



Papua New Guinea
Institute of Medical Research



2006-11

Scientific Report



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PNG Institute of Medical Research

SCIENTIFIC REPORT 2006-2011



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Abbreviations and Acronyms

ACT	Artemisinin-based Combination Therapy
AIDS	Acquired Immunodeficiency Syndrome
ARI	Respiratory Infection
ART	Antiretroviral Therapy
AusAID	Australian Agency for International Development
CDC US	Centers for Diseases Control
CPHL	Central Public Health Laboratory
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
IRB	Institutional Review Board (of PNGIMR)
I&I	Infection and Immunity
LLIN	Long-lasting Insecticide-treated Net
MRAC	Medical Research Advisory Committee
NACS	National AIDS Council Secretariat
NCD	Non-Communicable Disease
NDoH	National Department of Health
NIH	National Institutes of Health
NGO	Non-government organization
NHMRC	National Health & Medical Research Council, Australia
NMCP	National Malaria Control Program
PCV	Pneumococcal Conjugate Vaccine
PHDU	Population Health and Demography Unit
PPV	Pneumococcal Polysaccharide Vaccine
PI	Principal Investigator
PIH	Partnership in Health
PLHIV	People living with HIV
PNG	Papua New Guinea
PNGIMR	Papua New Guinea Institute of Medical Research
RDT	Rapid diagnostic test
SRHU	Sexual and Reproductive Health Unit
STI	Sexually transmitted infection
TB	Tuberculosis
UNSW	University of New South Wales
VBDU	Vector Borne Disease Unit
WHO	World Health Organization



Forward

This Summary Report presents key scientific achievements for the period 2006-2011 and demonstrates the Institute's dedication and commitment to policy-relevant public health research to improve the health and wellbeing of the people of Papua New Guinea.

This period has seen the Institute consolidate its earlier success in obtaining research funding from international donor agencies such as the US National Institutes of Health (NIH) and the National Health & Medical Research Council (NHMRC), Australia that have allowed the PNGIMR to conduct world-leading scientific research, particularly in the epidemiology, prevention and control of malaria.

This success would not have been possible without the support of the Government of Papua New Guinea and the Australian Agency for International Development (AusAID) who generously provided core funding support to the Institute during this period.

In 2011, recognizing the Institute's need to continue to address national health priorities, two new Units were formed by the dissolution of the Operations Research Unit (ORU): the Population Health and Demography Unit (PHDU); and the Sexual and Reproductive Health Unit (SRHU). These now join the Infection and Immunity and Vector Borne Disease Units and the recently created Environmental and Emerging Diseases Unit, representing an important realignment of research priorities within the Institute.

Professor Peter Siba
Director, PNG IMR



Acknowledgement

This report could not have been written without the dedicated input and support from research scientists and technical support staff at the PNG IMR. Particular thanks go to the Unit and Section Heads and to the Principal Investigators of individual research projects. The PNGIMR would also like to acknowledge the study participants and communities who took part in the research activities summarised in this report, without whom this work would not have been possible.

Infection and Immunity Unit



1. Infection and Immunity Unit

1.1.1 Overview

Our Mission is to conduct research that will improve our understanding of the major and emerging causes of illness and death in Papua New Guinea; with the aim of improving the health of all Papua New Guineans.

Within the Infection and Immunity Unit (I&I) there are two main research streams: respiratory infections and enteric infections. In both research streams we seek to conduct integrated cross-disciplinary research on the most important infectious diseases in PNG. The majority of our research projects include two or more of the research sections within I&I, and we actively collaborate with other units within the PNGIMR as well as with national and international partners to fulfill our mission.

1.1.2 Research Objectives

The work of I&I encompasses the following research objectives:

1. Investigate the aetiology of important illnesses in PNG, including acute respiratory illnesses, diarrhoea and febrile illness.
2. Investigate preventative strategies for the major causes of illness and death in PNG, playing particular focus on vaccine studies for prevention of *Streptococcus pneumoniae* infection.
3. Use modern techniques to better understand the epidemiology of infectious diseases in PNG.
4. Gain an insight into the relationship between pathogen, host and environment in the PNG context.

1.1.3 Achievements 2006 – 2011

Over the past five years, the unit have put together a team of senior scientists to conduct locally-relevant research. The team has come together through a combination of capacity building of local scientists and new recruitment. This work is supported by a team of excellent technical and research staff.

Through the formation of a collegiate team of researchers and the support of the Institute's senior management, I&I has been able to leverage external research funds and form new collaborations, which has helped increase the output of the unit. The unit has undertaken a variety of important research in the past five years,

particularly pneumococcal vaccine studies (PCV). In 2006 we commenced a 7-valent PCV trial to determine the safety and immunogenicity of the vaccine when given at 0-1-2 months and 1-2-3 months. We have demonstrated that the vaccine is safe and immunogenic when given at 0-1-2 months. We have also investigated the immune response of children who had received a pneumococcal polysaccharide vaccine (PPV) booster, as it has been speculated that PPV may dampen the immune response when given to young children. Our data do not support this finding, suggesting that the cheaper, broader coverage PPV could play an important role in preventing deaths due to pneumococcal infection in PNG.

Our enteric disease research has expanded in recent years. We have conducted surveillance of rotavirus infection in children at Goroka General Hospital and shown that rotavirus accounts for around 30% of all hospitalizations in children under 5 years with diarrhoea. These data will be used to determine the feasibility of a rotavirus vaccine in PNG. We have also evaluated typhoid fever diagnostic tests in an attempt to improve typhoid diagnosis in PNG. The unit has also participated in research to improve understanding of the epidemiology and transmission of cholera in PNG. In addition, we have collaborated with researchers from other units to gain data on the development of antimicrobial resistance in PNG. Current and future studies will monitor antibiotic resistance, as little data are obtained through hospital pathology laboratories due to the lack of routine services for bacteriological culture.

1.1.4 I&I Organizational structure

I&I is organized into three sections and at the end of 2011 had a workforce of approximately 25 scientific research staff working on more than 15 research projects.

Unit Head, **Dr Andrew Greenhill**

Section Heads

Bacteriology, **Dr Andrew Greenhill**

Virology, **Dr Paul Horwood**

Immunology, **Dr William Pomat**



1.2 I&I Research projects 2006-2011

- 1.2.1 Neonatal PCV Study
- 1.2.2 Neonatal Immunity Study
- 1.2.3 IgG/IgE Study
- 1.2.4 Typhoid Diagnosis
- 1.2.5 Influenza Surveillance
- 1.2.6 Rotavirus Surveillance
- 1.2.7 PiH Disease Surveillance
- 1.2.8 Neonatal PCV Follow-up Study
- 1.2.9 Epidemiology of *Vibrio cholerae*
- 1.2.10 HIV Co-infection Study
- 1.2.11 Avian Influenza Surveillance
- 1.2.12 Cholera Environmental Persistence
- 1.2.13 10v and 13v PCV Study
- 1.2.14 Aetiology of ARI & Meningitis
- 1.2.15 Kuru study

1.2.1 Neonatal PCV Study

Summary

Title: Neonatal immunization with pneumococcal conjugate vaccine in Papua New Guinea

Date commenced: November 2004

Project funding: Wellcome Trust, UK and NHMRC Australia

About the project

Rationale: A large clinical trial in California demonstrated the efficacy of the 7-valent pneumococcal conjugate vaccine (PCV7) when given at 2-4-6 months which led to the introduction of PCV in many industrialized countries. Earlier schedules are needed for PNG and other low-income countries where high intense carriage occurs early in life leading to disease at a young age. This study investigated safety and immunogenicity of PCV given at 0-1-2 or 1-2-3 months and compared immune response and carriage rates of *Streptococcus pneumoniae* to children who did not receive PCV.

Design: Of 400 mothers who assented, the newborn children of 318 mothers were recruited into the study. 280 children were followed up to 18 months of age. Children were randomized to receive PCV7 at 0-1-2 months, 1-2-3 months or no PCV. At 9 months a single dose of 23-valent pneumococcal polysaccharide vaccine (PPV23; also commonly referred to as Pneumovax) was given as a booster to all children. Blood, pernasal swabs and saliva were collected prior to vaccination and at various time points to 18 months of age.

Progress: Field component was completed in 2009, laboratory component continuing, particularly mucosal immunity and functional antibody assays.

Significance: Results show no deleterious effect of neonatal (0-1-2 months) PCV7 administration. PCV7 is immunogenic in PNG neonates and young infants, and both neonatal and early infant (1-2-3 months) schedules primes for immunologic memory for PCV7 serotypes. A booster response to PPV at age 9 months and sustained serotype-specific antibody concentrations to age 18 months was observed in both vaccine arms. PPV also induces good antibody responses for some pneumococcal serotypes that are not included in PCVs but commonly cause disease in PNG. Carriage of pneumococcus in the nasopharynx is often used to determine the effect of PCV. In the highlands of PNG 70% of neonates were colonized with *Streptococcus pneumoniae* by age 1 month and overall carriage rates did not vary between vaccine and control groups. Over 50 different pneumococcal serotypes have been isolated, demonstrating the diversity of carriage of pneumococcus. This can reduce the impact of the PCV on carriage as only a small proportion of carried pneumococci will be targeted by the vaccine. Indeed, at age 9 months, 68-78% of pneumococci were non-7vPCV serotypes. Multiple serotypes were more commonly identified in unvaccinated than vaccinated children. Studies of cellular immune responses show that early schedules of 7vPCV induce normal memory T-cell responses and do not interfere with general immune maturation.



Communicating information about pneumonia to mothers in Bena, Eastern Highlands province.

Contributors

Investigators: Deborah Lehmann (PI), John Reeder, Peter Siba, Suparat Phuanukoonnon, Peter Richmond, Pat Holt, Anita van den Biggelaar, William Pomat, Peter Jacoby.

Collaborating centres: PNG Institute of Medical Research; Goroka General Hospital, University of Western Australia, Telethon Institute for Child Health Research.

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1.2.2 Neonatal Immunity Study

Summary

Title: Differences in neonatal immune regulation in the 'developing' and 'developed' world: implications for neonatal vaccinations

Date commenced: 2008

Project funding: NHMRC Australia

About the project

Rationale: There is increasing evidence that functional state of immune system at birth is predictive of kinetics of immune maturation in early infancy. This maturation process can have major impact on early vaccine responses and can be key determinants of risks for communicable and non-communicable disease in later life. Most knowledge on immune maturation is derived from studies in developed countries: very little information pertaining to immune maturation in developing countries exists, where environmental and genetic risk factors differ.

Design: This study aims to investigate the process of immune maturation in PNG children in relation to neonatal immune responses, environmental and genetic factors.

Progress: Field component of the study was completed in 2010, laboratory component is continuing at the Telethon Institute for Child Health. Of 247 mothers recruited, 132 cord bloods were collected at birth. Stool samples were collected from mothers and indoor air pollution was measured in each household over a 24 hour period.

Significance: This study showed that high maternal parasite load and high indoor air pollution in traditional houses in the highlands of PNG may add to burden of respiratory diseases. However, neonatal immune functions were quiescent (not elevated) in this population compared to those living in modern environmental conditions, despite conditions that might be expected to activate the immune response.

Contributors

Investigators: Anita van den Biggelaar, Danielle Stanisc, Suparat Phuanukoonnon, Wendy Kirarock, William Pomat, Gerard Saleu, Christine Opa, Audrey Michael, Joanne Lisciandro, Susan Prescott, Pat Holt.



Staff explaining about pneumonia at the PNGIMR exhibition booth, Morobe Show, 2012.

Collaborating centres: PNG Institute of Medical Research; Goroka General Hospital; Modilon Hospital, Telethon Institute for Child Health Research, University of Western Australia.

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1.2.3 IgG/IgE Study

Summary

Title: The genetics of immunoglobulin E (IgE) in parasitized and allergic individuals

Date commenced: 2008

Project funding: UNSW Faculty Research Grant and NHMRC

About the project

Rationale: The pathway to protective immunity against helminth parasites remains unclear, but a conspicuous feature of the anti-parasite response involves production of IgE antibodies. These

antibodies are the product of a tiny fraction of circulating B cells, and their study has therefore always been problematic. The study of immunoglobulin gene sequences provides a means by which aspects of the biology of these important cells can be inferred, and by which light can be shed on the nature of the human anti-parasite immune response.

Design: This study aims to amplify and sequence large numbers of germline and rearranged antibody genes of different isotypes (IgG and IgE), so that the patterns of gene usage and patterns of somatic mutation can be determined in parasitized individuals.

Progress: Samples were collected in 2008, and have been under investigated since. Over 1000 IgE and IgG sequences were generated using Sanger sequencing. Next generation sequencing was then applied to generate additional sequences including IgE and IgG subclass-specific heavy chain genes, kappa chain rearrangement and unrearranged germline IGHV genes. Together these data allows an unprecedented view of the immune response in parasitized individuals. Sequences are still being generated from those samples, to more fully and accurately describe the genes that contribute to anti-parasite response.

Significance: These studies are the first detailed immunogenetic studies of immunoglobulin in Papua New Guinea and they have already demonstrated a number of surprising features about the immunogenetics of anti-parasite responses in Papua New Guineans:

1. We have shown that the germline immunoglobulin genes include many allelic variants that have never before been seen.
2. We have shown that light chain genes and the light chain gene repertoire is essentially indistinguishable from those seen in other human populations
3. We have shown that the IgE response in parasitized individuals has the mutational characteristics that have previously been associated with allergic IgE antibodies. In particular, the results suggest that the anti-parasite IgE response is not subject to the process of affinity maturation, which is a feature of the classic T cell-driven IgG response.

Contributors

Investigators: Andrew Collins, Yan Wang, Peter Siba, William Pomat, Katherine Jackson, Janet Rimmer, William Sewell, Bruno Gaeta.

Collaborating centres: PNG Institute of Medical Research; University of NSW, Sydney, Australia; Stanford University, USA; Royal North Shore Hospital, Sydney, Australia; Sewell, Garvan Institute, Sydney, Australia.

Publications

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1.2.4 Typhoid Diagnosis

Summary

Title: The evaluation of typhoid diagnostic systems for use in Papua New Guinea

Date commenced: April 2008

Project funding: PNGIMR Internal Grant (through AusAID core funding)

About the project

Rationale: Typhoid fever, caused by *Salmonella enterica* serovar Typhi, is one of the leading causes of fever in low-income countries. It often presents with non-specific signs and symptoms, making accurate clinical diagnosis very difficult. In PNG the Widal test remains the mainstay of diagnosis (alongside clinical diagnosis), however it is known to have poor sensitivity and specificity.

Design: We evaluated two commercially available kits, one prototype, and the currently used Widal test, comparing them to the traditional gold standard of blood culture, as well as a gold standard of blood culture plus real-time PCR. Febrile patients were recruited from the Goroka General Hospital outpatients and Lopi Urban Clinic in Goroka. For each diagnostic test we calculated the sensitivity, specificity, positive predictive value and negative predictive value.

Progress: Sample collection and laboratory analysis has been completed. Data analysis is nearing completion.

Significance: In general, the commercially available antibody based rapid detection methods do not significantly improve typhoid diagnosis in PNG. The prototype we evaluated had a sensitivity of 89% and a specificity of 85%. This is among the best performing typhoid rapid diagnostic tests that have been evaluated in a community setting. The prototype warrants further evaluation, but unfortunately will not be made commercially available in the foreseeable future as the manufacturer is no longer in business.

Contributors

Investigators: Andrew Greenhill (PI), Peter Siba, and the Infection and Immunity team at PNGIMR.

Publications

CONFERENCE PRESENTATIONS

1. The molecular detection of *Salmonella typhi* and other *Salmonella* species from blood using polymerase chain reaction. Siba V, Greenhill A, Horwood P, Siba P. Abstract in Program and Abstracts of the 46th Annual Symposium of the Medical Society of Papua New Guinea, Sep 2010, Wewak, PNG.
2. The evaluation of typhoid fever diagnostic systems for use in Papua New Guinea. Siba V, Greenhill A, Francis J, Lai M, Martin B, Vanuga K, Sehuko A, Solomon A, Siba P. Abstract in Program and Abstracts of the 45th Annual Symposium of the Medical Society of Papua New Guinea. Sep 2009, Port Moresby, PNG

1.1.5 Influenza Surveillance

Summary

Title: Sentinel surveillance for influenza

Date commenced: April 2008

Project funding: WHO (Global Influenza Surveillance and Response System)

About the project

Rationale: The PNG Institute of Medical Research (PNGIMR) is the National Influenza Centre (NIC) for PNG. As such we contribute to the global network to monitor for new and emerging influenza strains which may have pandemic potential.

Design: Nasopharyngeal samples are collected from patients presenting at sentinel clinics with the symptoms of influenza infection (WHO definition): An acute respiratory illness with onset during the last 7 days with, measured temperature $\geq 38^{\circ}\text{C}$, and cough. Nasopharyngeal samples are collected by nursing staff at sentinel sites and sent to the PNGIMR laboratories where they are tested for influenza A and B viruses using real-time PCR assays supplied by the US Centers for Diseases Control (CDC). Influenza A viruses are further characterized using a panel of real-time PCR assays to determine the haemagglutinin subtype (i.e. H1pdm, H1, H3 or H5). All positive samples are sent to the WHO Collaborating Centre in Melbourne for further characterization.

Progress: Ongoing with annual review.

Significance: Through this research PNGIMR is contributing to the global network to monitor for pandemic influenza outbreaks. This research is also helping to determine the role that influenza viruses play in pneumonia and other respiratory illnesses in PNG.

Contributors

Investigators: Paul Horwood (PI), Peter Siba, Marinho Jonduo, Jacinta Kono.

Collaborating centres: WHO Collaborating Centre for Reference and Research on Influenza, Melbourne.

Publications

CONFERENCE PRESENTATIONS

1. Viral pneumonia in Papua New Guinea Horwood PF. 2010. Papua New Guinea Pneumonia Colloquium, 2010, Goroka, Papua New Guinea,

2. Influenza surveillance in Papua New Guinea Jonduo MH, Suarkia DL, Jimmy S, Sumun S, Mauta L, Ropa B, Siba PM, Horwood PF. 2010. Papua New Guinea Medical Symposium. Wewak, Papua New Guinea. Abstract in Program and Abstracts of the 46th Annual Symposium of the Medical Society of Papua New Guinea, Sep 2010, Wewak, PNG.

1.2.6 Rotavirus Surveillance

Summary

Title: Sentinel surveillance for rotavirus

Date commenced: April 2008

Project funding: WHO Western Pacific Region Rotavirus Surveillance Network

About the project

Rationale: Rotavirus is the most important cause of acute gastroenteritis in children <5 years of age throughout the world. Two live attenuated vaccines have been licensed and proven efficacious for protection against rotavirus infections, namely RotaTaq (Merck) and Rotarix (GlaxoSmithKline Biologicals). The ability of these vaccines to protect against uncommon rotavirus strains is not fully understood. Therefore, it is important that baseline data is collected to determine which rotavirus genotypes are circulating in a population before vaccination, and that surveillance continues after vaccination to monitor for the emergence of new or uncommon strains.

Design: Stool samples are collected from the paediatric ward from the Goroka General Hospital from children presenting with the following definition: aged under 5 years with >3 loose motions in the previous 24 hours, no blood in the stool, and sample collected within 48 hours of hospitalization. Samples are transferred to the PNGIMR laboratory in Goroka where they are tested for rotavirus antigen using an enzyme linked immunosorbent assay (ELISA). All positive samples are sent to the WHO Collaborating Centre for further characterization.

Progress: Ongoing with annual review.

Significance: The newly developed rotavirus vaccines have been shown to greatly reduce morbidity and mortality of childhood gastroenteritis throughout the world. However, the ability of the vaccines to protect against uncommon genotypes is not well understood.

Contributors

Investigators: Paul Horwood (PI), Peter Siba, Sauli Bebes.

Collaborating centres: WHO Collaborating Centre for Rotavirus, Melbourne, Australia.



Working in the pathogens laboratory, a staff extracts DNA from samples.

1.2.7 PiH Disease Surveillance

Summary

Title: Sentinel surveillance of the major causes of febrile, respiratory and enteric diseases

Date commenced: 2009

Project funding: Partnership in Health Project (PiHP)

About the project

Rationale: The diagnosis of febrile illnesses is particularly poor in PNG and other low-income countries, where febrile patients are typically diagnosed as having either malaria or typhoid fever despite these diseases only causing 20-30% of fever in endemic areas. A detailed aetiological study is required to determine the true cause of fever in PNG. Similarly the full spectrum of pathogens involved in the aetiology of respiratory and enteric diseases is poorly understood.

Design: We are conducting surveillance of infectious diseases in the PiH demography sites. Clinical staff at health centres screen patients for signs and symptoms: patients with suspected acute respiratory infection, diarrhoea or febrile illness have specimens collected and analyzed for pathogens. A combination of rapid detection methods, traditional culture and molecular diagnostics are being used.

Progress: Sample collection has commenced in one of the four sites to date. We expect to commence sample collection at the remaining three sites during 2012. We have established numerous (>30) molecular assays to enable the sensitive detection of bacterial and viral pathogens associated with febrile, respiratory and enteric illnesses. We also have culture methods established for important bacterial pathogens.

Significance: This study will provide much needed data on the real causes of the main disease presentations (acute respiratory infection, diarrhoea and fever of unknown origin) in PNG. In determining the aetiology of these diseases, we will also trial PNG-appropriate diagnostic methods, and determine antimicrobial resistance patterns in isolated pathogens. These data could have important public health implications.

Contributors

Investigators: Paul Horwood (PI), Andrew Greenhill (PI), and the PIH team.

Collaborating centres: PNG Institute of Medical Research, University of Tokyo.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Arboviruses of human health significance in Papua New Guinea. Jonduo MH, Bande G, Horwood PF. PNG Med J. [In Press]

1.2.8 Neonatal PCV Follow-up Study

Summary

Title: Investigation of serotype-specific antibody persistence and B-cell memory at age 3 - 5 years following 23-valent pneumococcal polysaccharide vaccine at age 9 months in Papua New Guinean children previously primed with 7-valent pneumococcal conjugate vaccine

Date commenced: 2010

Project funding: PNGIMR (ICRAS); Telethon Institute of Child Health Research

About the project

Rationale: The PCV follow-up study was initiated following concerns that vaccination of children with pneumococcal polysaccharide vaccine (PPV23) at 12 months led to less responses at 18 months when children were challenged with a 0.1mg/ml dose of PPV23 (to mimic infection with *S. pneumoniae*). This interpretation arose from studies in Fiji that showed no marked increase in antibody GMC after vaccination with PPV23 at 12 months, especially in children initially primed with PCV. This is of great concern for PNG children as rates of carriage and diseases are higher than in Fijian children.

Design: The study was conducted in the Asaro Valley (Eastern highlands Province), recruiting 130 children from the Neonatal PCV study (as described previously) and 150 age-matched controls. Children were given a challenge dose of PPV at 3-5 years and followed up a month later for blood to be collected.

Progress: Of 289 children vaccinated at 9 months with PPV23, 150 were followed to 3-5 years of age and challenged with 0.1mg/ml dose of PPV23. 130 age-matched children (controls) were also given a challenge dose of PPV23. Blood was collected pre- and post-challenge dose of PPV23 to measure antibody GMC to serotypes 2, 4, 5, 7F, 9V, 14, 18C, 19F and 23F. Nasopharyngeal carriage was also investigated.

Significance: Generally lower GMC were measured in unvaccinated children than PPV23 challenged children. Protective IgG GMC $\geq 1.0\mu\text{g/mL}$ was detectable in 62.8 - 98.9% in previously unvaccinated children compared to 72.3 - 98.9% in PPV vaccinated children. IgG GMC $\geq 1.0\mu\text{g/mL}$ post-PPV challenge dose was 82.1 - 97.6% and 78.4 - 98.8%, in controls and PPV vaccinated children, respectively. Means fold rise in controls were higher as their antibody pre-challenge were lower (1.2 - 3.4 vs. 1.2 - 2.8 & 1.4 - 3.0 in PCV/PPV or PPV only). GMC were slightly lower in children less than 47 months compared to those greater than 48 months of age. Despite adequate immune responses, carriage rates were high pre- and post-challenge dose (>84%) in these children.

Contributors

Investigators: William Pomat, Andrew Greenhill, Peter Richmond, Deborah Lehmann, Jacinta Francis, Audrey Michael, Gerard Saleu, Christine Opa, Peter Jacoby, Anita van den Biggelaar, Peter Siba.

Collaborating centres: PNG Institute of Medical Research; University of Western Australia, Telethon Institute for Child Health.

Publications

CONFERENCE PRESENTATIONS:

1. High pneumococcal carriage in 3-5-year-old Papua New Guinea children following 9-month Pneumovax23 dose with or without prior 7-valent conjugate vaccine. Yoannes M, Michael A, Saleu G, Opa C, Greenhill A, Siba P, Pomat W, Lehmann D. 2011, 8th International Symposium on Pneumonia and Pneumococcal Diseases (ISPPD-8), Mar 2012, Iguacu Falls, Brazil.
2. No evidence of hypo-responsiveness following re-challenge at 3-5 years in PNG children vaccinated with Pneumovax at 9 months. Pomat W, Francis J, Orami T, Siba P, Greenhill A, Phuanookoonun S, Saleu G, Opa C, Lehmann D, Richmond P and PNG PCV Vaccine Trials Team. 8th International Symposium on Pneumonia and Pneumococcal diseases (ISPPD-8) Mar 2012, Iguacu Falls, Brazil.

1.2.9 Epidemiology of *Vibrio cholerae*

Summary

Title: The Molecular Epidemiology of *Vibrio cholerae* in Papua New Guinea

Date commenced: July 2010

Project funding: WHO PNG

About the project

Rationale: Cholera was first reported in PNG in mid-2009 and spread throughout lowland PNG. Given the previously cholera free status of PNG, there was considerable speculation regarding the origins of the disease. Moreover, there were fears that the causative organism, *Vibrio cholerae*, might mutate quickly in this non-endemic environment. PNGIMR conducted studies on the molecular epidemiology of *V. cholerae* in an attempt to better understand factors surrounding the introduction and spread of the disease in PNG. The study also provided an initial characterization of the pathogen in PNG, which may provide useful should future outbreaks occur.

