SACEMA
DST/NRF Centre of Excellence in Epidemiological Modelling and Analysis

Director: Alex Welte (alexwelte@sun.ac.za)
Research Manager: Lynnemore Scheepers (scheepersl@sun.ac.za)
Mailing address: Private Bag X1, Matieland 7602, South Africa
Physical address: 19 Jonkershoek Road, Stellenbosch, 7602, South Africa

Phone: +27 (0) 21 808 2589
Fax: +27 (0) 21 808 2586
Inquiries: info@sacema.com

Web site: www.sacema.com **Quarterly Epidemiological update:** www.sacemaquarterly.com

SACEMA NEWSLETTER

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NEWS:

Prof Brian Williams appointed to the Scientific Advisory Board of PEPFAR

Brian Williams, SACEMA Senior Fellow, has been appointed to the PEPFAR (Presidents Emergency Plan for AIDS Relief) scientific advisory board - the highest level body for helping the PEPFAR planners assess the scientific basis for funding strategy and programme evaluation. Brian has been a leading voice internationally in drawing attention to the importance of the transmission prevention aspect of effective treatment, and with this appointment SACEMA can continue advocating for consistent access to treatment for patients at all stages of infection while helping drive and implement the scientific agenda in support of evaluating tough choices facing implementers.

RESEARCH:

Incidence estimation

SACEMA continues to make a major impact on the world stage in the area of the estimation of HIV incidence – with particular reference to the application of biomarkers to the analysis of data from cross-sectional surveys. In this regard John Hargrove made an early contribution to the field through the analysis of data from the Harare ZVITAMBO study, suggesting a means of mathematically adjusting HIV incidence estimates to account for (known or estimated) rates at which people continue to test as recent (incident) infections when they are known to have been infected for long

periods – of the order of years. A recent re-evaluation of the situation, by John Hargrove, Hayden Eastwood and Cari van Schalkwyk shows that the algorithm leading to the originally suggested adjustment leads also to a solution identical to one produced, through an independent and mathematically more rigorous approach, by Alex Welte, Tom McWalter and Reshma Kassanjee. A paper on the subject has been submitted for publication. An important insight in both approaches is that incidence, and the mean recency period for the assay, should be estimated over a user-defined finite period.

A further paper is being prepared in which we address problem of estimating the mean recency period for the BED and similar assays. Is there an optimum method, or will a number of different approaches produce similarly acceptable results.

Hargrove continues to provide advice and support for workers in the region (in particular, Botswana, Zimbabwe and Kenya) on the use of BED in incidence estimation – and this work has also resulted in one new publication in 2011.

The tissue samples collected during the ZVITAMBO study continue to provide one of the richest, high-quality, sources for testing new methods in the area. Accordingly Hargrove is pursuing the possibility of utilising the samples to test two new methods under development at the Centers for Disease Control (CDC) in Atlanta, Georgia, USA.

Climate change

There is increasing world interest in the epidemiological effects of changes in global climate; in particular much has been published on the likely changes in the distribution of vector-borne diseases, especially in Africa. The majority of this work, however, has been carried out without reference to actual data on past and current levels of the vector(s) concerned. This is for the good and sufficient reason that these data are often entirely absent and, even where present, they are of limited scope and quality.

A shining exception to this rule does, however, exist in the data that have been collected over the past half-century at Rekomitjie Research Station, Zambezi Valley, Zimbabwe. These data have resulted from in-depth studies of the tsetse flies *G. morsitans morsitans* Westwood and *G. pallidipes* Austen and of three trypanosome species that they transmit to livestock and humans. At the same time workers at the Research Station have measured climatic variables such as temperature and rainfall. The biological data relate not only to changes in tsetse and trypanosome population levels with season and year, but also to much more detailed studies of changes in the age, gender and species structure over time.

Workers at SACEMA aim to analyse the changes in tsetse and trypanosome population levels and structure in the light of observed seasonal and longer-term fluctuations in temperature and rainfall. To this end John Hargrove has been interacting with Glyn Vale in efforts to consolidate climate data from Rekomitjie and, where necessary, from the nearest major weather station at Kariba airport. He has also travelled to the UK and had meetings with Profs Torr, Maudlin and Welburn in efforts to develop a project proposal aimed at securing funding to support a major effort to analyse this unique situation.

