

**Review of
DST/NRF Centre of Excellence in
Epidemiological Modelling and Analysis
covering the period 2006 to 2008**

16 to 18 February 2009

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EXECUTIVE SUMMARY

A review of the NRF Centre of Excellence in Epidemiological Modelling and Analysis (SACEMA) was held from 16-18 February 2009. The review covered the activities of the Centre from its inception in 2006 to 2008. The review panel consisted of three members, two from Canada and one from South Africa.

The progress that has been made by SACEMA over the three years since inception is truly impressive. Over 40 journal articles have been published and another 13 have been submitted for publication in prestigious international journals. Currently 29 students are registered for MSc and PhD degrees through five different South African universities and at least one European university. Collaboration with international institutions has provided support not only for research projects but also capacity building and supervision of students.

The research projects carried out by SACEMA cover many aspects of HIV/AIDS and TB and their co-interactions. These projects will be particularly useful to the National and Provincial Departments of Health in their efforts to reach their goal of halving HIV infections by 2012. In addition, SACEMA is expanding its research scope to include the modelling of other diseases of public health importance such as malaria, trypanosomiasis and African horse sickness.

Some of the key recommendations made by the panel include:

- Fostering a formal collaborative link between SACEMA, the National Department of Health and the National Institute for Communicable Diseases to the mutual benefit of all concerned. This is crucially important to South Africa's success in effectively combating the spread of diseases.
- Staffing and succession planning needs to be addressed and efforts to attract South African students into the field of epidemiological modelling need to be continued and expanded. The panel's suggestions on how to achieve these, itemized under the 'Recommendations' section below, are by no means considered to be the only options available.
- The provision of video conferencing facilities would greatly enhance the ability of SACEMA staff and students to communicate more effectively with each other and with international collaborators.

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BACKGROUND

The Department of Science & Technology (DST), through the National Research Foundation (NRF), has established seven physical or virtual Centres of Excellence (CoE) at various locations in South Africa. The aim is to concentrate existing research capacity and resources to foster long-term collaboration across disciplines thereby enhancing research excellence and capacity development. The Centres are sponsored by the DST and the programme is managed by the NRF.

The South African Centre for Epidemiological Modelling and Analysis (SACEMA) was established in 2006. Unlike the other CoE's that were based on applications from established researchers, SACEMA was established *de novo* on recommendations to the DST by a panel of experts that such a facility was critical to understanding the dynamics of disease transmission, in particular HIV and TB but including other diseases such as malaria and trypanosomiasis. The modelling and statistical fields of quantitative epidemiology represented a large gap in the South African skills base with relatively few local mathematicians or statisticians being drawn into them. As a result, SACEMA was established with a mission statement as follows:

"To establish, within South Africa, a leading research centre of excellence for quantitative modelling of the prevalence and management of disease in and transmission among hosts. The Centre will focus on the major health issues in Africa by:

- Developing the necessary human capacity and infrastructure to advance epidemiological modelling and analysis;
- Placing an initial emphasis on research into the epidemiology, control and management of HIV/AIDS and TB, extending this to malaria and other diseases as additional staff and funding become available;
- Providing a firm scientific basis for health policy and planning locally and nationally."

Professor John Hargrove was appointed as Director of SACEMA and the CoE is based at the Stellenbosch Institute for Advanced Study (STIAS) under the auspices of Stellenbosch University.

PURPOSE OF THE REVIEW

Reviews of both the Centres of Excellence and the NRF management of the programme are carried out at regular intervals. The purpose of the reviews is:

1) To assess the conception, implementation and management by the NRF of the CoE programme. The assessment of the performance of the individual CoE's in terms of their respective mandates forms part of this review.

2) To make recommendations for the future to enhance the DST/NRF programme and performance of the individual CoE's.

The scope of the review is a retrospective assessment of the CoE from the date of inception to June 2008, as well as a prospective view covering the future goals to which the CoE should strive. The performance of the CoE relative to the approved proposal submitted to the DST/NRF and its subsequent evolution under the guidance of the Advisory Board was assessed. The following key performance areas (KPA's) were addressed:

- **Research** – the main activity of the CoE, focused on the creation and development of new knowledge and/or technology.
- **Education and Training** – capacity building through masters and doctoral programmes, post-doctoral support, etc.
- **Information Brokerage** – providing access to a highly developed pool of knowledge, maintaining databases, promoting knowledge sharing, etc.
- **Networking** – collaborate with reputable individuals, groups and institutions.
- **Service Rendering** – providing information, analysis and advice to government, business and civil society.
- **Management** – leadership, staffing, host institution commitment, location, funding, strategic positioning and future plans.

REVIEW METHODOLOGY

Background documents were provided by the DST/NRF, such as the NRF Strategic Plan 2000, Vision 2015, Framework for Centres of Excellence, Guide to Funding of Centres of Excellence, and others. Documents provided by the CoE included a self-evaluation report, business plans for 2006, 2007 and 2008, annual progress reports and a Service Level Agreement of 2007.

The review panel convened in Stellenbosch during the period 16-18 February 2009. The panel was briefed by Dr Andrew Kaniki of the NRF on the purpose and scope of the review and the responsibilities of the panel in terms of the reporting. The panel conducted interviews with the Director of SACEMA, staff members, students and stakeholders (see Appendix 1) to gain insight into the key performance areas addressed below.

