BOTSWANA
HARVARD AIDS INSTITUTE
PARTNERSHIP
FOR HIV RESEARCH AND EDUCATION

ANNUAL REPORT 2014-2015

BHP "GETTING TO ZERO…!"

"Towards ending the AIDS epidemic by 2030"

1 Strategic Foundations

Vision

To be a world renowned institute of excellence in research and education on HIV/AIDS and emerging public health challenges.

Mission Statement

To fight against HIV/AIDS and emerging public health challenges through collaborative research, education, capacity building, and community engagement.

Core Values

a) **Botho:** An all-encompassing Setswana word which means, amongst others, 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 on and about studies will be handled with the utmost confidentiality.

b) **Beneficence:** All activities done at BHP shall be of relevance and benefit to those infected and/or affected by HIV/ AIDS in Botswana, regionally and globally. The knowledge generated through our research shall be availed to advise public health policy and shall be shared with the general public and scientific community for the benefit of mankind. We will be guided by the principle of 'Do No Harm' in our Research and related activities.

c) **Innovation:** BHP staff is committed to finding solutions to the HIV/AIDS pandemic. We shall endeavor to be continuously innovative and resourceful in our quest to understand the Human Immunodeficiency Virus and to discover a solution to its spread as well as the treatment of AIDS.

d) **Collaboration:** BHP recognizes that the fight against HIV/AIDS will not be won by one man or one institution. We commit and emphasize the importance of team work and collaborative research in our activities.

e) **Excellence:** To achieve our vision of being a 'World Renowned Institute of Research and Education' 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.

1 BHP at a Glance

Establishment

Botswana Harvard Partnership is a Not for Profit limited liability organisation, established through a partnership between the Government of Botswana, represented by the Ministry of Health, and Harvard University, represented by the Harvard T. H Chan School of Public Health's AIDS Institute. It was established in 1996 and registered as a limited liability company in 2009.

Business

Knowledge generation and knowledge dissemination through research, education and capacity building.

Board of Members

Prof David Hunter; Dean for Academic Affairs, HSPH; Mrs Joy Phumaphi, Ex-Minister of Health Botswana; Madisa Mine, Consultant Virologist BHHRL & MoH.

Prof Max Essex, Mary Woodard Lasker Professor of Health Sciences, HSPH; Prof Richard Marlink, Beal Professor of the Practice of Public Health, HSPH; Michael Kan, Executive Dean for Administration, HSPH.

Board of Directors

Prof Max Essex, Mary Woodard Lasker Professor Health Sciences, HSPH (Chairman); Prof Richard Marlink, Beal Professor of the Practice of Public Health, HSPH; Michael Kan, Executive Dean for Administration, HSPH; Dr Khumo Seipone, Director of Health Services, MoH; Mr Modise Modise, Ex- Permanent Secretary of Development, Office of the President; Dr George Matlho, General Manager, Botswana Vaccine Institute; Dr Joseph Makhema, Chief Executive Officer, BHP; Mrs Ria Madison, Chief Operations Officer, BHP (Ex Officio).

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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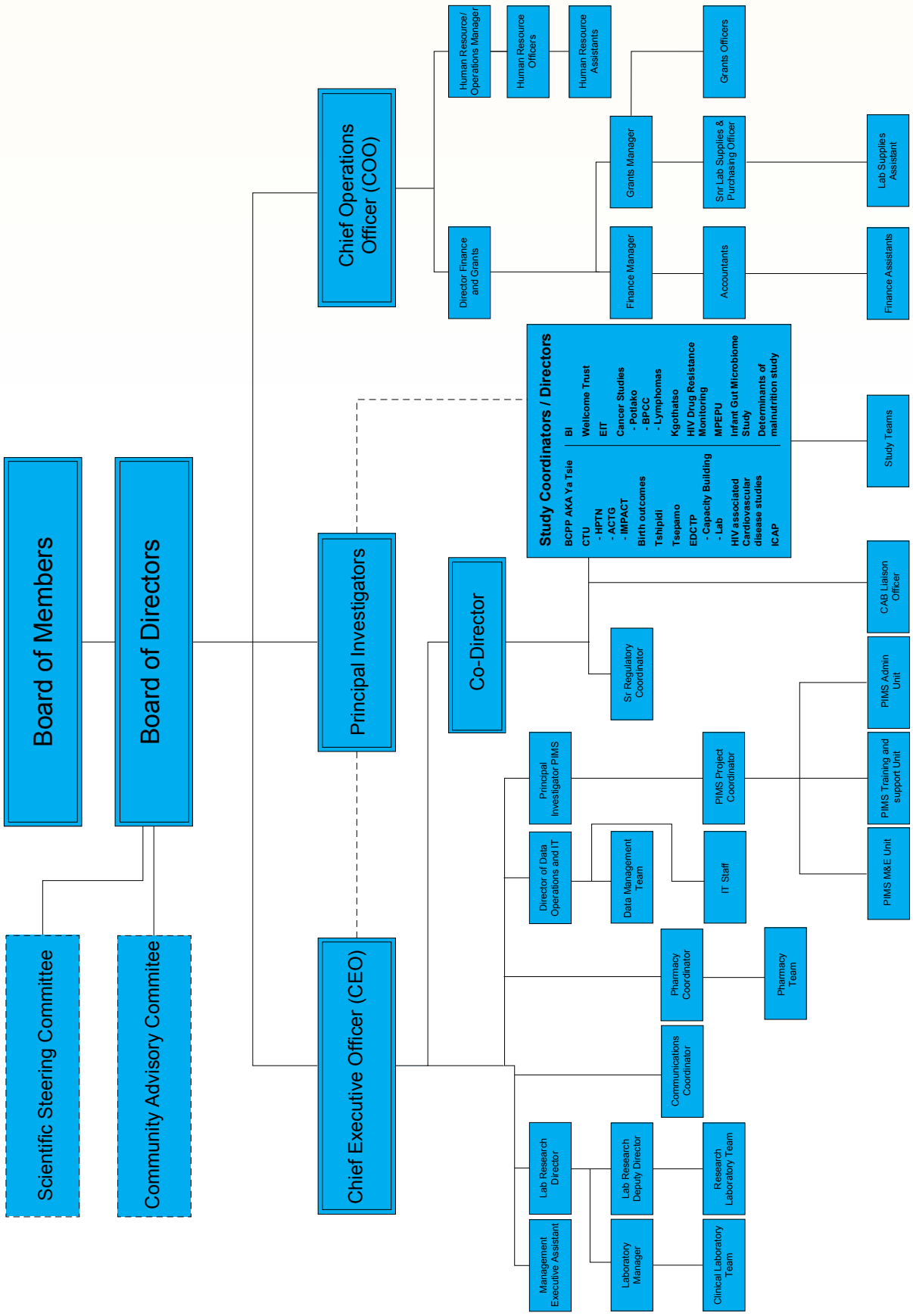
Company Auditors: Price Waterhouse Coopers,

Company Secretaries: DPS Consulting,

Company Attorneys: Armstrongs Attorneys, Notaries & Conveyancers

Main Bankers: Standard Chartered Bank & Stanbic Bank

3 BHP Organisational Structure



3 List of Abbreviations and Symbols

ACTG	AIDS Clinical Trials Group
ACTU	AIDS Clinical Trials Unit
AFB	Acid Fast Bacilli
AfriCan	Africa Canadian Partnership
AIDS	Acquired Immuno Deficiency Syndromme
AMP	Antibody Mediated Prevention
ANC	Anti-natal Clinic
ART	Antiretroviral Therapy
ARV	Anti-retroviral
BCPP	Botswana Combination Prevention Project
BED	Enzyme immune assay to determine recency of infection
BHHRL	Botswana Harvard HIV Reference Laboratory
BHP	Botswana Harvard AIDS Institute Partnership
BIDMC	Berth Israel Deaconess Medical Center
BMC	BioMed Central Journal (Open source journal)
BPCC	Botswana Prospective Cancer Cohort
BUP	Botswana University of Pennsylvania Partnership
CAB	Community Advisory Board
CDC	Centers for Disease Control and Prevention (USA)
CFAR	Centers for AIDS Research
CIN	Carcinoma in situ
CMV	Cytomegalovirus
CROI	Conference on Retroviruses and Opportunistic Infections
CTU	Clinical Trials Unit
DAIDS	Division of AIDS (at National Institutes of Health)
DMC	Data Management Center
DNA	Deoxyribonucleic Acid
DSMB	Data Safety Monitoring Board
EDC	Electronic Data Capture
ELISA	Enzyme-linked Immunosorbent Assay
FTE	Fulltime Equivalent
FY	Financial Year
GAGAS	Generally Accepted Government (USA) Auditing Standards
GCLP	Good Clinical Laboratory Practice
HAART	Highly Active Anti-retroviral Therapy
HBV	Hepatitis B Virus
HIV	Human Immunodeficiency Virus
HPTN	HIV Prevention Trials Network
HPV	Human Papilloma Virus
HR	Human Resource
HRDC	Health Research and Development Committee (Botswana's National Ethics Committee)
HRM	Human Resource Management System
HSPH	Harvard TH Chan School of Public Health
ICASA	International Conference in AIDS and STIs in Africa
IFRS	International Financial Reporting Standards
IMPAACT	International Maternal, Paediatrics, and Adolescents AIDS Clinical Trials
INH	Isoniazid
ISO	International Standards Organisation
LTBI	Latent Tuberculosis Infection
mAb	Monoclonal antibodies
MARS	Merck Africa Research Summit
Mayan	The open-source electronic data management system
MDR	Multi-Drug Resistant
MGH	Massachusetts General Hospital
MoH	Ministry of Health (Botswana)
MPhil	Master of Philosophy
MSc	Master of Science
NGS	Next Generation Sequencing
NHHRL	Nyangagbwe Hospital HIV Reference Laboratory
NHHRL	Nyangagbwe Hospital Reference Laboratory
NIH	National Institutes of Health
NUST	National University of Science and Technology (Zimbabwe)
OMB	Office of Management and Budget
PCR	Polymerase Chain Reaction
PhD	Doctor of Philosophy
PI	Principal Investigator
PMTCT	Prevention of Mother to Child Transmission
PPD	Pharmaceutical Product Development (Monitors)
PK	Pharmacokinetic study
pSMILE	Patient Safety Monitoring in International Laboratory
QGIT	Quantiferon TB in-Tube Assay
RPR	Rapid Plasma Reagin test
RPT/INH	Rifapentine/Isoniazid
SANAS	South African National Accreditation System
TB	Tuberculosis
THPA	Treponema Pallidum Haemagglutination test
UB	University of Botswana
UCLA	University College of Los Angels
USD	United States Dollar
USG	United States Government
UTT	Universal Test and Treat