GRADUATIONS:

Tinevimbo Shiri graduated with a PhD from the University of the Witwatersrand, on 19th July 2011. His thesis titled: "In-vivo dynamics of HIV-1 evolution" was supervised by Dr Alex Welte.

Mercy Kamupira graduated with a PhD from the University of Cape Town on 9th June 2011. Her thesis titled: "Dyad-related factors in HIV prevention" was supervised by Assoc. Prof Landon Myer from School of Public Health and Family Medicine, University of Cape Town.

We wish Tinevimbo and Mercy all the best with their future endeavours.

ACADEMIC EXCHANGES/VISITORS:

Aaron Lucas spent 10 weeks at SACEMA as part of his PhD. Dr Wim Delva supervised his research experience as Aaron worked to improve, modify and calibrate the stochastic simulation tool, SIMPACT. Aaron is at the midpoint of his PhD at Northwestern University Illinois, studying infectious disease modelling using operations research techniques. His main research interests lie in improving infectious disease control using simulation and dynamical systems modelling, and in particular network modelling. His home department is in Industrial Engineering and Management Sciences.

Nele Deprez, a medical student from Belgium is spending two months at SACEMA while working on her Master's dissertation built on the Sexual Network Study led by Dr Wim Delva. Nele's main task has been the statistical analysis of the survey data. She has also been involved in the fieldwork study in Khayelitsha Site C.

CAPACITY BUILDING & TRAINING EVENTS:

Clinic on the Meaningful Modelling of Epidemiological Data

Once again this year, in conjunction with our distinguished and energetic North American colleagues, SACEMA was proud to help mount the 11 day Clinic on **Meaningful Modelling of Epidemiological Data**, at AIMS from 30 May - 10 June 2011. A total of 32 students were selected to participate in the course: 8 North American students, 8 SACEMA students, 6 AIMS/Stellenbosch University Biomathematics Honours students, 1 Stellenbosch University Biomathematics MSc student, and 9 other African students (from Ghana, Nigeria, Tanzania, Malawi, Zimbabwe, South Africa). The mentoring and presenting team consisted of 5 North Americans and 5 SACEMA staff, while 11 AIMS postgraduates, researchers and tutors also participated. South African Universities

represented among the students were: UKZN, Venda, NWU, WITS, UNISA, Wits, Stellenbosch, and Rhodes. The goal of the Clinic was to engage participants in epidemiological modelling projects that use real data to grapple with practical questions in a meaningful way. Participants were encouraged to start collaborative projects with each other or the mentors, and continue this research on return to their home institutions.

Participants of the MMED clinic enjoying a cold day outdoors

Applications of Mathematics in Biology and Medicine

During the week 4-8 July 2011, thirty-four Honours or final year students from eight South African universities attended the course: **Applications of Mathematics in Biology and Medicine,** at the African Institute for Mathematical Sciences, Muizenberg. This event, co-sponsored by SACEMA and AIMS, has taken place annually since 2007 (skipping world-cup year) and has been known variously as the "SACEMA/AIMS Winter School", "Epi-intro Week", or "Outreach Week". Its purpose is to introduce South African students to the wide range of applications of the mathematical sciences in biology, demography, epidemiology, ecology and medicine, with a view to attracting talented students into postgraduate work in these areas. And, indeed, a fair number of past and present students were first drawn to study with AIMS or SACEMA through attending this course. The selection process this year was highly competitive and there is little doubt that among the thirty-four were some leading South African scientists of the future.

In planning the programme for the 2011 event we looked for people doing important work, not just in epidemiology but in other critical areas where mathematics is proving a powerful instrument of discovery. Equally, we looked for good communicators who could talk about their work in an exciting and attractive way that would motivate and inspire students. Eighteen presenters, from the Universities of Stellenbosch and Cape Town as well as from SACEMA and AIMS, gave interactive talks and computer practicals on such topics as: introduction to scientific computing, introduction to mathematical modelling, population projection, HIV/AIDS modelling, biotechnology and mathematics

in the 21st century, modelling the interactions between HIV and the immune system in humans, organisms and populations: mathematical applications in ecology, systems biology, modelling sexual networks in a township, bioinformatics of viral evolution, estimating HIV incidence from prevalence data, the impact of antiretroviral treatment (ART) on HIV transmission.