KEY PERFORMANCE AREAS

RESEARCH

In line with their mission statement, SACEMA has focussed mainly on the epidemiological modelling of HIV/AIDS and TB and the interactions between these two diseases. They have also recently extended their research scope to include malaria, trypanosomiasis and African Horse Sickness.

The broad areas of research undertaken by SACEMA are:

- HIV/AIDS
 - Surveillance tools
 - Population level analysis
 - Cellular/molecular modelling
 - Male circumcision
- Tuberculosis
 - Community level modelling
 - Modelling/diagnosis/treatment
- Modelling HIV and TB co-infection
 - Community level modelling at Masiphumelele
 - Community level modelling at Ravensmead/Uitsig
- Malaria population level modelling
- Trypanosomiasis tsetse population dynamics
- African Horse Sickness

Since its inception three years ago, SACEMA has produced an impressive track record of research outputs with publications in major peer-reviewed international biomedical and mathematical journals. These journals include *Plos Medicine*, *Plos ONE*, *AIDS*, *Journal of Mathematical Biology*, *Journal of Infectious Diseases*, *Journal of the Royal Society Interface* and *Mathematical Biosciences and Engineering*.

Many of the research articles have major public health implications, particularly the work on male circumcision which has received worldwide acclaim. The HIV/TB co-infection work, carried out in collaboration with the Desmond Tutu Centres for HIV and TB, is a pioneering study giving detailed insight into the complex dynamics between the two diseases and evaluating different control strategies using data from the Masiphumelele and Ravensmead/Uitsig areas outside Cape Town.

Furthermore, the work on the estimation of HIV incidence, led by the SACEMA Director John Hargrove, is directly relevant to South Africa's goal of halving HIV incidence by 2012. Measuring incidence is critical to the success of anti-HIV control strategies. HIV incidence has been impossible to realistically estimate in the past largely due to the difficulty of estimating the time when primary HIV infection occurred, and hence the rate of acquisition of new infections. SACEMA's work in this area provides a more realistic methodology for estimating incidence based on a sound mathematical framework. This will allow the Department of Health to base their policies and strategies on sound scientific evidence. Following the success of SACEMA in this area, they have been invited to provide leadership for establishing similar studies in Uganda and Kenya.

SACEMA researchers have presented their work at major conferences around the world. In addition, SACEMA has organised and co-organised various workshops and conferences over the years.

An impressive aspect of SACEMA's research work is that it has attracted fruitful collaborations from institutions both locally and internationally. These include the Universities of the Witwatersrand, Cape Town, Western Cape and KwaZulu/Natal, and the Onderstepoort Veterinary Institute in South Africa. In the USA: Johns Hopkins University, UCLA and Boston University as well as the Center for Discrete Mathematics and Theoretical Computer Science (DIMACS), based at Rutgers University, New Jersey. In Europe: Paris University and the Institut de Recherche pour le Developpement (IRD) Paris, France. In the UK: Greenwich University. In Africa: the University of Botswana and the National University of Science and Technology, Zimbabwe.

A list of SACEMA's research publications in peer-reviewed journals is given in Appendix 2. Another list of ongoing research projects is given in Appendix 3.

EDUCATION & TRAINING

Training is a major part of SACEMA's activities, and becomes even more important due to the enormous difficulties encountered in recruiting qualified researchers. Hence, SACEMA decided to undergo a shift in emphasis in favour of training.

Currently, SACEMA has 18 MSc students, 9 PhD students and 2 post-doctoral fellows. Close to two thirds of those students are based at universities all over South Africa other than the University of Stellenbosch. The students work on various topics, mostly concerned with the modelling of HIV/AIDS and TB, although some are working on related areas such as malaria.

The shortage of core qualified researchers to handle the training program necessitated that SACEMA increase its efforts to foster linkages with reputable international and national institutions notably DIMACS (USA), and the African Institute of Mathematical Sciences (AIMS) at Muizenberg outside Cape Town. These collaborations have significantly helped SACEMA increase its student population base, in addition to enhancing its international profile.

The Service Level Agreement requires that no fewer than 20 graduate students be on board within 3 years and that 50% of these students should be South African. The third and fourth requirements are that of the South African students, 50% should be black and 50% female. The first requirement has already been met and exceeded, and the second requirement has almost been met. The third and fourth requirements have not been met. Although all these goals are laudable, the last two appear somewhat unrealistic because of the inherent difficulty in attracting qualified South African students into mathematics. Further, the recent apartheid history, with the consequent dearth of black students, makes it quite difficult to attract qualified black students.

Nonetheless, SACEMA has continued to engage in constructive efforts to increase its student population. They have gone from 4 students in 2006 to 15 in 2007 and 29 in 2008.

In 2007, SACEMA has sponsored an introductory course, in collaboration with AIMS and the Centre for Actuarial Research (CARE), for final year undergraduate and honours students aimed at introducing them to the applications of mathematics in biology and medicine. SACEMA, in conjunction with the Department of Mathematical Sciences at Stellenbosch University, is jointly running bio-mathematics degree programmes at undergraduate and graduate levels. These programmes would have been impossible to offer without the presence of SACEMA.

Some of the students at SACEMA have made very good use of the opportunities available to them to form their own international networks through collaboration with other institutions.

