 participants took part in a discrete choice experiment survey. A publication on the findings is currently in review in a peer-reviewed journal. The main study findings were that women strongly favoured non-vaginally inserted and non-implanted PrEP compared to oral PrEP and preferred combination prevention methods for HIV, STIs and pregnancy over HIV prevention alone.

7) GETSA Study: The Genomic Epidemiology of Treponema Pallidum in Southern Africa

PI: Dr Chelsea Moroni, MD, MPH, PhD

The GETSA aims to determine the aetiology of genital ulcer disease in South Africa and Botswana and to conduct an analysis of Treponema pallidum genomes in swabs obtained from symptomatic individuals with suspected syphilis. There is limited epidemiological data of syphilis in the general population as most of the syphilis burden of disease estimates are derived from antenatal surveys and mathematical modelling. There is also a lack of Treponema pallidum genomic data from Sub-Saharan African with most genomes published in literature collected from Europe, the USA and Australia. Closing this gap and ensuring geographic inclusivity is urgently needed. The study started in October 2023 and has to date enrolled 57 participants.

8) RETI Study: Exploring bystander risks and benefits in HIV pre-exposure prophylaxis trials and opportunities for engagement

PI: Dr Chelsea Moroni, MD, MPH, PhD

This study aims to assess men and women's attitudes and preferences regarding male partner engagement in HIV prevention research and services for pregnant and breastfeeding women (PBFW) in Botswana through in-depth interviews. The sex partners of participants enrolled in HIV prevention trials may face both risks and benefits associated with research activities and are considered "bystanders." Currently, there are no guidelines related to managing the risks of bystanders in HIV pre-exposure prophylaxis trials (PrEP) and researcher obligations to bystanders are unclear. The RETI study commenced in June 2024 and has thus far enrolled two PBFW and their partners.

9) AAA Study: Planning for the "Antenatal micronutrients, Asprin and Azithromycin for maximum reduction of preterm birth related outcomes" trial.

PI: Dr Chelsea Moroni, MD, MPH, PhD

When a baby is born too early or too small, it presents a significant health challenge. In 2023, the term "small vulnerable newborns" was conceptualized to emphasize the increased vulnerability of premature, small for gestational age, or low birth weight infants. Small vulnerable newborns are at an increased risk of mortality, morbidity, developmental delays, chronic diseases and a lifetime of reduced well-being. In 2020, small vulnerable newborns accounted for one in four live births globally, with low- and middle-income countries bearing the greatest burden. There is an urgent need to develop and implement effective and scalable prevention strategies to reduce the risk of small vulnerable newborn births in resource-limited settings. Targeting factors such as poor maternal nutrition, inflammation, and infections with simple-to-deliver combination regimens in routine antenatal care may be of benefit.

Building on our work in STI screening and treatment in pregnancy and ancillary findings from our studies on gaps in maternal health and antenatal care in Botswana, the BSRHI team has received funding from Open Philanthropy USA to develop and plan for a large-scale randomized trial in Botswana and South Africa. This trial will investigate interventions in routine antenatal care to reducing preterm birth.

f) MALIGNANCIES STUDIES

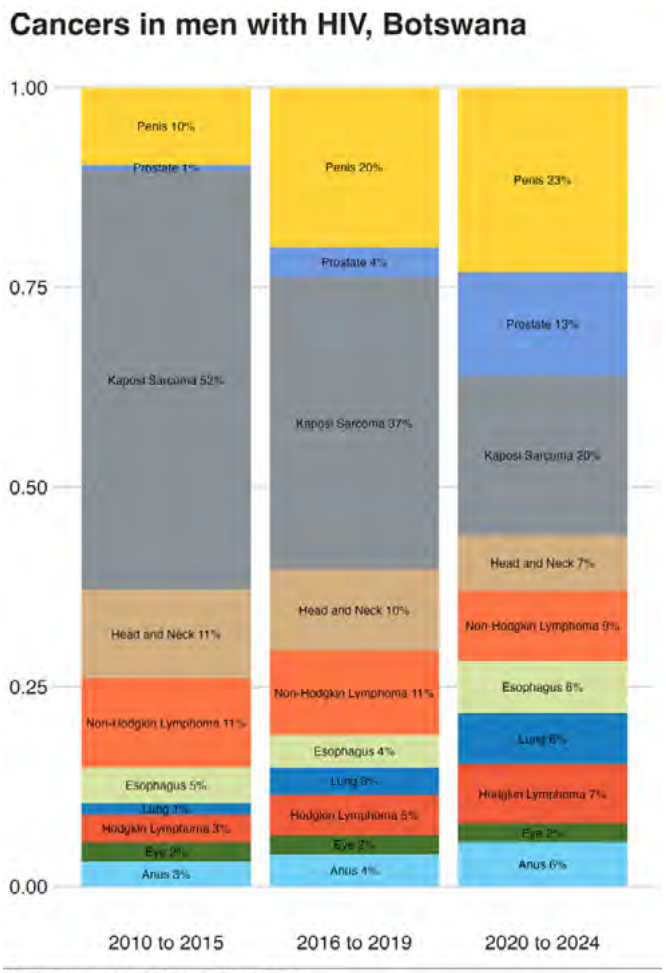
1) HIV and Malignancy in Botswana: An Observational Study of Medicine Toxicity of Concurrent Treatment and Clinical Outcomes (Thabatshe Study)

PI: Dr Scott Dryden-Petersen, MD, MSc

The Thabatse team continues its mission to understand and reduce the burden of cancer in Botswana and the region since 2010. This project has two main components: (1) an observational study tracking response and treatment toxicity in patients treated for malignancies, and (2) strengthening the cancer registry to evaluate cancer risk factors and longitudinal trends. Thabatse, one of the largest cancer cohorts in Africa (n=7,045), enrols consenting patients entering cancer care from principal treatment facilities in Botswana.

Patients are followed quarterly for five years, achieving a >98% retention rate, to assess key factors in cancer development, delayed treatment, and treatment outcomes. Findings from the Thabatse Cancer Cohort (TCC) have informed the Ministry of Health's cancer control plans, WHO guidance, and international NCCN treatment guidelines and is recognized as the leading source of global epidemiologic and outcomes data on cancer in the context of HIV.

The dedicated team driving groundbreaking cancer research



Thabatse cancer cohort, 2010 to 2024

Recent Findings:

• Thabatse cohort supported development of scientific agenda for IARC/WHO and US National Cancer Institute. Engels ES et al. Int J Cancer. 2024.
• Motswana breast cancer survivors with HIV experience similar quality of life gain following cancer treatment women without HIV. Dykstra MP et al. JCO Global Oncology 2024.
• People with HIV remain at substantially greater risk of HPV-associated cancer despite receiving ART for five or more years. ART does not reduce risk. Mendu M et al. CROI 2024.
• Large changes in cancers diagnosed in Botswana. Leading cancers shared with community members.

2) Potlako+: A Multilevel Intervention to Improve Timely Cancer Detection and Treatment Initiation in Botswana

PI: Dr Scott Dryden-Petersen, MD, MSc & Dr Neo M. Tapela, MD, MPH

The Potlako+ trial is a community-based, randomized study across 20 diverse communities, aiming to improve early cancer diagnosis and treatment initiation. This trial compares two groups and combines assessing both the effectiveness and implementation of an intervention designed to encourage earlier clinic visits for symptoms potentially indicating cancer, streamline diagnosis, and start timely cancer care.

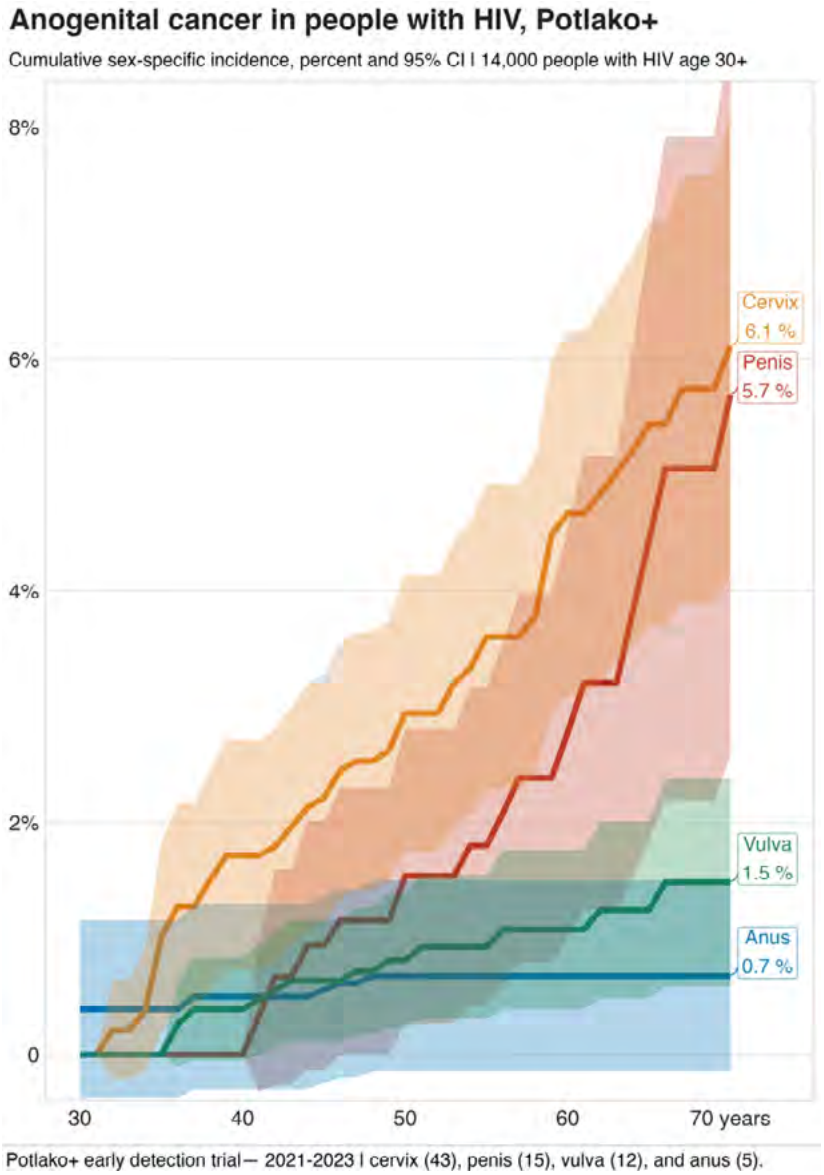
To achieve these goals, the trial includes community cancer education, diagnosis support, and care initiation. This is done through community campaigns, group education, information materials, health provider training, and onsite, longitudinal support for over 850 patients suspected of having cancer. Enrollment will conclude in November 2024, followed by study close-out activities.

Men's Pitso: Potlako + Study team educating men on cancers at Mandunyane Kgotla

Community members attending the Potlako+ Study Cancer Education session at Mmathethe

Recent Findings

• Community campaigns to increase community cancer knowledge, improve diagnosis and linkage-to-care for patients with cancer. The study conducted five community campaigns in Mandunyane, Nata, Mmathethe, Metsimotlhabe and Shoshong communities respectively. A total of 1519 community members were reached with cancer message and services. The project engaged several stakeholders, such as, but not limited to, Dikgosi and VDCs, DHMTs, Journey of Hope, Village Imaging, Tebelopele, VIA clinic, and Diagnofirm Medical Laboratories which provided free PSA and pap smear sample testing in Mmathethe and Metsimotlhabe communities. Special consultation facilities were offered to men, for cancer evaluation. A total of 60 cancer suspects were identified and navigated.
• Staff turnover and reshuffling has been one of the big challenges in maintaining teams that are trained and able to efficiently identify patients with symptoms suggestive of moderate or high risk of cancer.
• Interruptions of patient management systems affect patient appointments and linkage to care turnaround times.
• Burden of HPV-associated cancers is large among rural Batswana population living with HIV. Penile and cervical cancer are leading causes among older residents.



3) Evaluation of triage strategies and screening intervals in an HPV-based cervical cancer screening program in Botswana

PI: Dr Rebecca Luckett, MD, MPH

This is a follow-up study is aimed at improving cervical screening by evaluating screening algorithms using primary HPV testing followed by standard-of-care and novel triage strategies in women living with HIV in Botswana. It is also evaluating long term outcomes in an HPV based screening programme.

The study has enrolled 3000 women (both with and without HIV). In March 2023, the study-initiated follow-up re-enrolment among approximately 1,300 women living with HIV with plans for ongoing follow-ups to continue at 1, 2, and 3-year intervals depending on the results of baseline screening. So far, 529 participant have been re-enrolled. The study also started qualitative interviews with participants in the cohort in June 2024 to gain more in-depth understanding of women's knowledge, attitudes and practices regarding HPV cervical screening.

The HPV research team: Bridgette Wamakima, Salma Amin, Olorato Mokime, Janet Gaborone and Lorato Mochoba

g) NETWORK CLINICAL TRIALS

CTU PIs: Dr Shahin Lockman MD, MPH; Dr Joseph Makhema, MB. ChB, FRCP

Community members attending the Potlako+ Study Cancer Education session at Mmathethe

ACTG STUDIES

The ACTG is a global clinical trials network that conducts research to improve the management of HIV and its comorbidities; develop a cure for HIV; and innovate treatments for tuberculosis, hepatitis B, and emerging infectious diseases. The following studies are being conducted under the ACTG Network in Botswana:

1)PHOENIx (A5300B): Protecting Households on Exposure to Newly Diagnosed Index Multidrug Resistant TB patients.

Site PI: Ayotunde Omoz-Oarhe, MBBS

This study aims to assess the efficacy and safety of Delamanid, a novel anti-TB drug, compared to Isoniazid, the standard of care, in protecting high-risk Household Contacts (HHCs) from acquiring TB. The study aims to enrol 5,160 MDR-TB index cases and their household contacts across multiple study sites. Since the study began in 2019, Botswana has enrolled 49 participants out of a target of 300. Recruitment has been slower than anticipated due to a low burden of MDR-TB cases in Botswana. This has been compounded by local testing challenges due to shortages in GeneXpert cartridges, which has made it difficult to identify study participants. The study is projected to reach full enrolment in May 2025.

2)A5379: B-Enhancement of HBV vaccination in Persons Living with HIV (BEe-HIVe): Evaluation of HEPLISAV-B.

Site PI: Ayotunde Omoz-Oarhe, MBBS

The A5379 study enrolled adults living with HIV with a history of nonresponse to hepatitis B vaccination (HBV vaccine-experienced) and those living with HIV with no known prior history of HBV vaccination (HBV vaccine-naïve). The study evaluated a two-dose and a three-dose regimen of HEPLISAV-B, each compared to a standard three-dose regimen of ENGERIX-B in HBV vaccine-experienced participants. It also evaluated the efficacy of a three-dose regimen of HEPLISAV-B vaccine compared to historical response rates in the HBV vaccine-naïve participants.

Opened in 2022, the study enrolled 633 participants globally, including 29 in Botswana. Results from primary analysis were presented at the Conference on Retroviruses and Opportunistic Infections (CROI) 2024 in Denver, Colorado on March 6, 2024. The analysis showed that 93% of participants receiving two doses of the HepB-CpG vaccine and 99% receiving three doses of the HepB-CpG vaccine achieved a seroprotection response compared to 81% of those receiving three doses of the conventional hepatitis B vaccine. The most frequently reported adverse events were vaccination site pain, fatigue, headache, malaise, and myalgia. No unexpected safety issues were observed. The study closed to follow-up in July 2024.

3)A5356: A Phase II, Prospective, Randomized, Multicenter Trial to Evaluate the Efficacy and Safety/ Tolerability of Two Linezolid Dosing Strategies in Combination with a Short Course Regimen for the Treatment of Drug Resistant Pulmonary Tuberculosis (DR-TB).

Site PI: Ayotunde Omoz-Oarhe, MBBS

The A5356 trial is designed to evaluate the efficacy, safety and tolerability of two dosing strategies for Linezolid (LZD) in combination with a short course regimen for treating drug-resistant pulmonary tuberculosis (DR-TB). DR-TB is a major threat to human health worldwide, accounting for approximately 3.4% of all new TB cases. However, there is currently no “standard of care”, or single standardized treatment regimen recommended for all patients with DR-TB. Treatment generally requires longer duration (often extends 18 to 24 months) using second-line TB drugs that are generally more toxic and less active than first line therapies. This study aims to evaluate the efficacy, safety, and tolerability of an injectable-free short course regimen for treatment of drug-resistant-TB comparing, two dosing strategies of linezolid (LZD) combined with bedaquiline (BDQ), delamanid (DLM), and clofazimine (CFZ). The study will enroll adults aged 18 years and older, with or without HIV, who have recently been diagnosed with pulmonary DR-TB. The study opened in August 2022 and has enrolled 135 participants globally, including two in Botswana.

IMPAACT STUDIES

1) IMPAACT 2017 - Phase I/II Study of the Safety, Acceptability, Tolerability, and Pharmacokinetics of Oral and Long-Acting Injectable Cabotegravir and Long-Acting Injectable Rilpivirine in Virologically Suppressed HIV-Infected Children and Adolescents.

Site PI: Gaerolwe R. Masheto, MD

The primary objective of the study is to confirm the dosage and assess the safety, tolerability, acceptability, and pharmacokinetics (PK) of oral cabotegravir (CAB), long-acting injectable cabotegravir (CAB LA), and long-acting injectable rilpivirine (RPV LA) in virologically suppressed HIV-1 infected children and adolescents aged 12 to under 18 years.

