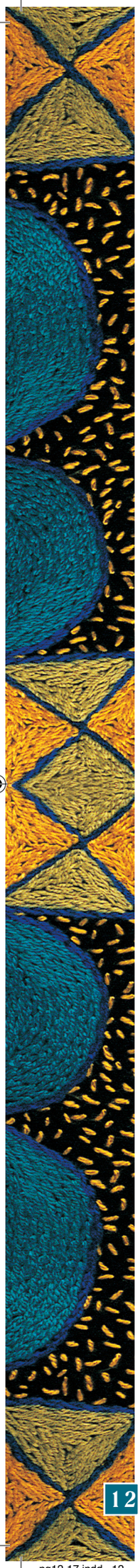

OPINION

IN DEFENCE OF RATIONAL AIDS ACTIVISM

How the irrationality of Act Up-Paris and others is risking the health of people with HIV or at risk of HIV infection

Nathan Geffen, Gregg Gonsalves

This article describes the irrational actions of Act Up-Paris and some other organisations in recent years. We have written it because their activities are threatening the development of new treatment and prevention technologies for people with HIV. They are also undermining scientific research programmes in developing countries.

The groups we discuss here couch their anti-science agenda in progressive rhetoric. They therefore persuade some well-intentioned people and organisations unfamiliar with HIV science to support their causes. But there is nothing progressive about hindering life-saving medical research. Act Up-Paris and the other organisations discussed here are endangering the lives of people with HIV; they have to be exposed.

THE SUCCESSES OF AIDS ACTIVISM

AIDS activists have led the struggle against HIV via successful campaigns for lower medicine prices, public sector programmes and increased international funding for HIV programmes. By sharing their skills and knowledge with each other – through informal networks of collaboration, training, publications and web-based information – AIDS activists have been the drivers of community health education programmes across the globe. Their efforts have enabled poor people in Africa, Eastern Europe, South America, the Caribbean and Asia to become community educators and more effective activists themselves. There is now a strong and vital global movement of AIDS treatment activists that has revolutionised how science is conducted, how health care is delivered, and how health care workers relate to their patients.

Community involvement in drug development and AIDS research has depended on the willingness of scientists to assist activists in learning the science of HIV/AIDS. This *ad hoc* scientific education has been critical in lifting community involvement beyond the tokenism of identity politics. Because people living with HIV – including women, gay men, drug users and people of colour – have learned the science of HIV/AIDS, they can engage with experts at the US National Institutes of Health (NIH), the US Food and Drug Administration (FDA), the World Health Organization (WHO) and other institutions on scientific issues, and offer a perspective grounded on sound evidence-based principles and methodology.

These are just some of the successes activists have helped to secure over the past 27 years. Despite these advances, many opportunities have still been lost: far too few people receive the treatment and prevention interventions they need, and all too often ideology has trumped science in delivering these services causing millions of avoidable new infections and deaths. But the global response to the epidemic would have been far worse without activism, with even more devastating consequences.

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THE RISE AND FALL OF RATIONALISM IN ACT UP-PARIS

Yet there are some AIDS activists whose actions and campaigns are counter-productive, even dangerous. Of course, every major activist group makes serious mistakes from time to time, be they factual, tactical or even ethical lapses. But some activist groups, in particular Act Up-Paris, have developed a pattern of irrational behaviour.

The organisation has in recent years actively worked to undermine cutting-edge life-saving HIV clinical research in Africa. Act Up-Paris used to be an effective activist group. In its earlier years under the leadership of Didier Lestrade and others, it worked closely with other groups in North America and Europe to forge the first relationships between activists and researchers. It made significant contributions to clinical trials and drug approval in Europe.

But in recent years the organisation has been taken over by new leadership that lacks a rigorous knowledge of HIV science and clinical trials and an understanding of the needs of people with HIV or at risk of infection in developing countries, or the nuances of modern political struggle outside of France. In particular, over the past few years, Act Up-Paris has targeted several clinical trials in developing countries as unethical without evidence to support their claims.

HOW ACT UP-PARIS SHUT DOWN TENOFOVIR TRIAL SITES

In 2004 - 2005, Act Up-Paris actions led to the shutting down of clinical trial sites examining pre-exposure prophylaxis with tenofovir in several countries around the world. The controversy over the tenofovir studies is complex, but throughout this period Act Up-Paris sought to exacerbate tensions between researchers and community groups rather than look for solutions that would have allowed these critical studies to continue.