INFORMATION BROKERAGE

In addition to producing 56 original scientific research manuscripts that have been published, accepted or submitted to peer-reviewed scientific journals, SACEMA hosts an annual research meeting for Board members and Stellenbosch University staff. Furthermore, SACEMA conducts a mathematical biology training programme in collaboration with DIMACS (Rutgers University) for African and African-American students annually. The first of such events was held at University of the Witwatersrand in 2006 (titled “Facing the Challenge of Infectious Diseases in Africa: The Role of Mathematical Modeling”) followed by a US-Africa Advanced Studies Institute on Mathematical Modeling of Infectious Diseases in Africa held at AIMS in 2007 and 2008. SACEMA was also involved in organizing other similar research and training events.

Information is shared with various universities and other institutions through the production of quarterly newsletters, which are distributed nationally and internationally. Important activities and research findings are disseminated through press releases via the University media office and items placed on the NRF web site.

NETWORKING

SACEMA has formed linkages with a number of universities within South Africa, and supports students and scientists in these universities. Thus, SACEMA is actively involved in the nurturing and development of mathematical biology in South Africa. Furthermore, in line with its mandate, SACEMA fosters very successful collaborations with major institutions around the world, such as DIMACS and AIMS, and has collaborative agreements with the University of the Witwatersrand, UKZN, UCT, NUST and Onderstepoort Veterinary Institute, and supports students at many of these institutions as well.

Nationally, collaboration has been established with the Agricultural Research Council for work on tsetse flies and horse sickness; the Desmond Tutu HIV Clinic for sponsoring students; the Centre for Actuarial Research for training students and for

work on male circumcision, and the Mathematics Department at the University of Stellenbosch for training and research supervision of students.

Internationally, SACEMA has collaborated with Professor Bertran Auvert, of the University of Paris, who conducted the first trial on male circumcision, voted by Time Magazine as the medical breakthrough of 2007, with UNAIDS and WHO in Geneva on the spread of HIV, and with CERN in Geneva also on the spread of HIV.

SERVICE RENDERING

SACEMA's research is highly relevant to the control of infectious diseases both in South Africa and in the broader community of SADC and sub-Saharan Africa. Measuring incidence, for example, is the very first step in assessing whether a particular intervention is working or not. In this respect, SACEMA has a critical role to play in assisting both the national and provincial Departments of Health.

SACEMA has a representative on the Research, Monitoring and Evaluation sub-committee of the South African National AIDS Committee (SANAC).

MANAGEMENT

SACEMA has a Management Board consisting of representatives from the University of Stellenbosch, MRC, Department of Health and DST/NRF to advise on and approve strategic management. It also has a Scientific Advisory Committee that provides advice on research direction.

The Director of SACEMA is responsible for developing strategic plans, providing overall scientific guidance, implementing decisions taken by the Board, administration, and in addition to all of this he actively does research, forms liaisons with national and international institutions, mentors students and post-doctoral fellows, and generates external funding.

The Director is assisted by a research manager and an administrative officer based in Stellenbosch. SACEMA has a co-ordinator for the project funded by the Canadian International Development Agency (CIDA) who is a full-time employee at Wits University in Johannesburg with 60% commitment to SACEMA.

REVIEW RESULTS ON KEY PERFORMANCE AREAS

1. Over the past three years, SACEMA has carried out very high quality research on the transmission dynamics and control of diseases of major public health importance to South Africa, notably HIV/AIDS and TB and their co-infection. This is very evident from the impressive list of high quality publications in top international journals, averaging 15 publications per annum. The research is conducted in collaboration with many reputable national and international institutions.

The facilities at SACEMA are very impressive and conducive to the production of excellent research and training. However, as SACEMA expands over the next few years, additional infrastructure will be needed for lectures, seminars and offices for students and visitors.

2. Student training and capacity building is excellent as noted above. SACEMA has come very close to meeting the Service Level Agreement targets in terms of number of students and addressing the gender and race issues. They are to be congratulated on this achievement. The atmosphere at SACEMA is very collegial and the students interviewed were extremely positive about their environment and the support given to them by SACEMA. However, there is a clear problem in recruiting qualified South African students and the Director is making a serious effort to create awareness (e.g., conducting workshops and short courses targeting under-graduates, initiating a bio-maths degree programme at Stellenbosch University) within the South African academic community to circumvent this problem.
3. Knowledge sharing and knowledge transfer takes place through seminar series, annual research meetings for SACEMA associates, production of quarterly newsletters which are distributed nationally and internationally. Important activities and research findings are disseminated through press releases via the University media office and items placed on the NRF web site.
4. SACEMA has established an extensive network for research collaboration with major institutions across the nation and internationally. These have resulted in major funding opportunities, joint research activities and training of students through workshops, conferences, short courses and research visits.
5. The ground-breaking work on the impact of male circumcision on HIV control has attracted major international attention. The work on co-infection of HIV and TB is also relevant to South Africa and results have been communicated to the Department of Health. The issue of designing better methods for estimating disease incidence will also assist South Africa's public health authorities in assessing the success of the stated goal of halving new HIV infections by 2012. Collaboration with the Western Cape Department of Health is proving to be extremely fruitful in assessing the impact of ARVs. However, a major constraint to advancing the epidemiological knowledge of transmission dynamics of HIV/AIDS and TB is the lack of access to data held by the National Department of Health.
6. SACEMA is very well managed and progress has been good despite difficulties in recruiting quality students, qualified staff and access to relevant epidemiological data. The Director is a very well-respected academic with international standing and with sound inter-personal and management skills.
7. Due to the highly inter-disciplinary nature of the research activities at SACEMA and variable background of SACEMA students in mathematics and biomedical sciences, it is essential that targeted extended courses are offered at SACEMA on the biology (epidemiology, immunology etc.) of the diseases

being studied as well as in some advanced but relevant mathematical and statistical disciplines.

