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We congratulate the Unit on all the achievements registered during this reporting period. The Unit has continued to make significant contributions towards its mission in research, capacity development and in the translation of research findings into policy and practice. The Unit continues to be an important partner whose achievements contribute to UVRI’s overall achievements as well.

The Unit’s work in the areas of HIV such as providing data on the epidemic and participation in research into new prevention technology are well known. Other work including understanding social behavioral risk factors in special groups and approaches to intervene, immunological and virological studies relevant for HIV vaccine discovery and improved therapeutic interventions are all making a significant impact.

We welcome the expansion into other emerging/re-emerging, endemic and neglected diseases, adding to the previous work in co-infections and TB that generated important data. This expansion will tap into the comparative advantage of the location in Uganda and at UVRI, a region known to have many microorganisms including epidemics and outbreaks of viral infections for which UVRI is an important research global player.

We also applaud the work in non-communicable diseases, already recognised to increasingly becoming a major health threat. It is our hope the Unit will explore more ways to collaborate with the wider UVRI institute in achieving its mission.

The Unit’s role in infrastructure and human capacity development is acknowledged. During this reporting period as an example the MRC has supported us to construct a UVRI canteen, co-funded with IAVI. They also supported the improvements of our roads and car parks. The Unit is an active player in the MUII, THRiVE and the EACCR-2, activities that are contributing to human capacity development and strengthening our links with Makerere University and other institutions within the region and beyond. There are many other areas where the institute is benefiting from the partnership with the Unit; we hope the Unit also feels that UVRI is a key partner for its successful functioning.

The Unit has undergone another major change as it transfers to the LSHTM. We and the Government of Uganda welcome and endorse these changes, which we hope will strengthen further and expand the activities of the Unit. LSHTM is an international teaching institution with whom we have had a long standing collaboration.

We thank MRC-UK for the continued funding, now running for another 5 years up to 2022, other funders and collaborators are also acknowledged and thanked. We wish to thank all the Unit staff for the good work done and wish them success as they embark on this new funding cycle and the transfer to the LSHTM.

Finally, during this reporting period, Dr Edward Katongole Mbidde retired as Director of UVRI, having served in this capacity for nearly ten years. I wish to extend my sincere thanks to the MRC/UVRI and MRC-UK for the support given to me over this period, without this support we may not have attained all the successes we witnessed.

In 2016, I handed over the leadership of this institution to Prof Pontiano Kaleebu. It is for this reason that we both give this foreword and wish the Unit success for the future.
It is nearly 30 years since the MRC/UVRI was established, to improve the understanding and control of the HIV epidemic in Uganda and globally, following a request from the Uganda Government to the United Kingdom (UK) Government. We completed our 4th quinquennium (QQ) March 2017 where we addressed emerging challenges arising from the changing HIV epidemic and associated diseases in Uganda and elsewhere.

After wide consultations, in the current QQ, which started April 2017, we have broadened our work beyond HIV to include other infections, neglected, endemic, emerging and re-emerging infections and expanded our work in non-communicable diseases (NCDs).

As a result, we have a new mission and vision and we have introduced a thematic approach to our research as explained below under Unit Themes. We have created new research Programmes and the science will be led and delivered through these various programmes. Research Platforms have also been created with the aim of providing an efficient and integrated support structure in order to maximise output. We also have various Research Support Services described later in this report.

**Key achievements in the past three years**

In this report, we provide the progress made over the last three years by the different Programmes, Platforms and Research support services.

**Important Research Findings**

We published results showing that in the rural population of Kyamulibwa there has been substantial improvements in life expectancy in the last 20 years, largely driven by reductions in HIV related mortality. However, among the approximately 90% of the population without HIV, there have been no substantive improvements in life expectancy since 1989. These results have implications for Uganda’s track to the 2040 vision, aimed at life expectancy of 60 years by then. We also showed that the increasing prevalence and reducing incidence may be due to ART uptake and a positive net HIV prevalence among in/out migrants.

We continue to find that HIV infection is high among the newly recruited women in GHWP (since 2013): prevalence (34%) and incidence (3.1/100 PYAR) by August 2017.

Despite the prevention and HIV counselling provided our more recent data indicates the high HIV in the fishing communities continues. The IAVI supported Open B protocol that enrolls high risk HIV negative people in the fisherfolk communities in Masaka and follows them quarterly, has shown that over a cumulative follow up period of 1691 person-years, we see HIV incidence of 3.73 per 100 person-years (95% CI 2.90 – 4.70). The HIV incidence rates by gender are 2.4 [1.7 - 3.4] and 7.6 [5.2 - 10.6] for males and females respectively. In similar fishing communities in Wakiso district, 64% of new infections can be attributed to drinking alcohol. Our studies in the Uganda Police Force found that though members of this group were willing to participate in research, the population studies may not be appropriate for HIV prevention activities due to the low incidence detected.

We have continued to participate in studies aimed at the discovery of New HIV Prevention Technologies (NPT). We were part of the large multi-centre study that found the Dapivirine vaginal ring to be safe and effective in reducing HIV infections by 31% among women at risk of HIV acquisition, the trial at our
site was funded by IPM. The ring was less effective with younger women. Currently we are participating in a follow-on, Open-Label Extension (OLE) trial to assess continued safety of and adherence to the Dapivirine (25 mg) vaginal ring in healthy, HIV-negative women, a phase Illb study.

During this reporting period, we have led and completed a phase I double blind placebo-controlled clinical trial to evaluate the safety and immunogenicity of the combination of DNA-HIV-PT123 and AIDSVAX®B/E in HIV-1-uninfected adult participants with or without underlying Schistosoma mansoni infection (IDEA EV06). The trial was sponsored by the EuroVacc Foundation and was conducted at both MRC/UVRI, Masaka and UVRI-IAVI centre, Entebbe among healthy adults aged 18-45 years. The vaccine regimen was well tolerated and induced strong gp120, gp140 and V1/V2 region-focused binding IgG and neutralising antibodies against tier 1 isolates. A follow on study EV07 about to end, is an open label phase I clinical trial to evaluate the effect of late boost on HIV-uninfected vaccinees from EV06 trial.

We also performed an MRC/DFID Global Trials funded feasibility study of HIV combination (HIVCOMB) intervention effectiveness in fishing communities in Uganda. While the intervention was successful with those who engaged with the trial, recruitment was challenging and follow-up poor, because of mobility among the target population.

In the area of treatment, we were part of the large USA NIH funded trial, The START trial where the main study showed that early ART, reduces the risk of serious AIDS-related illness, serious non-AIDS-related illness and death by 53% compared to deferring ART. We also completed the COSTOP study that indicated that cotrimoxazole can be safely discontinued among Ugandan adults on ART who have achieved sustained immune restoration as measured by a confirmed increase in CD4 cell count to 250 or more cells/ul. The study showed that compared to placebo, adults on ART who continued primary prophylaxis with cotrimoxazole had a significantly reduced risk of severe bacterial infections mainly bacterial pneumonias; episodes of symptomatic malaria and of hospitalization.

The Clinical Outcomes of Long-Term ART (CoLTART) in an African Cohort provided us a good platform to investigate the complications of long-term ART use in Uganda. For example, we found no differences in renal function between patients on Tenofovir and Non-Tenofovir containing ART regimens, this is reassuring, meaning that Tenofovir based first line ART can safely be initiated even in settings without routine renal function monitoring.

A study looking at switching at low HIV-1 RNA into fixed dose combinations, the (SALIF) Trial which we were part of, demonstrated non inferiority, in terms of virological suppression, of a fixed dose combination (FDC) of Tenofovir/Emtricitabine/Rilpivirine (TDF/FTC/RPV) and Tenofovir/Emtricitabine/Efavirenz (TDF/FTC/EFV) and with a comparable tolerability profile.

We conducted an open-label cluster randomised controlled trial to evaluate the effectiveness of follow-up counselling after Home Based HIV Counselling and Testing (HBHCT) on linkage to HIV care in south western (SW) Uganda. We found that follow-up counselling improved linkage to care, an important approach towards test and treat.

Our mental health research among HIV infected children and adolescents (the CHAKA study) found that the prevalence of emotional and behavioural problems was 31.6% and that of Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM -5) psychiatric disorders was 6.9% was 6.9%. The most prevalent emotional disorder category was anxiety problems (21.2%) while the most prevalent behavioural disorder category was attention deficit hyperactivity disorder (ADHD) related problems (6.1%). We conclude that, children and adolescents with HIV have a significant burden of emotional and behavioural problems including psychiatric disorders with considerable psychiatric comorbidity.
Among women who engage in commercial sex, we have examined factors associated with prompt ART or Test and Treat. Sex as a main job and young age for example were associated with lower odds of prompt ART.

The challenges faced by children, adolescents and adults adhering to ART long term have been highlighted in our social science research. Young people may not only experience the taking of daily pills as a burden, but also wrestle with managing life with HIV as they begin sexual relationships. Experimentation with missing doses to have a rest from pills, or to hide their status in a new relationship, can jeopardise long-term health. However, disclosing adherence challenges to carers and clinic staff can be difficult, particularly when the language of ‘treatment failure’ instils in young people a sense of personal failure and hopelessness particularly when ‘going on to second line drugs’ is couched as a last chance. Young people and adults need time to come to terms with life on ART, responses to questions in an environment where they do not feel judged and care that is responsive to changing emotional and physical needs.

Our work with key populations, such as female sex workers (FSWs) and people working in the fishing industry (or engaged in activities that support fishing), shows that perception of risk of HIV infection is often relationship and context specific, with women and men being less likely to use condoms with partners they regularly have sex with, than casual partners. Visual signs of ‘good health’ continue to be used to judge HIV-infection risk in a new partner with high alcohol consumption often lowering sexual inhibitions. Research with older people (50 years and older) living with HIV shows the barriers they can face accessing treatment, for example because of the stigma of being seen in a clinic or the challenge of travelling for care. Co-morbidities add to the challenges, although, ironically, older people accessing HIV-care may be more likely to receive support for hypertension and other conditions than an older people who are not living with HIV because of the provision of HIV services.

We show that when perform near full length sequencing of HIV (at least 5kb) approximately 50% of the HIV strains in Uganda are unique recombinants and recombination appears to be random. We provided data on the high rates of K65R and TAMs after 12 months on treatment in Ugandan patients on Tenofovir (TDF), mutations that can compromise first line regimens. A follow up study under the TenoRes Study Group for which we were part, looking at global epidemiology of drug resistance recorded drug resistance in a high proportion of patients after virological failure on a tenofovir-containing first-line regimen across low-income and middle-income regions. Effective prevention and surveillance of drug resistance is therefore crucial in our setting.

We have furthermore shown that pre-treatment drug resistance is very high in Uganda exceeding the 10% threshold NNRTI resistance set by WHO for changing first-line ART. This has led to the planned change of first line regimens to include dolutegravir an integrase inhibitor. We also showed high rates of pre-treatment NNRTI resistance in children under prevention of mother to child transmission (PMTCT) before introduction of Option B+, this reinforces the urgent need to overcome barriers to scaling up paediatric protease inhibitor-based regimens in sub-Saharan Africa and underscore the need to accelerate the study and approval of integrase inhibitors for use in young children.

By combining phylogenetic approaches with social-epidemiological studies, we demonstrated in the fishing communities that a large proportion of HIV sexual transmissions occur within households and within communities even in this key mobile population. In a more recent analysis we further show that most transmissions in the fishing communities are more recent and significantly more infections come from the surrounding general population to the FF than the other way. It means, when infections are introduced into these communities, transmissions occur at community level. Interventions therefore based on test and treat need to target both the FF communities and the surrounding general population.
The HIV superinfection (SI) studies indicate that SI can occur in the presence of neutralizing antibodies. However, in one of the only two studies so far, looking at genetically confirmed linked heterosexual HIV SI, we reported presence of moderately potent and broad anti-HIV NAb response prior to superinfection but not NAb activity against the superinfecting strain. The implications for vaccine design is the requirement to induce highly potent and broad Nab.

Our earlier studies indicated that treating mothers for worms during pregnancy resulted in an increased incidence of infantile eczema. We were concerned that the increased rates of eczema in infancy might translate to increased rates of asthma at school age. However, follow up of the cohort found that rates of most allergy-related conditions declined with age and cases of asthma were very few. The “hygiene hypothesis” implies that this decline in allergy-related conditions with age may be due to cumulative infection exposure – a hypothesis we plan to address in further analyses. Urticaria (a skin rash sometimes called “nettle rash” or, in Luganda, “ebilogologo”) followed a different pattern – a progressive increase in reported prevalence with age. This may reflect the urticarial responses directly induced by helminth infection.

Chronic helminth infections induce T-helper (Th2) and regulatory immune responses, and may interfere with the development of Th1 responses required to control many viral or bacterial infectious diseases. It has long been proposed that helminth co-infection might increase susceptibility to HIV infection. However, in our studies, we found no evidence that S. mansoni co-infection increased susceptibility to HIV or impaired the innate immune response among recently HIV-infected people. By contrast, for established infections, we found a benefit of hookworm treatment for HIV replication among EMaBS mothers. Also, we described associations between maternal hookworm and childhood malaria susceptibility and found a positive association between helminths (or malaria) and Kaposi’s Sarcoma Herpes Virus (KSHV). Together, these findings suggest that chronic helminth co-infection may impact little upon acquisition of new infections, but be detrimental to control of established infections.

As for susceptibility to infections, there is long-standing concern that helminth infection may impair the response to unrelated vaccines. In adolescents, we investigated effects of schistosomiasis on responses to the candidate booster TB vaccine, MVA85A: we found no adverse effect on the interferon (IFN)-γ response. However levels of Antigen 85-specific IgG4 were elevated among the schistosome infected children prior to the MVA85A booster immunisation – suggesting a schistosomiasis-associated bias in the antibody response to prior mycobacterial exposure, unaltered by the additional vaccination.

Furthermore, in a phase I double blind placebo-controlled clinical trial to evaluate the safety and immunogenicity of the combination of DNA-HIV-PT123 and AIDSVAX®B/E in HIV-1-uninfected adult participants mentioned earlier, there was a trend of lower responses in vaccinees infected with S. mansoni, which attained statistical significance with a number of antigens.

It has also been suggested that helminth infection impairs cognitive development and school performance. Our studies found minimal effects of helminths and their treatment, suggesting that these infections, on their own, may have little adverse effect on brain development.

We observe that where HIV is well managed like in our rural population cohort, NCD related deaths are now more frequent than communicable disease related deaths. Furthermore, we show that the prevalence of NCDs and of risk factors is higher in rural than in urban settings (37% overall in rural areas versus 31% in urban; the exception is Type 2 Diabetes (T2D) which, though rare everywhere in Uganda, is more frequent in urban settings (<0.5% of adult. As part of work on KSHV, we have shown that participants of the GPC have the highest prevalence of KSHV ever reported (>90%), with the infection occurring mainly in childhood; conversely, prevalence in urban settings in Uganda is generally slightly lower, particularly in children. In the GPC, the prevalence of abnormal liver function among adults may be as high as 40% and abnormal renal function of about 20%. The Uganda component of the multi-
centre H3A Diabetes Study looking at burden, spectrum and etiology of type 2 diabetes in sub-Saharan Africa was completed and analyses are underway.

Within the GPC, we have shown that exposure to oncogenic infections is much more widespread than risk factors typically associated with western lifestyles. The seroprevalence of Helicobacter pylori (H. pylori), Epstein Barr Virus (EBV), Kaposi’s sarcoma associated herpesvirus (KSHV) and Merkel Cell Polyomavirus (MCV) was >90%; high risk human papillomaviruses (HPVs), 58% (22% HPV 16, 28% HPV 18); human immunodeficiency virus (HIV), 10%; chronic Hepatitis B (HBV), 12%. For non-infectious risk factors, 6.5% of adults reported current daily smoking, 11% at least weekly drinking, 12% were overweight and 30% reported low levels of exercise. These results have implications if we are to effectively prevent NCDs in our populations.

The East African Chronic Diseases Research Project (EACDR) aimed at generating data on the burden of treatable chronic diseases (CDs) including HIV infection, design and implement health system interventions to improve management of CDs in primary care services in Uganda and Tanzania and to evaluate their impact in a randomized control study was completed. We showed that by providing basic facilitation and training, knowledge and competence of managing CD is enhanced.

In the area of emerging and re-emerging infections; through MRC funding and in partnership with the University of Glasgow Centre for Virus Research and UVRI, we have tested samples from humans and mosquitoes using Taqman real time PCR, metagenomics and serology but have not shown presence of the Zika virus. However, in the process of this work two viruses within the Rhabdoviridae, the Le Dantec virus and a novel rhabdovirus isolated from a patient in Arua currently named Adumi were identified. Further characterization of these viruses in underway. Prior to this work, we had through the UVRI, signed an MOU with the University of Glasgow for collaborative research and capacity development.

During this reporting period, we have conducted an Ebola vaccine trial. This study demonstrated that heterologous Ad26/MVA prime-boost vaccination against Ebola is well tolerated and highly immunogenic in healthy African adult volunteers, regardless of whether the dosing interval is 28 or 56 days. The funding was from the EU’s Innovative Medicines Initiative Ebola programme through the LSHTM and the French National Institute for Health and Medical Research (INSERM).

The Clinical Diagnostics Laboratory Services (CDLS) department in collaboration with other partners reported the emergence of low level ciprofloxacin resistant and multi drug resistant H-58 lineage Salmonella Typhi in Kampala. The laboratories in Entebbe, Mengo and Masaka maintained accreditation under Good Clinical Laboratory Practice (GCLP) by Qualagy and the Entebbe laboratory was accredited to ISO 15189 international standards. We continue to host the national and regional reference laboratory for HIV drug resistance determination, with WHO certification. Our biorepository has expanded and improved. We are the central biorepository hub for H3A diabetes study biobanking samples from 10 sites within 8 countries in Sub Saharan Africa. We hold more than 1 million samples with multiple aliquots from multiple local and international studies managing them accurately with Freezerworks specimen management software.

Over the last three years, the statistics section has served over 50 projects from setting up data bases to analyses. They have also fully implemented the OpenClinica database development platform, ensuring that the databases in use are compliant with Good Clinical Practice. By the end of 2017, we had 16 studies using this platform. In 2017, we also introduced another GCP complaint database platform, ODK (Open Data Kit), and implemented two studies on this platform. Staff have also participated in mathematical modelling and genetic statistics.
We have made efforts to build capacity in bioinformatics through infrastructure development, formal courses and hands on training, during this reporting period, the MRC funded Uganda Medical Informatics Center (UMIC) was launched. The Uganda Genome Project provides one of the largest study of its kind to date, comprising genome-wide data from 6,400 individuals from rural Uganda, and including whole-genome sequence from 1,978 individuals. Through this work, we demonstrate systematic differences in trait heritability between European and African populations, probably reflecting the differential impact of genetic and environmental factors on traits.

**Staff**

During this reporting period, staff numbers have increased from around 362 in 2015 to the current level of 395 (excluding students). Among those who joined are some senior staff like Suzanne Rupp, COO; Dr Jesus Salazar, senior virologist, Prof Moffat Nyirenda, NCD Theme and Programme Leader; Dr Christian Hansen, Head of Statistics; and Ayoub Kakande, Head of Data Management and others in different sections and programmes. I do welcome them. I also thank those who have left including those who have worked with the Unit at senior level like Prof Anatoli Kamali who was the Deputy Director; Dr Paula Munderi, who was Programme Leader for the Care Programme, Dr Jonathan Levin who was Head of the Statistics Section, Dr Gershim Asiki and Dr Sam Biraro both project leaders and Dr Jessica Nakiyingi Miiro who was a senior statistician among others. We have introduced the medical insurance scheme and annual director’s awards.

**Funding**

Our total funding exceeded £9.8 million pounds annually. In addition to MRC-UK core funding, our activities require additional funding which we obtain through attraction of additional external funding either through MRC supplementary awards or other funders. In the last three years, the external funding contributed about 47% of our operations. The largest external funders outside the MRC were EDCTP and Wellcome Trust. We have made significant improvement in generating external grant funding for the reporting period with more of 130% increase in awarded grants. Additionally we have strengthened capacity in the Grants Support Office to further support the scientific community and improve grants’ efficiency.
Infrastructure

We have continued to receive generous capital investments from MRC. In 2017 for example, the Unit received capital awards amounting to £812k plus £256k brought forward from the previous year and ran international tenders for assets including 21 new vehicles, 15 bio gram freezers, and a Laboratory Information Management Systems which will track samples from clinic, to analysis to store among others.

Some major projects included, a Data Centre established at the Kampala Office, linking Entebbe Main Data centre using fibre data and internet links replicating data to Entebbe on daily basis. The Internet Bandwidth requirements have increased from 10Mbps in 2014 across the Unit to 50 Mbps in 2017 shared across the six sites (two Hospital clinic offices, Entebbe, Masaka, Kyamulibwa and Kampala). In 2017 the Unit successfully implemented a phase one electrical upgrade at a cost of c £1m. This was a major infrastructure project increasing the electrical supply into the unit to include a new transformer station. Other equipments obtained included an ABI sequencer, next generation Miseq illumina, and a Luminex machine.

Training

We have maintained an excellent capacity-building programme with a mix of “on the job” and formal training and an emphasis on career development of staff. In the past three years, our training has extended to academic studies and short-term courses. For instance, 50 PhDs have been supported by the Unit of which 34 (Fig) are still on-going.

In the current QQ, in addition to the available training funds, MRC awarded an additional 200,000 pounds to support our post doc fellowships, which we are about to award. We continue to receive about 100 interns per year. We have strengthened linkages with key institutions such as Makerere University and participated in capacity building networks such as two Wellcome Trust funded ventures – the Makerere University–Uganda Virus Research Institute (UVRI) research training programme in Infection and Immunity (MUII) and Training Health Researchers into Vocational Excellence in East Africa (THRiVE) – plus the East African Consortium for Clinical Research (EACCR) funded by the European and Developing Countries Clinical Trials Partnership (EDCTP). Other training support has come through the IAVI funded-post docs and investigator initiated awards, EDCTP and Wellcome Trust fellowships among others.

Partnerships and collaboration

We have continued to maintain, expand and strengthen our partnerships, page ???? of this report lists some of the key partners. Our important partnership with UVRI has grown. We have worked
together in the areas of HIV prevention, laboratory testing and in studies around emerging, re-emerging infections. For the later, this has been further facilitated through the memorandum of understanding (MoU) between the Glasgow Centre for Virology Research and UVRI. Our partnership with Makerere University has been strengthened. UVRI has a long history of collaboration with Makerere, and this has been enhanced over the last decade through the development of a MoU and through the activities of MUII and THRiVE.

**Staff on different committees and peer reviews**

Our staff continue to sit on important National, Regional and International committees. We have had staff on the National ART, Drug resistance, Prevention and National laboratory committees. Internationally, staff sit on various WHO, UNAIDS and EDCTP committees and African Network of Cancer Registration. A number of staff peer review for scientific journals.

**Unit’s contribution to policy and practice**

It is important that results that will improve people’s health continue to be made available to decision makers in order to influence policy and practice. Page ?? of this report describes some of the important areas in this regard. We work very closely with relevant ministries and other stakeholders to ensure this approach is strengthened, involving them from the inception of research ideas and giving them representation at Unit advisory committee level. Staff are also encouraged to participate in national and global expert committees that advise on policy issues.

**Transfer to London School of Hygiene & Tropical Medicine (LSHTM)**

On 1st February, 2018, the MRC Units, The Gambia and the MRC/UVRI Uganda Research Unit formally joined LSHTM. These transfers are expected to build on the existing strong relationships between LSHTM and both Units, ensuring even stronger scientific collaboration as well as new career opportunities for researchers. The LSHTM and our unit have therefore created a new partnership that will boost research capacity into some of the current and emerging health issues in Africa and the world.

The relationship between MRC/UVRI and LSHTM dates back to the Uganda programme’s initiation in the 1980s, at the height of the HIV epidemic, with population studies crucial to understanding the course, the impact of the epidemic and interventions studies. There is also a long standing collaboration with the Tropical Epidemiology Group (TEG), and the Analysing Longitudinal Population-based HIV/AIDS data in Africa (ALPHA) network among others. The LSHTM is instrumental in the Unit’s capacity building programme with various staff undertaking post-graduate training at the School. Some of the Unit Senior staff are also faculty at the School. We are therefore excited to join the LSHTM and are optimistic about the numerous opportunities the partnership will provide to research teams both at the Unit and at the School. The transfer not only offers a wider platform for our researchers to train, practice and collaborate, but increases capacity and access to resources to undertake more cutting-edge medical research.

**New Unit name**

As a result of our broadened mission to include other infections beyond HIV and the inclusion of NCDs together with the transfer of the to LSHTM, the unit’s name has changed. We are now called Medical Research Council/Uganda Virus Research Institute and London School of Hygiene & Tropical Medicine Uganda Research Unit (MRC/UVRI and LSHTM Uganda Research Unit). These changes have been endorsed by the key parties, i.e the Uganda Government, the UK Government, the MRC and LSHTM requiring an addendum to the existing MOU.

**The challenges**

As we expand we continue to face space and accommodation challenges. Some of the critical areas include the limited space at our Mengo clinic. The expansion in Mengo will require obtaining additional land, a challenge at this stage. We also require creation of a clinical trial center in Entebbe, at the
moment most of our trials are being conducted in Masaka which is getting crowded. As we write this report though, we have obtained approvals from MRC for funding of this clinic and additional funds are expected from the Wellcome Trust. The research laboratories also need expansion in terms on offices and laboratory space. We will be approaching the MRC for support in this area.

