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

Director (outgoing): Professor John Hargrove (jhargrove@sun.ac.za)
Director (Incoming): Dr Alex Welte (Alex.Welte@wits.ac.za)
Research Manager: Ms Lynnemore Scheepers (scheepersl@sun.ac.za)
Administration: Mrs Natalie Roman (nroman@sun.ac.za)
Tel: +27 21 808 2589/2893 Fax: +27 21 808 2586
Mailing address: Private Bag X1, Matieland 7602, South Africa
Web site: http:www.sacema.ac.za Epidemiological update: www.sacemaquarterly.com

SACEMA NEWSLETTER
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The new decade is unfolding. The Director, staff and students of SACEMA would like to wish our friends and colleagues a very prosperous 2010 and hope that fruitful collaboration will continue to grow.

NEWS:

RESEARCH GRANT FOR RESEARCH ON AGE MIXING PATTERNS AND THE SPREAD OF HIV

The European Society of Contraception and Reproductive Health (ESC) has approved a research grant for the project **"Age disparate relationships, condom use and the spread of HIV among young men and women in Cape Town, South Africa"**.
The study will be conducted as a joint collaboration between SACEMA and Ghent University, and will address the following key questions:

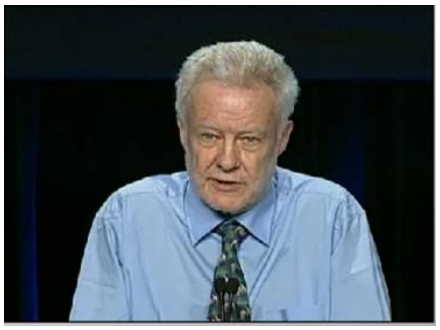
- What is the average age difference between male and female sexual partners?
- What is the variability around this mean age difference?
- Are larger age differences between the male and female sexual partner associated with (a) lower levels of condom use and (b) higher number of annual and life time sexual partners?
- Is condom use decreasing as a function of (a) age and (b) the duration of the relationship?

To this end, a detailed statistical analysis of age mixing patterns, condom use and partner exchange rate from the Cape Area Panel Study (CAPS) will be performed. Specifically, linear and non-linear mixed-effects models with hetero-skedastic errors will be fitted to the CAPS data.
Next, the effect of the observed patterns of age mixing and condom use on the spread of HIV will be assessed using the SIMPACT simulation software. SIMPACT is a new software package developed by

the International Centre for Reproductive Health at Ghent University in collaboration with SACEMA. It uses demographical, behavioural, epidemiological and clinical data to simulate the spread of HIV in the population and the expected impact of different HIV prevention and HIV treatment strategies. By simulating the HIV epidemic under the age mixing and condom use patterns observed in CAPS, compared to less disparate age mixing patterns described elsewhere, SIMPACT is able to "single out" the effect and importance of age disparate relationships and associated risk factors on the spread of HIV.

SACEMA'S PROFESSOR BRIAN WILLIAMS MAKES MAJOR PRESENTATION AT CROI CONFERENCE

On February 16th 2010 in San Francisco, Prof Brian Williams gave a presentation entitled, "Put Your Money Where Your Model Is: ART for the Prevention and Treatment of HIV/AIDS", as part of the 17th CROI (Conference on Retroviruses and Opportunistic Infections) conference (16-19 February 2010).



The big question at hand, as Brian formulated it, is: "Can we use treatment for prevention, not just for survival?" In his presentation, Brian referred to the arguments of David Ho (1995) and Julio Montaner et *al*. (2006), both of whom tried to answer this very question. In 1995 David Ho argued that, in the interest of the individual patient, HIV should be hit early and hard. With "hitting early" David meant that ART is to be started within one year of sero-conversion. This would reduce the likelihood that the infected person will develop resistant strains of the virus and ensure that the virus does not cause significant damage to the immune system before treatment is started. In 2006, Julio Montaner and his group argued that not only could ART be potentially useful for the individual patient but it might be possible to use highly active anti-retroviral treatment to curb the growth of the HIV epidemic and even to eliminate it. David Ho and Julio Montaner therefore both supported the argument that HIV should be hit early and hard, they were just driven by different end-goals. Brian expressed regret that David Ho's advice was not followed back in 1995, since according to the model the lives of 2 million people would have been saved by now.