As of 29 August 2022, the study achieved the global accrual target of 155 participants. Of these, 25 participants were enrolled from two Botswana sites (Gaborone and Molepolole). Currently, 24 participants are in the long-term safety follow-up extension after completing 96 weeks of study follow-up, while one participant was taken off study due to pregnancy.

The study continues to evaluate the safety, tolerability, acceptability, and pharmacokinetics of oral CAB, CAB-LA, and RPV-LA. The results from this study are anticipated to support the expansion of treatment formulation options for children and adolescents living with HIV-1 to improve adherence and treatment satisfaction.

2) IMPAACT 2026 - Pharmacokinetic Properties of Antiretroviral and Anti-Tuberculosis Drugs during Pregnancy and Postpartum.

Site PI: Gaerolwe R. Masheto, MD

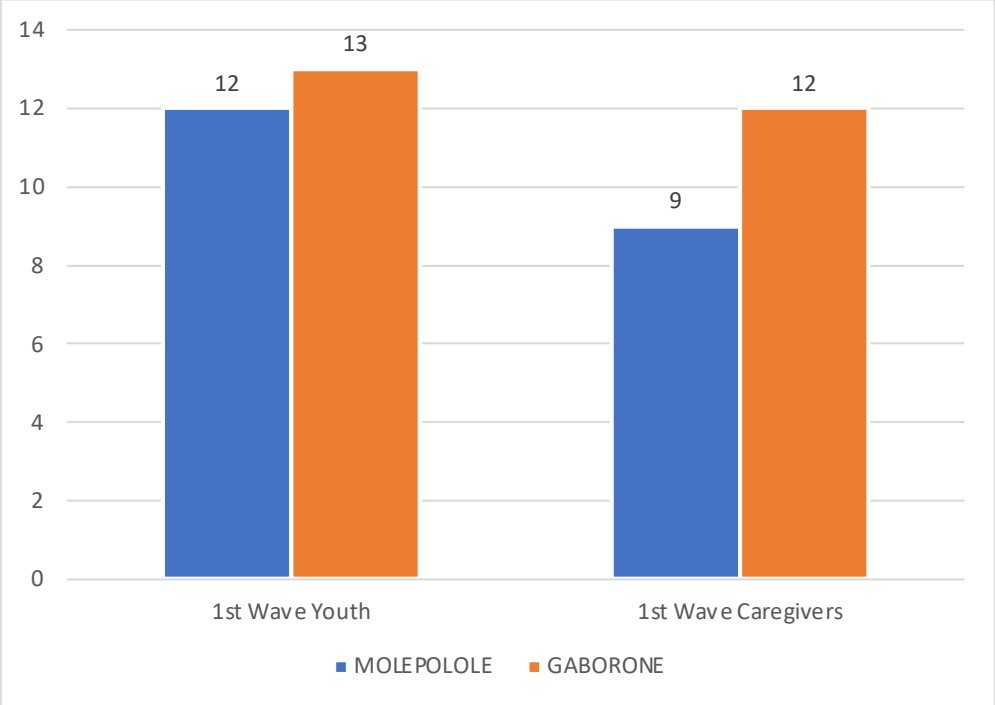
The primary objective of the study is to describe the pharmacokinetic (PK) properties of antiretroviral (ARV) and anti-tuberculosis (TB) drugs administered during pregnancy and postpartum. The study aims to enroll up to 325 women and their infants globally, including 10 women and their infants from Botswana. Even though the study was opened in April 2022, no participant has been enrolled yet due to challenges in identifying potential participants at the healthcare facilities where recruitment is taking place.

3) IMPAACT 2016 - Evaluating a Group-Based Intervention to Improve Mental Health and ART Adherence Among Youth Living with HIV in Low Resource Settings.

Site PI: Gaerolwe R. Masheto, MD

The IMPAACT 2016 study aims to evaluate whether a Trauma Informed-Cognitive Behavioral Therapy (TI-CBT) Intervention is associated with improved depression, anxiety, and/or traumatic stress symptoms in youth living with HIV, compared to a Discussion Control over a six-month period. The study aims to enroll up to 256 participants globally, with 56 participants from Botswana.

Botswana sites (Gaborone and Molepolole) have completed the study's Pilot Test in January 2024, enrolling 16 youth and caregiver pairs across both sites. The Molepolole completed the first wave (six youth sessions and two caregiver sessions) of the Randomized-Controlled Trial (RCT) part of the study in June 2024. The Gaborone site had not completed the first wave by the end of the reporting period (June 2024).



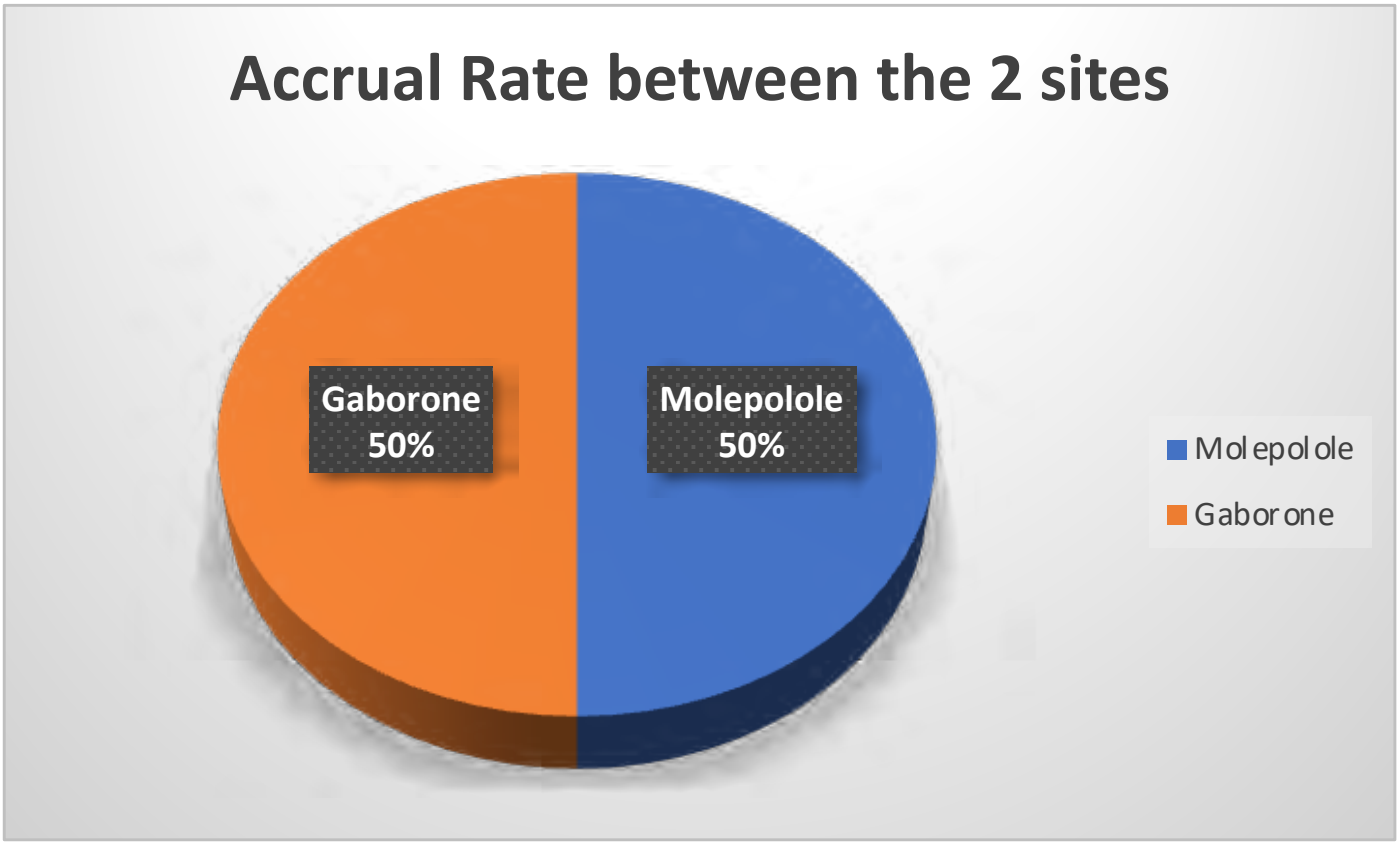
IMPAACT 2016 Wave 1 Accrual

4)IMPAACT 2036 - Phase I/II Study of the Safety, Tolerability, Acceptability, and Pharmacokinetics of Oral and Long-Acting Injectable Cabotegravir and Rilpivirine in Virologically Suppressed Children Living with HIV-1, Two to Less Than 12 Years of Age

Site PI: Gaerolwe R. Masheto, MD

The primary objectives of this cohort are to describe the repeat-dose pharmacokinetics of CAB + RPV (oral and injectable) through Week 24 and to assess the safety of the oral lead-in of CAB + RPV, and the safety of CAB + RPV (oral and injectable) over the same period (week 24). The global target is to enroll up to 90 participants and their parents/caregivers, with a plan to enroll up to 20 participants in Botswana.

A total of 16 participants (child and parent/caregiver pairs) have been enrolled across two sites since 6th Mar 2024, under Cohort 1, covering weight bands 1, 2, and 3. In May 2024, the study team requested and received approval from both local and Harvard ethics committees to increase the accrual target from 20 to 40 participants. The study is currently temporarily paused for interim data analysis.

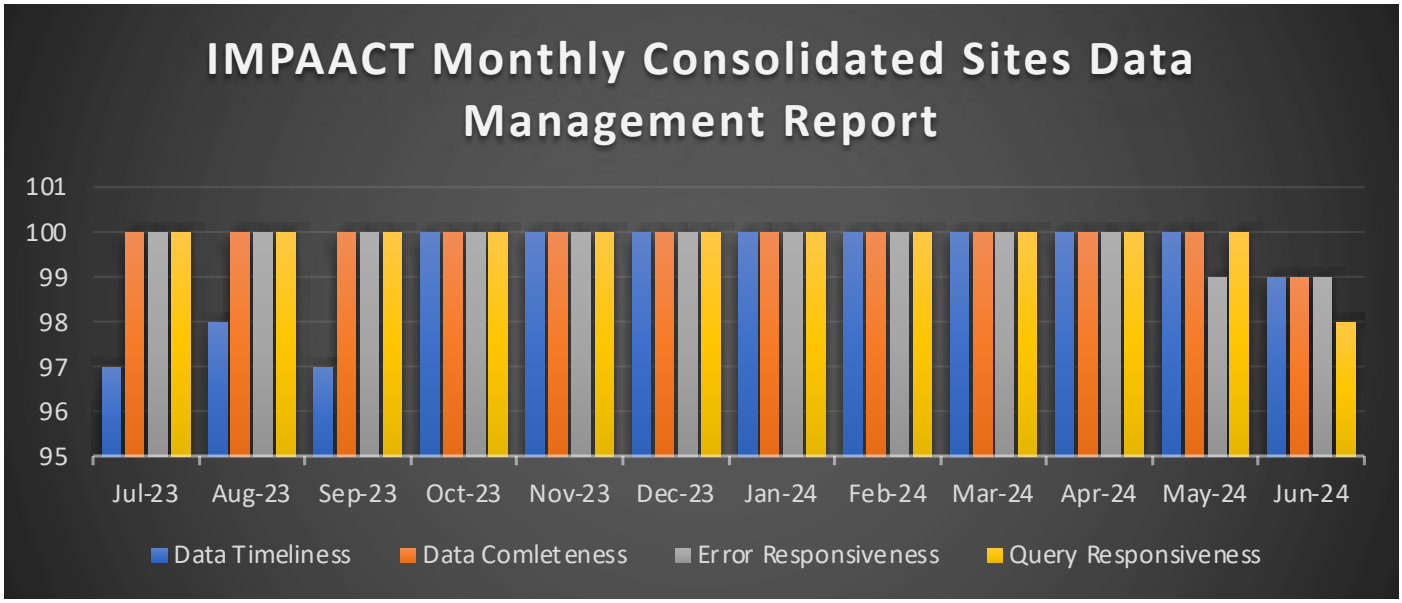


5)IMPAACT 2028 – Long-Term Clinical, Immunologic, and Virologic Profiles of Children who Received Early Treatment for HIV.

Site PI: Gaerolwe R. Masheto, MD

The primary objective of this study is to characterize the long-term clinical, immunologic, and virologic profiles of children who received early treatment for perinatally-acquired HIV. The study population consists of participants previously enrolled in the IMPAACT 2008 study. The target accrual for the Botswana sites is six participants, with five currently there enrolled across the Gaborone and Molepolole sites.

IMPAACT DATA MANAGEMENT REPORT_2023-2024



HPTN/HVTN STUDIES

HPTN / CoVPN Team

The HIV Prevention Trials Network /HIV Vaccine Trials Network (HPTN/HVTN) is a worldwide collaborative clinical trials network that develops and tests the safety and efficacy of interventions designed to prevent the transmission of HIV.

1) HPTN 084: A Phase 3 Double Blind Safety and Efficacy Study of Long-Acting Injectable Cabotegravir Compared to Daily Oral TDF/FTC for Pre-Exposure Prophylaxis in HIV-Uninfected Women.

Site PI: Dr Joseph Moeketsi Makhema, MB. Ch.B., FRCP

This is a Pre-Exposure Prophylaxis (PrEP) study being conducted among women at 20 sites across seven countries in Sub-Saharan Africa, including the BHP in Botswana. Participants who were willing to continue taking CAB-LA PrEP are being followed up in anticipation of receiving approvals for the use of CAB-LA as PrEP in the country following the study results. In the interim, the study product provider, ViiV Healthcare will continue providing CAB LA to participants who are willing to remain on PrEP for up to three years or until CAB LA becomes available through the national program, under a study called GSK221163. As of 16 August 2024, the site has been activated to transition eligible participants from the HPTN084 study to this study new study.

CoVPN STUDIES

1)CoVPN 3008: Multi-Centre, Randomized, Efficacy Study of an Early vs Deferred mRNA COVID-19 mRNA Vaccine in Regions with SARS-CoV-2 Variants.

Site PI: Dr Joseph Moeketsi Makhema- MB. ChB, FRCP

The study evaluated the safety and effectiveness of the Moderna COVID-19 mRNA vaccine across seven African countries. It included adults living with HIV, who may have weaker immune systems, as well as adults with other conditions, such as obesity or diabetes, which may increase the risk of severe COVID-19. The study aimed to assess how well the Moderna COVID-19 mRNA vaccine helped to prevent COVID-19 illness, including severe illness among participants. The study also compared how mRNA vaccine work in individuals who previously had COVID-19 compared to those who had not.

Study Summary

What was learned from comparing protection from COVID-19 among participants with a prior history of COVID-19 versus those without prior COVID-19?

• People with prior COVID-19 infection who got one vaccination before month 6 had a significantly lower chance of getting ill or severely ill from COVID-19 in the first 6 months after vaccination compared to people without prior COVID-19 at enrolment who got two vaccinations before month 6.

• This suggests that the combination of prior infection plus vaccination may provide even stronger protection against COVID-19 than vaccination alone. In other words, prior COVID-19 likely enhances the protection provided by vaccination.

How safe were the vaccines in the study?

• COVID-19 mRNA vaccinations were safe and caused few significant side effects, including in people living with HIV, people with past COVID-19 infections, and pregnant persons.

• When people had reactions, most were brief and mild. The most common reactions were pain in the area where the vaccination was given, headache, and feeling tired.

What else has been learned from the study so far?

A few participants who got COVID-19 infection continued to test positive for the virus for a long time, even after they felt well. Why this happens is being studied further. It is also being studied whether these longer infections result in more virus spread, and whether these longer infections result in the virus changing into a more harmful strain.

Source: CoVPN 3008 Study Summary Document, 3 June 2024, V1.0

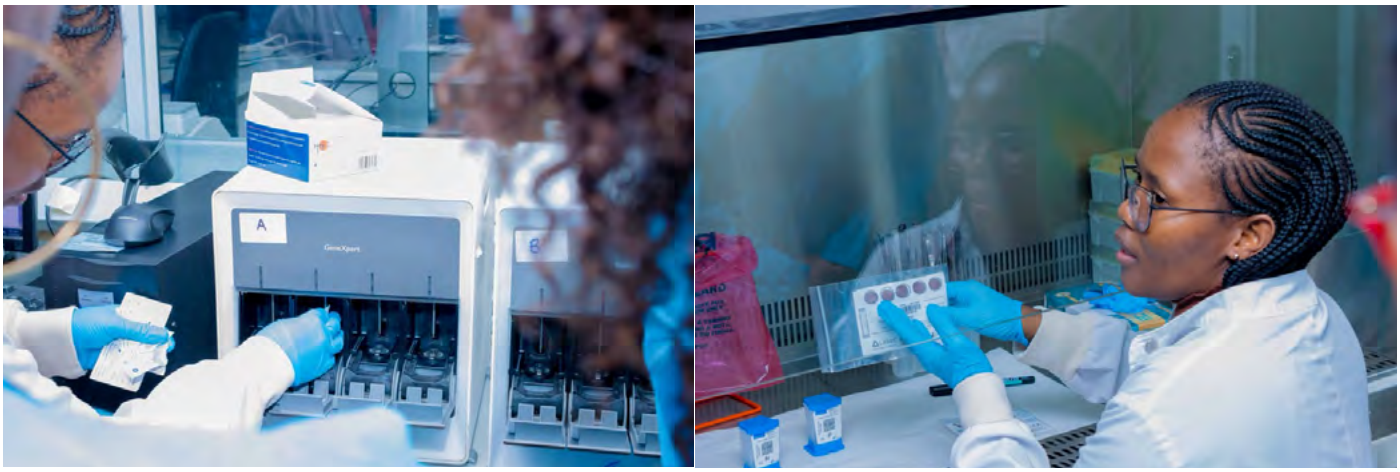
RESEARCH SUPPORT

1) Clinical Laboratory

The Botswana Harvard HIV Reference Laboratory (BHHRL) serves as the primary local laboratory for the Botswana Harvard Health Partnership (BHP). Throughout 2023-2024, BHHRL continued to support various clinical trials conducted by BHP and collaborating institutions. In addition to its research role, BHHRL partners with the Ministry of Health through the National Health Laboratory (NHL), contributing to national public health efforts, including providing laboratory testing support for the National ARV program.