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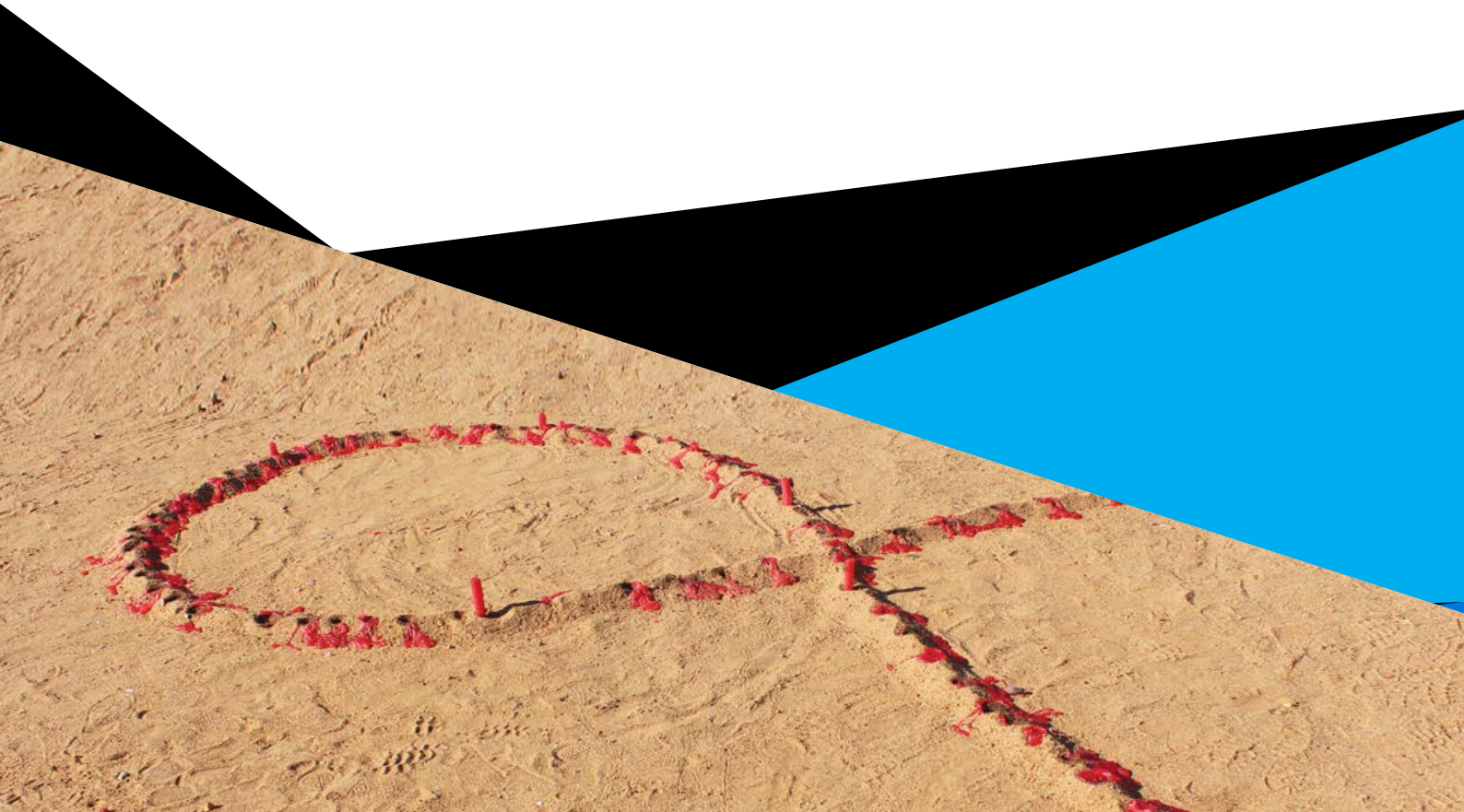


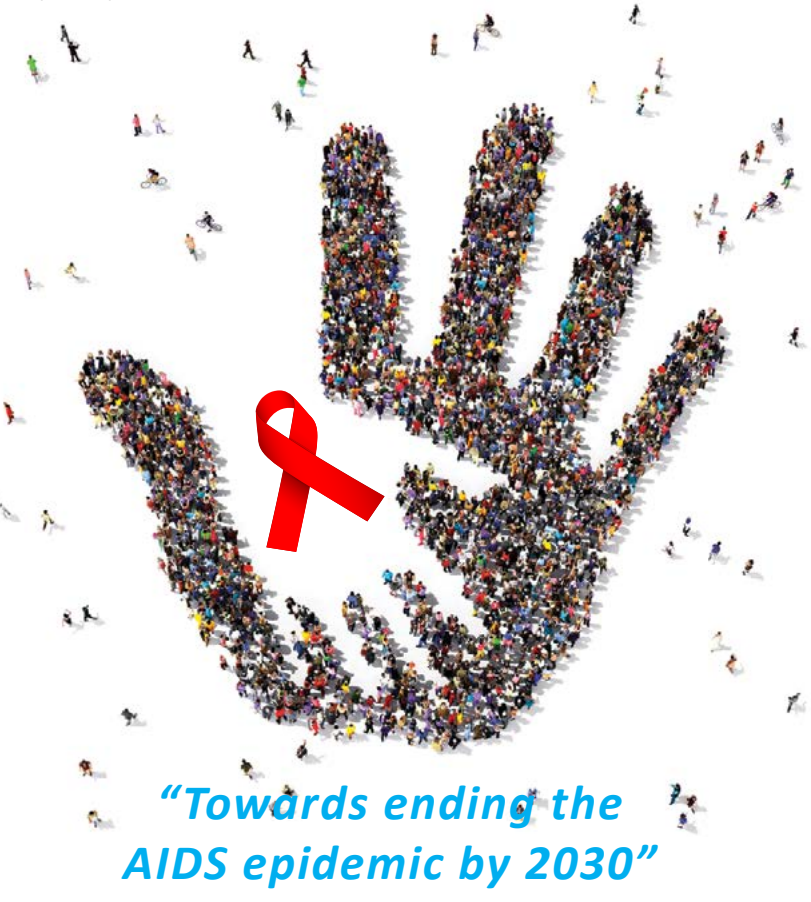
4 Chairman's Remarks

Professor MAX ESSEX
BHP CHAIRMAN

In the past, BHP and Harvard researchers have ensured that study data is presented to stakeholders to inform public health driven interventions. This has been authenticated by publishing findings in high impact, peer reviewed journals. BHP believes that mere sharing of the data may not be sufficient to achieve important public health outcomes and that active advocacy should be incorporated into BHP practices. BHP has resolved to present research outcomes as position papers and recommendations. In February 2015, a position paper cited evidence from the Mashi, Mmabana, Mpepu, and Tshipidi studies recommending that the national policy be revised to promote breastfeeding by HIV-infected women, given the fact that Botswana now offers triple antiretroviral treatment to all HIV-infected pregnant women. In November 2015, the Deputy Permanent Secretary of Botswana's Ministry of Health employed an outside consultant from the European Union to draft an infant formula feeding policy. The final policy submitted by an external consultant to Botswana's MoH, mirrors the policy paper submitted by BHP, and it also cites BHP studies. It is anticipated that when Botswana releases updated HIV treatment guidelines in April 2016, revised infant feeding guidelines will promote breastfeeding for all infants, regardless of maternal HIV-status.

