From the editorial board

This is the second newsletter from the DFID Knowledge Programme on HIV/AIDS and STIs. The Programme is funded by the Department for International Development, UK, and based at the London School of Hygiene and Tropical Medicine (LSHTM) and the Medical Research Council (MRC), Social and Public Health Sciences Unit, University of Glasgow. It has five Knowledge Areas: 1) Determinants of sexual behaviour; 2) Biological risk factors for HIV and STI transmission; 3) Factors affecting use and effectiveness of care and prevention services for HIV/AIDS and STIs; 4) Impact and cost-effectiveness of interventions against HIV and STIs; and 5) HIV/AIDS and STI prevention and care priorities and policies.

These newsletters provide a forum for the exchange of research within the Programme and introduce other relevant research from Programme members. They form a useful means to exchange information such as updates on projects underway, conferences, new grants, etc. Initially, the selected articles reflect the contents of our bi-annual scientific meetings in London (or Glasgow). Contributions from Programme members are invited. Please email comments and suggestions to: Tamsin.Kelk@lshtm.ac.uk. Also see the Programme's website at: http://www.lshtm.ac.uk/research/dfid/aids/

Philippe Mayaud, David Mabey, Graham Hart and Tamsin Kelk

Antiretroviral Drugs

Introduction

The vast majority of deaths from AIDS are in developing countries where there is poor access to treatment because drug prices are high and health systems for delivering drugs are weak. Antiretroviral drugs (ARVs), and particularly access to them, have attracted substantial attention in recent years.

International media headlines, for example from The Washington Post ‘As drug testing spreads, profits and lives hang in balance’ and from The Guardian ‘At the mercy of the drug giants’, attacked high drug prices. Others, such as The New York Times offered potential solutions: ‘Drug companies are vincible. The world’s AIDS crisis is solvable.’ Northern NGOs such as Oxfam and VSO have highlighted problems around drug companies, WTO/TRIPS and high drug prices. Southern NGOs have launched patients’ rights campaigns, demanding greater access to ARVs.

The Knowledge Programme is (or will be) conducting important research on antiretroviral therapy (ART), looking at alternative ways to deliver ART; trying to understand and strengthen the health systems that are necessary to sustain equitable access to ARVs for impoverished societies and individuals; estimating the level of financing required nationally and internationally to support ART; and examining the policy context in which campaigns on ARV accessibility are developing in countries and internationally.

Intermittent antiretroviral therapy

Ninety-five percent of HIV-infected people worldwide live in developing countries, two-thirds of them in sub-Saharan Africa. As the HIV epidemic progresses, although preventing new infections remains very important, the issue of treatment for HIV-infected people becomes more pressing.

Low-cost interventions with the drugs isoniazid and cotrimoxazole have been shown to be effective in the prevention of opportunistic infections. However, antiretroviral therapy (ART) will be required to achieve major reductions in morbidity and mortality. The problem here is one of cost. ART has been so expensive that it has been inaccessible to all but a privileged few in low-income countries. Prices are falling rapidly but cost remains an important barrier for the great majority of individuals in low-income countries.

However, ART is not all good news. Long-term ART is associated with considerable toxicity. Therefore, there has been considerable interest in “pulsed” or interrupted ART in order to:

- reduce long-term toxicity,
- promote adherence,
- reduce cost.

In light of this, a proposal has been put forward for a trial of continuous vs. interrupted ART among mineworkers in South Africa.

Alison Grant (Clinical Research Unit, LSHTM)
The politics of antiretroviral drugs

A number of international political developments have formed the background to the recent agenda for access to ARVs:

- global partnerships between governments or international agencies and private companies, e.g. the International AIDS Vaccine Initiative (IAVI) from 1996 and the UNAIDS Drugs Access Initiative from 1998, with the potential to increase funds for HIV/AIDS activities;
- an unprecedented level of NGO involvement, of both southern and northern NGOs;
- formation of the World Trade Organization and the TRIPs agreement, to standardise global trade rules and protect intellectual property;
- pressure on the pharmaceutical industry from negative public opinion and ‘ethical investors’;
- pressure on governments of wealthy nations, including debt relief and anti-globalisation campaigns.

Potential solutions put forward to the problems include:

- central drug purchasing funds (Global Health Fund);
- drug donations and price reductions by pharmaceutical companies.

Such quick-fix solutions are popular with politicians and company executives, but are often formulated by the international community with little representation from low-income countries. Assuming prices fall and more funds become available, is purchasing ARVs the best way to spend them?

Neglect of practicalities at national level

Even if drug prices are lowered, health systems for delivering them are a problem:

- central drug administrations are under-regulated, out of date and weakly monitored;
- peripheral distribution systems are inefficient;
- monitoring of viral load, CD4 cell counts, side effects or drug resistance is difficult;
- voluntary counselling and testing (VCT) is often not available;
- clinical capacity needs major improvement through training, supervision and technical support;
- should these services be integrated with others or are dedicated AIDS treatment centres more appropriate?

Solving these problems will require a huge resource investment, which will draw funds away from already stretched preventive and treatment activities.

