



BECAUSE WE CAN: CLASHES OF PERSPECTIVE OVER RESEARCHER OBLIGATION IN THE FAILED PrEP TRIALS

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ABSTRACT

This article examines the relationship between bioethics and the therapeutic standards in HIV prevention research in the developing world, focusing on the closure of the pre-exposure prophylaxis (PrEP) trials in the early 2000s. I situate the PrEP trials in the historical context of the vertical transmission debates of the 1990s, where there was protracted debate over the use of placebos despite the existence of a proven intervention. I then discuss the dramatic improvement in the clinical management of HIV and the treatment access movement, and consider how these contexts have influenced research practice. I argue that as HIV prevention trials oblige researchers to observe the rate at which vulnerable people under their care acquire HIV, there is an obligation to provide antiretroviral treatment to seroconverters and other health care benefits that fall within the scope of researchers' entrustment, both to avoid exploitation and to enact reciprocal justice. I argue against propositions that the obligations to provide specific benefits are vague, fall only upon researchers and sponsors, and create injustices by privileging the few over the many. Finally, I contend that the realisation of a broader standard of care in HIV prevention research broadens the role of research from being a simple tool to produce knowledge to a complex intervention that can play a part in the reduction of health disparities.

INTRODUCTION

This article focuses on the closure of the pre-exposure prophylaxis (PrEP) trials in the early 2000s and reflects on how the issues of justice and exploitation in clinical research played out in a context where HIV treatment activism had impacted upon the landscape of possibility.

It is my contention that unresolved issues concerning the obligations of HIV prevention researchers to research participants resurfaced in the context of the PrEP trials. The issue debated in the late 1990s was the use of placebo controls in vertical mother-to-child transmission research, which left the research community divided as to the nature and scope of researcher obligation. The issues that arose in the PrEP trials are closely related: concerning ancillary care, compensation for harm and access to antiretroviral therapy for sero-

converters. Rather than being another academic debate, however, communities became actively engaged in the question of what clinical research could, or should, offer to participants.

The PrEP controversy erupted seven years after the exposé in the *New England Journal of Medicine* about vertical HIV transmission trials which were placebo-based despite the existence of a proven intervention.¹

PrEP – pre-exposure prophylaxis – is an HIV prevention strategy, as yet unproven, that involves the use of antiretroviral medication prior to exposure to prevent

¹ P. Lurie & S.M. Wolfe. Unethical Trials of Interventions to Reduce Perinatal Transmission of the Human Immunodeficiency Virus in Developing Countries. *N Engl J Med* 1997; 337: 853–856; M. Angell. The Ethics of Clinical Research in the Third World. *N Engl J Med* 1997; 337: 847–849.

HIV infection.² This article looks at three PrEP trials that came to international attention: one that was to be conducted in Cambodia in a population of female sex workers; a second at three sites in Africa: Ghana, Nigeria and Cameroon, in a population of women at high risk of HIV infection; and a third in Thailand in injecting drug users. By 2005, the Cambodian trial and two of the three African trial sites had closed due to community objections to the conduct of the research, and activists were raising serious concerns about the Thai study. While there were differences in the specific issues at the respective sites the overwhelming concerns were access to treatment and/or prevention interventions, and medical care as part of the research package.³

Both the failed PrEP trials and the earlier placebo-controlled vertical transmission trials raise important ethical questions for researchers. What obligations do researchers have to participants? What role does context and circumstance play in determining obligation? How do ideas of fairness and reciprocity play out in the context of limited research funding and inadequate national health systems? I will argue that the researcher is obliged to protect the best interests of the research participants, insofar as these interests fall within the scope of the research study and to the extent that logistics allow. This obligation, arising from the imperative to avoid exploitation and grounded in reciprocal justice, should take precedence over the production of knowledge and potential benefits that may flow from this knowledge. In the case of HIV prevention studies, this may necessarily involve investment in infrastructure to facilitate treatment access post-trial. While this arguably increases the burdens placed upon researchers, it situates the production of knowledge appropriately within a relationship of care for the subject, rather than divorcing the research context from the clinical context.