The benefits created as we continue managing the HIV epidemic, with reducing incidence, means that conducting intervention trials becomes more complicated. We have a number of requests to participate in intervention studies but the population to conduct these are getting more and more limited.

For those who complete their PhDs, transitioning to Post doc levels comes with its challenges, especially in terms of winning independent grants. We are pleased that MRC offers some limited funding in this direction and other funders like EDCTP, Wellcome Trust and AREF, but this still remains a challenge.

In the past we have found a challenge in attracting senior level staff to key positions, but we hope that the transfer to the LSHTM will address this challenge as suitable candidates see better opportunities working under a University setting.

The future
We look to the future with a lot of optimism. There are new opportunities especially as far as research in concerned in the areas of emerging and re-emerging infections and NCDs. The transfer to LSHTM also comes with plenty of opportunities for research, winning grants and career progression. We will endeavour to continue with our capacity building efforts in order to create a generation on new young investigators that will move the Unit to the next level.

Some of the Future Research Activities
We will continue to study the HIV epidemic in the general population and in key populations i.e fisherfolk and women engaged in high-risk behaviours; providing important information on the epidemic to enable appropriate response. We will continue to gain more experience and information on the delivery of test and treat within the GHFW. The work in the above key populations will largely be funded by IAVI and PEPFAR respectively. We will continue to characterize by sequencing the transmitted and circulating HIV viruses, including studies to determine the transmission signatures in the transmitted viruses and biological characterization of these viruses.

Our GPC will continue to contribute to international collaborations, such as the ALPHA Network, the INDEPTH Cohort Consortium and the ANDLA (African Non-Communicable Disease Longitudinal data Alliance) collaboration. In addition, we have signed a Memorandum of Understanding with The AIDS Support Organisation (TASO) with a view to developing a platform for further studies of the health of HIV infected people living in real world conditions. Work with TASO has started on a study of integrating care on NCDs among people living with HIV and on long-term anti-retroviral therapy.

In the area of HIV vaccines; our partnership with IAVI will be strengthened within the USAID funded “Accelerate the Development of Vaccines and New Technologies to Combat the AIDS Epidemic (ADVANCE)”. This is aimed at advancing the design and development of HIV vaccines and biomedical prevention tools while ensuring they are effective and accessible for all in need. Under this is the VISTA programme, Vaccine Immunology Science and Technology for Africa, a new initiative aimed to strengthen and expand an international consortium of investigators in order to address gaps in HIV vaccine design. Under VISTA, MRC labs are being strengthened to perform viral inhibition, neutralization and generation of infectious molecular clones (IMCs). Another area we are expanding is related to viral sensitivity to the currently available broadly neutralizing antibodies. We are making pseudoviruses from our circulating strains to study their sensitivity to neutralization. We will also continue to identify participants with broadly neutralizing antibodies in our cohorts.
We will be part of the newly EDCTP funded phase IIb efficacy study of two DNA-Env protein/adjuvant, +/-MVA HIV-1 vaccine regimens with pre-exposure prophylaxis (PrepVacc). The Unit will play a central role in coordination, data management and immunological assays for this trial. We will be part of another EDCTP funded phase IIa vaccine trial the Globally Relevant AIDS Vaccine Europe-Africa Trials Partnership (GREAT) that will evaluate the safety and immunogenicity of 2 HIV vaccines (ChAdOx1- and MVA with conserved and mosaic HIV sequences).

We are to participate in the Combined HIV Adolescent PrEP and prevention Study, looking at the acceptability and feasibility of providing daily and on-demand PREP to adolescent boys and girls (CHAPPS), this is also funded by EDCTP.

Our research into mental health is expanding and with funding from the Welcome Trust, we have started studies to examine the epidemiology of HIV infection and risky sexual behaviour among severe mental illness patients. Our activities to integrate mental health into HIV care services for HIV infected children and adolescents (CHAKA+) will continue. Further work that has been launched is integrating the management of depression into routine HIV care in Uganda (the HIV+D trial).

We will be part of a phase II, open label, single arm trial to evaluate the pharmacokinetics, safety, tolerability and efficacy of TMC2778 (Rilpivirine RPV), in ART naïve HIV-1 infected children aged 6 to <18 years (PAINT). Janssen sponsors the study.

There are two USA NIH funded studies we are to continue; one is a study to investigate whether norethisterone enantate (NET-EN) can reduce the risk of recurrent bacterial vaginosis (BV) in women at high risk for HIV infection and another is continuing to follow participants in the START trial.

We have developed a Memorandum of Understanding with The AIDS Support Organisation (TASO) in order to study issues related with HIV as a chronic disease among others. TASO has the advantage of patient numbers and wider spread in the country. As mentioned above, work has started on a study of integrating care on NCDs among people living with HIV and on long term ART. Another planned study funded through our internally generated funds is to investigate the effect of HIV and ART on bone health among Ugandan on combination ART.

We are continuing to understand the social aspects of health and wellbeing for specified individuals and populations to inform the design, implementation and evaluation of interventions, as well as contribute to policy development. We will focus on different stages of the life course and specific populations: 1) Children and adolescents; 2) Key (at-risk) populations; 3) People 50 years and older. For example, our youth, mobility and health (including HIV) risk will investigate how this widespread rural-urban migration exposes young people to health risks and affects their health-related attitudes and behaviours. We will examine the barriers and facilitators of HIV ‘test and treat’ among key populations.

Under the Men and HIV prevention we will conduct research to look at the influence of different types of masculinity on treatment seeking, and then develop an intervention to address the barriers and facilitators of treatment seeking behaviours. Finally, we want to fill a gap by measuring the cost of illness or extent of impoverishment among older people and their caregivers as a result of lost livelihoods and paying for medication and/or health care in Uganda or elsewhere in East Africa.

Through PEPFAR funding, we will continue to participate in a number of HIV drug resistance activities, including surveillance, resistance development after second line failures among others. The Ministry of Health (MoH) has requested us to genotype patients failing on second line regimens.

Through funding from MRC, NIH and EDCTP, our HIV superinfection (SI) studies will continue to allow understand viral and immunological factors associated with superinfection but also to understand the
events surrounding HIV superinfection such as viral recombination. We are continuing with the PREPPIE study looking at the potential protective immune responses against HIV through PrEP in highly exposed populations. Gilead has provided the drugs for this study.

We will continue work on the impact of coinfections (notably malaria) on KSHV transmission. Under the Helicobacter pylori studies, we have secured funding from WHO International Agency for Research on Cancer to: i) subtype the bacterium in more detail and to identify drug resistance patterns and ii) study rates of re-infection following successful eradication as treatment for dyspepsia and heart burn. Work on conjunctival malignancies is on-going. The GlaxoSmithKline (GSK) kidney project will also continue.

We received a strategic award from the MRC for NCD research programme and additional funding from UK’s National Institute for Health Research (NIHR). Our research will include epidemiological studies, clinical and laboratory phenotyping, as well as intervention studies. These will include: Understanding local burden and drivers of gestational diabetes (GDM). This study is aimed at generating robust data on the burden, determinants and outcomes of GDM, in order to stimulate a policy response to address this challenge. In addition, using a combination of demographic, clinical and biochemical markers, will attempt to develop a risk scoring tool that might be used to identify women at high risk of GDM who should be targeted for screening. Phenotyping of type 2 diabetes with the aim to adequately understand the specific nature of diabetes in sub-Saharan Africa through detailed clinical and laboratory phenotyping that will lead to characterization of the clinical course of diabetes in this population; better understanding of the pathophysiology and rational use of available drugs, as well as provide new targets for therapeutic intervention.

We also plan to conduct a number of studies looking at the NCD-HIV interactions and this will involve the strong collaboration with TASO. We will examine whether treatment with metformin in HIV-infected individuals with prediabetes lowers the rate of progression to overt type 2 diabetes. Finally, we propose to study the long term impact of health systems intervention to improve care of NCDs

The goal of the new I-Vac programme is to further understand the impact of infection exposure on human immunological programming and health. Our overarching hypothesis is that chronic and cumulative infection exposure influences immunological mechanisms through active processes (during current infection), lasting epigenetic modifications, and genetic selection; that (therefore) some effects do not immediately respond to treatment; and that effects critically impact upon major health outcomes including vaccine responses and susceptibility to pathogens, allergy-related disease and metabolic conditions.

Other studies planned include the conduct of a phase I trial of the Rift Valley Fever (RVF) vaccine being developed by partners at Oxford University and studies aimed at understanding the role of pre-existing status of the immune system and presence of endemic infections on hepatitis B vaccine responses, this will also include gene profiling.

In the area of emerging and re-emerging infections, we will strengthen our collaborations with key partners and expand our involvement in the identification and characterization of new viruses, our plans currently are to make IMCs for the Le Dantec and Adumi viruses in order to study further its characteristics and to generate reagents for testing of these in the population. We are also part of a number of new funding applications for studies in emerging and re-emerging viral infections. We will develop further capacity in metagenomics and bioinformatics.

With funds from the Engineering and Physical Sciences Research Council to Imperial College, we will be part of a new initiative aimed at development of capacity for RNA vaccine manufacture. The UVRI Hub will establish a modular platform for RNA production consisting of training of core staff from Uganda in the UK in RNA manufacture, GMP process and regulation.
Looking at the above summary, the Unit will be well positioned to make significant contributions towards the control of some of the major health challenges we currently face. In the pages that follow in this report we provide some more details of the achievements and future plans.

Let me end by thanking all colleagues at the Unit, UVRI and its partners, the Uganda Ministry of Health, the funders especially MRC-UK and the communities where we conduct our research especially volunteers in our studies. I also thank the members of our outgoing scientific advisory committee for their contribution that shaped our science.

Thank you

Prof. Pontiano Kaleebu
MESSAGE - MRC-UK CEO

As you are aware there are a number of changes taking place at the MRC and at the MRC/UVRI Unit. First is the creation of the UK Research and Innovation (UKRI) an organisation in the United Kingdom created to direct research funding. It was established formally by the Higher Education and Research Act 2017 and brings together the seven existing research councils including the MRC, as well as Innovate UK and the Higher Education Funding Council for England as one unified body. The body was created in order to increase integrative and cross-disciplinary research. The position of Chief Executive (CE) at the MRC will cease from 1st of April 2018 and a new position of Executive Chair (EC) of the MRC has been created. For these reasons, I will be stepping down as MRC CE at the end of March 2018 and return to the University of Edinburgh before the launch of UKRI on 1st April after serving more than seven years as MRC CE. Professor Fiona Watt FRS has been selected to serve in the new position of the EC of the MRC when it formally becomes part of UKRI on 1 April 2018.

In May 2010, The MRC Council endorsed plans for a programme to transfer the majority of MRC intramural units to the university unit funding model. An important objective for the programme was that these new arrangements were expected to realise added value for both MRC and the University. Transferred units are owned and operated by universities; however, they are still part of the MRC family and MRC expectations that they will deliver excellent scientific output unchanged.

On the 1st February 2018, the Unit transferred to LSHTM. MRC/UVRI Uganda Research Unit and the London School of Hygiene and Tropical Medicine already enjoy a close strategic relationship and the transition will help crystallise further opportunities for joint working between the Unit and the University.

I’m also pleased to note that as a result of my initiative in 2014 to set up a High Level Advisory Group on Uganda (HAGU) under the chairmanship of Prof. Peter Piot, the unit’s activities have broadened into other infections and NCDs. The move into this direction was after consideration of the long term health research priorities for the country and the region.

As I leave MRC, I wish to take this opportunity to thank the Director and all staff for the good work done. The research of the Unit has helped develop an extensive body of knowledge and discovery which maintains the MRC’s position as a world-leader in medical research. I wish the Unit success.

Thank you

Prof. Sir John Savill
MESSAGE - LSHTM DIRECTOR

I would like to take this opportunity to send a warm welcome message on behalf of the staff and student community at the London School of Hygiene and Tropical Medicine (LSHTM) as MRC/UVRI joins our School. We anticipate this being the start of an exciting and successful endeavour for all of us and I look forward to the future.

The relationship between LSHTM and the Unit has existed for a long time since the inception of the Unit more than 25 years ago, when our School sent its staff to explore initiation of the MRC activities in Uganda and the first MRC/UVRI Director came from our faculty. Since then several other staff of the Unit, including two of its previous Directors, came from LSHTM, and we have worked together on a number of studies. By working even more closely together, we can develop the innovative and collaborative research projects needed to tackle major global health issues.

The transfer of the Unit to LSHTM involved considerable efforts from colleagues across all institutions, highlighting the positive and collaborative nature of our relationship. The coming together of our institutions should have many significant benefits, both for Uganda and globally. I look forward to our shared success.

Prof. Baron Peter Piot KCMG FMedSci
After wide consultations, we have broadened our work beyond HIV to include other infections and expanded our work in non-communicable diseases (NCDs). We are undertaking research in other important infections, such as tuberculosis (TB), schistosomiasis and soil transmitted helminths, where we have already established a track record of research. In addition, Uganda faces emerging infections, such as Ebola, Marburg, Yellow Fever, Zika and Rift Valley Fever, which are local and global priorities. Our data on mortality in rural Uganda, based on verbal autopsy, highlights the increasing mortality due to NCDs.

In view of the above, we now have a new Mission and Vision

Our mission for 2017-2022 is:
1. To conduct research to add knowledge and improve the control of infectious and non-communicable diseases both in Uganda, in Africa and globally
2. To contribute to the translation of research findings into policy and practice and
3. To build capacity for research in Africa.

Our vision is to build on the Unit’s past research achievements, and new opportunities, to contribute to the control of the HIV epidemic, of other infectious diseases, and of non-communicable diseases, in Uganda, the region and the world. We have also identified strategic aims of the Unit (Box 1).

Thematic approach. We have introduced a thematic approach to our research in order to maximise cross-Programme fertilisation and to create more opportunities for synergy of skills in the pursuit of the Unit goals, we have three Themes namely:
1. Research on the changing HIV/AIDS Epidemic (ROCHAE) leader to be appointed
2. Research on Endemic, Neglected, Emerging and Re-emerging infections (ENERI) led by Prof Alison Elliott.
3. Research to understand the risk factors and control of NCDs (STOP-NCD); led by Prof Moffat Nyirenda.

Theme leaders are providing overarching strategic leadership to the research Programmes within the Themes, thereby ensuring there is collaboration and added value. Themes will address specific research questions below:

**THE UNIT THEMES**

**SHIFTING BURDEN OF DISEASE LEADING TO THE CURRENT QQ 2017-2022**

**ROCHAE: Research on the Changing HIV/AIDS Epidemic**
1. What are the unique characteristics of the HIV epidemic in general and in high risk populations that may hinder meeting National and UNAIDS targets?
2. What are the best ways to deliver ART, what are the long term consequences of the expanded ART roll out, and can HIV be cured?
3. How can HIV prevention tools best be used, and can new tools for prevention be found?
4. What are the epidemiological, biological and genetic mechanisms of the interaction between HIV infection and non-communicable diseases?

**ENERI: Endemic, Neglected, Emerging & Re-emerging Infections**
1. How can we control infectious diseases and intervene to prevent local and global epidemics?
2. What are the overall impacts of infectious disease control on human health?

**STOP NCDs: Stop Non-Communicable Diseases**
1. What is the scale of, and forecast for, the NCD epidemic in Africa, and who will be most affected?
2. Are the physiology of, and risk factors for, African NCDs similar to those in HICs?
3. How can we intervene to stem the African NCD epidemic?

**New Programmes**

The science will be led and delivered through the various research programmes (Fig. 1). Supported by the three Themes, we have created 6 Programmes. Each of these programmes will deliver scientifically competitive research drawing from our strengths and achievements.

**Box 1. MRC/UVRI Uganda Unit, Strategic Aims**
1. Deliver excellent science
2. Strengthen partnerships and collaborations
3. Build human and infrastructural capacity
4. Attract external funding
5. Translate knowledge into policy and practice
A. HIV Intervention Programme
- Programme Leader, TBA.
This Programme has two broad areas within which there are specific projects a) Prevent acquisition of new infections in general and in key populations; b) Improve survival and quality of life among those infected. There is also a Mental Health component led by Prof Eugene Kinyanda that is addressing clinical trials preparedness and the integration of mental health into HIV care services.

B. HIV and Cancer Epidemiology Programme
- Programme Leader, Robert Newton.
This Programme builds on some of the activities of the former HIV Epidemiology and Prevention Programme, as well as greatly expanding the scope of our activities on cancer. The primary aims are to study i) the epidemiology of HIV infection in both general and in high-risk populations, ii) and to establish the burden and risk factors for non-communicable diseases (NCDs), particularly cancer.

C. Social aspects of health across the life course Programme
- Programme Leader, Janet Seeley.
The aim of the Programme is to further our understanding of the social aspects of health and wellbeing for specified individuals and populations to inform the design, implementation and evaluation of interventions, as well as contribute to policy development.

D. Pathogen Genomics, Phenotype and Immunity Programme
- Programme Leader Pontiano Kaleebu.
This Programme aims to conduct research that will lead to the better understanding of pathogen genomics in order to characterise diseases and epidemics for better control and to investigate virological, immunological and genetic factors required for the development of effective interventions against HIV-1. There is also the HIV transmission signatures component led by Dr Jesus Salazar.

E. Vaccines and Immunomodulation Programme
- Programme Leader, Alison Elliott.
This Programme will address the hypothesis that repeated and chronic infection exposure has a fundamental impact on immunological programming and hence on both infectious disease and NCD outcomes.

F. NCD Phenotype Programme
- Programme Leader, Moffat Nyirenda.
We received a strategic award from the MRC for NCD research programme (to complement QQ funding) in April 2017. The programme is addressing three key areas, namely: Understanding local burden and drivers of gestational diabetes; Phenotyping of type 2 diabetes and NCD-HIV interactions.

Research Platforms
We have created research platforms with the aim of providing an efficient and integrated support structure in order to maximise output (Fig 2). Each platform supports the minimum infrastructure and skills required to maintain research activity across the Unit and can be expanded by new funding when required for specific projects. They are intended to be dynamic and responsive to changing needs, and to provide the basis on which specific core and externally funded studies can readily build.

In the current QQ, we have strengthened our partnership with TASO, a non-governmental organisation caring for over 120,000 HIV affected individuals in Uganda.

Research Support Services
We also have various support services some of which are new (Fig 2). The new ones created are Grants Support Office, Bioinformatics and Compliance and Quality Assurance.
Prof. Anatoli Kamali - Head of Programme

Prof. Anatoli Kamali was the Deputy Director of the MRC/UVRI Uganda Research Unit on AIDS, and Head of the HIV Epidemiology and Prevention Programme until May-2016. Prof. Kamali has been involved in HIV/STI research since 1989, and has led several HIV intervention clinical trials. His main interest has been HIV epidemiology and evaluating HIV prevention strategies in Africa including HIV vaccine and vaginal microbicides.

Dr. Gershim Asiki – Senior Scientist

Dr Asiki was a Project Leader from 2008-2015. He coordinated epidemiological studies in fishing communities in preparation for future HIV efficacy trials, in addition to clinical trials on HIV/Schisoma mansoni co-infections. He also ran epidemiological studies in the General Population Cohort on HIV, Hepatitis B and C and non-communicable diseases.

Prof. Rob Newton - Senior Clinical Epidemiologist

Prof Newton was senior epidemiologist with the Epidemiology and Prevention Programme at MRC/UVRI. He is Professor of Clinical Epidemiology at the University of York, UK. He is also a Senior Visiting Scientist at the World Health Organisation’s International Agency for Research on Cancer. He is interested in the role of infectious agents and immune suppression in the aetiology of cancer and has particular experience of the conduct of epidemiological research on non-communicable diseases in sub-Saharan Africa.
**Programme Aim**

The primary aim of the programme was to study the epidemiology and prevention of HIV infection in both general and high-risk populations, and to establish the burden and risk factors for non-communicable diseases (NCDs). The epidemiological work of the programme encompassed three major cohorts (General Population Cohort, women at high risk of HIV-infection (Good Health for Women Project) and fisherfolk cohort), and several hospital-based studies. We also conducted work within the Uganda Police Force in Kampala. These cohorts provided a platform for epidemiology and prevention, basic science, HIV care, and social science research projects as well as contributing to wider international collaborations, such as the ALPHA Network (Analysing Longitudinal Population-based HIV/AIDS data in Africa), the INDEPTH Cohort Consortium and the NCD Risk Factor Collaboration (NCD-RisC).

**Epidemiology**

The **General Population Cohort (GPC)**, led by G. Asiki, A. Kamali and R. Newton continued to provide a useful source of information on trends in HIV incidence, prevalence and mortality, as well as a wealth of novel data on risk factors for cancers and other NCDs. In this cohort, national guidelines on the management of HIV were adhered to. The participation rate remained high with >95% of those present during survey recruited; of those >97% accepted VCT. The role of village reporters was enhanced, with successful vital registration of pregnancies, births, deaths and incident strokes. In addition, we introduced verbal autopsy to record cause specific mortality. Annual census and two biennial survey rounds of adults were completed. In 2016/17, we are conducting a survey of risk factors for HIV and for NCDs among children.

In relation to HIV, key findings from the GPC include substantial improvements in life expectancy over the last 20 years, largely driven by reductions in HIV related mortality. However, among the approximately 90% of the population without HIV, there have been no substantive improvements in life expectancy since 1989. We also showed that the increasing prevalence and reducing incidence may be due to ART uptake and a positive net HIV prevalence among in/out migrants.
**Good Health for Women Project (GHWP):** The GHWP cohort of women at high-risk of HIV-infection in Kampala led by J Seeley, A Kamali, M. Kuteesa and Y. Mayanja, continued to provide valuable data on HIV epidemiology and risk factors. The objective was to continue HIV epidemiology and social science research, as well as providing a platform for HIV prevention and basic science research. We continued to observe excellent retention beyond 36 months of follow up in both the women and their partners. The test-and-treat policy was implemented in August 2014. The median time to ART initiation was 3 months; 28% initiated ART within one month. Young women (≤24yrs) were less likely to initiate ART within one month. Uptake of ART was more likely after one year of implementing the ‘Test and Treat’ intervention. We continue to find that HIV infection is high among the newly recruited women in GHWP (since 2013): prevalence (34%) and incidence (3.8/100 PYAR). Reported condom use increased from 35% at enrolment to 73% at 36 months but inconsistent use remained high.

**Fisherfolk Cohort:** In preparation for future efficacy prevention trials, we followed an open HIV incident cohort (Led by Freddie Mukasa Kibengo) among high risk fishing communities to characterise the populations for efficacy prevention clinical trials. With a focus on high-risk behaviour, approximately 400 volunteers from fishing communities were followed quarterly. Enrolled volunteers were re-assessed for high risk every 12 months and those no longer at risk replaced with new ones. Despite the prevention and HIV counselling provided we observed that HIV incidence remained much higher compared to the general population; 4.00 and 0.56 per 100 PYAR respectively, with a rate ratio (RR) of 10.83 [95% CI 6.11-19.76]. This was higher among those aged 18-24 years, unmarried, and those with more than two sex partners in the past year; RR of 15.44, 22.99 and 19.29 respectively. Factors associated with high incidence were short duration in the community and unprotected sex. We also explored use of Biometric finger print technology (FPT) and preliminary data indicate that FPT could be a useful tool for tracking hard-to-reach populations-virtual cohort.

**Non-Communicable Disease Epidemiology**
We have shown in the GPC and in other cross-sectional surveys in urban settings (led by Rob Newton and G. Asiki), that: i) where HIV is well managed, NCD related deaths are now more frequent than communicable disease related deaths and ii) the prevalence of NCDs and of risk factors is higher in rural than in urban settings (37% overall in rural areas versus 31% in urban; the exception is Type 2 Diabetes (T2D) which, though rare everywhere in Uganda, is more frequent in urban settings (<0.5% of adults in rural areas versus 2% in urban centres). In addition, in rural Uganda, data from verbal autopsy suggested that the predominant causes of NCD deaths include: the malignant and non-malignant consequences of oncogenic infections, liver cancer and liver failure due to cirrhosis, and problems associated with hypertension, particularly stroke.

As part of work on KSHV, we have shown that participants of the GPC have the highest prevalence of KSHV ever reported (>90%), with the infection occurring mainly in childhood; conversely prevalence in urban settings in Uganda is generally slightly lower; particularly in children. In case-control studies of stroke nested within the GPC, we demonstrated the importance of hypertension as a cause. We completed the H3A Diabetes Study - a multi-centre study of the prevalence and environmental and genetic determinants of T2D in sub-Saharan Africa.

Our partnership with Wellcome Trust Sanger Institute, Cambridge, UK has led to important findings on genomics of cardiometabolic traits. We have genome-wide data from 6,400 individuals from rural Uganda including GPC. Alongside phenotype data, we provide a rich new genomic resource for researchers in Africa and globally.