For the presenters, the reward was the pleasure of talking about one's work to a group of such talented and enthusiastic youngsters, and the real possibility of enticing students to study and work in one's institution, field or project. For the students, the scientific and social programmes were probably equally important. Here is one response: “The week was an incredible experience, and has certainly given me much to think about. It was also a wonderful chance to meet so many different students from across the country. I'll certainly be recommending it to other students.”

Participants of the Applications of Mathematics in Biology and Medicine course: 4-8 July 2011

Introduction to Applied Biostatistics

A first for SACEMA was the workshop: **Introduction to Applied Biostatistics**, which took place 11-22 July 2011, at AIMS in Muizenberg, mounted in association with the University of KwaZulu-Natal (UKZN) and the University of Ghent, Belgium. Funded by the Flemish Inter-University Council (VLIR) under a project launched and managed by SACEMA's Dr Wim Delva, the purpose of this workshop was to provide an intensive training in the basic concepts and the most commonly applied methods of biostatistics, and so contribute to vital capacity building in this important field. From a large number of applicants, twenty five students were selected – mostly professionals and postgraduates in the health sciences, including about 10 SACEMA students. While most of the students were South African, a number came from other countries in the region. The lectures and practical sessions were undertaken by an experienced team of statisticians and teachers from UKZN: Prof Delia North, Prof Glenda Matthews, Prof Temesgen Zewotir, Dr Henri Moolman and Dr Shaun Ramroops; they were backed up by four tutors from SACEMA: Ms Cari Van Schalkwyk, Ms Hilmarie Brand, Mr Dieter

Winkler and Dr Guy Mahiane. This 2011 introductory workshop is seen as a pilot operation, and we expect it to be followed by annual workshops of a two tier nature: introductory and intermediate. These will be partially funded under the VLIR scheme until the fifth year, and it is hoped they will be self-sustainable thereafter.

A participant writes: "I am so appreciative of the opportunity afforded me to participate … I am now confident as to which statistical test I will be using when analysing the data for my PhD study. The knowledge gained will also be used in a lot of research projects that I will embark on in the department where I work. Thank you for the great hospitality, good accommodation and wonderful personnel … The excursion to Cape Point will add to the good memories of Cape Town, and will never be forgotten."

Participants of the Introduction to Applied Biostatistics workshop: 11-22 July 2011

Advanced Epidemiological Methods

The **Advanced Epidemiological Methods** seminar, presented under the auspices of SACEMA in March 2010 by Prof Matthew Fox of the University of Boston, proved so popular that we mounted it again this year, taking advantage of Matthew's plans to visit South Africa again. It took place in Stellenbosch, 15-19 August, with thirty-four participants, including six SACEMA students and people from many different institutions in South Africa, as well as a number from other countries. The commitment of participants was severely tested on a very cold Monday morning before the Neelsie heating system was correctly set, but it is believed all survived the temporary chill. Participants were invited to a lunchtime reception at SACEMA where they could meet SACEMA staff and students, and it is hoped some longer-term collaborations will ensue.

The aim of this unusually challenging and thought-provoking course was to deepen understanding of basic epidemiological concepts such as measures of effect, confounding, misclassification and selection bias, and to question the implications of various sources of bias. In exploring the basic

statistics used in epidemiological research, many subtle misunderstandings were revealed about what these statistics can tell us.

From Matthew Fox's introduction: “Throughout the course we will focus on the core concepts of validity and precision and will further develop our understanding of these central ideas. We will emphasize the development of skills that every doctoral level epidemiologist should have, skills that are both practical and marketable.”

Introduction to Epidemiology and Research Methodology

For the second year at SACEMA, we have been privileged to have Dr Jo Barnes present the course **Introduction to Epidemiology and Research Methodology** for our MSc students and the University of Stellenbosch Biomathematics Masters students. Combining vast experience with a contagious enthusiasm for the subject, Dr Barnes has visited SACEMA for Tuesday afternoon sessions over a number of months, patiently tolerating the interruptions caused by various workshops and seminars, and the course should conclude in the next few weeks.

UPCOMING TRAINING EVENTS:

Prof Jacek Banasiak: Population Dynamics (date in October to be confirmed).