THE DEBATE OVER PLACEBO CONTROLLED VERTICAL TRANSMISSION TRIALS

The issue of therapeutic standards in HIV prevention research came into sharp focus in 1997, when the *New England Journal of Medicine* published an article by Lurie and Wolfe,⁴ which condemned a series of clinical trials in

the developing world as unethical. The basis of their criticism was that interventions to prevent vertical (mother-to-child) transmission of HIV were being tested against placebo controls, despite the existence of a proven regimen established in 1994, known as the '076 regimen', named after the landmark trial ACTG076.⁵ Their critique was supported by an editorial by Marcia Angell,⁶ which compared the vertical transmission trial to the infamous Tuskegee experiment, which denied African American men access to proven syphilis treatment in order to study the natural history of the disease.

The practice of testing a new therapy against placebo when a proven therapy exists was explicitly proscribed by the *Declaration of Helsinki* (the 'Declaration'),⁷ an international document providing guidance on research ethics. The *Declaration of Helsinki* was adopted in 1964 by the World Medical Association and periodically updated. It is a descendent of the *Nuremberg Code* of 1949, which defined guidelines for the ethical conduct of human research in the aftermath of the trials of the Nazi doctors, but is somewhat more liberal than that code in its definitions of permissible research.⁸

Because the 1996 Declaration explicitly stated that placebo-controlled trials where proven interventions exist were unethical, it came under intense scrutiny and was subject to a number of revisions, which have been dealt with elsewhere.⁹ In the wake of this scrutiny, there ensued an international debate about research standards and the role of guidelines. The debate centred upon the themes of exploitation, the obligations of researchers to trial participants, the need for research to be responsive to the needs of the developing world and the requirement for scientific rigour.¹⁰ These issues were not resolved,¹¹ and they resurfaced in a different guise with regard to the ethical design of the PrEP trials.

² E. Mills et al. Designing Research in Vulnerable Populations: Lessons from the HIV Prevention Trials that Stopped Early. *Br Med J* 2005; 331: 1403–1406.

³ E. Mills et al. Media Reporting of Tenofovir Trials in Cambodia and Cameroon. *BMC International Health and Human Rights* 2005; 5 no. 6. Available at: <http://www.biomedcentral.com/1472-698X/5/6> [Accessed 13 Jan 2010].

⁴ Lurie & Wolfe, *op. cit.* note 1.

⁵ E.M. Connor et al. Reduction of Maternal-Infant Transmission of Human Immunodeficiency Virus Type 1 with Zidovudine Treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *N Engl J Med* 1994; 331: 1173–1180.

⁶ Angell, *op. cit.* note 1.

⁷ World Medical Association (WMA). 1996. *Declaration of Helsinki 1996*. Ferney-Voltaire, France: WMA. Available at: http://www.jcto.co.uk/Documents/Training/Declaration_of_Helsinki_1996_version.pdf [Accessed 22 Sept 2010].

⁸ B. Loff & J. Black. The Declaration of Helsinki and Research in Vulnerable Population. *Med J Aust* 2000; 172: 292–295; H. Wolinsky. The Battle of Helsinki. *EMBO Rep* 2006; 7: 670–672.

⁹ See for example, R. Macklin. After Helsinki: Unresolved Issues in International Research. *Kennedy Inst Ethics J* 2001; 11: 17–36.

¹⁰ Angell, *op. cit.* note 1; Lurie & Wolfe, *op. cit.* note 1; R. Levine. The Need to Revise the Declaration of Helsinki. *N Engl J Med*, 1999; 341: 531–534; H.E. Varmus & D. Satcher. Ethical Complexities of Conducting Research in Developing Countries. *N Engl J Med* 1997, vol. 337: 1003–1005.

¹¹ Macklin, *op. cit.* note 9.

THE HIV TREATMENT REVOLUTION AND ITS IMPACT

While the ethical debate over placebo-controlled trial in the developing world was raging in the journals, the landscape of HIV treatment (for those who could afford it) was being transformed in the clinics of the developed world. Research first presented in 1996, and consolidated in the years immediately following, radically changed the perception of HIV/AIDS as a terminal illness in wealthy countries. It was shown that HIV replication could be effectively suppressed using combination antiretroviral therapy (ART), and that this appeared to halt and even reverse immune damage in people with HIV. Although initial optimism about the possibility of a cure turned out to be misplaced, the prediction that HIV infection could become another chronic manageable condition has arguably come to pass – for some people and to some extent.¹²

By July 2000, at the International AIDS Conference in Durban, South Africa, the stark injustice of people dying of AIDS in the developing world while people lived indefinitely with HIV in the resource rich world was palpable. Treatment access had become the most significant political issue.¹³ The drug pricing policies and intellectual property regimes that made treatment inaccessible for the majority of people living with HIV became the news story from this conference, rather than some biomedical breakthrough.¹⁴