**HIV prevention**
We continued with HIV vaccine research and conducted two phase I trials. The first was a phase I double blind placebo-controlled clinical trial to evaluate the safety and immunogenicity of the combination of DNA-HIV-PT123 and AIDSVAX®B/E in HIV-1-uninfected adult participants with or without underlying
Schistosoma mansoni infection (IDEA EV06) (PI P. Kaleebu and Giuseppe Pantaleo). The vaccine was safe and immunogenic (see Basic Science). The second was a follow-up Open label phase I clinical trial to evaluate the effect of late boost on HIV-uninfected vaccinees from EV06 trial (IDEA EV07). Study follow-up ended in December 2017. Both trials were sponsored by the EuroVacc Foundation and were conducted at MRC/UVRI, Masaka and UVRI-IAVI centre, Entebbe among healthy adults aged 18-45 years. Funding was largely from the European Union and IAVI.

We conducted a study led by M. Kuteesa and Ubaldo Bahemuka, to access the feasibility and acceptability of establishing a cohort for HIV prevention research in the Uganda Police Force. We found that members of this group willing to participate in research may not be appropriate for HIV prevention activities due to the low incidence detected. We are investigating partnering to work in the areas of NCD.

We completed a Simulated Vaccine Efficacy Trial (SiVET) studies led by G. Asiki and Andrew Abaasa, aimed at assessing whether HIV high risk populations such as fishing communities and female sex workers can be enrolled, vaccinated and retained in a SiVET using standard 3-dose Hepatitis B vaccine as proxy for HIV vaccine. A total of 282 participants were enrolled into the study with 10 new HIV infections occurring within 309.1 person years of observation (PYO) giving HIV incidence of 3.2 [95% CI; 1.7-6.0]; 7 HIV infections in 231 PYO among men, HIV incidence of 3.0 [95% CI; 1.7-6.0] and 3 HIV infections among women in 78.1 PYO, HIV incidence of 3.8 [95% CI; 1.2-11.9].

Another similar SiVET study among women in GHWP was initiated, led by A Kamali and Y. Mayanja. This was a simulated interventional study that followed 290 HIV negative volunteers over 12-months and receiving hepatitis vaccine at months 0, 1 and 6. The study enrolled a total of 290 volunteers and there were 7 HIV infections (212.1 PYO) giving an HIV incidence 3.3/100 (95% CI; 1.6-6.9).

The Unit, led by A. Kamali and S. Kusemererwa was part of the International Partnership for Microbicides collaboration evaluating of Dapivirine Vaginal Ring for HIV prevention among women in a phase III placebo-controlled safety and efficacy trial in 7 centres in Uganda and South Africa (The Ring study, PI Zeda Rosenberg). The Dapivirine vaginal ring was found to be safe and effective in reducing HIV infections among women at risk of HIV acquisition by 31%. Although the ring was less effective with younger women.

HIV and worm co-infections are common in resource constrained settings and some studies have shown that these co-infections could lead to faster HIV progression. Of particular importance is S. mansoni which evades the immune system through strong immunoregulatory effects for the long-term survival of adult worms within the host. We conducted an open label randomized control trial to evaluate the effect of high intensity praziquantel (three monthly) versus low intensity praziquantel (annually) on viral load, CD4 counts and HIV clinical progression after 15 months of treatment. In communities with a high burden of both S. mansoni and HIV infection, intensive treatment of S. mansoni has benefits on parasitic clearance but does not delay HIV disease progression.

We performed a feasibility study of HIV combination (HIVCOMB) intervention effectiveness in fishing communities in Uganda. This was a parallel-arm cluster randomized pilot trial, with a pair of rural and urban communities allocated to intervention or control arm. Mapping and census were done prior to baseline sero-survey. Using census data, we randomly selected adults (≥18 years) stratified by age and sex, and resident for ≥3 months. While the intervention was successful with those who engaged with the trial, recruitment was challenging and follow-up poor, because of mobility among the target population. The study was led by A. Kamali, M. Kuteesa, Helen Weiss, J. Levin and J. Seeley.

We are part of an IAVI led 5-year (2016-2021) USAID funded activities: ‘Accelerate the Development
of Vaccines and New Technologies to Combat the AIDS Epidemic (ADVANCE). ADVANCE has four areas of focus: i) Understanding communities and cohorts leading to epidemiological studies, social science studies, and community engagement/research preparedness ii) Through Africa-centred science (also termed VISTA), engaging in the design and testing of new immunogens ADVANCE engages regionally-based researchers to utilize unique samples to identify modes of viral control iii) Clinical evaluation of vaccine candidates iv) Sustainable capacity building of scientists and institutions and transferring critical technologies and information.

We are part of the European HIV Vaccine Alliance (EHVA). This is using a multidisciplinary approach to HIV vaccine development in order to discover and progress novel vaccine candidates through the clinic. The project is funded by the European Union’s Horizon 2020 Research and Innovation Programme. The capacity built over the years to conduct HIV vaccine trials is being used to conduct vaccine trials of other pathogens. We conducted and concluded a phase 1 study led by Zacchaeus Anywaine to evaluate the safety, tolerability and immunogenicity of heterologous prime-boost regimens using MVA-BN®-Filo and Ad26.ZEBOV administered in different sequences and schedules in healthy adults.

This Ebola vaccine trial was funded by the European Union under the Innovative Medicines Initiative-1 and was coordinated by the London School of Hygiene and Tropical Medicine. In this study, Ad26.ZEBOV and MVA-BN-Filo vaccines were evaluated as heterologous prime-boost regimens, in which one study vaccine was used to prime a filovirus-specific immune response and the other study vaccine to boost the immune response 28 or 56 days later. This study demonstrated that heterologous Ad26/MVA prime-boost vaccination against Ebola is well tolerated and highly immunogenic in healthy African adult volunteers, regardless of whether the dosing interval is 28 or 56 days.

A follow on randomized, observer-blind, placebo-controlled, phase 2 study to evaluate the safety, tolerability and immunogenicity of three prime-boost regimens of the candidate prophylactic vaccines for Ebola Ad26.ZEBOV and MVA-BN-Filo in healthy adults, including elderly subjects, HIV-infected subjects, and healthy children in three age strata in Africa was also initiated. Enrolment started in January 2016 and was completed in September 2017. A total of 227 subjects were enrolled (137 healthy adults and elderly 18-70 years; 39 HIV positive adults 18-50 years; 31 adolescents 12-17 years and 20 children 4-11 years). 103 subjects completed follow-up and have been exited from the trial, 1 subject was withdrawn due to non-compliance and 2 subjects died of non-trial related deaths (1 adolescent and 1 HIV infected).

EBOVAC extended follow-up study: This is a multi-country, prospective, long-term clinical safety study designed to allow collection of pregnancy outcomes (including spontaneous/elective abortion, intrauterine death/stillbirth, information on delivery) following administration of Ad26.ZEBOV and/or MVA-BN-Filo for the prevention of Ebola virus disease among subjects who participated in a Phase 1, 2 or 3 clinical study. In addition, offspring from vaccinated female subjects who became pregnant with estimated conception within 28 days after vaccination with MVA-BN-Filo or within 3 months after vaccination with Ad26.ZEBOV in a Phase 1, 2 or 3 clinical study will be followed up to 60 months after birth.
Dr. Paula Munderi
- Head of Programme
Dr. Paula Munderi is a Physician and was Head of the HIV Care Research Program since 2005-2017. She is a graduate of Makerere University Medical School and a Fellow of the Royal College of Physicians (UK). Previously she worked at WHO Geneva, and as a Lecturer in the Faculty of Medicine, Makerere University.

Dr. Billy Mayanja Nsubuga
- Senior Scientist
Dr. Mayanja Billy Nsubuga is an epidemiologist and Senior Scientist at the Unit. He was Project Leader of the Complications of Long-Term Antiretroviral Therapy (CoLTART) study. He is a graduate of Makerere University Medical School and University of London.

Prof. Eugene Kinyanda
Prof. Eugene Kinyanda is Programme Leader Track for the mental health project at the Unit. He received a Medical Research Council/DFID (through an MRC/DFID African Leadership Award with the Global Centre for Mental Health at LSHTM, 2014-2016) and most recently, a Senior Wellcome Trust Fellowship (2017-2021). He trained as a psychiatrist at Makerere Medical School and got his PHD in suicidology from Norway.

Dr. Zacchaeus Anywaine
Dr. Zacchaeus Anywaine is an epidemiologist and senior scientist with an MBChB degree from Mbarara University of Science and Technology and a Master of Science in Clinical Trials from the University of London. He joined the MRC/UVRI Uganda Research Unit on AIDS as a clinician and has been an investigator on studies evaluating Microbicides for HIV, COSTOP and Ebola vaccine.
Dr. Sam Biraro
- Epidemiologist

Dr. Sam Biraro is a Clinical Epidemiologist, and was a Senior Scientist at the Unit. He led Health Systems and Chronic Disease Project until June 2015, and previously led the Kyamulibwa General Population Cohort. He is now the Uganda Country Representative for ICAP at Columbia University.

The HIV Care Research Programme conducted studies on treatment and care of people infected with HIV and a health systems research project on management of chronic HIV infection and other treatable chronic diseases (CDs).

The East African Chronic Diseases Research Project (EACDR) was aimed at generating data on the burden of treatable chronic diseases (CDs) including HIV infection, designing and implementing health system interventions to improve management of CDs in primary care services in Uganda and Tanzania and to evaluate their impact in a randomized control study. The project was a collaboration with the Mwanza Intervention Trials Unit (MITU) in Tanzania and LSHTM. We found a high prevalence of hypertension and its lifestyle risk factors; poor preparedness at all levels of health services and community perceptions and insights on NCDs present barriers to health service seeking. In consultation with national Ministry of Health partners, findings from phase I were used to design a health system intervention. The intervention succeeded in improving screening, treatment, monitoring, record keeping and referral of patients with treatable CDs at participating health centres; in-service training and supervision of frontline health workers. The overall PI was Prof Heiner Grosskurth and our team was led by Paula Munderi and Sam Biraro assisted by David Katende.

Strategic Timing of AntiRetroviral Treatment (START) Trial was a 6-year international multisite randomised controlled trial, designed to compare early versus deferred ART in treatment naïve adults. The Unit contributed 190 participants and our local PI was Dr P. Munderi, supported by Joseph Lutaakome. The START main study showed that early ART, reduces the risk of serious AIDS-related illness, serious non-AIDS-related illness and death by 53% compared to deferring ART. The effect of early treatment on AIDS was greater than on non-AIDS events. These results have contributed to the change of policy to advocate for test and treat which in addition to better treatment outcomes contributes to reduced transmission.

The COSTOP Trial, Safety of discontinuing Cotrimoxazole prophylaxis among HIV infected adults on ART in Uganda was completed led by Prof Heiner Grosskurth, Dr Paula Munderi, Jonathan Levin and Zacchaeus Anywaine as project leader. This was a 2000 patient, 3-year randomised placebo controlled trial designed to investigate whether primary prophylaxis with Cotrimoxazole can be safely discontinued among Ugandan adults on ART who have achieved sustained immune restoration as measured by a confirmed increase in CD4 cell count to 250 or more cells/μl. Key findings: The study showed that compared to placebo, adults on ART who continued primary prophylaxis with Cotrimoxazole had a significantly reduced risk of severe bacterial infections mainly bacterial pneumonias; episodes of symptomatic malaria and of hospitalization.
The Clinical Outcomes of Long-Term ART in an African (CoLTART) Cohort study was composed of 1093 adults attending the two MRC/UVRI clinics in Entebbe and Kyamulibwa who had been on ART for 5-10 years, created in July 2012 and closed in July 2015. Data from CoLTART provided valuable information on treatment related metabolic side effects and on long term cardiovascular morbidity and renal function among African patients. We found no differences in renal function between patients on Tenofovir and Non-Tenofovir containing ART regimens. Patients on Protease Inhibitor (PI) regimens had higher total cholesterol, lower high density lipoprotein, higher low density lipoprotein, higher triglycerides, and a higher atherogenic index for plasma than the non-PI regimen, but patients on Non-PI regimens had higher mean diastolic hypertension than those on PI regimens. Of the 36 patients failing on second line ART, 7 had major PI associated drug resistance mutations of whom five had high level resistance to ritonavir boosted Lopinavir and Atazanavir; with Darunavir as the only susceptible PI tested. Highlighting the need for HIV care programs in resource limited settings to start routine HIV viral load monitoring, targeted HIV drug resistance testing and availability of third-line ART regimens. The studies were led by Paula Munderi, Billy Mayanja and Joseph Lutakoome assisted by Ivan Namakoola.

We conducted an open-label cluster randomised controlled trial to evaluate the effectiveness of follow-up counselling after Home Based HIV Counselling and Testing (HBHCT) on linkage to HIV care in SW Uganda. HIV-infected adults (≥18 years) residing in 28 rural clusters were randomly allocated to control (referral to HIV care only) or intervention (referral & follow-up counselling) arms (14 clusters per arm). We found that follow-up counselling improved linkage to care. This was a PhD project for Dr Eugene Ruzagira.

Switching at low HIV-1 RNA into fixed dose combinations (SALIF) Trial was a multisite phase 3b clinical trial designed to demonstrate non inferiority, in terms of virological suppression, of a fixed dose combination (FDC) of Tenofovir/Emtricitabine/Rilpivirine (TDF/FTC/RPV) with Tenofovir/Emtricitabine/Efavirenz ((TDF/FTC/EFV); the latter being the preferred FDC for first line ART in Africa. 19 clinical study sites in 5 African countries and 4 in Thailand participated in the trial. MRC/UVRI functioned as the coordinating site for Uganda. From this study, switching to TDF/FTC/RPV was non-inferior to (TDF/FTC/EFV) in maintaining high rates of viral suppression, with a comparable tolerability profile.

During this reporting period, we expanded our mental health activities. Currently HIV/AIDS clinical trials in Africa do not routinely measure and control for adverse mental health factors yet these may be significantly impacting HIV disease progression and other clinical and behavioural outcomes.

Between 2014-2016, the Mental health among HIV infected Children and Adolescents in Kampala and Masaka, Uganda (the CHAKA study) was undertaken. 1,339 children and adolescents (CA) with HIV (CA-HIV; aged between 5-17 years) were recruited and followed up for 12 months with 3 assessments done at baseline, 6 months and 12 months. The prevalence of emotional and behavioural problems was 31.6% (95%CI: 29.1%-34.2%) and that of Diagnostic and Statistical Manual of Mental Disorders DSM-5 psychiatric disorders was 6.9% (95%CI: 5.6%-8.4%). The most prevalent emotional disorder category was anxiety problems (21.2%) while the most prevalent behavioural disorder category was attention deficit hyperactivity disorder (ADHD) related problems (6.1%). About a quarter (21.5%) of CA-HIV with at least one emotional problem had a comorbid behavioural problem, while more than half (59%) of the CA-HIV with at least one behavioural problem had a comorbid emotional disorder problem. In conclusion, CA-HIV were found to have a significant burden of emotional and behavioural problems including psychiatric disorders with considerable psychiatric comorbidity. This work was led by Prof Eugene Kinyanda assisted by Richard Mpango.

In the current funding cycle starting April, 2017, the above two programmes were modified to create a new HIV Intervention programme and a new HIV and Cancer Epidemiology Programme. In the subsequent pages, we present some of the progress since these changes.
Dr Freddie Mukasa Kibengo
Dr Freddie Mukasa Kibengo is a Scientist and Project Leader in the HIV Interventions Programme. He currently leads HIV vaccine research preparatory cohort studies among various key populations in Masaka, Uganda, HIV vaccine trials and Cryptococcal meningitis trials. His broad area of interest is interventional clinical studies particularly on HIV/AIDS Care and vaccine development for HIV and other emerging infections. He obtained his training as a physician at Makerere Medical School.

Dr. Joseph Lutaakome
Dr Joseph Lutaakome is a physician and project leader under the HIV Intervention Programme for over 10 years. Joseph holds an MBcHB from Mbarara University of Science and Technology, a Masters of Public Health from University of Manchester UK and Post graduate certificate in monitoring and evaluation from AMREF International Kenya. He has worked on a number of clinical trials including -DART, ARROW, COSTOP, SALIF, CoLTART.
**Dr. Eugene Ruzagira**
Dr. Ruzagira is a senior Scientist in the HIV intervention programme. He is the coordinator for PrEPVacc, a multisite phase IIb HIV vaccine trial that will be conducted in four countries in sub-Saharan Africa. Previously he led a number of IAVI supported studies in Masaka. He has recently obtained his PhD at the LSHTM.

**Dr. Richard Mpango (PhD)**
Richard S. Mpango is a clinical psychologist by background with an advanced diploma in child psychiatry. He joined the Unit in 2014 as a project leader of the CHAKA study. He is currently one of the project leaders of both the HIV+D and SMILE studies. In 2017 he participated in the development of the Child and Adolescent Mental Health Policy Guidelines in which publications from the Mental Health Project were referenced.

**Dr. Margaret Nampijja**
Dr. Nampijja is a developmental psychologist who has been with the Unit since 2002, initially with the Entebbe Mother and Baby Study. In 2017 she joined the Mental Health Project as one of the project leads of the HIV+D study. She is also the PI of a study that is evaluating the feasibility and acceptability of an early intervention programme that is aimed at improving early detection and intervention for young infants at high risk of neurodevelopmental delay and disability in Uganda.

**Dr. Sylvia Kusemererwa**
Dr. Sylvia Kusemererwa is a Scientist and a Project Leader. She joined the Medical Research Council in 2013 and coordinates the dapivirine vaginal ring microbicide studies for HIV prevention among high-risk women in Masaka, South western Uganda.
Work under the HIV Intervention Programme has two broad aims. Firstly, to prevent acquisition of new infections, and secondly to improve survival and quality of life among people living with HIV. To address these aims several scientific projects are being undertaken partly by the Unit, and partly through scientific collaboration with our long-term partners and institutions in Europe, USA and Africa. Our aim is to conduct HIV intervention research in these populations by building on recent advances in biomedical interventions, some of which we participated in, such as oral and topical pre-exposure prophylaxis (PrEP), and HIV combination prevention. This programme of work builds on our past successes and expertise in conducting HIV epidemiological research in key populations and, work on designing and evaluating HIV prevention, treatment and care strategies in Africa.

**Research on prevention of acquisition of new infections**

We continue to engage key populations such as fishing communities and female sex workers to understand how best we can evaluate new HIV prevention technologies in these populations. These data will help inform national policy on HIV prevention and care and enable us to identify acute and early HIV infection volunteers to enable immunological work within the basic science work. This involves community engagement, observational and epidemiology studies and socio-behavioural research.

In collaboration with International AIDS Vaccine Initiative (IAVI), we are participating in studies aimed at informing HIV vaccine design and to evaluate new candidates in phase I/II trials. We are also monitoring and defining populations at highest risk of HIV infection, estimate HIV incidence and volunteer retention, and to generate data that informs future clinical trial design and interventions in these key populations. The IAVI Protocol B (HIV Vaccine preparedness study) has been on since 2004. This enrolls high risk HIV negative people in the fisherfolk communities in Masaka and follows them quarterly. The study is an open cohort that has enrolled a total of 980 (664, 67.8% male). Of those enrolled, 591 (337, 57.0% male) volunteers have been withdrawn from the study so far. Sixty-three (63) new HIV infections have occurred over a cumulative follow up period of 1691 person-years resulting in an HIV incidence of 3.73 per 100 person-years (95% CI 2.90 – 4.70). The HIV incidence rates by gender are 2.4 [1.7 - 3.4] and 7.6 [5.2 - 10.6] for males and females respectively. This work is led by Dr. Freddie Mukasa Kibengo.

Under the IAVI “Accelerate the Development of Vaccines and New Technologies to Combat the AIDS Epidemic (ADVANCE)”. Under two major objectives i) conducting preclinical and clinical HIV vaccine R&D and ii) strengthening capacity for HIV vaccine and biomedical prevention research; we have been supported in the following areas: Follow a cohort of high risk men and women mentioned above; participate in the lake Victoria Health Research; conduct adolescent research, i.e feasibility of enrolling and retaining adolescents 15-25 years; community engagement; VISTA related activities (progress see P-GPI); a number of investigator initiated studies and support to training. After the departure of Prof Kamali, the ADVANCE activities are led by Prof Pontiano Kaleebu with a number of project leaders including Freddie Kibengo, Yunia Mayanja, Vincent Basajja, Jennifer Serwanga and Peter Hughes.

We are participating in a follow-on, **Open-Label Extension (OLE) trial** (DREAM study: Dapivirine Ring Extended Access and Monitoring/IPM 032) to assess continued safety of and adherence to the dapivirine (25 mg) vaginal ring-004 in healthy, HIV-negative women, Phase IIIb. In collaboration with the International Partnership for Microbicides (IPM), the Unit is part of a follow-on trial to IPM 027, to collect additional safety data and establish adherence to use of the ring in healthy, HIV-negative women with monthly (for three months) followed by 3-monthly research centre follow-up visits over 12 months. Of the 197 women who participated in the phase III trial at MRC, 78% (153/197) were eligible for screening into the OLE. We screened 136 participants and enrolled 121. This work is led by Dr Sylvia Kusemererwa.
A study to investigate whether norethisterone enantate (NET-EN) can reduce the risk of recurrent bacterial vaginosis (BV) in women at high risk for HIV infection is on-going. BV is highly prevalent among women in the GHWP cohort and is associated with HIV acquisition. There is evidence that hormonal contraceptives, including depot medroxyprogesterone acetate (DMPA), decrease BV recurrence; however, there is also evidence that DMPA increases the risk of HIV infection. Encouraging women to start or switch to an alternative progestin injectable such as NET-EN may mitigate HIV risk whilst decreasing the risk of recurrent BV. We are investigating the effect of NET-EN on vaginal microbiota. Recruitment into the trial began at the end of 2017. The PI is Dr Suzanna Francis, LSHTM, in-country co-Is Prof Seeley and Dr Yunia Mayanja.

The following three studies were recently funded by EDCTP and currently preparations are underway for their implementation: Globally Relevant AIDS Vaccine Europe-Africa Trials Partnership (GREAT) is an EDCTP funded phase IIa vaccine clinical trial that will evaluate the safety and immunogenicity of 2 HIV vaccines (ChAdOx1- and MVA). The overall PI is Prof Tom Hanke at Oxford University and MRC/UVRI co-PI P Kaleebu. The Improved 2nd generation tHIVconsX Conserved Mosaic targets functionally conserved regions of HIV-1 proteins common to all global variants important for replicative fitness. The efficacy is further enhanced by Bi-valent mosaic design to increase perfect epitope match to global variants to increase breadth and magnitude. The study population will consist of high risk individuals, and for the Unit these will be the high risk fishing communities around Lake Victoria in Masaka. Other sites will be in Zambia and in Kenya. We are upgrading clinics and laboratories that will be used for this study as the protocol is still being written up.

A combination efficacy study in Africa of two DNA - Env protein/adjuvant, +/-MVA HIV-1 vaccine regimens with pre-exposure prophylaxis (PrepVacc). We are part of a consortium funded by EDCTP to conduct an HIV vaccine phase 2b efficacy trial. This trial will test two immunization strategies, HIV DNA + gp120/alum and HIV DNA, MVA + gp140/MPLA to determine if these products protect against HIV-1 infection in Africa, in combination with universal PrEP covering the immunisation schedule. The trial has two stages i) The initial is the development of a HIV negative Registration cohort for future participation in a HIV vaccine study. The registration cohort is to recruit HIV negative volunteers at risk of HIV acquisition and prepare them for participation in an HIV preventative vaccine trial; ii) a phase Ib randomised blinded placebo controlled vaccine trial to demonstrate the efficacy of two vaccines - DNA-MVA/protein and DNA/protein immunisation strategies in preventing HIV infection in high-risk populations. This will be the first large efficacy trial in Africa, outside of South Africa and first fully European funded. The studies will be carried out in Uganda, Tanzania, Mozambique, and South Africa. The overall coordination for studies will be conducted by the MRC/UVRI and LSHTM Uganda Research unit and Imperial College. Overall PI is Prof Jonathan Weber, MRC/UVRI co-Pl is Prof Pontiano Kaleebu while Dr Eugene Ruzagira will be the trial Director. The registration cohort protocol has been developed and applications for ethical reviews are underway at the participating sites. The trial protocol is under development.

Combined HIV Adolescent PrEP and prevention Study: the acceptability and feasibility of providing daily and on-demand prep to adolescent boys and girls (CHAPPS) is a new EDCTP funded study about to start working with the Social Aspects of Health Across the life and PGPI programmes, aimed to compare and optimize PrEP and Post-exposure prophylaxis (PEP) regimes and optimize delivery in adolescent boys and girls in Africa. We hypothesize that on-demand PrEP will be highly acceptable/ feasible to administer to at-risk adolescents, that the number of PrEP pills required for insertive sex will be less than for receptive anal sex, that F/TAF (TAF/Emtricitabine) will provide greater protection than Truvada in PrEP and PEP and that the window period for PEP initiation will be greater than guidelines recommend. We will investigate the acceptability and feasibility of implementing daily and on-demand PrEP in adolescent boys and girls in South Africa, Uganda and Zimbabwe; to optimize the dosing schedule for on-demand PrEP regimens for insertive sex and to optimise the time frame for initiating PEP for insertive sex. Under this study there will be capacity built in performing explant tissue culture experiments. The overall PI for the study is Dr Julie Fox from Kings College London.
The HIV clinical trials preparedness studies among patients with severe mental illness in Uganda (SMILE Study) will examine the epidemiology (prevalence, incidence and associated/predictor factors) of HIV infection and risky sexual behaviour among patients with the severe mental illnesses (SMI) of Schizophrenia, Bipolar affective disorder and recurrent Major depressive disorder. To do this, we shall recruit and follow-up for 12 months 1,000 patients with SMI attending Butabika National Psychiatric Referral Hospital and Masaka Regional Referral Hospital. We shall undertake 3-monthly assessments of HIV status, HIV associated risky sexual behaviour and psychiatric symptomatology. A prospective clinical trials preparedness sub-study will also be undertaken to investigate the feasibility and acceptability of undertaking clinical trials among persons living with co-morbid SMI/HIV. To undertake this, a random sample consisting of 100 respondents with comorbid SMI/HIV will be enrolled and followed up for 12 months with 3 monthly assessments. We shall monitor willingness to be recruited into the study, drop-out rates and acceptability to participate in the study. As of the 8th April 2018 we had recruited 430 respondents into the Main Study and 4 respondents into the clinical trials sub-study.

