## SAMA's inward-looking approach to AIDS and ethics

**To the Editor:** Posted together with the February issue of *SAMJ* was a copy of SAMA's *Human Rights and Ethical Guidelines on HIV and AIDS – A Manual for Medical Practitioners*,[1] updating the 2001 edition to reflect changes in the response to the AIDS epidemic in South Africa, notably the increasingly accessible antiretroviral therapy (ART) in the public sector. SAMA seems not to encourage wide dissemination of, and discussion on, its Guidelines.

I moderate an online discussion forum on HIV Policy and Ethics for the Southern African HIV Clinicians Society. A recent case study concerned the thorny ethical issue of whether a surgeon with HIV/AIDS on ART had to disclose her HIV status to her patient after discovering blood on the inside of the first of her double gloves after surgery. I thought it appropriate to refer members of the discussion forum to the Health Professions Council of South Africa (HPCSA) Guidelines on *The Management of Patients with HIV Infection or AIDS*[2] (which replaced the South African Medical and Dental Council (SAMDC) Guidelines of 1994) and SAMA's new Guidelines. While the HPCSA Guidelines can be accessed, the latest SAMA Guidelines cannot be located on the Internet. (The URL on the HPCSA website referring to their Guidelines (http://www.hpcsa.co.za/hpcsa/UserFiles/File/Patient'sRightsCharter.pdf ) did not function at the time of writing, but the Guidelines could be accessed from secondary sources such as http://alp.org.za.dedi20a.your-server.co.za/images/upload/3rdAids%20finalss%20append.pdf (last accessed 29 May 2007)).

I requested, from SAMA's Human Rights, Law and Ethics Department and its Corporate Communications Department, an electronic copy of the Guidelines to post on the discussion forum website. I was informed that only SAMA members could access this on the SAMA website, while a hard copy was available in the *SAMJ*. Not being a SAMA member, a hard copy would cost R120, or alternatively R2 500 for an electronic copy that could be made available to special interest groups as a special concession from SAMA.

SAMA's position on its Guidelines is perplexing. In a devastating AIDS epidemic, it seems elementary that new knowledge, innovative ideas and technological advances are widely shared. While South Africa boasts an impressive legal framework, laws or policy have not adequately addressed every issue pertaining to HIV/AIDS. In lieu of law or policy, lawyers, AIDS organisations and medical practitioners are often guided by standards produced by medical and ethical bodies, which have invested skills and expertise in thinking through some of the complex implications of the epidemic, such as contained in SAMA's latest Guidelines. It follows that it is in the public interest for such documents to be made generally available, and for their use to be encouraged and promoted.

HIV/AIDS is not a purely medical issue, and for its devastating effects to be adequately contained, it is crucial that a wide range of expertise, resources, disciplines and skills are sourced. Restricting SAMA's Guidelines to an exclusive group of members of the Association who are chiefly medical professionals, or to those who can purchase a copy, does an injustice to the Association's approach and commitment to the epidemic. This seems petty and short-sighted, particularly as doctors and medical scientists debate whether it is ethical for access to new knowledge to be limited to paid-up subscribers of major medical journals.[3-5] SAMA's attitude harkens back, damagingly, to closed bureaucracies, institutional possessiveness and competitive small-mindedness. I therefore call on SAMA to seriously review its current position on restricting various documents and Guidelines to its members only, to make the HIV Guidelines freely available on the Internet, and to mail hard copies to all AIDS organisations and community-based organisations that may not have access to the Internet.

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## Pap smears in the Third World

**To the Editor:** A 73-year-old woman presented to the emergency unit at Polokwane Hospital complaining of chronic abdominal pain. When asked whether she had visited a health professional before, she produced an old referral letter from a general practitioner which read: 'It is not possible to do a Pap smear in a Third-World general practice.'