Design: Clinical isolates were obtained primarily through the Port Moresby General Hospital, which acted as the national reference laboratory during the cholera outbreak. Suspected isolates were also obtained from Madang, which has also lead to studies investigating the diagnosis of cholera. Molecular typing was conducted on representative isolates from throughout the country using variable number tandem repeat (VNTR) and multi-locus sequence typing (MLST) to determine the relatedness of isolates to each other and to isolates reported in the literature from other countries.

Progress: Due for completion in June 2012.

Significance: This research is of national and international significance. We have established that all isolates from around the country were very closely related (clonal), confirming the suspicion that the outbreak arose from a single pathogenic strain of *V. cholerae* that spread throughout lowland PNG. It is likely that this pathogenic strain was recently introduced to PNG. The PNG strain is closely related to Vietnamese strains; however, it is not possible to ascertain exactly where the pathogenic strain originated from or the route of introduction into PNG.

Contributors

Investigators: Andrew Greenhill (PI), Paul Horwood, Peter Siba.

Collaborating centres: PNG Institute of Medical Research; Port

Moresby General Hospital Pathology Laboratory, The PNG National Department of Health; World Health Organization, PNG.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Clonal Origins of *Vibrio cholerae* O1 El Tor Strains, Papua New Guinea, 2009-2011. Horwood PF, Collins D, Jonduo MH, Rosewell A, Dutta SR, Dagina R, Ropa B, Siba PM, Greenhill AR. Emerg Infect Dis 2011; 17: 2063-5.
2. Cholera in Papua New Guinea and the importance of safe water and sanitation. Horwood PF, Greenhill AR. In Review with WPSAR 2012. 3(1): doi 10.5365/wpsar.2011.2.4.014
3. Improved laboratory capacity is required to better respond to future cholera outbreaks in Papua New Guinea. Greenhill AR, Rosewell A, Kas M, Manning L, Latorre L, Siba PM, Horwood PF. In Review with WPSAR

CONFERENCE PRESENTATIONS

1. The epidemiology of cholera in Papua New Guinea. Greenhill AR, Horwood P, Collins D, Hilla M, Dutta SR, Siba P. 60th Annual Meeting of the American Society of Tropical Medicine and Hygiene. Dec 2011, Philadelphia, USA.
2. Molecular characterization of clinical isolates of *Vibrio cholerae* from Papua New Guinea. Horwood PF, Collins D, Hilla M, Dutta SR, Siba PM, Greenhill AR. The Australian Society for Microbiology 2011 Annual Conference, Jul 2011, Hobart, Australia.
3. Development of a molecular confirmatory test for *Vibrio cholerae* and other enteric pathogens in Papua New Guinea. Kas M, Siba P, Waiin B, Horwood P, Greenhill A. 47th Annual Symposium of the Medical Society of Papua New Guinea. Sep 2011, Kimbe, PNG
4. Cholera in Papua New Guinea: an additional burden on the health system in a resource limited setting. Greenhill AR. Invited key note address at the Australian Institute of Medical Scientists Tropical Division Conference, Jun 2011, Mackay, Australia.
5. The molecular epidemiology of *Vibrio cholerae*, the causative agent of cholera, in Papua New Guinea. Greenhill A, Collins D, Horwood P, Dutta SR, Laman M, Atua V, Manning L, Siba P. 46th Annual Symposium of the Medical Society of Papua New Guinea. Sep 2010, Wewak. PNG.

THESES

1. Enteric microbiota and its relationship to cholerae diagnosis by stool culture in Papua New Guinea. Kas M. Honours Thesis, University of Papua New Guinea.



Scientific officers analyzing samples of *V.Cholera* at the Institute's Laboratory.

1.2.10 HIV Co-infection Study

Summary

Title: An investigation into the causes of concurrent infections in HIV positive people in PNG: a greater knowledge will improve diagnosis and treatment

Date commenced: September 2010

Project funding: NACS PNG

About the project

Rationale: HIV remains a serious social and health threat in PNG. Much of the research to date has centered on social research aiming to better understand drivers of the epidemic. But little is known about the causes of illness in HIV positive people in PNG. This study aims to determine the major (infectious) causes of illness HIV-positive people, which due to the nature of HIV have an increased susceptibility to infectious diseases.

Design: This two-year cross-sectional multi-site study is investigating the aetiology and relative burden of infectious diseases in HIV-positive people in PNG. Sample collection was initially from Madang, Goroka and Port Moresby, with collection now being conducted in the latter mentioned two sites only. Participant recruitment takes place from HIV/STI clinics and hospital wards.

Progress: Recruitment has been slower than expected. This is perhaps in part due to the successful rollout of antiretroviral therapy (ART) in urban areas of PNG: people who adhere to ART have better immune function and are less likely to succumb to infectious diseases. The initial study design was to include Madang, Goroka and Port Moresby in the study. After over 12 months of sample collection in Madang, only ~20 samples had been collected: on this basis it was decided to cease sample collection from that site. We are concentrating on sample collection in Goroka and Port Moresby, and hope to increase recruitment in Port Moresby. We will continue to collect samples throughout 2012.

Significance: This study will provide much needed information on the infections that HIV positive people succumb to in PNG. A better knowledge of these infections will enable us to adopt appropriate diagnostic methods, use targeted treatments and explore appropriate interventions to prevent some infections.

Contributors

Investigators: Andrew Greenhill (PI), Peter Siba, Jeffrey Warner, Ivo Mueller, Suparat Phuanookoonun, Angela Kelly, Audrey Michael, John McBride.

Collaborating centres: PNG Institute of Medical Research; James Cook University.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Human immunodeficiency virus and respiratory disorders: clinical and diagnostic considerations. McBride WJ, Greenhill AR. PNG Med J 2010; 53(3-4): 169-75.

1.2.11 Avian Influenza Surveillance

Summary

Title: Surveillance and characterization of avian influenza viruses in Papua New Guinean poultry

Date commenced: March 2011

Project funding: St Jude Children's Research Hospital (Center of Excellence for Influenza Research and Surveillance), Memphis USA.

About the project

Rationale: The natural host for influenza A viruses are ducks and other aquatic bird species. Occasionally, these viruses can cross the species barrier and infect a diverse range of animals, including poultry, humans, pigs and horses. The recent spread of highly virulent H5N1 'bird flu' throughout Southeast Asia and other regions of the world resulted in massive numbers of poultry deaths and fears of a devastating human pandemic. We are conducting surveillance and characterization of avian influenza viruses in poultry populations throughout PNG to determine the epidemiology and ecology of these viruses.

Design: Avian samples (oropharyngeal swabs, cloacal swabs and serum) are collected from domestic poultry by the National Agriculture and Quarantine Inspection Agency (NAQIA). The samples are collected from sites all around PNG and sent to the PNGIMR laboratory in Goroka for analysis. Influenza A viruses are detected using real-time PCR. All positive samples are sent to the St Jude's laboratories for further analysis and characterization of influenza subtypes.

Progress: Ongoing (>1,600 samples collected); anticipated completion by mid-2012.

Significance: The close proximity of Papua New Guinea (PNG) to the outbreak region means that there is a high-risk of introduction of this virus due to bird migrations or the transport of poultry. Early detection of new or highly pathogenic influenza viruses in poultry populations must rely upon an effective and efficient surveillance system.

Contributors

Investigators: Paul Horwood (PI), Peter Siba, Marinjho Jonduo, Richard Webby, Pamela McKenzie, Nime Kapo.

Collaborating centres: St Jude Children's Research Hospital (Center of Excellence for Influenza Research and Surveillance) Memphis USA, PNG National Agriculture and Quarantine Inspection Agency (NAQIA).



Children drawing water from a well, in Madang.

1.2.12 Cholera Environmental Persistence

Summary

Title: Development of molecular surveillance tools for the monitoring of cholera outbreaks and analysis of the factors that influence cholera transmission.

Date commenced: June 2011

Project funding: PNGIMR ICRAS

About the project

Rationale: The natural habitat of *Vibrio cholerae*, the aetiological agent responsible for cholera, is an environmental organism whose natural habitat is water. The pathogenic strain of *V. cholerae* is likely to persist in the environment in PNG, giving rise to the risk that there will be ongoing transmission (or a new outbreak in the future). The ability to detect *V. cholerae* in the environment will assist researchers and public health authorities to predict future outbreaks, as increased numbers in the environment increases the risk of human disease.

Design: This two-year multi-disciplinary study commenced in mid-2011. The study will investigate:

1. The presence of *V. cholerae* in environmental water samples, and factors that influence the population dynamics of *V. cholerae* and;

2. Social and demographic factors that influence the transmission of cholera. The study will be conducted primarily in Lae, Morobe Province, and we will also trial our methodology in the Madang Province.

Progress: To date, the project has concentrated on an evaluation of methods to detect *V. cholerae* in the environment. This aspect of the study is nearing completion, and soon sample collection will commence in Morobe Province. The sociological survey will be conducted in mid-2012.

Significance: Environmental water sources are the reservoir of infection for cholera transmission. A greater understanding of this reservoir of infection in PNG will greatly improve our ability to predict, and hopefully prevent, future outbreaks.

Contributors

Investigators: Paul Horwood, Andrew Greenhill, Hebe Gouda, Marinjho Jonduo.

Collaborating centres: PNG Institute of Medical Research; PNG University of Technology, Lae; University of New South Wales.

1.2.13 10v and 13v PCV Study

Summary

Title: A study to determine the safety and immunogenicity of 10-valent and 13-valent pneumococcal conjugate vaccines in Papua New Guinean children

Date commenced: November 2011

Project funding: Exxon Mobil

About the project

Rationale: The primary aim of this study is to determine whether the pneumococcal conjugate vaccines PCV10 and PCV13 are safe and immunogenic in PNG infants for the serotypes in the respective vaccines to determine which is the most suitable for introduction into the national schedule.

Design: This randomized control trial will investigate the safety and immunogenicity of PCV10 and PCV13 in 200 children. 100 children will receive PCV10 and 100 will receive PCV13. At 9 months, 50 children in each arm will receive booster dose of PPV23 (Pneumovax) while the remaining 50 in each arm will not receive any booster vaccine. At 23 months, all children will receive a challenge dose (0.1mg/ml; which is one-fifth of a standard dose) of PPV23. Blood will be collected at various time points pre- and post-vaccination.

Progress: At the end of 2011, 17 children had been recruited, and 2 had completed all 3 doses of PCV. No adverse reactions to PCV have been documented to date.

Significance: This study will provide data to the National Department of Health (NDoH) about the safety and immunogenicity of PCV10 and PCV13. As NDoH intends to introduce PCV13 in 2013 into the national immunization schedule, results from this study will also inform NDoH of whether PCV10 and PCV13 are interchangeable should vaccine stock of PCV13 run out due to global demand.

Contributors

Investigators: William Pomat, Andrew Greenhill, Vela Solomon, Peter Richmond, Deborah Lehmann, Megan Passey, Peter Siba, William Lagani.

Collaborating centres: PNG Institute of Medical Research; National Department of Health, PNG; University of Western Australia, Telethon Institute for Child Health, Sydney University.

1.2.14 Aetiology of ARI and Meningitis

Summary

Title: The aetiology of acute lower respiratory tract infection and meningitis in hospitalized children from the Eastern Highlands Province, Papua New Guinea

Date commenced: First quarter, 2012

Project funding: Pfizer and PNGIMR ICRAS

About the project

Rationale: Pneumonia remains the single greatest cause of death in children in PNG, and the burden of acute respiratory infections (ARI) in the highlands of PNG is amongst the highest in the world. Meningitis also remains a major cause of serious illness and death in children in PNG and elsewhere. We have very little up to date data on the causes of pneumonia and meningitis in PNG. Previous studies found *S. pneumoniae* and *H. influenzae* to be the most important causes of moderate and severe pneumonia and meningitis in children. While this is likely to remain the case, we need to know which types are causing disease, as this will impact on vaccination strategy. Furthermore, we seek to determine which viruses are associated with influenza-like illness.

Design: We will conduct a case-controlled study to determine the causes of pneumonia and meningitis in children under 5 years of age. Study participants will be recruited from Goroka General Hospital paediatrics ward who meet the inclusion criteria (consistent with PNG guidelines for diagnosis and treatment of pneumonia and meningitis). We aim to enrol approximately 800 children over 18 months.

Progress: Ethics approval has recently been granted and patient enrolment will commence in the coming two months. Real-time PCR assays have been adopted for respiratory syncytial virus, parainfluenza viruses 1-3, metapneumovirus, rhinovirus, coronaviruses, adenoviruses and influenza viruses. Positive control material has been obtained from PathWest in Western Australia. We have culture methods established for diagnosis of *H. influenzae* and *S. pneumoniae*.

Significance: This study will provide essential data on the burden and aetiology of pneumonia and meningitis in children in highlands PNG. The resulting data will provide baseline data prior to the introduction of a pneumococcal vaccine, which will help us determine the impact of the vaccine.

Contributors

Investigators: Chris Blyth, Andrew Greenhill, Lea-Ann Kirkham, Deborah Lehmann, Trevor Duke, William Pomat, Ilomo Hwaihwanje, Jerry Tanumei, Megan Passey.

Collaborating centres: PNG Institute of Medical Research, University of Western Australia, Telethon Institute of Child Health Research, Goroka General Hospital.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Improving aetiological diagnosis of bacterial pneumonia and meningitis in PNG. Kirkham L-A, Smith-Vaughan HC and Greenhill AR. 2010. P N G Med J. 53(3-4): 139-146.

1.2.15 Kuru study

Summary

Title: PNGIMR Kuru Project

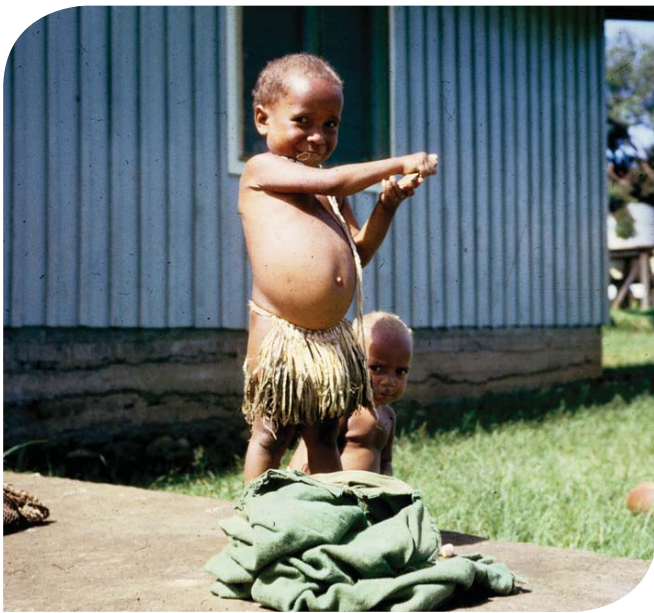
Date commenced: 1996

Project funding: Medical Research Council Prion Unit

About the project

Design: Kuru is a fatal degenerative brain disease restricted to the Fore people and their immediate neighbours in the Eastern Highlands of PNG. Research into kuru began in 1957, and by the mid-1980s the research responsibility had devolved entirely to the Papua New Guinea Institute of Medical Research (PNGIMR). Collaborative studies, with the Medical Research Council (MRC) Prion Unit, commenced in 1996. Kuru provides the principal experience of an epidemic human prion disease, and one that is now reaching its end. In addition to its intrinsic interest, it provided an opportunity to learn much of relevance to understanding variant Creutzfeldt-Jakob Disease (vCJD), also thought to be caused by dietary prion exposure (cattle infected with Bovine Spongiform Encephalopathy (BSE) prions). Indeed vCJD gave kuru a new global relevance. Kuru is also of wider importance to the history of medicine and human society, and the collaboration has documented cultural practices and traditions that would otherwise have been lost.

Progress: Collaboration was done between the PNGIMR and the MRC Prion Unit. Close links between the PNGIMR and the MRC Prion Unit (Director: Professor John Collinge) have been essential to the success of the kuru project. The collaboration was first established in 1996, when Professor Michael Alpers was Director of the PNGIMR. The collaboration continued under the directorship of Professor John Reeder, and has since been successfully maintained through the latest Director, Professor Peter Siba. Mr Lawrence Ungga is now Coordinator of the Kuru Project at the PNGIMR and is answerable to Professor Peter Siba. The research on kuru was approved in the very beginning by the Medical Research Advisory Committee when it was first constituted in 1962, and reaffirmed when the collaboration was set up (MRAC No 96.27).



Children from the local community in the Fore area.

Interaction with and support of local communities

Critically important from both the ethical and operational aspects is the full participation in the project of the communities involved. This is established and maintained through discussions with village leaders, communities, families and individuals. Though it is not the function of the project to engage in community development it has obtained funding from the British High Commission in Port Moresby and from UK charities to facilitate community development projects. This has included the establishment of primary schools that support over 500 children, and a number of village water supply projects. The project has held medical clinics in remote areas, instigated malaria eradication programs, HIV/AIDS awareness, and provided emergency medical treatment when required. When requested, clinical and logistic assistance has been provided to the local Ivingoi Health Centre.

Objectives of the programme

The objectives of this programme are listed below, and very substantial progress against them has been reported.

- Identify and study all remaining kuru patients; document the maximum incubation periods.
- Provide further data for accurate epidemiological modelling of the kuru epidemic to estimate key epidemic parameters.
- Document mortuary feast practices and traditional beliefs of the aetiology of kuru by interview of surviving participants and other members of the Fore community.
- Study the clinical features of current kuru patients and compare clinical and other diagnostic features with other human prion diseases, notably iatrogenic and variant CJD.
- Investigate for any evidence of maternal or other routes of kuru transmission.
- Identify genetic susceptibility factors to kuru by study of recent patients and archived samples, long-term survivors of multiple feast exposures and the normal Fore and adjacent

(exposed and unexposed) populations.

- Study the peripheral pathogenesis of kuru and tissue distribution of infectivity, and investigate the possibility of sub-clinical prion infection by analysis of blood samples.

Genetic studies on kuru susceptibility and incubation period. It is hard to overstate the importance of kuru in understanding the impact of genetic factors on a human prion disease epidemic. Kuru was huge both in terms of numbers of patients affected and the proportion of the population; also, it was orally acquired, as is assumed for vCJD. As the epidemic is coming to a close, it has been possible to identify patients with incubation periods over 50 years, who proved resistant to prion disease throughout their lifetimes. The clinical and genetic data acquired for these studies is without precedent. Much was learned about genetic susceptibility to prion disease and human evolution.

Much new information on the details of mortuary practices, and their place in Fore cosmology, has been obtained from the elders of many communities across the kuru region and beyond by the field team.

Maternal transmission of kuru

From the complete absence of kuru in children born to mothers with the disease after 1960 there is strong evidence that normal kuru is not transmitted vertically.

Epidemiological analysis of kuru records

The process of abstracting all the information from the field records obtained by Michael Alpers from 1979 to 2000 was completed. The data relating to all the real cases of kuru were entered into the kuru database, giving a total number of deaths from kuru, from 1957 to the present, of 2724.

Contributors

Investigators: John Collinge, Michael Alpers, Jerome Whitefield.

Collaborating centres: MRC Prion Unit, UCL Institute of Neurology, London, PNG Institute of Medical Research.

Publications

SCIENTIFIC JOURNAL ARTICLES (SINCE 2006)

1. Kuru in the 21st century – an acquired human prion disease with very long incubation periods. Collinge J, Whitfield J, McKintosh E, Beck J, Mead S, Thomas DJ, Alpers MP. 2006. *Lancet*. 367:2068-74.
2. A history of kuru. Alpers MP. *PNG Med J* 2007;50:10-9.
3. Kuru prions and sporadic Creutzfeldt-Jakob disease prions have equivalent transmission properties in transgenic and wild-type mice. Wadsworth JDF, Joiner S, Linehan JM, Desbruslais M, Fox K, Cooper S, Cronier S, Asante EA, Mead S, Brandner S, Hill AF, Collinge J. 2008. *Proc Natl Acad Sci USA*. 105: 3885-90
4. Introduction to 'The end of kuru: 50 years of research into an extraordinary disease'. Collinge J, Alpers MP. 2008. *Phil Trans R Soc B*. 363: 3607-12
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6. Some tributes to research colleagues and other contributors to our knowledge about kuru. Alpers MP. 2008. *Phil Trans R Soc B* 2008. 363:3614-3617.
7. An account of the last autopsy carried out on a kuru patient. Boone K. 2008 *Phil Trans R Soc B*. 363:3630.
8. The work of the Kuru Field Unit, Kuru Research Project of the Papua New Guinea

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2. The imminent disappearance of the disease kuru from Papua New Guinea. Alpers MP, Whitfield J, Collinge J, Gajdusek DC, Kuru Surveillance Team One Hundred Years of Tropical Medicine: Meeting the Millennium Development Goals. Program and Abstracts of the Royal Society of Tropical Medicine and Hygiene 1907-2007 Conference, 13-15 Sep 2007, London, England. (Also presented at the Conference on the End of Kuru: 50 Years of Research into an Extraordinary Disease, London, 11-12 Oct 2007).

CONFERENCE

The end of kuru: 50 years of research into an extraordinary disease

This meeting, organized by John Collinge and Michael Alpers, was held in London at the Royal Society on 11-12 Oct 2007. The 90 participants included representatives of every era of kuru research and the 2 Nobel Laureates in the field of kuru and prions, D. Carleton Gajdusek and Stanley Prusiner. The 15 Papua New Guineans who attended the meeting comprised the Director of the Papua New Guinea Institute of Medical Research, Professor Peter Siba, Dr Adolf Saweri, Chair of the PNGMR Council, associate research colleague Dr Ken Boone, present Fore staff members Mr W. Henry Pako and Mr Anderson Puwa, and 10 Fore former colleagues and friends of the early kuru researchers, including two women.

Sexual and Reproductive Health Unit



2. Sexual and Reproductive Health Unit

2.1.1 Overview

Our Mission is to conduct policy-relevant clinical, laboratory, qualitative and health systems research to improve the sexual and reproductive health of women and men in Papua New Guinea. The formation of the Sexual and Reproductive Health Unit (SRHU) in March 2011 represented a re-alignment of research priorities within the PNGIMR and a renewed commitment to robust, policy-relevant research to improve sexual, reproductive and maternal health in PNG. Prior to the formation of the SRHU, clinical, social and behavioural research in HIV/AIDS, sexual and reproductive health was carried out by the Operational Research Unit (ORU), in collaboration with the Infection and Immunity Unit (I&IU) where the HIV/STI Research Laboratory was previously located.

2.1.2 Research Objectives

The work of the SRHU is organized around seven key Research Objectives:

1. To investigate the epidemiology of HIV and STIs among general and at-risk populations in PNG and the key determinants of acquisition risk in these populations.
2. To increase knowledge of the socio-cultural and behavioural drivers of HIV and STIs and understand the lives of those affected.
3. To support the National Department of Health (NDoH) in the surveillance and diagnosis of HIV and STIs in PNG.
4. To support the NDoH and National AIDS Council (NAC) in evaluating the effectiveness of the national response to HIV and STIs in PNG.
5. To investigate biomedical strategies for the prevention of HIV and STIs in PNG.
6. To investigate the epidemiology of human papillomavirus (HPV) and cervical cancer in PNG, and strategies for their prevention, screening and clinical management.
7. To support the NDoH and partners to develop effective and locally-appropriate strategies to improve maternal health in PNG.



Staff working in the HIV/STI Research Laboratory.



The Red Ribbon, a show of the Institute's commitment to fight against HIV/AIDs through research in PNG. World Aids Day 2011, PNGIMR Headquarters, Goroka.

2.1.3 Achievements 2006 – 2011

In the past five years, the PNGIMR has led ground-breaking research in HIV, sexual and reproductive health that has directly informed public health policy in PNG. These include the first comprehensive study on people's experiences of antiretroviral therapy (ART of Living Study); population-based bio-behavioural surveys (Ten Sites Study; PASHIP); and a multi-disciplinary study to investigate the acceptability, epidemiological impact and feasibility of male circumcision for HIV prevention in PNG (MCAIS). A new cadre of PNG-based social scientists was created through a two-year AusAID-funded Cadetship Program in 2008 that significantly increased capacity within PNG to conduct high-quality, locally-led HIV social and behavioural research. The first longitudinal clinical cohort study in sexual health conducted in PNG was completed in 2011 (MCAIS) and the first ART drug resistance study is expected to be completed in early 2012, when a large-scale qualitative study on the prevention of mother to child transmission will also be completed (PMTCT Study).

In 2012, the SRHU is consolidating these achievements by conducting new research in two key priority areas: cervical cancer prevention and care; and maternal health. This research will provide the first population-based estimates of human papillomavirus (HPV) type-specific prevalence among women at different levels of sexual risk and inform future HPV vaccination policy; validate the scientific validity and operational feasibility of

new approaches to cervical cancer screening and prevention; and investigate women's experiences of pregnancy and childbirth, key determinants of adverse maternal health and new interventions for the prevention of maternal mortality and morbidity in PNG.

2.1.4 SRHU Organizational structure

The SRHU is organized into five sections and at end of 2011 had a workforce of over 40 scientific research and administrative support staff working on more than 20 research projects.

Unit Head, **Dr Andrew Vallely**

Unit Administrator, **Steven Aina**

Logistics Officer, **Jimmy Elliot**

Section Heads

HIV & Behavioural Research, **Dr Angela Kelly**

Clinical Research, **Dr Andrew Vallely**

HIV/STI, **Dr Claire Ryan**

Maternal Health, **Lisa Vallely**

Health Promotion, **Geraldine Maibani-Mitchie**

2.2 SRHU Research projects 2006-2011

NB: This section includes research projects carried out by the former Operational Research Unit (ORU) until March 2011.