The Integrating mental health into HIV care services for HIV infected Children and Adolescents in Kampala and Masaka, Uganda: Formative work (CHAKA+). The recently completed CHAKA study reported a prevalence for emotional and behavioural problems of 31.6% including 6.9% who had a Diagnostic and Statistical Manual of Mental Disorders (DSM-5) psychiatric disorder. Despite this burden, Adolescent HIV care services in the country do not provide mental health care. In this project, we plan to hold a consultative meeting with experts in the field to review CHAKA data in the context of best global practices for mental health care in childhood and adolescence. This will inform the conceptualisation of a mental health integration model for childhood and adolescent HIV care in Uganda. We shall then subject components of this model to pilot testing. These results will inform a bigger study application that will propose to further refine this model and later put it to trial.

The Integrating the management of depression into routine HIV care in Uganda (the HIV+D trial) will have two phases, the formative phase (to develop and pilot the model) and the cluster randomised trial (to put the model to trial). The formative phase has made the following progress: i) had a successful launch on the 2nd November 2017 where we received good media coverage; ii) completed the development of the Theory of Change Map (ToC Map); iii) have undertaken workshops with policy makers, mental health specialists, frontline health workers and community health workers to adapt the Health Activity Program (a behavioural activation based depression therapy) to the HIV care situation of Uganda. The mental health activities are led by Prof Eugene Kinyanda with Mr. Richard Mpango and Dr Margaret Nampijja as project leaders.

KAF 156 study is a phase 2 clinical trial testing a new molecule for treating malaria to be conducted in Masaka. The trial will be a multicentre study involving 15 African and Asian countries. It will involve adults and adolescents. The study is a hospital-based trial treating participants with uncomplicated malaria. The MRC/UVRI and LSHTM trial is led by Dr Sylvia Kushemererwa.

C-ASSERT study is a multicentre trial funded by the NIH. The study will be conducted together with Makerere-IDI, Mbarara University of Science and Technology (MUST) and MRC/UVRI Masaka. This is a clinical trial investigating fluconazole and sertraline vs. Fluconazole and placebo in management of
cryptococcal infection among HIV positive participants with serum CrAg positive blood but asymptomatic for Cryptococcal meningitis. It will be an outpatient study however participants who get meningitis will be admitted and managed as inpatients. Enrolment will be done at the MRC clinic in Masaka Regional Referral Hospital. Dr Fredrick Kibengo will lead the MRC/UVRI and LSHTM trial.

We are part of a phase II, open label, single arm trial to evaluate the pharmacokinetics, safety, tolerability and efficacy of TMC2778 (Rilpivirine RPV), in antiretroviral naïve HIV-1 infected children aged 6 to <18 years (PAINT). The study is sponsored by Janssen and is led by Dr. Joseph Lutaakome at the Unit. Study is recruiting with a completion date Dec 2021.

**Strategic Timing of Antiretroviral Treatment (START)-(NCT00867048.**

We continue to follow study participants for primary and secondary end points. The study is expected to end by Dec 2021. The study is in its extended follow-up of participants with over 95% retention rates and is led by Dr Joseph Lutaakome at the Unit and the funder/sponsor is University of Minnesota - Clinical and Translational Science Institute.

We have developed a study, currently undergoing review to investigate the effect of HIV and Antiretroviral Therapy (ART) on bone health among Ugandans on combination ART. This is a cross-sectional study. We aim at estimating the prevalence of both low bone mineral density (BMD) and fractures among ART naïve PLWH and those who are currently on lifelong combination antiretroviral treatment [cART], and HIV-negative individuals, and also determine the risk factors for low BMD among these individuals. The study is led by Dr Joseph Lutaakome and Dr Billy Mayanja.

We have developed a Memorandum of Understanding with The AIDS Support Organisation (TASO) in order to study issues related with HIV as a chronic disease among others. TASO has the advantage of patient numbers and wider spread in the country. We will:

- Plan collaborative research activities in population health including HIV and associated co-morbidities.
- Where appropriate and mutually agreed upon, jointly seek funding for these planned collaborative research activities.
- Share specialized personnel, equipment, physical facilities and support services in ways that will make the planned collaborative research activities cost effective.
- Develop a critical mass of health research professionals in order to contribute to improved health of the population.
- Contribute to body of knowledge in order to influence policy and programming for disease prevention and eradication through joint publications.

The following are other studies being planned:

**Sickle cell (HESTIA 3)** trial sponsored by AstraZeneca. This is a randomised, double blind, parallel group, multicentre, phase III trial evaluating the effect of Ticagrelor - a platelet aggregation inhibitor in preventing vaso-occlusive crises (VOCs) in sickle cell patients. Preparations for the study are underway. This work will be led by Dr Sylvia Kusemererwa

**RIFT Valley Fever Vaccine Trial.** This is a phase I trial testing ChAdOx-RBF Rift Valley Fever Vaccine developed by the Jenner Institute. The study will be performed with the I-Vac Programme team. The
primary objective is to assess the safety and immunogenicity of the vaccine. The study will be carried out in the United Kingdom and MRC/UVRI Masaka. The draft protocol has been developed, the study will be testing 3 vaccine doses versus placebo. Vaccine manufacturing process is slow but stability tests will be available 2018. It is proposed this work to form part of PhD for Dr Zac Anywaine.

The Lake Victoria Consortium: We are part of this consortium also called The Wavuvi Concern co-founded in 2014 as an interdisciplinary group of scientists, researchers and clinicians committed to improving the health of people living in Lake Victoria fishing communities. With funding from various sources including IAVI, we are conducting a FF mobility studies.

HIV AND CANCER EPIDEMIOLOGY PROGRAMME
Progress and Future Plans April 2017 & Beyond

Robert Newton- Senior Clinical Epidemiologist

Professor Newton became head of this new programme in 2017. This new Programme builds on some of the activities of the former HIV Epidemiology and Prevention Programme, as well as greatly expanding the scope of our activities on cancer. The primary aims are to study i) the epidemiology of HIV infection in both general and in high-risk populations, ii) and to establish the burden and risk factors for non-communicable diseases (NCDs), particularly cancer. The epidemiological work of the programme encompasses three major cohorts (rural General Population Cohort, high-risk female sex workers, Fisherfolk cohort), and several hospital-based studies of HIV, cancer, stroke and diabetes. We also conducted work within the Uganda Police Force in Kampala, although this cohort has now closed because of a low incidence of HIV. These cohorts provided a platform for many epidemiology & prevention and intervention, basic science, HIV Care, and social science research as well as contributing to wider international collaborations, such as the ALPHA Network (Analysing Longitudinal Population-based HIV/AIDS data in Africa), the INDEPTH Cohort Consortium and the ANDLA (African Non-Communicable Disease Longitudinal data Alliance) collaboration. In addition, we have signed a Memorandum of Understanding with The AIDS Support Organisation (TASO) with a view to developing a platform for further studies of the health of HIV infected people living in real world conditions. Work has started on a study of integrating care on NCDs among people living with HIV and on long term anti-retroviral therapy.

NCD Epidemiology: In the GPC, the prevalence of abnormal liver function among adults may be as high as 40% and abnormal renal function of about 20%. Anaemia is also common and varies substantially by age and sex. Further work on these factors is on-going in the cohort, together with a nested case-control study of stroke. The Uganda component of the multi-centre H3A Diabetes Study is complete and analyses are underway.

Cancer Epidemiology: Within the GPC, we have shown that exposure to oncogenic infections is much more widespread than risk factors typically associated with western lifestyles. The seroprevalence
of *Helicobacter pylori* (*H. pylori*), Epstein Barr Virus (EBV), Kaposi’s sarcoma associated herpesvirus (KSHV) and Merkel Cell Polyomavirus (MCPV) was >90%; high risk human papillomaviruses (HPVs), 58% (22% HPV 16, 28% HPV 18); human immunodeficiency virus (HIV), 10%; chronic Hepatitis B (HBV), 12%. For non-infectious risk factors, 6.5% of adults reported current daily smoking, 11% at least weekly drinking, 12% were overweight and 30% reported low levels of exercise. Exposure to aflatoxin was ubiquitous. Appropriate cancer prevention strategies must therefore target oncogenic infections and aflatoxin exposure, as well as factors associated with lifestyle, such as tobacco.

**KSHV:** As part of work on KSHV, we have shown that participants of the GPC have the highest prevalence of KSHV ever reported (>90%), with the infection occurring mainly in childhood; conversely prevalence in urban settings in Uganda is generally slightly lower, particularly among children. In view of this, we have developed a substantial programme of work on KSHV in collaboration with colleagues at the National Cancer Institute, USA and with a local PhD student (Angela Nalwoga). Since KSHV is transmitted in saliva, we have examined risk factors for viral shedding in saliva within the Entebbe Mother and Baby Study (EMaBS). Among mothers, 18% (64/300) shed KSHV in saliva compared to 40% (40/100) of children; boys were almost twice as likely to shed KSHV as girls (48% [27/56] versus 25% [13/44]; p=0.06). We have also studied genetic factors associated with immune response to KSHV and shown that certain variants within the HLA region may be key. Work on the impact of coinfections (notably malaria) on transmission is on-going.

**Helicobacter pylori:** Having shown in the GPC that by the age of 10 years, infection with *H. pylori* is ubiquitous and that associated morbidity and mortality is high, we have successfully secured funding to: i) subtype the bacterium in more detail and to identify drug resistance patterns and ii) study rates of re-infection following successful eradication as treatment for dyspepsia and heart burn.

**Human papillomavirus:** Cervix cancer is the commonest cancer in Uganda and we have shown that the underlying cause – HPV – is also common. Uganda is one of the first countries in Africa to vaccinate school girls against infection and so in 2018 we will begin a study to examine the impact of a national vaccination scheme on circulating subtypes of HPV. Since many girls either do not attend school, or leave early, it is important to measure the effect of HPV vaccination at a population level.

**Hepatitis B & C:** Chronic active hepatitis secondary to HBV remains common in Uganda and we have recently argued that it should be given the status of a neglected tropical disease. Work on HBV is ongoing as part of broader studies of risk factors for liver cancer and cirrhosis. HCV is less common but tends to kill around half of all infected people. We have recently treated HCV infected individuals in the GPC and have successfully cured all of them. To our knowledge this is the first demonstration of cure in East Africa and demonstrates the feasibility in an African context.

**HIV-related cancers:** We have secured funding for a case-control study of Kaposi’s sarcoma in Uganda and hope to begin recruitment in 2018. The focus of this work will be to understand co-factors for disease, with the intention of identifying modifiable risk factors and better understanding pathogenesis. In relation to haematological malignancies, we recently highlighted similarities and differences in the prevalence and subtypes of Monoclonal B-cell Lymphocytosis between Uganda and the UK that may reflect fundamental differences in the pathogenesis of B-cell lymphoproliferative disorders. Work on conjunctival malignancies is on-going.
Prof. Janet Seeley

Prof. Janet Seeley is head of Social Aspects of Health programme and Professor of Anthropology and Health at the London School of Hygiene and Tropical Medicine. Prof. Seeley holds a PhD in social anthropology. She has headed the social science team in the Unit since 2008. She held the same position in 1989-1993, when she was part of the team which established the Unit.

Dr. Catherine Kansiime (PhD)

Dr. Kansiime is the Study Coordinator/Project lead on Menstrual health interventions and School attendance among Ugandans (MENISCUS-2) at MRC/UVRI/LSHTM Uganda Research Unit. She has a Bachelor’s degree in Social Sciences, a Master’s degree in Clinical Epidemiology and Biostatistics and a PhD in Public Health all from Makerere University, Uganda. Dr. Kansiime has eight years’ experience in research and four years as Project Manager.

Dr. Agnes Ssali (PhD)

Dr. Agnes Ssali is a social scientist, trained in social work and social administration, social sector planning and management, and public health and holds a PhD in International Development. She has been with MRC since 2003 and is a focus area lead in social sciences for our work with key populations.
**Dr. Godfrey Sui (PhD)**

Dr Godfrey Sui is a Senior Scientist in the Social Aspects of Health Programme. He holds a PhD from University of Glasgow, UK. Godfrey’s PhD was funded by the Unit. He joined the Unit as a Post-Doc Fellow in 2012. Godfrey currently leads the parenting work in the programme.

**Dr. Joseph Mugisha**

Dr. Joseph Mugisha is a Senior Scientist in the programme, and one of the focus area leads. Mugisha holds a PhD in Epidemiology and population health from the London School of Hygiene and Tropical Medicine. He qualified as a medical doctor from Mbarara University of Science and Technology. He joined MRC in 2003 and has worked as a clinician, clinical trials coordinator, project leader and now senior scientist. He is a mixed methods researcher. His research interests are health and social issues associated with HIV and ageing in low and middle-income countries. He remains clinically active.

**Dominic Bukenya**

Mr. Bukenya Dominic is a scientist in the Social Aspects of Health Programme. He holds an MA in International Health from the University of Bergen, Norway. He joined the Unit in September 2008 as a scientific officer. His focus research areas lead to our work on chronic disease prevention, diagnosis, treatment uptake and adherence.

**Dr. Rwamahe Rutakumwa (PhD)**

Dr. Rwamahe Rutakumwa is a Senior Scientist in the Social Aspects of Health Programme. He holds a Ph.D in Rural Sociology from the University of Alberta, Canada. He joined the Unit as a Post-Doctoral Social Scientist in November 2012. He is a focus area lead for our work with children and adolescents.
Rachel Kawuma

Rachel is the focus area lead for our work with key population. Previously, she was a social science team leader contributing to projects on adolescent health, health system improvements and microbicide research trials. Rachel holds a Master’s degree in Counselling psychology.

Flavia Zalwango:

Flavia Zalwango is a Scientist in the Social Aspects of Health Programme. She holds a MA in Social Sector Planning and Management from Makerere University, Kampala and a MSc in Social Science (gerontology) from the University of Southampton, UK. She joined the Unit as a Social Scientist in November 2008. She is a project lead for our work with children and adolescents and a researcher on the Parenting Programme.

Kenneth R. Katumba:

Kenneth Katumba is a multi-disciplinary Health Economist with experience from France, West and Eastern Africa. He is the Health Economist at the Unit, carrying out a range of Health Economics Research. Kenneth has an MPH with a concentration in Health Economics from the French School of Public Health (EHESP).
SOCIAL SCIENCE PROGRAMME

The aim of the programme was to further our understanding of the structural drivers and social impact of HIV through the life course. Our research focused on three themes: 1. HIV across the life course; 2. HIV, relationships and vulnerable groups; and 3. the long-term social and economic impact of HIV.

1: HIV across the life-course

a. HIV in children and adolescents
i) Adhering to HIV treatment during adolescence: a multi method qualitative study in Uganda (PI Prof Tim Rhodes, LSHTM, Co-investigators Dr Sarah Bernays and Prof Janet Seeley, (funded by ESRC and MRC/UVRI core funding 2011-2016). This study was embedded within an international clinical randomised controlled trial (RCT) led by Prof Diana Gibb of University College, London). The RCT tested a new administration of HIV treatment for adolescents, known as Short Cycle Therapy (SCT), in which young people take their treatment for five days and then have two days off at the weekend. The social science sub-study provided essential evidence on context and experiences of taking part in a trial, finding that there is an urgent need to improve communication with young people regarding their adherence challenges to enable them to discuss ‘slippages’ and missed doses.

ii) Growing up in a setting with high HIV prevalence: a qualitative longitudinal study of young people in rural and urban settings in Uganda (PI Prof Janet Seeley with Dr Victor Musiime, JCRC and Makerere University, and Dr Sarah Bernays) (funded by ViiV Health Care 2014-2016). This longitudinal qualitative study traced the process of growing up with HIV in Uganda and the influence this has on young people’s preventive and treatment seeking behaviour.

iii) Risk perception, behaviour, and structural drivers of HIV among rural and urban adolescents and to inform the design of adolescent-friendly HIV prevention and vaccine development programmes (co-PIs Dr Rwamahe Rutakumwa and Flavia Zalwango) (funding IAVI investigator award). This study explored and compared rural and urban adolescents’ HIV risk perception and behaviour, and structural drivers of their HIV vulnerability in order to inform the design of a behavioural intervention for HIV prevention among this population sub-group. In addition, we investigated adolescents’ interest and future participation in HIV vaccine trials as well as barriers and facilitators of their participation in the trials.

iv) Odyssey Qualitative sub-study: how does moving onto second-line HIV treatment affect young people’s treatment engagement? (sub-study PI Dr Sarah Bernays, with Prof Seeley and Stella Namukwaya, MRC/UVRI). Funded by ViiV Healthcare through the PENTA Foundation 2017-2019. Embedded with the ODYSSEY trial (investigating second line ART among adolescents at JCRC) we are investigating the experiences of children and young people in the ODYSSEY trial being moved onto second line antiretroviral treatment (ART) (ODYSSEY B) on order to identify their support needs to maximize their adherence.

v) Developing measures of parent-child relationships – a tool development project (PI Dr Godfrey Siu with Prof Daniel Wight (Glasgow University), Prof Seeley and Flavia Zalwango) (funded by MRC Social and Public Health Science Unit [University of Glasgow] and MRC/UVRI core funding 2012-2017). We developed survey measures for parents and children aged 10-14 to investigate child outcomes associated with parenting styles and to evaluate parenting interventions, particularly those intended to modify authoritarian parenting.

vi) Parenting for good behaviour and respectability: Developing and piloting an intervention to reduce sexual and gender-based violence in Uganda (PI Dr Siu) (funded by Sexual Violence Research Initiative/
This project addresses familial processes that predict sexual and gender-based violence and child maltreatment in Uganda for the primary prevention of gender-based violence. We have developed and are testing a promising intervention that draws on pre-existing motivation in families: the concern for their respectability, largely achieved through children’s good behaviour and respect for parents.

vii) Young children’s behaviour and local constructs of parenting (PI Prof Mark Tomlinson, Stellenbosch University, in-country PI Dr Godfrey Siu) (funded by an anonymous donor through Stellenbosch University 2015-2016). This gathered essential basic data to inform work in Uganda and South Africa for an early parenting intervention aimed to reduce child aggression and behaviour disturbance. We worked with participants from the Good Health for Women Project clinic, Kampala collecting both quantitative and qualitative data.

b. Management of HIV as a chronic condition, including adherence

The Complications of Long-Term Antiretroviral Therapy in Uganda (CoLTART) (see HIV Care Programme) provided an opportunity to investigate through qualitative methods the individual and structural level reasons why some patients failed to adhere to ART and subsequently develop ART failure, despite the ART adherence counselling provided.

i) A qualitative sub-study of individual level factors associated with ART Adherence among participants in the Complications of Long-Term Antiretroviral Therapy in Uganda (lead Dominic Bukenya) (funded by MRC/UVRI core 2015-2016). We interviewed 60 CoLTART participants about challenges with sustained use of ART, including persistent feelings of stigma, problems combining taking drugs daily and treatment access while managing mobile-livelihoods.

ii) Reduction of early mortality in HIV-positive adults and children starting antiretroviral therapy (REALITY) – social science sub-study (PI Prof Diana Gibb, lead social scientist Prof Seeley with Rachel Kawuma) (funded by MRC/DFID/Wellcome, 2014-2016). This study, conducted in Uganda and Zimbabwe, was embedded in the REALITY trial which tested the effectiveness of interventions aimed at reducing excess HIV-related mortality and morbidity. Our findings showed that despite the availability of treatment many people did not consider themselves in need of ART because their health was ‘good enough’. Several had a limited appreciation that ART is about maintaining health, rather than restoring health to someone who is ill.

iii) Bottlenecks study: a qualitative investigation of the barriers and enablers to successfully navigating the HIV care system in the era of widespread ART availability (PI Dr Alison Wringe, LSHTM, Uganda lead Dominic Bukenya with Prof Seeley) (funded by Bill and Melinda Gates Foundation and Wellcome Trust through the ALPHA Network 2015-2016). This study in Uganda, Tanzania, Malawi and South Africa provided an opportunity to study and understand better how HIV-positive patients navigate the different care cascade stages.

iv) HIV Counselling in Uganda: Mapping the terrain (PI Dr Faith Martin, University of Bath, with Dr Josephine Birungi (The AIDS Support Organisation [TASO]), and Winfred Nalukenge (MRC/UVRI) and Prof Seeley (funded by the British Academy 2015-2016). The project mapped current counselling practice and training needs in TASO, providing valuable information on the need for the design and delivery of mental health interventions for counselling.

i) Optimising clinical care, treatment strategies and use of laboratories for ART roll out in Africa: The Lab-Lite Project (PI Prof Diana Gibb in collaboration in Uganda with JCRC. MRC/UVRI lead Prof Seeley, Health economics lead Stella Settumba/Kenneth Katumba, statistics lead Dr Sylvia Kiwuwa) (funded by DFID, 2011-2015). This built on the DART and ARROW projects to describe and compare national and inter-country delivery of training, clinical care and use of laboratories and monitoring in health centres in South African Medical Research Council and Bernard van Leer Foundation, Netherlands, 2013-2018).
national ART roll-out through a survey of representative sites.

c) Impact of HIV on older people

i) The direct and indirect effects of HIV/AIDS on the health and wellbeing of older people study (WOPS). Waves 2 and 3 (PI Dr Ties Boerma WHO, in-country PIs Prof Seeley and Dr Joseph Mugisha) (funded by NIA/NIH through WHO and MRC/UVRI core 2013-2019). This project was the second and third waves of a study conducted with a cohort of older people in 2010/2011. The study contributes evidence to guide the development and implementation of health programmes to meet older people’s needs, especially those living with or otherwise affected by HIV.

ii) Addressing the financial, social and health needs of older Ugandans: A feasibility study for a multi-level social protection intervention (PI Dr Enid Schatz, University of Missouri) (funded by University of Missouri, 2015). This project focused on Ugandans aged 60 and over to: (1) assess the feasibility of a large scale intervention that packages three levels of inter-related social protection for older Ugandans; and (2) prepare a grant proposal for a full-scale implementation of the intervention.

2: HIV, relationships and vulnerable groups

i) Enhanced HIV prevention in the Republic of Uganda under the President’s Emergency Plan for AIDS Relief (PEPFAR) Co-PIs Dr Edward Katongole Mbidde (UVRI) and Prof Seeley (funded through CDC, 2011-2018). This project scaled up the existing prevention interventions within the Good Health for Women Project. In addition to prevention activities related to safer sex and alcohol the project is now offering ART services to participants and providing enhanced treatment for the young children of clinic attendees. An evaluation of the programme led by Dr Agnes Ssali and Winfred Nalukenge has been conducted 2017-18.

ii) Structural drivers of HIV and other STI in fishing communities and women at high risk of HIV infection. Led by Martin Mbonye with Prof Seeley (funded by MRC/UVRI core 2011-2017). Building on work from the previous quinquennium, our purpose was to investigate the social context of sexual partnerships among women participating in the Good Health for Women Project and their regular partners and clients, as well as men and women in fishing villages in Masaka. The study complements the Basic Science programme-led Superinfection study and ‘HIV-1 Molecular Epidemiology in Uganda: the strains, distribution and spread of HIV-1 in Uganda’ (participants are also included from the General Population Cohort, Kyamulibwa for this second study).

iii) Understanding Adolescent Vulnerability: transactional sex and sexual exploitation in Central Uganda (funded by Oak Foundation 2015-2016), led by Dr Kyegombe (LSHTM and research associate MRC/UVRI) with Richard Muhumuza. The aim was to provide a detailed understanding of the norms, expectations, and contexts that shape and perpetuate the practice of transactional sex in urban and rural Uganda. The study was conducted in two sites, in Kampala and Masaka District.

iv) Biometric finger print technology for identification of prospective HIV prevention trial participants from fishing communities and enhancing retention in future trials. PI Martin Mbonye (funded by IAVI Investigator award). This project showed that it is possible to improve tracking of trial participants who are mobile and can contribute learning for interventions to improve linkage to care. This project was conducted in fishing sites in Masaka and Kalungu districts.

v) A cognitive behavioural and structural HIV prevention intervention for young Ugandan women engaging in high risk sexual behaviour (ZETRA). PI Dr Rachel King, UCSF, Prof Seeley co-PI (funding NIH R01 2016-2021). This project is with young women attending the Good Health for Women Project clinic. ZETRA is a randomized trial of a behavioural and structural intervention. The intervention focuses on repeat HIV testing and counselling every six months, and increasing and sustaining sexual risk reduction
behaviours to reduce STIs, HIV, and unplanned pregnancy.

v) Hormonal Contraception and Bacterial Vaginosis (HCBV): The effect of norethisterone enanthate on recurrent bacterial vaginosis among women at high risk for HIV infection PI Dr Suzanna Francis, LSHTM, in-country co-Is Prof Seeley and Dr Yunia Mayanja. (MRC new investigator grant for Dr Francis, 2017-2020). Bacterial vaginosis (BV) is highly prevalent among women in Africa and is associated with HIV acquisition. Developing robust treatment strategies to prevent recurrent BV is important for HIV prevention in key populations at high risk for HIV infection. This study investigates the effect of hormonal contraceptives on recurrent BV, vaginal microbiota and inflammatory markers among women at high risk for HIV in the Good Health for Women Project in Kampala, Uganda.