RECOMMENDATIONS

1. In addressing the issue raised in point 5 above, the panel recommends that the leadership of the DST should liaise with the National Department of Health (DoH) to encourage collaboration with SACEMA to the mutual benefit of both departments. It is to the advantage of everyone that the large databases in the possession of the DoH are shared and that the skills available at SACEMA are used to the full in providing the DoH with accurate estimates of HIV incidence that in turn, will inform policy making on designing strategies for achieving South Africa's goal of halving HIV incidence by 2012.
2. Formal collaboration with the National Institute for Communicable Diseases (NICD) should be established to promote data-sharing and build capacity in research on HIV/AIDS, TB and malaria. The NICD currently lacks modelling and statistical skills in its Epidemiology Division. Collaboration with SACEMA would clearly be synergistic and advantageous to all. The benefits of such a formal collaboration to the Department of Health, in addition to receiving advanced data analysis of the samples processed by the NICD, are immeasurable.
3. The issues of staffing and succession planning need to be addressed urgently. Currently, SACEMA has one scientist in Stellenbosch (the Director) and another based at Wits University (Dr. Alex Welte). At least one additional staff member should be appointed at the senior scientist level to be based in Stellenbosch. This person's role should be primarily research and over-seeing post-graduate training, and should also relieve the Director of some administrative responsibilities. Short-term (6 months) and long-term (1-2 years, e.g. for someone on sabbatical) contracts could be offered to international experts.
4. One way of addressing the staffing problem at SACEMA is to encourage the remote mentoring of post-doctoral fellows and graduate students by experts in the various areas. In this respect, the panel strongly recommends that the DST/NRF provide support to set up video conferencing facilities at SACEMA. This will facilitate interactions with students situated away from the SACEMA campus, as well as with SACEMA's collaborators in international and local institutions.
5. Targeted short courses should be given to provide broad background information on biology (e.g., immunology, epidemiology, parasitology) and mathematics (e.g., dynamical systems, advanced linear algebra, computational mathematics, statistical methods and optimization). This is necessary for a successful inter-disciplinary programme. Video-conferencing could help facilitate this. SACEMA should encourage its students to spend time with practicing biologists in their labs to better equip them with the biological insight they need for effective modelling.

6. The under-graduate workshop currently offered is a good way of promoting SACEMA and mathematical modelling in South Africa. It may be a good idea to expand this to include offering internships to high school and under-graduate students to work on projects with SACEMA students. SACEMA could also increase awareness amongst the public health people by giving seminars and workshops on the relevance of modelling to disease prevention and control.
7. SACEMA should continue with its spirited efforts to attract more South African students into mathematical modelling of diseases. It should devise an effective outreach strategy, particularly targeting black students. The panel has the view that the recent proposal, by a review panel for mathematical sciences in South Africa, to set up a national centre for mathematics in South Africa would undoubtedly help SACEMA achieve its objective of attracting more qualified South African students.
8. A new 5-year strategic plan for SACEMA should be drawn up within the near future to provide a detailed roadmap for SACEMA's growth and sustainability. This is necessary considering the fact that SACEMA's progress over the last three years has been phenomenal and has opened up new directions for research in this field.

APPENDIX 1

Review of the DST/NRF Centre of Excellence in Epidemiological Modelling and Analysis (SACEMA): List of interviewees

Briefing by representatives of the National Research Foundation

Dr Andrew Kaniki, Executive Director: Knowledge Fields Development
Ms Anke Rädcl, Professional Officer

Director of SACEMA

Professor John Hargrove

SACEMA team members / Staff

Dr Alex Welte: Research Fellow, Lead consultant: CIDA project
Dr Pieter Uys: Researcher
Ms Lynnemore Scheepers, Research Manager

SACEMA post-docs and PhD students

Dr Farai Nyabadza: Postdoctoral Fellow
Dr Simon Childs: Postdoctoral Fellow
Mr Carel Pretorius: PhD student, Stellenbosch University (SU)
Mr Joseph Ssebuliba: PhD student, SU
Dr Wim Delva: PhD student, University of Ghent
Mr Kazeem Okosun, PhD student, University of the Western Cape

SACEMA MSc students

Ms Bilkisu Abdulra'uf Bello, SU
Ms Geomira Sanga, SU
Ms Doreen Mbabazi, SU
Mr Bewketu Bekele, SU

External stakeholders

Dr Keren Middelkoop: Senior Investigator: Desmond Tutu HIV Centre
Prof Nulda Beyers: Director: Desmond Tutu TB Centre
Prof Abdalla Latif: Onderstepoort Veterinary Institute
Prof Wolfgang Preiser: Head: Division of Medical Virology, SU

SACEMA Board members

Prof Eugene Cloete: Dean of Science SU
Prof Doug Rawlings: previous Interim Dean of Science SU and previous Acting Board Chair
Prof Carl Lombard: Member of SACEMA Board and SACEMA Trust

Prof Fritz Hahne: Director: African Institute of Mathematical Sciences
Prof Bernard Lategaan: ex- Director: Stellenbosch Institute for Advanced Study
Prof Barry Green: Head: Mathematics Department SU,
Prof Fred Roberts: Director: DIMACS, Rutgers University (via teleconference)