Current on-going research continues to be selected and implemented collaboratively with the Ministry of Health to ensure relevance to Botswana's Public Health challenges. Following the new WHO treatment guidelines having recommended the Universal Test and Treat (UTT) strategy and the UNAIDS having set Country targets for 90% of all HIV infected people to know their HIV status; 90% of those diagnosed with HIV infection being on ART; 90% of all people on ART having undetectable HIV in their blood, referred to as the 90 - 90 - 90 targets by the year 2020: The ongoing Botswana Combination Prevention Project, BCPP also known as the "Ya Tsie" study offers opportunity for Botswana to develop tools and modalities, monitoring and evaluation systems, and capabilities of various healthcare operational systems.

These opportunities to develop new systems both at community and health care facility level would strengthen existing HIV/AIDS management systems in the MASA Programme based on research outcomes of the study. The Board of Directors is committed to support the BHP in its participation in such relevant studies and in its mandate.



5 Chief Executive Officer's Foreword

DR JOSEPH MAKHEMA
BHP Chief Executive Officer

As the leading HIV/AIDS research institution in Botswana BHP continues to undertake relavant research and capacity building to inform development of evidence driven scientific public health policies and programmes to mitigate against the HIV/AIDS epidemic in Botswana, regionally and internationally. Despite resource constraints due to increasing competition to attract grants and sponsorship to support ongoing activities, 2015 was a productive year for the BHP with continued success in various research and training programs.

During the year further consolidation and strengthening of administrative, operational and data systems in the support of research and training activities was undertaken. Both the financial audit and Generally Acceptable Government Audit Standard (GAGAS) reports for the year ended June 2015 were unqualified having benefited from system strengthening initiatives. All new research studies are now only implemented through electronic data capture, and there is ongoing archiving of case reports from previous studies with the aim of making BHP research activities paper-less.

2016 marks the last year of the current BHP Strategic Plan 2011-2016. There is general consensus that BHP still has a role and can make further valuable contributions in the fight against HIV/AIDS and other emerging Public Health challenges in Botswana and the region. Management has thus embarked on a process to begin preparations for the next Strategic Plan.

A strategic management decision was undertaken to collaborate with Institutions and partners with competitive advantages when applying for grants. These include ACHAP, Botswana-Baylor Children's Centre of Excellence and Botswana U-Penn Partnership to enhance possibility of positive outcomes while fostering collaborative linkages to facilitate synergism to improve and maximize programme efficiencies by working together across multiple areas in the public health sphere in Botswana.

2015 has seen successful BHP research ably supported by the laboratory which has maintained its ISO 17025 accreditation. The BHP/HSPH Botswana Combination Prevention Project "Ya Tsie Study" completed the first year base line survey in its 30 communities at the end of November 2015 and it has already provided valuable data and a manuscript submitted on the current 90-90-90 Botswana HIV epidemic control target as set by UNAIDS. BHP's Clinical Trials Unit is active in the HIV Prevention Trials Network having been competitively selected to participate in the HIV Prevention Trials Network (HPTN) Protocol 081. This study also called the Antibody Mediated Prevention (AMP) Study is a multisite multicenter, randomized, controlled, double-blind phase 2b study to evaluate the safety and efficacy of a broadly neutralizing monoclonal antibody (mAb) called VRC01 in reducing acquisition of HIV-1 infection. There are currently two ongoing (A5279 & A5282) and two new (A5316 & A5300) ACTG studies planned for early 2016, while the IMPAACT network has three ongoing (P1066, 1077HS & P1078) and one new study (P1093) scheduled to start early 2016. Furthermore the site has been identified for participation in at least three new designated studies (IMPAACT 2006, P1026S and IMPAACT 2005). The Early infant Treatment study is ongoing in Gaborone and Francistown with encouraging enrollment. Other active grants include, Head & neck cancer studies, drug resistance monitoring laboratory study, Birth Outcomes surveillance studies, including the effects of neuro-cognitive impairment following Anti Retro Viral drug exposure and research to underpin reasons for increased mortality among HIV-exposed uninfected children.

The BHP's citizen human resource research capacity was strengthened by the appointment of two Batswana as Research Associates, Drs M. Mosepele and N. Tapela both of whom are focused in careers in clinical and operational systems research by applying for their own grants to support their effort. This effort is also seen as strengthening BHP's strategic theme on capacity building.

We produced 21 publications in various scientific peer reviewed journals and at least 19 abstracts presented at various international meetings.

BHP remains committed to be true to it's mission of undertaking collaborative research and capacity building in the fight against HIV/AIDS and related public health challenges as we aim at meeting the ultimate universal target of ending the AIDS epidemic by 2030.

7 Organisational Excellence

Finance and Administration

BHP continues to strive for Organisational excellence consistent with its vision of becoming an Institute of research and training excellence. Focus has been on delivering quality services in the laboratory, administration, human resource, finance, grants and quality management supported by the development and installation of robust systems and operating procedures.

The BHP's Human Resources, Grants Management, Procurement, and Finance Department is complemented by a highly-qualified team with experience in financial and risk management, budgeting, grants management, procurement, auditing, project management, talent management, performance management, employee engagement and capacity building. BHP support services staff have worked with sub-grantees both in-country and internationally, primarily in sub-Saharan Africa. In accordance with organizational policy, BHP staff continually enhance their knowledge and skills through attendance of financial, grants and human resource trainings and workshops.

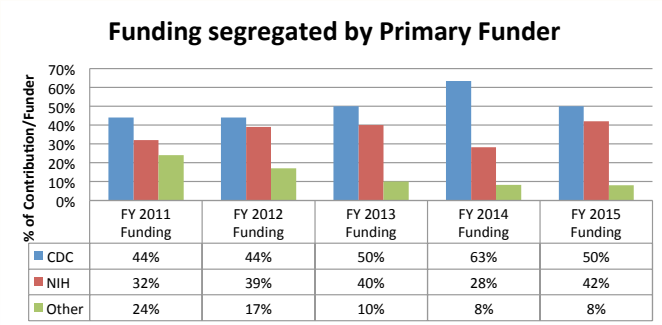
Grants and Procurement

The grants department absorbed the procurement function in FY2015 to ensure enhanced compliance with sponsor rules and regulations as relates to vendor selections and Sourcing strategy.

This department is responsible for the strategic management of a portfolio of over 30 grants 95% of which BHP is a subcontract to other institutions and 5% of which BHP is a prime recipient of sponsor funding. 92% of BHP's funding in the current year as in prior years is from USG Federal Donors being the Centre for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH); 8% of the remaining funding comes from non-traditional donors being the Welcome Trust, European and Developing Countries Partnership, the Paul Allen Foundation and the Botswana Government.

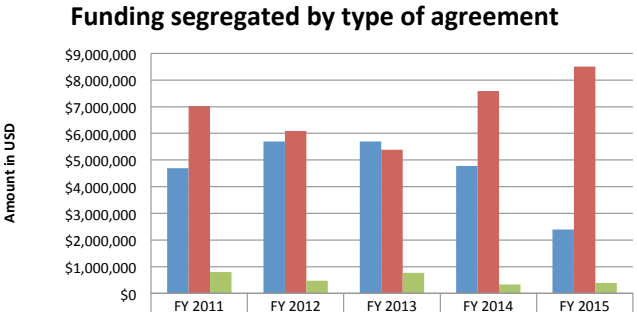
The following chart shows the total income competitively received by BHP over a period of 5 years, categorized by funder:

Chart 1: Funding over 5 years segregated by Primary Funder



	FY 2011 Funding	FY 2012 Funding	FY 2013 Funding	FY 2014 Funding	FY 2015 Funding
CDC	44%	44%	50%	63%	50%
NIH	32%	39%	40%	28%	42%
Other	24%	17%	10%	8%	8%

Chart 2: Funding over 5 years segregated by type of contract/agreement



	FY 2011 Funding	FY 2012 Funding	FY 2013 Funding	FY 2014 Funding	FY 2015 Funding
BHP Prime Awards	$4,690,911	$5,702,945	$5,700,698	$4,774,601	$2,385,222
Subcontracts	$7,026,599	$6,085,239	$5,380,795	$7,586,749	$8,503,607
Other	$793,045	$466,017	$764,395	$332,008	$387,102

The graph above shows decline of funding where BHP is the prime. This was mainly due to the non-renewal of the PEPFAR funding which has been supporting training initiatives by BHP. Given that BHP as an Institution expends more than USD500,000 annually and is funded 92% by the US Federal Government; it is required to comply with the requirements of Generally Accepted (US) Government Auditing Standards (GAGAS) and/or A133 audit requirements. To this end, BHP adheres to OMB cost principles and rules and regulations and for the year that ended June 2015, BHP attained an unqualified GAGAS audit with audit actions from the prior years fully implemented.