BHHRL ensures full coverage for all the clinical trials at BHP by offering a range of services such as receiving and processing samples, cell separations and cryopreservation, diagnostics, safety and monitoring, as well as specialized research assays. These services ensure high-quality testing for key assays required for the enrollment and management of study participants.

Owing to its compliance to Good Clinical Laboratory Practice (GCLP) guidelines, BHHRL is approved to offer laboratory services for clinical trials supported by the US National Institutes of Health (NIH) and the Division of AIDS (DAIDS) through networks such as ACTG, IMPAACT, HPTN and CoVPN. In 2023, BHHRL became the first lab in the region to successfully transition its accreditation from the ISO 15189:2012 standard to the new ISO 15189:2022 standard under the Southern African Development Community Accreditation Service (SADCAS). The transition underlines BHHRL's commitment to maintaining the highest standards of quality and competence in both medical laboratory services and research.



Laboratory Scientist doing Point of Care (POC) Testing

Activities of the Clinical Laboratory

- Processing and Accessioning
- Inventory and Archiving (Biorepository management)
- Safety Labs: Clinical Chemistry, Hematology
- Monitoring Labs: CD4, HIV Viral load,
- Molecular Assays: Diagnostic DNA PCR, HPV PCR, Chlamydia and Gonorrhea, HIV Drug Resistance, SARS-CoV-2 RT-PCR testing, Cepheid Gene Xpert assays (Point of Care HIV-1 Viral load, HIV-1 Qualitative, MTB/RIF, HPV and SARS-CoV-2).
- Serological Assays: Fourth generation HIV ELISA, Hepatitis B profiles, Hepatitis C Antibody, Syphilis RPR and TPHA, HIV-1 confirmatory assays (Geenius), Incidence Assays [Limiting Antigen, Avidity, Bio-Rad Avidity and BED capture enzyme immunoassay], QuantiFERON TB Gold Plus assay
- In-House Research Assays
- Referral Testing: TB (AFB, Molecular, culture and Drug Sensitivity), Cytology/Histology, and inflammatory cytokines).

The laboratory has registered all assays in External Quality Assurance (EQA) programs. Specimen volumes received in the laboratory were stable over the year, however the nature and type of lab visits led to an increase in processing intensity and complexity, for tasks such as pharmacokinetics sampling and PBMC isolation.

Prof Catherine Koofhethile analyzing results

The laboratory also maintains a specimen biorepository housing approximately 1,5 million samples across more than 40 ultra-low-temperature freezers and six liquid nitrogen storage facilities. To address freezer space challenges, in 2024 the laboratory initiated a sample archiving and freezer cleanup exercise to create more storage capacity.

BHHRL is also actively involved in several technical working groups, including Biosafety and Biosecurity and Molecular Testing for various pathogens and the Botswana Public Health Institute.

2) Regulatory Office

The BHP Regulatory Office plays a vital role in upholding research integrity and ensuring ethical compliance across all BHP research projects. During the reporting period, the office supported a total of 95 studies, with 25% of these being clinical trials. This highlights the office's critical role in ensuring regulatory compliance and maintaining the highest standards of ethical conduct within BHP's diverse research portfolio. During this period, 17 (16%) new applications were approved, and 12 (11%) studies were closed (Figure 1).

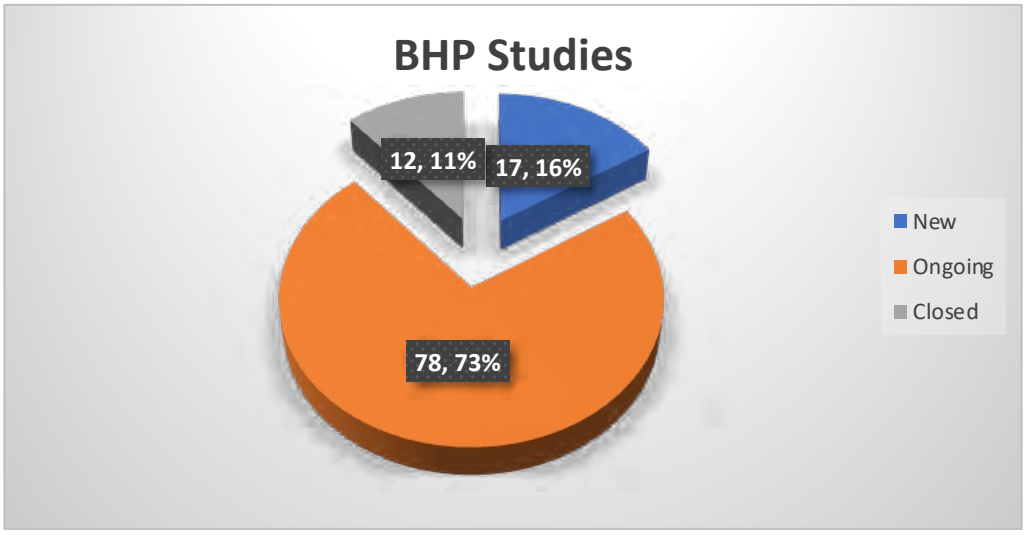


Figure 1: BHP Studies

Among the 17 new studies, nine were Principal Investigator initiated or were non-network studies, three were from the Research Lab for master's and PhD students or Early Career Researchers (ECRs) and five were network studies.

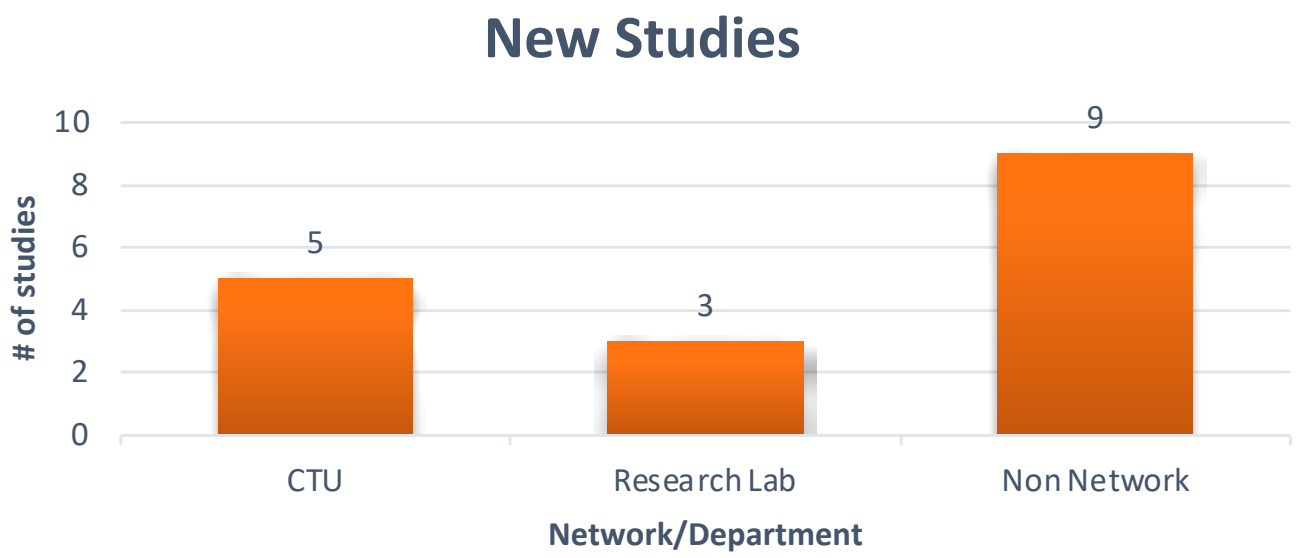


Figure 2: New Studies

Capacity Building

The Regulatory Office continued its commitment to capacity building through Responsible Conduct of Research (RCR) training. From September 5-8, 2023, the team conducted in-person RCR training for 23 participants. To date, 178 BHP staff and stakeholders have been trained, reinforcing the dedication to upholding research integrity across the organization.

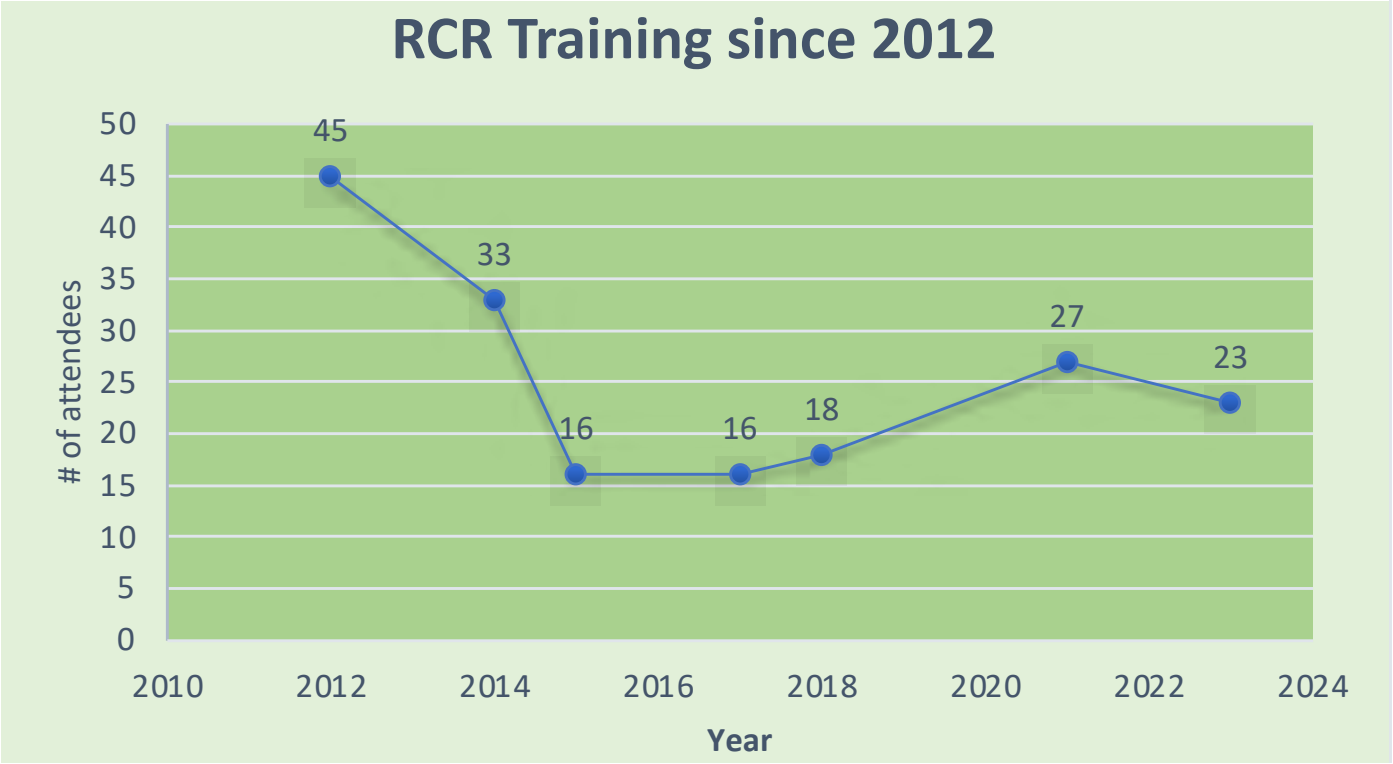


Figure 3: RCR Training

Poster Presentations

The BHP Regulatory Office continues to contribute to the global dialogue on research integrity through participating in international conferences. In this reporting period, the Regulatory team presented a poster at the Canadian Bioethics Society Conference, Montreal, Canada in May 29-31, 2024.

3) Community and Stakeholder Engagement

BHP Team at the World AIDS Day 2023 in Nata

Community and Stakeholder Engagement is enshrined in the ethics of clinical trials. This is further articulated in the UNAIDS Good Participatory Practice (GPP) updated in 2011, which has established a framework for community and stakeholder engagement. AVAC has taken initiatives to strengthen the capacity of community and stakeholder engagement practitioners and advocates globally. Engaging communities and stakeholders are crucial for building collaborative partnerships and ensuring that communities and stakeholders are actively involved in the research process as beneficiaries of research outcomes.

BHP employs several strategies to engage these important stakeholders, including:

1. BHP Community Advisory Board (CAB): Comprising of volunteers from various communities and Civil Society Organizations, the CAB's mandate is to bridge the communication gap between communities, civil society and researchers. Its mission is to ensure that research addresses public health needs and that communities receive accurate and timely information about studies and other health matters. Some CAB members represent BHP CAB in various committees and clinical trials network structures. Ms Baraedi Winnie Sento serves as Non-Scientist member of the University of Botswana Institutional Review Board (UB IRB) and co-chairs the ACTG Community Scientific Committee (CSS), while Ms Neo Monnapula and Mr Modiko Molefi are CSS members, and BHP CAB Chairperson, Mr Dichaba Siane is a member of the IMPAACT Network CAB Leadership Group.

Neo Monnapula

Winnie Sento

Modiko Molefi

Dichana Siane

2.Outreach to News Stakeholders: BHP actively identifies and engages new stakeholders, especially NGOs, to foster and maintain existing relationships. This year BHP connected with the following organisations:
- Mental Health Network of Botswana which offers free services to individuals experiencing mental issues.
- Botswana Substance Abuse Network (BOSASNET), which provides rehabilitation for people struggling with substance addiction.
- Sentebale, which provides psychosocial support to young people living with HIV.

Additionally, organised several meetings with stakeholders to share knowledge and up-to-date information in clinical trials:

1. HIV Cure Research Workshop: The target audience of the meeting was the Ministry of Health, partners, HIV service providers, communities, and students on attachment at the Botswana Harvard HIV Reference Laboratory (BHHRL). The purpose of the meeting was to introduce HIV cure research to the public. BHP partnered with Centre for Youth of Hope (CEYOHO) and HIV Cure Africa Acceleration Partnership (HCAAP). This meeting helped discover that many attendees had limited understanding of HIV cure research and primarily relied on social media and internet for information.

Group discussion during the HIV Cure Workshop

2. BHP Stakeholders Meeting: This important BHP stakeholder meeting, sponsored by Trials of Excellence in Southern Africa (TESA), was held on April 19, 2024. The purpose of the meeting was primarily to:

a. Facilitate interaction and foster appreciation of each other's mandate among researchers (BHP, UPENN,) Ministry of Health officials (policy makers, programme designers and implementors), civil society, research regulators (HRDC, UB IRB and BOMRA), and former study participants.
b. Enhance transparency in research and clinical trials by clarifying the roles of the various stakeholders.
c. Share experiences among former study participants.

The meeting was deemed successful, and there are plans to continue hosting similar annual meetings in the future.

Stakeholder Engagement Meeting on Advancing Clinical Trial

BHP CAB members, Dichaba Siane, Eddie Rantshilo, Lesego Tshwelane and Kgosi George Thwane participated in a panel discussion on integrating health services into HIV care as part of the InterCARE Study Annual Meeting held on the 28-30 May 2024. The aim was to gather community feedback on the study and help dispel misinformation.

The BHP Community Engagement Coordinator Ernest Moseki was invited to co-present at the ACTG-HPTN joint plenary session on 16 June 2024 at the Annual Network meeting. His presentation was titled "Reaching Populations with High HIV Incidence and Limited Access to services". CAB Member, Neo Monnapula also delivered a presentation on 11 June 2024 during the community sessions at the ACTG annual group meeting.

4) Pharmacy

Pharmacy Technician, Calvin Mongwaketse prepares study medication under a biosafety cabinet

The BHP Pharmacy Department provides pharmaceutical services to all studies involving study drugs. The department supports study participants and BHP personnel with Government concomitant medication for primary ailments. The scope of Pharmacy department includes:

• Submissions to Botswana Medicines Regulatory Authority (BoMRA) for all studies involving a study drug to ensure regulatory compliance.
• Validation and optimal operation of storage locations and equipment, including temperature monitoring to maintain medication efficacy and potency.
• Acquisition of storage, preparation, dispensing, inspections, and counseling of study participants on medications.
• Facilitation of pharmacy related monitoring, inspections and audits.

During the reporting period, the pharmacy department managed several on-going studies, including IMPAACT 2017, the A5300B PHOENIx study, EIT study, MOSO study, HPTN 084 and CoVPN 3008. Three protocols; IMPAACT 2036, A5356 and Tshireletso study, were opened during the reporting period.

Several protocols received BoMRA approval and are awaiting study implementation and these include A5394, A5416, A5417, A5409, the MMS Pilot study, the REVIVE study, rollover studies for IMPAACT 2017 and IMPAACT 2036, as well as for HPTN 083 and HPTN 084, and the CoVPN 3008 TB sub-study. IMPAACT 2042, Tatelo Plus study, HOPE-II study, AAA study and A5397 are still in the BoMRA approval process.