Cervical cancer is the commonest cause of cancer death among women in the developing world.[1] It is the duty and responsibility of every primary health care doctor to be able to assess patients with cervical abnormalities. This is particularly important in developing countries where the incidence of cervical cancer is high, with 30 - 100/100 000 women acquiring the disease.[1]

One of the principles of family medicine is that every consultation should be used as an opportunity for health

promotion and prevention. Failing to do a Pap smear is inexcusable and negligent.

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## Glibenclamide – what dose?

**To the Editor:** Doses of a wide variety of pharmacological agents currently used in clinical practice differ from the doses initially recommended at the time of drug registration.[1] Oral antidiabetic agents, in particular the sulphonylureas (SUs), so far lack this degree of post-approval evaluation.

The low cost and ready availability of SUs to the state make it a popular agent in the management of type 2 diabetes mellitus.

Manufacturers of glibenclamide are inconsistent and even in conflict in their recommendations on the maximum dose. This discrepancy in dose recommendation among the manufacturers has resulted in inappropriate doses of glibenclamide being prescribed.

An audit of the prescribing of glibenclamide at selected provincial institutions in KwaZulu-Natal showed that 25% of all dose unit packs dispensed comprised the 20 mg dose of glibenclamide (Table I).

From this audit it is not possible to determine whether these doses are associated with efficacy or safety issues. High dosage appears to have been used by centres supplying medication mainly to geriatric patients. There is controversy as to whether there is a linear relationship between dose and pharmacodynamic response. Various studies have suggested that SUs may have efficacy below doses recommended by manufacturers and that doses above half of maximal do not add to clinical benefit.[2-5] High-dose glibenclamide with its high potency and long duration of action carries the risk of prolonged hypoglycaemia, especially in the elderly and those with irregular eating habits. In addition, SUs may mask the severity of a myocardial infarction.[6]

While the cost of glibenclamide to the province is low because of the nature of the present tender system of purchase, it may become an issue if the single exit price for medicines from manufacturers is implemented.

In conclusion, this survey of glibenclamide usage in the greater eThekwini/Durban area confirms that the maximum recommended dose of 15 mg per day is being exceeded in public institutions.

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**Table I. Usage of 20 mg dose as inferred from number of pre-packed units of 112 glibenclamide tablets dispensed by provincial institutions in the greater eThekwini/Durban area in 2002/3**

| Centre | Number of 20 mg/day dose packs prepared in 2002 | Total of all packs prepared in 2002 | Percentage |
|---|---|---|---|
| A | 5 694 | 23 116 | 25 |
| B | 28 334 | 64 743 | 44 |
| C | 3 083 | 44 415 | 7 |
| D | 3 594 | 15 230 | 24 |
| E | 6 590 | 14 758 | 45 |
| F | 2 621 | 38 750 | 7 |
| Total | 49 916 | 201 012 | 25 |

## Condom failure in South Africa

**To the Editor:** It was with great interest that we read the recent editorial by Dr Khumalo[1] in which she expressed concern regarding potential condom failure in Africa. The issue of condom failure is certainly important and we were most alarmed by the lack of prevalence data on condom failure in South Africa. In her literature search Dr Khumalo did not find any research on the prevalence of condom failure in Africa aside from that in pregnant women.

We have been conducting HIV/AIDS behavioural surveillance research at a large public health clinic that provides sexually transmitted infection (STI) services in Cape Town and have collected data that can help shed light on this urgent problem. In anonymous behavioural surveys collected from 1 729 men and 470 women receiving STI services we have found that 41% of men and 37% of women have experienced condom failure, defined as a broken, torn, or slipped-off condom. In a subsample of 202 patients who reported condom failure, 12% had used oil-based condom lubricants that are known to degrade latex, such as hand creams, vaseline, or oils. In another separate subsample of 214 patients who had experienced condom failure, 7% reported having practised dry sex, although we do not know if the dry-sex practices were directly associated with condom failure. These rates of 30 - 40% of persons experiencing condom failure are similar to those reported in the US studies cited by Dr Khumalo.[2,3] Our behavioural surveillance data confirm that condom failure is prevalent in at least some high-risk populations in South Africa and may be of particular concern in the populations at highest risk. The causes of condom failure remain undocumented as we found only a minority of cases potentially attributable to improper use of lubricants or dry-sex practices.