- 2.2.1 HIV/STI Prevention Program Evaluation
- 2.2.2 Ten Site Study
- 2.2.3 Enhancing Pregnancy Outcomes Study
- 2.2.4 Strengthening HIV Social and Behavioural Research in PNG (Cadetship Program)
- 2.2.5 Young People's Study
- 2.2.6 Male Circumcision Acceptability and Impact Study (MCAIS)
- 2.2.7 PNG-Australia Sexual Improvement Program (PASHIP)
- 2.2.8 Violence against women and girls
- 2.2.9 The Art of Living Study
- 2.2.10 Women and men's experiences of PPTCT in PNG (PPTCT Study)
- 2.2.11 NACS Masculinities Study
- 2.2.12 HIV Drug Resistance Study
- 2.2.13 NACS HSV-2 / HIV Co-infection Study
- 2.2.14 Healthy Pregnancy Study
- 2.2.15 VIA Study
- 2.2.16 HPV Study
- 2.2.17 Sik bilong Mama Study, PNG
- 2.2.18 Pregnancy and childbirth study
- 2.2.19 Pregnancy Loss study
- 2.2.20 Maternal Health Survey
- 2.2.21 Syphilis Point of Care Tests
- 2.2.22 Health Workers Understanding of Syphilis Testing
- 2.2.23 Hosts Genetics and HIV Transmission

2.2.1 HIV/STI Prevention Program Evaluation

Summary

Title: Evaluation of HIV and STI Prevention Intervention Program for FSW and MSM – The Poro Sapot Project

Date commenced: 2004

Project funding: Family Health International

About the project

Rationale: The HIV and AIDS National Strategic Plan (NSP) provided the guiding strategies and objectives for HIV and AIDS prevention and control in PNG in seven focus areas. Save the Children in PNG (SCiPNG) were implementing HIV prevention programs among people considered at increased risk of HIV acquisition and through the Poro Sapot Project (PSP), providing services to female sex workers (FSW), men who have sex with men (MSM), and their sexual partners. The PNGIMR was tasked to conduct evaluative research to inform future national surveillance, monitoring and evaluation plans.

Design: A baseline assessment was conducted in 2004 and repeated in 2008. Formative qualitative research, social and geographical mapping were conducted to inform the final design of the baseline quantitative survey. The study was conducted among MSM and FSW in Port Moresby and among FSW in Goroka.

Progress: Completed in August 2007.

Significance: This research provided valuable data for national HIV prevention strategies among people at increased risk of HIV and STI infection in PNG. A summary report was disseminated to stakeholders and policymakers in Port Moresby at a national stakeholder's forum jointly organized by FHI and the PNGIMR in 2007.

Contributors

Investigators: Geraldine Maibani-Michie (PI), Dimitri Prybylski (Co-PI), William Yeka (Co-PI), Henry Brawn, Dorothy Kavanamur, Mckenzie Jikian, Don Colby and Ric Mateo.

Collaborating centres: PNG Institute of Medical Research; Save the Children in PNG; Family Health International, PNG; Family Health International, Asia Pacific Region; Vietnam-CDC-Harvard AIDS Partnership, Ho Chi Minh City, Vietnam.

Publications

SCIENTIFIC JOURNAL ARTICLES

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2. Evaluation of the Poro Sapot Project: Intervention-Linked Baseline and Post-Intervention Studies. PNGIMR, Dec 2007.

CONFERENCE PRESENTATIONS

1. Evaluation of STI and HIV Prevention Program for MSM in Port Moresby. Maibani-

Michie G, Kavanamur D, Jikian M, Yeka W, Prybylski D, Siba P. In: 43rd Annual Symposium of the Medical Society of Papua New Guinea, Port Moresby, 2007.

2. Occupational health and safety hazard for the marginalised. Maibani-Michie G, Kavanamur D, Jikian M. In: 42nd Annual Symposium of the Medical Society of Papua New Guinea, Madang, 2006.

3. Preliminary findings from a behavioural survey of FSWs in Port Moresby and Goroka - a pre-intervention assessment for HIV. Yeka W, Maibani-Michie G, Kavanamur D, Jikian M, Prybylski D. In: 41st Annual Symposium of the Medical Society of Papua New Guinea, Goroka, 2005.

4. Assessment of MSM intervention program in Port Moresby. Maibani-Michie G, Yeka W, Kavanamur D, Jikian M, Colby D, Prybylski D. In: 41st Annual Symposium of the Medical Society of Papua New Guinea, Goroka, 2005.

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2.2.2 Ten Site Study

Summary

Title: Capacity Strengthening for HIV research in Papua New Guinea

Date commenced: April 2004

Project funding: NHASP Project

About the project

Rationale: In 2004, robust HIV and STI prevalence data was limited in PNG due to the small number of sentinel surveillance sites in operation, and the low levels of HIV testing being conducted outside Port Moresby. No published or unpublished data describing the subtypes of HIV present in PNG had been reported, with the exception of a single case report in 1996 describing the transmission of HIV-1 subtype B from a mother to her child. There were also considerable uncertainties regarding the epidemiology of HIV and STIs in PNG, and the key socio-cultural and behavioural determinants associated with acquisition risk. A better understanding of these issues was considered critical to informing effective, locally-appropriate responses to the HIV epidemic in PNG.

Design: This bio-behavioural study used a combination of health facility and population-based surveys. Geographical sites were pre-determined based on the number of cases being reported. Participants were asked to take part in a behavioural interview and to provide biological specimens for the detection of STIs.

Progress: Completed in December 2007.

Significance: This study provided robust bio-behavioural data from ten geographical locations in PNG and significantly informed understanding of the HIV/STI epidemics among researchers, stakeholders and policy-makers in PNG, including the molecular epidemiology of HIV.

Contributors

Investigators: John Reeder (PI), Robert Oelrichs, Tony Lupiwa, Lawrence Hammer, Geraldine Maibani-Michie, Claire Ryan, Janet Gare, Jeremy Songovare, Pamela Toliman, Dorothy Kavanamur, Mckenzie Jikian, Herick Aeno.

Collaborating centres: PNG Institute of Medical Research; National Department of Health; The Burnet Institute, Melbourne.

Publications

CONFERENCE PRESENTATIONS

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5. The Relationship between age of sexual debut and sexual assault with HIV/STI infection: Findings from 11 sites across Ten Provinces. Lupiwa T, Maibani-Michie G, Toliman P, Hammer L, Yeka W, Mgong C, Reeder J, Siba P. In: 45th Annual Symposium of the Medical Society of PNG, Port Moresby, 2007.

6. Molecular epidemiology of HIV type 1 subtype in Papua New Guinea: phylogenetic analysis of HIV-1 subtypes B and C found in Papua New Guinea. Gare J, Ryan C, Reeder J, Oelrichs R, Siba P. In: 41st Annual Symposium of the Medical Society of Papua New Guinea, Goroka, 2005.

2.2.3 Enhancing Pregnancy Outcomes Study

Summary

Title: Enhancing pregnancy outcomes in Papua New Guinea

Date commenced: 2006

Project funding: UNICEF PNG

About the project

Rationale: PNG has a number of factors that contribute to poor pregnancy outcome, including geopolitical and socio-cultural contexts; pregnancy, birth and post-partum factors. This study sought to determine if community-based interventions (assessment and treatment of anaemia, micronutrient supplementation, malaria prevention, provision of anti-helminth medications, and assessment and referral for treatment of syphilis) could improve health outcomes for both mothers and their infants.

Design: Maprik (East Sepik Province) and Esa'ala (Milne Bay Province), malaria-endemic districts each with approximately 12,000 women of reproductive age and 2,000 births annually, were included in this cross sectional survey. Surveys took place at baseline (Oct-Dec 2006) and following the intervention (Nov-Dec 2007). Both surveys included qualitative interviews and the collection of biological specimens.

Progress: Completed in 2007.

Significance: The intervention reduced anaemia and malaria among study participants, and increased birth weight of newborn infants in Esa'ala. This study demonstrated the operational

feasibility and impact of a village health volunteer centered program for enhancing pregnancy outcomes in PNG.

Contributors

Investigators: Rachel Hinton (PI), Anatoly Abramov, Grace Kariwiga, AB Amoa, Ivo Mueller, Peter Siba, John Reeder.

Collaborating centres: PNG Institute of Medical Research; National Department of Health; UNICEF PNG.

2.2.4 Strengthening HIV Social and Behavioural Research in PNG (Cadetship Program)

Summary

Title: Strengthening HIV Social and Behavioural Research in Papua New Guinea

Date Commenced: September 2006

Project Funding: AusAID AHAPI Grant

About the project

Rationale: Since the first HIV diagnosis was made in PNG in 1987, medical models have dominated national, provincial and local-level responses to the national epidemic. There is little in the way of an indigenous social research tradition, which has led to a deficiency in demographic and social data on which to base local HIV prevention and education activities. This program was carried out in recognition of the need for a social research response to the HIV epidemic in PNG that is indigenous in its meanings and activities, sustainable in its application, and grounded in the local social-structural realities.

Design: The cadetship program was based on a philosophy of 'learning by doing'. 10 cadets were enrolled and undertook workplace training in HIV social and behavioural research, including training in a number of research methods, academic writing, conference presentations and proposal development.

Progress: Completed in September 2008.

Significance: This program significantly increased HIV social research capacity within PNG. On completion of the two-year cadetship program, trainees demonstrated skills in understanding the epidemiology and determinants of the HIV epidemic in PNG and worldwide; a wide range of HIV social research techniques; critical and scholarly thinking, carrying out 'real life' research projects (external and internal); writing for academic publication; oral presentations and applying for research funding.

Contributors

Investigators: Peter Siba, Heather Worth and Angela Kelly.

Collaborating centres: PNG Institute of Medical Research; University of New South Wales, Sydney.

Publications

SCIENTIFIC JOURNAL ARTICLES

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CONFERENCE PRESENTATIONS

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2. HIV Social Research and Biomedicine. Kelly A. In: 43rd Medical Symposium Specialist Meeting for STIs, HIV and AIDS: HIV Medicine and Social Research, 6-7th Sep 2007; Port Moresby, PNG: 2007.

3. Challenges of Abstinence in Papua New Guinea. Keleba K. In: 8th International Congress on AIDS in the Asia Pacific Region 19-23rd Aug 2007; Colombo, Sri Lanka: 2007.

4. Married women vulnerable to HIV infection in PNG. Kepa B. 8th International Congress on AIDS in the Asia Pacific Region 19-23rd August 2007; Colombo, Sri Lanka: 2007.

5. Sorcery, HIV & Women in PNG. Mek A, Kelly A. (2007). Paper presented at the 43rd Medical Symposium, Special Session on Biomedical Research, 3-7th Sep 2007; Port Moresby, PNG: 2007.

6. HIV and the Rural Enclaves of Papua New Guinea. Akuani F. In: 8th International Congress on AIDS in the Asia Pacific Region 19-23rd Aug 2007; Colombo, Sri Lanka: 2007.

7. Papua New Guinea's emerging dilemma with AIDS Orphans. Cangah B. In: 8th International Congress on AIDS in the Asia Pacific Region 19-23rd Aug 2007; Colombo, Sri Lanka: 2007.

8. Strengthening HIV Social Research in PNG. Emori R, Worth H, Siba P, Kelly A. In: 8th International Congress on AIDS in the Asia Pacific Region 19-23rd Aug 2007; Colombo, Sri Lanka: 2007.

2.2.5 Young People's Study

Summary

Title: Young People's attitudes towards sex, HIV and condoms in the Eastern Highlands

Date Commenced: 2007

Project Funding: Funded as part of the Strengthening HIV Social and Behavioural Research Program

About the project

Rationale: Young people are considered at high risk of HIV infection in PNG. Young people's attitudes towards sex and HIV are important determinants on the spread of the HIV epidemic in PNG.

Design: This study involved focus group discussions with 73 Grade 12 students from 3 secondary schools in Eastern Highlands Province. In total, eight gender-specific focus groups were held, of which five were with males and three with females.

Progress: Completed in 2008.

Significance: This study increased understanding about young people's attitudes and sexual behaviour in PNG and how these impact on the emerging HIV/STI epidemics.

Contributors

Investigators: Angela Kelly, Agnes Mek, Martha Kupul, Lucy Walizopa, Kritoe Keleba, Somu Nosi, Brenda Cangah, Barbara Kepa, Rebecca Emori, Frances Akuani.

Collaborating Centres: PNG Institute of Medical Research; University of New South Wales, Sydney.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Gendered talk about sex, sexual relationships and HIV among young people in Papua New Guinea. Kelly A, Worth H, Akuani F, Kepa B, Walizopa L, Kupul M, Emori R, Cangah B, Mek A, Nosi S, Pirpir L, Keleba K, Siba P. Cult Health Sex, 2010; 12: 221-232.

2. Christian discourses in young people's narratives of sex, condoms and HIV in the Eastern Highlands Province, Papua New Guinea. Kelly A, Walizopa L, Pirpir L, Emori R, Akuani F, Kupul M, Nosi S, Kepa B, Cangah B, Mek A, Keleba K, Worth H, Siba P. Catalyst 2009; 39:102-114.

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CONFERENCE PRESENTATIONS

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2. Young People's Perception of Sex: A qualitative study of the Secondary School Students of Eastern Highlands Province of Papua New Guinea. Mek, A, Pirpir, L, Cangah, B, Kupu, M, Kelly, A, Akuani, F, Emori, R, Walizopa, L, Nosi, S, Kepa, B, and Keleba, K. In: 44th PNG Medical Symposium 1-5th Sep 2008; Rabaul, East New Britain, Papua New Guinea: 2008.

3. The role of comfort in young people talking and learning about sex and HIV in Papua New Guinea. Walizopa L, Emori R, Nosi S, Akuani F, Kupul M, Kepa B, Cangah B, Mek A, Pirpir L, Keleba K, Kelly A. In: Australasian Society for HIV/AIDS Medicine Conference 16-20th Sep 2008; Perth, Australia: 2008.

4. Gendered talk about sex, sexual relationships and HIV in young people in PNG. Kelly A, Kupul M, Frankland A, Kepa B, Cangah B, Nosi S, Emori R, Walizopa L, Mek A, Pirpir L, Akuani F, Keleba K, Worth H, Siba P. In: Pacific STI & HIV Research Centre Conference, Fiji School of Medicine, 2nd Jul 2009; Suva, Fiji: 2009.

2.2.6 Male Circumcision Acceptability and Impact Study (MCAIS)

Summary

Title: Male circumcision for HIV prevention among at-risk men and women in Papua New Guinea: Acceptability, epidemiological impact, cost effectiveness and options for implementation

Date commenced: December 2007

Project funding: AusAID Australian Development Research Award (ADRA)

About the project

Rationale: A series of phase III clinical trials in Africa demonstrated the efficacy of male circumcision (MC) for the prevention of HIV infection in men and led WHO to recommend male circumcision for inclusion within comprehensive national prevention programs in high-prevalence settings. The potential role of MC for HIV prevention in countries experiencing lower prevalence HIV epidemics, such as PNG remains unclear.

Design: The Male Circumcision Acceptability & Impact Study, PNG (MCAIS) was a four-year multi-disciplinary community-based research program to investigate the potential of MC for HIV prevention in PNG. The study was conducted among general and at-risk populations at multiple sites in PNG, and had four principal components: qualitative research; mathematical modeling; health systems research; and longitudinal clinical cohort studies. A sub-study to investigate the notional acceptability of a vaginal microbicide surrogate for HIV prevention among women and men attending a sexual health clinic in Port Moresby was completed in 2010.

Progress: Completed in December 2011.

Significance: Research findings were presented at a Joint National Policy Forum on Male Circumcision for HIV Prevention in PNG held in Port Moresby in November 2011 in order to translate research evidence into public health action. The Forum was jointly coordinated and funded by MCAIS and was co-chaired by the PNG National AIDS Council Secretariat (NACS) and the PNG Sexual Health Society (SHS).

The Forum made three key recommendations:

1. the formation of a joint NDoH/NACS Policy Committee on Male Circumcision;
2. the establishment of an integrated Harm Reduction Program; and;
3. that future policy on wide scale roll-out of MC for HIV prevention in PNG be informed by a combination of:
 - (a) data from MC intervention pilot programs and;
 - (b) formative research on the potential protective effect of other forms of penile cutting. The MCAIS group has been asked to take a lead role in these future research activities.

Contributors

Investigators: Andrew Vallely (PI), Peter Siba (PI), John Kaldor (PI), Angela Kelly, Claire Ryan, John Murray, David Wilson, Richard Gray, Martha Kupul, Herick Aeno, Voletta Fiya, James Neo, Richard



Conducting awareness with men and boys group in a community in the Eastern Highlands Province.

Naketumb, Greg Law, Petronia Kaima, Zure Kombati, Joyce Sauk, Joyce Allan, Pamela Toliman, Lisa Fitzgerald, Peter Hill, Anna Tynan, Andrew Page, John Millan.

Collaborating centres: PNG Institute of Medical Research; Mt Hagen General Hospital; HOPE Worldwide, PNG; University of New South Wales, Sydney; University of Queensland, Brisbane; The Burnet Institute, Melbourne.

Publications

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2. "Now we are in a different time; various bad diseases have come." Understanding men's acceptability of male circumcision for HIV prevention in a moderate prevalence setting. Kelly A, Kupul M, Fitzgerald L, Aeno H, Neo J, Naketrumb R, Siba P, Kaldor JM, Vallely A. BMC Pub Health 2012; 12: 67
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2.2.7 PNG-Australia Sexual Improvement Program (PASHIP)

Summary

Title: Baseline Studies to support the PNG-Sexual Health Improvement Program

Date commenced: August 2008

Project funding: AusAID PNG

About the project

Rationale: PNG has among the highest prevalences of Sexually Transmitted Infections (STIs) in the Asia-Pacific region and there are concerns that these infections may be acting as important co-factors in the PNG HIV epidemic. Recognizing the importance of STIs and the need to support improved interventions, the PNG-Australia Sexual Health Improvement Program (PASHIP) was established to identify barriers to the effective implementation of STI control activities and to develop new interventions.

Design: This population-based bio-behavioural survey was conducted in seven provinces in partnership with five non-government organizations (NGOs) involved in implementing STI prevention programs. Participants were asked to take part in a behavioural interview and to provide biological specimens for the detection of STIs. Participants in the general community were recruited by random household sampling while respondent driven sampling (RDS) was used for hidden and hard to reach populations, such as female sex workers and male youth. Progress reports were presented biannually at Progress Review Group (PRG) meetings.

Progress: Completed in August 2010.

Significance: This study provided one the first indications that adult HIV prevalence in PNG was lower than previously estimated, a finding subsequently validated by NACS/NDoh in 2010 when



A research assistant interviewing a study participant in Southern Highlands Province for the PASHIP study.

national adult prevalence was revised to 0.9%. A final report was completed and launched during the November 2011 PRG meeting in Port Moresby.

Contributors

Investigators: Peter Siba (PI), Tony Lupiwa, Geraldine Maibani-Michie, Claire Ryan, Janet Gare, Gavin Edward, Alois Ralai, Martha Kana, Joshua Nembari, Primrose Homiegombo, Jeremy Songovare, Janet Totave, McKenzie Jikian, John Kaldor and Handan Wand.

Collaborating Centres: PNG Institute of Medical Research; National Department of Health; Save the Children in PNG; Anglicare PNG; CARITAS; CAMPAS; Burnet Institute, Melbourne; Kirby Institute, University of New South Wales, Sydney.

Publications

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2.2.8 Violence against women & girls

Summary

Title: Best practices in addressing violence against women and girls in Melanesia and East Timor

Date commenced: January 2008

Project Funding: Sub-contract from PATH (funded by AusAID Office of Development Effectiveness)

About the project

Rationale: Violence against women and girls is a serious public health issue in many countries, including PNG. In order to provide evidence of best practices in addressing violence against women and girls this study examined local community programs and initiatives. This was part of a wider study of violence against women and girls in Melanesia and East Timor.

Design: This study used a number of qualitative methods including in-depth interviews, focus group discussion and participatory learning activities including Venn diagrams in Eastern Highlands and Chimbu Provinces.

Progress: Completed.

Contributors

Investigators: Angela Kelly (PI), Peter Siba, Martha Kupul, Barbara Kepa, Agnes Mek and Kritoe Keleba.

Collaborating Centres: PNG Institute of Medical Research; University of New South Wales, Sydney.

Publications

CONFERENCE PRESENTATIONS

1. Tribal fighting, violence against women and girls and HIV in PNG. Kupul M, Mek A, Kepa B, Kelly A. In: Australasian Society for HIV Medicine Conference, 16-20th September 2008; Perth, Australia: 2008.

2.2.9 The Art of Living Study

Summary

Title: The art of living: The social impacts of ART on PLWHA in Papua New Guinea

Date commenced: January 2008

Project Funding: PNG National AIDS Council

About the project

Rationale: Since late 2003 there has been global momentum in expanding access to antiretroviral therapies (ART) in low and middle-income countries. The benefits of ART are at least twofold: people living with HIV (PLHIV) are expected to have a better quality of life with less morbidity and mortality; and ART can restore individuals to active participation in the social and economic activities of their families and communities. In order to monitor the impact of ART programs on the lives of people, we need to complement routine clinical and laboratory monitoring and evaluative measures and develop further our understandings of the experiences of PLHIV who are enrolled in such programs. To do this we must examine the behavioural and sociocultural outcomes for PLWHA on ART, which will, amongst other things, help us, better understand the determinants of success on therapy.

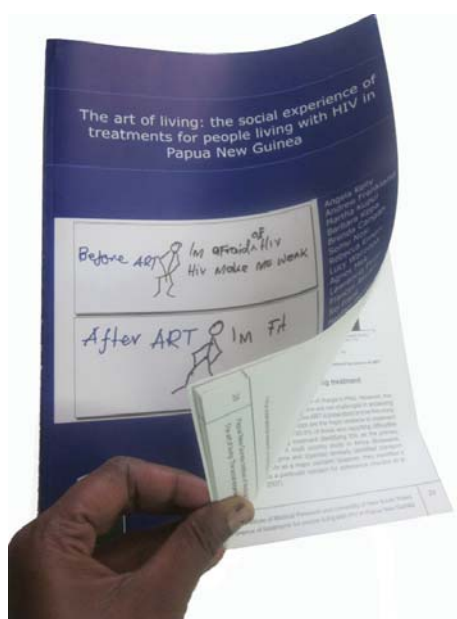
Design: This study engaged a mixed-method research approach across six provinces (National Capital District; Morobe, Chimbu, Eastern, Western and Southern Highlands Provinces). Methods included; survey, in-depth interviews (IDIs) and visualization techniques. The quantitative component of the study involved a cross-sectional survey of 374 people with HIV who had been taking ART for more than two weeks. A non-probability, convenience sampling approach was used. The questionnaire gathered information on demographics; knowledge and beliefs of HIV and ART; stigma and discrimination; health and well-being; disclosure; food security and alcohol use; adherence to treatment; sexual practices; and access to services. Of these survey participants 36 also agreed to participate in an IDI. Participants were recruited through HIV treatment clinics, NGO's and PLHIV groups.

Progress: Completed in 2009.

Significance: The findings of this study and the study recommendations (developed in consultation with people living with HIV) are informing National HIV Policy and programming in PNG.

Contributors

Investigators: Angela Kelly (PI), Heather Worth, Peter Siba, Martha Kupul, Andrew Frankland, Agnes Mek, Barbara Kepa, Lawrence Pirpir, Brenda Cangah, Frances Akuani, Somu Nosi, Rebecca Emori, Lucy Walizopa.



The ART Report Book.

Collaborating Centres: PNG Institute of Medical Research; University of New South Wales, Sydney.

Publications

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4. The Art of Living: Key findings from PNG's first study of People Living with HIV on ART (PNG). Kelly A, Kupul M, Frankland A, Kepa B, Cangah B, Nosi S, Emori R, Walizopa L, Mek

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2.2.10 Women & men's experiences of PPTCT in PNG (PPTCT Study)

Summary

Title: Women and men's experiences of PPTCT in Papua New Guinea: a gendered socio-cultural analysis of barriers and facilitators for program engagement

Date commenced: January 2009

Project Funding: AusAID Australian Development Research Award (ADRA)

About the project

Rationale: Prevention of parent to child transmission (PPTCT) programs have been designed and implemented in PNG in order to reduce the risk of HIV transmission during pregnancy, delivery and feeding. In order for the national PPTCT program to be successful, greater program engagement with women and their male partners is required. Women and men's experiences of PPTCT programs have been studied in detail in other settings such as in Africa, but have not previously been investigated in PNG.

Design: This qualitative study involved both longitudinal and cross-sectional qualitative interviews. In order to understand the experience of HIV testing at antenatal clinics (ANCs), both women who tested HIV-positive and HIV-negative were interviewed as well as male partners and key informants involved in the delivery of PPTCT in PNG. Participants were recruited through ANCs, NGOs and government departments in Western Highlands Province and National Capital District. In total 168 interviews were conducted with women, men and key informants. 78 HIV-positive women took part in in-depth interviews (IDIs). Of these, 24 were interviewed three times, 16 twice and 38t once. 12 HIV-negative women underwent one IDI. 18 men whose wives had undergone

HIV testing were interviewed. Of these, one was interviewed three times, nine twice and seven once. 28 Key Informant Interviews (KIIs) were also conducted.

Progress: To be completed in June 2012.

Significance: This study will inform national HIV prevention policy and practice in PNG.

Contributors

Investigators: Heather Worth (PI), John Kaldor (PI), Angela Kelly (PI), Martha Kupul, Lisa Vallyely, Ruthy Neo, Voletta Fiya, Grace Karawiga and Glen Mola.

Collaborating Centres: PNG Institute of Medical Research; University of Papua New Guinea; Port Moresby General Hospital; UNICEF PNG; International HIV Research Group and the Kirby Institute, University of New South Wales, Sydney.

2.2.11 NACS Masculinities Study

Summary

Title: Qualitative longitudinal study to investigate constructions of masculinity, sexuality and agency among male youth in Papua New Guinea

Date commenced: January 2010

Project funding: National AIDS Council Secretariat, PNG

About the project

Rationale: A more sophisticated understanding of 'how gender works' and how it connects with other forces that structure people's social and sexual lives is a clear priority in counties such as PNG that are experiencing complex and emerging HIV epidemics.