Currently the World Health Organisation (WHO) recommends starting ART at a CD4 count of 350 per micro-litre. At present South Africa has a prevalence of about 16 percent and incidence and mortality between 1 and 2 percent. The average HIV infected person infects about 7 others in his/her infectious period. This means that if transmission is reduced by 7 times, HIV should be eliminated. If the current strategy regarding ART is not changed, then according to Brian there is every reason to believe that everything will go on much as it is at present. If, however, from this year, everybody is tested for HIV once a year on average and antiretroviral treatment is started as soon as somebody is found to be HIV positive, then there is every reason to believe that transmission could be stopped and incidence be brought close to zero within 5 years. If this strategy, called "Test and Treat", is followed, mortality will be reduced to very low levels.

The natural question to ask next is: if antiretroviral therapy is going to be given to people infected with HIV in the hopes of suppressing their viral load, keeping them alive and reduce their infectivity, why not give people ART before they get infected? This is the rationale behind PrEP, Pre-Exposure Prophylaxis, whereby which all HIV negative people are put on ART. In order to compare PrEP with Test and Treat, it is assumed that we have universal coverage and complete protection. In the long term PrEP does rather better than Test and Treat in reducing HIV prevalence but that is only because people already infected with HIV are not treated and therefore left to die from HIV. This way people already infected with HIV are cleared out of the way more quickly which makes the results of PrEP

appear better in the long term. This, however, is completely unethical. Leaving HIV infected people untreated also cause the number of people that will die under PREP to be larger than the number of people that will die under Test and Treat. In order to obtain the best result, PrEP should be combined with Test and Treat. Brian suggested that ART be given as prophylaxis (PrEP) to high risk groups as well as to younger people in high prevalence settings and that the Test and Treat methodology, whereby which individuals are tested once a year and put on ART as soon as they are found to be HIV positive, should be followed in low prevalence settings as well as be applied to older people in high prevalence settings.

A study conducted in Harare in 1997-2000 involving about 14 000 postpartum women confirmed that, at least in the case of postpartum women, it is in the interest of the individual patient to start ART as soon as the patient is found to be HIV positive. In the study mortality for one year was measured against the CD4 count of the women participating in the study. It was found that postpartum women infected with HIV with a CD4 count of 1000 are still almost 4 times more likely to die than postpartum women who are HIV negative. Also, no matter how high your CD4 count is, you are at least 2.5 times as likely to die as an HIV negative postpartum woman. The conclusion was that postpartum women who are HIV positive are at much greater risk of dying than HIV negative postpartum women, even if they have very high CD4 counts, and should therefore be offered ART. Bearing in mind the most important directive in the Hippocratic Oath, “first do no harm”, it is clear that these women should be started on ART immediately and kept on ART for life.

There are also side benefits to hitting HIV early and hard. Most people do not die of HIV but of the opportunistic infections like TB which they get as a consequence of having HIV. Before HIV came along there were about 200 TB cases per 100 000 people in South Africa. HIV has driven this number up by a factor of 3. There is reason to believe that ART will reduce TB transmission by about 60 percent. Hence, if universal coverage is achieved there will be a significant reduction in TB.

One of the possible arguments against the use of ART for prevention by means of interventions like Test and Treat and PrEP, is the resulting cost. The sooner treatment is started, the more person-years there will be to deal with. If people are put on ART immediately, then many more people will need to be put onto ART in the next 40 years. This will, however, according to the model, save about 3 million lives. Even though it seems natural that using ART for prevention would be much more expensive than the current policy, the model suggests that combining the Test and Treat methodology with PrEP will require a large initial investment, but in the long term will have roughly the same cost implications as the current policy. Cost is therefore not the limiting issue. Two other issues which must be considered when looking at the counter-arguments for Test and Treat, are drug resistance and acceptability. Brian believes that drug resistance is important and should be monitored, but should not stop Test and Treat from being implemented. Based on a study conducted in Kenya where 41 000 people volunteered to be tested, given that the test was free of charge and that they were provided with a free bed-net and a free drinking-straw, Brian is positive that if ART is offered to people they will accept it. According to Brian, the real problem is mobilisation of health systems: “if we were going to do this, could we actually get the drugs out there, provide the services, do the monitoring and do the follow-up?”