Only two antiretroviral drugs were listed on the World Health Organization's (WHO) essential drug list in 2000 and these were both listed for prevention rather than treatment (AZT and nevirapine – both to prevent vertical transmission). Even Bactrim, the basic antibiotic used to prevent two common opportunistic infections in people with AIDS, was grossly underutilised in Africa.¹⁵

¹² K. Bhaskaran. Changes In The Risk Of Death After HIV Seroconversion Compared with Mortality in the General Population. *JAMA* 2008; 300: 51–59; The Antiretroviral Therapy Cohort Collaboration. Life Expectancy of Individuals on Combination Antiretroviral Therapy in High-Income Countries: A Collaborative Analysis of 14 Cohort Studies. *Lancet* 2008; 372: 93–299.

¹³ See for example, B. Whyte. Nelson Mandela Calls for Unity at the XIIIth International AIDS Conference in Durban, South Africa. *B World Health Organ* 2000; 78 (9): 1169. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2560854/pdf/0042-9686_78_9_1169a.pdf [Accessed 21 Feb 2010].

¹⁴ N. Geffen. 2000. What Happened in Durban? A South African Perspective. *The Body* September/October. Available at: <http://www.thebody.com/content/art13213.html> [Accessed 21 Feb 2010].

¹⁵ South African Department of Health. 2000. *Report on the 13th International AIDS Conference, Durban, 9–14 July 2000: Summary Report of Major Issues, Conclusions and Recommendations*. Pretoria, South Africa: South African Department of Health: section 7.3. Available at: <http://www.doh.gov.za/aids/docs/13conf00.html> [Accessed 21 Feb 2010].

AIDS Coalition to Unleash Power (ACT-UP) New York. 2000. *WHO Sold Out to Big Pharma*. New York, NY: ACT-UP New

Five major pharmaceutical companies announced a partnership with UNAIDS to reduce drugs costs for Africa at the Durban conference,¹⁶ but this news was greeted by activists with 'caution and scepticism', due to concerns that such programs would come with complicating conditions that could prevent access to generic antiretrovirals.¹⁷

By 2003, the treatment access movement that had begun at the grass roots and non-governmental organization (NGO) levels went mainstream. The WHO announced its '3 by 5' program, which framed universal access to HIV treatment (and prevention), for those who needed it, as a human right. Its specific target was to gain ART for three million people by the year 2005. While this target was not reached, the program developed policy and infrastructure that greatly facilitated later scale-up. In addition to addressing barriers like distribution and pricing, this program devised simplified systems of ART prescription that required minimal health service support. This assisted in removing structural barriers to access.¹⁸

Two other international events had major impacts on access to ART. The first was the United Nations General Assembly Special Session on AIDS (UNGASS 2001), which spawned the Global Fund for AIDS, Tuberculosis and Malaria. The second was the President's Emergency Fund for AIDS Relief (PEPFAR), first announced in the United States President's State of the Union address in 2003.

From being considered untenable in resource-poor settings, ART was now hailed as 'an appropriate, rational and cost-effective investment choice for developing countries'.¹⁹

THE ROLE OF COMMUNITY PROTEST IN THE PrEP TRIAL CLOSURES

Having foreshadowed the failure of the PrEP trials due to community protest, I will now discuss in more detail the

York. Available at: <http://www.actupny.org/reports/durban-who.html> [Accessed 3 Mar 2010]; D.G. McNeill. 2000. Agencies Urge Use of Affordable Drug for H.I.V. in Africa. *New York Times* (online) 6 April. Available at: <http://www.nytimes.com/2000/04/06/world/agencies-urge-use-of-affordable-drug-for-hiv-in-africa.html?pagewanted=1> [Accessed 13 Jan 2010].

¹⁶ A. Diarra. Making a Public-Private Partnership Work – An Insider's View. *B World Health Organ* 2001; 79: 795–796.

¹⁷ ACT-UP, *op. cit.* note 15; J.S. James. Access to Treatment Worldwide: From Talk to Action at Durban. *Aids Treatment News* 2000; #347. Available at: <http://www.aegis.org/pubs/atn/2000/ATN34703.html> [Accessed 21 Feb 2010].

¹⁸ WHO-UNAIDS. 2005. *The 3 by 5 Initiative: Treat three million people with HIV/AIDS by 2005*. Geneva, Switzerland: WHO. Available at: <http://www.who.int/3by5/en/> [Accessed 21 Feb 2010].