3: The long-term social and economic impact of HIV

Analysis from work on this theme in the previous quinquennium work has continued and has been published. We developed new ideas and carried out one innovative project under this theme.

i) Susceptibility to HIV: the use of hope as a property for targeting interventions. An exploratory study in Uganda and Tanzania co-PI Prof Tony Barnett (LSHTM) and Prof Seeley (MRC/UVRI core 2012-2013 for data collection; continued collaboration with other countries). We developed an understanding of the use and meaning of the concept ‘hope’ in the Ugandan and Tanzanian settings; tested the existing ‘Snyder scale’ to measure individual hope and hopelessness; and examined whether an association exists between hope and variables associated with individual and group HIV susceptibility. Our findings from Uganda show how hope and hopelessness as experienced by individuals and groups reflect their experience of the opportunities and constraints offered by the structures within which they live. We are currently analysing the Tanzania data and data from similar studies in Bangladesh and South Africa.

iii) Developing a robust and supportive ethical and governance framework for genomic research in Africa – an exploratory study in Ghana, Uganda and Zambia co-PI Prof Michael Parker (University of Oxford) and Prof Seeley with Dr Rwamahe Rutakumwa (funded by Wellcome Trust through University of Oxford, 2015-2018, [Prof Parker]). This project is linked to the H3Africa consortium projects (see Epidemiology and Prevention) and is contributing to the development of an ethics and governance framework for genomics in Africa.

Social science contributions to other Programmes

In addition to the projects above the Social Science programme has made important contributions to other Programmes work:

Epidemiology and Prevention Programme
Inputs to ‘The epidemiology and genetics of communicable and non-communicable diseases in the General Population Cohort in Kyamulibwa, Uganda’ and associated projects. The social science component of the pilot ‘Uptake and impact of HIV combination (HIVCOMB) interventions on HIV incidence among fishing communities in Uganda’ which was led by Prof. Kamali. We are contributing to a discrete choice experiment study assessing the acceptability of PrEP among fisherfolk in Uganda, and there is a social science component in the GSK funded project on renal disease.

HIV Care Programme
There were social science sub-studies (qualitative and health economics) of the Improving the health systems response to chronic diseases in Africa (PI Prof Heiner Grosskurth), in addition to the COLTART substudy, described above.

Basic Science Programme/Epidemiology and Prevention Programme
Social science studies related to the ‘Superinfection project’ and the ‘Molecular epidemiology project’ are described under Focus area 2 (section 2: HIV, relationships and vulnerable groups) above.
Co-infection Studies Programme

Early neurodevelopmental outcomes after neonatal encephalopathy in Uganda: Neurodevelopmental follow-up of the ABAaNA cohort at 12-15 months. (PI Dr Cally Tann) We contributed to qualitative design, data collection and analysis and writing up.

LaVIIISWA social science sub-study – Community perceptions about interventions to control schistosomiasis in Koome sub-county, Mukono district. Interviews and group discussions were undertaken in selected sites in the LaVIIISWA project area to find out what people think about control measures, now that the LAVIIISWA project has finished.

Brief for future (2017 onwards): Social Aspects of Health across the Life Course Programme

The aim of the programme is to further our understanding of the social aspects of health and wellbeing for specified individuals and populations to inform the design, implementation and evaluation of interventions, as well as contribute to policy development. This programme focuses on different stages of the life course and specific populations: 1) Children and adolescents; 2) Key (at-risk) populations; 3) People 50 years and older. Each focus area is led by two or three Ugandan senior members of the programme team. In addition to the on-going projects described in the previous section, projects which have begun in 2017, groups by focus area, include:

Children and adolescents (led by Dr Rwamahe Rutakumwa, Dr Catherine Kansiime and Flavia Zalwango)

i) Youth, mobility and health (including HIV) risk: a qualitative longitudinal study of young rural migrants to urban centres PI Prof Seeley, co-I Dr Bernays (LSHTM) with Africa Health Research Institute (South Africa) (funded by MRC/UVRI core and ViiV Health Care 2017-2018). This longitudinal study investigates how this widespread rural-urban migration exposes young people to health risks and affects their health-related attitudes and behaviours. Mobility and the specific vulnerabilities associated with adolescence, coupled with sexual violence, drug and alcohol use, unemployment and poverty, continue to drive HIV incidence.

ii) ‘Menstrual health interventions and School attendance among Ugandans (MENISCUs-

Key populations (led by Dr Godfrey Siu, Dr Agnes Ssali and Rachel Kawuma)

i) Barriers and facilitators of HIV ‘test and treat’ among key populations PI Prof Seeley with Rachel Kawuma. In December 2013, the Uganda Ministry of Health (MoH) approved “Test and Treat” programmes for certain key populations for HIV prevention, such as sex workers (SW) fisherfolk (FF), military and police personnel and prisoners. We are investigating potential interpersonal, relationship and structural factors that create barriers to the uptake of HIV treatment of key populations in Uganda to contribute to improvements in uptake. We aim to develop this work further with TASO.

ii) Men and HIV prevention (PI Martin Mbonye [PhD candidate] supervisors Dr Godfrey Siu and Prof Seeley) funded by THRIVE. Our findings from the REALITY trial, and other research, show that men
seek HIV-treatment late, and once in treatment may not be retained in care. Some men are at particular risk of being lost to care. Building on Godfrey Siu’s PhD research, Martin Mbonye has commenced his research to look at the influence of different types of masculinity on treatment seeking, we will develop an intervention to address the barriers and facilitators of treatment seeking behaviours.

Older people (led by Dr Joseph Mugisha and Dominic Bukenya)

i) The direct and indirect effects of HIV/AIDS on the Health and wellbeing of older people study (WOPS). Wave 3&4 PI Dr Boerma (University of Manitoba) and Dr Chatterji (WHO), in country co-PIs Prof Seeley and Dr Mugisha. (funding by NIA/NIH through WHO). The overall goal is to contribute evidence to guide the development and implementation of health programmes to meet older people’s needs, especially those living with or otherwise affected by HIV. A detailed survey was repeated in 2017 and will be repeated in 2018-2019 with approximately 600 people aged 50 and over in Kalungu, Masaka and Entebbe, using the tool and approach used in Waves 1, 2 and 3.

ii) Leaving no one behind: Identifying approaches to improving HIV treatment outcomes among older Ugandans PI Prof Seeley, co-Is Dr Enid Schatz (University of Missouri) Dr Mugisha, Dr Joel Negin (University of Sydney) and Prof Helen Weiss (LSHTM). This early phase study addresses the gap in knowledge on older persons’ barriers to ART access and adherence in sub-Saharan Africa (SSA), and will revise and strengthen theory on the role that social support and community play in ART access and adherence. We will develop an effective intervention to address older Ugandans’ ART access and adherence and their feelings of stigma and social isolation.

iii) The cost of illness among older people in Uganda PI Kenneth Katumba, funding MRC/UVRI core. Our past and current work documenting the direct and indirect effects of HIV on older people, and developing social protection interventions for older people, has not included work on costing from the patient or health system perspectives. To our knowledge no studies have measured the cost of illness or extent of impoverishment among older people and their caregivers as a result of lost livelihoods and paying for medication and/or health care in Uganda or elsewhere in East Africa. This work is being nested within WOPS Wave IV (2018)

iv) Developing a wellbeing index for the evaluation of public health interventions in Uganda: Capabilities and happiness measures PI Dr. Giulia Greco, co-Is Kenneth Roger Katumba and Prof Seeley, funding MRC Fellowship (Dr Greco). The overall aim of this project is to develop a broad outcome measure based on the Women’s Wellbeing Index developed in Malawi. The validity of the measure in Uganda will be tested and policy use of the wellbeing measure investigated.

Other projects

i) Cultural, social and economic influences on ongoing S. mansoni transmission, despite a decade of mass treatment, and the potential for change PI Dr Poppy Lamberton, Glasgow University (funding GCRF). Our aim is to understand better how people living in endemic communities manage their risk of schistosomiasis and how they might change their behaviour if additional resources were provided. This project has two overlapping parts. In part one, we will work directly with communities who experience a lot of schistosomiasis to establish how people currently try to reduce the risk of infection for themselves and their families as well as the risk of passing those infections on through open defecation. In the second part, information gathered above will be incorporated into household surveys to measure what is needed to change an individual’s behaviour.

Key collaborations and funding

We list individual collaborators and funding sources above. We continue to build our internal and external collaborations, working with, for example, Makerere University, TASO, district health services, LSHTM, University of Glasgow and WHO staff.
BASIC SCIENCES PROGRAMME
Achievements March 2015- April 2017

PATHOGEN GENOMICS, IMMUNITY AND PHENOTYPE PROGRESS
Future Plans April 2017 & Beyond.

Professor Pontiano Kaleebu
- Head of Programme

Prof. Pontiano Kaleebu is the Director of the MRC/UVRI & LSHTM Uganda Research Unit and Director Uganda Virus Research Institute. He also heads the Pathogen Genomics Phenotype and Immunity Programme. Prof. Kaleebu holds a medical degree from Makerere University, a Diploma in Immunology and a PhD from the University of London now Imperial College. He was admitted to the Fellowship of the Faculty of Medicine, Imperial College, London in 2011 and to the Fellow of the Royal College of Physicians-Edinburgh in 2015. He leads the EDCTP East African Networks of Excellence. He serves on many National and International committees including chairing the National HIV drug resistance working group. His main research interest includes HIV vaccine research especially understanding protective immune responses, HIV diversity and resistance to ARVs.

Dr. Jesus Salazar
- Programme Leader Track

Dr. Salazar is an immunologist/virologist with >35 years of research experience in premier institutions in the US, Mexico, Israel, and Uganda. His participation in the Center for HIV/AIDS Vaccine Immunology (CHAVI) consortium (2005-2012) allowed the dissection of the genetic identity, evolutionary pathways and biological properties of HIV-1 transmitted/founder viruses; these studies rank in the top 1% of highly-cited researches (Thomson Reuters). His research interest includes mechanisms underlying HIV-1 transmission bottleneck through a comprehensive and systematic analysis of the HIV-1 strains being transmitted and spread in Uganda. Other activities include the genetic identification and characterization of zoonotic viruses with outbreak/pandemic potential and capacity building in virus discovery and diagnostics.
Dr. Pietro Pala
- Senior Immunologist

Dr. Pietro Pala is interested in T-cell mediated immunity against viruses, particularly influenza, herpes simplex, respiratory syncytial virus, which he investigated at NIMR (UK), Ludwig Institute (CH), SmithKline Beecham Biologicals (Belgium) and Imperial College London. He joined the Uganda Unit to focus on HIV-1. He is trying to understand how HIV-1 can circumvent immune responses: why is there no natural immune mediated clearance of HIV infections? Why don’t some people become infected despite considerable exposure to HIV? Why do others acquire superinfections while they have apparently strong immune responses to an initial HIV infection and what are the implications for HIV vaccines? How do previous or concurrent immune responses to other pathogens influence HIV acquisition, progression to AIDS or the response to vaccines? His current project investigates whether T cell responses against HIV-1 can develop in highly exposed women that are protected from infection by pre-exposure prophylaxis.

Dr. Jennifer Serwanga (PhD)
- Cellular Immunologist

Dr. Jennifer Serwanga is a Ugandan senior scientist (Immunology) within the PGPI programme. She received her PhD from Murdoch University, Western Australia, and believes that there is no single right approach to combating HIV-1 AIDS. She has thus trained in a range of disciplines to enable evaluations of HIV specific T cell and B cell responses that may be relevant for vaccine formulation. She evaluated the neutralizing antibody responses to the first HIV vaccine trial in Uganda and has widely contributed to the understanding of immunological correlates of protection from HIV disease progression. She is involved in Ebola vaccine development currently in clinical trials; polio end game implementation, and in understanding the coevolution of neutralizing antibody breadth to clade A and D infection.

Dr. Deogratious Semwanga (PhD)
- Senior Research Scientist

Dr. Deogratius Ssemwanga is a Molecular Virologist and a Senior Scientist in the Pathogen Genomics, Phenotype and Immunity Programme. He is involved in studies to investigate the Virological and Immunological correlates of HIV-1 superinfection. His other research interests include studies on HIV-1 drug resistance and molecular epidemiology of HIV-1 in Uganda. He is involved in H3ABionet, a network tasked to develop bioinformatics capacity in Africa’s BRecA (Bioinformatics Research Capacity in Africa, 2017-2022) project that will establish Bioinformatics programs at Makerere University. He was recently awarded an EDCTP career development fellowship to study the Immunological Selection of Recombinants following HIV-1 Superinfection (2016-2019).
Dr. Sheila Balinda (PhD)  
- Molecular Virologist

Sheila Balinda is a Molecular Virologist and received her Doctoral training under a sandwich program (btw. Makerere University and University of Copenhagen), an MSc in Applied Molecular Microbiology (University of Nottingham) & BSc Biochemistry (Makerere University). She has been involved in the management of the Affordable HIV drug resistance test for Africa (ART-A) and Pan African studies to evaluate HIV Resistance (PASER). Currently, a postdoctoral fellow at the Unit working on the determination of biological properties of HIV founder viruses relative to the non-transmitted using Infectious Molecular clones (IMCs), a project funded by IAVI-VISTA program. In addition, she lectures in an honorary capacity at Makerere University, College of Health Sciences.

Dr. Jacqueline Kyosiimire Lugemwa (PhD)

Jackie’s PhD research work was on Virologic and Immunologic studies of HIV-1 infected Long term non progressors and Rapid progressors in Uganda. This study was undertaken as part of the GISHEAL (Genetic and Immunological studies of HIV-1 infected European and African Long-term non progressors) project funded through the European Union. The main objective of this study was to examine and define immune and host genetic correlates of protection against disease progression mediated by HIV-1-specific CD8+ and CD4+ T-cells. After her PhD, she has worked as a study investigator/ Scientist on a study investigating microbial translocation and T-cell activation in HIV ART-treated patients that stop or continue taking Cotrimoxazole prophylaxis in Uganda.

Dr. Zacchaeus Anywaine  
- Senior Scientist

SEE BIO ON PAGE 23
Dr. Fredrick Lutwama - Scientist

Dr. Fredrick Lutwama received training in Medicine and Surgery from Makerere University College of Health sciences. He then joined the Infectious Diseases Institute at Makerere where he worked on studies that evaluated the performance of less expensive laboratory assays for monitoring patients treated with ARVs and the DART study. He subsequently joined the South African Tb Vaccine Initiative at the University of Cape Town, South Africa to undertake his PhD training in Clinical sciences and Immunology. He is currently a postdoctoral research scientist on the VISTA program at MRC/UVRI. Fredrick research project focuses on assessing the sensitivity of HIV-1 envelope clones isolated from participants in the Lake Victoria basin to a panel of broadly neutralizing antibodies. These studies will contribute to our understanding of how we can improve the design of immunogens for use in novel HIV-1 vaccines.

Brief of the past aims and key achievements

In the past three years, the Basic Sciences Programme aimed at increasing our understanding of the virology and immunology necessary to prevent and treat HIV-1 infection. The Programme focused on six themes: Theme 1, Molecular virology studies to better understand the epidemic, and the development of resistance to HIV drugs. Key findings include a report led by P. Kaleebu and C. Watera showing high rates of K65R and TAMs after 12 months on treatment in Ugandan patients on Tenofovir (TDF). A follow up study under the TenoRes Study Group for which we were part, looking at global epidemiology of drug resistance recorded drug resistance in a high proportion of patients after virological failure on a tenofovir-containing first-line regimen across low-income and middle-income regions. Effective surveillance for transmission of drug resistance is therefore crucial. These observations have stimulated discussions nationally and internationally as to how to preserve this important drug being used for PrEP in addition to being a first line recommended drug of choice.

We have furthermore shown that pre-treatment drug resistance is very high in Uganda exceeding the
10% threshold NNRTI resistance set by WHO for changing first-line ART. This has led to the planned change of first line regimens to include dolutegravir an integrase inhibitor. We also showed high rates of pre-treatment NNRTI resistance in children under PMTCT before introduction of Option B+, this reinforces the urgent need to overcome barriers to scaling up pediatric protease inhibitor-based regimens in sub-Saharan Africa and underscore the need to accelerate the study and approval of integrase inhibitors for use in young children.

Our work under PANGEA (PI Deenan Pillay, A.L. Brown and others) shows that using near full-genome HIV sequence data rather than small genome regions like pol, improves use of phylogeny to study epidemics.

Finally, in the fishing communities, in a study led by Silvia Kiwuwa Muyingo, we demonstrated that a large proportion of HIV sexual transmissions occur within households and within communities even in this key mobile population. The findings suggest localized HIV transmissions and hence a potential benefit for the test and treat approach even at a community level, coupled with intensified HIV counselling to identify early infections. Theme 2, Virological and host factors associated with HIV-1 superinfection. Key findings include, the identification for the second time ever, of linked transmission with samples from a superinfecting person before SI, providing opportunities to study this phenomenon in order to contribute further to understanding of protective immune responses (led by Deo Ssemwanga and Andy Redds). We have also demonstrated that HIV-1 superinfection can occur both in the presence, and in the absence of broadly neutralizing antibodies as demonstrated by Jennifer Sserwanga. Theme 3, Potential protective immune responses against HIV through PrEP in highly exposed populations, the PREPPIE study led by Pietro Pala. The study aims to test whether allowing more HIV exposure over time might eventually induce protective immunity. This is a proof of the concept that immunity to HIV might be achieved if the initial infections are hampered by chemoprophylaxis, simulating vaccination with a live attenuated virus strain. Progress: Enrolment and follow up continues. Theme 4, Impact of worm co-infections on HIV immune responses. Key findings, so far our data does not support the hypothesis that S. mansoni down modulates innate or HIV-specific Th1 responses in HIV/S. mansoni-coinfected individuals, work that formed part of Andrew Obuku’s PhD project. Theme 6, Immune responses to HIV vaccine candidates. A phase I double blind placebo-controlled clinical trial to evaluate the safety and immunogenicity of the combination of DNA-HIV-PT123 and AIDSVAX®B/E in HIV-1-uninfected adult participants with or without underlying Schistosoma mansoni infection (IDEA EVO6) was completed. The trial was sponsored by the EuroVacc Foundation and was conducted at both MRC/UVRI, Masaka and UVRI-IAVI centre, Entebbe among healthy adults aged 18-45 years. Key findings include: The vaccine regimen was well tolerated and induced strong gp120, gp140 and V1V2 region-focused binding IgG and neutralising antibodies against tier 1 isolates. There was a trend of lower responses in vaccinees infected with S. mansoni, which attained statistical significance with a number of antigens. Other studies included:

• ROUTINE AUDIT - MASAKA LABS
• LAMBU LANDING SITE
an immunological substudy of the CO-STOP trial led by Jackie Kyosimire and Pietro Pala, aimed at investigating whether the beneficial effect of use of co-trimoxazole prophylaxis in HIV disease is due to reduced microbial translocation from the gastrointestinal tract (leaky gut) and immune activation.

• a study led by Jackie Kyosimire to look at the effect of pre-existing immune status and endemic infections on Hepatitis B vaccine mediated immune responses among HIV negative adult Ugandans.

• studies led by Pietro Pala looking at the Immunologic and Proteomic Biomarkers of Endemic Burkitt’s Lymphoma.


• participation in Zika research in order to study whether Uganda is vulnerable to a Zika virus epidemic (PI P. Kaleebu, others Jesus Salazar (further information below).

• participation in the evaluation of HIV Rapid HIV tests to come up with alternative testing algorithms for Uganda led by P Kaleebu. As a result of this work, Uganda has adopted a new HIV Rapid Test algorithm.

• in collaboration with Glasgow CVR MRC Unit (Emma Thompson) and Wellcome Trust Sanger Institute (WTSI) Manj Sandhu, we genotyped hepatitis C positive samples for the GPC and found that the samples are genotypes 4 (rarely described variants) and the second genotype 7 (nearly 30% different from genotype 7a which is the only reported genotype 7 of HCV).

• as part of the International Collaboration for the Genomics of HIV, work led by Manj Sandhu we have identified a novel region on chromosome 1 that appears to influences set point Viral Load.

In the current funding cycle starting April, 2017, the above programme was modified to become a programme to study pathogen genomics, phenotype and immunity. Below, we present some of the progress since these changes.

Pathogen Genomics, Immunity and Phenotype Progress and future plans

This new Programme builds on progress made under the previous Basic Sciences Programme and aims to conduct research that will lead to better understanding of pathogen genomics in order to characterise diseases and epidemics for better control and to investigate virological, immunological and genetic factors required for the development of effective interventions against HIV-1. We want to take advantage of a) well characterised cohorts and biobanks b) Unit track record in intervention trials c) investment in new technologies in genomics, immunological assays and bioinformatics and d) established collaborations. The Programme is focusing on key objectives and targets under four major projects and additional smaller studies that are largely be externally funded. These activities are conducted in collaboration with the other four Unit Programmes and under the HIV and ENERI Themes.

We are continuing to monitor the HIV epidemic by characterising the circulating HIV-1 subtypes especially in recent infections and use near full length genome sequencing to understand better the increasing recombinant viruses using better bioinformatics tools. We are using molecular in combination with social-epidemiological and modelling approaches to provide novel avenues to monitor epidemic trends and transmission dynamics, and to contribute to targeted interventions through the identification of transmission clusters and hotspots. Part of this work is forming a PhD project for Nicholas Bbosa.

HIV drug resistance (HIVDR) is emerging as one of the most important challenges to ART roll out for both care and prevention, more so in resource limited areas characterized by the use of limited ARV regimens, stock outs, regimen change based on available supply and often limited use of viral load (VL)
testing to monitor treatment outcomes. We are expanding our drug resistance studies in collaboration with colleagues at UVRI (Christine Watera, Edward Mbidde) and the Ministry of Health to contribute to improved interventions. We are well positioned to provide such data being a National and Regional Reference laboratory for HIV DR and active participants in related national activities.

We are undertaking a comprehensive and systematic analysis of HIV-1 viruses representing the subtypes and recombinant forms circulating in Uganda to elucidate if transmitted/early HIV-1 viruses have recurrent patterns (signatures) that distinguish them from chronic viruses, work led by Jesus Salazar.

We propose to strengthen our work in antimicrobial resistance (AMR) currently acknowledged as a rapidly emerging threat to the management and treatment of infectious diseases globally. Besides HIV, our focus will be on enteric diseases, bloodstream infections and STIs.

We are continuing the MRC funded studies aimed at understanding whether Zika virus exists among humans, primates and mosquitos in Uganda and conduct studies to molecularly characterize the Zika genome.

In the process of looking for Zika and working in partnership with other colleagues at UVRI (Julius Lutwama, Robert Downing, Jonathan Kayondo) and MRC-Glasgow University (Emma Thompson), other viruses are being identified such as the Le-Dantec (LDV) and a new Adumi viruses.

Our studies to understand the events surrounding HIV superinfection (SI) continue. Deo Ssemwanga obtained an EDCTP fellowship to study recombination events during superinfection. Through this work we have strengthened our capacity to perform HIV neutralization assays led by Jennifer Serwanga. This information will contribute to knowledge on protective immune responses and viral evolution.

We are continuing with the PREPPIE study (led by Pieto Pala) looking at the potential protective immune responses against HIV through PrEP in highly exposed populations. Gilead has provided the drugs for this study.

We are participating in other studies to contribute to HIV Vaccine research and development. These are largely IAVI funded and to a lesser extent the European Union and EDCTP. Studies include conduct of trials and basic science studies aimed at HIV vaccine research and development (R & D). EDCTP has funded our first efficacy phase 2b trial, PrepVacc aimed to test two immunization strategies using experimental HIV DNA and Env protein/adjuvant, with or without MVA boosting, to determine if they protect against HIV-1 infection in Africa with universal Pre-Exposure Prophylaxis covering the immunisation schedule. This work is led by Prof J Weber at Imperial College with P Kaleebu as the MRC/UVRI co-PI and Eugene Ruzagira as Trial Director. The study will enrol 1668 high risk participants across 5 clinical sites in Africa. MRC/UVRI will play a lead role in a number of activities including data management and laboratory assays (See also HIV Intervention Programme).

Another study is The Globally Relevant AIDS Vaccine Europe-Africa Trials Partnership (GREAT) that will evaluate in a phase I/IIa clinical trial the safety and immunogenicity of tHIVconsvX vaccines and to demonstrate the feasibility of an efficacy trial in the at risk populations and with diverse clades at four sites in Kenya, Uganda and Zambia. GREAT is a collaboration bringing together different partners led by Prof Tom Hanke at the University of Oxford. The tHIVconsvX vaccine will be evaluated in 168 volunteers, in Uganda this will be in the fishing communities around Lake Victoria. The vaccines are inserted in Chimp adenovirus for prime and in MVA for the boost.