Design: This two-year multi-disciplinary community-based research program is investigating the role that individual, community and cultural constructs of masculinity, male sexuality and sexual agency have in determining sexual behaviour among young men in PNG, and specifically, their role in promoting behaviours known to increase the risk of HIV and STIs among men and women. The study will be conducted in Eastern and Western Highlands Provinces, PNG where 50-60 in-school and out-of school male youth aged 16-17 years will be recruited into a qualitative longitudinal research study and followed up 3 monthly for 12 months.

Progress: Literature review on masculinities and male sexuality in Melanesia completed Nov 2010. Baseline multi-method qualitative research completed in four sites in Eastern and Western Highlands (Jun-Nov 2011). Qualitative longitudinal study among male youth started recruitment in rural district in Eastern Highlands Province, February 2012.

Significance: This research addresses a clear gap in current knowledge about masculinities and male sexuality in the context of the HIV epidemic in PNG. It will provide information vital to evidence-based public health policy development. The study is also expected to directly inform the implementation of new

national programs designed specifically to address male sexual and reproductive health.

Contributors

Investigators: Andrew Vallyely (PI), Angela Kelly, Lisa Fitzgerald, Peter Siba, Maxine Whittaker, John Kaldor, John Millan, Joyce Sauk, Herick Aeno, James Neo, Zure Kombati.

Collaborating centres: PNG Institute of Medical Research; University of New South Wales, Sydney; University of Queensland, Brisbane.

2.2.12 HIV Drug Resistance Study

Summary

Title: An investigation into HIV drug resistance and subtype distribution in the Highlands of Papua New Guinea

Date commenced: May 2010

Project funding: National AIDS Council Secretariat, PNG

About the project

Rationale: Antiretroviral therapy (ART) for the treatment of HIV infection has been rapidly scaled up in PNG. ART drug resistance can occur due to virological factors, but it can also be influenced by sub-optimal drug intake, which in turn can be influenced by the patient's adherence level and health seeking behaviour, including the patient's access to the clinic to maintain the drug supply.

Design: We aimed to determine the prevalence of transmitted and acquired drug resistance, and also to investigate behavioural factors that could contribute to the development of drug resistance. The HIV drug resistance study is a bio-behavioural survey aiming to recruit 100 ART naïve individuals and 100 ART experienced individuals from Michael Alpers Clinic in Goroka and Tininga Clinic in Mount Hagen. ART experienced individuals will be followed up 1-2 years after their initial appointment to determine if there are any changes in their drug resistance profile. Blood samples collected on filter paper will be sent to the PNGIMR laboratory for DNA extraction and drug resistance analysis. Subtype is determined via standard phylogenetic protocols.

Progress: Recruitment of phase one is complete, and drug resistant analysis for the Mount Hagen samples is complete. There was no evidence of transmitted drug resistance, and two patients had evidence of acquired drug resistance. All samples analyzed to date were HIV type 1 subtype C. An interim report has been released to clinic collaborators.

Significance: Monitoring HIV drug resistance on a population level is of paramount importance when there are limited drug options available. This investigation will provide the first information regarding HIV drug resistance in the highlands of PNG. It will serve as an evaluation of treatment programs and will help to identify areas of potential improvement.

Contributors

Investigators: Claire Ryan (PI), Janet Gare, Peter Siba, Matthew David, Petronia Kaima, Zure Kombati.

Collaborating centres: PNG Institute of Medical Research; Tininga Clinic, Mt Hagen General Hospital; Michael Alpers Clinic, Goroka General Hospital; The Burnet Institute, Melbourne.

2.2.13 NACS HSV-2 / HIV Co-infection Study

Summary

Title: Defining the epidemiological relationship between HIV-1 and HSV-2 in the Highlands of Papua New Guinea

Date commenced: June 2011

Project funding: National AIDS Council Secretariat, PNG

About the project

Rationale: Genital herpes, caused by the *Herpes simplex* Type-2 virus (HSV-2) is considered an important biological co-factor in the transmission of HIV infection in many highly-affected countries, such as those in East and Southern Africa. No data is currently available on HSV-2 epidemiology in PNG and the role that genital herpes may play in the national epidemic therefore remains unclear.

Design: This project will investigate the epidemiology of HSV-2 among 100 HIV sero-positive and 200 HIV sero-negative individuals attending sexual health clinics in the Highlands Region of PNG and investigate the performance of different diagnostic assays for the detection of HSV-2.

Progress: Stakeholder consultation and site preparation was completed in 2011. Study recruitment will commence in mid-2012.

Significance: This will be the first study on HSV-2 / HIV co-infection conducted in PNG and together with the STIs in Pregnancy Study, will greatly increase understanding regarding the role of genital herpes in the HIV epidemic in PNG.

Contributors

Investigators: Claire Ryan (PI), Andrew Vallely, John Kaldor, Peter Siba, Zure Kombati, Petronia Kaima, Cassey Simbiken.

Collaborating centres: PNG Institute of Medical Research; Goroka General Hospital; Mt Hagen General Hospital; University of New South Wales, Sydney; The Burnet Institute, Melbourne.

2.2.14 Healthy Pregnancy Study

Summary

Title: The epidemiology of sexually transmitted infections (STIs), including human papillomavirus (HPV), among pregnant women attending antenatal clinics at four sites in Papua New Guinea

Date commenced: June 2011

Project funding: PNG Partnership in Health Program

About the project

Rationale: PNG has one of the highest rates of cervical cancer in the world with an estimated age-standardized incidence of 40 / 100,000 compared to 6.0 / 100,000 in Australia. Cervical cancer is the most common cancer among women in PNG and a leading cause of premature death (age-standardized mortality of 22.6 / 100,000). An estimated 1500 women die every year in PNG due to cervical cancer. Despite this disease burden, no large-scale surveys have been conducted to establish the prevalence of human papillomavirus (HPV) among general or at-risk populations of women. The only survey published to date was conducted among 114 women in Eastern Highlands Province in the mid-1990s, which reported a 33% prevalence of HPV-16/18. In addition, although national surveillance of HIV and syphilis in pregnancy is able to provide robust prevalence estimates, there have been no large-scale population estimates of other STIs in pregnancy, such as chlamydia.

Design: This cross-sectional bio-behavioural survey will investigate the epidemiology of sexually transmitted infections, including human papillomavirus (HPV), HIV and Herpes simplex Type-2 (HSV-2) among 1000 women attending antenatal clinics in four provinces in PNG.

Progress: Following ethical approval and clinical site preparation, study recruitment commenced in Eastern Highlands Province in December 2011 and will proceed to Central, Madang and Southern Highlands Provinces in the first half of 2012.

Significance: This study will provide the first general population level estimates of HPV-type prevalence, and is expected to inform future policy on HPV vaccination and cervical cancer prevention in PNG. The study will also provide the first general population level estimates of HSV-2 prevalence in PNG, considered an important co-factor for HIV transmission in many generalized heterosexual HIV epidemics.

Contributors

Investigators: Claire Ryan (PI), Andrew Vallely (Co-PI), John Kaldor, Handan Wand, Lisa Vallely, Suparat Phuanukoonnon, Peter Siba, Glen Mola, Greg Law, John Millan, Glennis Rai, Sepehr Tabrizi.

Collaborating centres: PNG Institute of Medical Research; National Department of Health, PNG; University of New South Wales, Sydney; The Burnet Institute, Melbourne; Royal Women's Hospital, Melbourne.

Publications

CONFERENCE PRESENTATIONS

1. Human papillomavirus (HPV) infection among general and at-risk populations in Papua New Guinea. Valley A, Ryan C, Mola G, Siba P, Kaldor J. In: 47th Annual Symposium of the Medical Society of Papua New Guinea. Kimbe, West New Britain; 2011.

2.2.15 VIA Study

Summary

Title: Cervical cancer screening using visual inspection with acetic acid (VIA) and its relationship to cervical cytology and high-risk human papillomavirus (HR-HPV) infection among women attending Well Woman Clinics in Papua New Guinea

Date commenced: April 2011

Project funding: AusAID PNG

About the project

Rationale: Cervical cancer is the most common cancer among women in PNG and a leading cause of premature death. Visual inspection with acetic acid (VIA) for cervical cancer screening has been evaluated in a variety of resource-limited settings and found to compare favourably with Pap smear cytology and histological biopsy, but has not been formally evaluated in PNG.

Design: This study will investigate the prevalence of VIA-detectable cervical abnormalities; cervical intraepithelial dysplasia; high-risk human papillomavirus (HR-HPV) infection; and the behavioural and biological determinants associated with risk, among women attending Well Woman clinics in Eastern and Western Highlands Provinces, PNG. This research will also establish the operational feasibility of providing a rural outreach VIA plus cryotherapy ('test and treat') service and investigate the acceptability of 'test and treat' among women and their sexual partners.



Staff from the Well Women's Clinic at the Goroka General Hospital checking out the new VIA equipments.

Progress: Ethical approvals, clinical training (in Thailand), procurement of essential equipment (cervical cryotherapy units) and clinical site preparation were completed at the end of 2011. Study recruitment to start in mid-2012 once VIA services are fully established at participating centres.

Significance: The study will determine the acceptability and operational feasibility of VIA plus cryotherapy ('test and treat') as an intervention for cervical cancer screening and treatment among urban and rural populations in PNG, and is being conducted in order to inform future national policy on cervical cancer screening.

Contributors

Investigators: Andrew Valley (PI), Claire Ryan, John Kaldor, Glen Mola, Antonia Kumbia, Benny Kombuk, Handan Wand, Lisa Valley, Angela Kelly, Joanne Goyen, Phillip Baird, Greg Law, Peter Siba.

Collaborating centres: PNG Institute of Medical Research, National Department of Health, PNG, HOPE Worldwide, PNG, Mt Hagen General Hospital, Save the Children in PNG; University of New South Wales, Sydney; The Burnet Institute, Melbourne.

Publications

CONFERENCE PRESENTATIONS

1. The human papillomavirus epidemic in Papua New Guinea: Overview of prevention, screening and treatment. Mola G. In: 47th Annual Symposium of the Medical Society of Papua New Guinea. Kimbe, West New Britain; 2011.

2.2.16 HPV Study

Summary

Title: Human papillomavirus (HPV) infection among women attending sexual health clinics in Mt Hagen, Goroka and Port Moresby, Papua New Guinea

Date commenced: June 2011

Project funding: PNGIMR ICRAS Program / AusAID PNG

About the project

Rationale: An estimated 1500 women die every year in PNG due to cervical cancer. Despite this disease burden, no large-scale surveys have been conducted to establish the prevalence of HPV among general or at-risk populations of women.

Design: This cross-sectional bio-behavioural survey will investigate the epidemiology of HPV and other sexually transmitted infections among women attending sexual health clinics in three provinces in PNG.

Progress: Ethical clearance and clinical site preparation was completed in December 2011; study recruitment has started in February 2012.

Significance: This study will provide the first estimates of HPV-type prevalence among women at increased risk of HIV/STI acquisition in PNG and will inform future policy on cervical cancer screening and prevention.

Contributors

Investigators: Andrew Vallely (PI), Claire Ryan (Co-PI), John Kaldor, Handan Wand, Peter Siba, Greg Law, Petronia Kaima, Zure Kombati, Joyce Sauk, Sandra Yamuwe, Lisa Vallely, Glen Mola, Nola N'drewei, Sepehr Tabrizi.

Collaborating centres: PNG Institute of Medical Research; National Department of Health, PNG; HOPE Worldwide, PNG; Mt Hagen General Hospital; Save the Children in PNG; University of New South Wales, Sydney; The Burnet Institute, Melbourne; Royal Women's Hospital, Melbourne.

Publications

CONFERENCE PRESENTATIONS

1. Human papillomavirus (HPV) infection among general and at-risk populations in Papua New Guinea. Vallely A, Ryan C, Mola G, Siba P, Kaldor J. In: 47th Annual Symposium of the Medical Society of Papua New Guinea. Kimbe, West New Britain; 2011.

2.2.17 Sik bilong mama Study, PNG

Summary

Title: Meanings and beliefs of cervical cancer, its causation, prevention and treatment in Papua New Guinea

Date commenced: October 2011

Project funding: AusAID PNG

About the project

Rationale: Cervical cancer is the most common cancer among women in PNG and a leading cause of premature death. Despite this disease burden, no research to date has been conducted to investigate traditional and contemporary socio-cultural contexts, meanings and understandings of cervical cancer causation, prevention and treatment in PNG. Without this understanding, policy makers and health care professionals will find it difficult to design appropriate, acceptable and effective public health intervention programs for cervical cancer in PNG.

Design: This mixed-method qualitative study will investigate socio-cultural contexts of cervical cancer in three provinces in PNG currently involved in piloting new cervical cancer screening and prevention programs in order to inform future national prevention and care strategies, including HPV vaccination and cervical screening programs.

Progress: Ethical approvals were obtained in December 2011. Participant recruitment to start in mid-2012.

Significance: This research will inform the development of locally-appropriate behaviour change communication strategies designed to increase awareness of cervical cancer prevention and treatment; to reduce stigma and discrimination associated with cervical cancer; and to increase the acceptability and uptake of cervical cancer prevention and care services in PNG.

Contributors

Investigators: Angela Kelly (PI), Andrew Vallely, John Kaldor, Glen Mola, Antonia Kumbia, Benny Kombuk, Alex Golpak, Lisa Vallely,

Primrose Homiehombo, Jane Jones, David Wood, Peter Siba.

Collaborating centres: PNG Institute of Medical Research; National Department of Health, PNG; HOPE Worldwide, PNG; Mt Hagen General Hospital; Kimbe General Hospital; University of New South Wales, Sydney.

2.2.18 Pregnancy and childbirth study

Summary

Title: Women's experiences of pregnancy and childbirth in Upper Bena, Unggai Bena District, Eastern Highlands Province, Papua New Guinea

Date commenced: October 2011

Project funding: PNGIMR ICRAS Program

About the project

Rationale: PNG has one of the highest maternal mortality ratios (MMR) in the world. The National Department of Health (NDoH), together with key partners and stakeholders, are concerned at low antenatal care uptake, low uptake of services for supervised births, and the high and rising MMR in PNG. NDoH and partners also recognise the importance of qualitative research to identify issues surrounding choices and decision making processes relating to the uptake of maternal health services.

Design: This mixed-methods study will explore women's choices and decisions regarding place of birth together with perceptions, beliefs and health seeking behaviour surrounding pregnancy, childbirth and the postnatal period. Focus group discussions (FGDs) with both men and women; in depth interviews (IDIs) with women who have given birth, and semi structured interviews with key health informants will allow the research team to explore issues experienced and perceived by women, and identify barriers to appropriate and timely health care.

Progress: FGDs and IDIs began in December 2011 following ethical approval in PNG and Australia. Key Informant interviews (KI) and recruitment of women into a longitudinal cohort started in January 2012. Collection of health facility data relating to maternal health activities, follow-up interviews for women in the longitudinal cohort, and KI to be completed by May 2012.

Significance: This study will identify specific constraints to the delivery and uptake of maternal health services in rural communities in Eastern Highlands Province, and inform future provincial and national public health policy and practice.

Contributors

Investigators: Lisa Vallely (PI), Primrose Homiehombo, Julie Liviko, Angela Kelly, Andrew Vallely, Voletta Fiya, Andrea Whittaker, Caroline Homer.

Collaborating centres: PNG Institute of Medical Research; Eastern Highlands Provincial Department of Health, PNG; University of New South Wales, Sydney; University of Queensland, Brisbane; University Of Technology Sydney.

2.2.19 Pregnancy Loss study

Summary

Title: Spontaneous and induced abortion: A mixed methods hospital-based study from two sites in Papua New Guinea

Date commenced: September 2011

Project funding: AusAID PNG / Marie Stopes PNG

About the project

Rationale: PNG has one of the highest maternal mortality ratios (MMR) in the world with an estimated 733 maternal deaths per 100,000 live-births; sepsis due to unsafe abortion is a leading cause of maternal mortality. A recent study at Goroka General Hospital (GGH) and a behavioural surveillance survey among “high risk” women in Port Moresby (USAID/FHI 2011) highlighted that induced abortions were being carried out in unsafe situations, as previously also reported by Jenkins et al (1994). Aside from these studies, there is limited information in PNG relating to spontaneous or induced abortion. Consultation with key National Department of Health stakeholders and other partners identified unsafe abortion as a priority research area for PNG, particularly the types of complications requiring hospital treatment following pregnancy loss, and the reasons that women in PNG resort to induced abortion.

Design: This multi-disciplinary study combines clinical, quantitative and qualitative research methods. A 6-month prospective collection of clinical data of all cases admitted due to suspected abortion (induced or spontaneous) will be carried out in selected wards at GGH and Port Moresby General Hospital (PMGH). In-depth interviews will be conducted with women admitted to hospital following a miscarriage or for post-abortion care. Key informant interviews will be carried out with health care workers at GGH and PMGH.

Progress: Ethical approval was obtained in December 2011; study recruitment to start March 2012.

Significance: This study will identify why and where women seek induced abortion and provide information relating to post-abortion care services for women accessing health services. The findings of this research are expected to inform future health service delivery and public health policy on maternal health in PNG.

Contributors

Investigators: Lisa Vallely (PI), Primrose Homiehombo, Antonia Kumbia, Glen Mola, Joseph Pauru, Angela Kelly, Andrea Whittaker.

Collaborating centres: PNG Institute of Medical Research; National Department of Health, PNG; Goroka General Hospital; Port Moresby General Hospital; University of Queensland, Brisbane, Australia.

2.2.20 Maternal Health Survey

Summary

Title: Maternal and Child Health in 4 sites in PNG: A quantitative and qualitative survey

Date commenced: September 2011

Project funding: PNG Partnership in Health Project (PiHP)

About the project

Rationale: In PNG there are an estimated 733 maternal deaths per 100,000 live births; more than two thirds of maternal deaths occur within the first week after childbirth. The majority of maternal deaths occur in rural areas and are due to poor service provision and lack of access to and use of available services. A maternal death is frequently accompanied by a stillbirth or early neonatal death; in PNG there are 29 neonatal deaths per 1,000 live births. Low birth weight and neonatal sepsis are the main causes leading to neonatal death. The Maternal Health Survey will estimate the uptake of maternal and infant health services, and women's perceptions and experiences of pregnancy and childbirth, in four sites in PNG.

Design: Cross sectional survey among 1000 women aged 15-44 years at four health and demographic surveillance sites (Central, Madang, Eastern and Southern Highlands Provinces).

Progress: Ethical approval in PNG and Australia obtained Mar 2012; study to start mid-2012.

Significance: Aside from periodic demographic and health surveys (DHS) there is little information in PNG relating to maternal health and practices during and following childbirth in the community. This research will provide policy-relevant information on barriers to accessing maternal and child health (MCH) services and provide insights into the beliefs, practices and experiences surrounding pregnancy and childbirth.

Contributors

Investigators: Lisa Vallely (PI), Primrose Homiehombo, Suparat Phuanukoonnon, Peter Siba, Glen Mola, Andrea Whittaker, Caroline Homer.

Collaborating centres: PNG Institute of Medical Research; National Department of Health, PNG; University of Queensland, Brisbane; University of Technology, Sydney.

2.2.21 Syphilis Point of Care Tests

Summary

Title: A Laboratory Evaluation of Rapid Point of Care Tests for Syphilis

Date commenced: May 2011

Project funding: Funded as part of NHMRC Program Grant (PI – J Kaldor, UNSW)

About the project

Rationale: Antenatal clinic surveillance and periodic surveys indicate that syphilis is one of the most common STIs in PNG. Syphilis can be effectively treated with penicillin. Thus if an early diagnosis is established, and therefore the case treated, complications associated with pregnancy, including congenital syphilis, can be prevented. Furthermore, in the general adult population, early detection and treatment of syphilis will greatly assist disease control.

There are many rapid point of care (RPOC) tests available for the detection of syphilis. These typically use fingerprick whole blood, serum or plasma samples and can be performed at the point of care. The implementation of a new diagnostic tool in PNG needs to be carefully considered. As many health workers lack extensive training, it is imperative that diagnostic algorithms are kept simple, and employ tools that are known to work effectively in this setting. We therefore aim to compare the performance of RPOC tests for syphilis against current reference standard tests, and to assess the operational characteristics of each test. This study will provide data that will lead to field trials of RPOC tests in PNG.

Design: This is a multi site study involving reference laboratories in PNG, Melbourne and Sydney, Australia. For PNG, a well-characterized, archived serum from 1000 patients was selected on the basis of previous laboratory results. All sera were blinded and tested on five different RPOC tests.



Two syphilis testing kits that are currently used in testing syphilis in PNG.

Progress: A training workshop was conducted in Melbourne in May 2012 before the study commenced in PNG. Testing was completed by end-2011 and data analysis will be completed by Jun 2012.

Significance: The best performing syphilis RPOC test will be chosen for field trials in PNG. This will help to standardise syphilis testing in the country and will improve the quality of results.

Contributors

Investigators: Claire Ryan (PI), Tawarot Kurumop, Rebecca Guy, Louise Causer, John Kaldor, Peter Siba.

Collaborating centres: PNG Institute of Medical Research; The Burnet Institute, Melbourne; The Kirby Institute, University of New South Wales, Sydney; Victorian Infectious Disease Reference Laboratory, Melbourne; South Eastern Area Laboratory Services, Sydney.

2.2.22 Health Workers Understanding of Syphilis Testing

Summary

Title: An investigation of health workers understanding of syphilis testing in PNG

Date commenced: June 2011

Project funding: PNGIMR ICRAS Program

About the project

Rationale: Syphilis can cause serious adverse effects during pregnancy, including stillbirth and congenital syphilis. The PNG Safe Motherhood/Obstetrics Group has approved the use of a TPHA syphilis rapid test in rural antenatal clinics (ANCs). Whilst it is acknowledged that this may result in the over-diagnosis and subsequent over-treatment of syphilis, this is considered favourable to the potential risks of congenital syphilis and other neonatal complications. Informal interviews conducted at multiple clinical sites in PNG indicate that health care workers (HCWs) have not been trained in the use of TPHA rapid tests, that there are differences in how much blood is used, and how long before results are being read. Information gathered at relevant meetings, most notably the PASHIP reference group meeting in November 2010, has highlighted the confusion of many health workers in ANCs and sexual health clinics about syphilis testing and the correct interpretation of results.

Design: We aim to visit at least three ANCs and two sexual health clinics in at least three provinces in each region of PNG (Highlands, Islands, Momase and Southern). Following informed consent, all health workers based at these facilities will be invited to take part in a short interview based questionnaire aiming to seek basic information regarding the health workers understanding of syphilis testing, diagnosis and treatment. We will also seek information on the level of training health workers received in the performance of a rapid test and the interpretation of results.

Progress: Ethical approval was obtained in January 2012. Interviews to start in April 2012.

Significance: Data collected within this study will inform National Department of Health training guidelines for syphilis testing, and enable the harmonization of testing protocols. This will lead to more accurate diagnosis, treatment, and better outcomes for patients in PNG.

Contributors

Investigators: Claire Ryan (PI), Tawarot Kurumop, Justin Pulford, Andrew Vallely, Greg Law.

Collaborating centres: PNG Institute of Medical Research; Burnet Institute, Melbourne; Kirby Institute, University of New South Wales, Sydney; National Department of Health.

Significance: The results from this study will provide the first data on the association between CCR5 genotypes and CCR5 expression, and correlation between CCR5 expression and viral propagation in individuals from PNG. A better understanding of the virus-cell interactions within the PNG epidemic influenced by unique host genetics, at the population level, will shape public health policy for this region.

Contributors

Investigators: Claire Ryan (PI), Paul Gorry, John Reeder, Peter Zimmerman, Barne Willie, Bangan John, Scott Sieg, John Tilton, Rajeev Mehlotra, Michael Roche.

Collaborating centres: PNG Institute of Medical Research; The Burnet Institute, Melbourne, Case Western Reserve University, Cleveland, Ohio.

2.2.23 Hosts Genetics & HIV Transmission

Summary

Title: Characterization of novel CCR5 genotypes influencing the emerging and unique HIV-1 epidemic in Papua New Guinea

Date commenced: February 2012

Project funding: Australian Centre for HIV and Hepatitis Virology

About the project

Rationale: HIV transmission can be influenced not only by behaviour and the use of condoms and microbicides, but also by virological factors and host genetics. HIV uses CCR5 as the predominant co-receptor for its transmission to humans. Since this discovery, it is observed that alterations in CCR5 gene expression can impact HIV infection dynamics and disease progression. Laboratory tests of virus invasion and propagation also provide important insight regarding HIV strain virulence. Levels of CCR5 expression have not been characterized in the PNG population.

Design: We will extract genomic DNA from 50 blood samples from PNG, and genotype CCR5 Single Nucleotide Polymorphisms with established assays. For comparison, we will genotype 50 samples collected from North American random blood donors. In addition to genotyping, we will sequence the CCR5 gene (4.5 kb) to capture any other polymorphism which may be unique to PNG individuals. We will perform flow cytometry assays to analyze CCR5 expression patterns on PBMCs from PNG and North American samples. We will perform in vitro infection assays with PBMCs from PNG and North American samples, already characterized for CCR5 genotypes and co-receptor expression in Aim-1, using highly sensitive multicolour flow cytometric assays that specifically identify memory CD4+ T cell subsets that can fuse with and become productively infected by a R5-tropic HIV-1 isolate. The research plan undertakes an innovative translational component through direct involvement of the PNG Institute of Medical Research scientific staff. Two PNGIMR staff members are in residence at Case Western Reserve University, in Cleveland, Ohio and use the proposed studies as their Master's Degree thesis projects.

Progress: Sample processing to begin in May 2012.

Population Health and Demography Unit



3. Population Health and Demography Unit

3.1.1 Overview

The Population Health and Demography Unit (PHDU) was formed alongside the Sexual and Reproductive Health Unit (SRHU) in March 2011, following the dissolution of the former Operational Research Unit (ORU). The PHDU focuses on assessing large-scale trends in health and disease by applying an interdisciplinary population-based research approach. The unit's current emphasis is on the evaluation of large-scale health interventions implemented at national or sub-national levels and the assessment of changes in health trends related to large-scale development projects. It aims to provide evidence on the impact of interventions and on determinants of health and disease at implementation and policy level. In consideration of changes in disease patterns related to social and economical developments, the PHDU is planning to expand into the areas of Non-Communicable Diseases, Cancers and Lifestyle Conditions as well as Health Systems and Health Economics. Activities carried out by the PHDU encompass clinical, biomedical, social, behavioural, epidemiological and health systems studies and span across several diseases. Health and Demographic Surveillance Sites (HDSS) are maintained as the backbone for monitoring morbidity, mortality and causes of death, and as a platform for population-level studies on a variety of health problems. Due to the cross-cutting nature of this work the PHDU aims to collaborate closely with other IMR units that have a more disease-specific focus.