¹⁹ J.P. Moatti et al. Antiretroviral Treatment for HIV Infection in Developing Countries: An Attainable New Paradigm. *Nat Med* 2003; 9: 1449–1452.

circumstances under which the trials were closed, the issues raised by protesters and how these concerns relate both to the bioethical discourse about standard of care and the political movement for universal treatment access.

Four different clinical trials of the experimental HIV prevention strategy known as 'PrEP' had begun by 2005, with sites in Africa and Asia, and with planning underway for further trials in the Americas. All of the trials investigated the safety and/or efficacy of the antiretroviral drug tenofovir,²⁰ in preventing HIV infection.²¹ The rationale for the number of trials was the need to explore the intervention in a variety of high risk contexts (i.e. in sexual activity, both gay and straight, and injecting drug use) and in different genders and body types.²²

Three of these trials became the focus of adverse attention: the Cambodian trial in female sex workers, the African trial in high-risk women with sites in Cameroon, Nigeria and Ghana, and the Thai trial in injecting drug users. The fourth trial, studying tenofovir in high risk 'men who have sex with men' (MSM) in Malawi, was terminated without fanfare for reasons that remain unpublished. Allegations were made that the trials were unethical on the basis of not collaborating sufficiently with communities, providing selective and biased information about potential adverse effects, and being unwilling to provide comprehensive health insurance for participants.²³ Each trial had a US sponsor: the Cambodian trial was sponsored by the United States' (US) National Institute of Allergy and Infectious Diseases (NIAID) and Family Health International (FHI); the African trial again by FHI and the Thai trial by the US Centers for Disease Control and Prevention (CDC).²⁴

US sponsorship was the root cause of unrest in the Thai trial, as it targeted injecting drugs users. According to the *Declaration of Helsinki* 2000, participants in a drug trial should be assured of the best current prophylactic method – meaning in this instance, clean injecting equipment. The US, however, neither acknowledged the 2000 version of the Declaration nor would its government

allow the provision of injecting equipment. Bleach was provided to clean equipment, but this is sub-optimal; the US claims that its actions are in line with Thai policy, were disputed.²⁵

The Cambodian trial

In Cambodia the contentious issues were: concerns about the long-term safety of tenofovir in HIV negative people; access to care, especially ART, post-trial; the level of HIV prevention counselling to be provided to participants; pre- and post-test HIV counselling; and the limited involvement of the community in the study design.²⁶ In particular, the issue of compensation was extremely problematic. Under US law research sponsors are not required to provide free medical care or compensation for participants injured in clinical research.²⁷ Although medical care would be available for participants from the research facility for the duration of the trial, it was unclear whether prospective participants understood this, and at any rate there was no provision for medical care after the trial, apart from access to ART for seroconverters through the then-fledgling national program. It is not clear that the preferential access to ART for trial participants was well understood, as access to ART was cited as a key issue by protesters.

Adverse effects of the study drug, especially potentially serious long-term ones, became a very significant focus of attention for the prospective study participants, who were often the sole breadwinner for families, the survival of whom depended on the commercial sex worker being fit for work.²⁸

The problem of compensation was apparent to the study investigators early on, as Page-Shafer et al. note in their article in the *Lancet*:

During 2003, we consulted with [other] investigators who had faced similar issues in other developing

²⁰ Later trials added the drug emtricitabine (FTC) combined with tenofovir in a single tablet, under the brand name Truvada. See for example listings on trial registries, available at: <http://www.controlled-trials.com/mrct/trial/438173/%27HIV+infection%27+AND+prevention> [Accessed 3 Mar 2010].

²¹ AIDS Vaccine Advocacy Coalition (AVAC). 2005. Will a Pill a Day Prevent HIV? New York, NY: AVAC. Available at: <http://www.avac.org/ht/a/GetDocumentAction/i/3116> [Accessed 13 Jan 2010]; A. Forbes. Moving Towards Assured Access to Treatment in Microbicide Trials. *PLoS Med* 2006. 3 (7): e153: 980–983.

²² K. Page-Shafer et al. HIV Prevention Research in a Resource-Limited Setting: The Experience of Planning a Trial in Cambodia. *Lancet* 2005; 366: 1499–1503.

²³ Mills et al. *op. cit.* note 2; Mills et al. *op. cit.* note 3.