Our partnership with IAVI has expanded into the newly USAID funded programme; Accelerate the Development of Vaccines and New Technologies to Combat the AIDS Epidemic (ADVANCE) (led by Mark Feinberg and Fran Priddy, others Anatoli Kamali and Jill Gilmour IAVI). It is aimed at advancing
the design and development of HIV vaccines and biomedical prevention tools while ensuring they are effective and accessible for all in need.

The VISTA programme, Vaccine Immunology Science and Technology for Africa (led by Jill Gilmour at Imperial College and P Kaleebu as Steering Committee chair) is part of ADVANCE, a new initiative aimed to strengthen and expand an international consortium of investigators in order to address gaps in HIV vaccine design. There are three key areas: Virology: Fully characterize transmitted virus; Immunology: Identify targets and immune responses and Clinical trials: Develop and test novel vaccines and build capacity. Under this programme, MRC labs are being strengthened to perform viral inhibition, neutralization and generation of infectious molecular clones (IMCs). Already our scientists (Anne Kapaata and Sheila Balinda) have participated in the generation of IMCs at Emory University in Prof Eric Hunters laboratory. This work is now being continued in our laboratories. Jesus Salazar has also introduced additional assays for IMC, involving synthetic synthesis of IMCs. We have also embarked on another IAVI supported study to determine the neutralization sensitivity of different Ugandan HIV strains on different broadly neutralizing monoclonal antibodies, work led by Fred Lutwama.

We are part of a newly funded EDCTP study “Combined HIV African Prevention studies: On demand Truvada and F/TAF pre-exposure and post-exposure prophylaxis to protect adolescents from HIV”. For this multi-centre study, led by Julie Fox, at Kings College, London, our laboratory will be involved in studies that include determining the minimum PreP dose required for ex-vivo protection, using resected fore skin, ex vivo tissue explant experiments; comparison of the efficacy of FTAF and Truvada; and impact of PrEP on mucosal inflammation gene expression and microbiome.

In collaboration with Immunomudulation Programme, we are preparing for the conduct of a phase I trial of the RVF vaccine being developed by partners at Oxord University led by George Warimwe and Adrian Hill, University of Oxford.

We are part of a new award by the Engineering and Physical Sciences Research Council (EPSRC) to participate in developing Future Vaccines Manufacturing Research Hub. Led by Prof Robin Shattock from Imperial College, London with Prof. P. Kaleebu as the MRC/UVRI co-PI, we plan to train in the production of RNA vaccine and training in GMP process, product release and characterisation. Our focus will be on training to make and design RNA vaccines with an emphasis on those most needed in Uganda - i.e. research and discovery. We will acquire equipment to make RNA vaccines according to GMP but not in a GMP building but GMP modular rooms. We will show we can make candidate vaccines in Uganda and validate them in preclinical models.

Finally, and again working with the Immunomudulation Programme, we continue with the studies aimed at understanding the role of pre-existing status of the immune system and presence of endemic infections on hepatitis B vaccine responses. This work forms part of IAVI investigator initiated award to Jackie Kyosimire-Lugemwa.
Professor Alison Elliott
- Head of Programme

Prof. Alison Elliott is the Unit’s Theme Leader for Endemic, Neglected, Emerging and Re-emerging Infectious Diseases and also heads the Immunomodulation and Vaccines Programme. She is Professor of Tropical Medicine at the London School of Hygiene and Tropical Medicine. She is Director of the Makerere University – Uganda Virus Research Institute Centre of Excellence for Infection & Immunity Research and Training (MUII-plus).

Prof. Elliott holds a degree in Natural Sciences from the University of Cambridge, a medical degree from the University of London, a Diploma in Tropical Medicine, and a doctorate in medicine from the University of Cambridge. She is a Fellow of the Royal College of Physicians, and of the African Academy of Sciences.

Prof. Elliott serves as a member on a number of National and International committees including that of the Uganda Ministry of Health Neglected Tropical Diseases Technical Committee and of the Advisory Board of THRiVE (Training Health Researchers into Vocational Excellence). Her main research interests include tuberculosis and helminths, and the impact of chronic, immunomodulating infections on outcomes including vaccine responses, infectious disease susceptibility and non-communicable diseases.

Dr. Anne Wajja – Senior Scientist

Dr. Anne Wajja is an experienced clinical trials physician whose principal research interest is in vaccines, particularly for tuberculosis. She holds a medical degree from Makerere University in Uganda and a Masters degree in Epidemiology from the University of Toronto in Canada. Before joining the MRC/UVRI and LSHTM Unit she worked at the Infectious Diseases Institute of the Makerere College of Health Sciences where she headed a 5-year European and Developing Countries Clinical Trials Partnership (EDCTP) and Aeras funded Tuberculosis vaccine preparedness programme in the Iganga/Mayuge Demographic Surveillance Site. She joined the Unit in October 2013 to run a clinical trial using the candidate tuberculosis vaccine MVA85A, to investigate the impact of Schistosoma mansoni co-infection on the vaccine-induced immune response.
Dr. Harriet Mpairwe
- Senior Scientist

Dr Harriet Mpairwe is a Wellcome Trust Training Fellow, clinical epidemiologist and senior scientist. She joined the Unit as a volunteer having graduated in Medicine at Makerere at the top of her class. She held Wellcome Trust Masters and PhD fellowships and spearheaded work on the effects of prenatal exposure to helminths on eczema risk in infancy. She is now responsible for studies on asthma at the Unit. In 2010 she won the TWAS ROSSA prize for young African Scientist in Applied Medical Sciences. She is an affiliate of the African Academy of Sciences.

Dr. Richard Sanya – Scientist

Dr Sanya qualified in Medicine at Makerere University, and undertook a Masters in Medicine in Internal Medicine at Makerere with a research project focusing on asthma, before becoming a lecturer and head of department of internal medicine at Gulu University. He joined the Unit in March 2014 to lead the Lake Victoria Island Intervention Study of Worms and Allergy-related diseases (LaVIISWA). He then developed a research project, supported by an extension of the LaVIISWA trial, to investigate the effects of helminths and their treatment on metabolic outcomes, particularly insulin resistance, and won a MUII PhD fellowship to support this work.

Maggie Nampijja - Scientist

SEE BIO ON PAGE 27
Dr. Steve Cose – Immunologist

Dr Steve Cose is an immunologist with a background in studies of immunological memory and tissue-specific immunity in animal models. He undertook his PhD at Monash University, Melbourne, Australia, followed by post-doctoral studies at the Edward Jenner institute for Vaccine Research in the UK, and the UCONN Health Centre in the USA, before taking up a Lectureship at the University of Bristol, UK. He joined the Unit in 2009 as lead immunologist for MUII. He developed and launched the Immunology in the Tropics course which has now taken place 13 times, offering training to 365 students from 21 different countries. This year, for the first time, the course was held in The Gambia. Within the I-Vac Programme Steve has been responsible for a study on the impact of maternal latent tuberculosis infection on the infant response to BCG and has supported 3 postdocs, 10 PhD and 18 Masters students.

Infectious diseases remain a major cause of morbidity in tropical, low-income countries but effective vaccines are still lacking for many poverty-related and neglected infectious diseases. Concurrently, non-communicable diseases (NCDs) are an emerging threat.

Over the past three years, the Co-infection Studies Programme (CISP; now Immunomodulation and Vaccines Programme) has been working to address the hypothesis that infectious exposures result in fundamental immunological changes with consequent effects (both beneficial and detrimental) on health outcomes including
vaccine immunogenicity and efficacy, and susceptibility to infectious, inflammatory and metabolic diseases.

Population-based cohorts underpin our work. The Entebbe Mother-and-Baby Study (EMaBS) birth cohort, now a Unit platform, was initiated in 2003 as a trial of anthelminthic treatment during pregnancy and early childhood. When the children were nine years old, a total of 1,201 were seen for allergy-related evaluations. At age 10-11 years, 1,119 were assessed for blood pressure. Follow up still continues (Figure 1A).

In 2012 we initiated the Lake Victoria Island Intervention Study on Worms and Allergy-related diseases (LaVIiSWA), a cluster-randomised trial of intensive versus standard anthelminthic intervention (Figure 1B). Twenty-six fishing villages were randomised to standard mass drug administration (MDA: praziquantel annually for schistosomiasis, albendazole semi-annually for nematodes) versus intensive MDA (praziquantel and triple-dose albendazole quarterly). Allergy- and helminth-related outcomes were assessed in a survey of 3,175 people, after three years’ intervention. The trial was then extended for a further year for more detailed investigation of parasitological outcomes and to assess the metabolic effects of worm infections and their treatment.

To provide comparable data from an urban comparison population, an urban survey among 1,500 people took place in Entebbe during 2017 (Figure 1C).

Helminths and allergy-related disease
Helminth (worm) infections are “master immunoregulators” and there is evidence that they may be particularly good at switching off allergy-like responses (which probably evolved in mammals to protect against them). In the EMaBS cohort, a major, early finding was that treating mothers for worms during pregnancy resulted in an increased incidence of infantile eczema. These results were compatible with a protective effect of pre-natal helminth exposure against allergic conditions and further analyses showed that maternal hookworm infection modified risks associated with classical risk factors for eczema (atopy, family history, gender), supporting a protective effect established very early in life. We were concerned that the increased rates of eczema in infancy might translate to increased rates of asthma at school age.

However, follow up of the cohort found that rates of most allergy-related conditions declined with age and cases of asthma were very few (Figure 2). The “hygiene hypothesis” implies that this decline in allergy-related conditions with age may be due to cumulative infection exposure – a hypothesis we plan to address in further analyses.

Urticaria (a skin rash sometimes called “nettle rash” or, in Luganda, “ebilogologo”) followed a different pattern – a progressive increase in reported prevalence with age. This may reflect the urticarial responses...
directly induced by helminth infection.

### Table 1. Comparison of allergy-related outcome prevalence between urban (EMaBS) and rural (LaVIISWA) Ugandan children

<table>
<thead>
<tr>
<th></th>
<th>Urban EMaBS children (age 9 years) (n=1030)</th>
<th>Urban EMaBS children (age 9 years) (n=1030)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheeze in last 12 months</td>
<td>3.6% (2.5, 4.9)</td>
<td>3.0% (1.5, 6.1)</td>
</tr>
<tr>
<td>Eczema, UK diagnostic criteria</td>
<td>1.7% (1.0, 2.7)</td>
<td>0</td>
</tr>
<tr>
<td>Rhinitis in last 12 months</td>
<td>4.7% (3.4, 6.1)</td>
<td>3.6% (1.7, 7.8)</td>
</tr>
<tr>
<td>Urticarial rash in last 12 months</td>
<td>15.7% (13.6, 18.1)</td>
<td>8.1% (4.9, 13.0)</td>
</tr>
<tr>
<td>Skin prick test positive, House dust mite (HDM)</td>
<td>18.9% (16.6, 21.5)</td>
<td>8.2% (4.4, 14.8)</td>
</tr>
<tr>
<td>Allergen specific IgE, HDM, ng/ml, median (IQR)</td>
<td>183 (0, 368)</td>
<td>1730 (200, 3750)</td>
</tr>
</tbody>
</table>

To our surprise, baseline LaVIISWA results showed no inverse helminth-allergy associations. Instead several positive associations were observed. Despite these findings within the island population, island children showed a lower prevalence of allergy-related outcomes compared to children from outside the islands: the more urban EMaBS children. This was particularly so for urticaria and skin prick test responses, which are directly related to atopy (allergy-related immune responses mediated by Immunoglobulin (Ig)E and histamine release (Table 1 and Figure 3). By contrast, island children had markedly elevated allergen-specific IgE. This suggests an impact of helminth infection on the IgE:histamine release link - which PhD fellow Gyaviira Nkurunungi is investigating further in our new Project 3. These allergy-related results emphasise the importance of pre-natal helminth exposure and the “protective” effect associated with high helminth transmission environments, despite complex associations with active helminth infections.

### Helminths and susceptibility to other infectious diseases

Chronic helminth infections induce T-helper (Th)2 and regulatory immune responses, and may interfere with the development of Th1 responses required to control many viral or bacterial infectious diseases. It has long been proposed that helminth co-infection might increase susceptibility to HIV infection. However, in LaVIISWA communities, and in collaborative studies with the Unit’s HIV Programmes, we found no evidence that *S. mansoni* co-infection increased susceptibility to HIV or impaired the innate immune response among recently HIV-infected people. By contrast, for established infections, we found a benefit of hookworm treatment for HIV replication among EMaBS mothers. Also, we described associations between maternal hookworm and childhood malaria susceptibility and, with Rob Newton, investigating oncogenic viruses, we observed positive associations between helminths (or malaria) and Kaposi’s Sarcoma Herpes Virus (KSHV). Together, these findings suggest that chronic helminth co-infection may impact little upon acquisition of new infections, but be detrimental to control of established infections, with important implications for our further work on control of oncogenic infections (Project 2).

### Helminths and vaccine responses

As for susceptibility to infections, there is long-standing concern that helminth infection may impair the response to unrelated vaccines. In adolescents we investigated effects of schistosomiasis on responses to the candidate booster TB vaccine, MVA85A: we found no adverse effect on the interferon (IFN)-γ response (Figure 4A). But levels of Antigen 85-specific IgG4 were elevated among the schistosome infected children prior to the MVA85A booster immunisation – suggesting a schistosomiasis-associated bias in
the antibody response to prior mycobacterial exposure (Figure 4B), unaltered by the additional vaccination. We undertook a review of current literature on this topic. We concluded that that helminth infection may influence response to unrelated vaccine responses in various ways. These include biasing the response to a Th2 profile or suppression of responses; while, in some cases, there may be no effect. The impact of exposure may differ between toxoids (such as tetanus), live vaccines (such as measles), and live, non-replicating vaccines (such as MVA85A); and between injected vaccines and those taken orally. Outcomes may also depend on helminth species and age at helminth exposure. We planned to investigate this further in the up-coming quinquennium project 1.

Infections and cognitive development

It has been suggested that helminth infection impairs cognitive development and school performance, but the data supporting this is limited and controversial. Many studies on the topic are observational and therefore helminth infection is confounded by poverty, malnutrition and other infections. The EMaBS trial offered an opportunity to identify causal, but reversible, effects of pre-natal and early childhood helminth infections on cognitive development. Dr Maggie Nampijja undertook this work for her PhD studies (Figure 5). She found minimal effects of helminths and their treatment, suggesting that these infections, on their own, may have little adverse effect on brain development. In separate studies, Dr Cally Tann investigated the role of infection as a contributor to neonatal encephalopathy (NE) – brain damage occurring around the time of birth and an important contributor to early death and disability. She found that neonatal sepsis and inflammation of the placenta extending into the tissues of the umbilical cord were both strongly associated with NE, independent of other events around the time of delivery. This indicated that infections do contribute to NE in Africa. Follow up of affected infants highlighted the huge challenges that face families supporting disabled children in this setting and Dr Tann and Dr Nampijja are now, together, exploring interventions that may improve outcomes for children and families, under the Social Science Programme and Mental Health group at the Unit.

Immunomodulation and Vaccines (I-Vac) Programme, future plans

The goal of the new I-Vac programme is to further understand the impact of infection exposure on human immunological programming and health. Our overarching hypothesis is that chronic and cumulative infection exposure influences immunological mechanisms through active processes (during current infection), lasting epigenetic modifications, and genetic selection; that (therefore) some effects do not immediately respond to treatment; and that effects critically impact upon major health outcomes including vaccine responses and susceptibility to pathogens, allergy-related disease and metabolic conditions (Figure 4).
The main focus of our new work is on vaccine responses, addressing the contribution of infectious exposures to population differences in vaccine immunogenicity (Project 1). We are also continuing to conduct allergy-related and metabolic studies. Building on recent findings, exploiting unique platforms that we have established, we aim to determine the effects of infectious exposures (prenatal, cumulative life-time and current, active exposures) on health outcomes comprising:

### Project 1: Vaccine immunogenicity
Among adolescents in the EMaBS cohort we will investigate the effects of prior, life-course infection exposure on responses to vaccines including a novel booster regimen for tuberculosis (ChAdOx1 85A/MVA85A), on BCG revaccination, on yellow fever and HPV immunisation.

### Project 2: Infectious disease susceptibility – focussing on oncogenic viruses
Using samples from the LaVIISWA trial we are investigating the effects of helminth infection and its treatment on KSHV and hepatitis B replication.

### Project 3: Asthma phenotypes and allergy-related effector mechanisms
In case – control studies we are exploring the phenotypes of asthma and risk factors for asthma in Ugandan school children. As well, using samples from our urban and rural population studies, and from the asthma studies, we are investigating the role of allergen-specific and glycan-specific antibody profiles in allergy-related disease risk.

### Project 4: Infection, inflammation and cardio-metabolic risk
Within the EMaBS cohort, analyses are in progress to evaluate the effects of life-time infection exposure on blood pressure and metabolic outcomes. As well, follow up of the LaVIISWA communities to four years has been completed with samples collected to assess the impact of helminth exposure and treatment on insulin resistance and other metabolic outcomes.

To obtain deeper insights into mechanisms by which infections have their effects, we plan complementary studies (for which funding is available, or being sought elsewhere):

### Project 5: on the mediating role of the microbiome

### Project 6: on the mediating role of epigenetic modifications
Disease epidemiology has changed rapidly in Africa. About a decade or so ago, African health services were dealing principally with infectious diseases. While these continue to have a high burden, chronic non-communicable diseases (NCDs) are increasingly becoming major contributors to morbidity and mortality in the region. Following a recent strategic review, the Unit recruited Prof Moffat Nyirenda to establish and lead the NCD research theme.

**Prof. Moffat Nyirenda - Diabetologist/Endocrinologist**

Moffat Nyirenda is a Diabetologist/Endocrinologist and Professor of Medicine at LSHTM, and NCD Theme Leader at MRC/UVRI & LSHTM Research Unit. His previous appointments include Director of Malawi Epidemiology and Intervention Research Unit, Professor of Research at the College of Medicine (Malawi) and Associate Director of Malawi-Liverpool-Wellcome Trust Clinical Research Programme. Moffat’s research interests lie in mechanistic understanding of the aetiology of NCDs including associations between early environmental insults and the risk of cardiometabolic disorders, and using cross-cutting approaches to examine the interactions between infection and NCDs.”

**Dr. Barnabas Natamba - Senior Scientist**

Dr. Barnabas Natamba is a senior scientist and postdoctoral fellow in the NCD Theme at MRC/UVRI & LSHTM Uganda Research Unit. He holds a BSc in Food Sciences and Technology (Makerere University), Masters in Public Health (Hebrew University), and PhD in Nutritional Sciences (Cornell University). Barnabas recently joined the Unit to begin to develop a programme of research on linkages between nutrition and NCDs.”

**The NCD research team and research**

We received a strategic award from the MRC for NCD research programme (to complement QQ funding) in April 2017. We have since made significant progress in building a team and developing the research, leveraging the local expertise, infrastructure and partnerships. Our research will include epidemiological studies, clinical and laboratory phenotyping, as well as intervention studies – examples of which are given below.

*Understanding local burden and drivers of gestational diabetes*

Gestational diabetes (GDM), when not properly managed, is associated with significant morbidity to the mother and child. The true burden of GDM in Uganda (and most African countries) is not known, because of a lack of high quality studies. Moreover, GDM is currently diagnosed using relatively expensive
approaches and applying various criteria. However, we do not know how well these different approaches are suited to the African setting. This study is aimed at generating robust data on the burden, determinants and outcomes of GDM, in order to stimulate a policy response to address this challenge. In addition, using a combination of demographic, clinical and biochemical markers, will attempt to develop a risk scoring tool that might be used to identify women at high risk of GDM who should be targeted for screening.

Phenotyping of type 2 diabetes
It is becoming increasingly clear that type 2 diabetes is not a single entity, but a complex group of conditions that involves genetic, metabolic, and clinical heterogeneity; it can arise from perturbations in distinct pathways in glucose metabolism (such as decreased insulin secretion, increased gluconeogenesis, insulin insensitivity, or increased glucose uptake in the intestine) whose contribution may differ between populations. We can therefore not assume that the Western stereotype, on which current guideline and practice are based, is necessarily going to be the right one for Africa. The limited data available, including from our recent studies, suggest that NCDs (including type 2 diabetes) occur in younger people in Africa than in developed countries – with the majority of individuals with diabetes or hypertension under 50 years old. In addition, unlike in high-income countries where these disorders are classically associated with obesity, most individuals affected had body mass index within the normal range. The biological mechanisms for this apparent heightened susceptibility are unknown, but may relate to environmental exposures, particularly early in life, can influence long term risk of disease (perhaps by affecting organ size or via epigenetics); for example, undernutrition during the prenatal period or childhood has been associated with substantially increased risk of diabetes and cardiovascular disease in adulthood.

This work aims to adequately understand the specific nature of diabetes in sub-Saharan Africa through detailed clinical and laboratory phenotyping that will lead to 1) characterization of the clinical course of diabetes in this population (including description of the prevalence and determinants of micro- and macrovascular complications), 2) better understanding of the pathophysiology (including the contributions of beta cell dysfunction and insulin resistance), and to identify novel biomarkers for the risk of developing diabetes and its progression, 3) rational use of available drugs, as well as provide new targets for therapeutic intervention. We will also have established a cohort of well-characterized individuals in Africa for future interventional studies in diabetes and related disorders. This work with contribute to Davis Kibirige’s PhD, and has attracted a strategic collaboration with Prof Andrew Hattersley in Exeter (who leads the premier international group on diabetes characterisation) with a recent joint application for further funding to UK’s National Institute for Health Research (NIHR).

NCD-HIV interactions
One of the key strands of our research is to understand the interface between NCDs and infection, notably HIV. This work will capitalise on the strong collaboration between MRC/UVRI & LSHTM Research Unit and The Aids Support Organisation (TASO), a pioneer non-governmental not-for-profit organization that provides HIV/AIDS support and care; TASO follows up over 75,000 individuals living with HIV at its 12 service centres and 4 regional offices covering most parts of Uganda. In collaboration with Liverpool School of Tropical Medicine, we recently won an award from NIHR to establish a Group and to develop research partnerships and a large research programme on integration of HIV and NCD (diabetes and hypertension) care; currently, HIV care with ART provision are delivered as stand-alone services, while services for diabetes, hypertension and other NCDs remain very limited. Importantly, individuals...
with HIV infection have increased prevalence of NCD comorbidity. We will conduct early phase studies to identify potential benefits and likely harms for HIV infection and NCDs in order to inform the development of the large research programme. This work will be led by Dr Josephine Birungi who has been Research Manager at TASO, but currently seconded to MRC/UVRI & LSHTM Research Unit to undertake a PhD.

In a separate study, we are interested in examining whether treatment with metformin in HIV-infected individuals with prediabetes lowers the rate of progression to overt type 2 diabetes. This is based on the premise that HIV+ persons are at increased risk of prediabetes (and diabetes), and that metformin has been shown to slow progression in the general population. This work is being led by Dr Ivan Namakoola, and these data will inform a large phase III trial.

**Long term impact of health systems intervention to improve care of NCDs**

This work follows from a recently completed intervention study, the health systems and chronic disease project (HSCDP), to improve the quality of diabetes and hypertension care through training, treatment guidelines, and provision of essential medicines and equipment. The intervention showed a two-fold increase in preparedness of the health facilities for NCD care and a six-fold improvement in the quality of care for NCD patients. The new work is designed to examine whether these improvements are sustained in the medium and long term, and to determine factors that influence this sustainability. This work will be led by Dr David Katende who was the coordinator of the HSCDP and will undertake this work as part of a PhD study.
Peter Hughes Head - Clinical Diagnostic Laboratories

Peter joined the MRC/UVRI Uganda Research Unit in 1999 where he supervised the laboratory component of a pneumococcal vaccine trial. He has since led the development of the Clinical Laboratory from a small ‘clinic based’ operation to a fully comprehensive laboratory service covering all disciplines of the diagnostic laboratory with the capacity to fully support the Unit and collaborators in all aspects of clinical diagnostics. In 2007 he was appointed to Head of Clinical Laboratories. All laboratories operate under GCLP compliance with Entebbe site awarded ISO15189 accreditation in 2016.

Currently the laboratory network consists of four laboratory sites within Uganda. The Central laboratory is located in Entebbe and was selected as the central testing centre for the Africa H3A diabetes study. Alongside the clinical laboratory is a vast biorepository holding over 3 million biological samples, with collections dating back to the early 1990's.

The MRC/UVRI Clinical Diagnostic laboratories (CDLS) are a key component of all the research studies conducted by the Unit. The central laboratory in Entebbe and those in Kyamulibwa, Masaka and Kampala have, over the years, expanded from small scale establishments using simple rapid methods to highly developed multidisciplinary laboratories capable of providing high quality and sophisticated diagnostics.

The laboratories are fitted with state of the art equipment, which has promoted comprehensive provision of services for haematology, microbiology, serology, biochemistry and molecular diagnostics. The facilities include a Biorepository to store and maintain the vast collection of biological material which have been collected by researchers since the inception of the Unit. The laboratories have considerable experience in Quality Assurance (QA) procedures and are regularly audited by external organisations such as PPD, CLS (South Africa) and the MRC Clinical Trial Unit. The laboratories in Entebbe, Mengo and Masaka maintain accreditation under Good Clinical Laboratory Practice (Qualagy) and the Entebbe laboratory is accredited to ISO 15189 international standards of competence for clinical laboratories. The laboratories are fully compliant with local regulations and all staff as well as the laboratories are certified by the Uganda Allied Health Professionals.