APPENDIX 2

SACEMA PUBLICATIONS 2006 - 2008

HIV at molecular and cellular level

1. Ouifki, R. & Witten, G. (2007) Stability analysis of a model for HIV infection with RTI and three intracellular delays. *BioSystems* doi:10.1016/j.biosystems.2008.05.027
2. Shiri, T. & Welte, A. (2008) Transient antiretroviral therapy selecting for common HIV-1 mutations substantially accelerates the appearance of rare mutations. To appear in *Theoretical Biology and Medical Modelling* **5**, 25 doi:10.1186/1742-4682-5-25
3. Ouifki, R. Welte, A. & Pretorius, C. (2008) A model of HIV infection with two viral strains and cytotoxic T-lymphocyte response under structured treatment interruptions. *South African Journal of Science* **104**, 216-220 (2008).

Male circumcision

4. Williams, B.G., Lloyd-Smith, J.O., Gouws, E., Hankins, C., Getz, W.M., Hargrove, J.W., de Zoysa, I., Dye, C. Auvert, B. (2006) The potential impact of male circumcision on HIV in sub-Saharan Africa. *PLoS Medicine* **3**, e262.

Association between HSV2 and HIV

5. Cowan, F.M., Pascoe, S.J.S., Barlow, K.L., Langhaug, L.F., Jaffar, S., Hargrove, J.W., Robinson, N.J., Latif, A.S., Bassett, M.T., Wilson, D., Brown, D.W.G., & Hayes, R.J. (2006) Association of genital shedding of herpes simplex virus type 2 and HIV-1 among sex workers in rural Zimbabwe. *AIDS* **20**, 261-268.

HIV prevalence

6. Mahomva, A., Greby, S., Dube, S., Mugurungi, O., Hargrove, J., Rosen, D., Dehne, K-L., Gregson, S., StLouis, M., Hader, S. (2006) HIV prevalence and trends from data in Zimbabwe, 1997-2004. *Sexually Transmitted Infections* **82**, (Supplement STI): i42-i47
7. Humphrey, J.H., Nathoo, K.J., Hargrove, J.W., Iliff, P.J., Mutasa, K., Moulton, L.H., Chidawanyika, H., Malaba, L.C., Zijenah, L.S., Zvandasara, P., Ntozini, R., Zunguza, C.D., Ward, B.J. & ZVITAMBO study group. (2007) HIV-1 and HIV-2 prevalence and associated risk factors among postnatal women in Harare, Zimbabwe. *Epidemiology and Infection* **135**, 933-942.
8. Hargrove, J.W., Williams, B.G. (2007) Income inequality and HIV prevalence. Response to: Piot P, Greener R, Russell S. Squaring the circle: AIDS, poverty and human development. *PLoS Medicine* **4(10)**, e314.
9. Tavengwa, N.V., Piwoz, E.G., Iliff, P.J., Moulton, L.H., Zunguza, C.D., Nathoo, K.J., Hargrove, J.W., ZVITAMBO study group & Humphrey, J.H. (2007) Adoption of safer infant feeding and postpartum sexual practices and their relationship to maternal HIV

status and risk of acquiring HIV in Zimbabwe. *Tropical Medicine and International Health* **12(1)**, 97-106.

10. Hargrove, J. (2008) Migration, mines and mores: the HIV epidemic in southern Africa. *South African Journal of Science* **104**,53-61

HIV incidence

11. Humphrey, J.H., Hargrove, J.W., Malaba, L.C., Iliff, P.J., Moulton, L.H., Mutasa, K., Zvandasara, P., Nathoo, K.J., Mzengeza, F., Chidawanyika, H., Zijenah, L.S., Zunguza, C.D., Ward, B.J. & the ZVITAMBO Study Group. (2006) HIV incidence among post-partum women in Zimbabwe: risk factors and the effect of vitamin A supplementation. *AIDS* **20**, 1437-1446.
12. Welte, A. (2008) Relating Incidence to 'Recent Infection' Prevalence: Application to HIV. *South African Journal of Science* **104**, 199-202.
13. Welte, A., McWalter, T.A. & Barnighausen, T. (2008) A Simplified Formula for Inferring HIV Incidence from Cross-Sectional Surveys Using a Test for Recent Infection. *AIDS Research and Human Retroviruses* (accepted).

HIV mortality

14. Zvandasara, P., Hargrove, J.W., Ntozini, R., Chidawanyika, H., Mutasa, K., Iliff, P.J., Moulton, L.H., Mzengeza, F., Malaba, L.C., Ward, B.J., Nathoo, K.J., Zijenah, L.S., Mbizvo, M., Zunguza, C., Humphrey, J.H. & the ZVITAMBO Study Group (2006) Mortality and morbidity among post-partum HIV-positive and HIV-negative women in Zimbabwe: risk factors, causes, and impact of single-dose postpartum vitamin A supplementation. *Journal of Acquired Immune Deficiency Syndrome* **43**, 107-116.

Genetics of HIV

15. Lajoie, J., Hargrove, J.W., Zijenah, L.S., Humphrey, J.H., Ward, B.J. & Roger, M. (2006) Genetic variants in non-classical MHC class I HLA-E and HLA-G molecules are associated with risk of heterosexual HIV-1 infection. *Journal of Infectious Diseases* **193**, 298-301.