3.1.2 Research Objectives

The PHDU's mission is to conduct policy-relevant interdisciplinary research with the aim to understand population-level changes and determinants of health and disease in Papua New Guinea.

The unit's goals are:

1. To establish and maintain local interdisciplinary research capacity with a focus on population-level research and flexible to adapt to changing health research priorities.
2. To strengthen the priority research areas of;
 - (a) Health Systems Research & Health Economics and;
 - (b) Non Communicable Diseases, Cancers and Lifestyle Conditions.
3. To establish and maintain Surveillance Sites as platform and

framework for conducting population-level studies.

4. To apply a mixed-methods approach to identify and investigate health problems and underlying determinants at a policy, systems and population level.
5. To conduct policy-relevant research along the continuum of health policy development – implementation of interventions and projects – evaluation of health impact.
6. To build on the Institute's capacity in disease-focused research in the development and application of population-level studies.

3.1.3 Achievements 2006 – 2011

The separation of the former ORU into the PHDU and Sexual and Reproductive Health Units was a direct consequence of the success and fast growth of the former ORU. The expansion of sexual and reproductive health activities consequently resulted in the formation of a separate dedicated unit. The PHDU successfully contributed to the evaluation of the first Goba Fund malaria grant to PNG (Round 3) and subsequently managed to establish itself as a Sub-Recipient of the Round 8 Global Fund malaria grant in charge of the country-wide overall evaluation of the National Malaria Control Program. An additional major project which is still in development is the health impact assessment of the PNG LNG natural resource project. The latter provided an ideal opportunity to revive existing and establish new Health and Demographic Surveillance Sites in four locations. Complemented by the Sentinel Sites with demographic surveillance of the Round 8 evaluation, the PHDU is in the process of establishing a strong framework for the assessment of demographic and health trends across PNG. Between 2006 and 2011, the ORU/PHDU (excluding sexual and reproductive health research activities) secured project funding in excess of 9.5 million US\$, almost 90% of which were secured between 2009 and 2011. Major funding agencies are The Global Fund and PNG LNG (Esso Highlands) while smaller grants came from the Department of Higher Education, Japan, the German Ministry of Education and Research, the Bill and Melinda Gates Foundation and PNG IMR ICRAS.



The unit's current emphasis is on the evaluation of large-scale health interventions implemented at national or sub-national levels and the assessment of changes in health trends related to large-scale development projects.

3.1.4 PHDU Organizational Structure

The structural organization of the PHDU reflects its two major research programs (Partnership in Health and Malaria Control Section) as well as the strategic objective to strengthen the priority research areas Health Systems and Health Economics as well as Non-Communicable Diseases, Cancers and Lifestyle Conditions. The Malaria Control section comprises activities related to the Evaluation of the National Malaria Control Program and related studies on malaria control interventions. The Partnership in Health section comprises activities under the health and demographic surveillance research component of the PNG LNG Partnership in Health Program. Of particular importance is the overlap of activities in the area of health and demographic surveillance systems.

Unit Head, **Dr Manuel Hetzel**

Section Heads

Malaria Control Project, **Dr Manuel Hetzel**

Health Systems & Health Economics

Non-Communicable Diseases, Cancers & Lifestyle Conditions

Partnership in Health Project, **Dr Suparat Phuanookoonun**

3.2 PHDU Research Projects 2006-2011

NB: This section includes research projects carried out by the former Operational Research Unit (ORU) until March 2011.

- 3.2.1 East-PNG Study
- 3.2.2 *Helicobacter pylori* Study
- 3.2.3 Behavioural Studies on Tuberculosis in PNG
- 3.2.4 Acceptability of ITPi
- 3.2.5 Global Fund Bednet Project
- 3.2.6 AL Effectiveness Study
- 3.2.7 National Malaria Control Program Evaluation: Malaria Household Survey
- 3.2.8 National Malaria Control Program Evaluation: Sentinental Sites Surveillance
- 3.2.9 Antimalarial Drug Resistance Monitoring
- 3.2.10 National Malaria Control Program Evaluation: Health Facility Survey
- 3.2.11 Partnership in Health Project
- 3.2.12 Cause of Death Study
- 3.2.13 Barriers to Mosquito Net Use
- 3.2.14 Home Management of Malaria (HMM) Study
- 3.2.15 RDT Test Performance
- 3.2.16 Antimalarial Drug Quality Study
- 3.2.17 G6PD Study
- 3.2.18 Durable Lining Study
- 3.2.19 PiH Project - Nutrition Study
- 3.2.20 PiH Project - Non-Communicable Diseases Study

3.2.1 East-PNG Study

Summary

Title: Evaluation and alleviation of environmental burden due to subsistence transition (EAST) in Papua New Guinea – elucidation of health impact

Date commenced: June 2007

Project funding: University of Tokyo (Department of Higher Education, Japan)

About the project

Rationale: Most communities in Papua New Guinea undergo a very rapid transition from traditional subsistence agriculture to cash-economy. Such transition entails the introduction and release-accumulation of chemical substances, such as pesticides and food additives (through the purchase of processed foods), into the local ecosystem, which in turn may affect not only the health and survival of the people, but also the safety of local produce.

Design: Cross sectional prospective study; target regions are Asaro valley (Eastern Highlands), Tari basin (Southern Highlands), Nomad-Bosavi area (Western Province/Southern Highlands), Maprik hill (East Sepik), Madang area (Madang), and Port Moresby (NCD). In each region, three to five communities with different extent of modernization/urbanization will be selected. The sample will include approximately 400 participants in each region (each household with head, spouse, and children) from whom biological samples (urine, saliva, blood, and scalp hair) will be collected. At the same time, environmental samples (drinking water, ash, major food items) will be collected in each region. In both, environmental and biological samples, pesticides, heavy metals, essential elements, and bio-marker contents will be determined. Also, explanatory chemical analyses for pesticides and POPs will be conducted to reveal the expansion of the lists of identified chemicals.

Progress: Ongoing.

Significance: This study will provide evidence to mitigate the environmental/health burden due to agricultural development.

Contributors

Investigators: Masahiro Umezaki (PI) and Suparat Phuanukoonnon, Gwendalyn Vengiau, Kazumi Natsuhara Tsukasa Inaoka, Kazuhiro Suda, Shingo Odani, Takuro Furusawa, Beno Elepan Pupang, Ivo Mueller.

Collaborating Centres: PNG Institute of Medical Research; University of Tokyo.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Diet and physical activity among migrant Bougainvilleans in Port Moresby, Papua New Guinea: association with anthropometric measures and blood pressure. Vengiau G, Phuanukoonnon S, Siba P, Umezaki M. Am J Human Biol [In Press]

3.2.2 *Helicobacter pylori* Study

Summary

Title: Analysis of the phylogenetic structure and geographic distribution of the gastric pathogenic bacterium *Helicobacter pylori* in people from Papua New Guinea

Date commenced: February 2008

Project funding: ERA-NET Pathogenomic Network, German Ministry of Education & Research

About the project

Rationale: Two prehistoric migrations peopled the Pacific. One reached New Guinea and Australia, and a second, more recent, migration extended through Melanesia and from there to the Polynesian islands. These migrations were accompanied by two distinct populations of the specific human pathogen *Helicobacter pylori*, called hpSahul and hspMaori, respectively. hpSahul split from Asian populations of *H. pylori* 31,000 to 37,000 years ago, in concordance with archaeological history.

Design: A cross-sectional study to collect 140 gastric biopsy specimens from PNG highlanders who had gastric ulcer or upset. The specimens were cultured, genotyped and compared with results from other countries.

Progress: Completed.

Significance: The study provided proof of the genetic association between *H. pylori* from Melanesian Papua New Guinea and Indigenous Australia. The hpSahul populations in New Guinea and Australia have diverged sufficiently to indicate that they have remained isolated for the past 23,000 to 32,000 years. The second human expansion from Taiwan 5000 years ago dispersed one of several subgroups of the Austronesian language family along with one of several hspMaori clades into Melanesia and Polynesia, where both language and parasite have continued to diverge.

Contributors

Investigators: Mark Achtman (PI), Yoshan Moodley, Suparat Phuanukoonnon, Peter Siba.

Collaborating centres: PNG Institute of Medical Research; Max Planck Institute for Infection Biology, Germany.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. The peopling of the Pacific from a bacterial perspective. Moodley Y, Linz B, Yamaoka Y, Windsor HM, Breurec S, Wu JY, Maady A, Bernhöft S, Thiberge JM, Phuanukoonnon S, Jobb G, Siba P, Graham DY, Marshall BJ, Achtman M. Science 2009; 323(5913): 527-30.

3.2.3 Behavioural Studies on Tuberculosis in PNG

Summary

Title: Knowledge, Attitude and Practice (KAP) of Tuberculosis (TB) in Selected Pilot Sites in Papua New Guinea

Date commenced: August 2008

Project Funding: The Global Fund to Fight AIDS, Tuberculosis and Malaria

About the project

Rationale: The National TB program, with support from the Global Fund, developed Behaviour Change Communication (BCC) materials to increase community awareness on tuberculosis and to promote public and private DOTS services. The implementation of these materials was done in several pilot sites prior to nationwide roll-out. This survey aimed to provide data to inform the development of appropriate key messages on TB prevention and control for the population groups covered in the project sites. Moreover, it was intended to contribute to refining the TB class and other TB prevention-related activities with the aim of improving health seeking behaviour of people in the target communities.

Design: This cross-sectional community-based study was conducted as a series of household surveys and included a complementary qualitative research component to illicit data on process and meaning. Qualitative data was gathered from care providers and patients' lived experiences of tuberculosis and community leaders' perceptions of TB and care provisions. The study was conducted in pilot implementation sites selected by NDoH based on the local burden of TB.

Progress: Completed in 2010.

Significance: The study revealed a low level of awareness of TB with 60 % of respondents not aware of the disease. It found a lack of adequate knowledge of the causes of TB (below 45% in all five sites, except Milne Bay) and no respondent mentioned knowledge of BCG immunization for prevention. This indicates a great need



Study staff conducting community awareness on TB in a community in the Eastern Highlands Province.

in scaling-up TB campaigns, as the advocacy, communication and social mobilization (ACSM) activities don't appear to be impacting the community to make a difference in KAP towards TB. KAP studies (KAP+) should be prioritized and reported so that impact and outcomes can be measured as the current TB control program is being rolled out. Only a minority indicated positive attitude or reaction of seeking treatment which needs to be advocated and strengthened through ACSM.

Contributors

Investigators: Peter Siba (PI) , Geraldine Maibani-Michie (Co-PI), Jimmy Elliot, Rebecca Emori, Somu Nosi, Melvin Kualawi, Paul Aia, Rajenda Parasad.

Collaborating centres: PNG Institute of Medical Research; NDoH and Provincial Divisions of Health; World Vision-PNG.

Publications

REPORTS

1. Report on the Knowledge, Attitudes and Practice (KAP) of Tuberculosis (TB) in Selected Pilot Sites in Papua New Guinea. PNG Institute of Medical Research, Goroka, Dec 2009.

2. Knowledge, Attitudes and Practice (KAP) of TB in NCD, Madang, Morobe, EHP, Milne Bay and Simbu (series of six provincial reports). PNG Institute of Medical Research, Goroka, Apr 2010.

CONFERENCE PRESENTATIONS

1. Knowledge Attitude and Practice (KAP) of TB in Madang Province. Emori R, Kualawi M, Elliot J, Nivia H, Siba P, Maibani-Michie G. In: 46th Annual Symposium of the Medical Society of Papua New Guinea. Wewak, PNG; 2010.

3.2.4 Acceptability of IPTi

Summary

Title: Acceptability of Intermittent Preventive Treatment in infants (IPTi) interventions in Papua New Guinea

Date commenced: September 2008

Project funding: IPTi Consortium (Bill and Melinda Gates Foundation)

About the project

Rationale: Although the acceptability research published to date provides a comprehensive insight into community responses to IPTi delivered in sub-Saharan Africa, there are no published data on the acceptability of IPTi in other settings. Given that IPTi has the potential to reduce malaria-related morbidity and mortality in infants in other regions with a significant level of malaria mixed endemicity (*Plasmodium falciparum* and *Plasmodium vivax*), such as South-East Asia or Oceania, it is crucial to ensure that IPTi is socially and culturally acceptable in distinct social and cultural settings outside of sub-Saharan Africa. This study complements a trial with IPTi conducted by PNGIMR.

Design: This qualitative study investigated the acceptability of the IPTi intervention among study participants of an IPTi trial, health service providers, and the wider communities in Madang and Maprik (East Sepik).

Progress: Completed.

Significance: This study provides crucial information to support the IPTi introduction in PNG. IPTi fits well with local health cultures, appears to be accepted easily and has little impact on attitudes towards childhood immunization or malaria prevention. The study adds to the evidence indicating that IPTi could be rolled out in a range of social and cultural contexts.

Contributors

Investigators: Robert Pool (PI), Suparat Phuanukoonnon, Christopher Pell, Leanne Straus, Nicolas Senn, Ivo Mueller.

Collaborating centres: PNG Institute of Medical Research; CRESIB, University of Barcelona.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Community response to intermittent preventive treatment of malaria in infants (IPTi) in Papua New Guinea (PNG). Pell C, Straus L, Phuanukoonnon S, Mueller I, Senn N, Gysels M, Pool R. *Malar J* 2010; 9: 369.

3.2.5 Global Fund Bednet Project

Summary

Title: PNG/The Global Fund Round 3 malaria control program evaluation 2008-2009

Date commenced: June 2008

Project funding: The Global Fund to Fight AIDS, TB and Malaria

About the project

Rationale: In 2003, PNG successfully submitted a proposal for the free distribution of long-lasting insecticide treated mosquito nets (LLIN) and expansion of confirmed diagnosis and appropriate treatment of malaria to The Global Fund. The grant was implemented by the National Department of Health and Rotarians Against Malaria (RAM) between 2004 and 2009. The aim of the evaluation program was to assess, at a population level, the

outcomes and impact of the Global Fund supported program. A particular focus was the free distribution of LLINs.

Design: The Bednet Project was designed as a comprehensive evaluation scheme comprising cross-sectional household surveys and malaria surveillance in Sentinel Sites. Household surveys included visits to the nearest health facility to assess availability of malaria treatment. Sentinel Site activities included malaria case surveillance in a health facility and household, prevalence and entomology surveys in nearby villages. Cross sectional surveys were carried out in randomly selected villages and the nearby health facility in 17 provinces. Sentinel Sites were located in Yapsie (Sandaun Province), Dreikikir (East Sepik), Finschhafen and Mumeng (Morobe), Sausi (Madang), Tabibuga (Western Highlands) and Wipim (South Fly).

Progress: Completed in August 2009.

Significance: Findings of the evaluation were compiled in a final report and presented to the National Department of Health (NDoH) and other stakeholders. Key results were presented to the NDoH and the media in March 2011 and subsequently featured in local newspaper articles and on Radio New Zealand. The final evaluation report formed part of the overall reporting to the Global Fund. It demonstrated that the implementation of the LLIN distribution campaign led to a significant increase in net ownership across PNG. Usage of nets by children and pregnant women remained comparably low at around 40%. While the program missed the Global Fund targets of 80% ownership and usage, the report concluded that it significantly improved net coverage in PNG. The results of this evaluation project also featured.

Contributors

Investigators: Ivo Mueller (PI), Leo Makita (PI), Peter Siba (PI), Manuel Hetzel, Gibson Gideon, Lisa Reimer.

Collaborating centres: PNG Institute of Medical Research; National Department of Health and Provincial Divisions of Health, PNG; Lutheran Health Services, PNG; Evangelical Brotherhood Church, PNG.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Ownership and usage of mosquito nets after four years of large-scale free distribution in Papua New Guinea. Hetzel MW, Gideon G, Lote N, Makita L, Siba PM, Mueller I [submitted to *Malaria Journal*]

2. Multiplex Assay for Species Identification and Monitoring of Insecticide Resistance in *Anopheles punctulatus* Group Populations of Papua New Guinea. Henry-Halldin CN, Nadesakumaran K, Keven JB, Zimmerman AM, Siba P, Mueller I, Hetzel MW, Kazura JW, Thomsen E, Reimer LJ, Zimmerman PA. *Am J Trop Med Hyg* 2012; 86: 140-151.

3. High Throughput Multiplex Assay for Species Identification of Papua New Guinea Malaria Vectors: Members of the *Anopheles punctulatus* (Diptera: Culicidae) Species Group. Henry-Halldin C, Reimer L, Thomsen E, Koimbu G, Zimmerman A, Bosco Keven J, Dagoro H, Hetzel MW, Mueller I, Siba P, Zimmerman PA. *Am J Trop Med Hyg* 2011; 84: 166-173.

4. An integrated approach to malaria control in Papua New Guinea. Hetzel MW. *PNG Med J*, 2009, 52: 1-7.

REPORTS

1. Papua New Guinea/The Global Fund Round 3 Malaria Control Programme Evaluation 2008/2009: Results from Cross-Sectional Surveys and Sentinel Sites. Hetzel MW, Gideon G, Mueller I, Siba PM. PNG Institute of Medical Research, Goroka; March 2010.



A boy receiving his free treated mosquito nets.

CONFERENCE PRESENTATIONS

1. The changing epidemiology of malaria in Papua New Guinea. Hetzel MW, Barnadas C, Gideon G, Tarongka N, Iga J, Morris H, Siba PM, Mueller I. In: 60th Annual Meeting of the American Society of Tropical Medicine and Hygiene. Philadelphia, USA; 2011.

2. Treatment Seeking Behavior for Fever Patients and the Availability of Malaria Diagnostic Tools and Treatment in Health Facilities. Gideon G, Hetzel MW, Makita L, Mueller I, Siba P. In: 46th Annual Symposium of the Medical Society of Papua New Guinea. Wewak, PNG; 2010.

3. Evaluation of the Global Fund Round 3 Malaria Grant 2004-2009. Hetzel MW, Gideon G, Ningi T, Makita L, Siba P, Mueller I. In: 45th Annual Symposium of the Medical Society of Papua New Guinea. Port Moresby, PNG; 2009.

3.2.6 AL Effectiveness Study

Summary

Title: Artemether-Lumefantrine clinical effectiveness study

Date commenced: June 2008

Project funding: AusAID

About the project

Rationale: As part of the new malaria treatment policy which was endorsed in 2009, the National Department of Health (NDoH) is introducing artemether+lumefantrine (AL) as new first-line treatment for malaria. AL is an artemisinin-based combination therapy (ACT) that has proven effective in a trial conducted in PNG by the IMR and collaborators from the University of Western Australia (Karunajeewa et al. 2008). The aim of this study is to compare the proven in-vivo efficacy of AL with the drugs real-life clinical effectiveness when it is implemented in a routine health care setting. A reduced effectiveness may for example be related to treatment adherence issues.

Design: The study is designed as an open-label two-arm randomized controlled trial. Patients in the effectiveness arm will receive the first dose of AL under full supervision in Gurney Health Centre, Milne Bay; the following doses will be taken at home, as in real-life clinical practice and according to the national treatment guidelines. Patients in the efficacy arm (comparison group) will receive all doses of AL as directly observed treatment in the health facility, in order to establish the efficacy of the drug. The study enrolls outpatients aged 6 months to 10 years with a history of fever and a positive rapid diagnostic test for malaria. All patients will be followed up actively for 42 days, but patients in the effectiveness arm will be seen for the first follow-up date only on day 3, i.e. after the expected completion of the treatment course.

Progress: Enrolment of patients ongoing.

Significance: This study is expected to provide essential information about how well AL works in routine clinical practice. It can contribute to a better and more comprehensive understanding of factors which might hamper clinical and community effectiveness of AL. Such information will allow the National Malaria Control Program to adapt treatment strategies in order to achieve a high health impact with ACT.

Contributors

Investigators: Manuel Hetzel (PI), Ivo Mueller (PI), Peter Siba (PI), Livingstone Tavul, Leo Makita, Tim Davis, Gilchrist Oswyn, Inoni Betuela.

Collaborating centres: PNG Institute of Medical Research; National Department of Health, PNG; Milne Bay Provincial Health Authority, PNG; The University of Western Australia School of Medicine & Pharmacology, Freemantle.

3.2.7 National Malaria Control Program Evaluation: Malaria Household Survey

Summary

Title: PNG & The Global Fund Round 8 malaria control program evaluation plan 2009 – 2014: repeated country-wide household surveys on malaria

Date commenced: October 2009

Project funding: The Global Fund to Fight AIDS, TB and Malaria Round 8 Grant

About the project

Rationale: Since 2009, the National Malaria Control Program (NMCP) has been supported by PNG's second Global Fund grant ("Round 8" malaria grant). Over five years, over one hundred million USD will be invested in scaling up malaria control interventions with the aim to dramatically reduce malaria morbidity and mortality in PNG. This includes the distribution of long-lasting insecticide treated nets (LLIN), the introduction of artemisinin-based combination treatment (ACT) for malaria, the scaling-up of rapid diagnostic tests and microscopy, and advocacy and behaviour change communications for the prevention and response to malaria. The program is implemented by the National Department of Health, Rotarians Against Malaria (RAM), Population Services International (PSI) and the Divine Word University/Diwai Pacific Ltd. As a sub-recipient of the Round 8 grant, PNGIMR is in charge of independently evaluating the outcomes and impact of the Round 8 interventions. Activities include repeated country-wide household surveys assessing coverage with malaria control interventions alongside the community prevalence of malaria parasitaemia.

Design: Country-wide household surveys are conducted twice over the grant period in a random sample of villages across all provinces. In each village, 30 households are randomly sampled. Interviews are conducted with household heads and all members of the households are eligible for blood collection. Semi-structured interviews cover questions about mosquito net ownership and usage as well as the clinical presentation of and treatment seeking for recent illness episodes. Blood samples are collected on slides for diagnosis by light microscopy.

Progress: Baseline survey was concluded in July 2011. Follow-up survey scheduled for October 2013.

Significance: Findings from this survey provide the key data for the Global Fund's grant Performance Framework (one of three impact evaluation indicators and all four outcome evaluation

Contributors

Investigators: Ivo Mueller (PI), Manuel Hetzel (PI), Peter Siba (PI), Lisa Reimer, Justin Pulford, Seri Maraga.

Collaborating centres: PNG Institute of Medical Research; National Department of Health & Provincial Health Authorities, PNG; Evangelical Church of PNG; Evangelical Brotherhood Church, PNG; Lutheran Church, PNG; United Church, PNG; Walter & Eliza Hall Institute, Melbourne; University of Queensland, Brisbane; Barcelona Centre for International Health Research, Spain.

Publications

REPORTS

1. PNG & The Global Fund Round 8 Malaria Control Programme Evaluation 2009 – 2014: Preliminary Report on Year 2 Outcome and Impact Indicators (2011). Hetzel MW, Cuervo-Rojas J. Papua New Guinea Institute of Medical Research, Goroka, 2011.

CONFERENCE PRESENTATIONS

1. Global Fund Round 8 Malaria Grant: Programme Evaluation & Operational Research. Hetzel MW, Makita L, Siba P, Mueller I. In: 45th Annual Symposium of the Medical Society of Papua New Guinea. Port Moresby, PNG; 2009.

3.2.9 Antimalarial Drug Resistance Monitoring

Summary

Title: The in vitro and in vivo assessment of antimalarial drug resistance to first- and second-line drugs for uncomplicated malaria in Papua New Guinea

Date commenced: November 2009

Project funding: The Global Fund to Fight AIDS, TB and Malaria Round 8 Grant

About the project

Rationale: In 2009, the NDoH of Papua New Guinea will introduce artemether-lumefantrine (AL) as a new national first-line treatment for uncomplicated malaria and dihydroartemisinin-piperaquine (DHA-PPQ) as second-line treatment. The principal purpose of this study is to continuously monitor the sensitivity of malaria parasites to these two drugs and provide the NDoH with regular and accurate information about antimalarial drug resistance in PNG.

Design: The study is designed as standard in vivo efficacy trial complemented by an in vitro component. Children aged 6-10 years are enrolled and followed up for 42 days. Two sites, one in Milne Bay and one in East Sepik were chosen.

Progress: In vivo monitoring of resistance against AL started in Milne Bay.

Significance: This study will provide NDoH with essential data on the development of drug resistance following a baseline assessment by Karunajeewa et al. (2008). The data is essential for continuously assessing the usefulness of currently deployed antimalarial drugs.

Contributors

Investigators: Livingstone Tavul (PI), Ivo Mueller (PI), Manuel Hetzel (PI), Peter Siba (PI), Tim Davis, Ingrid Felger.

Collaborating centres: PNG Institute of Medical Research; National Department of Health, PNG; The University of Western Australia, Perth; Swiss Tropical and Public Health Institute (Swiss TPH), Basel.

3.2.10 National Malaria Control Program Evaluation: Health Facility Survey

Summary

Title: PNG & The Global Fund Round 8 malaria control program evaluation plan 2009 – 2014: repeated countrywide survey of malaria case management pre- and post-implementation of a revised malaria treatment protocol

Date commenced: January 2010

Project funding: The Global Fund to Fight AIDS, TB and Malaria Round 8 Grant

About the project

Rationale: As part of the GFATM supported national malaria control program, a new national malaria treatment protocol (NMTP) will be implemented in health facilities across PNG from late 2011 onwards. The aim of this study is to monitor the implementation of the revised NMTP with emphasis on the availability of diagnostic and treatment resources, health worker knowledge and training, and adherence to the revised malaria case management protocols.

Design: Repeat countrywide cross sectional survey completed at randomly selected health facilities pre- (baseline) and post- (1, 2 and 3 years) implementation of a revised national malaria treatment protocol.

