THEMED ABSTRACTS

Malaria

Jacky Snoep (US): *Towards whole body modelling of glucose metabolism in malaria patients: from biochemistry to disease state*

The key diagnostic for poor chances of survival of malaria patients is lactic acidosis and hypoglycemia. The aetiology of these disease states are still poorly understood. We have used a bottom up approach to model glucose metabolism of the malaria parasite Plasmodium falciparum, and extended the model to the infected red blood cell during different stages of the parasite's life cycle. The metabolic activity of a red blood cell increases dramatically after its infection by Plasmodium, and we are currently constructing whole body models to estimate the contribution of this increased metabolic rate towards the changed glucose metabolism in malaria patients. In my talk I will focus on the construction and validation of the mathematical model for glucose metabolism of the Plasmodium infected red blood cell, and on the application of the model for drug target identification.

Maynard Meiring (MSc, US, Prof Jacky Snoep): *From rupture to invasion: A new framework and set of equations to describe the dynamics of the parasite P. falciparum*

Research question: Can a consistent mathematical model within an appropriate and reliable framework be constructed to describe and model the dynamics of the P. falciparum parasite during the cycle transition stage of malarial infection?

The pathology of malaria is defined by the consequences of the asexual erythrocyte cycle (fever, anaemia, body aches, nausea, etc.). This cycle takes approximately 48 hours and terminates with the release of daughter parasites from ruptured schizonts (mature infected cells) which are free to invade more susceptible erythrocytes and repeating the cycle. The stage between rupture and re-invasion is termed "cycle transition" and is arguably the most important stage since it will determine the overall parasitaemia throughout the infection. Factors affecting the invasion rate/efficiency will be carefully considered. Some of these include multiple invasion, the parasite multiplication rate and the selectivity index, among others. A reliable framework will be set up together with a consistent mathematical model to describe the dynamics of the free parasite population.

Mbhekiseni Khumalo (MSc, WITS, Dr Benn Sartorius): *Correlation between surrounding environmental conditions and malaria incidence in selected sub-districts of Mpumalanga Province, South Africa (2001 – 2010)*

Methodology: The study setting was Mpumalanga Province, study design was retrospective ecological study design and study population was Mpumalanga residents. The study outcome was malaria incidence, explanatory variables was daily rainfall, temperature and relative humidity. The analysis was divided into descriptive and inferential statistics analysis. Mean (SD) or Median (IQR) was computed for numerical data and percentages for categorical data. ANOVA and Chi-square tests were used to detect significant differences in continuous and categorical variables respectively

across the three districts. The Pearson correlation was used to assess for significant correlations between malaria incidence and environmental conditions. The Kulldorff spatial scan statistics was used to detect for significant clustering of malaria cases in space-time. The Poisson regression model was used to identify and quantify factors significantly associated with malaria risk.

Results: The results that have been obtained from the on-going analysis are presented and more results are to come .....

Discussion and conclusion: The remote sensed-satellite meta-data is currently being extracted for further analysis. These findings are interim from an on-going analysis therefore more results are still to be obtained.

HIV

Bewketu Bekele (PhD, US, Dr Rachid Ouifki & Prof Wim Delva): *Modelling the impact of early HIV treatment: scaling up HIV testing and retention on HIV treatment*

We present a mathematical model to study the impact of increasing retention in HIV treatment and scaling HIV testing. The model considers current CD4 count threshold for ART initiation. Health outcomes, such as new HIV infections, HIV deaths averted, and person years on ART will be compared for different ART retention scenarios.

Cynthia Mazinu (MSc, US, Prof Wim Delva): *Estimating HIV treatment Coverage in South African ART clinics based on the time trend of the CD4 count distribution at ART initiation and a dynamic epidemiological model*

In this study, we present a more inclusive method of estimating HIV treatment coverage. We apply descriptive statistics to capture the time trend of the CD4 count distribution at ART initiation in selected ART clinics in South Africa. The statistical results have been used to adjust and calibrate the mathematical model to reproduce the number in need of treatment.