Following the EMA audit, the DAIDS Pharmaceutical Affairs Branch (PAB) visited the site to gather feedback on the audit. Pharmacist, Ms. Obonwe Pule, represented the site at the HPTN and ACTG annual meetings in Boston, sharing sights from the EMA experience with other pharmacists involved in network trials. The department has authored or updated several general pharmacy standard operating procedures (SOPs) to reflect improvements identified during the audit.

As per the new DAIDS PAB guidelines, the pharmacy transitioned to the use of temperature recording data loggers from Dickson Wheelchair temperature recorders as part of the storage location temperature recording.

Challenges

• Inconsistent study drug order processing from the drug sponsors/suppliers and the BoMRA import permit.
• Delayed transit times from international destination, affecting the timely supply and delivery of study product to the site.
• Overstocking of up to a minimum of six months' supply of study product to prevent stock out leading to shortage of pharmacy storage.
• Limited space for the accumulated paper records due to an increase in protocols involving large participant volumes and large study drug consignments.
• Lack of an electronic pharmacy management and dispensing platform to reduce paper records.
• High increase of study protocols that require high level of preparation and time-consuming preparations of study product
• Limited personnel, creating pressure and increasing the risk of errors during study product preparation.

5) Department of Software Engineering and Data Management

The Software Engineering and Data Management Center (SE & DMC) is a cornerstone in supporting clinical and research studies, enhancing data integrity and availability through a dedicated team of software engineers, data managers, and a scalable data management system. The SE & DMC team works to ensure that each research protocol data record is complete, accurate, compliant, auditable, confidential, secure, and accessible.

The following are some of the department's key achievements:

Laboratory Information System (LIS) Replacement
In an ongoing effort to improve laboratory information systems, the SE & DMC has been working for over 10 months to identify a long-term, cost-effective LIS solution that meets evolving lab requirements. This initiative aims to enhance the efficiency, scalability, and robustness of lab data management.

Sample Inventory Cleanup
In collaboration with the laboratory team, SE & DMC recently completed a comprehensive cleanup of sample storage inventory. This cleanup process ensures an accurate understanding of available samples, making space for new ones, and facilitating the upcoming Data Warehouse project, which will centralize data storage.

FLOURISH Study Data Capture
One of SE & DMC's most complex projects, the FLOURISH Study Data Capture, supports ongoing research with multiple study cohorts and distinct enrollment criteria. Although a single-site study, it has enrolled participants from prior BHP studies, requiring an intricate data management approach to track and analyze this diverse participant pool.

Data Warehouse Project
Currently underway, the Data Warehouse project is transforming the lab's data handling practices. Designed to house sample and clinical data across various systems, this biorepository will allow researchers to access comprehensive datasets for future studies. By integrating data updates across systems, the warehouse will enable principal investigators to identify sample availability efficiently, fostering new research avenues and publications.

Challenges

Staffing and Financial Support: The department faces an ongoing challenge in retaining specialized staff essential to advancing its goals. Limited grant funding restricts the department's ability to offer competitive salaries, resulting in difficulty recruiting and retaining skilled personnel. Training new staff is a lengthy process, which adds pressure as current staff are often preoccupied with high-priority projects and tight deadlines.

Graduate Training Program Limitations: The department has also struggled to establish a graduate trainee program to develop future specialized talent. Space constraints and limited resources have made it challenging to accommodate additional trainees who could gain valuable experience and strengthen the department.

Scope Management and Understanding: The scope of the department's work is often not fully understood, leading to scope creep and unmet expectations. This misalignment can result in underestimating the full-time effort (FTE) required for projects, as some principal investigators do not clearly define project requirements from the outset.

DECODING DATA: Software Engineers and Developers analyzing study data.

6) Information Technology

Florence Mafoko, IT Officer, monitoring internet connectivity performance

The IT department's primary focus for the year 2023 - 2024 has been to enhance IT infrastructure and improve cybersecurity measures to meet the growing needs of the organisation.

1. Infrastructure Upgrades

Network Cabling Replacement: The department modernised the internal network within BHHRL building and replaced the old network cabling with high-performance cabling to improve data transmission speed and reduce latency. This upgrade has significantly improved network reliability, ensuring consistent connectivity for all users and devices.

Network Server Enhancement: To accommodate the increasing number of employees and devices, network servers were upgraded to support up to 1,000 devices, effectively doubling the previous capacity. This upgrade has improved network connectivity and performance for all users and devices, thereby supporting operational efficiency.

2. Cyber Security Measures

VPN Server Upgrade: To bolster cyber security, the latest technologies were implemented. The existing VPN server migrated to a new server the latest encryption and multi-factor authentication. All new VPN accounts are created on the new server, enhancing the security protocols for remote access. This transition not only strengthens data protection but also provides secure access to sensitive information for all remote employees.

3. Challenges and Solutions

• As more personnel shift to working online, accessing cloud systems and collaborating with external partners, the strain on our current bandwidth has increased significantly.
• Many teams are experiencing slow internet speeds and disruptions, affecting productivity and collaboration.
• The department is implementing systems to actively monitor bandwidth usage, aiming for fair distribution among users to ensure optimal performance.
• We are actively exploring Starlink as an alternative solution. This initiative aims to boost internet speeds and reliability for teams that are heavily reliant on online resources.

Despite these challenges, the IT Department at BHHP has made significant progress in enhancing infrastructure and cyber security over the past year. Ongoing efforts to monitor and improve bandwidth, alongside investigating innovative solutions like Starlink, reinforces the Department's commitment to maintaining a secure and efficient IT environment. These upgrades not only support current operational needs but also lay a robust foundation for future growth.

11

Capacity Building & Training

1) Research Laboratory

The BHP research laboratory is a dynamic team of research fellows at various training stages dedicated to addressing public health challenges in Botswana, the region and globally. The group operates under the guidance of Dr Simani Gaseitsiwe, Prof. Sikhulile Moyo and Dr Rosemary Musonda. Dr Motswedi Anderson who has received substantial funding from Wellcome Trust, Africa Research Excellence Fund (AREF) and Sub-Saharan African Network for TB/HIV Research Excellence (SANTHE), plays a pivotal role in leading the viral hepatitis research agenda.

Also central to BHP's research efforts is Professor Catherine K. Koofhethile, a Principal Investigator who transitioned to BHP after completing her postdoctoral fellowship at Harvard T. H. Chan School of Public Health (HSPH). Prof Koofhethile leads the HIV Cure basic science research focused on adolescents and young adults living with HIV. Prof Koofhethile has in the past year received several awards and grants including the NIH K43, SANTHE -PTI, Johns Hopkins CFAR Africure, and the Ministry of Communications, Knowledge and Technology (MCKT) Research award to advance HIV cure research in Botswana.

Dr Simani Gaseitsiwe, Natasha O. Moraka and the team have also received a grant from Botswana's Department of Research, Science and Technology (DRST), Ministry of Communications, Knowledge and Technology. This funding supports the BHP161 Tekodiso study which evaluates the epidemiologic, clinical, and virological characteristics of individuals recently HIV diagnosed individuals initiating ART in Botswana. The study also seeks to determine the prevalence of coinfections, such as HBV and their impact on HIV treatment outcomes in recently HIV diagnosed individuals. A sub-study led by Dr Motswedi Anderson has also been included to co-enroll within the Tekodiso study. The study aims to determine the profiles and association of human leukocyte antigen (HLA) and killer-cell immunoglobulin-like receptors (KIR) genotypes on hepatitis B infection phenotypes, and outcomes in individuals with HIV.

The lab has international collaborators who assist in the supervision of fellows working in areas where there is limited local capacity. Fellows are registered with various academic institutions, including the University of Botswana (UB), Botswana International University of Science and Technology (BIUST), Stellenbosch University (SU), University of Cape Town (UCT), University of Witwatersrand (WITS) and University of KwaZulu-Natal (UKZN).

Key research focuses in the laboratory include Bioinformatics, HIV drug resistance, HIV incidence and tools for determining HIV incidence, HIV viral diversity, potential for broadly neutralizing antibody (bnAbs) in therapy and prevention, HIV-1 subtype C reservoir characterization, Viral hepatitis, TB incidence and molecular epidemiology, HPV molecular epidemiology, noroviruses and sapoviruses. The fellows are supported by several capacity building grants which include:

Active Capacity Building Grants

No.	Grant	Awardee/s
1	TESA III	Dr Rosemary Musonda
2	SANTHE II (SANTHE-Gates and SAF)	Dr Simani Gaseitsiwe
3	Fogarty D43	Prof. Sikhulile Moyo
4	Fogarty K43	Prof. Sikhulile Moyo
5	AREF	Dr Dorcas Maruapula
6	Fogarty HBNU	Dr Gaerolwe Masheto
7	Fogarty G11	Prof. Catherine Koofhethile Dr Motswedi Anderson Dr Simani Gaseitsiwe
8	SANTHE II Path -to- Independence	Prof. Catherine Koofhethile
9	SANTHE II Path -to- Independence	Dr Motswedi Anderson
10	Ministry of Communications, Knowledge and Technology (MCKT)	Prof. Catherine Koofhethile
11	NIH Johns Hopkins CFAR Africure	Prof. Catherine Koofhethile
12	NIH Fogarty- K43	Prof. Catherine Koofhethile

TESA III

The Trials of Excellence in Southern Africa (TESA) consortium, now in its third phase (TESA III), aims to develop, strengthen and expand clinical research capacities across Southern Africa by consolidating nodes of excellence for conducting clinical trials. TESA focuses on high quality research addressing infectious diseases with severe morbidity and mortality in the region, including TB, HIV and Malaria. TESA III supports 15 institutions from nine African and three European countries, coming together to strengthen and enhance the capacities for clinical research in Southern Africa, and to strengthen the North-South and South-South collaborations.

BHP, as the consortium's reference laboratory for HIV, plays a crucial role by offering training in HIV drug resistance and related techniques. In September 2022, BHP hosted scientists from the Biomedical Research and Training Institute (BRTI) in Zimbabwe for hands-on training in HIV drug resistance testing, including experiment setup, RNA isolation, PCR, sequencing, mutation analysis, and drafting SOPs for laboratory accreditation. Through the TESAIII grant, BHP supported students to attend data analysis and manuscript writing bootcamp organized by UTH, Zambia., This training equipped students with essential skills needed to advance their academic and professional growth.

BHP also supported graduate students to attend and present their project findings at international conferences, including the Conference in Retroviruses and Opportunistic Infections (CROI), Conference on Liver Disease in Africa (COLDA) , 8th Botswana International AIDS conference and AIDS 2024 among others.

TESA III Trainees

• Bonolo Phinius, PhD candidate (University of Botswana)
• Ontlametse Choga, PhD candidate (University of Botswana)
• Nametso Kelentse ,PhD in Medical Sciences (University of Botswana, graduated in 2023)
• Doreen Ditshwanelo, MSc in Biological Sciences (Botswana International University of Science and Technology, graduated in 2023.)

TAGENDI Fellowship Program

The TESA Addressing Gender and Diversity Regional Gaps in Clinical Research Capacity (TAGENDI) PhD fellowship program was launched to support female PhD candidates from TESA member countries, including Botswana, South Africa, Angola, Mozambique, Namibia, Eswatini, Malawi, Zambia, and Zimbabwe in collaboration with European country partner institutions from the Netherlands, Portugal, Spain, and France. Botswana's TAGENDI PhD Fellow is Tuelo Mogashoa who is registered with Stellenbosch University, South Africa.

SANTHE 2.0

The Sub-Saharan African Network for TB/HIV Research Excellence (SANTHE) is a multinational network of multidisciplinary experts dedicated to empowering African scientists and combating HIV, Tuberculosis and HIV/TB co-infection through pioneering basic, clinical and translational research. SANTHE aims to shape and drive locally relevant basic, clinical and translational research in Africa.

SANTHE 2.0's strategic focus includes the following:

- A cutting edge HIV and TB research programme.
- An innovative training and capacity building programme.
- The facilitation of a strong institutional network for research excellence as a pathway to intellectual and financial independence for African researchers and their institutions.
- Community engagement to ensure meaningful translational research and public health and community impact.

The SANTHE Network seeks to address the syndemic of HIV and TB as a critical public health crisis through basic science, translational research, and collaborative mobilization across sectors.

SANTHE 2.0 Fellows
- Natasha Onalenna Moraka, PhD Candidate (University of Botswana)
- Wonderful Tatenda Choga, PhD Candidate (University of Botswana)
- Linda Mpofu-Dobo, PhD Candidate (Botswana International University of Science and Technology)
- Dorcas Maruapula, Postdoctoral Fellow

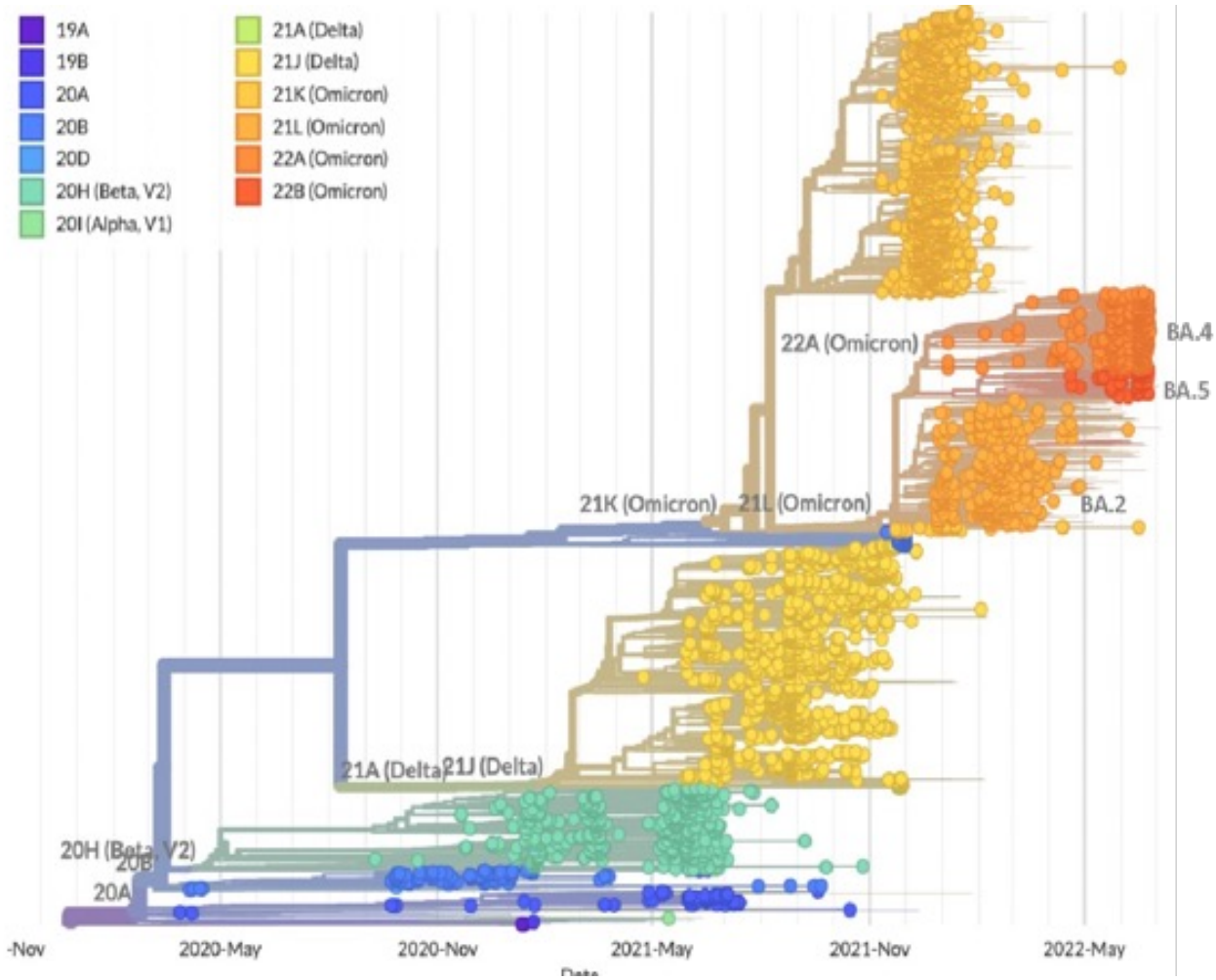
Highlights of Projects in the reporting period

- Genomic Surveillance of SARS-COV-2
- Immune Responses to SARS-CoV-2 following vaccination
- Deep Sequencing of HIV for analysis of diversity and drug resistance
- Analysis of Drug Resistance in Low-level viremia
- Compartmentalization of HIV
- Determining HIV recency as a cross-sectional measure of HIV incidence
- Determining broadly neutralizing antibody (bNAb) resistance using machine learning.
- Determining HIV envelope characteristics associated with bNAb resistance
- Prevalence of Hepatitis B virus the population-based household surveys
- Drug Resistance among Highly Treatment experienced individuals
- HPV genotyping and diversity
- HIV-1 Subtype C reservoir characterization studies

Pathogen Genomics and Surveillance of SARS-COV-2 Variants

The Botswana Harvard HIV Reference Laboratory played an important role in Botswana's COVID-19 response and the genomic surveillance of SARS-CoV-2. In collaboration with the Ministry of Health and Botswana COVID-19 Taskforce, BHP initiated genomic sequencing efforts to monitor SARS-CoV-2 variants within the country. To date, BHP has contributed 4700 SARS-CoV-2 whole genome sequences to the Global Initiative on Sharing All Influenza Data (GISAID).