The controversy essentially began as a local issue between researchers from the USA and Australia and an organisation representing sex workers in Cambodia, with the local NGO claiming they had not been consulted in the preparations for the study nor received sufficient assurances that sex workers infected during the course of the study would have access to health care for their HIV infection.

The issue of post-trial care for clinical trials is a key one, but the solution is difficult and in this case needed lengthy discussion among stakeholders in Cambodia about how to address it. For instance, since people infected during the study would probably not get sick and need treatment for a decade, how would care that would be needed years in the future be assured? What is the responsibility of the local health system to provide AIDS treatment to all its citizens, not just clinical trial participants?

However, instead of attempting to deal constructively with these issues, Act Up-Paris led demonstrations at the International AIDS Conference in Bangkok in 2004 accusing Gilead, the manufacturers of tenofovir (which had no involvement with the study), and the study investigators of unethical conduct.

In addition, Act Up-Paris through its networks in francophone Africa flamed controversy about another tenofovir study being planned in Cameroon. A local Cameroon group and Act Up-Paris charged that inadequate counselling had been provided to trial participants, though at a meeting on the tenofovir studies in Seattle in 2005 neither group could adequately describe the deficiencies in the counselling protocol or its implementation and the description offered was contradicted by others involved with the study.

The tenofovir trials raised a host of issues around the conduct of clinical trials in developing countries, including post-trial care, informed consent, counselling of trial participants, the availability of other prevention interventions for participants in both control and experimental arms of the studies, and community involvement in study design and conduct. These issues are relevant to all HIV prevention research trials and, in part, clinical research overall in developing countries. However, what is needed to move the dialogue on the conduct of clinical trials forward in developing countries is an evidence-based, methodical and rational discussion of all these operational considerations. The difficulty in addressing these issues means there are no easy answers; partnership between all stakeholders is needed to resolve them. Though there were real issues around the tenofovir studies, Act Up-Paris sought to inflame the debate, was cavalier in offering evidence of wrong-doing, and often demanded impractical solutions to key issues.

With the closure of several of the tenofovir studies, it became difficult to ascertain the effectiveness of this potentially important new tool in HIV prevention, as the statistical power of the remaining studies was too weak to offer a reliable answer to the question. Act Up-Paris is responsible for this delay in answering a critical question in AIDS research, one that could potentially lead to a new intervention preventing millions of new HIV infections.

HOW ACT UP-PARIS TRIED TO DISCREDIT A HIGHLY SUCCESSFUL AFRICAN TRIAL

In 2006, Act Up-Paris attempted to discredit the DART trial. This trial, sponsored by the British Medical Research Council, took place in Uganda and Zimbabwe. It examined two questions: whether antiretrovirals can be administered in the absence of routine laboratory tests, and whether patients can take structured treatment interruptions.[1] The idea of treatment interruptions was to reduce side-effects and the inconvenience of having to take pills daily for life. It would also reduce costs. Unfortunately, structured treatment interruptions do not work; they increase the risk of morbidity and mortality. DART was one of three major trials that showed this, though it found a statistically significant effect for morbidity, not mortality (2 per 100 patient-years versus 8.6 per 100 patient-years).

Act Up-Paris's response was to accuse the DART investigators of endangering the lives of trial participants who were interrupting treatment and to disrupt the speech of one of the DART researchers, James Hakim, a Zimbabwean researcher, given at the 2006 International AIDS Conference in Toronto. They shouted during Hakim's speech and held up banners saying shame. They also distributed a pamphlet making a series of false allegations about the ethics and science of the trial. When they finished their demonstration one of the DART scientists, Paula Munderi, presented data showing 94% survival at 2 years and a 17-fold reduction in mortality compared with pre-antiretroviral data in this cohort. Unfortunately the Act Up-Paris demonstrators had left before Munderi spoke.