Vusie Lokothwayo (MSc, WITS, Dr Eustasius Musenge): *A comparative study on the determinants of HIV infection in Swaziland and Ethiopia*

Swaziland is a small country in Southern Africa with a population of 1.1 million, and has the highest HIV prevalence in the world of 26%. Ethiopia on the other hand is located in the Eastern part (horn) of Africa with a population of 74 million people, and has one of the lowest HIV prevalence rates with an adult prevalence of 1.5%. The main aim of the study was to explore and compare the main determinants of HIV infection in Ethiopia and Swaziland. Both countries are in the sub-Saharan Africa region, and it remains a question how they have such HIV prevalence differences. In the light of this, findings of this study will contribute evidence to inform policy and planning in the Ministry of Health as well as other sectors involved in HIV work on best practices that can contribute to the reduction of HIV incidence in Swaziland

Faikah Bruce (MSc, US, Dr Leigh Johnson & Prof Alex Welte):
Understanding the impact of an HIV intervention package for adolescents

With the high HIV prevalence among young people in South Africa, HIV prevention programs that target adolescents are vital in reducing HIV incidence in this high risk population. We develop a stochastic individual-based model that estimates the HIV incidence among adolescents over a relatively short period of time. The model is then used to simulate the impact of an HIV prevention package among adolescents participating in a hypothetical randomized controlled trial (RCT). The simulation aims to assist with the design of a RCT by determining which components to include in

an HIV prevention package to achieve the greatest effectiveness, as well as determining the sample size requirements for an optimally powered trial.

Moise Muzigaba (PhD, UWC, Prof Thandi Puoane):
The WHO 10-step treatment modality for severe malnutrition in the context of HIV/AIDS comorbidity: An operational research in the Eastern Cape Province

During my presentation I will build on my last slides to give an in-depth description of specific research questions relating to the epidemiological component of my PhD project. These questions have recently been honed down following a series of discussions with my supervisor and a SACEMA-based mentor and were not presented at the last research days meeting. I will then provide an overview of the new concepts I have introduced in the qualitative component of the research project, specifically the evaluation of the service utilization and organization structure within participating facilities. I will then conclude with an account of the progress to date and the plan moving forward, including specific targets as well as how, when and with which resources they are to be reached.

Anna Grimsrud (PhD, UCT, Prof Landon Myer): *Retention in care from ART programmes in resource-limited settings: temporal trends and models of care for stable patients*
This presentation will provide an update on work towards my PhD focussing on trends, risk factors, and models of care to improve retention in South Africa's antiretroviral treatment programme. An analysis on temporal trends in patient characteristics and programme outcomes from 25 cohorts in eight resource-limited countries will be presented. In addition, an overview of the rapid implementation of the Adherence Club model for stable patients at a large public clinic with Cape Town will be provided.

Temitope Sokoya (PhD, UP, Dr Martin Nieuwoudt & Dr Theresa Rossouw): *Immune activation in HIV-infected patients on HAART*

Persistent immune activation, despite adherence to antiretroviral regimens, is a major challenge facing clinicians in the treatment of human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS). Excessive immune activation is a major force driving HIV-1 replication and progression to AIDS. The persistence of inflammation during ART is associated with poor CD4+ T cell recovery, suboptimal therapeutic gains and an increased risk of other non-AIDS-related diseases, especially in patients who begin therapy after their CD4 T cells drop below 200 cells/µl. This study will focus on elucidating cellular level immune mechanisms with the ideal of guiding therapeutic strategies by which to reverse the activated state.

Rashmika Singh (MSc, UKZN, Prof Glenda Matthews): *Methods in Survival Analysis and applications to HIV Incidence Estimation*

The dissertation will consider modelling HIV survival data obtained from antenatal clinics using non-parametric, semiparametric and parametric methods, and regression models. Prevalence and incidence are two key measures of disease with reference to HIV. The main focus of the dissertation is to first model the cross-sectional seroprevalence data, thereafter, estimation of the hazard of infection, prevalence rates and incidence rates will be considered

Morna Cornell (PhD, UCT, Prof Landon Myer): *Mortality among patients after transfer compared with patients not transferred from 3 South African antiretroviral therapy cohorts*

Over the past 10 years, antiretroviral therapy (ART) programmes have undergone rapid expansion. There are now numerous large ART programmes in developing countries, many of which face

serious human resource constraints. Although some programmes report the proportion of patients who are transferred out (TFO), little is known about their mortality after transfer. In this study, we use data linked to the National Population Register to explore mortality among TFO patients after transfer compared with patients who were not transferred from the site of ART initiation.