Progress: Baseline survey (2010) completed. Follow-up survey 1 (2011) completed. Follow-up survey 2 to commence in April 2012.

Significance: This study will provide timely information to the National Department of Health and National Malaria Control Program partners regarding the implementation progress of the new malaria treatment protocol. The baseline rounds found poor provider compliance with the newly implemented protocol and concluded with recommending refresher training alongside the continued roll-out.

Contributors

Investigators: Ivo Mueller (PI), Manuel Hetzel (PI), Peter Siba (PI), Justin Pulford.

Collaborating centres: PNG Institute of Medical Research; National Department of Health, PNG; Provincial Health Authorities, PNG; The University of Queensland, Brisbane; Walter & Eliza Hall Institute, Melbourne; Barcelona Centre for International Health Research, Spain.

Publications

REPORTS

1. Papua New Guinea/Global Fund Round 8 Malaria Control Program Evaluation 2009-2014: Report of the Baseline Health Facility Survey 2010. Pulford J, Kurumop S, Hetzel MW, Mueller I, Siba PM. PNG Institute of Medical Research, Goroka, May 2011.

CONFERENCE PRESENTATIONS

1. Malaria case management in Papua New Guinea: Preliminary findings from a nationwide health facility survey. Hurim S, Pulford J, Hetzel MW, Mueller I, Siba PM. In: 46th Annual Symposium of the Medical Society of Papua New Guinea. Wewak, PNG; 2010.

2. Global Fund Round 8 Malaria Grant: Programme Evaluation & Operational Research. Hetzel MW, Makita L, Siba P, Mueller I. 45th Annual Symposium of the Medical Society of Papua New Guinea. Port Moresby, PNG; 2009.

3.2.11 Partnership in Health Project

Summary

Title: Partnership in Health (PiH) project: Monitoring the impact of the PNG Liquid Natural Gas (PNG LNG) project on the health of population in project impact and control communities

Date commenced: July 2010

Project funding: Esso Highlands Ltd., PNG-LNG

About the project

Rationale: The Exxon-Mobile led PNG Liquid Natural Gas (PNG LNG) project is the largest ever resource project in the history of Papua New Guinea. Once fully operational, it will contribute substantially to the PNG gross national product, employ several thousand staff and provide royalties to landowners and taxes to the Government. The project will thus contribute very significantly to the development of PNG. As any other major resource projects, the PNG LNG will have a significant impact on the life-style and health of people in the project impact areas. This project seeks to monitor the impact of the project on affected populations by comparing longitudinal demographic and health trends in project affected and comparison communities using health & demographic surveillance systems (HDSS). Demographic surveillance will include birth and mortality trends, migration events (in-, out- and internal migration) as well as socio-economic and educational factors while monitoring of health trends will focus on burden of key infectious and non-communicable diseases (NCD). For operational purposes, the HDSS platform including demographic/mortality studies as well as NCD components are implemented by the PHD Unit while the components related to sexual and reproductive health, and bacterial and viral diseases (such as vector borne, diarrhoeal, respiratory diseases) are implemented by other IMR units.

Design: An HDSS includes both continued, basic demographic monitoring (i.e. births, deaths, and migrations) and evaluation of health trends. An HDSS thus aim to assess the overall risks/benefits to individual households on the sound platform of close surveillance demographic dynamics. In order to monitor the short, medium and long-term impact, the locations for the health monitoring include the LNG project affected population in

Hiri district near Port Moresby, and Hides in Southern Highlands Province. In order to monitor health trends in the general PNG population (and provide a comparison to the situation in the project affected areas) the IMR will also (re-) establish two comparison sites in the Asaro Valley (Eastern Highlands) and Karkar Island (Madang).

Significance: This study will help to determine if and how the PNG LNG project impacts on the health and life-style of PNG populations by comparing demographic and health trends in project impact and comparison communities. The HDSS's will provide information on the overall risks/benefits to individual households on the platform of close surveillance of demographic dynamics. The project will further provide an evidence base for the design, implementation and monitoring of curative and preventative interventions targeting pneumonia, TB and STIs. In addition, it will serve as a platform for training local biomedical scientists.

Contributors

Investigators: Peter Siba (PI), Joe Burton (PI), Suparat Phuanukoonnon, Hebe Gouda, Ian Riley, Justin Pulford, Andrew Greenhill, Paul Horwood, Paul Harino, Harry Poka, Patricia Rarau, Seri Maraga, Gwendalyn Vengiau, Elias Namosha, Mexy Kakazo, Inoni Betuela, Angela Kelly, Claire Ryan, Andrew Valley.

Collaborating centres: PNG Institute of Medical Research; University of PNG, Port Moresby; Telethon Institute of Child Health Research, Perth; University of Queensland, Brisbane; Swiss Tropical and Public Health Institute, Basel; University of New South Wales, Sydney.



Papa Village from a distance. It is one of the four study sites of the PiH project.

3.2.12 Cause of Death Study

Summary

Title: Cause of death: improving measures of mortality by cause

Date commenced: 2010

Project funding: National Health and Medical Research Council (NHMRC)

About the project

Rationale: Given the lack of reliable cause of death (COD) data in most parts of the developing world, new methods are required to estimate COD patterns from low cost or existing data collections. COD data are a critical input into public health analyses for understanding epidemiological patterns and trends; for assessing their social, economic, cultural, and technological determinants of mortality; and for allocating scarce resources for public health and medical care; they are an essential component of burden of disease estimates. In PNG only hospital deaths are used for official COD statistics. Hospital deaths, however, are a biased sample of population deaths. It would be possible to use hospital COD data to estimate population cause specific mortality fractions (CSMFs) if the probability – by age, sex, and cause – were known that a person who died would die in hospital. The aim of this project is to calculate this probability.

Design: Deaths occurring in the community will be collected through the Health and Demographic Surveillance System (HDSS) within the Partnership in Health Project. Deaths will be followed up with verbal autopsy interviews - diagnoses of COD based on family histories. We will also collect covariate data from all deaths in the HDSS and from all deaths in the hospitals serving the HDSS population. Both sources of data will be employed to estimate the probability of a person who dies in hospital by age, sex, and COD.

Significance: The findings from this study will significantly improve our understanding of the mortality trends in Papua New Guinea, help to improve the currently available health information system and will inform decisions about health service delivery and public health interventions.

Contributors

Investigators: Ian Riley, Alan Lopez, Chris Murray, Rafael Lozano, Hebe Gouda.

Collaborating centres: PNG Institute of Medical Research; University of Queensland, Brisbane.

3.2.13 Barriers to Mosquito Net Use

Summary

Title: A qualitative investigation of the reasons why some Papua New Guineans who own long lasting insecticide treated nets (LLIN) choose not to use them

Date commenced: October 2010

Project funding: GFATM Round 8 Malaria Program Operational Research Grant

About the project

Rationale: The mass distribution of mosquito nets is a central component of the current national malaria control strategy in PNG. Unfortunately, evidence suggests that many individuals who own or have access to a mosquito net do not reliably sleep under it. Few studies have sought to examine the reasons why a mosquito net owner may choose not to use his or her net. Accordingly, this study was designed to address this gap in part and provide locally relevant data to the national malaria control program implementing partners.

Design: In-depth interviews (n=44) with individuals identified as owning, but not using, a mosquito net the night prior to interview. Participants were purposively sampled from four provinces across PNG during the course of a countrywide household survey.

Progress: Completed in December 2011.

Significance: This study is the first of its kind to examine reasons for mosquito net non-use amongst net owning individuals as a primary research focus via a qualitative methodology. It was anticipated that the resulting findings would broaden understanding in this relatively unexplored area and potentially inform interventions that may usefully promote greater mosquito net use amongst this population or alternative strategies to further reduce their risk of malaria infection.

Contributors

Investigators: Justin Pulford (PI), Manuel W Hetzel, Tania Oakiva, Angeline Angwin, Miranda Bryant, Ivo Mueller.

Collaborating centres: PNG Institute of Medical Research; Population Services International (PSI), Papua New Guinea.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Reported reasons for not using a mosquito net when one is available: A review of the published literature. Pulford J, Hetzel MW, Bryant M, Siba PM, Mueller I. Malaria Journal, 2011; 10:83.

REPORTS

1. Reported Reasons for Not Using a Mosquito Net When One is Available: A Review of the Published Literature and a Compilation of Recent Household Survey and In-Depth Interview Data. Pulford J, Oakiva T, Hetzel MW, Bryant M, Angwin A, Mueller I, Siba PM. PNG Institute of Medical Research, Goroka, Feb 2012.

3.2.14 Home Management of Malaria (HMM) Study

Summary

Title: Preparatory work towards a pilot of home management of malaria (HMM) in Papua New Guinea

Date commenced: February 2011

Project funding: GFATM Round 8 Malaria Program Operational Research Grant

About the project

Rationale: Population Services International (PSI) has been contracted to conduct a pilot of home management of malaria (HMM) in phase two of the PNG/GFATM Round 8 National Malaria Control Program grant. The aim of this study is to provide background information to PSI and the Malaria control program implementing partners that might usefully inform what type of HMM model (or models) may be best suited for use in PNG.

Design: In-depth interviews (n=44) with individuals who have experienced a recent febrile episode in four sites across PNG, a review of published evidence pertaining to HMM, and a stock take of HMM programs currently operating in PNG.

Progress: Data collection complete, data analysis currently underway, anticipated completion date of March 31st 2012.

Significance: This project will help PSI determine which model (or models) of HMM may be best suited to pilot in a PNG context. The study findings will also further understanding of malaria response and treatment seeking behaviours in a range of setting across PNG.

Contributors

Investigators: Justin Pulford (PI), Manuel W Hetzel, Angeline Angwin, Miranda Bryant, Ivo Mueller.

Collaborating centres: PNG Institute of Medical Research; Population Services International (PSI), Papua New Guinea; University of Queensland, Brisbane.



Villagers receiving their free treated mosquito nets.

3.2.15 RDT Test Performance

Summary

Title: Investigation of polymorphisms in *Plasmodium falciparum* hrp2, hrp3, aldolase and pldh genes and their predicted impact on malaria rapid diagnostic test performance

Date commenced: June 2011

Project funding: GFATM Round 8 Malaria Program Operational Research Grant

About the project

Rationale: It is recommended to perform a biological diagnosis before initiating any malaria treatment. Because of the easiness of use of the rapid diagnostics tests (RDTs), especially in remote areas, they are considered as a valuable alternative to traditional diagnosis methods such as microscopy. However, it has been reported that polymorphisms (or deletions) in the genes coding for the parasites proteins detected by these tests could have an impact on their sensitivity. We propose in this project to explore these genes in archival and newly collected PNG samples. We will first identify the presence of polymorphisms that may have an impact on the RDTs sensitivity in *P. falciparum* isolates collected in Madang, and secondly, to assess the prevalence of these polymorphisms in parasites collected in other regions of the country.

Design: Laboratory-based testing in PNGIMR, Goroka, and Walter and Eliza Hall Institute, Melbourne, will be conducted on existing blood samples collected from multiple sites across PNG.

Progress: Completed in February 2012.

Significance: The reported findings provide valuable information to the National Department of Health with respect to the usage of malaria RDTs in PNG. In particular, the findings provide necessary information to help inform which malaria RDT tests, from the many types available on the market, will be best suited for use with PNG populations.

Contributors

Investigators: Celine Barnadas (PI), Ivo Mueller, Elisheba Malau, Moses Laman, Laurens Manning.

Collaborating centres: PNG Institute of Medical Research; Walter and Eliza Hall Institute, Melbourne; The University of Melbourne, Melbourne.

Publications

REPORTS

1. Investigation of genetic polymorphisms in *Plasmodium falciparum* hrp2, hrp3, aldolase and pldh genes and their predicted impact on the performance of malaria rapid diagnostic tests in Papua New Guinea. Malau E. The University of Melbourne, Melbourne, Australia, October 2011.

3.2.16 Antimalarial Drug Quality Study

Summary

Title: Quality of anti-malarial drugs at the provider level in Papua New Guinea

Date commenced: June 2011

Project funding: GFATM Round 8 Malaria Program Operational Research Grant

About the project

Rationale: This study aims to assess the quality of antimalarial drugs at the level of health care providers in order to reflect more adequately the drug quality to which malaria patients are exposed. The study will initially include samples from different levels of formal health care facilities (hospital, health centre and aid post. If additional funding can be secured, the study will extend this survey to informal providers.

Design: Drug samples will be collected from all levels of health service provision (area medical store, hospital, health centre and aid post) from all four regions of PNG. Qualitative assessment of presence/absence of active ingredient and dissolution of tablets will be conducted via Minilab technology at CPHL, Port Moresby. Quantification of the amount of active ingredient in each drug sample will be conducted via high performance liquid chromatography (HPLC) or liquid chromatography-mass spectrometry (LC-MS) at University of Western Australia, Perth.

Progress: IRB and MRAC approval obtained. Sample collection completed. Analysis currently underway.

Significance: This study is the first of its kind to provide countrywide data on the quality of anti-malarials available at all levels of the government run health care network. The findings will usefully inform future decision making regarding anti-malarial procurement and quality assurance processes.

Contributors

Investigators: Manuel W Hetzel (PI), Nancy Bala, Evelyn Lavu, Justin Pulford, Inoni Betuela, Tim Davis.

Collaborating centres: PNG Institute of Medical Research, Central Public Health Laboratories (CPHL), Port Moresby; University of Western Australia, Perth.

3.2.17 G6PD Study

Summary

Title: Evaluation of the frequency of glucose-6-phosphate dehydrogenase (G6PD) deficiency and genotypic characterization of deficient phenotypes in populations from four regions of Papua New Guinea

Date commenced: October 2011

Project funding: GFATM Round 8 Malaria Program Operational Research Grant

About the project

Rationale: Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common human enzyme defect and one of the most common genetic disorders worldwide. G6PD deficiency is known to confer protection to individuals against malaria, yet it represents a main challenge in regards to vivax malaria treatment. Primaquine, the only drug available to cure *Plasmodium vivax* latent liver stages, causes hemolysis in G6PD severely deficient individuals. G6PD deficiency in PNG seems to be extremely heterogeneous; however, further research is needed to reliably identify the frequency with which the G6PD deficiency occurs in febrile patients and to identify the genotypic characterization of deficient phenotypes.

Design: This study is investigating the frequency of the G6PD deficiency in 1000 febrile patients attending four health centres in PNG. Genotypic characterization of G6PD deficiency will be examined in a randomly selected sample (n=6000) of the general population in the catchment areas of the respective health centres.

Progress: IRB approval obtained, MRAC approval pending. Sample collection to commence once MRAC approval obtained.

Significance: In Papua New Guinea (PNG), primaquine has been recommended by the National Department of Health in addition to an artemisinin combination therapy for the treatment of vivax malaria for non-G6PD deficient individuals. It will therefore be important to provide data on the frequency of G6PD deficiency among *P. vivax* infected patients susceptible to receive primaquine and among the general PNG population in order to assist the National Department of Health with the implementation of this treatment policy.

Contributors

Investigators: Celine Barnedas (PI), Inoni Betuela, Anna Rosanas, Manuel Hetzel, Leanne Robinson, Ivo Mueller, Jonah Iga.

Collaborating centres: PNG Institute of Medical Research, Walter and Eliza Hall Institute, Melbourne.

3.2.18 Durable Lining Study

Summary

Title: Feasibility and acceptability of insecticide treated plastic sheeting (ITPS) for vector control in Papua New Guinea

Date commenced: December 2011

Project funding: PNGIMR ICRAS Grant

About the project

Rationale: Insecticide treated plastic sheeting (ITPS) is a wall covering that acts against indoor resting mosquitoes for a period of 3-5 years. ITPS has been proposed as a complementary malaria control tool. Previous studies with ITPS have shown good acceptability; however, they have focused on African and Asian settings. Accordingly, this study will investigate the feasibility and acceptability of introducing ITPS across different settings in Papua New Guinea.

Design: The ITPS product will be installed in 10 homes in each of four study sites across PNG, inclusive of urban, highlands, lowlands and islands areas. Installation feasibility and subsequent acceptability of ITPS will be examined at baseline (installation) and four-week follow-up via structured survey and in-depth interview with participating householders.

Progress: Ethical approval obtained January 2012. Installation in first study site to commence February 2012.

Significance: Prior to embarking on a major study investigating the effectiveness of ITPS in PNG (incl. its impact on transmission and, ultimately, malaria prevalence and clinical episodes), preparatory studies are required to investigate the technical feasibility and acceptability of introducing ITPS across different settings in PNG. This inquiry will assist in informing future considerations of the desirability and feasibility of incorporating this new technology into the national malaria control program.

Contributors

Investigators: Justin Pulford (PI), Manuel W Hetzel (PI), Anthony Tandrapah (PI), Jo-An Atkinson, Tanya Russell.

Collaborating centres: PNG Institute of Medical Research; University of Queensland, Brisbane.



Installing plastic sheeting in a home in Masumave, Eastern Highlands Province.

3.2.19 PiH Project - Nutrition Study

Summary

Title: Monitoring nutritional change as a result of economic development in the Papua New Guinea

Date commenced: 2011

Project funding: Esso Highlands Ltd., PNG-LNG

About the project

Rationale: Expanded economic developments including modernization and urbanization influence people's lives in the communities. There is still much debate on the health impact of such developments. In some countries and populations changes bring about increased food supplementation and improve living standards reducing infectious diseases. On the other hand, the development brings changes in diets and causes of inactivity resulting in increased risk of NCDs. The nutrition research component of the Partnership in Health (PiH) project will extensively investigate diets and physical activities, which are major contributing risk factors to NCDs. The change in diets from a low fat and sugar diet to high sugar and saturated fat diet is an important risk factor which is often exacerbated by reduced physical activity. This study will also explore the issue of malnutrition which remains a major problem in PNG contributing to the prevalence of infectious diseases. By establishing the nutritional status of the populations and their food consumption patterns, the main risk factors of NCD and malnutrition issues can be identified.

Design: A sample population from the Health and Demographic Surveillance System (HDSS) within the Partnership in Health Project will be studied over a five-year period. Dietary and physical activity information will be collected and nutritional status surveys will be carried out. Data will be analysed and compared by sites, within site by sub-populations, sex, and age groups.

Progress: Pilot studies of 24 hr recall (nutrition) and physical activity have been completed. Preliminary analysis is being conducted. Tools will be finalized based on the outcome of the pilot studies.

Significance: This study will help to identify how and to what extent diet and physical activity contribute to the health transition in PNG populations impacted by the rapid economic developments. This information can assist the National Department of Health to develop appropriate health promotion and other preventative measures.

Contributors

Investigators: Suparat Phuanukoonnon, Hebe Gouda, Gwendalyn Vengiau.

Collaborating centres: PNG Institute of Medical Research; University of Queensland, Brisbane.

3.2.20 PiH Project - Non-Communicable Diseases Study

Summary

Title: A survey of Non-Communicable Diseases and associated risks factors in five sites across Papua New Guinea

Date commenced: 2012

Project funding: Esso Highlands Ltd., PNG-LNG

About the project

Rationale: The rapid rate of economic development currently occurring in PNG, attributable in large part to mining and natural resources and large scale liquefied natural gas (LNG) projects suggests an increase in Non-Communicable Diseases (NCDs) is inevitable. Accordingly, it is prudent to establish prevalence rates for NCDs (Diabetes Mellitus type 2, Hypertension, Acute Coronary syndrome, stroke, chronic lung diseases and cancers) and their associated risk factors (unhealthy diet, sedentary lifestyle, obesity, smoking and excessive alcohol consumption) in the early stages of this development boom so that subsequent changes may be identified and appropriate public health interventions developed and implemented in a timely manner.

Design: This study is a component of the Health and Demography Surveillance System (HDSS) established as part of the Partnership in Health Project. The HDSS is designed to monitor a range of demography, social and health issues in four sites across PNG. This

will include two communities in PNG LNG impact areas. NCD study will consist of a cross sectional survey conducted in each of the four HDSS sites over a five year period or until the target sample size of 4800 randomly selected individuals has been reached. The survey will include completion of a standardised questionnaire adapted from the WHO STEPS NCD risk factor survey, selected physical measurements and biological sample collection. In each site, a total of 1200 survey participants aged between 15-64 years and stratified according to gender and age (15-29, 30-34, 45-65) will be recruited.

Progress: Protocol developed and submitted for ethical review. Data collection scheduled to begin in August 2012.

Significance: This study will establish the prevalence of selected NCDs and their associated risk factors in five study sites across PNG. Furthermore, it will provide a baseline data set and surveillance system that will allow longitudinal monitoring of NCDs and associated risks factors in the respective study sites.

Contributors

Investigators: Patricia Rarau, Justin Pulford, Gwendalyn Vengia, Suparat Phuanukoonnon, Hebe Gouda.

Co-Investigators: Isi Kevau, Ian Riley, Robert Scragg, Chris Bullen, Geoffery Marks, Masahiro Umezaki, Ayako Morita.

Collaborating centres: PNG Institute of Medical Research; University of PNG, Port Moresby; University of Auckland; University of Queensland, Brisbane; University of Tokyo.

Vector Borne Disease Unit



4. Vector Borne Disease Unit

4.1.1 Overview

Our Mission is to conduct policy-relevant clinical, epidemiological, and laboratory research to better understand, diagnose, treat and prevent malaria and filariasis in PNG, in order to assist in developing evidence-based control programs.

Since its inception in the mid 1970s the Vector Borne Disease Unit (VBDU) has consistently been among the world's leading endemic country based research institution working on malaria and other vector borne diseases. Among its many achievement rank the conduct of one of the first malaria vaccine and insecticide treated bed net trials, extensive research on antimalarial drug and drug resistance, basic molecular parasitology, immunology and host genetic research on malaria and filariasis, in-depth studies of the epidemiology, treatment and prevention of *Plasmodium vivax* (*P. vivax*) and the pivotal trial establishing the use of mass drug administration for the elimination of lymphatic filariasis. In all its endeavors the VBDU aim to conduct research that, at the same time is globally excellent and locally relevant. Local relevance is achieved through close links with the PNG national and provincial malaria & disease control program, global excellence is assured by maintaining a large collaborative network with partners in Australia, Europe, USA and Asia.

4.1.2 Research Objectives

The work of the VBDU is organized around nine Key Research Objectives:

1. To test existing and develop novel antimalarial drug treatments and study patterns of antimalarial drug resistance.
2. To evaluate preventative drug treatment and improved vector control interventions.
3. To describe clinical presentations of malaria in children and pregnant mothers and identify key pathological processes.
4. To study the epidemiology and transmission of malaria (with a special focus on *P. vivax*).
5. To study the effect of vector control interventions on parasites and the mosquito vector species.
6. To investigate natural acquisition of immunity to malaria and determine correlates of protection as a bases of future malaria vaccine trials.
7. To monitor the impact of increased vector control on filariasis transmission.
8. To develop and evaluate improved and novel anti-filarial treatment regimens for mass drug administration (MDA).
9. To study immune status and disease patterns in a population with endemic filariasis before and after MDA has been introduced.

4.1.3 Achievements 2006 – 2011

The major achievement of the VBDU for 2006-2011 is the establishment of a highly policy relevant clinical and epidemiological research program (collaboration with colleagues from Australian Universities). As part of this, VBDU has conducted;

1. a large series of efficacy and pharmaco-kinetic studies both on evaluating existing and novel antimalarial treatments for children and pregnant women. This work has formed the basis for the new PNG standard antimalarial treatment guidelines;
2. two very large clinical trial for the prevention of malaria in children (completed 2011) and pregnant mothers (ongoing) and;
3. in-depth studies on severe malaria and non-malarial illness in Madang Province that will help to revise PNG policies for



Doing follow-up for a study in the Albimana area.

prevention and clinical practice in these high risk groups. In addition, 3 paediatric cohort studies conducted in East Sepik province, demonstrate the high burden of *P. vivax* in general and the large contribution of relapsing *P. vivax* in particular in young children, highlight the importance to include an appropriate anti-relapse treatment (using primaquine) in the PNG guidelines.

In line with the increased clinical research program, the VDBU now employs six clinicians (up from 0 in 2005). In parallel with this new program the VDBU continued to expand its studies in to the basic biology of Plasmodium parasites-host-vector interaction with a particular focus on studies on parasite diversity, the natural acquisition of immunity, host genetic adaption to malaria and in-depth studies on the ecology of malaria vector in both Madang and East Sepik Province. The VDBU also collaborates with the Population Health and Demography Unit in the monitoring and evaluation of the PNG National Malaria Control Program (supported by Global Fund Round 3 & 8 grants) and investigated the impact of long-lasting bednets (LLINs) on malaria transmission. In the areas of filariasis the VDBU unit continued groundbreaking studies that help set the global agenda for the elimination of lymphatic filariasis by conducting both a long-term follow-up of populations 8 years after MDA, investigating the impact of LLINs on filariasis transmission and developing improved drug combination for MDA.

Last, but not least, between 2006-2011 the VDBU published >100 scientific publications and raised >60 million Kina in external

research funding (covering both in-country and overseas costs). In addition to its scientific output, the VDBU made significant contribution to the training of PNG national scientists. Between 2006 and 2011 the number of local science and medical graduates employed in the VDBU increased from six to twenty, among whom three staff have enrolled in PhD programs, seven have completed MSC and eight have completed BSc Honours degrees.

4.1.4 VDBU Organizational structure

The VDBU has two laboratories and field sites in Madang and Maprik and is organized into five sections. At end-2011, the Unit had a workforce of over 150 scientific research and administrative support staff working on more than 20 research projects.