²⁴ While the Cambodian study was sponsored by FHI, its funding was provided by a direct grant from the Bill and Melinda Gates Foundation. See Page-Shaffer et al. *op. cit.* note 22.

²⁵ A. Chua et al. The Tenofovir Pre-Exposure Prophylaxis Trial in Thailand: Researchers Should Show More Openness in Their Engagement with the Community. *PLoS Med* 2005; 2: 1044–1045.

²⁶ Page-Shafer et al. *op. cit.* note 22, p. 1499; A. Forbes & S. Mudaliar. 2009. *Preventing Prevention Trial Failures: A Case Study and Lessons for Future Trials from the 2004 Tenofovir Trial in Cambodia*. Washington, DC: Global Campaign for Microbicides; 12. Available at: <http://www.global-campaign.org/clientfiles/Cambodia.pdf> [Accessed 28 Apr 2010].

²⁷ R. Steinbrook. Compensation for Injured Research Subjects. *N Engl J Med* 2006; 354: 1871–1873.

²⁸ Tenofovir Trial in Cambodia, film, directed by Women's Network for Unity. Cambodia: Women's Network for Unity, 2008. Available at: <http://www.drpetra.co.uk/blog/womens-network-for-unitys-account-of-the-tenofovir-trial> then go to: <http://blip.tv/file/1418090> [Accessed 3 Mar 2010]; J. Fawkes. The Cambodian PrEP Trial: The Sex Workers' Perspective. Powerpoint presentation to *The 2nd Symposium on Microbicides and HIV Biomedical Prevention*, Sydney, 14 July 2008.

countries, and considered various options for the assistance of people with long-term health problems that could be attributed to their participation in trials, including insurance schemes, lump-sum payments, and the establishment of long-term contracts for the provision of clinical services. None of these options fits with the policies of our funding agencies.²⁹

Tensions between the researchers and the sponsors are evident in the above quotation, and also in a later comment that in response to rising evidence of misinformation about the trial in the community, the two universities collaborating in the study – the University New South Wales and the University of California – sought to place the trial protocol on their respective websites, but were denied permission to do so by the sponsors.³⁰

Of note, it was not merely access to ART for seroconverters that the Cambodian sex workers sought,³¹ – as mentioned above, arrangements for access had been made by the investigators, with ART supplied in line with the WHO guidelines for treatment in resource-limited settings.³² The workers also sought ways to manage the risk of long term illness or injury caused by the experimental drug.³³

In a short documentary film, *Tenofovir Trial in Cambodia*,³⁴ made from the perspective of the sex worker group Women's Network for Unity, it is clear that the prospective participants believed that the trial would expose them to significant harms, such as the possibility of requiring new kidneys due to drug toxicity. While in some respects such a fear is disproportionate (tenofovir has an excellent safety profile compared with other anti-retrovirals), it underscores the difficulties of communicating clearly and honestly about issues like risk across the vast epistemic divide between researchers and very poor women with minimal access to education, whose very daily survival appears to depend upon being sceptical.

The specific demand made by the Women's Network for Unity was for health insurance to cover any potential long-term adverse events from the trial drug (referred to in the film as 'life' insurance),³⁵ for a period of 30 to 40 years post-trial. What they were offered instead was US\$3 per month for participation.

²⁹ Page-Shafer et al. *op. cit.* note 22.

³⁰ Page-Shafer et al. *op. cit.* note 22.

³¹ Weijer and Le Blanc (2006) discuss the Cambodia trial as if this were the sole reason for the protest. Other sources quoted in note 25 attest that a major concern was long-term health issues resulting from a trial related injury – in particular, from kidney damage. See C. Weijer & G.J. LeBlanc. The Balm of Gilead: Is the Provision of Treatment to those Who Seroconvert in HIV Prevention Trials a matter of Moral Obligation or Moral Negotiation? *J Law Med Ethics* 2006; 34.4: 793ff.

³² Forbes, *op. cit.* note 26.

³³ *Ibid.*

³⁴ *Tenofovir Trial in Cambodia*, *op. cit.* note 28.

³⁵ Forbes & Mudaliar, *op. cit.* note 26, p. 13.