All staff undergo GCLP training as well as GCP and all staff are encouraged to take part in CME activities. There is support for staff to attend short workshops and further education where appropriate, as well as continuous on-site training. The section supports staff capacity building and all have obtained BSc with some progressing to MSc awards. An internal promotion system is in place to further encourage and retain staff who have excelled over the years.

The primary objectives of the section are;

1. To provide a high quality ‘safety testing’ and clinical diagnostic support services to the core MRC/UVRI clinical studies and trials, as well as other collaborative studies undertaken by the Unit.
2. Maintain a database of all specimens collected and stored at the facilities
3. Establish the Entebbe laboratories as a Centre of Excellence in clinical laboratory, for the region.

Achievements over the past 3 years
The laboratory has a long history of successfully working with Clinical Trials in the area of Microbicides and HIV vaccine. Currently there is work on an Ebola vaccine through the Masaka laboratory and soon will start studies on Malaria

The Entebbe laboratory is the central laboratory for a multi-African site study into diabetes. The laboratory has been organising the collection and shipment of samples from across sub Saharan Africa for storage and creating a database in the biorepository. These are samples, which will be stored over the long term and made available to researchers for further study. Testing of a subset of the samples will be carried out in Entebbe laboratory later this year.

As well providing the diagnostic platform for research, the laboratory also opens its facilities where there is need to support national health issues. This was illustrated by the support given to the investigations into a typhoid outbreak in Kampala. The microbiology department was able to process the samples collected to identify positive cases of typhoid by cultures and provide the antibiotic sensitivity data so that the correct treatments could be administered. Through the collection and investigation of the isolates, the laboratory has been able to provide valuable information on the characteristics of the infecting strains of typhoid that were present in the outbreak. In collaboration with Wellcome Trust Sanger Institute, Cambridge, these studies indicated the emergence of low level ciprofloxacin resistant and multi drug resistant H-58 lineage Salmonella Typhi in Kampala.

The laboratory was central to the evaluation of various HIV rapid tests coming up with a new National Algorithm.

The Biorepository has been improved with now 3 full time well trained staff. We hold more than 1 million samples with multiple aliquots from multiple local and international studies managing them accurately with Freezerworks specimen management software. We are the central biorepository hub for H3A diabetes study biobanking samples from 10 sites within 8 countries in Sub Saharan Africa.

In order that the work carried out by the laboratory is to a high standard, international benchmarks of accreditation in the laboratory quality have been attained. The laboratory has been accredited under ISO 15189; competence for clinical laboratories, and undergoes annual assessments to ensure the standards are being maintained.

SOME OF THE LAB STAFF IN MASAKA (LEFT) AND ENTEBBE (RIGHT)
## Summary of MRC/UVRI cohorts over the reporting period

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Status</th>
<th>Original study aim</th>
<th>Design</th>
<th>Date Period</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cohorts (Population Platform)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>General Population Cohort (GPC) in Kyamulibwa subcounty (Kalungu District)</td>
<td>On-going</td>
<td>To examine trends in prevalence and incidence of HIV infection and their determinants.</td>
<td>Longitudinal observational study - Open cohort</td>
</tr>
<tr>
<td>2</td>
<td>Fisherfolk (Masaka and Kalungu)</td>
<td>On-going</td>
<td>To estimate the annual incidence of HIV infection, characterize early HIV infection, and prepare clinical trial sites for HIV preventive vaccine efficacy trials for which volunteers from this study cohort may be recruited.</td>
<td>Prospective, open cohort, observational cohort</td>
</tr>
<tr>
<td>3</td>
<td>Lake Victoria Island Intervention Study on Worms and Allergy-related diseases (LaVIIISWA), Koome sub-county, Mukono district</td>
<td>On-going</td>
<td>1. To describe the phenotypes, prevalence and risk-factors for allergy (wheeze, asthma, eczema and atopy) in island communities in Uganda; 2. To investigate effects of interventions against helminths on allergy-related outcomes, and on helminth-induced morbidity.</td>
<td>Cluster-randomised trial</td>
</tr>
<tr>
<td><strong>Cohorts (Clinical Platform)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Entebbe Mother and Baby Study (EMaBS), Entebbe</td>
<td>On-going</td>
<td>Current aims: 1. to investigate associations between allergy phenotypes at school-age and exposures before birth and below five years of age; 2. to investigate associations between early life exposures and blood pressure (and other cardiovascular disease risk factors) at school age.</td>
<td>Birth cohort. Originally a randomised controlled trial</td>
</tr>
<tr>
<td>5</td>
<td>Good Health for Women Project (GHWP), Kampala</td>
<td>On-going</td>
<td>To establish high risk cohorts and to conduct research on HIV and STIs and assess suitability of cohorts for future HIV prevention trials. Document prevalence of HIV and other STIs at enrolment and their determinants. Estimate incidence of HIV and STIs and trends of risk factors.</td>
<td>Longitudinal observational study - closed cohort (initially): now open</td>
</tr>
<tr>
<td>6</td>
<td>The AIDS Support Organisation (TASO)</td>
<td>In development</td>
<td>To follow the long term health of people living with HIV</td>
<td>Longitudinal observational open cohort study</td>
</tr>
<tr>
<td><strong>Cohorts (Others)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>IAVI protocol B Open Cohort, Fisherfolk Masaka</td>
<td>On-going</td>
<td>To estimate the annual incidence of HIV infection, characterize early HIV infection, and prepare clinical trial sites for HIV preventive vaccine efficacy trials for which volunteers from this study cohort may be recruited.</td>
<td>Prospective, open cohort, observational study</td>
</tr>
<tr>
<td>Cohort</td>
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<tr>
<td>8</td>
<td>On-going</td>
<td>To investigate factors limiting access to HIV prevention interventions and to determine the feasibility of conducting HIV combination effectiveness trial among HIV vulnerable fishing communities in Uganda.</td>
<td>Parallel arm cluster randomised control trial</td>
<td>2014-2015</td>
</tr>
<tr>
<td>9</td>
<td>On-going</td>
<td>To evaluate clinical, laboratory, immunologic and viral markers of disease progression in volunteers with recent HIV infection to prepare for preventive HIV vaccine efficacy trials.</td>
<td>A prospective, multi-center, observational study</td>
<td>2006-Ongoing</td>
</tr>
<tr>
<td>10</td>
<td>On-going</td>
<td>To evaluate treatment outcomes among patients enrolled in care.</td>
<td>Longitudinal observational study - Open cohort</td>
<td>2009-todate</td>
</tr>
<tr>
<td>11</td>
<td>On-going</td>
<td>To determine risk factors for Hepatitis infections and disease outcomes.</td>
<td>Longitudinal observational-Closed</td>
<td>2011-todate</td>
</tr>
<tr>
<td>12</td>
<td>On-going</td>
<td>To investigate the effect of intensive treatment with praziquantel on HIV diseases progression.</td>
<td>Open label randomised controlled trial</td>
<td>2012-todate</td>
</tr>
<tr>
<td>13</td>
<td>On-going</td>
<td>To determine whether immediate initiation of ART is superior to deferral of ART until CD4+ declines below 350 cells/mm3 in terms of morbidity and mortality in HIV-1 infected persons ART naive with CD4+ above 500 cells/mm3.</td>
<td>Open label randomised controlled trial</td>
<td>2012-2016</td>
</tr>
<tr>
<td>14</td>
<td>On-going</td>
<td>To demonstrate non-inferiority in terms of percentage of subjects who have plasma HIV-1 RNA levels &lt;400cp/ml after 48 weeks randomised treatment with TDF/FTC/RPV vs TDF/FTC/EFV using a modified FDA snapshot method.</td>
<td>Open label randomised controlled trial</td>
<td>2013-2016</td>
</tr>
</tbody>
</table>
Dr Christian Holm Hansen - Head of Section

In November 2017, Dr Christian Hansen took up the position as head of the Statistics and Data Management section. Christian is a senior member of the management team taking overall responsibility for the statistics and data section and joins us with expertise in medical statistics, research methodology and data management after working in clinical research and epidemiology in both industry and academia in the UK and elsewhere. He has been with the LSHTM since early 2014 and is a member of the TEG within the School. Before joining the Unit, he was based in Mwanza, Tanzania where he headed the medical statistics section at Mwanza Intervention Trials Unit (MITU). Christian has a background in mathematics and statistics and holds a PhD in Medical Statistics from the University of Edinburgh where he also worked from 2008-2014 as a Research Fellow with the MRC Hub for Trials Methodology Research, and as a Senior Clinical Trials Statistician at Edinburgh Clinical Trials Unit.

Mr Ayoub Kakande, MSc Head of Data Management

Ayoub Kakande was appointed Head of Data Management at the unit in November 2017. He is currently developing a generic data management plan for the unit and is in the process of ensuring that all unit data are stored on GCP compliant databases. Prior to moving to the MRC/UVRI, Ayoub worked in data management in the Makerere John Hopkins University collaboration (MUJHU) for 11 years. He holds a Master’s degree in ICT Management, Policy & Architectural Design, and a Bachelor’s degree in computer science.

Dr Rebecca N. Nsubuga, PhD

Dr Rebecca Nsubuga is a Senior Scientist (Statistician/Modeller) within the unit since 2008. Up to June 2016 she was a project leader of the Calibration and Analysis of Complex Individual-based Stochastic Models project (PI: R. White, LSHTM) and she leads
the mathematical modelling work in the unit. Since 2016 she has also been leading the genome-wide association studies (GWAS) work and currently works on GWAS analysis of chronic kidney disease in the GPC. Rebecca holds a visiting professorship at Hasselt University, Belgium. She previously worked as a lecturer at Makerere University, at the Department of Mathematics where she was based for 12 years. Rebecca holds a PhD from The University of Edinburgh, Scotland, a Master’s degree in Biostatistics from Limburgs Universitair Centrum (now Hasselt University), Belgium and a Bachelor of Science in Mathematics degree from Makerere University.

Dr. Sylvia Kiwuwa Muyingo (PhD)

Dr Sylvia Kiwuwa Muyingo is a senior statistician within the Unit and is involved in the design and analysis of clinical, epidemiological and basic science experiments. She received her PhD in Biometry from the University of Tampere, School of Health Sciences (Finland) and an MSc Medical Statistics from the LSHTM (UK) after graduating in Statistics and Economics from Makerere University. Sylvia’s main research interests include development and application of statistical methods for longitudinal studies. This involves understanding health disparities in the distribution of disease, health outcomes, including medication adherence and understanding how population genomics plays a key role.

Dr. Jessica Nakiyingi Miiro (PhD)

At the time of leaving the Unit in 2017, Jessica was a Senior Statistical Epidemiologist after completing a PhD from the University of London. Jessica was the project leader and site coordinator for ALPHA (Analysing Longitudinal Population-based HIV/AIDS data on Africa) Network studies, a network of 10 sites from 6 sub-Saharan countries from 2010, and co-ordinated the female arm of the MENISCUS (Menstrual Hygiene and Safe Male Circumcision Promotion in Ugandan Schools) project from 2015. For capacity building activities, Jessica was involved in in-house mentoring and training of Statistics and Epidemiology courses.

Her research interests are in areas of epidemiology (field, clinical, social, and statistical), public health, and statistical methodology. Recently, her research has concentrated on HIV infection trends; adult and child mortality; adolescent health; social impact of HIV i.e. education; fertility; and orphan hood.
Statistics Section brief

The Statistics section provides statistical support for all projects involving quantitative data in the Unit. The support consists of providing statistical input to study proposals and during protocol development, database creation, data entry, data processing and data management, ensuring that good quality data is provided for the projects and overseeing data analysis and inputting into interpretation (including report writing and contributing to scientific publications). Senior staff in the section also carry out methodological research. In addition, the section is involved in training and capacity building activities through running training courses ranging from database development platforms and basic statistics courses to more advanced courses such as the two-week intensive courses in Epidemiology and Statistics and Advanced Statistical Methods in Epidemiology. The two-week courses are delivered in collaboration with colleagues based at the London School of Hygiene and Tropical Medicine and elsewhere and have previously attracted participants from East and West Africa. The section also receives support from the MRC Tropical Epidemiology Group (TEG) within the London School with a couple of TEG statisticians dedicated to working on research projects undertaken by our unit.

Achievements

The section has carried out its mandate of supporting the various unit programmes; serving over 50 projects with the setting up of databases, data entry, data management and analysis. The section statisticians together with our TEG collaborators analysed data from observational and intervention studies, contributing to manuscripts for journal publications, conference presentations and to analysis to inform new grant proposals. The section has played a key role in various trials e.g. EV07 (An open label phase I clinical trial to evaluate the effect of late boost on HIV-uninfected vaccinees from EV06 trial); EV06 (A phase I double blind placebo-controlled clinical trial to evaluate the safety and immunogenicity of the combination of DNA-HIV-PT123 and AIDSVAX®B/Ein HIV-1- uninfected adult participants with or without underlying Schistosoma mansoni infection) and COSTOP (Safety of discontinuing cotrimoxazole prophylaxis among HIV infected adults on anti-retroviral therapy in Uganda). On these trials the section was involved in the design, database development, of the producing reports for the Data & Safety Monitoring Committee meetings and final analysis. With this expertise in trials, the section was selected to be the main data management centre for a multi-centre trial, PrEPVacc (an HIV pre-exposure vaccine trial) involving five international study sites from four countries. Staff also presented at local and international conferences and workshops; with one winning a Discovery Health clinical excellence award for best clinical paper by a non-South African delegate at the 7th South African AIDS Conference, Durban, South Africa 2015.

Prof. Jonathan Levin

At the time of his departure in 2015, Jonathan was Head of the Statistics Section at the Unit. He currently is Professor of Biostatistics in the School of Public Health at the University of Witwatersrand.

He has a B.Sc. from the University of the Witwatersrand, an MSc (Numerical Computation) from the University of Manchester, an MSc (Biometry) from the University of Reading and a PhD in Biometry from the University of Natal.

His interests are in statistical aspects of Randomised Controlled Trials, including Cluster Randomised Trials, the analysis of clustered data and in teaching Biostatistics to Health Professionals.
Over the last three years the section has fully implemented the OpenClinica database development platform, ensuring that the databases in use are compliant with Good Clinical Practice. By the end of 2017 we had 16 studies using this platform. In 2017 we also introduced another GCP complaint database platform, ODK (Open Data Kit), and implemented two studies on this platform. Going forward, we are using OpenClinica as the default database development platform with ODK and REDCap (Research Electronic Data Capture) as the alternative platforms.

The unit embraces the increasing demand of sharing data in order to maximise usage of data generated using public resources. We developed a data sharing policy and the unit now has an operational data sharing policy to enable timely access to data by researchers.

**Capacity building of section staff**

In order to ensure data quality all data management staff were trained in the three GCP compliant database platforms, OpenClinica, ODK and REDCap. Staff were also trained in statistics and the use of STATA software. This will enable data managers to develop more robust data cleaning programs.

**Research by Senior Staff**

To increase the output of statistician-led publications and to enhance the statistical methodology development of our staff, over the years, our statisticians have attended short courses internationally and won travel grants to visit external centres to undertake methodological training. In 2015-2017, our staff contributed to 58 (14 (2015); 15 (2016), 29 (2017)) peer reviewed publications, including seven first author publications. One of them a methodological publication on analyses combining phylogenetic and epidemiological Data.

**Projects within the Section**

The section has continued to be an active member of the Analysis Longitudinal Population-based HIV/AIDS data on Africa (ALPHA) Network under the lead of Dr Jessica Nakiyingi-Miiro. Over the review period, the ALPHA work in the section, funded by a three-and-a-half year grant from Bill and Melinda Gates Foundation, was mainly about analysis of deaths among HIV-infected adults since the introduction of antiretroviral treatment. The section was also a collaborator on the mathematical modelling work led by Prof Richard White (LSHTM) and coordinated by Dr Nsubuga in our section. This project which had its final meeting in June 2016 enabled us to dig more into our data and contribute to methodological work. This collaboration resulted in five publications with one further manuscript currently under review. We disseminated the public health component of this work to the Uganda Ministry of Health in June 2016 and also produced a policy brief which can be accessed from the unit website.
Our senior staff are now engaging in genetic statistics and held a GWAS workshop facilitated by Dr Fasil Tekola-Ayele (NIH) in December 2016. Following that, the staff started working on a GWAS analysis of chronic kidney disease in the General Population Cohort, a project lead by Dr Robert Newton within our unit. In December 2017 our section put on a more advanced workshop involving GWAS methods and work is currently ongoing to finalise the GWAS analysis for write-up and eventual publication.

Statistics training

Our section has put on a number of short courses over the past three years including Basic and Intermediate Statistics, and in collaboration with MRC TEG, the two-week intensive courses mentioned above, alternating between the two intensive courses each year. Our courses in basic and intermediate statistics are predominantly aimed at MRC/UVRI staff and typically attracts over 20 participants. The two-week intensive courses also attract over 20 participants typically with five or more international participants.

The section continued building links with sister organisations in Uganda through seminars and supervision (three PhDs awarded where our statisticians gave support), and by participating in short courses as attendees or facilitators. We also participated as joint organisers of international workshops hosted in Uganda such as the International Biometric Society Uganda Group workshop in 2015.

We also expanded our external links beyond LSHTM to include Makerere University (joint organisation of the R & Micro Array and Bioinformatics courses), Infectious Diseases Institute (courses in Missing data analysis) and Hasselt University.

DATA MANAGEMENT PLATFORM

Under the current five-year plan, the section was restructured to include a data management platform managed by a senior data manager with independent management roles. With this change, the head of section is relieved of the day-to-day data management responsibilities. In 2017, Mr. Ayoub Kakande was recruited as the head of the data management platform. Plans are underway to streamline our data management operations to further ensure efficiency and high quality data output.

Current and past statisticians in the review period


TEG Support

Prof Helen Weiss, Ms Kathy Baisley, Dr Emily Webb, Mr Stephen Nash.

STATISTISTICS TEAM- MENGO

STATISTICS TEAM- ENTEBBE
Beatrice Dhaala

Beatrice Dhaala is the Principle Systems Manager for the Uganda Medical Informatics Centre (UMIC). She oversees the daily operations of UMIC and plans and implements system improvements and upgrades. She also provides advice and guidance to the users of the facility and ensures compliance to the computing policies with emphasis on software and data security.

Prior to joining UMIC, Beatrice worked with the Directorate for ICT Support (DICTS) in Makerere University where some of her various job functions included IT management, systems development and integration, service and skills management and quality assurance.

We have made efforts to build capacity in bioinformatics through infrastructure development, formal courses and hands on training. Our staff have participated in analyses of studies that have included host genetics such as NCD and genomics; Analyses of Africa Genome Resource (3000 human genomes)- African Partnership on Chronic Disease Research (APCDR), NGS for HIV super infection and emerging diseases and the Gates funded PANGEA full length HIV sequences. Our staff have also participated in organization of courses including those funded by Makerere University/UVRI Infection and Immunity Research Training Programme (MUII) and Human Heredity & Health in Africa (H3A).

The UMIC infrastructure and ancillary systems with a total of 2,048 cores and 16TB of RAM was finalised on July 2016 and is currently supporting major programmes in Africa in bioinformatics and genomic research such as H3A, IAVI, TrypanoGEN (TPG), MUII and those of our Unit.

Our staff have continued to made use of several bioinformatics using softwares installed on the server e.g. BEAST, RAxML, COMET, SCUEAL, IVA, etc. and have developed several scripts to run these programs.
The Iterative Virus Assembler (IVA) has been setup to assemble NGS reads, generate consensus sequences and filter viral from non-viral or human genomes within data sets. The Unit has a repository of HIV molecular sequence data (~2TB of data) under PANGEA/Molecular Epidemiology studies and is involved in molecular characterization and phylogenetic-based analyses.

Bayesian phylogenetic inferences have been performed on these data sets utilizing UMIC’s high power computing capability to reconstruct the spatial-temporal dynamics of HIV-1 transmission in different population subgroups. We will continue to build automated pipelines to combine various bioinformatics programs to perform HIV sequence analysis processes and implement phyloscanner to screen for co-infections from sequenced viral genome and transmission networks.

Other staff have trained in HIV superinfection NGS analyses and in the use of HyDRA a user friendly web based bioinformatics platform that will be used for NGS of HIVDR from our illumina Miseq including detection of minority populations.

We have collaborated with UVRI and University of Glasgow (CVR) to build further capacity in metagenomics analysis in an effort to discover new and re-emerging viruses.

Our senior staff are now engaging in genetic statistics. The staff are working on a genome wide association study (GWAS) analysis of chronic kidney disease (CKD) in the GPC. The EMaBS genetic data is also being analysed and transferred to the UMIC to allow access for studies on the genetics.

The Uganda Genome Project provides one of the largest study of its kind to date, comprising genome-wide data from 6,400 individuals from rural Uganda, and including whole-genome sequence from 1,978 individuals. Through this work, we demonstrate systematic differences in trait heritability between European and African populations, probably reflecting the differential impact of genetic and environmental factors on traits. We hope this resource will be used by our scientists to study other diseases.

The Wellcome Trust Sanger Institute, The University of Cambridge and the Unit are now formal partners with the USAID funded IAVI programme (2016-2021), with UMIC providing a computational resource to host, curate and manage data generated across the IAVI regional programmes.

**OPERATIONS DEPARTMENT**

**Suzanne Rupp - Chief Operating Officer**
The following report provides an overview of departments supporting science including procurement and stores, human resource, information technology, estates, research support office and finance. The services of communications and engagement and clinical diagnostic lab services fall within the operations department but are the subject of individual reports. We have focused across all operations departments to providing improved transparency, improve collaboration with the scientific community, improve internal controls and efficiency and importantly improve cross functional planning. We continue to work closely with our stakeholders and to promote the science of the unit where opportunities arise.
A significant amount of work was undertaken in the last six months of 2017 to support due diligence requests generated by the LSHTM pending formal transfer.

Procurement headed by Isaac Odong

Procurement is critical to scientific delivery and is managed from Entebbe supporting the field stations at Mengo, Kyamulibwa, and Masaka. The supply chain is supported through both local and international purchasing. Imports to the unit are managed through our contracted freight forwarding company with significant attention paid to import documentation to aid local clearance. Goods are imported from UK, Europe and the US and often require special attention whereby supplies need to be transported as cold chain with constant monitoring from point of supply to arrival in MRC stores. Larger capital project purchases have required 40 foot containers shipped by sea to Mombasa and then by land to Entebbe. The procurement teams manage the shipping processes dependent upon cost, stock sensitivity and urgency of need.

The department have taken a strategic decision to improve costing and reduce administration through the contracting of suppliers for critical and high turnover items. National tenders have been utilized to conclude contracts for the supply of drugs, lab sundries and consumables, office consumables and stationery. Evidence has shown that this reduces lead-time, stabilizes prices, harmonizes and consolidates servicing of biosafety, analytical and cryogenics equipment. There continues to be a focus to improve internal controls with ongoing revision to SOPs and conducted dissemination trainings in all the field stations. Procurement activities are monitored through intranet reporting and real time updating.

In 2017, the unit received capital awards and ran international tenders for assets including 21 new vehicles, 15 bio gram freezers, and a Laboratory Information Management Systems which will track samples from clinic, to analysis to store. The unit is purchasing a boat for the islands. These activities generated £130k savings against budget.

As mentioned earlier key component of regular procurement activities is importation of supplies from abroad, which require compliance with regulatory requirements. The Unit holds tax and import exemptions and we met with the Directors of these organisations to improve communication as the underlying rules often change without prior notification putting goods clearance at risk. For 18/19 the focus is on improvement to supply chain planning through education and training and to improved management of transport fleet consumables to improve cost reduction.

Human resources and administration headed by Godfrey Kalungi

The human resource and administration department has focused on acquisition development and retention of staff to support scientific research. Highlights of the main achievements over the last three years include.
• Introduction of the medical insurance scheme
• Introduction of the 24-hour Group personal accident insurance cover for all staff.
• Annual salary surveys and increments to staff as approved by management.
• Timely job evaluations and commensurate remunerations for both new and old positions.
• Staff promotion scheme to allow for growth and recognize excellent achievements.
• Creation of data bank for potential recruits for some key positions and a rehiring system for former staff.
• Use of the internship and disabled internship schemes to identify competent and talented individuals.
• Annual performance management training sessions to all staff.
• Introduction of the staff wellbeing programme with different annual activities.
• Introduction of the annual director’s awards to recognize exceptional achievements.
• Through training, covered the different training needs for staff raised in their appraisals.
• Improved safety and security monitoring across the unit.
• Review of staff policies and procedures.

A number of job roles have changed over the period and the unit needs to conduct another job evaluation and salary survey so as to appropriately remunerate positions to boost retention and attract more competent talent competitively. We are looking to automate HR systems to ease recruitment, leave management, induction eLearning, performance management, through creation of a self-service platform possibly using LSHTM systems.

Information Technology (IT)
Headed by Mr. E. Ssennyonjo
The IT Section continues to offer an effective, efficient and economical high quality IT/IS services (data and voice) in support of research and administrative functions. The Team effectively manages a large-scale storage sub-system, with high-performance computing (HPC) for scientific applications like Bioinformatics, virtualisation technologies and other cutting-edge scientific equipment.