This contribution enabled BHP to track the lineages and variants of concern in circulating in the country, providing critical data on the global understanding of viral evolution and to inform vaccine design. Notably, BHP scientists, alongside South African colleagues, were the first in the world to sequence and share the first genomes of the Omicron variant. This was achieved with limited resources, leveraging and building on pathogen genomics capacity developed over years in various projects. This work has resulted in several high impact publications and earned national and international recognition.



Research on Broadly Neutralizing Antibody (bNAb) Resistance Using Machine Learning

Supported by SANTHE and NIH Fogarty, Natasha O. Moraka leads research on determining the resistance patterns observed in adults with documented seroconversion from the proviral sequences from adults with documented HIV-1 seroconversion (N=140) from a population-based household study (Botswana Combination Prevention Project, 2013-2018). The study used proviral HIV-1C sequences from adults with documented HIV-1 seroconversion in Botswana to determine HIV drug resistance mutations and predict (in silico) resistance to 33 known broadly neutralizing antibodies (bNAbs) using the bNAb-ReP algorithm (https://github.com/RedaRawi/bNAb-ReP).

Further information on this data was introduced through to analyzing variable region characteristics (VC) in HIV-1 seroconverters and compared them with predicted bNAb resistance/sensitivity using machine learning techniques. The findings the importance of evaluating HIV env variable region characteristics (VC) from sequence data, to determine the optimal vaccine design and best bNAb combinations to use for neutralization of highly variable HIV-1 subtype C. This work was presented at CROI 2024 as a poster with a New Investigator IAS scholarship as well as an oral and poster presentation at CAVD 2024. Ms. Moraka was part of 15 international early career investigators (ECIs) and the only one from Botswana sponsored to attend by the Bill and Melinda Gates foundation. Her abstract was among the top five selected by Dr Trevor Mundel as one of the most cutting-edge abstracts for CAVD2024. The final manuscript was published in Scientific Reports journal, doi: 10.1038/s41598-023-44722-2. PMID: 37875518.

Natasha Moraka presenting an oral abstract at the CAVD 2024 conference

At CAVD 2024 meeting, Dr Simani Gaseitsiwe delivered an oral presentation on “How AI/machine learning prediction models might predict potential resistance or susceptibility to neutralization of regional HIV-1 strains.” He highlighted that high mutation rate of HIV-1 strains in Sub-Saharan Africa leads to differences in neutralization capacity of different bNAbs. Therefore, the best bNAb combinations and sensitivity prediction can be evaluated using deep learning/ in silico techniques. The accuracy of prediction models remains an area of interest in HIV vaccine design especially in high HIV endemic countries with low capacity to evaluate vaccine and cure strategies like Botswana.

Bioinformatics and Next Generation Sequencing

During the reporting period, BHP facilitated Training in Bioinformatics and Next Generation Sequencing. The course was hosted in collaboration with the University of Cape Town and H3ABioNet consortium. This course intended to equip participants with the essential bioinformatics skills to analyze NGS data, covering sequencing technologies, algorithmic theory, and principles of bioinformatics, with focus on practical computational sessions for a variety of applications such as QC, alignment, assembly, variant calling, RNA-Seq and ChIP-Seq.

Graduations and Thesis Defense

Ten research fellows progressed academically, with Bonolo Phinius, Ontlametse Choga, Kabo Baruti and Wonderful Choga submitting their PhD theses while Patrick Mokgethi upgraded to PhD. Boitumelo Zuze, Teko Masuku, Basetsana Phakedi, Tsholofelo Ratsoma, Kesego Motsumi, Bonolo Molefe, Patience Motshosi and Gorata Mpebe registered for MPhil programmes at the University of Botswana.

Research Highlights

Conferences and Workshops

- Over the past reporting period, the research lab participated in 38 conferences and workshops, reflecting its active engagement in global and regional scientific dialogues. Major events attended included prominent gatherings like AIDS 2024 in Munich, CROI 2024 in Denver, and IAS 2023 in Brisbane, as well as regional meetings such as the SAPRIN Conference in Johannesburg and the Antimicrobial Resistance Summit in Gaborone. These conferences and workshops provided invaluable opportunities for knowledge exchange, collaboration, and capacity-building across a range of topics.

Climate Change Conference

Academic Achievements

- Wonderful T. Choga graduated cum laude with a Master of Science in Medicine (Human Genetics) from the University of Cape Town.
- Wonderful Choga was also awarded a prestigious Rockefeller Foundation Graduate Fellowship for Bioinformatics training under the mentorship of Prof Tulio de Oliveira in Stellenbosch University in South Africa.

Postdoctoral and Fellowship Opportunities

- Dr Kaelo Seatla was one of 10 selected fellows for African Postdoctoral Training Initiative (APTI), which is implemented by African Academy of Sciences (AAS) in partnership with the U.S. National Institutes of Health and the Bill & Melinda Gates Foundation. Dr Seatla is studying genotypic and phenotypic HIV drug resistance and spread of HIV and applying these skills to emerging pathogens in Botswana.
- Dr Kaelo Seatla's work on HIV drug resistance was featured in the Harvard University Center for HIV AIDS Research (HU CFAR) July 2023 Newsletter.
- Wonderful Choga received the Computational Biology Mentored Fellowship Award through SANTHE in partnership with the Ragon Institute, Washington University School of Medicine in St. Louis, USA, and the Université catholique de Louvain.

Awards for Women in Science

- Bonolo Phinius awarded the L'Oréal-UNESCO For Women in Science 2023 Young Talents Sub-Saharan Africa Award.

Community Engagement and Media Appearances

- Natasha O. Moraka participated as guest on Botswana Television Silent Shout programme and Duma FM, discussing HIV/AIDS during Month of Youth Against AIDS on March 4th and 14th, 2024 respectively.

- Natasha O. Moraka invited to Ministry of Health "Holiday Hygiene" panel discussion as panelist on 15th December 2023.
- Natasha O. Moraka and Tuelo Mogashoa spoke at Gaborone Senior secondary School's Career Week as guest speakers and alumni on 31st August 2023.
- Prof. Catherine K. Koofhethile discussed HIV cure research on Botswana Television (BTV) and delivered keynote addresses on HIV cure strategies at workshops in Kenya.
- Prof Koofhethile also presented on HIV cure research at the HIV Cure Literacy Project led by Center of Youth of Hope (CEYOHO) and at BHP's HIV Cure Workshop in collaboration with HIV Cure Africa Acceleration Partnership (HCAAP).

International Recognition
- Natasha O. Moraka received one of 15 worldwide Early Career Investigator Scholarships from the Bill & Melinda Gates Foundation to attend and present at the 19th Collaboration for AIDS Vaccine Discovery (CAVD) Annual Meeting in Seatle, USA (6th – 8th February 2024).
- Moraka was also elected as an investigator with the ACTG's Reservoirs, Remission and Cure Transformative Science Group (TSG).
- Bonolo Phinius elected as an investigator with the ACTG's Hepatitis Transformative Science Group (HEP TSG).

Research Excellence
- The Tekodiso study received high marks for protocol and regulatory compliance in TESA CRA placement review.

Scientific Contributions and Awards
- Dr Dorcas Maruapula awarded Charles Burcher award for best oral presentation at INTEREST conference.
- Dr Dorcas Maruapula awarded Africa Research Excellence Fund (AREF) fellowship award.
- Professor Catherine Koofhethile was appointed an adjunct Professor at University of Venda (UNIVEN), South Africa, and awarded four research grants (NIH Fogarty K43, SANTHE-PTI, Johns Hopkins CFAR Africure and MCKT Research awards) to establish her independent research programme.

2) The BHP Clinical Capacity Building Initiative at Scottish Livingstone Hospital

The BHP Clinical Capacity Building Initiative, a collaboration between Botswana Harvard Health Partnership (BHP), Beth Israel Deaconess Medical Center (BIDMC) in Boston, and Oregon Health & Science University (OHSU) in Portland, was launched in 2011. This initiative supports healthcare capacity building in Botswana through clinical education, quality improvement, and research. The program provides clinical training to University of Botswana (UB) medical students and residents as well as Ministry of Health (MOH) medical officer interns, medical officers, nurses, and other healthcare staff in collaboration with local partners. The program promotes healthcare systems through quality improvement and research. In addition, the program regularly provides opportunities for rotating U.S. residents and fellows to participate in clinical, educational, quality improvement, and research efforts.

The initiative began at Scottish Livingstone Hospital (SLH) and in Kweneng East (now Kweneng) District, where the Internal Medicine program continues to focus. The Obstetrics & Gynaecology (OBGYN) and Anaesthesia & Critical Care programs were also founded at SLH but have since transitioned to the University of Botswana (UB) and Princess Marina Hospital (PMH) to support residency training.

Obstetrics & Gynaecology
With support from BHP, the OBGYN residency training programme at UB is now in its fifth year and has now graduated the country's first cohort of specialists. Over the past year, BHP hosted four visiting OBGYN Residents, the Queenan Maternal-Fetal Medicine high-risk specialist for the third year in a row, a Global Health Fellow, and surgical specialists in urogynecology over the past year. These visitors helped support clinical education and quality improvement activities, training both residents and faculty. Interdisciplinary collaborations continue in critical care, ultrasound, and neonatal resuscitation.

Dr. S. J. Hanson has served as the OBGYN Site Director for the last two years, leading educational programs for both the UB Master of Medicine (MMED) residency training programme and the OBGYN Department at PMH. Dr Hanson's work included coordinating subspecialists, technical training in surgery and ultrasound, facilitating simulation and outreach efforts, as well as departmental wellness programming. Dr. Rebecca Luckett has continued to support the program and has transitioned the UB OBGYN residency training Programme Director (APD) role to Dr Hanson. Dr Luckett continues to provide support to the faculty and MMED research projects.

Anaesthesia & Critical Care
The Anaesthesia and Critical Care Program focuses primarily in developing and supporting the UB Anaesthesia residency program, which is now in its fifth year, with the first residency cohort set to return in 2025. The cohort of 2023 are in the process of transitioning to South Africa. The class of 2024 is the largest cohort for the University of Botswana with seven residents. The program has hosted four international senior anaesthesia residents, who contributed to the teaching and training of first-year residents.

The program has faced the challenges of limited functionality of main theatres and the attrition of senior staff, which has left only one consultant anaesthetist employed by the Ministry of Health at Princess Marina Hospital.

Collaborative efforts are underway with Princess Marina Hospital, University of Botswana, Beth Israel Deaconess Medical Centre and Boston Children's Hospital and Kids OR to support the development of subspeciality modules of training for obstetric and paediatric anaesthesia. Once agreed by all parties, the modules will be presented to MOH for approval and budget support. The goal is to increase the maternal and paediatric safety within their care journey respectively for pregnancy and when presenting for surgery. This, as a byproduct, will ensure that the residents can stay in Botswana longer before transitioning to South Africa to complete their training.

Meanwhile, Dr Ed Clune continues to support the program remotely in his new role as Director of Global Health for Anesthesia at Beth Israel Deaconess Medical Centre.

Internal Medicine
The Internal Medicine programme, based at SLH, is led by Dr. Kesegofetse Chabaesele. The programme focuses on clinical education as its primary pillar, while supporting partner-led quality improvement and research activities. It facilitates clinical education for multiple groups of learners, including UB fifth-year medical students, first-year UB Family Medicine residents, Medical Officer Interns assigned to SLH under the Botswana Medical Internship Training Program, as well as learners from across the world. Teaching is delivered through a variety of modalities in both inpatient and outpatient settings, with particular focus on cross-cutting streams: Point-of-Care Ultrasound (POCUS), simulation, and resuscitation (ACLS/BLS).

During 2023-2024 reporting period, the programme hosted two Global Health Fellows from BIDMC and fifteen US-based Internal Medicine and Family Medicine residents. Programme leadership and rotating trainees continue to contribute to the design and implementation of quality improvement initiatives for the SLH Medicine Department as well as multiple research projects at SLH and across Kweneng District, with emphasis on clinical problems prevalent in the district and medical education.

In addition to engaging in clinical care, education, and quality improvement at SLH, the Medicine programme participates in the Ministry's primary health care revitalization activities by conducting outreach activities focused on clinical education and quality improvement in primary care facilities across Kweneng District Health Management Team (DHMT). These includes engaging stakeholders at various levels of the primary care system as well as collaborating with visiting US partners specializing in Primary Care. The program hosted an OHSU Primary Care specialist for two weeks in early 2024, to develop a modular primary care curriculum and facilitated educational activities at multiple primary care facilities, including Thamaga Primary Hospital, Letlhakeng Clinic, and Phuthadikobo Clinic. This curriculum will complement the existing inpatient curriculum currently in use for interns rotating at SLH, will expand to cover Family Nurse Practitioners, Medical Officers, and General Nurses. It will also expand on hybrid refresher trainings conducted over the past year via WhatsApp and in-person workshops, focusing on diagnosis and management of diabetes, hypertension, and cardiovascular disease risk factors. Additionally, as part of the expansion of primary care outreach services, the Medicine Site Director, Fellow, and supporting faculty participated in the Ministry's Airborne Specialists initiative, which flies specialists to hard-to-reach areas such Hukuntsi and Tsabong.

Senior faculty members from OHSU and BIDMC visited Botswana for the first time since COVID-19. This visit was instrumental in facilitating discussions between Botswana and US-based partners, strengthening collaboration with important stakeholders such as the Ministry of Health and Kweneng DHMT. During this visit, a high-performing SLH medical officer intern sponsored to a renal conference in the US, exemplifying the program's commitment to fostering bidirectional learning and scholarly activities.

Beyond clinical training at SLH, the Medicine program provides mentorship for career progression and research engagement to a broad group of trainees, ranging from UB medical students to junior staff at SLH. Over the past year, numerous mentees have successfully obtained placement in graduate training programs, including MMed programs in a variety of specialties, as well as new employment in both the public and private sectors. This includes the successful match of a former SLH Medical Officer to the OHSU Internal

Medicine Residency Program – the first programme mentee to match at a collaborating US academic medical center to date. Two SLH Medical Officers have been identified to participate in the recently established Clinical Observership Program at OHSU, pending confirmation of funds to support their travel to the US. There are ongoing efforts to identify sustainable funding for this initiative for future, as the program aims to send a minimum of two promising candidates annually to the US to participate in clinical observerships in Internal Medicine and/or Family Medicine. Dr. Sara Schwanke Khilji continues to support the program part-time, focusing on bidirectional training opportunities and ongoing research programs.

RESEARCH STUDIES (MEDICINE):

i.) Patient Care Delivery and Clinical Outcomes, Scottish Livingstone Hospital: Characterization and Identification of Quality Improvement Opportunities Following the Onset of the COVID-19 Pandemic.

PIs: Dr. Kesegofetse Chabaesele, Dr. Roger Shapiro

Prior to the onset of the COVID-19 pandemic, a prospective observational cohort study was conducted at SLH to support analysis of healthcare delivery and clinical outcomes of patients admitted to Scottish Livingstone Hospital (SLH). This mixed retrospective and prospective observational cohort study builds upon that prior work, by compiling routinely collected data from the SLH inpatient wards to describe the spectrum of major presenting conditions, clinical outcomes, mortality, and related risk factors since the advent of COVID-19. The study aims to identify important changes in burden of disease and practice patterns before and after COVID-19, and to compile data that will enable better alignment and evaluation of quality improvement interventions at SLH.

ii.) Perceptions of Prevalence, Impact, and Management of Post-Acute Sequelae of SARS-CoV-2 Infection among Healthcare Workers in Kweneng District, Botswana.

PIs: Dr. Sara Schwanke Khilji, Mrs. Ditebogo J Mokone.

Botswana reported its first case of SARS-CoV-2 case in March 2020, but the prevalence of post-acute sequellae of SARS-CoV-2 infection (PASC) and its impact on the health system in Botswana are unknown. Given the novelty of the PASC syndrome, healthcare providers have to date received little systematic training regarding evaluation and management of long-COVID symptoms. The study used a mixed methods approach, combining cross-sectional survey of healthcare workers and key informant interviews to assess participants' perceptions of PASC burden, impact, and current management at the district level in Kweneng District, Botswana. The study has been completed and dissemination is in progress.

iii) Evaluation of Prevalence of Pericardial Effusion and Associated Risk Factors in Patients with Pulmonary Tuberculosis in the Kweneng District, Botswana.

PIs: Dr. Mahmoud Abu Hazeem, Dr. Kesegofetse Chabaesele

Tuberculosis (TB) remains the leading cause of morbidity and mortality in Botswana. However, there is limited data on extra-pulmonary manifestations of TB, with anecdotal evidence of underreporting of TB pericardial effusion specifically. Point-of-care ultrasound (POCUS) shows potential for rapidly identifying TB pericarditis, which could improve patient treatment and outcomes. This cross-sectional study seeks to evaluate the prevalence of and identify risk factors for pericardial effusion in patients with pulmonary TB in Kweneng District, Botswana. Data collection is ongoing.

iv) Supporting Continued Education on Non-communicable Disease Management for Outpatient Healthcare Providers in Kweneng District, Botswana during COVID-19.