Tenofovir Trial in Cambodia does not distinguish between misinformation, conspiracy theories³⁶ and the substantive issue of fair compensation for trial harms. Where it succeeds, is in foregrounding the profound depths of exploitation, trickery and violence to which these women have been subjected, which makes their level of suspicion of authority all too understandable. Extreme poverty, gang rape, systemic discrimination and abandonment by NGOs – that obediently dropped work with sex worker groups so as to meet the requirement for getting US funding during the George W. Bush Administration – form the background for negotiations.³⁷

In a memorable riposte, one Cambodian sex worker in the film dismisses the charge that the action of the Women's Network for Unity has denied her a chance to contribute to humanity. 'What has humanity ever done for me?' she asks.³⁸

Trust – identified by the investigators as a key component in working with communities – would be an elusive commodity, and deservedly so.³⁹ Indeed, the record of drug companies in providing reasonable access to drugs, to the populations in which they (the drugs) were tested, is not good: in Brazil, where the human papilloma virus (HPV) vaccine was tested, it is now sold at higher price than in the US.⁴⁰

On August 13, 2004 the Cambodian Prime Minister, Hun Sen, put an end to the trial (which had ethics approval in Cambodia, Australia and the US), stating that: 'Cambodian people are not waste, and Cambodia is not a waste bin', and researchers should take their trials elsewhere.⁴¹ Of note however, the sex workers had indicated a willingness to continue negotiations, so long as they were party to the decision-making processes from the earliest stages and their lives and wellbeing were considered appropriately in the development of the research design.⁴²

The African trials

Six months after the termination of the Cambodian trial, the Cameroon site of the African PrEP trial was halted by the Minister of Public Health. Activist concerns were related to: the level of HIV prevention counselling provided – there were only eight counsellors for 400 women,

³⁶ Conspiracy theories presented included a belief that sex workers were deemed expendable people upon whom dangerous drugs could be tested with impunity.

³⁷ Forbes & Mudaliar, *op. cit.* note 26, pp. 9–10

³⁸ *Tenofovir Trial in Cambodia*, *op. cit.* note 28.

³⁹ B. Loff et al. Unethical Clinical Trials in Thailand: A Community Response (letter). *Lancet* 2005; 365: 1618–1619.

⁴⁰ J. Beloqui. 2008. *International Rectal Microbicides Advocates* (listserv communication). Philadelphia, PA: Critical Path Project. Available at: http://critpath.org/pipermail/rectalmicro_critpath.org/2008-November/000564.html [Accessed 13 Jan 2010].

⁴¹ Loff et al. *op. cit.* note 40.

⁴² *Ibid.*

the lack of female condom provision (only male condoms were provided) and alleged inadequate preparation for ART provision. Indeed, the informed consent document explicitly stated that the trial would not provide ART to seroconverters, a stance that was informed by the notion that supplying ART in a context where it was not generally available would constitute undue inducement.⁴³ Trial seroconverters would be referred to existing NGO sources, which the activist group ACT-UP Paris described as overburdened, with treatment provision for 10,000 individuals, while 40,000 people were already in need.⁴⁴

In addition to these substantive concerns, Mills et al.⁴⁵ cite widespread, inaccurate rumours that the investigators would deliberately inject participants with HIV, or that the tablets themselves contained HIV. These rumours appear to have their provenance in an argument advanced by the activist group ACT-UP Paris, who were involved in the protests, that the provision of inadequate HIV prevention counselling to participants was a back-door method of increasing HIV infection in the cohort.

Following an inquiry, the Ministry of Public Health issued a number of administrative requirements, including formal site accreditation and more regular reporting. The trial, however did not resume. A month later, the Nigerian trial site closed after it was determined that the site did not comply with operational and laboratory procedures.

In 2006, data from the Ghanaian site alone from the African trial was reported at the International AIDS Conference in Toronto, Canada. Tenofovir appeared to be safe in HIV negative people, results showed, but the sample size was too small to show statistically significant efficacy.⁴⁶

The Thai trial

Despite significant disquiet about ethical issues, the Thai PrEP trial targeting injecting drug users, which opened in 2005, has not stopped. The Thai Drug Users' Network and the Thai AIDS Treatment Action group cite as ethical violations, the failure to provide participants with sterile injecting equipment, lack of meaningful community consultation, lack of commitment from the sponsors

to promoting the safety of participants enrolled in the trial, assured access to tenofovir for participants for one year only post-trial and no agreement to work with the Thai Ministry of Public Health towards securing price reductions of tenofovir after the trial.

The lack of consultation with communities and the failure to negotiate access to the experimental product, if effective, flouts both the letter and the spirit of key guidance documents.⁴⁷ The failure to provide sterile injecting equipment, however, is most problematic because it is an established, effective intervention,⁴⁸ which reliably reduces HIV acquisition in this population. Non-provision exponentially increases the likelihood of seroconversions during the trial and thus exploits participants' vulnerability to HIV acquisition by denying them a proven intervention.