Major Projects
• 2014 - The MRC Africa Backup Project was awarded in response to increased requirements from funding bodies. The aim of the project was to ensure research data is both secured, protected and available when required by the community. The IT team created a Virtual Private Network (VPN) between the Ugandan office and MRC Harwell that ensures the replication of all research data to MRC Harwell UK repositories on a daily basis; thus protecting this valuable resource.
• 2015 - A Data Centre was established at the Kampala Office, linking Entebbe Main Data centre using fibre data and internet links replicating date to Entebbe on daily basis.
• 2016 - Deployed a secure wireless infrastructure to facilitate mobile users across the five sites (Kyamulibwa, Masaka, Kampala, Entebbe and Hospital Clinics.
• 2017 - Implemented Eduroam facilities for all collaborators who subscribe to the service in their partner countries via federated services using the Research and Education network (NRENs) for researchers.
• Internet Bandwidth requirements have increased from 10Mbps in 2014 across the unit to 50 Mbps in 2017 shared across the six sites (two Hospital clinic offices, Entebbe, Masaka, Kyamulibwa and Kampala).
Going forward, we continue to reduce telephone costs using existing data/fibre networks by eliminating call trunks between departments that are geographically dispersed yet have similar functions. The transfer to LSHTM requires some changes in the IT infrastructure including a change of UK back up and interfacing between local systems and the LSHTM accounting software, Agresso.

**Estates and Transport headed by Kamya Epaineto**

Estates management continues to be hampered by low funding for ongoing maintenance. Improved visibility has been the focus of estates operations in the last two years to improve transparency of work requirements, consolidate work requests and to aid prioritisation. To this end the unit has implemented an estates management scheduling tool across its four sites which is accessed by users and used to raise and track work requests. The next phase of this project will be to input the MRC fleet to enable digital monitoring of maintenance and to improve long term planning. Additionally, the unit are assessing a fleet management system to improve fuel and resource management and cost charging opportunities.

In 2017 the unit successfully implemented a phase one electrical upgrade at a cost of c. £1m. This was a major infrastructure project increasing the electrical supply into the unit to include a new transformer station. Upon completion of these works the unit successfully applied for a phase two upgrade which will take the power into the offices and labs and reduce electrical fluctuations thereby reducing the need for inverter controls. A consulting firm has been appointed to provide the detailed specification ahead of works commencing in May 2018.

Recent smaller estates projects have focused on reconfiguration of existing space to improve space usability in Mengo, Entebbe and Masaka. A further tranche of funding was granted for Mengo reworks including new clinical space, improved office space and an increase to local storage. These works are expected to complete in 2018. The Estates team recognize the needs for better flexible accommodation to support unit programs.

We are delighted to announce that MRC has agreed to fund a new clinic research centre at a total cost c. £800k on land adjacent to the unit owned by UVRI. Details of the grant are being finalized and subject to a donation of £200k from Wellcome Trust.

**Research Support Office (RSO) headed by Mariam Nanteza**

The RSO has now been established and SOP’s written to assist with scientific funding proposals. All grants are now formally reviewed to ensure consistency of application and full economic costings. A large scale review has been undertaken on all cost drivers to ensure recovery of costs. This has increased the cost element of applications but does ensure that the unit will be recovering monies where the funder allows. Where there is a shortfall management will determine if we use core funding in support of new programmes. With the merger of LSHTM talks are ongoing regarding the need to apply TRAC costing to some Research Council grants. Initial reviews suggest there may be shortfalls in funding allocated and discussions are underway to ensure the unit is not disadvantaged by these changes. During the year to Nov 17 the RSO processed 23 external grants to the sum of £18.5m as lead investigators.
Finance headed by Monica Badaru
The finance team continues to operate tight internal controls enabling them to support external audit with no significant issues raised. The team deliver to the proposed month end timelines and reporting requirements as determined by Head Office. The team are working on the integration with LSHTM systems as the previous Oracle system is being replaced by Agresso. More flexibility has been granted to the unit especially regarding international procurement which will require a slight change in working practice and cash flow management.

RESEARCH COMPLIANCE AND QUALITY ASSURANCE

Geofrey Kimbugwe
Head- Research compliance and quality assurance

My background is Medicine and Surgery (MB ChB), and I am currently pursuing a Master’s of Science in Public Health. I have 5 years’ research experience to include clinical trials conduction and management, with two published papers. I have worked as a sub investigator on several phase 1 and phase 2a HIV vaccine and phase 1 and phase 2 Ebola/Marburg vaccine trials as well as high risk HIV cohort development and interventional studies, in addition to heading a key population HIV clinic.

Bernadette Nayiga Kalanzi-Clinical Research Coordinator

Bernadette joined the Unit in 2006 as study nurse, with a diploma in registered Comprehensive Nursing and later was sponsored by the Unit to undertake a post graduate diploma and Master of Science in Clinical Trials from London School of Hygiene and Tropical Medicine, University of London, which she completed in 2015. Upon completion she was promoted to Clinical Research coordinator a position she has held up to date. Her major role is to ensure that studies conducted by the Unit are compliant with ICH GCP, approved protocols, Standard Operating procedures (SOPs) and regulatory requirements.
Stephen Musemeza is the Quality Assurance Manager at MRC Unit. He has over Seven years’ experience in Quality Assurance Management. Stephen provides strategic leadership for the Unit’s quality improvement initiatives through routine audits staff training to ensure continuous process improvement and is responsible for ensuring the Unit’s compliance with all applicable local and external requirements to the established GCLP and ISO 15189 standards.

This section will undergo some restructuring in order to integrate, strengthen and expand this activity. This is to support the many clinical and laboratory studies in the Unit that require GCP, GCLP QA and other compliance and regulatory requirements. The Office will continue to assist investigators with Research Compliance involving among others protocol development, regulatory approvals and all the other complex aspects relating to research in human subjects. The section will also have an independent clinical research coordinator responsible for coordinating study approvals, compliance with GCP and GCLP as well as trial monitoring across the Unit. Quality Assurance will also fall under this section, to ensure that the laboratory quality management system is established, implemented and maintained in accordance with GCLP or ISO 15189 standards, participate in internal and external quality audits as directed by Management, coordinate laboratory accreditation and external audit activities, and to train personnel on quality management system activities among others.

The Unit has over 80 ongoing studies majority of these are either non interventional or Investigator initiated Clinical studies. During this reporting period, The Unit submitted the highest number of proposals (44%) to the UVRI REC. Whereas the sponsor contracts external monitors for Clinical Trials, for Investigator Initiated studies and observation studies this role is undertaken by research compliance section. We have set up minimum requirement for study start up to guide Principal Investigators and study coordinators on what needs to be in place before study commencement. We have conducted/ participated in site initiation visits and monitored investigator initiated studies as well as conducting site support visits across the four field sites.

The section actively participated in the Unit transfer activities. One other achievement was the Unit being accredited as a CPD provider. The section leads an in house ICH GCP training team. A number of templates have been developed aimed at ensuring study tools are uniform and is working towards ensuring that all SOPs for common procedures are standardised across the Unit.

We plan to set up an independent Clinical Trials Units to better support the implementation of quality control procedures across the Unit.

Laboratory Quality Assurance
As mentioned above, the MRC Laboratories including research labs had external assessments to become fully accredited under GCLP a prerequisite for clinical trial studies and the CDLS ISO 15189:2012 accreditation.

Our Laboratory external quality performance has greatly improved with more subscriptions to external testing programmes/schemes like CAP, RCPA, UKNEQAS, VQA, EQAPOL etc which is a key factor in determining the overall laboratory performance to generate credible research data.

We have updated our ELTEK systems that continuously monitor temperature of the stored specimens to guarantee their integrity. The equipment testing capacity as well as sample storage has greatly improved following the acquisition of more advance state of the art equipment in the different sites. Finally, the CDLS labs have put in place a laboratory information management system that will improve turnaround time of lab results and enhance lab service delivery in terms of result reporting.
The Communications and Public Engagement section is responsible for the translation of the Unit's research into policy and practice both locally and internationally and is guided by a strategy developed through a consultative process with staff, management and other stakeholders.

The section coordinates both internal and external communications, including branding and materials’ development and production and brings together communications and community mobilization activities with the aim to support the Unit’s research, through the effective engagement with various stakeholders at local, national and international levels.

Using various platforms such as online presence, Newsletters, media relations and stakeholder events etc., the section promotes the Unit’s stakeholder engagement for input into our work, sharing updates and dissemination of results.

Our audiences
- Unit staff
- Study participants/community members, Local Governments
- Study sponsors, funders, partner institutions etc.
- Regulatory authorities, Government agencies and Policy makers
- General public (National, regional and International)

COMMUNICATIONS AND PUBLIC ENGAGEMENT SECTION

Pamela Nabukenya Wairagala - Communications and Public Engagement Officer

Pamela leads the Unit’s communications and public engagement, with particular focus on building and sustaining visibility of the Unit’s work among stakeholders at national, regional and international levels. Her responsibilities include internal communications, stakeholder engagement, brand management, media relations, digital products, content generation, materials development and production among others.

She has worked as a Communications Specialist and Consultant with private, Non-Government Organizations (NGOs) as well as government Ministries, Departments and Agencies. Her areas of interests include development communications, community and public engagement and the strategic role of communication in organizational management.

A COMMUNITY LIAISON STAFF ENGAGES WITH STAKEHOLDERS

Community Liaison Officers and community mobilisers at the field stations spearhead the mobilization of community members to promote understanding of and participation in the Unit’s work through community events, one-on-one meeting as well as working with peer leaders.

The Unit works with a Community Advisory Board (CAB) at each of the field stations to strengthen two-way link processes between the research sites and local stakeholders. Each CAB comprises of not more than 20 members who may include political, administrative, religious and cultural leaders, medical professionals, local media, Community-based / non-governmental organizations, people living with HIV/AIDS, study participants as well as the general community. Membership to the CAB is by appointment by the respective constituencies and endorsement by the community leadership.
TRAINING (2015-2018)

1. Strategy
We combine focus – on sustaining and developing a world class research Unit – with outreach – supporting capacity development at Uganda Virus Research Institute (UVRI), in Uganda and the region, and for international global health. The components of our strategy are:

a. Partnership
b. Building support staff and systems
c. Supporting research career development

The Unit runs a competitive selection processes to attract and identify the best staff and trainees. Furthermore, it conducts annual appraisals and needs assessments to identify weaknesses and training gaps; workshops and short courses (local and international) to address identified needs; support for higher degrees; travel opportunities for knowledge exchange, training, broadening of research experience; supervision and mentorship. Figure 1 illustrates the number of training requests realised by category from the 2017 needs assessment. In addressing needs related to the Unit’s core functions, the training office works in collaboration with other sections and departments to ensure that the identified gaps are addressed appropriately. Opportunities to cover the gaps include targeted trainings and higher degrees.

1. Achievements
In the past three years, our training has extended to academic studies and short-term courses. For instance, 50 PhDs have been supported by the Unit of which 34 are still on-going. Early this year Unit has finalised selections of four postdoc fellows who will commence later on this year. Support is targeted at applications for “pump-priming” funds that have promise for future substantive funding. Students take their courses on either full-time or part-time basis, and locally or internationally. The flexible study options enable staff to grow their careers. Universities in which our students acquire knowledge and skills are seen in table1.

Table 1: Universities of our Masters and PhD Students during this reporting period

<table>
<thead>
<tr>
<th>University of Technology and Management University</th>
<th>Uganda Christian University</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edinburgh Business School-Heriot Watt University</td>
<td>Makerere University</td>
</tr>
<tr>
<td>Mbarara University of Science and Technology</td>
<td>University of Cape Town</td>
</tr>
<tr>
<td>London School of Hygiene and Tropical Medicine</td>
<td>University of Amsterdam</td>
</tr>
<tr>
<td>International Correspondence Schools Ltd</td>
<td>Medical University Graz</td>
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<tr>
<td>Makerere/Stellenbosch</td>
<td>University of Manchester</td>
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<tr>
<td>University of New South Wales</td>
<td>University of Antwerp</td>
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<tr>
<td>Ben Gurion University</td>
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</tr>
</tbody>
</table>

With experiences acquired from different countries – United Kingdom, Austria, South Africa, Israel, Belgium, Netherlands and Uganda – the Unit is equipped with staff that can handle world-cutting edge research.

Over the past three years, we have conducted various trainings related to bioinformatics and advanced laboratory methods and analyses; GCP, GLCP, IATA certification; safe handling of liquid nitrogen, boat safety, defensive driving, waste management, first aid and firefighting. Besides, various topics are covered through continuing medical education sessions that are held monthly in the different clinics.

Key areas of formal teaching have been in statistics (the Uganda Intensive and Advanced Courses in Statistics and Epidemiology run at UVRI; teaching in Tanzania at the Kilimanjaro Christian Medical University) in immunology (Immunology in the Tropics) and in qualitative research (in the Makerere-led “Training Health Researchers into Vocational Excellence” [THRiVE] consortium).
Table 2: Special Achievements in Capacity Development Partnerships

| MRC/UVRI, UVRI and the MRC’s Centre for Vaccine Research at Glasgow University. This was realised in the work of a joint (European) post-doctoral fellow and a joint (Ugandan) PhD student, using the new UVRI MiSeq to investigate causes of febrile illness and mosquito-borne viruses through RNA sequencing, and the award of a new MRC grant (£150,000) for the investigation of Zika virus in Uganda |
| The award of new funding to MUII (£4,500,000) and THRiVE (£5,000,000). |
| IAVI-supported VISTA initiative through USAID funding aimed at strengthening and expanding an international consortium of investigators in order to address gaps in HIV vaccine design. Through this initiative new assays and technologies are being introduced including HIV epitope mapping, viral inhibition assays and staff are training at Emory University, USA, in generation of infectious molecular clones |

We have enhanced our capacity to hold training events, seminars and symposia through the MRC-Wellcome Trust co-funded training building. Scientific seminars are conducted on a monthly basis in which staff get to know of recent developments in research within the Unit and across the world. Highlighted achievements in each of the three strategy areas are shown in the following sub sections.

Table 3: Bioinformatics Courses

| Dates | Courses |
| 6-9 July 2015 | Bioinformatics in the Tropics “Introduction to The development of a regional reciprocal bioinformatics analysis techniques for next monitoring network (through EAACR), for generation sequencing data” UVRI (MUII and Unit clinical trials, and on-line resources for staff; THRiVE, H3ABioNet, KEMRI-Kilifi, Africa training in Good Clinical Practice (GCP) Centre) |
| 14-16 Sept 2015 | Gene expression data analysis (wGoCrLkpshop) (MUII – and Unit staff in collaboration withhCwa.gselobWaelhsetearltnhtrainingcentre.tghn.org Reserve University) |
| 14-18 March 2016 | In-house Next Generation Sequencing workshop on Minority HIV drug resistance facilitated, UVRI, Public Health Agency of Canada. Funded by MRC |

1.1 Partnerships

Through partnerships in capacity development we receive support and expand opportunities, and contribute skills and opportunities to others. UVRI and Makerere University are key local capacity development partners. Special achievements in capacity development partnerships worth noting are listed in table2. We lead major regional capacity development consortia – the EDCTP-funded East African Consortium for Clinical Research (EACCR; www.eaccr.org; director P. Kaleebu) the Makerere University – UVRI Centre of Excellence for Infection and Immunity Research (MUII-plus; www.muii.org. ug; director A. Elliott) and the African Partnership for Chronic Disease Research (APCDR; https://www.cambridgetrust.org/partners/african-partnership-for-chronic-disease-research; (co-director P Kaleebu) and participate in others including (THRiVE; www.thrive.or.ug; UVRI lead J. Seeley). Key international capacity development partners are the LSHTM (which offers discounted PhD fees), and research partners who host placements in their laboratories and teach our courses. Partnerships have also facilitated bioinformatics trainings as seen in table 3, which shows selected courses that have run in the previous three years.

1.2 Building support staff and systems

The Unit aims to attract, and support career progression for talented individuals in research administration. The Unit is a leading participant in the UVRI internship programme which attracts about 300 applications and places over 100 interns per year (more than half with the MRC Unit). About 45% of all placements are in research support disciplines. Importantly, some of the best interns have been recruited to MRC employment. A senior nurse in the Co-infection Studies Programme (CiSP) was trained (through EACCR) as a trial monitor and has worked on studies and trials in CiSP and Epidemiology and Prevention, and elsewhere in the region.

Figure 2: UVRI internships 2015
The Unit supports the Eastern Africa Research and Innovations Management Association and contributed an acclaimed session on HIV research at the inaugural conference in 2015.

1.3 Research Career Development

Through our research career development framework illustrated in figure 3, we support our staff to reach the maximum of their abilities.

The Unit also offers important opportunities for international trainees. As well as internship and elective experience, we have supported 29 international visiting researchers for Masters or PhD, early work experience or post-doctoral training; these are formative experiences and steps for a career in global health.

In developing research careers, the Unit has a career development plan that comprises:

a. Mentoring: Through collaboration with MUII and funding from both MUII and MRC Head Office, the Unit has this year initiated a mentorship scheme. Senior Unit staff and international partners have volunteered as mentors; peer mentorship is also encouraged. The first cohort of mentors/mentees has already been trained and is leading the initiative while the next cohort is planned for 2019.

b. Leadership: Workshops (cohorts 1 and 2) were conducted in March and December 2017. Participants of cohorts 1 and 2 will facilitate forthcoming trainings in a bid to strengthen leadership capacity in the whole Unit at large.

c. Grant writing club: This is a forum in which scientists discuss their proposals that await submission. Besides, this is an avenue in which junior scientists develop their potentials for grant writing. Grant club meetings are usually held every last Friday of the month. Senior staff give their experience how they approach grant writing and share their experience of grant review panels and what they are looking for. In addition, a formal workshop on grant writing for post-doctoral scientists will be held in March 2018, as part of the Unit’s contribution to the new Crick African Network.

d. Seminar topics: In the UVRI seminar series, several topics are discussed that enhance capacity of Unit staff. Some topics that are discussed include communication skills, paper writing, critical thinking, networking and community engagement.

2. Summary

Experiences from previous years have led to the development of a five-year training plan (2017-2022) in a coherent strategy for developing capacity for both scientists and support staff at the Unit and for the region. In implementing the capacity development strategy of the Unit, the training office works in collaboration with supervisors, project leaders, heads of sections, heads of programmes and theme leaders to ensure learning gaps for staff are addressed timely and appropriately.
• HIV incidence and prevalence data generated continued to be used by the Ministry of Health (MoH), Uganda and by World Health Organisation/Joint United Nations Programme on HIV/AIDS (WHO/UNAIDS) to inform the understanding of national and global HIV trends.
• Data on life expectancy provided relevant information for Uganda’s Vision 2040
• New data on pre-treatment HIV drug resistance has recently led to a change on the first line treatment use of Dolutegravir
• Information on HIV vaccine research in the country.
• Results of the International Partnership on Microbicide (IPM) sponsored microbicide trial of the Dapivirine ring which indicate they could be an important HIV prevention option for those at risk.
• First evidence of the benefits and risks of discontinuing cotrimoxazole prophylaxis (COSTOP study) among HIV positive adults stable on ART. We propose to present a paper discussing the cost effectiveness of providing cotrimoxazole prophylaxis especially with the current test and treat in those with whose immunity is not yet compromised. Probably it’s not cost-effective where malaria is low
• START trial results that have shown the benefit of starting ART when CD4 counts are more than 500 cells/mm3. START results have influenced revisions of global HIV treatment guidelines, which today recommend initiating antiretroviral therapy upon diagnosis of HIV infection.
• Evaluation of new HIV rapid test algorithms which led to a change in the National HIV testing algorithm.
• Information on the burden of various NCDs and weaknesses of the health systems and areas for intervention.
• We are to draft a note to the Ministry of Health and Foreign affairs on the lack of evidence so far of circulation of Zika virus. This will be a basis for the provision of travel guidelines to those visiting Uganda.
• A community-based trial showed that a counselling intervention provided subsequent to HIV testing and referral for care improved linkage to care and ART initiation among HIV-positive adults identified through home-based HIV testing and counselling. This may be an important approach for promoting immediate linkage to ART in the context of the test and treat policy.
• DNA + protein HIV vaccine co administration, a new approach to candidate vaccine delivery.
• The CDLS in collaboration with other partners reported the emergence of low level ciprofloxacin resistant and multi drug resistant H-58 lineage Salmonella Typhi in Kampala.
• The SALIF study contributed to the introduction of Rilpivirine as a first line drug and the current use of the fixed dose combination (FDC) of Tenofovir/Emtricitabine/Rilpivirine (TDF/FTC/RPV) in some countries, especially where pre-treatment resistance is low.
• We produced, and shared with MoH, a policy brief from our mathematical modelling work, highlighting the effect of various scenarios of the costs and ART scale-up options on HIV incidence in Uganda. For example, we showed that if we valued each DALY averted at a minimum of USD210, then removing the CD4 threshold for ART initiation was highly likely to be cost-effective and would result into a reduction of up to 9% in HIV incidence 15 years later.
• LaVlISWA (Lake Victoria Island Intervention Study on Worms and Allergy-related diseases) results show intensive praziquantel treatment alone is unlikely to be the solution to schistosomiasis control in high-transmission hot-spots.
Our activities were guided by the scientific advisory committee who met annually. Below are the members during this reporting period.


**MRC HEAD OFFICE AND THE INFECTION AND IMMUNITY BOARD**

We continued to get support and advice from MRC head office. For this we thank the contributions of Dr. Jonathan Pearce, Dr. Morven Roberts, Amy McGregor and Paul Tait. We thank The MRC Management Board and the Estates Department for the support provided. We also thank Prof Paul Moss the chair of the II Board.
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Agincourt Study, South Africa
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Boston University, School of Public Health, USA Butabika National Psychiatric Hospital, Uganda
Case Western Reserve University, Ohio, USA
CDC Uganda
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H3A Type 2 Diabetes Consortium
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Imperial Cancer Research Fund, UK
Imperial College (St Mary’s Hospital and Chelsea and Westminster), UK
INDEPTH collaboration
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International Agency for Research on Cancer, Lyon, France
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Microsoft Research, Redmond, WA, USA
Institute Nazionale Tumori, Naples, Italy
Institute of Molecular Medicine, Oxford
School of Public Health, Makerere, Uganda
Institute of Tropical Medicine, Antwerp, Belgium
Institute of Women’s Health, Institute Pasteur, France
Instituto Nacional de Saúde, Ministry of Health, Maputo, Mozambique
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International Association of Suicide Prevention (IASP), Oslo, Norway
International Partnership on Microbicides, USA
Johns Hopkins University, USA
Joint Clinical Research Centre Kampala (JCRC), Uganda
Joint United Nations Programme on AIDS (UNAIDS), Geneva Switzerland
KEMRI/Wellcome Trust Research Institute, Kilifi, Kenya
Kilimanjaro Christian Medical Centre, Moshi, Tanzania
Kitovu Mobile Care Programme
Leiden University Medical Centre, The Netherlands
Liverpool School of Tropical Medicine
London School of Hygiene & Tropical Medicine, UK
Loyola University Medical School, USA
Makerere University College of Veterinary Medicine Animal Resources and Biosecurity (COVAB)
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Makerere University, College of Natural Sciences Makerere University, School of Graduate Studies
Makerere University- Johns Hopkins University Research Collaboration, Uganda.
Malawi - Liverpool – Wellcome Trust Clinical Research Programme
Masaka Regional Referral Hospital, Uganda
Microbicide Development Programme (MDP)
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Makerere University School of Biological Sciences
Microsoft Research, Redmond, WA, USA
Mildmay Centre Lubowa, Uganda


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PICTORIAL

STAFF AT THE MENGO FIELD STATION

THE UNIT RECEIVED A FLEET OF 21 VEHICLES AS PART OF THE CAPITAL BIDS FROM MRC-UK

PART OF THE ENTEBBE BASED OPERATIONS TEAM

STAFF AT THE ARCHIVES SECTION IN ENTEBBE

LAB STAFF IN KYAMULIBWA PREPARE TO DRAW BLOOD FROM ONE OF THE SHEEP AT THE FIELD STATION. THE BLOOD IS USED TO SUPPORT LAB-BASED RESEARCH WORK.
PART OF THE MASAKA BASED STAFF TEAM

SOME OF THE SENIOR SCIENCE TEAM

KYAMULIBWA STAFF

UNIT STAFF IN ONE OF THE LABS IN ENTEBBE

ART STORES IN KYAMULIBWA
CELEBRATING 25 YEARS OF RESEARCH THROUGH PARTNERSHIPS (1989-2014)

OFFICIAL OPENING OF THE MENG FIELD STATION BY THEN MINISTER OF HEALTH, HON. ELIODA TUMWESEIGYE

DR. ROBERTS AND THE UNIT DIRECTOR AT THE COMMISSIONING OF THE MENG FIELD STATION

A CROSS-SECTION OF GUESTS AT THE 25-YEAR ANNIVERSARY CELEBRATIONS IN ENTEBBE

RECOGNITION OF PEER LEADERS AT THE MENG FIELD STATION

SOME OF THE GUESTS ON A GUIDED TOUR OF THE NEWLY COMMISSIONED MRC CLINIC
MRC/UVRI AND LSHTM UGANDA RESEARCH UNIT

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