Stigma of HIV/AIDS

HIV/AIDS efforts have been muted in many developing countries because of political and cultural stigma. Lack of leadership has been a part of this, with politicians such as Mbeki (South Africa), Moi (Kenya) and Mugabe (Zimbabwe) voicing populism, conspiracy theories or religious fundamentalism. Successful programmes (e.g. in Uganda, Thailand) have been founded on open debate of: sexual behaviour and moral responsibility; distributive justice and access to care; social capital and community support structures. This requires relatively democratic political systems, free media and civil society representation.

Rich countries’ HIV/AIDS efforts relied on political activism. In the United States, activism by middle class gay communities helped generate research funds and government support for new services/treatments, as well as promoting the rights of people with HIV/AIDS. In Europe, open discussion of the benefits of needle exchange facilitated political support for these controversial programmes. Such political debate is rare in developing countries.

An agenda for action and research

In the face of practical reality ARVs could drop off the political agenda as quickly as they rose onto it, as politicians’ enthusiasm wanes under the weight of implementational problems. This would be a waste, since the political resources mobilised could be used to improve health systems and access to care in general.

Doing nothing is not an option. In most countries, ARVs are now available on the black market. Illegal prescription will lead to toxic side effects and viral resistance. Licensed prescription will do little more in the current health care environment. Issues to be addressed include: appropriate ARV regimens for poor countries; evaluation of technical and managerial resources required; assessing financial costs of scaling up; relative merits of integrated or dedicated care.

Political reform is also necessary. Fundamental political change is required, with attention to poverty, power and equity. Initial activities might include: delivering ARVs to limited morally uncontentious groups (prevention of MTCT, victims of rape and needle stick injuries); fostering innovative debate on the ethics of treatment access where there is no free press, democracy and limited literacy; mobilising popular support for action through political initiatives with elected officials, community representatives and people with HIV/AIDS. These activities should be determined locally and appropriate to context.

Finally, international political reform is needed to:

- involve a wider range of constituencies in international debates;
- re-balance representation of poor versus powerful interests at global fora;
- take greater care over public-private partnerships to ensure influence of powerful industry does not outweigh concerns of the poor.


The economics of expanding access to anti-retroviral treatment

As part of the Commission on Macroeconomics and Health, established in January 2000 under the direction of the World Health Organisation, researchers investigated the likely costs of scaling-up ARV treatment for HIV/AIDS. The analysis included all countries in sub-Saharan Africa.
and every nation with a per capita GNP of less than $1200.

Three major variables influenced the costs:
- the population in need,
- change in coverage,
- unit costs.

Additional infrastructure costs related to providing a package of care for HIV were also calculated, including investment in health facilities and recruitment and training of new personnel.

It is estimated that less than 1% of people currently living with HIV/AIDS and with access to health services receive ARVs. The researchers built costs on a baseline extrapolated from current available data for 2002 to produce three scenarios reflecting different coverage levels:

2007A - conservative estimates based on scaling-up within existing health system capacities to deliver ARVs to 10% of patients with access to health services;
2007B - cost estimates assuming substantial investment in current health systems to increase coverage to 45% of this group;
2015 - costs consistent with long-term investments in delivery and infrastructure to provide ARV treatment for 65% of people living with HIV/AIDS.

As Table 1 shows, the estimated annual amount that would be required from 2002 to scale-up ARV treatment to these levels would be US $0.8-1.2 billion, 4.2-5.8 billion and 6.8-9.2 billion, respectively. This analysis assumed that ARVs would only be delivered in the context of strengthened clinical management of HIV-related illnesses. An additional US $6.8-7.1 billion would be required annually to provide this for 70% of patients by 2015.

Table 1. Estimated costs of ARV treatment for HIV/AIDS

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<td>(US$ millions, 2002)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>All countries</td>
<td>855</td>
<td>1517</td>
<td>4275</td>
<td>5783</td>
<td>6846</td>
<td>9190</td>
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<td>All low income</td>
<td>691</td>
<td>937</td>
<td>3454</td>
<td>4683</td>
<td>5646</td>
<td>7597</td>
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<tr>
<td>All middle income</td>
<td>164</td>
<td>220</td>
<td>822</td>
<td>1100</td>
<td>1201</td>
<td>1593</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>720</td>
<td>970</td>
<td>3588</td>
<td>4850</td>
<td>5818</td>
<td>7784</td>
</tr>
<tr>
<td>East Asia &amp; Pacific</td>
<td>34</td>
<td>46</td>
<td>169</td>
<td>231</td>
<td>255</td>
<td>348</td>
</tr>
<tr>
<td>South Asia</td>
<td>87</td>
<td>120</td>
<td>437</td>
<td>602</td>
<td>665</td>
<td>911</td>
</tr>
<tr>
<td>Eastern Europe &amp; Central Asia</td>
<td>6</td>
<td>8</td>
<td>29</td>
<td>39</td>
<td>39</td>
<td>53</td>
</tr>
<tr>
<td>Latin America &amp; Caribbean</td>
<td>9</td>
<td>12</td>
<td>44</td>
<td>60</td>
<td>70</td>
<td>94</td>
</tr>
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</table>


The researchers considered both the drug and infrastructure costs that are required to deliver ARVs. Even if drug prices fall significantly, the financial barriers to implementing ARV treatment are still almost insurmountable for the vast majority of low and middle-income countries, without substantial international effort.