In December 2015, the Grants Management Team working with the corresponding Principal Investigator, Dr. Neo Tapela, submitted BHPs first NIH grant to the National Cancer Institute. This was a complicated multi-site grant submission and outlined plans to establish a

7 Organisational Excellence (CONT.)

Non-Communicable Disease Regional Research Center of Excellence. The grant is currently pending study section review. However, the Grants Team, led by Tryphinah Lungah, worked diligently to support Dr. Tapela. Ultimately, the grant included 5 subcontracts, including University of Botswana, University of Witwatersrand in South Africa, University of Pennsylvania, Harvard T.H Chan School of Public Health and Massachusetts General Hospital and reflected collaborative effort from Botswana's Ministry of Health. This opportunity demonstrated BHPs ability to seek NIH funding through local investigators. Capacity building for Dr. Tapela and the Grants Team was offered by Drs. Shahin Lockman, Scott Dryden-Peterson and Kate Powis.

Finance

The Finance Department exists to provide effective management of BHP's funds through implementation of sound financial management processes. The department has in place a robust PASTEL Evolution, ERP which enables compliance with International Financial Reporting Standards (IFRS), Generally Accepted (US) Government Auditing Standards (GAGAS) and facilitates multi-currency cost allocation across the 30+ grants within BHP's portfolio.

During the period under review, BHP recorded an asset base of $1, 283,368; revenue of $10, 570, 741 and expenditure of $12, 492, 685. These indicators are monitored on a monthly basis and co-reported to the Grants department. Furthermore, the department is responsible for the strategic management of an Admin Budget of $1,292,611 and provides financial analysis and forecasts in support of strategic sustainability initiatives.

Reflective of the organization's maintenance of a sound internal control environment designed to provide reasonable assurance that the transactions are accurately recorded, and to curb misuse and fraud, an unqualified statutory audit (in accordance with the International Standards on Auditing) result was obtained for period July 2014 to June 2015.

Due to the financial constraints on BHP's administration budget, the department has implemented cost cutting measures which are designed to contain costs within the administrative structure. These measures include;

i) BHP's Archiving Department has vacated rented office space as at the end of October 2015, reducing the monthly rental to $1,528.91 and overall admin budget by $12,231.26.

ii) BHP's Procurement function has been centralized and subsumed under the Finance and Grants Department to ensure more controlled and cost effective procurement as well as maximize project spending which ultimately drives and determines the available levels of the admin budget.

iii) The value add from our critical business partners is being carefully reviewed and resulted in a reduced insurance premium for FY2016 that generated savings of approximately $20,000 and a new vendor for the provision of fuel for BHP's motor vehicle fleet under terms that will allow for greatly enhanced controls and improved fuelling logistics that will save both time and money.

iv) Recruitment for operational support staff has been frozen under a staff rationalization exercise with the aim of generating savings in payroll.

Human Resources

The Human Resources Department is a central enabler of BHP's business objectives. It currently has five staff members which serve a complement of 314 employees. HR has a critical role in ensuring that BHP's employees are supported in driving key business objectives.

Over the past year, the department has focused on continuous improvement to increase efficiency and accountability, while improving services to employees and streamlining administration.

As BHP continues to integrate continuous improvement into business planning, the human resources department plays a critical role in ensuring that we have a high-performing and engaged workforce equipped to deliver results for the partnership.

Achievements of HR

The HR department made the following studies over the past year;

I) The implementation of the company salary structure to ensure consistency in remuneration and to increase retention rate of the critical positions.

7 Organisational Excellence

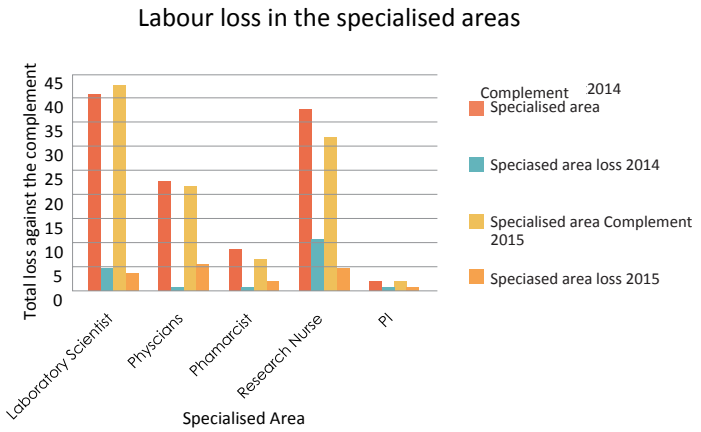
II) The procurement of Orange HRM as an Employee Self Service system which yielded efficiencies in administering vital HR functions and services such as leave application, time sheets and a Performance Management system.

III) The introduction of the training tracker. The office of the Training Coordinator has developed a training tracker and in-house training schedule for coordinators, to create a platform that helps grow staff into leadership roles. In the near future HR aims to add a training records management module in Orange HRM to monitor and manage all training as opposed to the current manual process.

Figure 1. Graph showing capacity building activities

BHP spent significant time on short and long term training of employees to increase productivity and effectiveness. Expected impact includes; Increased productivity, innovation, confidence and quality of work.

Figure 2: Staff retention by speciality



The chart in figure 2 depicts labour trends in specialized areas.

These were due to close-out of projects such as PEPFAR Master Trainer & Mpepu studies which employed specialists. However BHP made a significant effort to absorb the majority of staff into other ongoing projects

Capacity Building and Education Highlights

A key strategic theme and mandate of BHP is to inform, educate, and build research capacity for both researchers and the community. This is attained by growing and mentoring up coming researchers. This is fostered through special skills training at BHP by learning various skills and or carrying out some research projects. A number of staff obtained different trainings and attended both international and national conferences.

Conferences and Trainings

The year in review was successful in applications and attendances at various conferences. Six members of the Research Lab attended at AfriCan Forum 2 that was held from the 16th-18th February 2015 in Johannesburg, South Africa. AfriCan was an African-Canadian partnership that focuses on capacity building in HIV prevention and intervention research.

Key Conferences attended during the year include: CROI 2015 which was held from 23th-26th February 2015 at Seattle, Washington (USA); Keystone Symposium conference themed "HIV Vaccines" held from 22nd-27th March 2015 in Banff, Alberta, Canada; The 15th International Symposium of Viral Hepatitis and Liver diseases in Berlin (Germany) 26-28th June 2015; the International Meeting on Molecular Biology of Hepatitis B Viruses held 4th-8th October 2015 in Bad Nauheim (Germany) and the 7th H3Africa Consortium meeting in Washington DC (USA) from the 11th- 16th October 2015.

A Research Lab intern, Wonderful Choga attended the prestigious Merck Africa Research Summit (MARS). MARS was organized by Merck in collaboration with UNESCO, the Cambridge-Africa Programme at the University of Cambridge, and Universita di Roma, Italy on the 19th and 20th October 2015. The BHP was also represented at the ICASA confrence on the 29th November-4th December 2015 in Harare (Zimbabwe).

Trainings

The beginning of the year was marked with two fellows (Thabo and Prisca), attending Genetic Association Course at the University of Botswana. The course focused on analysis of NGS data and rare variant calling. Wonderful

7 Organisational Excellence (CONT.)

Choga attended Grant Writing and Research Conduct trainings that were held from 12th-13th August 2015 at the University of Botswana. Motswedi attended a 10 day rigorous training in Intermediate Biostatistics where she was taught application of R programming for Statistics from the 19th-28th August 2015 in Durban (South Africa). Prisca attended Proteomics Training Course from 4th-9th October 2015 at J. Craig Venter Institute (Rockville, USA). The training focused on hands on practicals in short-gun proteomics and mass spectrometry.

The BHP Data Management Centre

The BHP Data Management Centre is proudly entering it's 15th year of operation. The department has successfully managed data for numerous trials over the years. For each trial the main deliverable remains unchanged; – a highly available, protocol compliant, fully audit-able research-grade dataset. This position change gained momentum in 2010 with the start of development of electronic research data systems to make data management a fully electronic effort from point-of-care to final analysis. 2015 completed that transition with the closure of the last of the paper-based trials.

The data management center team

The resulting electronic research data management systems are all based on the customizable modules of the in-housed developed "EDC". The "EDC" software modules are the product of the data management and research team's years of experience in collecting, managing and delivering research-grade clinical trial data. All protocols at BHP now use electronic data collection. The development of the "EDC" is a continuous effort by the developers to capture into generalizable software modules the lessons learned from each new research protocol. The "EDC" modules are the data management centre's institutional memory and the building blocks for all deployments. 2015 saw further refinement of important EDC modules in the informed consent process, specimen chain-of-custody, laboratory integration, patient registration, appointment management, data collection schedule management, case report form entry logic and flow, patient contact management, adverse event management, offline data collection for household surveys, field-level data encryption, data audit trails, and data export. The developers create and refine these modules as the most logical and cost-effective approach to research trial data management. Each protocol brings new challenges. Each deployment informs the next and strengthens the groups ability to deliver protocol compliant research-grade data cost-effectively.

Digitising documents from previous paper based clinical trials

As an example, the Botswana Combination Prevention Project (BCPP) presented unique challenges for data management. In particular the DMC had to create electronic data systems to collect complex research-grade longitudinal patient-level data and specimen offline in households in remote villages with little or no Internet connectivity and have that data available to the laboratory and investigators in Gaborone and Boston nightly. For this the team developed secure data synchronization modules for the EDC to enable research assistants to collect complex data asynchronously in households without any data networks or internet. The EDC encryption module was enhanced to ensure the protection of participant data in the event that a collection device was lost or stolen.