Nishila Moodley (PhD, WITS, Prof Glenda Gray): *Modelling the impact of dual HIV and HPV vaccine strategies among adolescents in a resource constrained setting*

The availability of two prophylactic Human Papilloma Virus (HPV) vaccines, coupled with a potential prophylactic Human Immuno-deficiency Virus (HIV) vaccine delivered to adolescents through a sexual and reproductive health (SRH) platform developed at school level represents a significant, potent primary prevention strategy against cervical and penile cancer and HIV within a highly susceptible group. This study aims to estimate the impact of HPV and HIV dual vaccination preventative strategies on the HIV epidemic, cervical and penile cancer and ano-genital warts burden when administered to school-going adolescents as part of the school health programme envisaged under the primary health care (PHC) reengineering model. Mathematical modelling of the factors related to demography, sexual behaviour and disease characteristics would provide insights in evaluating the effects of the dual vaccination strategies. To the knowledge of the researcher, this study would represent the first testing of this dual vaccination concept in South Africa. The study is conceptualized specifically for the completion of a PhD in public health by publications.

Yusentha Balakrishna (MSc, UKZN, Prof Henry Mwambi): *Estimating the force of infection from prevalence data*

By knowing the force of infection, we can ascertain the high risk factors of the disease as well as the effectiveness of awareness programmes and treatment strategies. Since the work of Hugo Muench in 1934, many methods of estimating the force of infection have been developed, each with their own advantages and disadvantages. We explore the wide array of methods available to us and previous work done in estimating the force of HIV infection amongst antenatal clinic attendees.

Diabetes/*traditional medicine usage*

Dineo Nkholise (MSc, UWC, Prof Gail Hughes) *The use of traditional herbal medicine in conjunction with prescribed medicine for the management of diabetes in rural & urban areas of South Africa*

Information on the use of traditional herbal medicine is not very well documented or available in South Africa. Past studies have shown that there is prominent use of traditional medicine especially among the black population. Studies are also continuously showing the increase in the rate of non-communicable diseases among these communities especially those in urban areas. The purpose of the study is therefore to investigate the use of traditional medicines by diabetes patients and whether they use traditional medicines or not, and if so, what are the benefits or drawbacks of this form of treatment. The study also aims to investigate whether or not these diabetes patients use the traditional medicine simultaneously with their conventional prescribed diabetes treatment.

Metabolic syndrome/*genetic markers of risk*

Tanya Maistry (PhD, UKZN, Prof D P Naidoo): *Genetic contribution to the risk for metabolic syndrome: an investigation of candidate gene polymorphisms related to lipid and carbohydrate metabolism*

The literature provides limited description of the molecular mechanisms underlying the metabolic syndrome (Yamada *et al.*, 2008). In the context of the metabolic syndrome the relative contribution of genetic patterns to the pathogenesis of cardiovascular diseases and type 2 diabetes mellitus requires further investigation (Groop *et al.*, 2000). This study therefore aims to evaluate gene polymorphisms as potential genetic determinants for metabolic syndrome in a high risk Indian community. This investigation will be conducted on 1000 subjects from the Phoenix Lifestyle Project. Blood samples for lipids, glucose and insulin estimations were drawn from the cubital vein. Lipoprotein profile, glucose and insulin levels were documented. Genetic analyses will be conducted by standard techniques

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Stroke/*ethnobotanic treatment study*

Happy Mamadisa (MSc, UWC, Prof Gail Hughes & Prof Thandi Puoane): *Ethnobotanical study of traditional herbal medicines used for the treatment of stroke in the Western Cape, South Africa.*

The current ethnobotanical study aims to identify and document traditional herbal medicines used by patients and recommended in the management of stroke by traditional healers of Langa Township in the Western Cape, South Africa. This is a cross sectional, descriptive study utilising both quantitative and qualitative data collection methods. Quantitative methods will be used to identify and recruit stroke participants from the Prospective Urban and Rural Epidemiology (PURE) study, determine their demographic characteristics, clinical/medical history; specifically stroke, their use and pattern of THM. Qualitative study methods are aimed at identifying and documenting the indigenous knowledge of traditional healers on the use of THM for stroke specifically: name of the plant, plant parts used, mode of preparation, dosage and route of administration. The study will provide a better understanding of THM's used for the management of stroke and potentially identify additional traditional herbal medicines that are used in the Western Cape for stroke.