PI: Dr. Sara Schwanke Khilji

Non-communicable diseases (NCDs) are the leading cause of death and illness worldwide, with 85% of premature deaths from NCDs occurring in low-and middle-income countries. In Botswana, NCD management is challenging due to high rates of HIV/AIDS compounded by the rising cases of chronic diseases like hypertension and diabetes. A continuing professional development (CPD) program supporting NCD training for primary care health workers in Kweneng District was implemented in 2019 through a series of workshops and mentoring sessions. This pilot study evaluates the impact of a follow-up mobile phone-based education program on providers' knowledge, adherence to NCD management guidelines, and achievement outcomes. The study also assesses the acceptability and feasibility of a mobile phone-based program for NCD content delivery and evaluation. This work is supported by a grant from the Tartar Trust. Data collection is complete, and a manuscript is in preparation.

v) Assessing Educational Experiences Across Specialties Among Medical Officer Interns in Botswana

PIs: Dr. Thato Moshomo, Dr. Sara Schwanke Khilji

The Medical Internship Training Programme (MIT), launched by the Botswana Ministry of Health, the Botswana Health Professions Council (BHPC), and the UB Faculty of Medicine, was created to provide standardize and improve internship training across Botswana. The MIT's aim is to equip Medical Officer Interns with skills needed to practice independently as generalists in the Botswana's public health system, particularly in remote and rural areas. To ensure consistent learning outcomes across MIT training sites, assessment instruments are needed for gauging interns' self-perceived readiness for independent practice and to objectively measure their clinical knowledge. This project seeks to evaluate the feasibility, utility, and performance of two novel evaluation tools which measure medical knowledge across all four core specialties and perceived preparedness for independent clinical practice upon completion of internship, as well as to identify areas for improvement in MIT training. Enrollment has been completed and data collection is in progress.

3) Botswana Global Oncology Outreach (BOTSOGO)

Tumor Board Meeting

The Botswana Oncology Global Outreach (BOTSOGO) is a capacity-building initiative that unites Botswana's public and private oncology sectors with Harvard's oncology community to enhance the quality of cancer care. BOTSOGO has sustained a monthly tumor board to support clinician and nurse education on cancer management. During reporting period, a total of four tumor board meetings were held to advance knowledge and improve care practices in cancer management.

12

Public Policy & Advocacy

Ditlamelo Mareme from the Clinical Trials Unit (CTU) engaging with the public about BHP clinical trials

The BHP is committed to ensuring that the knowledge generated through its research is actively shared to inform public health policies and benefit the public, scientific community, and humanity. BHP maintains continuous public engagement to raise awareness of public health challenges and BHP's research, underscoring the importance and impact of its research for those it serves.

The organization regularly hosts events such as Journal Club meetings, Tumor Board discussions, Kgotla Meetings, Community Advisory Board meetings, Community Stakeholder Engagement gatherings, Health Exhibitions, and STEM Expos. Research findings are shared with the Ministry of Health (MOH) and presented at various international conferences to foster greater understanding and collaborative action.

BHP also actively introduces new studies to the MOH and other key stakeholders for guidance and to secure support. Key research insights and achievements are made accessible to the public and policymakers through presentations, media briefings, interviews, and press releases. BHP's dedication to high-quality research is further evidenced by its publication record, with 95 manuscripts published in reputable peer-reviewed journals and 34 abstracts presented at international conferences during reporting period.

BHP staff continues to contribute their expertise through participation in various technical committees and working groups organized by the MOH and international research networks. They collaborate extensively with international researchers, demonstrating BHP's commitment to teamwork. Together with Community Advisory Board members, BHP staff actively participate in over 22 committees and teams, reinforcing the organization's collaborative efforts and dedication to advancing public health knowledge and practice.

13

Operational Excellence

Acting HR Manager, Omphile Masuku and Senior HR Officer, Tebogo Akanyang

1) Human Resources

This report outlines the achievements, challenges, and initiatives of the Human Resources Department (HR). Over the year, the HR team has focused on fostering a culture of excellence, inclusion, and professional growth, effectively meeting the diverse needs of BHP's workforce and contributing to the organization's success.

Diversity and Manpower Strength

BHP is dedicated to creating an inclusive culture that values diversity among its employees. As of June 2024, the staff complement was 273, including 21 non-Batswana. The graph below indicates the number of staff per month for the period under review.

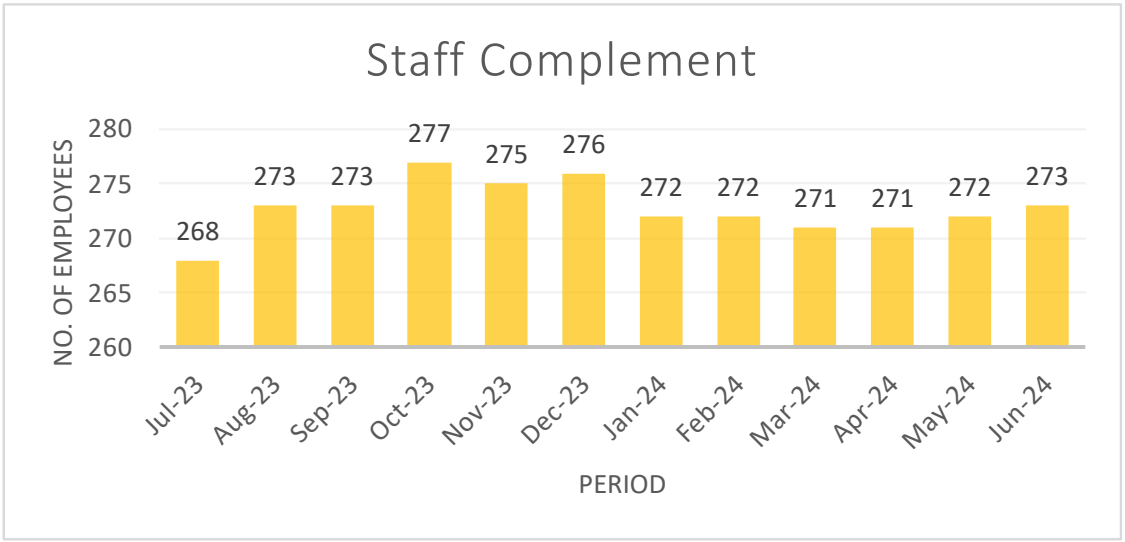


Figure 1: Staff Compliment trend per month

Gender Distribution

BHP is committed gender diversity throughout all cadres with a keen interest in promoting women in Science and the Medicine. Figure 2 indicates gender distribution in BHP.

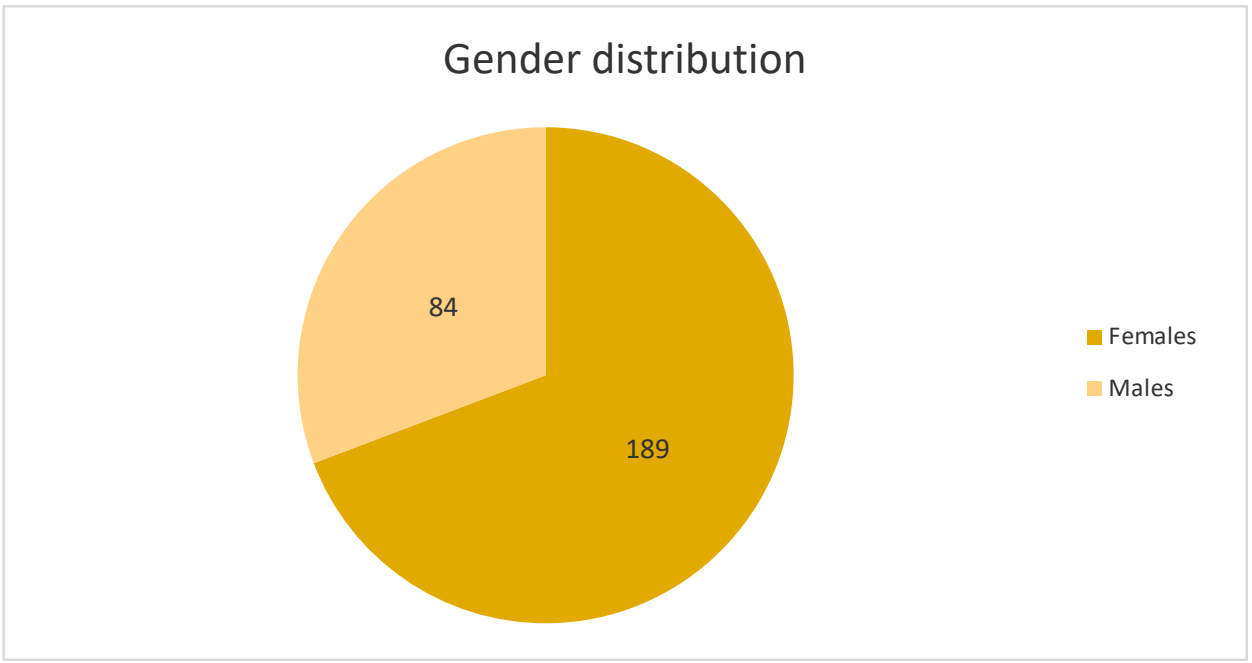


Figure 2: Gender Distribution

Human Resources Strategic Initiatives

a. Leadership and Management Skills Training

The HR department, in collaboration with Line Managers, organized a series of training sessions to enhance the leadership and management skills of their staff. A total of 46 employees participated, with 19 supervisors attended a "Leadership Skills for Supervisors" course on May 28, 2024, while middle and senior managers attended a "Leadership and Management Skills for Middle and Senior Managers" course on May 30-31 and June 6-7, 2024.

b. Medical Aid

BHP provides full (100%) medical aid coverage for all employees. They can now choose between Bomaid Scheme B and Botsogo Ruby plans, allowing them to select a healthcare package that best meets their needs and those of their families.

c. Annual Staff Engagement

One of the staff engagement meetings

To ensure open communication between management and staff, the Executive management held staff engagement meetings across all BHP sites. These sessions aimed to share the organization's status updates and provide feedback on previously raised concerns. This initiative underscores BHP's commitment to a transparent, inclusive, and responsive culture. These meetings are essential for ensuring every team member's voice is heard, fostering a positive work environment, enhancing communication, and aligning staff with organisational goals.

d. Training and Development

Capacity building at BHP focuses on research methodology, laboratory skills training and academic mentoring of students and early career investigators performing mentored research. Senior laboratory and clinical investigators serve as mentors to the research fellows, often in collaborative mentorship teams with one another and with other international investigators. Fellows pursuing MSc and PhD degrees are registered with various academic institutions including University of Botswana (UB), Botswana International University of Science and Technology (BIUST), Stellenbosch University, University of Cape Town, University of Witwatersrand, University of KwaZulu Natal, and the London School of Hygiene and Tropical Medicine. Currently BHP has eight employees pursuing MSc/MPhil and eight pursuing PhDs at various academic institutions.

e. Organisational Culture and Employee Engagement

The BHP culture and engagement activities reflects the company's commitment to fostering a positive work environment, promoting teamwork, supporting good cause, and enhancing communication and engagement. These initiatives have contributed to a more cohesive and motivated workforce.

i) Leteisi Day

To celebrate independence in style, BHP employees wore Leteisi in recognition and celebration of Botswana Day. This was also meant to promote a fun and positive enjoyable work environment essential for employee satisfaction and engagement.

One of the staff engagement meetings

ii) End of Year Event

BHP hosted an end of year event to celebrate and recognize staff efforts, foster teamwork and map a foundation for the coming year.

BHP Staff at the 2023 End of Year Event

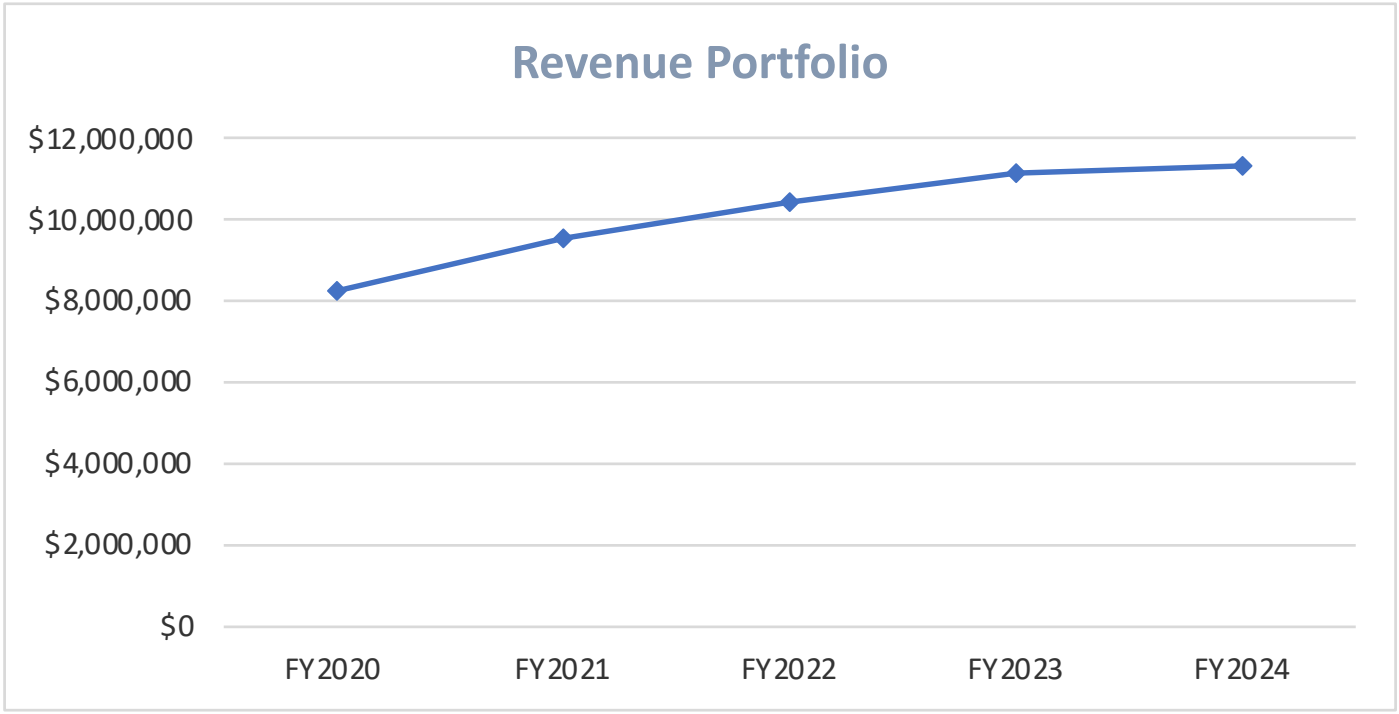
2) Finance and Grants

Grants Team bonding and recharging outside the office

Over the fiscal year 2023/2024, the department has successfully administered more than 100 awards from multiple donors. This effective administration is borne by the day-to-day activities that promote compliance, due diligence, prudence and timely reporting.

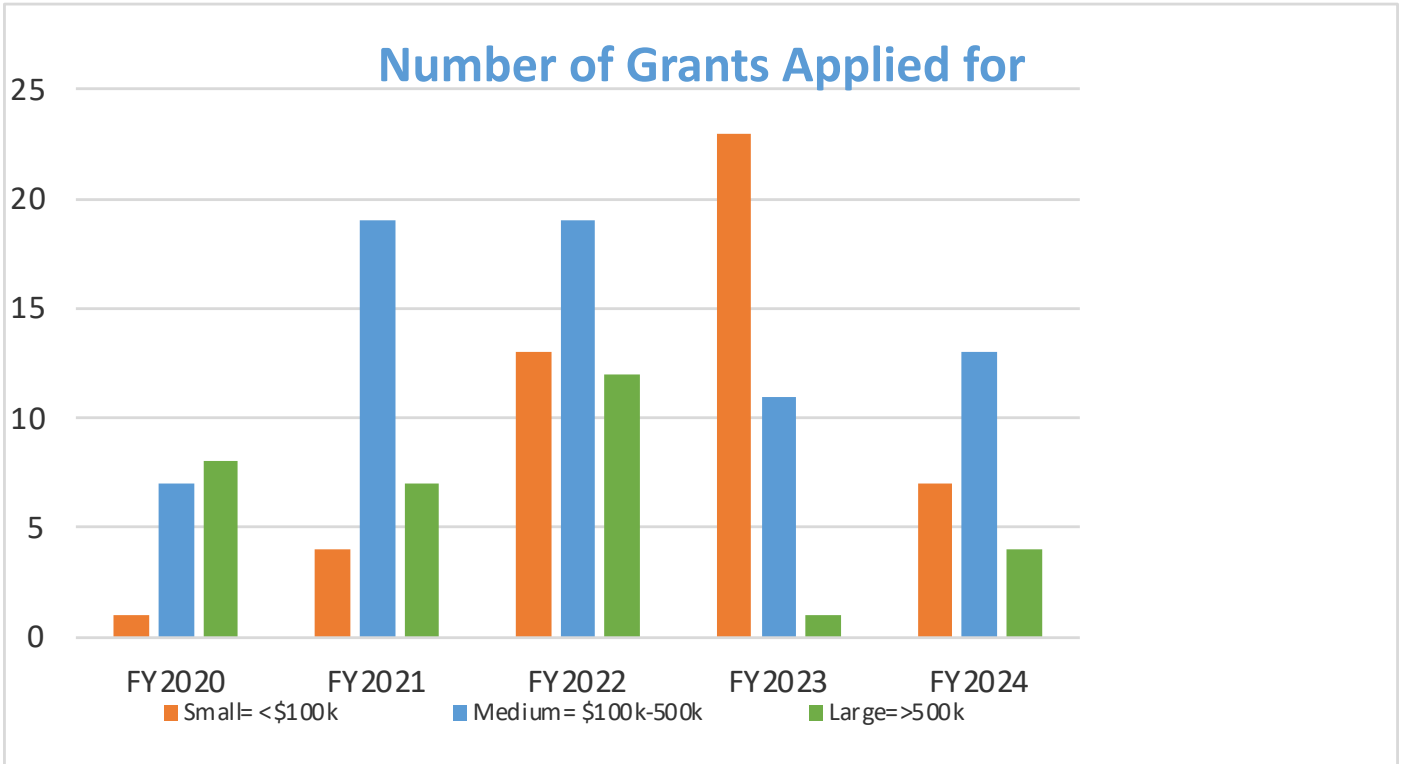
1. Funding Portfolio

The below graph depicts a 5-year funding trend with FY2024 reflecting a slight increase of 1.7% revenue from FY2023.