Brian concluded his presentation with the prediction of the theoretical model, namely that Test and Treat, possibly in combination with PrEP, could eliminate HIV transmission in 5 to 10 years and HIV infection in 40 years. He reminded everyone that, like every other model, this one also first needs to be tested for its practicality. However, Brian believes that theoretical models carry much weight and concluded his presentation with a quote by Ulanowicz (1988): “If one is caught in a dark maze, it is better to light a candle than to repeatedly walk into the walls. Those who dismiss theoretical models seem concerned with only the darkness and not the maze.”

Brian repeated his presentation at the AAAS (American Association for the Advancement of Science) annual meeting which was held in San Diego this year (18-22 February). As a result of Brian’s

presentations in San Francisco and San Diego SACEMA received a lot of publicity, and the Director gave interviews to a number of local and international radio stations.

A link to the presentation given by Prof Brian Williams is given below:
http://app2.capitalreach.com/esp1204/servlet/tc?c=10164&cn=retro&e=12334&m=1&s=20431&&espmt=2&mp3file=12334&m4bfile=12334&br=80&audio=false
The presentation has also been picked up by the BBC. See the following link:
http://news.bbc.co.uk/2/hi/science/nature/8526690.stm

SACEMA STUDENTS
March 2010 MSc and PhD Graduates

We are pleased to announce that the following SACEMA-supported students graduated in March 2010:

Doreen Mbabazi obtained an MSc from the University of Stellenbosch under the supervision of Dr Rachid Ouifki. Her thesis was entitled "Modelling Mixed Infection in TB and TB-HIV Co-infection". Doreen has already started her PhD studies at SACEMA. She will be working on the cost-effectiveness of interventions regarding HIV, TB and Malaria under the supervision of Dr Rachid Ouifki.

Bewketu Teshale Bekele obtained an MSc

from the University of Stellenbosch under the supervision of Dr Farai Nyabadza and Dr Rachid Ouifki. His thesis was entitled "Modelling Tuberculosis Transmission Dynamics in Children and Adults in the Presence of Vaccination". Bewketu has already started his PhD studies at SACEMA. He will be working on modelling the potential impact of early HIV treatment on the HIV and TB epidemics in South Africa under the supervision of Dr Rachid Ouifki.

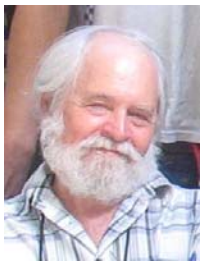
Doreen Mbabazi and Bewketu Teshale Bekele both got distinctions for their MSc's. We congratulate them on this wonderful achievement. They have also started their PhD studies at SACEMA.

Jordache Ramjith obtained an MSc from the University of Kwazulu Natal under the supervision of Prof Glenda Matthews. His thesis was entitled "Modelling survival data".

Geomira Sanga obtained an MSc from the University of Stellenbosch under the supervision of Dr Farai Nyabadza and Dr Aziz Ouhinou. Her thesis was entitled "Mathematical Modelling of the Impact of Undiagnosed and Diagnosed Untreated Infectious Individuals on Tuberculosis Dynamics".

We wish these students all the best with their future endeavours.

NEW FACES AT SACEMA



Following the NRF Review in February 2009, in which it was recognised that the SACEMA Director needed support to oversee the vital area of capacity building and postgraduate training, an experienced University teacher and educational consultant, Dr Gavin Hitchcock, was invited to visit SACEMA for a month to evaluate the whole training enterprise and give direction in capacity-building. After observing the working life of the SACEMA community, and interviewing students, staff, supervisors and associates, Dr Hitchcock submitted a report in July 2009. In view of the urgency of some of his recommendations, Dr Hitchcock was invited as Academic Visitor to SACEMA for six months, January to June 2010, to initiate implementation, and to prepare the way for a permanent Training person. In the first three months, he has been involved in organising courses, lectures, seminar series, research days and workshops, designing future research initiation programmes, and re-thinking overall strategy for student admissions, supervision and evaluation.

Hayden Eastwood, a Post Doc, joined SACEMA in January. He obtained his PhD from University of Edinburgh at the end of 2008. He will be working on estimating HIV incidence using the BED method.