Rheumatoid Arthritis/*Multistate chronic dynamic disease modelling*

Eustasius Musenge (WITS, work done with Hodkinson B, Ally M, Meyer PWA, Anderson R, and Tikly M): *Rheumatoid Arthritis disease progression in a South African cohort: Multistate chronic dynamic disease modelling*

Disease activity in Rheumatoid arthritis (RA) patients   is measured by a 28 joint disease activity score (DAS28), with patients on treatment generally moving from high disease activity (DAS38 >5.1) to moderate, low disease activity and eventually remission (DAS 28 <2.8).Functional disability as measured by the health assessment disability index (HAQ-DI) is a function of disease activity early in the disease. We modelled RA disease activity and functional disability as stochastic multistate models using MLE and Bayesian inference. We fit, a three state model and a four state model for the HAQ-DI and DAS28 respectively, with death as one of the states. The MLE model transition intensities were computed from sets of Kolmogorov differential equations based on the time-homogenous Markov theory, which were modelled with and without covariates. Bayesian inference allowed us to model the unexplained heterogeneity in transition intensities among individuals by introducing random effects and priors to the modelling. Longitudinal data used were from 171 patients enrolled in a observational cohort in Johannesburg and Pretoria, South Africa. The average time patients spent in severe, moderate (mild) or remission was 8.0, 1.3 and 7.0 months respectively. Better functionality was associated with good and faster progression from

severe to remission. Model goodness techniques together with rates of disease progression plots were used to assess the model best fitting our data. In conclusion we advocate that patients should be treated until the disease activity score is in remission or lowest possible to enable greater physical functionality whilst alleviating disability and mortality due to RA. We also motivate for public health and interventions for people to present early at most within two years of onset of disease before much bodily damage is incurred to enable better response to treatment.

Chronic non-communicable diseases

Thandi Puoane (UWC): *PURE-ifying research on chronic non-communicable diseases in South Africa: the birth of PURE study at UWC*

Mitigating chronic non-communicable diseases (CNCDs) is beyond knowledge and choice; it's beyond developing extra-cognitive abilities in individuals in the hope that they limit their exposure to the risk factors of these diseases or simply make healthier choices. Responding effectively to the growing burden of CNCDs has more to do with addressing societal and biologic pathways, from environmental causes (such as mal-adaptation to urbanization) to primordial predispositions (such as genetics and obesity) as well as adequately managing the primary risk factors (such as high blood pressure or abnormal blood glucose) which lead to these health problems. It is about identifying and addressing the "*cause-of-the-cause*" of this group of health conditions.

Informed by this and building on our initial work with Community Health Workers (CHWs) in peri-urban communities in South Africa, the SoPH joined a global consortium of health researchers led by the Population Health Research Institute of McMaster University, Canada, and involving 17 upper-, middle- and low-income countries in the Prospective Urban and Rural Epidemiology (PURE) study in January 2009.
The study seeks to scientifically document the root-causes of the traditional risk factors for CNCDs by following-up over 150,000 adults aged 30 to 75 years for 12 to 15 years and collecting individual-, household-, community- and national-level information about them.

National data collected include information on policy and economic indicators that influence health; community level information include social and environmental factors that affect health such as measurements of the built environment, neighborhood walkability, access to healthy food etc. Household level data focuses on family structure, income and housing; while data at an individual level is about physical activity, diet and psycho-social behaviors. Detailed bio-medical measurements including weight, height, body mass index, body circumference, lung function tests, electrocardiographs, blood and urine analyses are all conducted.

General/Multi-disease

Eben Du Toit (PhD, UP, Prof I K Craig):   *Pinning control of disease networks*

Within the interdisciplinary academic field of network science, a recent research question focuses on the measured outcomes seen if large complex networks are subjected

to control at particular nodes, as opposed to all of the nodes in the network. Within epidemiology, the networks approach is well-known and studied and it is acknowledged that a multilevel approach could provide new insights and answers.