As stated by Dr Khumalo, there are interventions that reduce condom failure and there are now brief counselling interventions that increase condom uptake and proper use in STI patients tested in South Africa.[4,5] We must also remember that condoms succeed in preventing pregnancy, STI and HIV infection far more often than they fail. We therefore applaud Dr Khumalo's call for more research as well as evidence-based guidelines that include skill-building techniques for improving correct and consistent use of condoms.

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## Overestimation of the South African HIV incidence using the BED IgG assay?

**To the Editor:** We thank Rehle *et al*. for their important study of HIV incidence in South Africa,[1] which we read with great interest. We agree with the authors that the incidence of HIV in South Africa is probably extremely high, particularly among young women, and believe that the study will help us focus HIV prevention efforts on appropriate subgroups. We have serious concerns, however, about the applicability of the BED IgG assay to the South African HIV epidemic. In light of recent evidence, we are concerned that Rehle *et al*. have overstated the true absolute incidence of HIV in South Africa.

As the name implies, the BED assay was developed using sequences from HIV subtypes B, D and E.[2] To compensate for imperfect sensitivity and specificity, Rehle *et al*. use a correction factor based on McDougal *et al*.'s study of subtype B virus.[3] Given that the majority of HIV infections considered by Rehle *et al*. were (apparently) of subtype C,[1] the applicability of the McDougal correction, and indeed of the BED assay itself, to these samples is problematic. More questions arise in light of a recent report by Karita *et al*.[4] that the BED assay does not perform well in subtype C virus infections; investigators found a specificity of 71% (95% confidence interval (CI) 54 - 84%),[4] substantially different from one estimate of specificity used in the McDougal correction[3] (94% for infections more than 360 days in the past). In addition, Karita *et al*. found that using the BED assay with the McDougal correction resulted in overestimation of incidence in prospective Ugandan samples (subtype not available, but probably A and D[5]), reporting a corrected BED incidence of 6.4% and a true incidence of 1.3 - 1.7%.[4]

We are therefore concerned that the incidence figures reported by Rehle *et al*. may be overestimates. If indeed these figures are incorrect, this will make future comparisons with more accurate measures of incidence difficult and could lead to spurious conclusions with regard to the course of the epidemic. Given these concerns and the current UNAIDS recommendation against using the BED assay for incidence estimation,[6] it would be helpful if the authors clarified their findings with a quantitative sensitivity analysis of their estimates. Until the BED assay has been further validated, we

believe that BED-derived estimates of HIV incidence must be interpreted with caution.

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**Drs Rehle, Shisana, Parker and Puren reply:** Westreich and colleagues express concerns about the applicability of the BED capture enzyme immunoassay to the South African epidemic with HIV subtype C as the predominant HIV clade.

The BED assay uses a multi-subtype peptide designed to cover all major HIV subtypes, not just subtypes B, E and D as its name may imply. The three main variants of the immunodominant region of gp41 were used to synthesise the BED peptide (B Parekh, Centers for Disease Control (CDC) – personal communication). These consensus sequences are well preserved and the inclusion of those sequences from the three subtypes B, E and D was found to be sufficient to cover all major (group M) subtypes of HIV prevalent in different areas of the world.[1] The BED peptide is equivalently reactive among these HIV subtypes as assessed by saturation binding and end-point titres.