Unit Head, **Dr Inoni Betuela**

Maprik Laboratories & Field Site Manager, **Lawrence Rare**

Madang Laboratories & Field Site Manager, **Andrew Raiko**

Section Heads

Immunology & Microscopy, **Dr Leanne Robinson**

Entomology, **Dr Lisa Reimer**

Molecular Parasitology, **Dr Anna Rosanas**

Data Management, **Thomas Adiguma**

Clinical Trials/ Studies, **Supervised by Project Clinicians**

4.2 VBDU Research Projects 2006-2011

- 4.2.1 Intermittent preventative treatment for prevention of malaria and anaemia in infancy (IPTi)
- 4.2.2 Molecular epidemiology *P. falciparum* and *P. vivax* infections in young PNG children
- 4.2.3 Natural acquisition of immunity to *P. falciparum* and *P. vivax*
- 4.2.4 Population genetic analyses of *P. falciparum* and *P. vivax* diversity and evolution of drug resistance
- 4.2.5 Paediatric severe malaria study
- 4.2.6 Primaquine Studies
- 4.2.7 Artesunate-Pyronaridine and Artemisinin-Nephthoquine combination therapies in Papua New Guinean children with uncomplicated malaria (Standard Treatment trial II)
- 4.2.8 Pharmacokinetics of piperaquine in pregnancy
- 4.2.9 Antimalarial drug combinations in pregnancy
- 4.2.10 IPTp Study
- 4.2.11 The contribution of relapsing infection to the burden of *P. vivax* in PNG
- 4.2.12 Neonatal Infection Study
- 4.2.13 The ecology of mosquito vectors of malaria and filariasis
- 4.2.14 Mosquito parasite interactions and filariasis transmission in Papua New Guinea
- 4.2.15 Malaria transmission potential of the *Anopheles punctulatus* species complex
- 4.2.16 Survey for insecticide resistance in the major vectors of Papua New Guinea
- 4.2.17 International Centre of Excellence for Malaria Research (ICEMR) Study
- 4.2.18 The epidemiology of malaria transmission in PNG (TransEPI) project
- 4.2.19 Fetal Immunity to Malaria
- 4.2.20 *Plasmodium Vivax* in Pregnancy (PregVAX) Study
- 4.2.21 Epitope-based identification of novel Plasmodium antigens for malaria vaccine development

4.2.1 Intermittent preventative treatment for prevention of malaria and anaemia in infancy (IPTi)

Summary

Title: Randomised placebo-controlled trial of intermittent administration of sulphadoxine-pyrimethamine (SP) plus amodiaquine (AQ) or artesunate (AS) for the prevention of malaria and anaemia in infants

Date commenced: 2005, field work completed 2010, primary outcomes, acceptability and economic studies published 2012, supplementary studies on impact of IPTi on acquisition of immunity and drug resistance ongoing

About the project

Rationale: This study aims at proving; if providing 3-4 full courses of antimalarials during EPI contact at 3, 6, 9 and 12 months would result in a significant reduction in the incidence of malaria and anaemia in infants 3-15 months of age.

Design:

a) Randomised, placebo-controlled trial of 1121 children randomised to receive a full course of SP plus AQ, SP plus AS or placebo at 3, 6, 9 and 12 months. Primary efficacy follow-up until 15 months with an additional 6 months of follow-up to exclude the risk of a post-intervention rebound.

Progress: Completed and published.

b) Immunological studies: Measurement of responses to a panel of *P. falciparum* and *P. vivax* antigens in a random sub-sample of children from both control and intervention arms.

Progress: Ongoing.

Significance: The results of this study have strong justification for the development and field testing for a PfEBA/PfRH combination and PvDBP vaccines.

Contributors

Investigators: Ivo Mueller (PI), John Reeder, Leanne Robinson, Louis Schofield, James Beeson, Danielle Stanistic, Nicolas Senn, Patricia Rarau, Stephen Rogerson.

Collaborating centres: PNG Institute of Medical Research; Walter & Eliza Hall Institute, Melbourne, Australia; University of Melbourne, Melbourne, Australia.



Publications

SCIENTIFIC JOURNAL ARTICLES

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2. RDT-based management of malaria: an effectiveness study in Papua New Guinean infants with *P. falciparum* and *vivax* malaria. Senn N, Rarau P, Manong D, Salib M, Robinson L, Siba P, Reeder JC, Rogerson S, Genton B, Mueller I, 2012. *Clinical Infectious Diseases*, 54, 644-51.

3. Community response to intermittent preventive treatment of malaria in infants (IPTi) in Papua New Guinea (PNG). Pell C, Straus L, Lupiwa S, Phuanukoonnon S, Mueller I, Senn N, Siba P, Gysels M, Pool R. 2010. *Malaria J*, 9, 369.

4. The economic cost of malaria among young children on households in Papua New Guinea: a focus on intra-country variation. Sicuri E, Davy C, Marinelli M, Oa O, Ome M, Siba P, Conteh L, Mueller I, 2011. *Health Policy & Planning*, (Epub ahead of print)

5. Seeking Treatment for Symptomatic Malaria in Papua New Guinea. Davy C, Sicuri E, Ome M, Lawrence-Wood E, Siba P, Warvi G, Mueller I, Conteh L, 2010 *Malaria J*, 9:268

4.2.2 Molecular epidemiology *P. falciparum* and *P. vivax* infections in young PNG children

Summary

Title: Studies of the burden and genetic complexity of *P. falciparum* and *P. vivax* infection and disease in children 1-4 years of age

1. Describe the burden of malarial infections and disease in children 1-4yrs. of age

2. Determine the interactions between *P. falciparum* and *P. vivax* infections

3. Investigate genetic diversity and dynamics of *P. falciparum* and *P. vivax* clonal infections

4. Determine association of malarial risk with host immune responses and host genetic polymorphisms

Date commenced: 2006, field work completed, laboratory work and analyses ongoing.

About the project

Rationale: These studies aimed to provide a better understanding of both host and parasites factors that affect a child's risk of infection and clinical disease. Particular foci of the studies are investigation of *P. vivax* and *P. falciparum* mixed infections, the study of the dynamics of individual *P. falciparum* and *P. vivax* clones and gaining a better understanding of the processes leading to the very rapid acquisition of immunity to *P. vivax*.

Design:

- **Longitudinal cohort** of 264 children followed for 16 months using active and passive surveillance in Ilaia, East Sepik Province.
- **Molecular epidemiology:** All PCR positive *P. falciparum* and *P. vivax* infections were genotyped. Analyses of genetic diversity and force-of-infection completed, analyses of cross-species interactions are still ongoing. **Progress:** Ongoing.

• Immunological and host genetic determinant of malaria risk:

Basic assessment of cellular and humoral immune responses and typing of common red blood cell polymorphism and KIR genotypes completed. In-depth immunological assays and publication in progress. **Progress:** Ongoing.

Progress: Completed in 2007 and published in 2010.

Significance: The results of this study confirmed that *P. vivax* is the primary source of malaria infections and disease in children <2 years of age and that children acquired substantial immunity to *P. vivax* by the age of 3-4 yrs. Importantly, the study defined a new molecular epidemiological measure, the molecular force of infection (molFOI) and demonstrated its central role in explaining difference in risk of *P. falciparum* malaria in young children.

Contributors

Investigators: Ivo Mueller (PI), Enmoore Lin, Leanne Robinson, Ingrid Felger, Louis Schofield, James Beeson, Danielle Stanicic, Anna Rosanas, Peter Zimmerman, John Reeder.

Collaborating centres: PNG Institute of Medical Research; Swiss Tropical & Public Health Institute, Basel Switzerland; Walter & Eliza Hall Institute, Melbourne, Australia; Case Western Reserve University, Cleveland OH, USA.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Multiplicity and diversity of Plasmodium vivax infections in a highly endemic region in Papua New Guinea. Koepfli C, Ross A, Kiniboro B, Smith T, Zimmerman P, Siba P, Mueller I, Felger I, 2011. PLoS Neglected Diseases, 5, e1424.
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8. The Force of Infection: Key to understanding the epidemiology of Plasmodium falciparum malaria in Papua New Guinean children. Mueller I, Schoepflin S, Smith TA, Benton KL, Bretscher MT, Lin E, Kiniboro B, Zimmerman PA, Speed TP, Siba P, Felger I, in press. PNAS.

4.2.3 Natural acquisition of immunity to *P. falciparum* and *P. vivax*

Summary

Title: Studies on the acquisition of cellular and humoral immunity to *P. falciparum* and *P. vivax* and their association with protection against infections and disease.

1. Study cellular and humoral immune responses to *P. falciparum* and *P. vivax* in children 5-14yrs of age
2. Determine their association with protection against infections and clinical illness

Date commenced: 2003, field work completed 2005, laboratory work and analyses ongoing.

About the project

Rationale: These studies aim at gaining a better understanding of naturally acquired immunity to malaria in order to inform rational design and testing of malaria vaccines.

Design:

• **Longitudinal cohort** of 206 children followed for 6 months using active and passive surveillance in Mugil, madang province.

Progress: Completed in 2005, published 2007.

• Immunological and host genetic determinant of malaria risk:

Basic assessment of cellular and humoral immune responses and typing of common red blood cell polymorphism and KIR genotypes completed. In-depth immunological assays and publication in progress.

Progress: Ongoing.

Significance: The results of this study have strong justification for the development and field testing for a PfEBA/PfPRH combination and PvDBP vaccines.

Contributors

Investigators: Ivo Mueller (PI), Pascal Michon, Leanne Robinson, Louis Schofield, James Beeson, Danielle Stanicic, Chetan Chitnis, Chris King.

Collaborating centres: PNG Institute of Medical Research; Walter & Eliza Hall Institute, Melbourne, Australia; Case Western Reserve University, Cleveland OH, USA; International Centre for Biotechnology & Genetic Engineering, New Delhi, India.

Publications

SCIENTIFIC JOURNAL ARTICLES

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5. Cellular TNF, IFN- γ and IL-6 responses: correlates of immunity and risk of clinical *Plasmodium falciparum* malaria in children from Papua New Guinea. Robinson LJ, D'Ombain MC, Stanisic DI, Bernard N, Taraika J, Richards JS, Beeson JG, Michon P, Mueller I, Schofield L, 2009. *Infection & Immunity*, 77, 3033–43.

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8. Naturally-acquired antibodies to erythrocyte binding antigens of *Plasmodium falciparum* are associated with protection from malaria and high density parasitemia. Richards JS, Stanisic DI, Fowkes FJ11, Tavul L, Dabod E, Thompson JK, Kumar S, Chitnis CE, Narum DL, Michon P, Siba P, Cowman AF, Mueller I, Beeson JG, 2010 *Clinical Infectious Disease*, 51, e50–60.

9. Evidence that the erythrocyte invasion ligand PfRh2 is a target of protective immunity against *Plasmodium falciparum* malaria. Reiling L, Richards JS, Fowkes F, Triglia T, Chokeyindachai W, Michon P, Tavul L, Cowman AF, Mueller I, Beeson JG, 2010. *Journal of Immunology*, 185, 6157–67

10. Quantifying the importance of MSP1-19 as a target of growth-inhibitory and protective antibodies against *Plasmodium falciparum* in humans. Wilson DW, Fowkes, FJY, Gilson PR, Elliott SR, Tavul L, Michon P, Dabod E, Siba PM, Mueller I, Crabb BS, Beeson JG, 2011. *PLoS One*, 6, e27705.

4.2.4 Population genetic analyses *P. falciparum* and *P. vivax* diversity and evolution of drug resistance

Summary

Title: Studies on genetic diversity of different *P. falciparum* and *P. vivax* population and monitoring of molecular markers of resistance to Chloroquine(CQ) and Sulphadoxine-Pyrimethamine(SP).

Date commenced: 2005, field work completed 2010, molecular analyses and publication ongoing.

About the project

Rationale: These studies aim at understanding the population structure of local *P. falciparum* and *P. vivax* parasites populations.

Design:

• **Population genetic studies:** cross-sectional surveys of multiple populations in Madang and East Sepik provinces. Genetic typing for *P. falciparum* and *P. vivax* parasites for both neutral micro-satellite makers and candidate vaccine antigens. **Progress:** field work completed, molecular analyses and publication ongoing.

• **Evolution of CQ and SP resistant *P. vivax*:** Genotyping of single nucleotide polymorphisms and flanking regions of PvMDR1 and PvDHFR genes in samples collected between 1991 and 2010 in East Sepik and Madang province. **Progress:** Ongoing.

Significance: The results of this study have shown strong differentiation of *P. falciparum* but not *P. vivax* parasites in different location in Madang and East Sepik Province. The studies in *P. vivax* drug resistance aim to given insight both into the mechanisms of CQ and how resistance arose in Madang and East Sepik Province

respectively.

Contributors

Investigators: Alyssa Barry, Ivo Mueller, John Reeder, Tim Davis, Celine Barnadas.

Collaborating centres: PNG Institute of Medical Research; Walter & Eliza Hall Institute, Melbourne, Australia; The Burnet Institute, Melbourne, Australia.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. A new high-throughput method for simultaneous detection of mutations associated with *Plasmodium vivax* drug resistance in pvdhfr, dhps and mdr1 genes. Barnadas C, Kent D, Timinao L, Iga J, Gray LR, Siba P, Mueller I, Thomas PJ, Zimmerman PA, 2011. *Malaria Journal*, 10, 282.

2. Population genetic analysis of the *Plasmodium falciparum* 6-cys protein Pf38 in Papua New Guinea reveals domain-specific balancing selection. Reeder JC, Wapling J, Mueller I, Siba PM, Barry AE, 2011. *Malaria Journal*, 10, 126.

3. Multilocus haplotypes reveal variable levels of diversity and population structure of *Plasmodium falciparum* in Papua New Guinea, a region of intense perennial transmission. Schultz L, Wapling J, Mueller I, Ntsuke PO, Senn N, Nale J, Kiniboro B, Buckee CO, Tavul L, Siba PM, Reeder JC, Barry AE, 2010 *Malaria Journal*, 9, 336.

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4.2.5 Paediatric severe malaria study

Summary

Title: In-depth Studies of severe paediatric malaria on other severe illnesses in PNG children (Surveillance of children admitted to Modilon Hospital, Madang / Case-Control study of severe malaria, severe - non-malaria, uncomplicated malaria and healthy community controls)

Date commenced: 2006, clinical studies completed in 2011, laboratory work, analyses and writing ongoing.

Project funding: National Health & Medical Research Council, Malaria Genetic Epidemiology Network (MalariaGEN).

About the project

Rationale: The last in-depth studies of severe malaria in PNG were done in the mid 1990s. Since then drug resistance has increase dramatically with recognition of *P. vivax* as no longer 'benign' but an important source of severe illness. In addition, all past in-depth studies of other major severe diseases in PNG children (e.g. pneumonia, meningitis, encephalitis, etc) has either been done in the Highlands or Port Moresby. Additional in-depth data from other coastal PNG populations are therefore very important for policy decisions.

Design: A general surveillance of all children admitted to the paediatric ward of Modilon Hospital, Madang, was established. All children with severe malaria and or signs and symptoms of severe bacterial illness had an in-depth assessment including: malaria

diagnosis, blood and (where indicated) CSF bacterial cultures, haematology and biochemistry. In order to compare clinical presentations in severely ill children with uncomplicated malaria and healthy children; uncomplicated malaria cases were enrolled through Modilon outpatient and village clinics, while healthy community controls were enrolled in the villages of origin of the severe malaria cases.

Significance: These were the first comprehensive studies of severe paediatric illness on the North Coast of PNG. Clinical presentations of Papua New Guinean children with severe malaria due to *P. vivax* were investigated and published. Furthermore, these studies have resulted in changes to the local paediatric and adult medicine guidelines. These translational changes include; the incorporation of ceftriaxone for all suspected bacterial meningitis patients, local reference intervals for biochemistry and haematological values and diagnostic algorithms for acute bacterial meningitis and febrile seizures. They also provided important additional information on major bacterial pathogens such as Methicillin Resistant Staph Aureus in severely ill paediatric and adult surgical patients. Data from these studies provided essential information for the ongoing reviews of the paediatric and the adult standard treatment guidelines of PNG. The bacterial meningitis and febrile seizure studies contributed to MMed Sci degree awarded to Moses Laman in 2009.

Contributors

Investigators: Tim Davis, Ivo Mueller, Laurens Manning, Moses Laman, Peter Siba.

Collaborating centres: PNG Institute of Medical Research, School of Medicine and Pharmacology, University of Western Australia; Walter & Eliza Hall Institute, Melbourne, Australia.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Lumbar puncture in children from an area of malaria-endemicity who present with a febrile seizure. Laman M, Manning L, Hwaihanje I, Vince J, Aipit S, Mare T, Warrel J, Karunajeewa H, Siba P, Mueller I, Davis TME, 2010. *Clinical Infectious Disease*, 51, 534-40.
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3. Features and prognosis of severe malaria caused by *Plasmodium falciparum*, *Plasmodium vivax* and mixed *Plasmodium* species infection in Papua New Guinea children. Manning L, Laman M, Law I, Bona C, Aipit S, Teine D, Warrell J, Rosanas-Urgell A, Lin E, Kiniboro B, Vince J, Hwaihanje I, Karunajeewa H, Michon P, Siba P, Davis TME, Mueller I, 2011. *PLoS One*, 6, e29203.
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12. Bloodstream infections caused by resistant bacteria in surgical patients admitted to Modilon Hospital, Madang. Asa H, Laman M, Greenhill A, Davis TME, Siba P, Maihua J, Manning L. *PNG Medical Journal*; 2011. In press.

13. A histopathologic study of fatal pediatric cerebral malaria caused by mixed *Plasmodium falciparum*/*Plasmodium vivax* infections. Manning L, Rosanas-Urgell A, Laman M, Edoni H, McLean C, Mueller I, Siba P, Davis TME. *Malaria Journal*. 2012. In press.

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Figure 1:
Light microscopy of brain tissue obtained from children dying from cerebral malaria due to mixed *Plasmodium falciparum*/*P. vivax* infections. In panel A (Patient 1), occasional mature forms of *P. falciparum* were seen (Giemsa stain, magnification x400). In panel B (Patient 2), malaria pigment and numerous *P. falciparum* trophozoites and schizonts are visible within the microvasculature (Giemsa stain, magnification x400). In panel C (Patient 3), there is acute chromatolysis of neurons and early infiltration by neutrophils from adjacent vessels at the edge of an area of infarction. The cerebral blood vessel (lower left) was normal and no malaria parasites were seen (magnification x 400).

Figure is from Manning L, Laman M et al, *Malaria Journal*, 2012

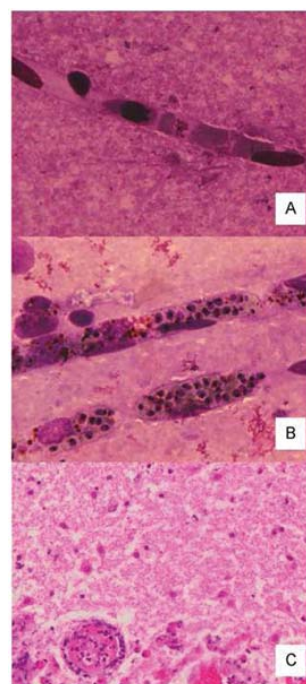
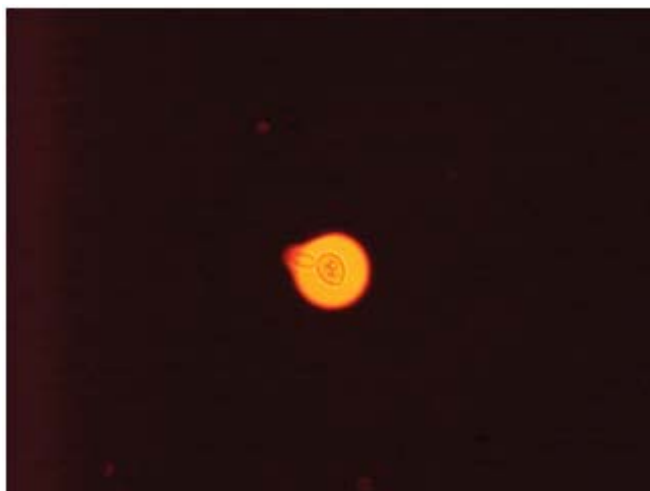


Figure 2: Indian ink staining of centrifuged cerebrospinal fluid (Magnification x400) showing a budding form of *Cryptococcus neoformans* var. *gattii*.

Figure is from Laman M, Hwaiwhanje I et al, Tropical Doctor: 2010, 40(1):61-3.



4.2.6 Primaquine Studies

Summary

Title: Studies to improve guidelines for the treatment of *P. vivax* malaria in PNG:

1. Safety and tolerability of primaquine in 1-10 yr old PNG children
2. Pharmacokinetic profile of single doses of 0.5mg/kg and 1mg/kg in children aged 5-10yrs
3. Safety, Tolerability and Pilot efficacy of Short course, High dose primaquine treatment for liver stages of *Plasmodium vivax* infection

Date commenced: 2008, ongoing in phases.

About the project

Rationale: These studies aimed to provide data on the safety, tolerability and pilot efficacy of short course, high dose primaquine in Papua New Guinean children. The National Malaria Control Program Strategic plan 2009-2013 of the Papua New Guinea National Department of Health clearly states as Strategies 2.8.5 and 3.2.7 the importance of developing strategies for *P. vivax* malaria relapse treatment and the capacity for G6PD diagnosis at the hospital level and implement primaquine treatment for *P. vivax* malaria.

Design:

• **Study 1:** The safety and tolerability of primaquine in G6PD normal children 1-10yrs old was a placebo controlled study as part of two longitudinal cohort studies conducted in East Sepik Province. **Progress:** Completed in 2009 and published in 2012.

• **Study 2:** The pharmacokinetic study involved 28 healthy G6PD normal children aged 5-10yrs whose parents consented to the study. **Progress:** Completed in 2011, Methodology paper, submitted for publication 2012.

• **Study 3:** In this study 120 G6PD normal children aged 5-10 yrs with confirmed *P. vivax* malaria will be treated with coartem and primaquine (PQ) in stepwise manner, 40 children will receive PQ, 0.5mg/kg for 14 days (currently recommended regimen), 40 children 1mg/kg PQ daily for 7 days, the safety and tolerability in these two groups compared before enrolling the last 40 children to receive 1mg/kg twice daily for 3 and a half days if the 7 day course was safe. This is a health center based study. The children in the short course, high dose study will be admitted and safety parameters monitored closely. **Progress:** Awaiting Pharmacokinetic study results.

Significance: Research findings from these studies are the first to report on the safety and tolerability of primaquine in children less than 10 years old. Currently there is very little or no safety data for primaquine in this age group with the highest burden of *P. vivax* infection and disease. Primaquine was shown to be safe and well tolerated. The short course, high dose primaquine if safe will improve compliance and be compatible with the ACT regimens for *P. vivax* relapse malaria. Primaquine will be a useful tool for *P. vivax* malaria prevention, control and elimination in the future and assist the National Department of Health in the implementation of the 2009-2013 Strategic plan. The funding is contributing to PNGIMR's capacity building program. The different studies will contribute to Dr Inoni Betuela and Dr Moses Laman's PhD thesis.

Contributors

Investigators: Inoni Betuela, Ivo Mueller, Quique Bassat, Peter Siba, Tim Davies, Pedro Alonso, Kevin Batty, Leanne Robinson, Anna Rosanas, Brioni Moore, Moses Laman, John Benjamin, Madhu Page-Sharp, Kenneth Ilett.

Collaborating centres: PNG Institute of Medical Research; School of Medicine and Pharmacology, University of Western Australia; Centre of International Health and Research, Barcelona, Spain; School of Pharmacy, Curtin University, Bentley, Western Australia.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Tolerability and safety of primaquine in Papua New Guinean children 1 to 10 years of age. Inoni Betuela, Quique Bassat, Benson Kiniboro, Leanne J Robinson, Anna Rosanas-Urgell, Danielle Stansic, Peter M Siba, Pedro L Alonso, Ivo Mueller. Antimicrob Agents Chemother, 2012; DOI:10.1128/AAC.05566-11 (E-pub ahead of print, 17 Jan 2012).

CONFERENCE PRESENTATIONS

1. Relapses are contributing significantly to the risk of *P. vivax* infection and disease in Papua New Guinean children 1-5 years of age - effect of primaquine treatment. Inoni Betuela, Anna Rosanas, Benson Kiniboro, Danielle Stansic, Lorna Somol, Elisa De Lezzari, Quique Bassat, Hernando del Portillo, Peter M Siba, Pedro L Alonso, Ivo Mueller. European Congress of Tropical Medicine and Hygiene, 2011, Barcelona, Spain.

4.2.7 Artesunate-Pyronaridine and Artemisinin-Naphthoquine combination therapies in Papua New Guinean children with uncomplicated malaria (Standard Treatment trial II)

Summary

Title: Artesunate-Pyronaridine and Artemisinin-Naphthoquine combination therapies in Papua New Guinean children with uncomplicated malaria

Date commenced: January 2011

Project funding: NHMRC Australia Research Grant held by Prof Tim Davis (CI-A).

Scholarship funding: PhD scholarship from AusAID awarded to Moses Laman

About the project

Rationale: While artemether-lumefantrine has been shown to be effective against *Plasmodium falciparum*, it has very little effect on suppressing initial relapses from *P. vivax* infections. In addition, the twice daily dosing for three days raises issues of potentially poor compliance and thus risk of developing drug resistance. Therefore, search for second generation ACTs which can be taken daily are needed to improve compliance and prevent resistance to ACTs developing.

Design: This is an open-label, randomized parallel-group trial assessing the safety, tolerability and efficacy and comparing the study drugs to artemether-lumefantrine the current recommended ACT for use in PNG.

Progress: The study is in progress, with initial safety data for artesunate-naphthoquine shown to be safe and well tolerated.

Significance: The results from this trial will add to the existing ACTs and assess their efficacy in suppressing initial *P. vivax* relapses. Modifications to the current treatment options can be made on evidence-based decisions from studies in Papua New Guinea. Significant contribution to PNGIMR and PNG's capacity building in funding of Moses Laman's PhD scholarship to do his PhD with Professor Timothy Davies, University of Western Australia.

Contributors

Investigators: Moses Laman, Tim Davies, Kenneth Illet, Kevin Batty, Ivo Mueller, Peter Siba, Francis Hombhnanje, Inoni Betuela, Laurens Manning, Brioni Moore, John Benjamin.