The reason for the lack of sterile injecting equipment is contested: the CDC website claims it is the result of Thai government policy, but this is vigorously denied in correspondence appearing in *The Lancet* that claims there is no such Thai policy; instead it is suggested that it was the US government policy which precluded provision (this was changed in 2009 with the sweeping changes brought in by the Obama administration).⁴⁹

Regarding ART provision, there is a national treatment program in Thailand, but the Thai Drug Users' Network claims systemic discrimination toward drug users by that service, and that very few of the 50,000 Thais on ART are injecting drug users.⁵⁰

⁴³ E. McGrory, A. Irvin & L. Heise. 2009. *Research Rashomon: Lessons from the Cameroon Pre-exposure Prophylaxis Trial Site*. Washington, DC: Global Campaign for Microbicides – PATH: 27. Available at: <http://www.global-campaign.org/clientfiles/Cameroon.pdf> [Accessed 5 May 2010].

⁴⁴ ACT-UP Paris. 2008. *ACT-UP-Paris and Treatment Activism*. Paris, France: ACT-UP Paris. Available at: <http://www.actupparis.org/article3482.html> [Accessed 12 May 2009].

⁴⁵ Mills et al. *op. cit.* note 2.

⁴⁶ L. Peterson et al. Tenofovir Disoproxil Fumerate for Prevention of HIV Infection in Women: A Phase 2, Double-Blind, Randomized, Placebo-Controlled Trial. *PLoS Med* 2007; 2: e27.

⁴⁷ Such as Guidelines 11,12 and 13 of the Council for International Organizations of Medical Sciences (CIOMS) *International Ethical Guidelines for Biomedical Research Involving Human Subjects* 2002, available at: http://cioms.ch/publications/guidelines/guidelines_nov_2002_blurb.htm [Accessed 3 Mar 2010]; Articles 6, 17, 32 and 33 of the Declaration of Helsinki 2008, available at: <http://www.wma.net/en/30publications/10policies/b3/17c.pdf> [Accessed 3 Mar 2010] and Guidance points 4, 5 13 and, depending upon the contested legality, 14 of the UNAIDS Ethical Considerations in HIV Preventive Vaccine Research 2000, available at: http://data.unaids.org/publications/IRC-pub01/JC072-EthicalCons_en.pdf [Accessed 3 Mar 2010]. It should be noted that the 2002 UNAIDS guidelines do not discuss provision of established HIV behavioural prevention such as condoms and clean injecting equipment under standard of care requirements, rather they position it as 'risk reduction measures' under 'informed consent' and only require provision of clean injecting equipment where it is legal to do so. The later UNAIDS guidelines, Ethical Considerations in Biomedical HIV Preventions Trials (2007) adopts a new category 'standard of prevention' (Guidance point 13) to define the control arm in HIV prevention trials. Available at: http://data.unaids.org/pub/Report/2007/jc1399_ethical_considerations_en.pdf [Accessed 24 Sept 2010].

⁴⁸ This is the language used in the CIOMS guidelines regarding placebo use. Guideline 11, CIOMS, *op. cit.* note 44.

⁴⁹ S. Jintarakanon et al. Unethical Clinical Trials in Thailand: A Community Response (letter). *Lancet*, 2005; 365: 1617–1618.

⁵⁰ K. Alcorn. 2005. Thai Tenofovir Trial Runs into Trouble after Ethics Protests from Drug Users. *NAM Aidsmap* 10 March. Available at: <http://www.aidsmap.com/en/news/AF0B8B91-A54B-4632-9736-03F66FE37CF5.asp> [Accessed 14 Jan 2010].

Given the strength of the ethical objections to the Thai trial, it seems remarkable that it has remained open, and continues recruiting, while the other trials closed. As to the reason why, I can only guess that this is concerned with the illegality of drug use in Thailand: Chua et al.⁵¹ mention that long prison terms and even the death sentence are norms for drug-related offenses. Police have wide discretionary powers, and there have been an alleged 3,000 extra-judicial executions. These factors arguably add up to a population who will not want to make too much fuss or attract too much attention for fear of reprisal.