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Geo-location and mapping services were developed to guide research assistants to pre-identified households. Comprehensive software change management and version control procedures were implemented to help the developers respond to the needs of a very dynamic protocol and to enable them to confidently deploy software updates remotely without fear of disrupting the remote research team activities.

The IT department played an important role in supporting the data management centre as well as the other departments of BHP. Together with an outside vendor, BHP IT built a research data network that extends to each of the 30 research communities for the BCPP. The network creates a single point of connection for the research team in each village. The IT team provided comprehensive technical support, connection monitoring, inventory management, backup, recovery services and secured data access. The demands of the BCPP forced the IT team to upgrade their skills and make better use of automation, monitoring and virtualization. In 2015 the team rolled out the following;

1) A new HR system;
2) An electronic document management inventory and asset management system;
3) Upgraded the BHP mail systems;
4) Virtualized all critical systems;
5) Upgraded and redesigned the overall BHP wide-area network, improved access for remote users and significantly improved access to online resources.

The Archive department finally put a dent in BHP's paper archive amassed over the last ten years. Approximately 40% of the documents have been digitized into Mayan, the open-source electronic data management system installed for the department by the BHP IT team. A team of seven people scan documents and keyword tag documents into Mayan. Their effort is measured not in pages but in kilograms scanned per day per person. Once documents have been scanned the paper is audited against the corresponding electronic record in Mayan before being shipped to a nearby shredding facility where BHP staff supervise the shredding to make sure all documents, some of which are confidential, are completely destroyed. The result of all this effort is that documents can be accessed by authorized users online and BHP is able to convert filing rooms back to precious laboratory space.

Plans are now underway to secure funding to get each department to scan documents in real time to avoid further build-up of paper-bulk in future.

The IT team having a light moment.

7 Organisational Excellence

Networking, Collaborations and Strategic Partnerships

The establishment and management of strategic partners is critical for an organisation since these partnerships contribute to the success of the organisation. This could be in the form of community engagement with government structures, bilateral, or multilateral partnerships.

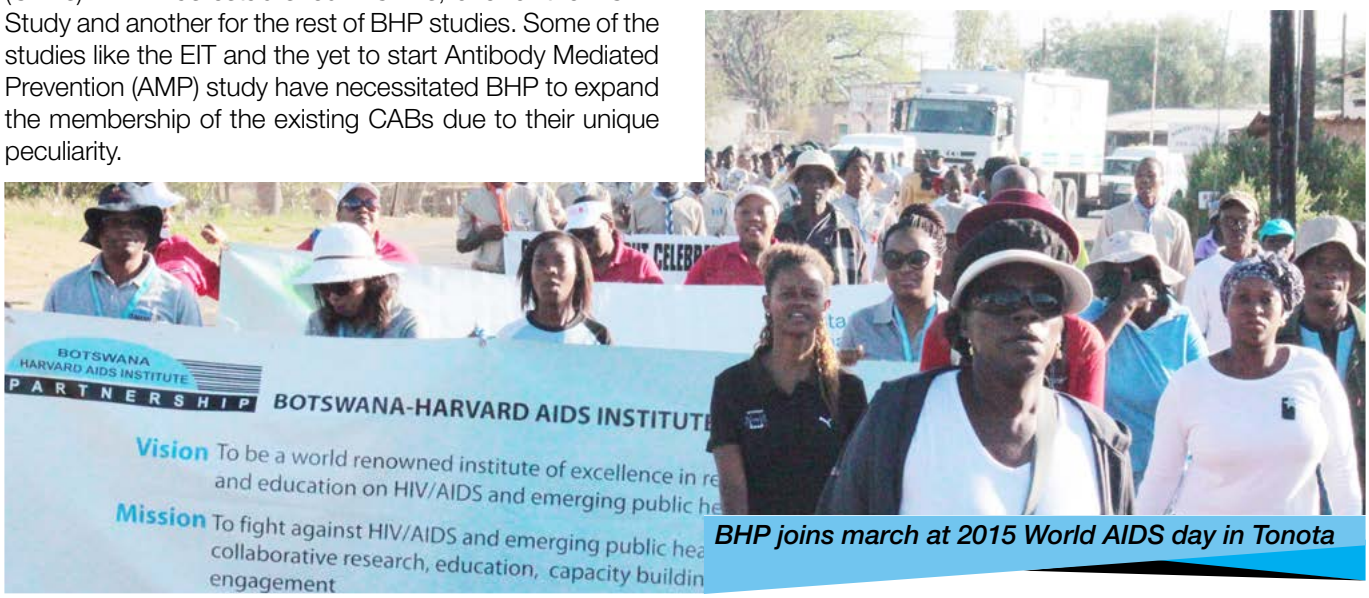
Community Engagement Team with Kgosi Kgari Sechele III of Molepolole

In line with this thinking BHP Community engagement has become an essential component of research involving human beings. In fact, there is a suggestion that community engagement should form part of the criteria to be considered during ethical review of research proposals. Common community engagement activities include those done through Community Advisory Boards (CABs). BHP has established 2 CABs, one for the BCPP Study and another for the rest of BHP studies. Some of the studies like the EIT and the yet to start Antibody Mediated Prevention (AMP) study have necessitated BHP to expand the membership of the existing CABs due to their unique peculiarity.

The BHP community engagement & Francistown team at 2015 World AIDs day in Tonota

During the reporting period of 2014-2015, BHP continued to nurture and grow existing collaborations with existing partners which include MGH, BIDMC, MoH, University of Kwa-zulu Natal for the SANTHE Project, University of Botswana, University of Cincinnati, and Botswana International University of Science and Technology (BIUST) are ongoing (with Masters and PhD projects underway).

One of the highlights of the year was a visit by the Tanzanian ministerial delegation who had come to learn and benchmark work done by BHP. Towards the end of the year BHP joined various stakeholders to attend the annual World AIDS day in Tonota and we set up a stall where people were engaged on different issues relating to both HIV and other public health issues.



BHP joins march at 2015 World AIDS day in Tonota

8 Research Highlights

Research remains the core business for BHP. This consists of laboratory, clinical and community based research. BHP is affiliated to various National Institutes of Health sponsored international networks as a Clinical Trials Unit, and it undertakes country relevant Clinical research. CTU consists of the AIDS Clinical Trials Group (ACTG), International Maternal, Paediatric and Adolescent Clinical Trials (IMPAACT) and HIV Prevention Trials Networks (HPTN). BHP also undertakes Investigator Initiated Protocols. While the initial focus of research was on HIV/AIDS, this has progressively expanded to include interaction between HIV infection and other Non-Communicable diseases like cardiovascular diseases, malignancies, tuberculosis and metabolic diseases.

Developing and mentoring new researchers for both personal career development and for long term sustainability of the organisation is one of the vital components of this program. This is done through on the job lab training, protocol and abstract writing, exposure to national and international conferences either as presenters or participants, and formal postgraduate training.

Network Research Projects

Clinical Trials Unit (CTU)
This remains an anchor grant for BHP. The grant also provides opportunity for local scientists to attend international conferences and annual network meetings where over 10 officers were sponsored to go, and attend other scientific meetings such as CROI. While BHP has enrolled in several protocols during the reporting period, a major constraint has been in the delay in finalizing Institutional Review Board (IRB) approval from the Health Research and Development Committee (HRDC). This has resulted in BHP missing out on being awarded some protocols.

Active protocols from research networks conducted under the CTU included the following;

a) Evaluating Pharmacokinetic Interactions with Vaginal Ring Contraceptives and Antiretroviral Therapy

The primary objective of which is to estimate the effect of ongoing ART containing either once daily ATV/r or EFV, in addition to two or more nucleosides/nucleotides, on the pharmacokinetic (PK) exposure of etonogestrel and ethinyl estradiol in HIV-infected participants at day 21 after placement of the etonogestrel/ethinyl estradiol vaginal ring (NuvaRing).

So far the study has enrolled 2 participants since the study opened in November 2015. There were limited slots to enroll participants by the time our site was approved and hence the limited number of enrolees.

b) Study of MDR TB Cases and Their Household Contacts: Operational Feasibility to Inform PHOENIx Trial Design

The study opened in December 2015. The study's objective is to describe the feasibility of identifying, recruiting, and characterizing adult MDR TB index cases and their adult and child household contacts. Second objective is to describe the prevalence of LTBI, TB disease, and HIV infection among adult and child household contacts. 2 MDR TB cases and 1 household index have been enrolled. Screening is ongoing.

c) Phase III Clinical Trial of Ultra-Short-Course Rifapentine/Isoniazid for the Prevention of Active Tuberculosis in HIV-Infected Individuals with Latent Tuberculosis Infection

The main objective here is to compare the efficacy of a 4-week daily regimen of weight-based RPT/INH to a standard 9-month (36 weeks) daily INH regimen for TB prevention in HIV-infected individuals. The study opened in October 2012. Since opening we enrolled 422 participants. All have finished the study medication and are on follow up. Some have finished the study and have gone off study.

d) A Randomized Trial to Compare An HPV Test-And-Treat Strategy To Cytology-Based Strategy For Prevention of CIN 2+ In HIV-Infected Women

The primary objective in this trial is to evaluate the effectiveness of immediate cryotherapy in HIV-infected women with high risk HPV compared to a cytology-based strategy, which is the standard of care, by comparing cumulative CIN2+ rates. The study was highly successful. Enrollment was fast reaching our target of 60 at each site on time. Most (only 10 remaining) have finished their follow up and are off study.