Collaborating centres: PNG Institute of Medical Research; Divine Word University, PNG; School of Medicine and Pharmacology, University of Western Australia; Curtin University, Australia.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Artemisinin-naphthoquine combination therapy for uncomplicated pediatric malaria: A pharmacokinetic study. Batty K, Salman S, Moore B, Benjamin J, Lee ST, Page-Sharp M, Pitus N, Illet K, Mueller I, Hombhnanje F, Siba P, Davis TME, 2012. Antimicrobial Agents & Chemotherapy, 2012 [in press].

2. Artemisinin-naphthoquine combination therapy for uncomplicated pediatric malaria: A tolerability, safety and preliminary efficacy study. Benjamin J, Moore B, Lee ST, Senn M, Griffin S, Lautu D, Salman S, Siba P, Mueller I, Davis TME, 2012. Antimicrobial Agents & Chemotherapy, 2012 [in press].

4.2.8 Pharmacokinetics of piperazine in pregnancy

Summary

Title: Pharmacokinetics of piperazine in pregnancy

Date commenced: 2010

Project funding: NHMRC Australia Research Grant held by Prof Tim Davis (CI-A)

About the project

Rationale: With the spread of chloroquine resistance throughout PNG, there is urgent need to find safer alternative drugs for pregnant women to improve maternal and child health.

Design: The study will involve 30 pregnant mothers (gestation >14 weeks), randomized to two treatment groups, aged-matched with 30 non-pregnant women. Half of the pregnant mothers will receive dihydroartemisinin-piperazine and the other half piperazine (PQ) plus sulfadoxine-pyrimethamine (SP) as a single dose with the first dose of PQ.

Progress: On-going.

Significance: Adds new knowledge on antimalarial drugs for pregnancy and contributes to a Master thesis being conducted by John Benjamin.

Contributors

Investigators: John Benjamin, Brioni Moore, Tim Davies, Ivo Mueller, Inoni Betuela, Peter Siba, Laurens Manning, Moses Laman.

Collaborating centres: PNG Institute of Medical Research; School of Medicine and Pharmacology, University of Western Australia.

4.2.9 Antimalarial drug combinations in pregnancy

Summary

Title: A safety, tolerability, pharmacokinetic and preliminary pilot efficacy study of azithromycin plus piperazine as intermittent preventative treatment in pregnant Papua New Guinean women

Date commenced: 2010

Project funding: Malaria in Pregnancy Consortium (MIPc) grant to PNG Institute of Medical Research (PIs Peter Siba, Ivo Mueller, Tim Davis).

About the project

Rationale: Safe and effective antimalarial treatment in pregnancy are needed to replace chloroquine plus sulfadoxine-pyrimethamine.

Design: A group of 30 consenting pregnant women aged >18yrs will be recruited and receive three daily doses of azithromycin plus piperazine (AZ-PQ) followed by determination of efficacy of optimal AZ-PQ dose for prevention of malaria in pregnancy.

Progress: Ongoing.

Significance: This study will provide initial data for Papua New Guinean women, which may lead to further clinical trials of azithromycin plus piperazine – one of the few potential short-term replacements of chloroquine and SP as a drug for prevention and treatment of malaria in pregnancy.

Contributors

Investigators: Brioni Moore, John Benjamin, Moses Laman, Tim Davies, Stephen Rogerson, Peter Siba, Ivo Mueller, Inoni Betuela, Maria Ome, Regina Wanganapi.

Collaborating centres: PNG Institute of Medical Research; School of Medicine and Pharmacology, University of Western Australia; Melbourne University.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. The pharmacokinetic properties of azithromycin in pregnancy. Salman S, Rogerson SJ, Kose K, Griffin S, Gomorai S, Baiwog F, Winmai J, Kandai J, Karunajeewa HA, O'Halloran SJ, Siba P, Ilett KF, Mueller I, Davis TME. *Antimicrobial Agents & Chemotherapy*, 2010; 54: 360-6.

4.2.10 IPTp Study

Summary

Title: Intermittent Preventative Treatment with Azithromycin (AZ) and sulphadoxine-pyrimethamine (SP) for the prevention of malaria in pregnancy (IPTp)

Date commenced: 2008

Project funding: Malaria in Pregnancy Consortium (funded Bill & Melinda Gates Foundation) grant to University of Melbourne (Professor Stephen Rogerson) and PNGIMR (Peter Siba, Ivo Mueller).

About the project

Rationale: Establish the efficacy of 3 doses of AZ plus SP for the prevention of malaria in pregnancy and congenital transmission of STIs.

Design: Pregnant mothers randomised to two treatment arms, AZ plus SP and chloroquine plus SP (current standard treatment).

Progress: Field study will end in November 2012, results will be available in 2013.

Significance: This study will provide evidence for the utility of AZ-combinations for the prevention of malaria and STIs in pregnancy and assist with reformulating regional and national guidelines for the prevention of malaria in pregnant mothers. Master Thesis studies for Maria Ome and Regina Wanganapi.

Contributors

Investigators: Stephen Rogerson, Ivo Mueller, Peter Siba, Maria Ome, Regina Wanganapi, Alex Umbers, Holger Unger.

Collaborating centres: PNG Institute of Medical Research; University of Melbourne; Walter & Eliza Hall Institute.

4.2.11 The contribution of relapsing infection to the burden of *P. vivax* in PNG

Summary

Title: The contribution of relapsing infection to the burden of *P. vivax* infection in PNG children and their impact on parasite diversity and host immune responses

Date commenced: 2008

Project funding: Cellex Consortium (Cellex Foundation, Barcelona, Spain) grant to PNG Institute of Medical Research, Swiss National Science Foundation held by Ingrid Felger and NHMRC Australia program grant (Louis Schofield) and project grant (Ivo Mueller).

About the project

Rationale: This study aims to determine the contribution of relapsing infection from long-lasting liver-stage to the burden *P. vivax* infection and disease and study their impact on parasite diversity and host immune responses.

Design: In 2 longitudinal cohorts in children 1-5 years (Ilaita 2008) and 5-10 years (Albimana 2010) in East Sepik province, studied the effect of removing long lasting liver-stages with primaquine treatment on the subsequent risk of *P. vivax* infection and disease. Parallel molecular and immunological studies are investigating the effect of removing these liver-stages on parasites diversity and host immune responses.

Progress: Started in 2008, field work completed in 2010, laboratory and statistical analyses ongoing.

Significance: Relapses from long lasting liver-stages are the major obstacle to the control and eventual elimination of *P. vivax*. By quantifying the contribution of relapsing infections, the study will improve our understanding of the biology of these 'hidden' parasites stages and provide additional support for the implementation of anti-relapse therapy in the PNG national treatment guidelines. PhD projects of Inoni Betuela.

Contributors

Investigators: Inoni Betuela, Leanne Robinson, Ivo Mueller, Peter Siba, Anna Rosanas, Quique Bassat, Pedro Alonso, Hernando del Portillo, Ingrid Felger, Louis Schofield.

Collaborating centres: PNG Institute of Medical Research, Walter & Eliza Hall Institute Melbourne, Barcelona Centre for International Health Research, Swiss Tropical & Public Health Institute.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Comparison of diagnostic methods for the detection and quantification of the four sympatric *Plasmodium* species in field samples from Papua New Guinea Anna Rosanas-Urgell A, Mueller D, Betuela I, Barnadas C, Iga J, Zimmerman PA, del Portillo HA, Mueller I, Felger I, 2010.. *Malaria Journal*, 9, 361

4.2.12 Neonatal Infection Study

Summary

Title: Evaluating the causes of perinatal and neonatal illness and death in Papua New Guinea

Date commenced: 2009

Project funding: Malaria in Pregnancy Consortium

About the project

Rationale: Malaria and bacterial infections contribute significantly to infant mortality rates in PNG. The babies of mothers in the IPTp study offers an opportunity to study the effects of treatment which has both antimalarial and antimicrobial properties.

Design: A cohort of 500-600 babies from mothers participating in the IPTp study will be followed up for 4 weeks.

Progress: Ongoing.

Significance: Understanding the causes of perinatal and neonatal infections will lead to preventative treatment to improved survival of the newborn and mothers.

Contributors

Investigators: Stephen Rogerson, Maria Ome, Regina Wanganapi, Andrew Greenhill, Ivo Mueller, Holger Unger, Naomi Pomat, Inoni Betuela, Alex Umbers.

Collaborating centres: PNG Institute of Medical Research, Melbourne University, Modilon General Hospital.



Entomology field staff checking for mosquito eggs from samples collected in study sites.

4.2.13 The ecology of mosquito vectors of malaria and filariasis

Summary

Title: The ecology of mosquito vectors of malaria and filariasis:

1. Studies of vector ecology in Madang and East Sepik

2. Determine the impact of Insecticide Treated Nets (ITN) distribution on vector ecology and behaviour

3. Determine the vectorial capacity of local Anophelines for the transmission of malaria and filariasis

Date commenced: 2007, field studies completed in 2012, laboratory work, analyses and writing ongoing.

Project funding: National Institutes of Health, US.

About the project

Rationale: With >10 distinct malaria vectors, PNG has one of the most diverse vector faunas in the world. Several of these vector species are morphologically nearly identical and molecular techniques are thus needed to accurately speciate PNG anopheline. To-date the ecology, biting behaviour and vectorial capacity of most of these species have not been appropriately determined. By comparing mosquito biting rates and times prior and after ITN distribution, it is possible to better understand and predict their effects on the local vector populations.

Design: Since 2008 regular entomological surveys have been conducted on the Madang North Coast and the Drikikir area in East Sepik. In addition, vector colonies have been re-established at the IMR entomology section, which are now being used in experiments to determine the vectorial capacity for transmission of malaria and filariasis.

Significance: This work is providing essential data for the evaluation of the impact of the National Malaria Control Program. In particular, it has shown that within one year of ITN distribution mosquito bite rates are reduced by ~80% but peak biting is shifting outdoors and into the early evening. If sustained, the later effect may limit the effectiveness of ITNs as the main vector control tool in PNG. This work has contributed to the BSc Honours of John Keven and Gasi Koimbu.

Contributors

Investigators: Ivo Mueller, Lisa Reimer, Peter Siba, Peter Zimmerman.

Collaborating centres: PNG Institute of Medical Research; Case Western Reserve University, Cleveland, Ohio; University of Wisconsin, Madison, WI, USA.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Pyrethroid Susceptibility in Natural Populations of the *Anopheles punctulatus* Group (Diptera: Culicidae) in Papua New Guinea. Keven J, Henry-Halldin C, Thomsen E, Mueller I, Siba P, Zimmerman P, Reimer L, 2010. *American Journal of Tropical Medicine & Hygiene*, 83, 1259 – 1261.

2. High Throughput Multiplex Assay for Species Identification of Papua New Guinea Malaria Vectors: Members of the *Anopheles punctulatus* (Diptera: Culicidae) Species Group. Henry-Halldin C, Reimer L, Thomsen E, Zimmerman A, Keven JB, Dagoro H,

Hetzel M, Siba P, Mueller I, Zimmerman PA., 2011 American Journal of Tropical Medicine & Hygiene, 84, 166-73.

3. Multiplex assay for species identification and monitoring of insecticide resistance in *Anopheles punctulatus* group populations of Papua New Guinea. Henry-Halldin CN, Nadesakumaran K, Keven JB, Zimmerman A, Siba P, Mueller I, Hetzel MW, Kazura JW, Thomsen E, Reimer LJ, Zimmerman PA, 2012. American Journal of Tropical Medicine & Hygiene, 86, 152-158.

4. Filarial worms reduce *Plasmodium* infectivity in mosquitoes. Aliota MT, Chen CC, Dagoro H, Fuchs JF, Christensen BM, 2011 PLoS Negl Trop Dis. 8;5(2):e963.

5. Are insecticide-treated bednets more protective against *Plasmodium falciparum* than *Plasmodium vivax*-infected mosquitoes? Bockarie MJ, Dagoro H, 2006, Malar J, 5:15.

CONFERENCE PRESENTATIONS

Numerous presentations at PNG Medical Symposium as well as at the American Society of Tropical Medicine & Hygiene.

4.2.14 Mosquito parasite interactions and filariasis transmission in Papua New Guinea

Summary

Title: Mosquito parasite interactions and filariasis transmission in Papua New Guinea:

1. Determine the impact of melanization immune responses on the development of *W. bancrofti* in anopheline mosquitoes in Papua New Guinea

2. Evaluate the impact of mosquito anti-filarial worm response on the development of *P. falciparum*

Date commenced: 2011

Project funding: National Institutes of Health, Fogarty International Center.

About the project

Rationale: Successful development of filarial worm or *Plasmodium* parasites is affected by the innate immune response of mosquito vectors, but the impact of vector immune responses on transmission of these parasites in endemic areas has seldom been evaluated. In addition, the impact of co-infection with filarial worms and *Plasmodium* parasites on transmission of disease is unknown.

Design: To understand these mosquito-parasite interactions and their ramifications on parasite transmission, controlled mosquito feeding experiments will be performed using blood with known microfilaria and/or gametocyte densities. Mosquitoes will be critically examined for the fate of ingested parasites; thereby assessing the impact of the melanization immune response on parasite development as well as the impact of co-infections on parasite transmission.

Significance: In order to achieve successful results in the ongoing campaigns for malaria and lymphatic filariasis control and/or elimination, it is critical that we gain a better understanding of the natural interactions between different parasites where they co-occur.



Contributors

Investigators: Bruce Christensen, Lisa Reimer, Peter Siba.

Collaborating centres: PNG Institute of Medical Research, University of Wisconsin, Madison, Case Western Reserve University, Cleveland Ohio.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Filarial worms reduce *Plasmodium* infectivity in mosquitoes. Aliota MT, Chen CC, Dagoro H, Fuchs JF, Christensen BM, 2011 PLoS Negl Trop Dis. 8;5(2):e963.

CONFERENCE PRESENTATIONS

Numerous presentations at PNG Medical Symposium as well as at the American Society of Tropical Medicine & Hygiene.

4.2.15 Malaria transmission potential of the *Anopheles punctulatus* species complex

Summary

Title: Malaria transmission potential of the *Anopheles punctulatus* species complex:

1. Determine malaria transmission potential of the primary malaria vectors of Papua New Guinea

2. Examine mixed *Plasmodium* infections in *An. punctulatus*

Date commenced: 2011

Project funding: National Institutes of Health.

About the project

Rationale: The burden of malaria is influenced by the ecological and physiological characteristics of the human host, parasite, and vector populations. While disease epidemiology in human populations, *Plasmodium* population structure, and the ecology of vectors is relatively well understood; the physiological parameters of the vector species and how they interact with malaria parasites has received little attention. In addition, relatively little attention has been given to mixed *Plasmodium* species infections in mosquitoes and how this might alter transmission dynamics.

Design: Mosquito feeding experiments will be performed using blood with known gametocyte densities. Mosquitoes will be critically examined for the fate of ingested parasites.

Significance: Malaria epidemiology is heavily influenced by host, vector and parasite diversity. In many endemic areas around the world, there exist multiple species or strains of both parasite and vector. Understanding these complex parasite-parasite and parasite-vector interactions is crucial to understanding the dynamics of transmission.

Contributors

Investigators: Lisa Reimer

Collaborating centres: PNG Institute of Medical Research, Case Western Reserve University, Cleveland Ohio.

4.2.16 Survey for insecticide resistance in the major vectors of Papua New Guinea

Summary

Title: Evaluation of insecticide resistance in anopheline mosquitoes of Papua New Guinea and implications for malaria prevention

1. Determine susceptibility to insecticides currently used in Papua New Guinea
2. Determine efficacy of used bednets on a standard susceptible population of *An. punctulatus* from Papua New Guinea

Date commenced: 2009

Project funding: Rotary Against Malaria

About the project

Rationale: The resistance status of malaria vectors in PNG has not been determined. In the 1970's, control failures were observed with DDT use. It is unclear if insecticide resistance played a role and if resistance remains in those populations. In light of ongoing ITN campaigns and IRS programs in Papua New Guinea, an understanding of insecticide resistance in the vector population is urgently needed. It is essential to detect resistance early so that mitigation and monitoring can be implemented and the efficacy of insecticide-based control preserved. It is also unclear if ITN will maintain their effect under local conditions of use. This study will contribute to the success of ITN and IRS programs and will help us preserve a susceptible vector population for more effective control.

Design: Anopheline larvae were collected from areas around the country with variable insecticide use histories. Adult mosquitoes were exposed to deltamethrin and lambda-cyhalothrin according to WHO protocols and knockdown times as well as mortality were measured.

Significance: Currently, Papua New Guinea is investing considerable resources in implementing an IRS program as well as distributing ITNs. However, little is known about the resistance profile of local mosquito populations or the effectiveness of available insecticides. In order to make informed decisions about

the insecticides used for IRS programs in PNG and the frequency of application, we must test their efficacy under local conditions. Furthermore, the success of any insecticide based control method hinges on the ability to detect and monitor resistance mechanisms in the local population.

Contributors

Investigators: Lisa Reimer, Ivo Mueller, Peter Siba.

Collaborating centres: PNG Institute of Medical Research, Case Western Reserve University, Cleveland Ohio.

Publications

SCIENTIFIC JOURNAL ARTICLES

1. Pyrethroid Susceptibility in Natural Populations of the *Anopheles punctulatus* Group (Diptera: Culicidae) in Papua New Guinea. Keven J, Henry-Halldin C, Thomsen E, Mueller I, Siba P, Zimmerman P, Reimer L, 2010. American Journal of Tropical Medicine & Hygiene, 83, 1259 – 1261.

CONFERENCE PRESENTATIONS

Numerous presentations at PNG Medical Symposium as well as at the American Society of Tropical Medicine & Hygiene.

4.2.17 International Centre of Excellence for Malaria Research (ICEMR) Study

Summary

Title: Impact of vector control on human immunity to malaria and genetic complexity of *P. falciparum* and *P. vivax* in two holoendemic areas of Papua New Guinea

Date commenced: 2011

Project funding: National Institutes of Health, PI James Kazura, Case Western Reserve University.

About the project

Rationale: The ongoing, intensified control program is resulting in very significant reduction of the malaria burden throughout PNG. This study aims to investigate the impact of this control effort on the relationships between parasites, human host and mosquito vector.

Design: Over seven years the project will conduct four cohorts (2 each in children 1-5 year and 5-12 years) and four cross-sectional population surveys in East Sepik and Madang provinces. In parallel, in-depth entomological studies of changes in vector behaviour and vector ecology and on human immune responses to malaria will be conducted.

Progress: Field work starting in 2012, ongoing through to 2018.

Significance: By better understanding changes to host-vector-parasites interaction causes, it will be possible to make recommendation for improving the ongoing and design optimised future control efforts.

Contributors

Investigators: Leanne Robinson, Inoni Betuela, James Kazura, Peter Siba, Ivo Mueller, Lisa Reimer, Chris King, Louis Schofield, Peter Zimmerman, Tom Burkot, Ingrid Felger.

Collaborating centres: PNG Institute of Medical Research; Case Western Reserve University; Walter & Eliza Hall Institute; Swiss Tropical & Public Health Institute; James Cook University, Australia.

4.2.18 The epidemiology of malaria transmission in PNG (TransEPI) project

Summary

Title: The Epidemiology of *Plasmodium spp.* transmission in Papua New Guinea: Research studies to determine the dynamics of malaria transmission stages in host and vector: bottlenecks and their impact transmission and parasite population diversity

Date commenced: 2012

Project funding: NHMRC Australia Research Grant (to Walter & Eliza Hall Institute) and Bill & Melinda Gates Foundation grant (to Barcelona Center for International Health Research)

About the project

Rationale: This study aims to characterise in detail the transmission dynamics of *Plasmodium spp.* in PNG and determine its impact on parasite-vector interactions.

Design: In two cross-sectional surveys (2010 Madang, 2012 East Sepik) and three longitudinal cohorts (5-10 years in Albimana (2010, ESK), 5-12 years in Mugil (MAD, 2012) and 1-5 year s Ilaia (2013, ESK), the study will determine the risk factors for *Plasmodium spp.* gametocyte carriage and study the temporal associations between the presence and complexity of asexual and sexual *Plasmodium spp.* infections. In parallel, the study will investigate the relationship between the presence and density of gametocyte in a blood samples and its infectivity to local vectors by conducting a series of standard mosquito membrane feeding assays.

Progress: Starting in 2012, ongoing through to 2014.

Significance: The proposed studies will provide the first in-depth assessment of the processes involved in transmission of malaria in PNG. Knowledge on the gametocyte carriers in a population, when gametocytes are most prevalent and what are the determinants of infectivity to the mosquito vector are essential not only for improving the implementation of current control tools, but even more so for the development of novel interventions aimed at the interruption of local transmission. The study will provide training opportunities both a local PNG medical and three scientific graduates.

Contributors

Investigators: Inoni Betuela, Leanne Robinson, Ivo Mueller, Peter Siba, Lisa Reimer, Ingrid Felger, Jetsumon Sattabongkot, Quique Bassat, Nigel Beebe, Dyann Wirth.

Collaborating centres: PNG Institute of Medical Research; Walter & Eliza Hall Institute; University of Queensland; Barcelona Centre for International Health Research; Swiss Tropical & Public Health Institute; Mahidol University Bangkok; Harvard School of Public Health.

4.2.19 Fetal Immunity to Malaria

Summary

Title: Fetal immunity to malaria study

Date commenced: 2012

Project funding: National Institutes of Health (USA) grant held by Chris King, William Pomat (Local IMR PI)

About the project

Rationale: This study aims to determine the effect of in-utero exposure to malaria on the development of infant immune responses and the risk of malaria and all cause morbidity in the first three years of life.

Design: ~350 children born to mothers participating in the IPTp study (see above) will be enrolled into the study. Immune responses in fetal cord blood will be studied and the presence and timing of in-utero malaria exposure. Children will then be followed to 3 years of age to determine the association of these responses with risk of malaria and all cause morbidity in the first 3 years of life.

Progress: Fieldwork starting in early 2012.

Significance: Malaria infections during pregnancy may not only impact the mother's health and reduce the baby's birth weight but by affecting the natural acquisition of immunity could also impact on the risk of malaria and other illnesses during early childhood. This study will provide an in-depth understanding of the effect of malaria infection during pregnancy and infant immune responses and health and will thereby provide further evidence for the importance of appropriate control of malaria during pregnancy.

Contributors

Investigators: Leanne Robinson, Chris King, William Pomat, Peter Siba, Stephen Rogerson, Ivo Mueller.

Collaborating centres: PNG Institute of Medical Research, Case Western Reserve University, Cleveland (USA), University of Melbourne, Walter & Eliza Hall Institute Melbourne.

4.2.20 *Plasmodium Vivax* in Pregnancy (PregVAX) Study

Summary

Title: To investigate the epidemiology of *P. vivax* malaria in pregnancy in Papua New Guinea.

Date commenced: 2008

Project funding: Malaria in Pregnancy Consortium

About the project

Rationale: Approximately 25 million pregnant women exposed to malaria annually live in areas where *Plasmodium vivax* is endemic. While the effects of falciparum malaria in pregnancy have been well characterized and are responsible for considerable maternal and infant morbidity and mortality, surprisingly little is known about the impact of *P. vivax* infection during gestation. This project aims to describe the epidemiological and clinical features of vivax malaria in pregnancy. In addition, we will determine if there are pregnancy-specific *P. vivax* immune responses and genotypically and phenotypically characterize the parasites of the placenta.

Design: A cohort study of 2000 pregnant women identified at the hospital/health center during routine antenatal clinic (ANC) visits, independent of their gestational age and parasitological status, and are able and willing to give informed consent to participate in the study. Active and passive follow-up to monitor participants until delivery.

Progress: Field work completed in 2012, analysis on-going.

Significance: Gain insight into the burden of *P. vivax* in pregnancy and investigate associations with poor pregnancy outcomes and severe disease. Contributed to the BSc Hons of Heather Huaupe.

Contributors

Investigators: Maria Ome, Danielle Stanisic, Sarah Hanieh, Honor Rose, Regina Wanganapi, Leanne Robinson, Heather Huaupe, InoniBetuela, Alex Umbers, Holger Unger, Clara Menendez, Ivo Mueller, Stephen Rogerson, Hernando del Portillo, Carlota Dobaño, Alfredo Meyer, John Aponte.

Collaborating centres: PNG Institute of Medical Research, Melbourne University, Walter & Eliza Hall Institute Melbourne, Barcelona Centre for International Health Research.

4.2.21 Epitope-based identification of novel *Plasmodium* antigens for malaria vaccine development

Summary

Title: Epitope-based identification of novel *Plasmodium* antigens for malaria vaccine development

Date commenced: 2008

Project funding: NIH, Denise L. Doolan (PI)

About the project

Rationale: The recent availability of the genomic sequences of *Plasmodium* parasites and their corresponding proteome, and the development of innovative and high throughput technologies, allow for a new approach to malaria vaccine development. We hypothesize that we can identify novel targets of protective immunity to malaria by applying cutting edge molecular immunology technologies to identify, on a genome-wide scale, those antigens recognized by T cell responses (or antibody responses) in individuals with life-long exposure to malaria. Those antigens could be prioritized on the basis of immune reactivity and may represent excellent candidate antigens for vaccine development. It is anticipated, therefore, that the work proposed here will facilitate the development of an effective malaria vaccine by identifying promising vaccine antigens; such a vaccine would be of considerable future benefit to the PNG community involved in this research as well as other populations in PNG and elsewhere for whom malaria remains a significant public health threat.

Design: Cross-sectional study of 400-500 Papua New Guinean adults aged 20 years and over residing in areas of high malaria transmission.

Progress: Fieldwork completed in 2010, analysis on-going.

Significance: Antigens prioritised on the basis of immune reactivity may represent excellent candidate antigens for vaccine development. It is anticipated, therefore, that that the work proposed here will facilitate the development of an effective malaria vaccine by identifying promising vaccine antigens; such a vaccine would be of considerable future benefit to the PNG community involved in this research as well as other populations in PNG and elsewhere for whom malaria remains a significant public health threat.

Contributors

Investigators: Denise Doolan, Ivo Mueller, Leanne Robinson, Patricia Rarau, Jack Taraika, Danielle Stanisic, Peter Siba, Bruno Douradinha, Angela Trieu.

Collaborating centres: PNG Institute of Medical Research, Queensland Institute of Medical Research, Walter & Eliza Hall Institute.