Damian joined SACEMA in January as a new PhD student. He was an in-house SACEMA student in 2007 and 2008 and obtained his MSc in December 2008. He will be working on his PhD with Dr Rachid Ouifki and Prof John Hargrove on modelling the control of tsetse and African trypanosomiasis through insecticide treated cattle in South-Eastern Uganda**.**

Lynnemore Scheepers, SACEMA's Research Manager is currently on maternity leave. SACEMA congratulates Lynnemore on the birth of her son, Logan.

Hilmarié Brand, a Mathematical Statistics Masters student at the University of Stellenbosch joined SACEMA in February as acting Research Manager, standing in for Lynnemore Scheepers, until the end of June.

EVENTS:

Maths Social

The annual University of Stellenbosch Mathematics Social was hosted by SACEMA on 5 February in the STIAS garden. Students arrived in mathematically-inspired fancy-dress, and as a recreation the World Cup Dance, the DISKI, was taught to the assembled company by a lady from Stellenbosch Municipality. The Director of SACEMA, John Hargrove, informed the maths students about the work done at SACEMA and gave them a tour of the premises.

Visit from the Minister of DST

On 12 February the Minister of DST, Mrs Naledi Pandor, as well as others from DST, came to visit SACEMA. Prof John Hargrove, Director of SACEMA, welcomed Mrs Pandor to SACEMA and introduced her to the staff and students, who all gathered to meet her. The Director gave the Minister an overview of SACEMA, its founding, its organisational structure, the research being done, and the typical profile of SACEMA-supported Masters and PhD students. He also detailed the organisations, besides the NRF, that are funding SACEMA. The Minister spoke very encouragingly about the work being done at SACEMA, especially on HIV and TB.

The Minister asked whether non-infectious diseases were also being modelled, and showed interest in the studies on Malaria and African Horse Sickness. She asked about progress on capacity building, and the Director outlined steps taken by SACEMA, but explained that, while the SACEMA community was enriched by students from many other African countries, it was not easy to recruit sufficient South Africans. The Minister emphasised how important postgraduate training was to the future of the country, acknowledging the difficulties of finding qualified and talented South Africans for entry into PhD programmes and reaffirming the DST's commitment to addressing this need.

SACEMA Research Days

The annual SACEMA Research Meeting was held at STIAS, Stellenbosch, 9-10 March 2010. At the meeting SACEMA staff and SACEMA-supported students gave presentations on progress made in their research over the past year.

After each presentation, opportunity was given to ask questions. This was beneficial, not only to the listeners in that it gave them the opportunity to gain clarity regarding certain issues, but also to the presenters in that they could be given useful pointers and directed to potential collaborators. The meeting gave students two distinct kinds of opportunity. Firstly, listening to other presentations on research topics similar to their own encouraged them to learn about different ways to tackle the problem at hand. Secondly, by listening to presentations on research topics differing from their own, students' horizons were broadened and they obtained a better understanding and knowledge about the multi-disciplinary field of Epidemiology in general.

In response to feedback regarding Research Meetings held in previous years, the number of social events forming part of the Research Meeting was increased so as to allow more time for students to get to know each other and talk informally about their work. On the evening of the 8th of March all attending the Research Meeting enjoyed snacks in the reception area of the SACEMA office – this served as a nice ice-breaker before the Research Meeting commenced on the morning of the 9th. A braai was held at SACEMA on the evening of the 9th, and the Research Meeting culminated in a lovely dinner at Beads restaurant in Stellenbosch on the 10th.

Overall the Research Meeting was a great success and we thank all who presented for their efforts and enthusiasm.

Management Board Meeting

The SACEMA Management Board meeting was held at the Wallenburg Centre, Stellenbosch on 11 March 2010 at 9am.

Board of Trustees Meeting

The SACEMA Board of Trustees meeting was held at the Wallenburg Centre, Stellenbosch on 11 March 2010 at 2pm.

RESIGNATIONS:

On the 26th of February SACEMA said goodbye to Carel Pretorius who was a member of the SACEMA family for 4 years as well as SACEMA's first in-house PhD. Carel was a valued colleague and a dear friend to many at SACEMA. He will be greatly missed. SACEMA wishes him and his wife, Monica, all the best for their new life in Connecticut, USA.