8 Research Highlights

e) **P1066 - A Phase I/II, Multicenter, Open-Label, Noncomparative Study of the International Maternal, Pediatric, Adolescent AIDS Clinical Trials (IMPAACT) Group to Evaluate the Safety, Tolerability, Pharmacokinetics, and Antiretroviral Activity of Raltegravir (Isentress™, MK-0518) in HIV-1 Infected Children and Adolescents**

The overall objective of this study is to evaluate safety, tolerability and pharmacokinetics of Raltegravir in HIV 1 infected children and adolescents. The project is closed to accrual and only 1 participant is still on follow up.

f) **1077HS - HAART Standard Version of the PROMISE Study: Promoting maternal and Infant Survival everywhere**

The study is designed to determine whether continuation of HAART after delivery or other pregnancy outcome reduces morbidity and mortality compared to discontinuation and re-initiation of HAART according to current standards of care.

The study is closed to accrual and patients, following START study results which showed benefits of lifelong HAART regardless of CD4 level at diagnosis, are being initiated on lifelong treatment.

g) **P1078 - A Phase IV Randomized Double-Blind Placebo-Controlled Trial to Evaluate the Safety of Immediate (Antepartum-Initiated) Versus Deferred (Postpartum-Initiated) Isoniazid Preventive Therapy Among HIV-infected Women in High TB Incidence Settings**

The Primary Objective of this study is to compare overall safety and toxicity of immediate versus deferred INH preventive therapy in HIV-infected pregnant women enrolled at ≥ 14 through ≤ 34 weeks gestation (34 weeks, 6 days). The study has achieved the enrollment target of 120 participants and they are currently at follow up stage.

h) **P1093 - Phase I/II, Multi-Center, Open-Label Pharmacokinetic, Safety, Tolerability and Antiviral Activity of GSK1349572 (Dolutegravir), a Novel Integrase Inhibitor, in Combination Regimens in HIV-1 Infected Infants, Children and Adolescents**

This is a new protocol whose primary objectives are to select a dolutegravir dose for chronic dosing; to determine the safety and tolerability of the dose, to evaluate the steady-state pharmacokinetics of dolutegravir in combination with other antiretrovirals and to determine the dose of dolutegravir that achieves a targeted AUC24 (primary PK endpoint) and C24h (secondary PK endpoint) in children and adolescents. Regulatory approvals have been received and project is to start in the 1st quarter of 2016.

Overall the projects performed very well. They all reached their planned targets with regards to maintaining high retention level of participants (94% for ACTG and 96% for IMPAACT), maintaining high standards of quality resulting in having clean reports from PPD and/or Westat Study monitors, (98.5% for ACTG and 99.5% for IMPAACT). HPTN had one study, HPTN 052, wind down during 2015, but also competed and got given opportunity to be a site for HPTN 081. Enrolment will be starting in 2016. As part of capacity building, the local co-investigators have submitted an abstract and request to the HPTN leadership to do retrospective data analysis of the HPTN 052 data.

Investigator Initiated Projects

a) **TSHIPIDI STUDY: Effects of HIV and ARV Exposure on Child Health and Neuro development, Botswana**

The study was opened to enrollment on 31 May 2010 and since then until July 2012 we enrolled 949 mothers (474 mothers HIV-infected & 475 mothers HIV-uninfected) and 910 infants. Enrollment was completed on 31 July 2012. Last infant born in December 2012 and Infants were followed up until age 2.

Data analysis on this study is on-going. We had an abstract presented at Botswana International Nurses Conference in November 2015 and a second abstract has been accepted for presentation at CROI 2016. One manuscript on unintended pregnancies, contraceptive use and future child bearing desires among HIV-infected and HIV-uninfected women in Botswana was accepted and is under publication in BioMed Central Public Health Journal (Author: Ms G. Mayondi). Another manuscript on haematological reference ranges nearly complete (Author: Mr. S. Moyo).

8 Research Highlights

b) Determinants of Malnutrition Study

This cross-sectional observational study was funded by the Centers of Disease Control and Prevention and carried out in 5 health districts in Botswana with medium to high reported rates of malnutrition in children under the age of 5. All data was collected on BHPs open source electronic data capture (EDC) system. A formal report of the study's findings was accepted by Botswana's Ministry of Health (MoH) in January 2015. As a result of study findings, policy changes have been made including more frequent monitoring of height for children under the age of two attending Child Welfare clinics, and identification of infants/children at risk for malnutrition prior to actually meeting malnutrition criteria with planned interventions to prevent rather than manage malnutrition.

The Divisions of Nutrition and Food Control and Sexual and Reproductive Health are working to develop programmatic support to ensure that pregnant women are gaining weight appropriately during pregnancy, as low birth weight was a significant risk factor for a finding of stunting, wasting or underweight. The study also highlighted the existence of overweight and obesity among children under the age of five. The Division of Nutrition and Food Control is working to develop programming to address childhood over nutrition, as result of the study.

In November 2015, UNICEF sponsored a regional meeting entitled "Nutrition Partnerships and Investments: An Imperative towards Sustainable Development". In the program, the background section cited findings from the Determinants of Malnutrition study carried out by Botswana Harvard Partnership, and Dr. Kate Powis, the study's Principal Investigator, was an invited speaker, presenting the study's key findings to representatives from Botswana, Namibia, Zimbabwe and Swaziland. Two different publications from this study are currently submitted to peer-reviewed journals.

C) Longitudinal Analysis of Changes in Infant Gut Microbiome and Immune System Functioning

Approximately 28% of infants born in Botswana are born HIV-exposed but remain uninfected. Despite escaping HIV infection, these HIV-exposed infants face 2- to 4-fold higher mortality rates compared with infants born to HIV-uninfected women. Death is predominantly due to infectious causes, specifically respiratory illnesses and diarrheal disease. An infant's gut microbiome trains their nascent immune system and it is biologically plausible that, since an infant's initial inoculation of gut microbiome is acquired from their mother, HIV-exposed uninfected infants acquire an aberrant gut microbiome from their immunocompromised mother. Dr. Kate Powis received an R21 grant funding from the National Institute of Allergy and Infectious Diseases to study the evolution of the gut microbiome of breastfed infants and correlate gut microbiome profiles with markers of immune function. This two-year study opened for accrual in Gaborone in December 2015 and will enroll 48 HIV-infected pregnant women and their uninfected infants, as well as 44 HIV-uninfected pregnant women and their infants. All data for the study is captured electronically on BHP's open source Electronic Data Capture System (EDC).

d) Botswana Prospective Cancer Cohort (BPCC)

This study has three components; HIV and Malignancy in Botswana, an observational study of the incidence, toxicity of concurrent treatment, and clinical outcomes. The primary aims are to evaluate the important risk factors for cancer in Botswana including HIV and to describe the response to treatment for patients without HIV, with HIV but not yet on HAART, and those with HIV and on HAART. HPV AND HIV associated head and neck squamous cell carcinoma in Botswana, the objective of the study is to determine the proportion of squamous cell carcinoma of the head and neck that is associated with HPV infection, the causative HPV types and the role of HIV infection in the risk of these cancers

e) Advancing the diagnosis and the treatment of lymphomas in Botswana:

The study aims to Clarify the precise histological diagnoses of identified lymphomas by WHO criteria 2. To expand local capacity for diagnosing lymphomas. Currently 1750 patients have been enrolled and the recent establishment of Francistown as a research site should enhance enrolments from the north of the country.

f) Potlako: Improving access to timely oncology care in Botswana

This study involves the implementation and evaluation of the impact of multi-component programmatic interventions to improve timely access to oncology care among individuals at public health facilities in Botswana. Interventions include establishing care navigator/ coordinator nurse role, deploying an SMS platform for coordination and communication such as through the use of automated appointment reminders (to patients) and results delivery (to clinicians), transport support for vulnerable patients, and clinician training and long-

8 Research Highlights

term mentorship on triage and referral of patients with suspected cancer. Primary endpoints for impact assessment are time to cancer treatment, and stage at cancer diagnosis.

The study has been approved by the IRBs and consultations with stakeholders and community leadership is ongoing. Training will start soon with the aim of initiating the study in March 2016.

g) Kgothatso: Characterizing barriers to diagnosis and treatment and developing early detection strategies for male ano-genital HPV-associated malignancies in Botswana.

This is a three-pronged study that aims to

a) characterize incident anogenital cancers in Botswana, including HPV serotyping,

b) define barriers to men accessing services for diagnosis and treatment of penile and anal cancer, through case-control design employing semi-structured questionnaires, and

c) development of training program to facilitate appropriate evaluation, triage and referral of male patients with anogenital complaints incorporating findings from (b).