In May 2006, an incidence validation meeting was held at the CDC where new study results were presented from China, Cote d'Ivoire, South Africa, Thailand, Uganda, the USA and Zimbabwe to address the concerns expressed by the UNAIDS Reference Group in December 2005.[2,3] Working groups developed guidelines with detailed adjustment procedures for the estimation of HIV-1 incidence in cross-sectional, population-based serosurveys.[4] Two separate studies showed similar misclassification rates among subtype B and subtype C infections and proposed their own adjustment formulae[5] (and Hargrove J, *et al*., 'Improved HIV-1 incidence estimates using the BED Capture Enzyme Immunoassay' – in review).

Values for the imputed variables for both adjustment factors were validated in 2 532 specimens from 1 192 people with known date of seroconversion in HIV-1 subtypes B and C. The key imputed value in these adjustments is the false recent rate among long-term (> 1 year) infected people. It is 5.57% in both adjustments (1-γ in McDougal's adjustment is equal to ε in Hargrove's adjustment). Therefore, the McDougal and Hargrove adjustments have only been validated for HIV-1 subtypes B and C where the proportion of long-term infection misclassifying as recent infections were quantified. The performance of these adjustments in populations with HIV-1 subtypes A, D and E is not yet known and is being validated.

The study of Karita *et al*.[6] quoted by Westreich and colleagues questions the validity of the adjustments applied in our analysis. However, in view of the large samples from which the McDougal and Hargrove adjustments were derived, a major limitation of the analysis by Karita *et al*. was the small sample size used in the BED performance assessment in subtype C specimens – only 117 samples from 26 Zambian volunteers. Furthermore, based on previous analysis of HIV subtype C seroconverter samples (Ethiopia, Zimbabwe) done at the CDC we have applied a window period of 180 days in our incidence calculation. This is in contrast to the window period of 153 days used by Karita *et al*.

In order to examine the plausibility of our HIV incidence estimates we compared the adjusted BED estimates with estimates derived from mathematical modelling, using the ASSA2003 AIDS and Demographic model.[7] BED HIV incidence in the population aged 2 years and older was 1.4%, compared with 1.3% estimated by the ASSA model. A BED HIV incidence rate of 2.4% was found among individuals aged 15 - 49 years. The modelled HIV incidence was 2.2% for this age group. We therefore conclude that the adjusted BED HIV incidence estimates appear to provide plausible national HIV incidence estimates for South Africa.

Notwithstanding these encouraging results we remain actively involved in further validation studies not limited to the BED-CEIA but will also explore the suitability of testing algorithms involving, for example, antibody avidity testing. There is emerging consensus that validated laboratory based tests are the method of choice to estimate national HIV incidence and assess the impact of national prevention programmes.


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## African section of e-journal *Rural and Remote Health*

**To the Editor:** We read with interest the *SAMJ* article 'Scope and geographical distribution of African medical journals active in 2005' by Siegfried *et al*.,[1] and would like to bring to your readers' attention the recent launch of an African section of the e-journal *Rural and Remote Health* (*RRH*). This regional section has a particularly African flavour, owing to its own editorial board and peer-review panel, but is under the umbrella of the international journal.

We hope that the African section will add to the initiatives described by Siegfried *et al*. and address some of the issues raised in their article. *RRH* is an international, peer-reviewed, open-access journal. It is Medline-listed. It aims to offer wider world exposure for quality African research in the area of rural and remote health care education, policy and practice. We believe the issues of rural and remote health are relevant to most of Africa.

Because *RRH* is an electronic journal it affords authors timely publication on an article-by-article basis. In addition, the electronic format means that *RRH* is not geographically bound, and therefore offers rural and remote authors and users an all-of-Africa approach to publication.

In a recent *RRH* editorial to coincide with the launch of the African section, we recognised the impact of inadequate access to information on the problems of health and health care in Africa.[2] We also discussed the issue of inequity in access to the Internet, which has been highlighted for urgent attention by the Commission for Africa,[3] and recent initiatives to improve the current situation of variable access.[4,5] We offer the African section of *RRH* as a small contribution towards this.

The Journal can be accessed at www.rrh.org.au. Users should select 'African section' from the main menu on the home page.


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