Estimating incidence: BED

16. Barnighausen, T., Wallrauch, C., Welte, A., McWalter, T.A., Mbizana, N., et al. (2008) HIV Incidence in Rural South Africa: Comparison of Estimates from Longitudinal Surveillance and Cross-Sectional cBED Assay Testing. *PLoS ONE* **3(11)**, e3640. doi:10.1371/journal.pone.0003640
17. Hargrove, J.W., Humphrey, J.H., Mutasa, K., Parekh, B.S., McDougal, J.S., Ntozini, R., Chidawanyika, H., Moulton, L.H., Ward, B., Nathoo, K., Iliff, P.J., Kopp, E. & the ZVITAMBO Study Group. (2008) Improved HIV-1 incidence estimates using the BED capture enzyme immunoassay. *AIDS* **22**, 511-518.

Malaria and mosquito population modelling

18. Torr, S.J., Della Torre, A., Calzetta, M., Costantini, C., Vale, G.A. (2008) Towards a fuller understanding of mosquito behaviour: use of electrocuting grids to compare the odour-orientated response of *Anopheles Arabiensis* and *An quadriannulatus* in the field. *Medical and Veterinary Entomology* **22**,93-108
19. Nyabadza, F. (2008) Modelling the role of prophylaxis in malaria prevention. *International Journal of Biological and Medical Sciences* **1(1)**,18-23

Tsetse and trypanosomiasis

20. Bett, B, Randolph, T.F., Kitala, P., Gathuma, J., Hargrove, J., Vale, G., McDermott, J. Using a mathematical model to predict the impact of a synthetic tsetse repellent on trypanosomosis transmission in cattle when used alone or in integrated strategies. Proceedings of the International Scientific Council for Trypanosomiasis Research and Control (ISCTRC) Luanda, Angola, 1-5 October, 2007 (in press).
21. Bett, B., Randolph, T.F., Irungu, P., Nyamwaro, S., Murilla, G., Kitala, P., Gathuma, J., Hargrove, J., Vale, G., McDermott, J. An assessment of the impact of a synthetic tsetse repellent technology on the incidence of trypanosomosis in cattle managed under pastoral production systems in Kenya. Proceedings of the International Scientific Council for Trypanosomiasis Research and Control (ISCTRC) Luanda, Angola, 1-5 October, 2007 (in press).

HIV and TB

22. Magombedze, G., Garira, W., Mwenje, E. (2006) Modelling the human immune response to mycobacterium tuberculosis in the lungs. *Journal of Mathematical Biosciences and Engineering* **3(4)**, 661-682.
23. Magombedze, G., Garira, W., Mwenje, E. (2006) Mathematical modelling of chemotherapy of human TB infection. *Journal of Biomedical Systems* **14(4)**, 509-553.
24. Magombedze, G., Garira, W., Mwenje, E. (2007) In-vivo mathematical study of co-infection dynamics of HIV-1 and Mycobacterium Tuberculosis. *Journal of Biological Systems* (accepted).
25. Bacaer, N., Ouifki, R., Pretorius, C., Wood, R. & Williams, B. (2008) Modeling the joint epidemics of TB and HIV in a South African township. *Journal of Mathematical Biology* **57(4)**, 557-593.

HIV and drug therapy

26. Kgosimore, M. & Lungu, E.M. (2006) The effects of vertical transmission on the spread of HIV/AIDS in the presence of treatment. *Mathematical Biosciences and Engineering* **3(2)**, 297-312.
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2. Ouifki, R., Welte, A. & Pretorius, C. A model for the interaction between the immune system and two strains of HIV with Structured Treatment Interruptions. *Presented at the Conference on Biomathematics in Africa, 23-26 January 2007. University of Cape Town, Cape Town, South Africa.* <http://www.mth.uct.ac.za/Biomaths/2007/>
3. Welte, A & Walwyn, D. Mathematical Modelling of Acute Infection: What Can it Tell Us About the Challenges of Vaccine Design? *Poster presented at the International AIDS Vaccine Conference, Cape Town, 13-16 October 2008.*
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- 8.** Bacaër, N., Ouifki, R., Pretorius, C. & Wood, R. Modelling the joint epidemics of TB and HIV in a peri-urban community in South Africa: what are the prospects for control? *Presented at 38th Union World Conference on Lung Health, 8-2 November 2007, Cape Town, South Africa.* <http://www.worldlunghealth.org/Conf2007/website2/>
- 9.** Lungu, E. Anti-tuberculosis resistance in patients co-infected with HIV and TV. *Paper presented at CMS-MITACS joint conference, 31 May – 3 June 2007, University of Manitoba, Winnipeg, Canada.*
- 10.** Lungu, E.M., Kgosimore, M. & Nyabadza, F. HIV – TB Model: The Botswana experience. *Paper presented at Modelling diseases in Africa workshop, 25-27 June 2007, Stellenbosch, South Africa.*
- 11.** Lungu, E.M., Kgosimore, M. & Nyabadza, F. HIV – TB Co-infection model in the presence of TB drug resistance. *Paper presented at MITACS workshop, 30 May - 3 June 2007 Winnipeg, Manitoba, Canada.*
- 12.** Lungu, E.M., Kgosimore, M. & Nyabadza, F. Treatment of HIV/AIDS with imperfect drugs and behavioural implications. *Paper presented at South African Mathematical Sciences conference, 26 November – 3 December 2007, Windhoek, Namibia.*
- 13.** Lungu, E.M. & Chigidi, E. Modeling HIV/AIDS with treatment. *Paper presented at Africa Canada summer school, 19 – 29 August 2008, University of Botswana, Gaborone, Botswana.*
- 14.** Chigidi, E. & Lungu, E.M. Modeling HIV/AIDS with treatment in the presence of drug resistance. *Paper presented at Africa Canada summer school, 19 – 29 August 2008, University of Botswana, Gaborone, Botswana.*
- 15.** Nyabadza, F. Can we learn from animal adaptations in HIV prevention? *Proceedings of the Southern Africa Mathematical Sciences Association (SAMSA) Conference, Windhoek, Namibia, 27-30 November, 2007.*
- 16.** Koga, E. & Lungu, E.M. A Reaction-Diffusion model for transport related diseases. *Paper presented at Africa Canada summer school, 19 – 29 August 2008, University of Botswana, Gaborone, Botswana.*
- 17.** Uys, P. A threshold value for the time delay to TB diagnosis. *Poster presented at the 38th Union World Conference on Lung Health, 8-12 November 2007, Cape Town, South Africa.*
- 18.** Uys, P.W. Delays in diagnosing TB: Causes and Consequences. *Paper presented at the 38th Union World Conference on Lung Health, 8-12 November 2007, Cape Town, South Africa.*
- 19.** Ouifki, R. & Pakdaman, K. Small delays induced oscillations for a class of differential equations with state dependent delay. *Paper presented at the Marrakesh International Conference and Workshop on Mathematical Biology, January, 3-8, 2008, Marrakesh, Morocco.* <http://euromedbiomath.free.fr/m2008/>