Research into the application of control systems theory, and in particular optimal control techniques in public health interventions for infectious diseases is still young. The application of pinning control strategies, as a network science related technique, is of particular interest here. Pinning control strives to drive a dynamic network along a predetermined trajectory towards a particular outcome or consensus. This trajectory may be the reduction of the effect of a combined set of risk factors for disease, elimination of disease balanced with physical resources within an intervention scenario, or finding an optimal drug scheduling and timing regime for influencing a targeted portion of a population as opposed to the now much-researched within-host viral dynamics.

Eddy Kimba (PhD, UKZN, Prof Jacek Banasiak): *A Singularly Perturbed SIS Model with Age Structure*

We present a preliminary study of an SIS model with basic age structure and focus on a disease with quick turnover, such as influenza or common cold. In such a case the difference between the characteristic demographic and epidemiological times naturally introduce two time scales in the model which makes it singularly perturbed. Using the Tikhonov Theorem we prove that for certain classes of initial conditions the nonlinear structured SIS model can be approximated with very good accuracy by lower dimensional linear models.

Renier Van Rooyen (MSc, US, Prof Paul Mostert & Dr Martin Nieuwoudt): *Investigating the Effectiveness of Bayesian Estimators for Parametric Survival Models Using Noninformative Prior Approach*

Bayesian Statistics will be used to derive estimators for unknown parameters in three parametric survival models: the compounded Exponential, compounded Rayleigh and compounded Weibull distributions. Frequentist properties of these estimators will be considered in a simulation study to judge their performances with regards to at least two different loss functions (squared error loss and linex loss) and a variety of noninformative prior distributions, including Jeffreys' priors, reference priors, probability matching priors and MDI (maximal data information) priors. Application to a data set will hopefully exhibit the usefulness of these estimators in accurately modelling the versatility of the hazard rate in any given circumstance.

Rendani Netshikweta (MSc, UV, Dr Winston Garira): *A mathematical modelling framework of infections with free-Living pathogen in the environment*

The environment is the reservoir of most infectious diseases and many pathogens emerge or re-emerge because of the changes on the environment. The standard procedure for developing models for infections with free-living pathogen in the environment is to consider an interactions triad of host, pathogen and environment. However, most researchers, when modelling such infectious, focus only on the transmission that occurs either between host and host, or host and vector. In our study we will develop a mathematical model framework that will accommodate environmental transmission.

Mbuso Mntambo (PhD, UWC, Prof Thandi Puoane & Prof Steve Reid) *Development of a public health model of community participation in the KwaZulu-Natal health care system*

Community participation is an educational and empowering process in which the people, in partnership with those who are able to assist them, identify the problems and the needs and

increasingly assume responsibilities themselves to plan, manage, control and assess the collective actions that are proved necessary.

The essential elements of community participation, therefore, are: empowerment, Partnership, Inclusiveness, Shared responsibility for health, Approved methods and systems for ongoing participation and development.
In KwaZulu-Natal, community participation is not integrated into the Primary Health Care system. This is due to lack of framework describing the systems and processes for involving communities as well as monitoring the response to the involvement processes. As a result, community participation is often understood as mere availability of governance structures, in particular Hospital Boards and Clinic Committees. The aim of this study is to assess and understand community participation in the KwaZulu-Natal Primary Health Care system, as well as to assess community participation challenges for the purpose of developing and testing a community participation model.

The study is being implemented in three phases, as follows:

PHASE 1: Situational analysis
PHASE 2: Developing and piloting the model
PHASE 3: Evaluating the model projects and finalizing the model

The situational assessment was conducted across five levels of the Primary Health Care spectrum which are households, clinic, hospital, sub-district (also called municipal) and district level. For each level, both the service provider and the community components were studied. During situational assessment, semi-structured interviews were used to understand the extent of participation by various community structures, methods used as well as challenges experienced by both service providers and communities. Observations were used to study the processes of community health promotion events. Data collected from the situational assessment were used to develop a pilot model for community participation. To test the model, four projects based on the model principles were identified and are being implemented in the four sub-district by the researcher. The projects are: Anti-teenage campaign, Training of clinic committee, Facilitation of participatory health promotion event, and establishment of an HIV/AIDS support group.

The pilot implementation of the projects will be evaluated by participants and by the PHC forums. The results of model evaluation will be used to finalize the public health model of community participation for KwaZulu-Natal PHC system.