Lilani Kumaranayake (Health Policy Unit, LSHTM)

Useful websites

Centers for Disease Control and Prevention (CDC)
Global AIDS Program:
http://www.cdc.gov/nchstp/od/gap/strategies/4_4_antiretrovirals.htm

HIV InSite, University of California San Francisco:
http://hivinsite.ucsf.edu/InSite.jsp?page=ar-drugs

International AIDS Society:
http://www.ias.se

Pan American Health Organization:
http://www.paho.org/English/HCP/HCA/antiretrovirals _HP.htm

WHO Initiative on HIV/AIDS & Sexually Transmitted Infections:
http://www.who.int/HIV_AIDS/frist.html

Conference Report

Society for Adolescent Medicine, 6-9 March 2002, Boston, USA

This was the annual meeting of the US Society for Adolescent Medicine. It focused almost exclusively on adolescent medicine in the United States, with a few presentations and posters on adolescent medicine in Europe. Most of the participants were medical doctors or nurses.

I had been invited to give a talk on the MEMA kwa Vijana Project (Adolescent Sexual & Reproductive Health Intervention Trial) in Mwanza, Tanzania as part of the first session they have ever had on International Adolescent Health. The other talks were on work in Switzerland, Sweden and Australia. The session was popular, and all the talks in the session will be published in the Journal of Adolescent Health.

There was only one other talk in the whole 4-day programme about work in a developing country: a cross-sectional survey of reported sexual behaviour of students attending 39 secondary schools in Plateau State, Nigeria. Research Assistants (medical students) administered a 96-item self-completion questionnaire. 4218 students completed the questionnaire, mean age 16.4 years, 53% male. 1513 questionnaires (36%) were excluded from the analysis because of important inconsistencies. 'Ever had sex' was associated with parental death, neither parent having been to primary school, family polygamy, and a low score for "family connectedness" (41% were from polygamous families). 34% of female respondents reported having had an induced abortion, and 36% reported having had "forced sex" (8% of male respondents reported forced sex). [Presenter: Gail Slap, Director of Adolescent Medicine, Children's Hospital Medical Center, Cincinnati, Ohio]

A talk by George Patton of the Gatehouse Project in Melbourne, Australia was very interesting. The intervention was to feed back the results of a series of questionnaires, etc with staff of secondary schools, students in one year of the same schools, and their parents about their views on each other and their school, smoking behaviour, illicit drug use, satisfaction with school and life in general, and school performance etc to the parent/teacher associations and school management. Outcomes such as smoking behaviour, illicit drug use, satisfaction with school and life in general, and school performance were then measured in a different cohort of students in the same year of these schools 2 years later. These "after" results were then compared with the "before" results in the same schools and in other schools.
that were joining the programme. Major improvements were detected. Process indicators showed that the intervention schools had initiated quite a lot of changes in the light of the feedback they had been given and that this had greatly improved the 'connectedness' of the students with each other, their teachers, and their parents. [Presenter: George Patton, Director, Centre for Adolescent Health, Royal Children's Hospital, Parkville, Victoria, Australia]

Sophia Yen and colleagues (US) studied bacterial vaginosis comparing FemExam®, pH & amines Testcard, Papanicolaou smear, and Nugent's criteria in 2157 otherwise healthy female military recruits. 27% were positive for BV using Nugent's criteria. The commercial FemExam® test strip is based on a test for both pH and amines.

<table>
<thead>
<tr>
<th>Results vs Nugent's criteria:</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH and amines positive</td>
<td>9%</td>
<td>99%</td>
</tr>
<tr>
<td>pH or amines positive</td>
<td>73%</td>
<td>66%</td>
</tr>
<tr>
<td>pH pos amines pos or neg</td>
<td>2%</td>
<td>67%</td>
</tr>
<tr>
<td>Amines pos pH pos or neg</td>
<td>1%</td>
<td>97%</td>
</tr>
<tr>
<td>Papanicolaou smear pos</td>
<td>2%</td>
<td>79%</td>
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</table>

Cherie Boyer reported on an evaluation of an intervention to reduce HIV/STDs in adolescents living in high STD prevalence neighbourhoods in California. Youth peer educators were trained to waylay other youth on the street and administer a 15 minute questionnaire to them about their age and sexual experience, an STD/HIV risk assessment, and questions to assess their stage or readiness to get an HIV/STD screening test. 86% of the youth who were waylaid were African Americans. Similar repeat questionnaires were conducted in 810 of those who had gone through the system. The results showed some (rather slight) improvements in knowledge, but not much change (if any) in self-perceived risk, or in willingness to have an HIV or STD test.

David Ross
(Mema kwa Vijana ASRH Intervention Trial, Mwanza, Tanzania)

Selected New Publications


Details of Programme research output areas are given on page 1. A more extensive list of publications is available on our website: http://www.lshtm.ac.uk/research/dfid/aids/

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