Appendix 3.

Summary of the research areas in which SACEMA has been involved. This includes an indication of the relevant projects pursued within those areas. Shaded cells indicate student (MSc or PhD) projects

Area of study	Project participants (shaded projects are student degree studies)	Activities
HIV/AIDS		
Surveillance tools	J. Hargrove(SACEMA) W. Preiser (Medical Virology, Stellenbosch University), <i>et al.</i>	Development of BED method for estimating HIV incidence
	A. Welte (SACEMA and School of Computational & Applied Maths, Wits University) T. McWalter (School of Computational & Applied Maths, Wits University)	Theoretical development of general methods for estimating incidence from cross-sectional surveys
	E. Marinda (School of Public Health, Wits University) J. Levine (Medical Research Council, Uganda) L. Moulton (School of Medicine, Johns Hopkins University, Maryland, USA)	Understanding the BED Capture Enzyme Immunoassay (CEIA): Measuring HIV-1 Incidence in Cross-Sectional studies
	R. Sewpaul (School of Statistics & Actuarial Science, UKZN) H. Mwambi (School of Statistics & Actuarial Science, UKZN)	Estimate age and time incidence of HIV infection in childbearing women using serial prevalence data from KwaZulu-Natal
Population level analysis	J. Hargrove (SACEMA) B. Williams (WHO, Geneva)	Trends in HIV incidence, prevalence, mortality in Zimbabwe.
	J. Hargrove(SACEMA) T. Porco (Francis I. Proctor Foundation for Research in Ophthalmology, Dept of Epidemiology and Biostatistics, University of California).	Age-structured model for changes in HIV prevalence among ANC attendees in Harare.
	J. Hargrove (SACEMA)	Analysis of roots of heterogeneity in HIV prevalence in African nations.
	R. Ouifki (SACEMA) F. Nyabadza (SACEMA)	HIV model structured by CD4 count and WHO stages.
	S. Woldeesenbet (School of Public Health, UWC) D. Jackson (School of Public Health, UWC)	Modelling effects of infant feeding strategies on HIV free infant survival and MtC transmission rates
	P. Kruger (Dept. Statistics & Actuarial Science, Stellenbosch University) A. Neethling (Dept. Statistics & Actuarial Science, Stellenbosch University)	An investigation of sequential/ adaptive sampling techniques applied to North West Univ's HIV/AIDS project
	R. Kuo (School of Statistics & Actuarial Science, UKZN) G. Matthews (School of Statistics & Actuarial Science, UKZN)	Statistical HIV modelling in the presence of missing data
	M. Maskew (Dept. of Medicine, Wits)	Simplification of treatment monitoring