This study is being conducted in partnership with BUP/UPenn and has received NIH funding (CFAR administrative supplement)

The protocol is under review at the IRBs and the anticipated start date is April 2016

h) HIV-associated Cardiovascular Disease Studies

Three pilot studies on HIV and Cardio Vascular Risk conducted by Dr Mosepele Mosepele, completed enrolment. These were:

a) Pilot study on risk of atherosclerosis and immune activation among HIV-infected patients
b) Pilot study on association between gut microbiome and atherosclerosis / immune activation among HIV-infected patients
c) Pilot study on association between atherosclerosis and cognitive function among HIV-infected patients. Analysis is ongoing with expected subsequent manuscripts.

A workshop on "Approach to CVD risk assessment & management among HIV-infected patients" was held on the 30th April 2015 with Dr Linda Hemphill from the Heart Center, Massachusetts General Hospital Boston as expert guest speaker.

i) A Randomized Study of Cotrimoxazole Prophylaxis and Longer Breastfeeding Duration to Improve Survival among HIV-Exposed Infants in Botswana (Mpepu Study)

This study was prematurely terminated by the DSMB in April 2015 after data showed that there was no difference in survival between infants on cotrimoxazole prophlaxis and those not. Close out has successfully been completed and data that had already been collected is still being analysed.

j) BHP Early Infant Treatment Study (EIT): A Clinical Treatment Trial of HIV+ Infants in Botswana

The overall objective of this study is to determine whether very early antiretroviral treatment (ART) initiation in HIV-infected infants limits the seeding of viral reservoirs and maintains immune responses such that a prolonged period off ART is possible.

This is a study intended to push the frontier of HIV management towards cure. It was designed to enrol a total of 50 HIV infected who are to be followed for a duration of 96 weeks to 192 Weeks. Recruitment is on-going in Gaborone and Francistown areas since the last quarter of 2015. Due to Botswana's very successful PMTCT program, the number of infants who are HIV infected is very small and this is resulting in very slow enrolments. It is hoped that with recruitment and deployment of a full time recruiter at Selibi Phikwe, one of the towns with highest HIV prevalence, enrolment rates may increase. So far only 11 HIV infected infants have been enrolled into the study.

k) NOVEL STRATEGY FOR HIV DRUG RESISTANCE MONITORING IN DEVELOPING COUNTRIES

The purpose of the research study is to study the form of HIV in Botswana that is present in newly diagnosed individuals including pregnant women, as well as to study the form of HIV that is resistant to current HIV medications. The target was to enroll 600 HIV positive pregnant mothers. The study started in 2012 and currently only 378 participants have been enrolled. Enrollment has been delayed at times mainly due to the unavailability of HIV testing kits at public health facilities where recruitment takes place. The study will be closing down early 2016.

8 Research Highlights

QUALITY MANAGEMENT AND REGULATORY SERVICES

The BHP regulatory office continues to anchor the implementation of human subjects research according to acceptable local and international compliance guidelines and standards. In order to achieve and maintain the desired standards the organisation focused on capacity building initiatives for BHP. This included training of 16 people on Responsible Conduct of Research, bringing the total number trained since the inception of this course in 2012 to 84. It is in BHP's plans to develop research auditing teams to strengthen quality of research implementations as well as credibility of data that is being produced at BHP. In the long run it is envisaged that such a team could be engaged in auditing and monitoring studies conducted by other role players in the country.

Clinical Trials Laboratory

The Clinical Trials Laboratory of BHHRL continued to provide the needed coverage for all the clinical trials at BHP providing requisite data, from processing labs, cell separations and cryopreservation, diagnostic, safety and monitoring, as well as specialized research assays, to providing high quality testing for the key assays for enrollment and management of study patients. Consistent with our mandate, to implement and sustain a quality management system, BHHRL was audited by SANAS and maintained its ISO 17025 Accreditation Status. BHHRL also conducted a management review to assess adequacy and effectiveness of quality management system.

BHP research laboratory team

The Laboratory's continued competence to conduct the assays for the studies is reviewed monthly by US National Institutes (NIH) of health sponsored Patient Safety Monitoring in International Laboratories (pSMILE). Over 15 trainings were conducted on the quality management system, GCLP, Safety for lab and clinic staff, technical assessing techniques, basic first aid/life support, fire marshal and several technical assay training.

BHP scientist hard at work!

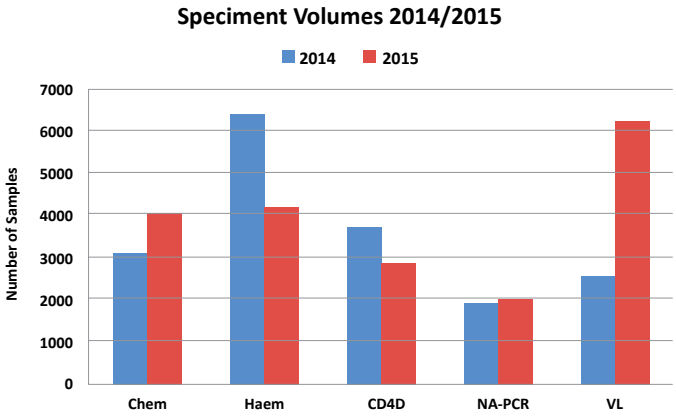
Clinical Trials Laboratory Support

Laboratory activities were expanded to areas outside Gaborone to support Clinical Trials Activities. BHP is working with a network of Ministry of Health Regional laboratories to support studies. The Establishment of laboratory operations in Northern and Central Regions presented a number of unique opportunities for BHP research and strategic agenda, and also some unique requirements/challenges for coordination, administrative, physical space as well as technical support structures. BHP opened laboratory operations with a base in the Nyangagbwe Hospital HIV Reference Laboratory (NHHRL), and within the Nyangagbwe Hospital Reference Laboratory (NHRL). NHHRL conducts CD4, Viral Load and Early Infant Diagnosis (DNA PCR). The hospital laboratory does a wide range of clinical tests including haematology, clinical chemistry, serology, TB microscopy and Cytology/ Histology services. Both laboratories have been accredited to ISO 15189 international standards. BHP collaborated with the NHHRL/NHRL to enhance the GCLP requirements obtain DAIDS approval for clinical trials.

8 Research Highlights

Clinical Assays and Workload

The Clinical Laboratory: Processing and Accessioning, Inventory and Archiving; Clinical Chemistry, Haematology, CD4, Viral load, Diagnostic DNA PCR, HPV PCR, Chlamydia and Gonorrhea, HIV Drug Resistance; Serological Assays including HIV ELISA, Hepatitis B profiles, Hepatitis C Antibody, Syphilis RPR and TPHA, HIV-1 Western Blots, Incidence Assays [Limiting Antigen, Avidity, Bio-rad Avidity and BED], Quantiferon TB in-Tube Assay (QGIT), Cepheid Point of Care Viral load and Gene Expert TB. Several research assays in-house or through referral laboratories are available including TB (AFB, Molecular, culture and Drug Sensitivity), Cytology/Histology, and inflammatory cytokines. Although sample volumes were mostly stable in 2015, the nature and type of visits were increasing in processing intensity and complexity, for instance pharmacokinetics sampling, rapid turnaround DNA PCR.



Specimen Management and Inventory

The specimen management continues to provide significant contribution to the success of studies and the scientific agenda for BHP by storing, with high quality, specimens crucial for answering current and future research questions. A number of Masters and PhDs students, University of Botswana Interns, visiting Fellows and Scholars have benefited from well-archived specimens. The lab currently has stored over 1.3 million specimens. The demand for maintenance of the infrastructure and data support is growing. Currently the specimen management is supported by a partial FTE of a data manager and lab assistants.

Laboratory specimen freezers

Laboratory Research

The research lab is hub for basic science research training in HIV and related public health issues. The Research Lab has a vibrant team of research associates, research fellows, interns and graduate and undergraduate students, each working on individual research projects. 2015 was particularly one of the successful years in the research lab with a number of international presentations and manuscripts/ abstracts writing by the team. There were 4 PhDs, 3 Masters/MPhil, 4 Research Fellows, and 4 Interns. The research lab hosted 3 undergraduate students from Harvard University and Smith College, 2 international scholars from the University of Cincinati, 1 Medical Student from UCLA and Post-Doc. Collaborations with other academic institutions continued to grow locally and internationally.

One of the major highlights of 2015 was the presentation of our research in regional and international scientific conferences, as well as awards presented to some BHP stuff. These included young investigator scholarship awards and prizes in international forums, and a number of resulting publications.

8 Research Highlights (CONT.)

Below is a description of research Fellows and selected individual projects and internships.

Research fellows, students and interns 2015

Sikhulile Moyo is a PhD student at University of Stellenbosch (South Africa). His main interests are viral phylogenetics, evolutionary bioinformatics and biostatistics. He currently works on a project aiming at using phylogeny and viral diversity to characterize early founder viruses with complementary application of serological assays for detecting HIV recency. In this project HIV recency assays are used to select samples for sequencing in addition to unique sample sets of seroconverters from previous studies. The project explores the novel application of viral genomic variation and coalescence models to determine recency of infection. Moyo is expected to complete his studies during the early part of 2016. He has published some manuscripts towards his PhD and contributes towards design, implementation and analysis of on-going BHP studies.