Participants in the DART trial, on all arms, actually did remarkably well. The trial has provided yet another example of how antiretroviral treatment can be implemented successfully in poor-resource settings. Although the trial found that patients in the structured treatment interruption arm had more serious adverse events, the interruptions were terminated once this was determined and all patients were put on continuous therapy. Three patients died out of 137 (2.4%) in an initial structured treatment interruption pilot. In two arms – consisting of a total of 813 patients – comparing continuous treatment versus structured interruptions, 9 patients died, 5 from the interruption arm and 4 from the continuous arm. The death rates in both arms of the study are low and when compared with high mortality in the general population living with HIV in both Uganda and Zimbabwe, show a strong benefit for antiretroviral therapy overall. [2,3]

No evidence has been brought forward to support Act Up-Paris's claims that there was inadequate consent or that patients were not given appropriate support and care. TAC wrote a letter to Act Up-Paris pointing out the errors in some of their allegations. We asked them to either provide evidence to support their claims or to apologise and withdraw them. Act Up-Paris responded defensively, repeating many of their earlier claims but producing no evidence.[4*]

SOMO'S ATTEMPT TO DISCREDIT HIVNET 012

Another European activist organisation making irrational claims about HIV science is the Dutch-based Centre for Research on Multinational Corporations (Stichting Onderzoek Multinationale Ondernemingen – SOMO). It published a briefing on what the organisation calls examples of unethical clinical trials.[5] We are only familiar with three trials in the list. No rational activist would hold these up as unethical, at least not for the reasons cited by SOMO. Two are the tenofovir and DART trials discussed above, and SOMO's attacks are largely based on the critique launched against these studies by Act Up-Paris. The third is the HIVNET 012 trial that took place in Uganda, which readers of this journal will know found that a single dose of nevirapine to mother and child reduces the risk of mother-to-child transmission of HIV by about half. The aim of the trial was to find a simple, affordable method of reducing paediatric HIV infections that could be implemented easily in poor countries.

The controversy surrounding HIVNET 012 has been widely reported in both the popular and scientific press. Initially, in December 2004, John Solomon of the Associated Press (who has recently become editor of the right-wing *Washington Times*) erroneously reported that there had been serious irregularities in the study, which took place in the late 1990s. These false charges became exaggerated in the media, with some commentators comparing the HIVNET 012 study to the infamous Tuskegee experiment that deprived African-American men of a proven cure for syphilis in a study conducted in the United States between 1932 and 1972.[6] Since 2004, these claims have been used by pseudo-scientists who deny the link between HIV and AIDS to undermine the provision of nevirapine in South Africa and elsewhere.

It was certainly not a perfect trial; indeed, a perfectly conducted clinical trial is extremely rare. Also, it has been criticised – notably by former *New England Journal of Medicine* editor Marcia Angell and respected consumer rights activist Ralph Nader's organisation, Public Citizen – for having had a placebo arm when it was already known that AZT was effective at reducing transmission.[7] Consequently the trial protocol was changed so that the control group used a very short-course AZT regimen instead of placebo. The fact that this regimen was shorter than the AZT intervention known to work is a legitimate criticism of HIVNET 012. But it was one that was debated openly in which reasonable arguments were put forward by both sides. Furthermore, the trial protocol was approved by an ethics committee.

However, this is not the criticism that has made HIVNET 012 the subject of intense media attention, nor is it the one highlighted by SOMO. Instead SOMO reports several partly true minor allegations about the trial and several major untruths including that 14 deaths went unreported.[†] The only references they provide for their allegations are the inaccurate Associated Press articles by John Solomon, not independent reviews or scientific papers.

*Act Up-Paris claimed to receive information about their allegations from a trial participant. Yet this person failed to attend a meeting with the researchers to discuss his concerns nor does the name he has used correspond with anyone on the trial.

[†]The independent review of HIVNET 012 conducted by the Institute of Medicines states 'In its review of HIVNET 012 records, the committee finds no evidence of and only a very limited opportunity for either unreported deaths or erroneous reports of deaths.'