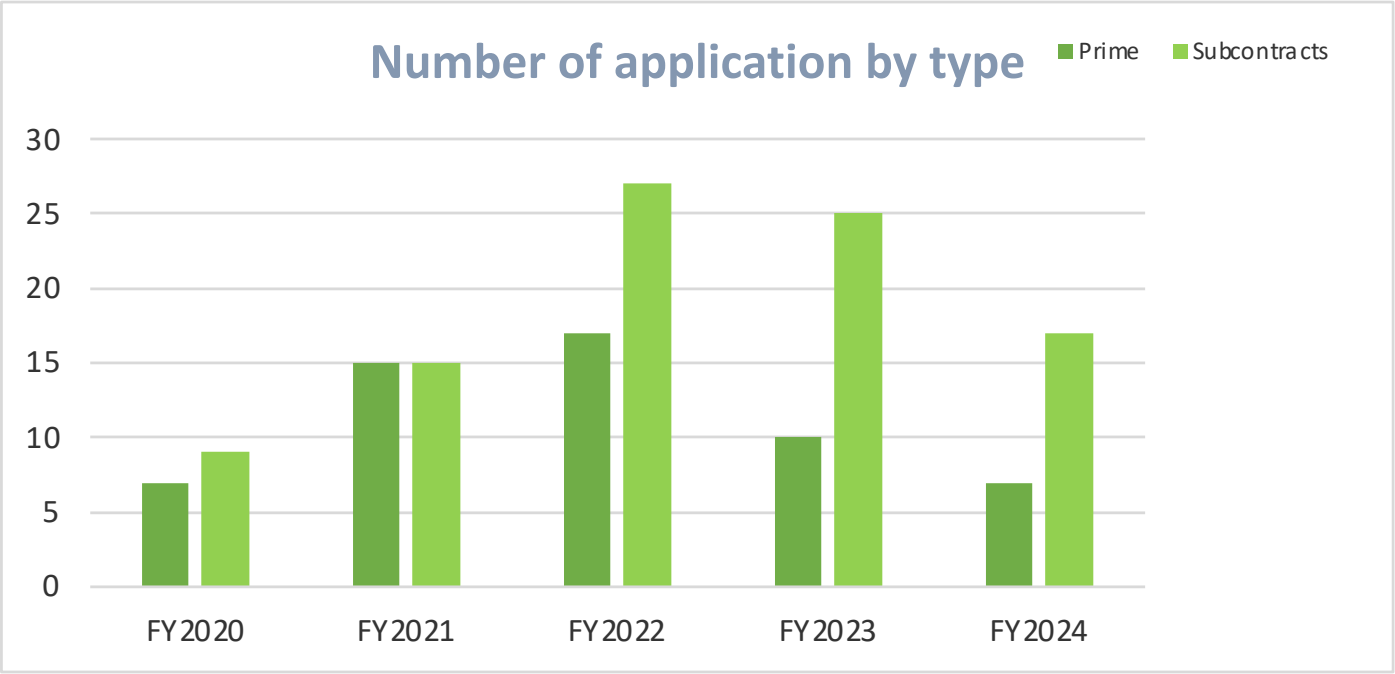
2. Number of Grants Applied For

Twenty-four (24) grant applications (a 31% decline from FY2023) were submitted during the year under review. Of the 24 submitted, seven were small grants, 13 were medium grants, and four were large grants. The table below shows the institution's application efforts over a five-year period.



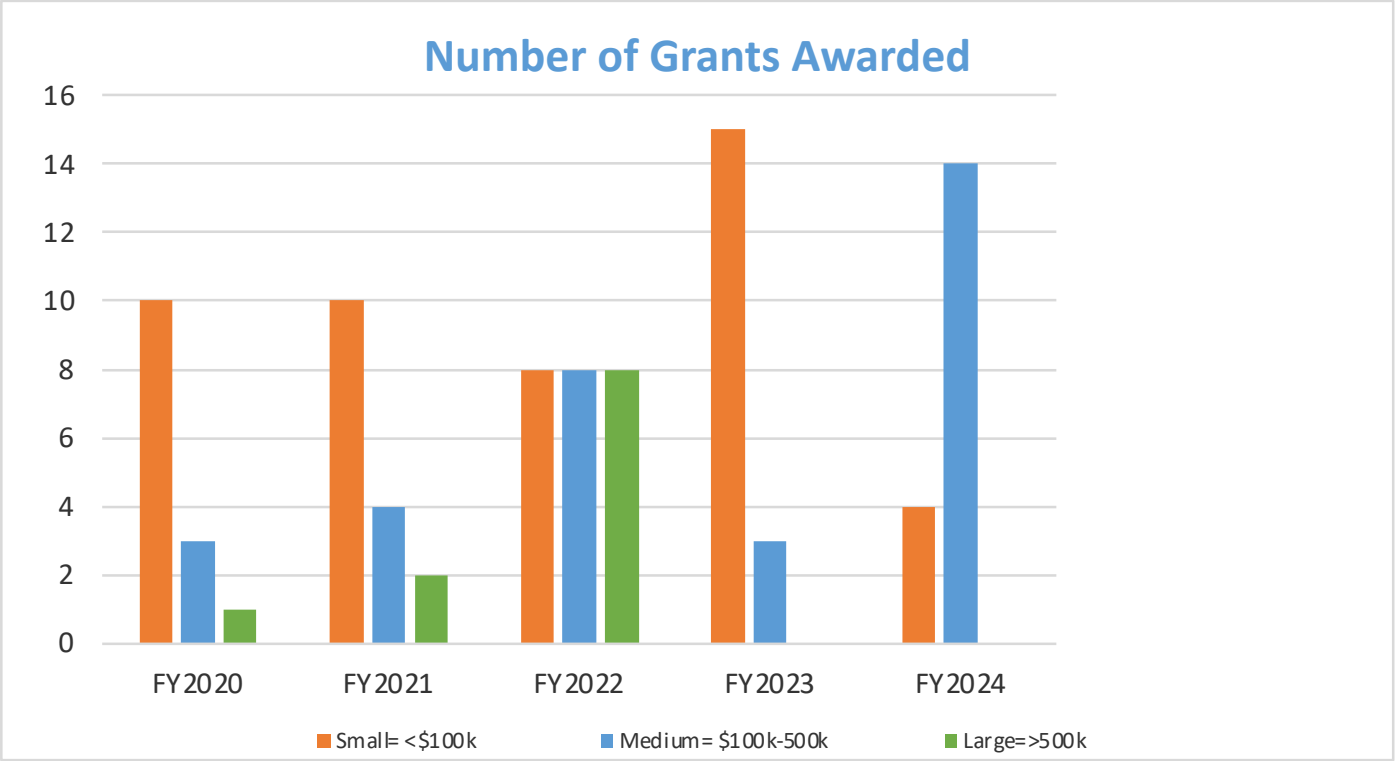
3. Number of Applications by Award Type

The table below shows the number of applications submitted to sponsors during the reporting period, being 17 prime awards and seven subcontracts.



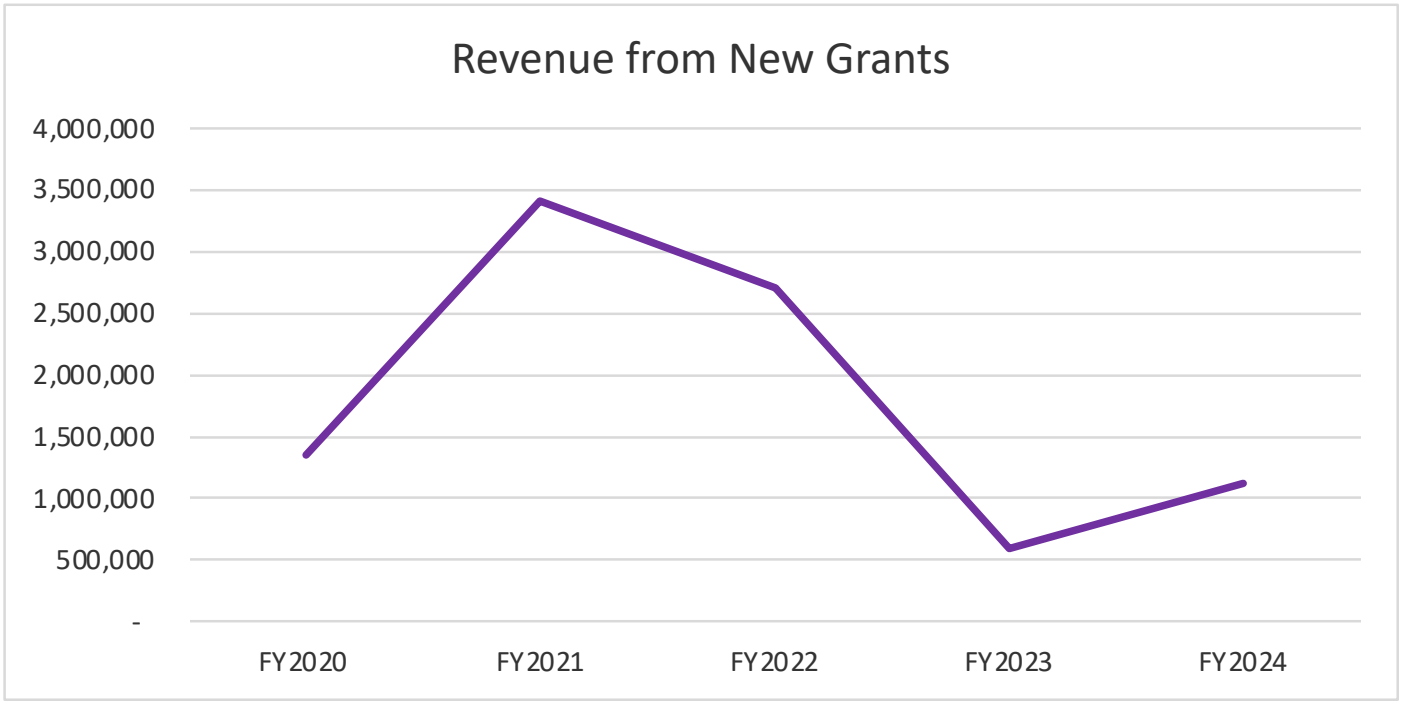
4. Number of Applications Awarded

Eighteen (18) out of 33 cumulative applications were successfully awarded in FY2024, of which four were small sized while 14 were medium sized grants.



5. Revenue From New Grants

Revenue from new applications increased to $1.1m from $0.586m in FY2023. There is a notable effort of grant application success from both the local and international Principal Investigators (PIs).



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Sustainability

The BHP has embarked on a two-tier fund development drive to help sustain and grow its critical missions of training, capacity building and research. BHP and affiliated supporters have embarked upon initiatives to raise additional funds, including targeted philanthropic activities in Botswana and across the globe. Domestic fund-raising efforts are primary aimed at raising capital for critical infrastructure (space, laboratory, pharmacy and clinical equipment).

International fund-raising efforts are primarily aimed at raising funds for core research needs (direct support of citizen Principal Investigator led research, the development of citizen Early-Stage Principal Investigators, and participation in international conferences and thinktanks). In support of international fundraising efforts, BHP has partnered with Myriad USA and their partner Every.org to accept donations from outside Botswana on BHP's behalf.

This partnership has established a Friends of Botswana Harvard Account to facilitate the receipt of philanthropic gifting by international donors, whether individuals, foundations or corporations.

Donations through Myriad USA from US based donors are tax deductible. The BHP continues to invest in supporting and developing early career investigators from Botswana and the rest of Africa, including building grant writing capabilities, and over the next strategic planning period, mentor and develop local early career investigators.

Empowering the future of Science: BHP thrives for sustainability to continue driving science forward for Botswana and the world

15

Annexure A: Publications

1. Impact of Hepatitis Delta Virus Infection on the Selection of Hepatitis B Surface Antigen Mutations. Baruti K, Choga WT, Phinius BB, Phakedi B, Bhebhe L, Mpebe GGA, Motshosi PC, Ratsoma T, Moyo S, Jongman M, Anderson M, Gaseitsiwe S. Genes (Basel). 2024 Jul 25;15(8):982. doi: 10.3390/genes15080982. PMID: 39202343.

2. Designing an implementation science clinical trial to integrate hypertension and cardiovascular diseases care into existing HIV services package in Botswana (InterCARE). Youssouf N, Mogaetsho GE, Moshomo T, Gaolathe T, Ponatshego P, Ramotsababa M, Molefe-Baikai OJ, Dintwa E, Kiki T, Van Pelt AE, Steger-May K, Bogart LM, Jaffar S, Gala P, Wang D, Seipone K, Bennett K, Hurwitz KW, Kebotsamang K, Hirschhorn LR, Mosepele M. Trials. 2024 Jul 29;25(1):510. doi: 10.1186/s13063-024-08333-0. PMID: 39075506.

3. Molecular Characterization of Hepatitis B Virus in People Living with HIV in Rural and Peri-Urban Communities in Botswana. Phinius BB, Choga WT, Anderson M, Mokomane M, Gobe I, Ratsoma T, Phakedi B, Mpebe G, Bhebhe L, Gaolathe T, Mosepele M, Makhema J, Shapiro R, Lockman S, Musonda R, Moyo S, Gaseitsiwe S. Biomedicines. 2024 Jul 14;12(7):1561. doi: 10.3390/biomedicines12071561. PMID: 39062134.

4. Novel use of local analgesia prior to intramuscular magnesium sulphate injection compared to mixed local analgesia with magnesium sulphate to reduce pain: a randomised crossover study in patients being managed for eclampsia and preeclampsia. Jamieson M, Luckett R, Hofmeyr GJ. Front Pain Res (Lausanne). 2024 Jul 11;5:1376608. doi: 10.3389/fpain.2024.1376608. eCollection 2024. PMID: 39055104.

5. Prevalence of sexually transmitted infection in pregnancy and their association with adverse birth outcomes: a case-control study at Queen Elizabeth Central Hospital, Blantyre, Malawi. van der Veer C, Kondoni C, Kuyere A, Mtonga F, Nyasulu V, Shaba G, Morroni C, Gadama G, Gadama L, Kawaza K, Dube Q, French N, Lissauer D, Freyne B. Sex Transm Infect. 2024 Jul 23: sextrans-2024-056130. doi: 10.1136/sextrans-2024-056130. Online ahead of print. PMID: 39043612.

6. Quantitative outcomes of a type 2 single arm hybrid effectiveness implementation pilot study for hypertension-HIV integration in Botswana. Moshomo T, Gaolathe T, Ramotsababa M, Molefe-Baikai OJ, Mogaetsho E, Dintwa E, Gala P, Ponatshego P, Bogart LM, Youssouf N, Seipone K, Van Pelt AE, Bennett K, Jaffar S, Ilias M, Tonwe V, Hurwitz KW, Kebotsamang K, Steger-May K, Hirschhorn LR, Mosepele M. Implement Sci Commun. 2024 Jul 22;5(1):80. doi: 10.1186/s43058-024-00620-w. PMID: 39039609.

7. Low Prevalence of Nirmatrelvir-Ritonavir Resistance-Associated Mutations in SARS-CoV-2 Lineages from Botswana. Choga WT, Bareng OT, Moraka NO, Maruapula D, Gobe I, Ndlovu NS, Zuze BJL, Motshosi PC, Seru KB, Matsuru T, Boitswarelo M, Matshaba M, Gaolathe T, Mosepele M, Makhema J, Tamura TJM, Li JZ, Shapiro R, Lockman S, Gaseitsiwe S, Moyo S. Open Forum Infect Dis. 2024 Jul 2;11(7):ofae344. doi: 10.1093/ofid/ofae344. eCollection 2024 Jul. PMID: 39015352

8. Diagnostic Prediction Model for Tuberculous Meningitis: An Individual Participant Data Meta-Analysis. Stadelman-Behar AM, Tiffin N, Ellis J, Creswell FV, Ssebambulidde K, Nuwagira E, Richards L, Lutje V, Hristea A, Jipa RE, Vidal JE, Azevedo RGS, Monteiro de Almeida S, Kussen GB, Nogueira K, Gualberto FAS, Metcalf T, Heemskerk AD, Dendane T, Khalid A, Ali Zeggwagh A, Bateman K, Siebert U, Rochau U, van Laarhoven A, van Crevel R, Ganiem AR, Dian S, Jarvis J, Donovan J, Nguyen Thuy Thuong T, Thwaites GE, Bahr NC, Meya DB, Boulware DR, Boyles TH. Am J Trop Med Hyg. 2024 Jul 16;111(3):546-553. doi: 10.4269/ajtmh.23-0789. Print 2024 Sep 4. PMID: 39013385.

9. Community dialogue to enhance understanding of beliefs, behaviours and barriers to care for people living with liver disease and HBV infection in KwaZulu Natal, South Africa. Ngwenya B, Anderson M, Mpanza N, Mbokazi W, Zuma L, Khoza T, Sukali G, Waddilove E, Delphin M, Iwuji C, Mhlongo N, Majozi N, Seeley J, Upton J, Harling G, Matthews PC, Edwards A. J Virus Erad. 2024 Jun 10;10(2):100378. doi: 10.1016/j.jve.2024.100378. eCollection 2024 Jun. PMID: 38983867.