	University) M. Fox (School of Public Health, Boston University, USA)	strategies in HIV-infected patients on antiretroviral therapy in SA
	J. Ramjith (School of Statistics & Actuarial Science, UKZN) G. Matthews (School of Statistics & Actuarial Science, UKZN)	Applying survival analysis models to CAPRISA data
	M. Kamupira (School of Public Health, UCT) L. Myer (School of Public Health, UCT)	DYAD-related factors in HIV prevention
Cellular/molecular modelling	T. Shiri (School of Computational & Applied Maths, Wits University) A. Welte (SACEMA and School of Computational & Applied Maths, Wits University)	In-vivo viral strain dynamics relating to drug resistance in HIV infection
	J. R-Ratsimihah (Institute of Infectious Disease and Molecular Medicine, UCT) C. Seiohge (Institute of Infectious Disease and Molecular Medicine, UCT)	Modelling HIV-1 escape from CTL responses
	K. Cawse (School of Computational & Applied Maths, Wits University) D. Sherwell (School of Computational & Applied Maths, Wits University)	A new model of population dynamics of HIV-1 strains in vivo
	J. SSebuliba (SACEMA) R. Ouifki (SACEMA) F. Nyabadza (SACEMA)	Modelling host-viral dynamics
	G. Mwanga (School of Computational & Applied Maths, Wits University) A. Welte (SACEMA and School of Computational & Applied Maths, Wits University)	Dynamical Models of Acute HIV Infection: Application to Interpretation of Seronegativity/RNA-Positivity Survey Data to Estimate HIV Incidence.
	C. Pretorius (SACEMA) A. Welte (SACEMA and School of Computational & Applied Maths, Wits University)	Investigating viral parameter dependence on cell and viral life cycle assumptions.
Male circumcision (MC)	B. Auvert (University of Paris) & SACEMA	Operationalising MC in South Africa
Microbicide modelling	W. Delva (University of Ghent, Belgium) M. Temmerman & S. Van Steelandt (UG)	Modelling microbicide impact on HIV in Kenya
Tuberculosis		
Community level modelling	A. Welte (SACEMA and School of Computational & Applied Maths, Wits University) C. Pretorius (SACEMA)	Microsimulation modelling of Masiphumelele data (HIVMM).
	F. Nyabadza (SACEMA) R. Ouifki (SACEMA)	Paediatric TB modelling.
	B. Bekele (SACEMA) F. Nyabadza (SACEMA)	Modelling Tuberculosis Dynamics in children and adults.
	R. Dunbar (Desmond Tutu TB Centre) F. Nyabadza (SACEMA)	Modelling of Ravensmead/Uitsig data

Modelling diagnosis/treatment	P. Uys (SACEMA)	Effects of delays in TB diagnosis and treatment
	G. Magomedze (Dept. Applied Mathematics, National University of Science & Technology, Zimbabwe) W. Garira (Dept. Applied Mathematics, National University of Science & Technology, Zimbabwe)	Modelling pathogenesis of Mycobacterium tuberculosis infection and treatment
	P. Uys (SACEMA)	Analysis and modelling of changing CD4 levels during antiretroviral therapy
TB and HIV co-modelling		
	M. Maba (Dept. of Mathematics, UKZN, Durban) P. Leach (Dept. of Mathematics, UKZN, Durban)	Statistical modelling to understand the complex relationship between HIV and TB
	T. Mzolo (Dept. of Mathematics, UKZN, Pietermaritzburg) H. Mwambi (Dept. of Mathematics, UKZN, Pietermaritzburg)	TB and HIV: Singularity and Symmetry analyses
	D. Kajunguri (SACEMA) F. Nyabadza (SACEMA) R. Ouifki (SACEMA)	HIV-TB co-infection.
	N. Bacaer (IRD, Paris, France) R. Ouifki (SACEMA) C. Pretorius (SACEMA)	Modelling the joint epidemics of TB and HIV in a South African township: Prospects for control.
	D. Mbabazi (SACEMA) R. Ouifki (SACEMA)	Modelling the joint epidemics of TB and HIV; the effect of exogenous reinfection.
	G. Sanga (SACEMA) F. Nyabadza (SACEMA)	Modelling the Detection and Delayed Treatment on Tuberculosis Dynamics.
	B. Abdulra'uf Bello (SACEMA) B. van der Ventel (Physics Dept. Stellenbosch University)	Theoretical modelling of drug-resistant HIV.
Malaria		
Population level modelling	G. Vale (Natural Resources Institute, University of Greenwich, UK)	Modelling malaria and mosquito population dynamics
	T. Marijani (SACEMA) E. Lungu (University of Botswana, Gaborone)	Modelling the role of immunity on the spread of malaria
Trypanosomiasis		
Tsetse population dynamics	J. Hargrove (SACEMA)	Modelling the dynamics of pupal production and survival.
	S. Childs (SACEMA) J. Hargrove (SACEMA)	Developing joint model for tsetse and trypanosome population dynamics.
	J. Hargrove (SACEMA) S. Childs (SACEMA)	General theory for the efficacy of aerial spraying of tsetse
	J. Hargrove (SACEMA) S. Chown (CIB, Stellenbosch University)	Modelling the responses of tsetse to climate change

	J. Terblanche (Dept. of Entomology, Stellenbosch University)	
African Horse Sickness	G. Vale (Natural Resources Institute, University of Greenwich, UK) & OVI	Development of electrocuting devices for sampling Culicoides
General population analysis	B. Sartorius (School of Public Health, Wits University) K. Kahn (MRC/Wits Rural Public Health & Health Transitions Research Unit, School of Public Health, Wits University)	Spatio-temporal patterns of mortality in rural north-east South Africa
Distributed Computing (BOINC)	C. Pretorius (SACEMA) R. Mateer (SACEMA)	Development of BOINC portal for HIVMM
Mathematical modelling and analysis of gene regulatory networks	R.Ouifki (SACEMA) [with K. Pakdaman and others]	Mathematical modelling and analysis of systems with delay: gene regulation and transition regime in neural networks
Delay differential equations	R.Ouifki (SACEMA) [with K. Pakdaman & others]	Mathematical analysis of the effect of small delays on: (i) dynamics of differential systems (ii) harmonic oscillators
Statistical development	C. Muller (Dept. Statistics & Actuarial Science, Stellenbosch University) P. Mostert (Dept. Statistics & Actuarial Science, Stellenbosch University)	Biostatistical studies