Unmentioned in the SOMO report is that the HIVNET 012 trial has been evaluated several times for ethical and scientific lapses. It has never been found by any of these reviews to have made a serious ethical breach. The US Institute of Medicine conducted an independent review of HIVNET 012. The chair of the investigating panel described their findings: 'The data from the HIVNET 012 study ... are sound and reliable. ... Our confidence in the trial's data and findings is based on several factors, including evidence that the study's design was both scientifically sound and *ethically implemented* [our emphasis].[8]

Interestingly, omitted from SOMO's long list of unethical trials is one of the worst such cases. Matthias Rath is an entrepreneur who has established multinational vitamin-selling operations. He has made a fortune selling his products at exorbitant prices by claiming, falsely, that vitamin supplements treat almost every serious disease including asthma, heart attacks, AIDS and, more recently, bird flu. With the implicit support of South Africa's Minister of Health and Director-General of Health, he ran an unauthorised illegal clinical trial in Cape Town. There are a myriad of ethical problems with the trial and several deaths have been documented. The evidence is public and yet Rath has not been prosecuted, or even stopped.[9]

SOMO, if it was genuinely interested in stopping unethical trials, could make a difference in the effort to stop Rath. This is because he runs his European operations in Holland. A systematic campaign against Rath might have been of tremendous assistance in our efforts in South Africa to bring Rath to justice.

Maybe the motives behind the irrational behaviour of organisations like SOMO and Act Up-Paris can be understood by SOMO's failure to mention Rath's trial. Science writer Jon Cohen has written about what he terms pharmanoia, the irrational fear and/or hatred of pharmaceutical companies and their products: 'The protest against Gilead is one example of pharmanoia, the extreme distrust of drug research and development that's sweeping the world. ... By overplaying unproved but sensational misdeeds, Big Pharma's watchdogs obscure serious ones – like the inane lawsuit that 39 drug makers filed against the South African government in 1998 to block it from making generic versions of anti-HIV drugs. The scattershot approach also draws attention away from a critical and increasingly complicated issue that AIDS has pushed to the fore ...'[10]

There is a view, with some justification, that pharmaceutical companies conspire with Western governments to protect their business interests, even at the expense of patients. SOMO, Act Up-Paris and the other organisations discussed here have taken this view to an ideological extreme, in which the actions of pharmaceutical companies and HIV clinicians are always presumed to be unethical, irrespective of the evidence. Consequently, these organisations are unable to evaluate facts that do not fit into this world-view. The actions of an alternative medicine seller, Matthias Rath, who ran a deadly trial in cahoots with a developing country government, do not fit neatly into this ideology and are therefore ignored.

HOW SEVERAL ORGANISATIONS ARE TRYING TO DERAIL A CIRCUMCISION PROJECT

Less known than the irrational attacks on the tenofovir trials, HIVNET 012 and DART, is the attempt by Act Up-Paris and several other organisations to derail an important prevention study in Orange Farm, Johannesburg.

Following the successful Orange Farm circumcision trial, the lead researcher Bertran Auvert rightly believes that he has a duty to follow up the trial by making circumcision widely available to the community. After all, the Orange Farm community helped show that circumcision reduces HIV transmission. Surely the community should be given the opportunity to benefit from it. Few uncircumcised Orange Farm men could afford to pay for their circumcisions, so Auvert applied to ANRS to fund a community study of male circumcision.

It is a 5-year programme that, in its first 2 years, will offer circumcision to about 20 000 uncircumcised men aged 18 - 39. The study protocol includes counselling and the offer of HIV testing. Patients with HIV will be referred to Orange Farm's clinic, which provides antiretrovirals. Critically, it will help answer some outstanding operational questions about circumcision.

The researchers will evaluate impact on the community's knowledge and attitudes. It will support existing means of prevention such as sexual behaviour change, condom use, sexually transmitted infection behaviour and voluntary counselling and testing, and the spread of HIV and the herpesvirus (taken from the project proposal).

Four French activist organisations, Act Up-Paris, Aides, Sidaction and TRT-5, have written a letter to ANRS attacking the trial protocol and attempting to stop it. The letter's header, in large capital letters, states 'WARNING TO THE DIRECTOR OF THE ANRS REGARDING THE PLANNED ANRS TRIAL 12126' (we have a professional translation of the original letter, which was written in French).

The writers describe themselves as a 'task group' that 'opposes the setting up of the study in its current form'. They make a series of false claims. For example, they claim the intervention is not 'part of a complete set of HIV prevention measures' which should include 'advice,

access to testing, treatment of sexually transmitted infections, promotion of safe sex, easy access to male and female condoms, promotion of their proper and regular use'.