Terence Mohammed is a research fellow and an MPhil student at the University of Botswana. He is currently compiling his MPhil thesis entitled "Molecular characterization of HIV-1c gp120 in recently and chronically infected individuals in Botswana". This project involves sequencing of the env gp120 gene with ABI 3130XL sequencer; bioinformatics and phylogenetics analysis of the sequences to understand the characteristics of the envelope which is a promising candidate in vaccine and therapeutics development. Terence Mohammed is expected to complete his studies in 2016.

Mompati Mogwele is a research fellow working on a project titled "HIV drug resistance in newly diagnosed HIV-infected infants" in which he uses Sanger sequencing to genotype the HIV strains then apply sequence analysis skills and phylogenetics to HIV sequences for inference of drug resistance.

Kerapetse Prisca Thami is a research fellow, bioinformatician, currently performing statistical analyses for on-going Research Lab projects. She also performs projects in which she investigates single nucleotide polymorphisms in the human genome and determines their effect on disease susceptibility and differential antiretroviral drug metabolism using real-time Polymerase Chain Reaction (PCR) and statistical analysis.

Motswedi Anderson is a research fellow and a student at the University of Botswana pursuing an MPhil. She works on a project titled "Prevalence and Molecular characterization of Hepatitis B virus in HIV infected individuals in Botswana" as part of her MPhil/PhD requirements. This project involves immunological and molecular characterization of the HBV in patients treated with Tenofovir. This project is almost near completion and the first findings have been published in a BMC journal article in August 2015. There are plans to upgrade Ms Anderson to PhD at the University of Botswana.

Dorcus Maruapula is a research fellow and a student at the University of Botswana; she enrolled at the UB for an MPhil program in March 2015. Dorcus is working on a project that determines prevalence of HIV drug-resistance profiles of ante-natal care (ANC) samples using a novel derivative of Allele Specific PCR called PANDAA. The findings of this project will be wrapped up in her MPhil thesis.

Thato Iketleng is a PhD student at University of Kwa-Zulu Natal (South Africa). Mr Iketleng works on a project entitled "Using Genomics in a demographically and clinically well-defined cohort to understand M. tuberculosis transmission dynamics and drug resistance in a hyper-endemic setting in rural KwaZulu-Natal".

Thabo Diphoko is also a research fellow and a PhD student at the University of Botswana. Thabo's PhD project is entitled "Investigating low-level drug resistance in HIV-1 c and the impact of the mutations on treatment outcomes in the population of Botswana". This project drug resistance mutations shall be inferred through next generational sequencing (NGS) with Roche 454 GS Junior sequencer. This project is the first NGS platform in Botswana to be applied in analysis of drug resistance.

Philimon Sebogodi and Baitshepi Mokaleng, have each successfully completed 3 months training in Advanced Molecular Virology at Harvard School of Public Health, Harvard, Boston. The fellows have since returned to the Research Lab to apply the new skills obtained on Long Range HIV Genotyping for Drug Resistance to on-going researches.

Wonderful Choga is a research intern and a student at the National University of Science and Technology (NUST) (Zimbabwe). He works on a project entitled "Prevalence and Molecular characterization of Hepatitis B virus in blood donors in Botswana". Mr Choga will complete his BSc in 2016.

8 Research Highlights (CONT.)

Ms Kenanao Kotokwe is a research intern working on characterization of early infection of HIV using serological and genotyping assays.

Ms Boitumelo Seraise is a research intern working on HIV drug resistance and the newly acquired Canadian Vaccine.

Natasha O. Moraka, is a recent graduate of the University of Botswana working on HPV and HIV-associated Head and Neck Squamous Cell Carcinoma in Botswana, and Characterizing congenital transmission of CMV from mothers to exposed infants.

Some of the fellows/students in the research Lab

8 Research Highlights

Clinical Trials

BHP continues to succeed in attracting funding for clinical trials protocols for both network trials or investigator initiated projects. The organisation has also increased the number of local Principal Investigators (PIs) who are submitting their own protocols and applying for funding. These achievements address one of the main goals of BHP which is to mentor and grow a pool of local investigators who would ensure long term credibility and sustainability of the organisation.

Community Research: Botswana Combination Prevention Project (BCPP) AKA Ya Tsie Study

The BCPP project is a study conducted collaboratively by the Ministry of Health (MoH), Centers for Disease Control and Prevention (CDC) and the Botswana Harvard Partnership (BHP). It started in the last quarter of 2013 and it is envisaged that it will be completed in 2018. This is an HIV prevention study with overall objective of determining whether implementation of an enhanced combination prevention package can significantly reduce population-level, cumulative HIV incidence in 16-64 year old residents in Botswana over a period of 36 months. BHP is responsible for evaluating the effects of the interventions through following a sample of about 20% of residents in 30 communities spread over different geographic regions of Botswana.

BCPP is the largest community based study ever undertaken by BHP and thus came with opportunities and challenges never experienced before by the organization. These included logistical challenges of recruiting and retaining a large (about 60) mobile research team, ensuring effective transportation system for moving field teams from one community to the other every 3 to 4 weeks, moving supplies and specimen transportation between the headquarters and the teams at the 30 research communities. Other Challenges Include ensuring functioning data collection and communication systems that would provide real time data flow to the headquarters as well as to the other collaborators, challenges of sensitizing and mobilizing the communities, often very different in culture and tradition, to have the buy-in and take part in the project in large numbers, and to keep communication channels open between all moving parts of the study both within BHP including with the Harvard T. H Chan Public school of health, CDC and the funders.

EQUIPPED FOR SUCCESS: Mobile office, GPS, Consent form, Electronic Data Capture System, HIV testing kits, CD4 Point of Care machine, Determined and Experienced Research Assistant

Research assistant doing home based HIV testing and Counseling.

Foot soldiers team behind success of BCPP. The fight against HIV is on!

8 Research Highlights

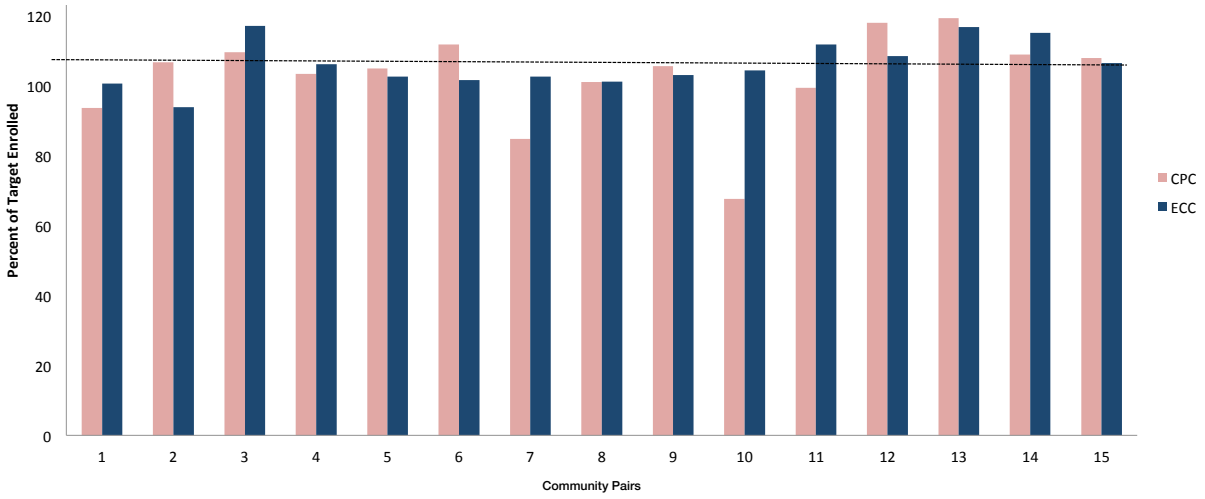
Undertaking community research and observing cultural sensitivities, BCPP men in the kgotla

Since the study started in 2013 through 2014 there were several challenges and progress of the study was very slow. However, some lessons were learned and systems accordingly improved.

2015 became a year when BCPP teams excelled in all they did. The whole year the team stuck to the agreed study time-lines although occasionally teams had to be split to ensure that there is no delay in getting to the next community. The teams rearranged the sequence of study communities to be visited if for whatever reason it was found that the scheduled time to enter the community was not ideal because at that time a significant number of residents were going to be outside the community, and where enrollments proved to be a challenge, innovative ways were devised to improve recruitment of participants.

Despite all these challenges, BCPP Ya Tsie Team reached a milestone of completing the first round of the study, that is, conducting field work in all the 30 communities by the end of November, 2015. The team did so with very high success rates of over 90% in all the 30 communities. This success reflects on the organizational skills, study team's determination and focus, teamwork, and having a purpose. BHP has grown in its capabilities of doing community based studies with quality and excellence.

Percent of Actual BHS Baseline Enrollment to target by Pair and Intervention



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Notes

"Towards ending the AIDS epidemic by 2030"

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