PUBLICATIONS:

1. Biccard BM, **Kassanjee R, Welte A.** (2011) Is it possible to decrease the incidence of peri-operative stroke associated with acute peri-operative beta-blocker administration? *Anaesthesia*, 66(2): 73-83.
2. **Delva W,** Verguet S, **Hargrove J, Williams B,** Sheneberger R, Stander T, **Welte A.** (2011) Treatment-centred prevention: an integrated biomedical and social approach to HIV prevention. *AIDS* 25:1435–1437.
3. Dye C, Bourdin Trunz B, Lonnroth K, Roglic G, **Williams BG**. (2011) Nutrition, Diabetes and Tuberculosis in the Epidemiological Transition. *Plos One* 6(6): e21161 (1-7)
4. **Hargrove JW,** Humphrey JH, Mahomva A, **Williams BG,** Chidawanyika H, Mutasa K, Marinda E, Mbizvo MT, Nathoo KJ, Iliff PJ (2011) Declining HIV prevalence and incidence in perinatal women in Harare, Zimbabwe. *Epidemics* 3: 88 – 94.
5. **Hargrove, J. W. Ouifki, R. & Ameh, J. E.** (2011) A general model for mortality in adult tsetse (*Glossina* spp). *Medical and Veterinary Entomology*, 25, doi: 10.1111/j.1365-2915.2011.00953.x.
6. Incidence Assay Critical Path Working Group (2011). More and Better Information to Tackle HIV Epidemics: Towards improved HIV Incidence Assays. *PLos Medicine* 8(6): e1001045 (1-6)
7. **Johnstone-Robertson SP, Hargrove J, Williams BG** (2011) Antiretroviral therapy initiated soon after HIV diagnosis as standard care: potential to save lives? *HIV/AIDS – Research and Palliative Care* 3: 9 – 17. DOI 10.2147/HIV.S7278
8. **Kassanjee R, Welte A, McWalter TA,** Keating SM, Vermeulen M, Stramer SL, and Busch MP. (2011) Seroconverting Blood Donors as a Resource for Characterising and Optimising Recent Infection Testing Algorithms for Incidence Estimation. *PLoS ONE* 6(6): e20027 (1-8)

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10. Lawn SD, Ayles H, Egwaga S, **Williams B**, Mukadi YD, Santos Filho ED, Godfrey-Faussett P, Granich RM, Harries AD. (2011) Potential utility of empirical tuberculosis treatment for HIV-infected patients with advanced immunodeficiency in high TB-HIV burden settings. *International Journal of Tuberculosis and Lung Disease* 15(3):287-295
11. Lawn SD, Harries AD, **Williams BG,** Chaisson RE, Losina E, de Cock KM, Wood R. (2011) Antiretroviral therapy and the control of HIV-associated tuberculosis. Will ART do it? *International Journal of Tuberculosis and Lung Disease* 15(5):571-581
12. Marinda ET, Moulton LH, Humphrey JH**, Hargrove JW et al .** (2011) In utero and intra-partum HIV-1 transmission and acute HIV-1 infection during pregnancy: using the BED capture enzyme-immunoassay as a surrogate marker for acute infection. *International Journal of Epidemiology*; 1–10 doi:10.1093/ije/dyr055
13. Torr SJ, Chamisa A, **Vale GA**, Lehane MJ and Lindh JM. (2011) Responses of tsetse flies, Glossina morsitans morsitans and Glossina pallidipes, to baits of various size. *Medical and Veterinary Entomology*, doi: 10.1111/j.1365-2915.2011.00647.x
14. **Uys P,** Marais BJ, **Johnstone-Robertson S, Hargrove J, Wood R** (2011) Transmission elasticity in communities hyperendemic for tuberculosis. *Clinical Infectious Diseases* 52:1399–1404.
15. **Welte A, Hargrove J, Delva W, Williams B**, Stander T. (2011) How different are the costs and consequences of delayed versus immediate HIV treatment? *South African Medical Journal.* 10(101.6)377-378
16. **Williams B,** Wood R, Dukay V, **Delva W,** Ginsburg D**, Hargrove J,** Stander M, Sheneberger R, Montaner J, **Welte A** (2011) Treatment as prevention: preparing the way. *Journal of the International AIDS Society* **14** (Suppl 1)