But on the contrary, the study protocol includes voluntary counselling and testing for participants and counselling on sexually transmitted infections and safer sex. Symptomatic sexually transmitted infections will be treated. The project will work with the health facilities in Orange Farm and ensure that participants who test HIV-positive will get antiretroviral treatment if indicated.

Act Up-Paris *et al.* claimed there was a lack of clarity regarding the approach to the South African ethics committee. It's not clear what they meant, but the protocol has been approved by the Wits University's ethics committee.

They also claimed that local organisations and authorities had not been consulted. This is despite the researchers working, for many years now, with groups in Orange Farm. They have also consulted with TAC, AIDS Consortium and provincial government officials.

Act Up-Paris *et al.* also claimed that there was virtually no local collaboration with South African social scientists. Yet one of the lead investigators is Dirk Taljaard, a South African social scientist who was an investigator in the previous circumcision study in Orange Farm.

Even if any of the above allegations were valid, surely the correct approach would have been for Act Up-Paris *et al.* to write a very different style of letter to the researchers and ANRS, one that recommended improvements. Instead, they wrote their complaint months before the project was scheduled to start without first giving the investigators an opportunity to address their concerns.

ATTACKS ON THE NONOXYNOL-9 RESEARCHERS

One of the signatories of the letter to ANRS denouncing the circumcision study is Marie de Cenival of Sidaction. She has been centrally involved in Act Up-Paris for many years. Her irrational actions are particularly concerning. In July 2007, at a conference on women and AIDS in Nairobi, she stood up during a session on a panel discussion on microbicides and accused the panel members of killing 900 women. She was referring to a study of a nonoxynol-9 gel (N-9) called the COL-1492 trial. Perhaps, the most bizarre aspect of her allegation is that none of the panellists were investigators on this trial! (Personal communications with scientists and activists in altendance at the Nairobi conference.)

During the study, 59 women became HIV infected out of 892 women on the N-9 gel arm as opposed to 45 new infections in the control arm, where women received a placebo, a gel that did not contain N-9. Consequently the trial was stopped. Obviously a negative result, where the tested product performs worse than placebo, is tragic. Yet the infection rate in the N-9 arm was lower than the background infection rate in the community, possibly because of the counselling and care incorporated into the trial for both sets of women, i.e. those receiving the N-9-containing gel and those receiving a placebo. There was nothing close to 900 deaths. Nonoxynol-9 does not work. This was an unfortunate and unexpected scientific result. But de Cenival's accusation was false.

THE CONSEQUENCES OF IRRATIONAL ACTIVISM

The trials discussed here that irrational activists have attacked were all conducted in developing countries, mainly African, with the involvement of scientists in those countries. Three outstanding African scientists, Peter Mugyenyi, Paula Munderi and James Hakim, played a leading role in the DART study. Conducting high-quality science in Africa, especially outside South Africa, is difficult. Not only do scientists have to contend with a lack of finance, equipment and facilities, they now also have to contend with what amounts to a concerted campaign to unfairly discredit their work.

As TAC's chairperson Zackie Achmat wrote in the prologue to Sipho Mthathi's and his letter to Act Up-Paris, 'Their unsubstantiated hysteria has undermined support for AIDS research and sowed unnecessary fear and suspicion about research among people living with HIV/AIDS across the world.'

Act Up-Paris's actions have done a great disservice to people living with HIV and those at risk of HIV transmission. Our appeals to their leaders to stop their harmful actions have been met by scorn and contempt. There are worrying indications that other organisations, from SOMO in Holland to well-respected French AIDS groups including Aides, Sidaction and TRT-5, are buying into Act Up-Paris's irrational critiques and ideologically driven methodologies – their 'pharmanoia'. We find this a dangerous development in AIDS activism and one which demands that AIDS activists around the world speak up against this trend. It does not give us any pleasure to have to take this step. Both of the authors of this piece have been critics of AIDS research, drug and vaccine and microbicide development for many years. We are not asking for *carte blanche* for researchers to do what they please in our countries. However, our criticisms of clinical research need to be factually sound.

Scientific research is the reason why technology exists that renders HIV infection a chronic lifelong infection, as opposed to the death sentence it used to be. The significant investment into that research and the high quality with which most of it has been conducted are in large part due to the efforts of activism. As activists

we should not allow that success story to be undone by irrational behaviour. The consequences will be deadly.

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