10. Association between maternal HIV status and postpartum depressive symptoms in Botswana. Mmasa KN, Liu Y, Jao J, Malee K, Legbedze J, Sun S, Kgole S, Masasa G, Mmalane M, Makhema J, Mafa N, Abrams EJ, Powis KM, Bonner LB. AIDS Care. 2024 Jul 8:1-6. doi: 10.1080/09540121.2024.2373398. Online ahead of print. PMID: 38976581.

11. How much could anemia-related interventions reduce the HIV disparity in adverse birth outcomes? Caniglia EC, Zash R, Diseko M, Mayondi G, Mabuta J, Mmalane M, Makhema J, Jacobson DL, Bengtson AM, Lockman S, Shapiro R, Swanson SA. Am J Epidemiol. 2024 Jul 4: kwae160. doi: 10.1093/aje/kwae160. Online ahead of print. PMID: 38965743.

12. Impact of efavirenz on hormone-positive breast cancer survival in women living with HIV. Johnson AT, Ntloedibe T, Mendez Reyes JE, Matshaba MS, Dryden-Peterson SL, Chiao EY. AIDS. 2024 Jul 15;38(9):1439-1442. doi: 10.1097/QAD.0000000000003912. Epub 2024 Jun 27. PMID: 38932749.

13. Hepatitis B Virus Prevalence among HIV-Uninfected People Living in Rural and Peri-Urban Areas in Botswana. Anderson M, Mangogola T, Phinius BB, Mpebe G, Aimakhu CO, Choga WT, Phakedi B, Bhebhe LN, Ditshwanelo D,

Baruti K, Mpofu-Dobo L, Othusitse L, Ratsoma T, Gaolathe T, Makhema J, Shapiro R, Lockman S, Moyo S, Gaseitsiwe S. Microorganisms. 2024 Jun 15;12(6):1207. doi: 10.3390/microorganisms12061207. PMID: 38930589.

14. High prevalence of albuminuria among adult males living with HIV in Botswana. Mosepele M, Ponatshego P, Molebatsi K, Williams C, Mokgatlhe L, Lockman S, Youssouf N, Gross R, Jarvis J, Wang D, Jaffar S. Sci Rep. 2024 Jun 23;14(1):14432. doi: 10.1038/s41598-024-65099-w. PMID: 38910157

15. A mixed methods approach identifying facilitators and barriers to guide adaptations to InterCARE strategies: an integrated HIV and hypertension care model in Botswana. Gala P, Ponatshego P, Bogart LM, Youssouf N, Ramotsababa M, Van Pelt AE, Moshomo T, Dintwa E, Seipone K, Ilias M, Tonwe V, Gaolathe T, Hirschhorn LR, Mosepele M. Implement Sci Commun. 2024 Jun 20;5(1):67. doi: 10.1186/s43058-024-00603-x. PMID: 38902846.

16. Improving management of first and second stages of labour in low- and middle-income countries. Hofmeyr GJ, Moreri-Ntshabele B, Qureshi Z, Memo N, Hanson S, Muller E, Singata-Madliki M. Best Pract Res Clin Obstet Gynaecol. 2024 Jul; 95:102517. doi: 10.1016/j.bpobgyn.2024.102517. Epub 2024 Jun 14. PMID: 38902106.

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Annexure B: Abstracts

1. Rilpivirine-associated resistance mutations among virologically suppressed people living with HIV-1 in Botswana: implications for cabotegravir-rilpivirine use. D. Maruapula1, N.O. Moraka, O.T. Bareng, P.T. Mokgethi, W.T. Choga, K.K. Seatla, N. Kelentse, T. Gaolatlhe, M. Pretorius-Holme, J. Makhema, V. Novitsky, R. Shapiro, S. Moyo, S. Lockman, S. Gaseitsiwe. IAS 2023, the 12th IAS Conference on HIV Science. Brisbane, Australia, virtually from 23 to 26 July 2023. Eposter

2. Incidence of occult hepatitis B virus among people living with HIV in Botswana. M. Anderson, B.B. Phinius, B.K. Phakedi, L.N. Bhebhe, N. Tlhabano, P. Motshosi, D. Ditshwanelo, K. Baruti1, G. Mpebe1, W.T. Choga, D. Glebe, J.T. Blackard, S. Moyo, A. Kramvis, S. Gaseitsiwe. IAS 2023, the 12th IAS Conference on HIV Science. Brisbane, Australia, virtually from 23 to 26 July 2023. Eposter.

3. No impact of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) on maternal mortality or infant adverse birth outcomes in Botswana during the Omicron era. J. Banga, M. Jackson-Gibson, M. Diseko, E. Caniglia, G. Mayondi, J. Mabuta, R. Luckett, S. Moyo, P. Lawrence, M. Mosepele, S. Lockman, J. Makhema, R. Zash1,3, R. Shapiro, IAS 2023, the 12th IAS Conference on HIV Science. Brisbane, Australia, virtually from 23 to 26 July 2023. Eposter.

4. Positive Predictive Value of HIV Serological Tests in HPTN 084 Trial. M. Hosseinipour, E. Voldal, B. Hanscom, S. Eshleman, E. Piwowar-Manning, Y. Agyei, K Nyarota, F Angira, S. Dadabhai, D. Gadama, BG Mirembe, P. Hunidzarira, S. Innes, D Kalonji, J. Makhema, P Mandima, A. Marais, J Mpendo, P Mukwekwerere, N Mgodi, V Naidoo, P Nahirya Ntege, H Nuwagaba-Biribonwoha, E Roos, N Singh, B Siziba, E Spooner, J. Farrior, S. Rose, L. Soto-Torres, J Rooney, A.R. Rinehart, R Landovitz, M.S. Cohen1, S. Delany-Moretlwe, on behalf of the HPTN 084 study team. IAS 2023, the 12th IAS Conference on HIV Science. Brisbane, Australia, virtually from 23 to 26 July 2023. Oral Abstract.

5. Initial PrEP product choice: results from the HPTN 084 open-label extension. S. Delany-Moretlwe, B. Hanscom, F. Angira, S. Dadabhai, D. Gadama5 B. Mirembe, M. Bhondai, S. Innes, D. Kalonji, J. Makhema, P. Mandima, A. Marais, J. Mpendo, P. Mukwekwerere, N. Mgodi, V. Naidoo, P. Nahirya Ntege, H. Nuwagaba-Biribonwoha, E. Roos, N. Singh, B. Siziba, E. Spooner, J. Farrior, S. Rose, E. Piwowar-Manning, M. Burton, L. Soto-Torres, J. Rooney, A. Rinehart, M. Cohen, M. Hosseinipour, HPTN 084 study team. IAS 2023, the 12th IAS Conference on HIV Science. Brisbane, Australia, virtually from 23 to 26 July 2023. Oral Abstract.

6. Neural tube defects and major external structural abnormalities by antiretroviral treatment regimen in Botswana: 2014-2022. R. Zash1, M. Diseko, L.B. Holmes, D. Jacobson, E. Caniglia, S. Brummel, G. Mayondi, J. Mabuta, C. Fennell, T. Makoni1, T. Gaolathe, S. Lockman, J. Makhema, R. Shapiro. IAS 2023, the 12th IAS Conference on HIV Science. Brisbane, Australia, virtually from 23 to 26 July 2023. Eposter.

7. Analytical treatment interruption among African women and Peruvian men & transgender individuals with early ART initiation +/- VRC01 circulating at HIV acquisition: early observations of viral rebound & control. S. Karuna1, K. Bar, A. deCamp, P.-C. Yu, D. Grove, P. Andrew, C. Orrell, J. Gallardo-Cartagena, R. De La Grecca, A. Takalani, M. Villaran, L. Gama, T.-W. Chun, J. Sanchez, J. Valencia, J. Montenegro-Idrogo, S. Dadabhai, C.-A. Mathew, J. Makhema, F. Laher, R. Cabello, M. Casapia, M. Hosseinipour, N. Mgodi, R. Tressler, L. Soto-Torres, M. Cohen, J. Currier, J. Eron, L. Corey, AMP ATI Study Teams. IAS 2023, the 12th IAS Conference on HIV Science. Brisbane, Australia, virtually from 23 to 26 July 2023. Eposter.

8. Low HIV transmission among high-risk infants receiving post-natal prophylaxis in Botswana. Gbolahan Ajibola, Oganne Batlang, Maureen Sakoi-Mosetlhi, Sikhulile Moyo, Molly Pretorius Holme, Tendani Gaolathe, Modiegi Diseko, Max Kapanda, Jessica Mafa-Setswalo, Sean Brummel, Kathleen Powis, Shahin Lockman, Joseph Makhema, Daniel Kuritzkes, Mathias Lichterfeld, Roger Shapiro. IAS 2023, the 12th IAS Conference on HIV Science. Brisbane, Australia, virtually from 23 to 26 July 2023. Poster.

9. Predicted bnAb resistance and HIV envelope characteristics of adults with seroconversion in Botswana. Natasha Onalenna Moraka. SANTHE Consortium Annual Meeting, 13-14 July 2023, Lusaka Zambia.

10. Evaluating HIV reservoirs in infants and adolescents in Southern Africa: Advancing HIV cure research. Catherine Kegakilwe Koofhethile. SANTHE Annual meeting 2023, 12-13th July 2023, Lusaka Zambia. Oral Abstract.

11. Occult Hepatitis B virus among people with HIV in rural and peri-urban communities in Botswana. Bonolo Phinius. Global Hepatitis Summit 2023, 25th - 28th April 2023, Virtual, Poster.

12. Approaches to interdisciplinary research in One Health. Sikhulile Moyo. Conference on Climate Change and Pandemic Preparedness, 26-27 October 2023, German Embassy Gaborone, Botswana

13. Role of pathogen genomics in Public Health: Lessons from HIV and COVID-19 towards pandemic Preparedness. Sikhulile Moyo. The 11th EDTCP forum. 07-10 November 2023, Paris, France.

14. Treatment outcomes of low-level viremia among adults living with HIV on dolutegravir-based first line

antiretroviral therapy in Botswana. Ontlametse T Bareng. The 11th EDTCP forum. 07-10 November 2023, Paris, France.

15. Impact of Multi-Class Antiretroviral Drug-Resistant Variants on Newly Approved Antiretroviral Therapy (ART) Among People Living with HIV in Botswana. Nokuthula S. Ndlovu. The 11th EDTCP forum. 07-10 November 2023, Paris, France.

16. High Proportion of False-Positive HIV Results with Point-of care Birth Testing in Botswana. Gbolahan Ajibola, Nyaladzi Maphorisa, Aischa Niesar, Terence Mohammed, Maureen Sakoi-Mosetlhi, Oganne Batlang, Sikhulile Moyo, Molly Pretorius Holme, Kathleen M. Powis, Shahin Lockman, Joseph M. Makhema, Mathias Lichterfeld, Roger Shapiro. Conference on Retroviruses and Opportunistic Infections, 2024 Denver, Colorado from March 3-6, 2024, Poster Presentation

17. No Early Signal That DTG Improves 24-Week Viral Suppression in Infants in Botswana Maureen Sakoi-Mosetlhi, Gbolahan Ajibola, Oganne Batlang, Kenneth Maswabi, Molly Pretorius Holme, Kathleen M. Powis, Shahin Lockman, Michael D. Hughes, Joseph M. Makhema, Daniel R. Kuritzkes, Mathias Lichterfeld, Roger Shapiro. Conference on Retroviruses and Opportunistic Infections, 2024 Denver, Colorado from March 3-6, 2024, Poster Presentation.

18. Predictive Markers for Sustained Viral Suppression on Dual bNAbs During ART Interruption in Children. Jaspreet Banga, Bryan S. Nelson, Gbolahan Ajibola, Terence Mohammed, Nyaladzi Maphorisa, Oganne Batlang, Maureen Sakoi-Mosetlhi, Molly Pretorius Holme, Kathleen M. Powis, Shahin Lockman, Michael D. Hughes, Joseph M. Makhema, Daniel R. Kuritzkes, Mathias Lichterfeld, Roger Shapiro. Conference on Retroviruses and Opportunistic Infections, 2024 Denver, Colorado from March 3-6, 2024, Poster Presentation.

19. Hypertension in Pregnant Persons with and Without HIV and by dolutegravir versus efavirenz exposure at conception in the Tsepamo Study. Denise L. Jacobson, Modiegi Diseko, Judith Mabuta, Ellen Caniglia, Kathleen Powis, Lynn Yee, Joseph Makhema, Shahin Lockman, Roger Shapiro and Rebecca Zash. Conference on Retroviruses and Opportunistic Infections, 2024 Denver, Colorado from March 3-6, 2024, Poster Presentation.

20. A Target Trial of Preconception Switch from Nevirapine- to Dolutegravir-Based ART on Birth Outcomes. Ellen C. Caniglia, Rebecca Zash, Modiegi Diseko, Judith Mabuta, Mompati Mmalane, Shahin Lockman, Gloria Mayondi, Gaerolwe Masheto, Joseph Makhema, Roger Shapiro. Conference on Retroviruses and Opportunistic Infections, 2024 Denver, Colorado from March 3-6, 2024, Poster Presentation

21. Evaluating research integrity awareness: An assessment among Botswana research institutions. Sekoto, T., Sebaka, A., Zwinila, M., Seonyatseng, N., Ikgopoleng, K., & Okui, A. L.). Poster presented at the Canadian Bioethics Society Conference, Montreal, Canada. May 29-31, 2024.

22. Integrating STI screening in antenatal care: Data from Botswana so far. Moshashane N, Mussa A, Wynn A, Bame B, Ryan R, Ndlovu N, Ramontshonyana K, Tamuthiba L, Morroni C. Poster presentation at the Botswana Ministry of Health 3rd National Research Symposium (Gaborone, Botswana) – February 2024.

23. Effect of antenatal Chlamydia trachomatis and Neisseria gonorrhoeae screening on post-delivery prevalence and vertical transmission in Gaborone, Botswana. Mussa A, Wynn A, Ryan R, Babalola CM, Hansman E, Simon S, Bame B, Moshashane N, Masole M, Wilson ML, Klausner JD, Morroni C. Poster presentation at the Institute for Regeneration & Repair Symposium 2024, The University of Edinburgh (Edinburgh, UK) – May 2024.

24. Evaluating research integrity awareness: An assessment among Botswana research institutions. Sekoto, T., Sebaka, A., Zwinila, M., Seonyatseng, N., Ikgopoleng, K., & Okui, A. L. May29-31,204. Poster presented at the Canadian Bioethics Society Conference, Montreal, Canada.

25. High Prevalence of Depression and Anxiety in Women Without HIV and Women with HIV on DTG-ART. Kebaiphe Moabi. Conference on Retroviruses and Opportunistic Infections, 2024 Denver, Colorado from March 3-6, 2024, Poster Presentation.

26. Neurodevelopment in Children Exposed in Utero to Dolutegravir- or Efavirenz-Based ART in Botswana. Adam Cassidy. Conference on Retroviruses and Opportunistic Infections, 2024 Denver, Colorado from March 3-6, 2024, Poster Presentation.

27. Predictive Markers for Sustained Viral Suppression on Dual bNAbs During ART Interruption in Children. Jaspreet Banga. Conference on Retroviruses and Opportunistic Infections, 2024 Denver, Colorado from March 3-6, 2024, Poster Presentation.

28. Long-Term ART Is Not Associated with Reduced Anogenital Cancer Risk: A Case-Cohort Study. Maanasa Mendu. Conference on Retroviruses and Opportunistic Infections, 2024 Denver, Colorado from March 3-6, 2024,

Poster Presentation.

29. Hypertension in a Randomized Trial of DTG vs EFV-Based ART in Pregnant and Postpartum Women. Risa Hoffman. Conference on Retroviruses and Opportunistic Infections, 2024 Denver, Colorado from March 3-6, 2024, Poster Presentation.

30. Breast Milk Transfer and Infant Exposures to DTG, TAF, and TFV: Results from IMPAACT 2010/VESTED. Jeremiah Momper. Conference on Retroviruses and Opportunistic Infections, 2024 Denver, Colorado from March 3-6, 2024, Poster Presentation.

31. Variable HIV-1 C Env Characteristics Associated with Predicted bNAb resistance in Botswana. Natasha Moraka. Conference on Retroviruses and Opportunistic Infections, 2024 Denver, Colorado from March 3-6, 2024, Poster Presentation.

32. High Genetic Diversity of Rifampicin-Resistant Mycobacterium Tuberculosis Strains in Botswana. Tuelo Mogashoa. Conference on Retroviruses and Opportunistic Infections, 2024 Denver, Colorado from March 3-6, 2024, Poster Presentation.

33. Safety Outcomes in Trial of COVID-19 10 mRNA Vaccine Among People Living with HIV in Sub-Saharan Africa. Hudson Aaron. Conference on Retroviruses and Opportunistic Infections, 2024 Denver, Colorado from March 3-6, 2024, Oral Presentation.

34. mRNA Vaccine Versus Hybrid Immunity Against COVID-19 Among People with HIOV During Omicron wave. Hudson Aaron. Conference on Retroviruses and Opportunistic Infections, 2024 Denver, Colorado from March 3-6, 2024, Oral Presentation.

The Botswana Harvard Health Partnership (BHP) has successfully concluded its 2023-2024 annual reporting period, showcasing impactful research and capacity building achievements aligned with its five strategic themes: Research Excellence, Capacity Building and Training, Operational Excellence, Public Policy and Advocacy, and Sustainability.

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