The impact of the activism

The activism surrounding the PrEP trials has generally been met with disapproval from the wider community of people involved in HIV research. Joep Lange, who co-chaired the fifteenth International AIDS Conference in Thailand, which was disrupted by PrEP trial protesters, claimed that the activist group ACT-UP Paris, in particular, used methods of ‘uninformed demagoguery [and] intimidation’.⁵² Lange’s anger at the failure of the PrEP trials is based on three key issues: the demonstrated need for new biomedical HIV prevention strategies, which he deems to be foiled by the trial closures; the fact that it is demonstrable that the researchers in the Cambodia trial did, in fact, consult with community groups (but arguably not the right groups, and not well enough); and thirdly, that the protests were led from outside, motivated by the ‘misguided ethical imperialism’ of ACT-UP Paris.⁵³ While it is undeniable that there were elements of sensationalism and misinformation in the protests, this does not mean that there were no substantive issues involved. As the measured analysis written by the investigators from the Cambodia trial makes clear, the issue of compensation for harms was pertinent, but the trial sponsors would not negotiate.⁵⁴

During the controversy over the design and implementation of PrEP trials, provision of ART for seroconverters was treated as one of several requirements to ensure that participants got fair recompense for their participation. The sex workers involved in the protests were more interested in health care generally, particularly in the event of a catastrophic side effect like kidney failure, than ART alone. This demand for fair access to ongoing healthcare made by the PrEP protesters demonstrates a

concept of equity at work, one where people – including trial participants – are assumed to have the same basic rights to life saving treatment regardless of where they live. This, of course, is a tenet of the treatment access movement: that universal access is a human right.

The experience of the PrEP trials shows that even very vulnerable populations have an expectation that if they undertake risks, they earn an entitlement to benefits that comprehensively offset those risks. Further, that they should be consulted in the determination of the nature of those benefits.

THE BIOETHICS RESPONSE TO THE UNIVERSAL ACCESS MOVEMENT

Although access to ART in the developing world remains inadequate, the universal access movement has created political impetus to redress this and programmatic interventions to facilitate it. These changes create the context where it can be argued that obligations to research participants have changed due to external circumstances. This fits with the tenet that ‘we can only morally require of people to do what they are capable of doing, or what it is reasonable to ask’,⁵⁵ commonly expressed as ‘ought implies can’. The argument that treatment provision in prevention trials is too burdensome, while always contestable, is now clearly untenable.

Ruth Macklin (2006) contends that arguments against obligatory provision of ART in prevention trials were based on the assumption that either the researcher or the sponsor would have to bear the cost. Now that treatment access programs are in place and partnerships between treatment and research programs are being forged, that assumption has been overturned. Within the new context of treatment access programs, she suggests an obligation to provide ART has arisen.⁵⁶

The problem for bioethics becomes how to theorise the source of the obligation. The obligation is not grounded in compensatory justice, argue both Slack et al.⁵⁷ (2004) and Weijer and Le Blanc,⁵⁸ as HIV acquisition is not caused by trial participation but by risk behaviour, against which participants are explicitly counselled. Causation is a necessary condition of compensatory claims. If the prevention technology itself does not cause the HIV infection (so the argument goes), then the infection arises from the participant’s own behaviour.

⁵¹ Chua et al. *op. cit.* note 25.

⁵² J.M. Lange. We Must Not Let Protestors Derail Trials of Pre-Exposure Prophylaxis for HIV. *PLoS Med* 2005; 2(9): 833–834. Available at: <http://www.plosmedicine.org/article/info:doi%2F10.1371%2Fjournal.pmed.0020248> [Accessed 13 Jan 2010].

⁵³ *Ibid.*

⁵⁴ Page-Shafer *op. cit.* note 22.

⁵⁵ R. van der Graaf & J.J.M. van Delden. What is the Best Standard for the Standard of Care in Clinical Research? *Am J Bioethics* 2009; 9(3): 35–43.

⁵⁶ R. Macklin. Changing the Presumption: Providing ART to Vaccine Research Participants. *Am J Bioethics* 2006; 6: W1–W5.

⁵⁷ C. Slack et al. Provision of HIV Treatment in HIV Preventive Vaccine Trials: A Developing Country Perspective. *Soc Sci Med* 2005; 60(6): 1197–1208.

⁵⁸ C. Weijer & G.J. LeBlanc. *op. cit.* note 31.

The individualism that underpins this argument and the avoidance of addressing the structural determinants of HIV risk is problematic.⁵⁹ An eighteen year old sex worker who has unprotected sex in Durban, South Africa has a much greater risk of being infected with HIV than her sister in Sydney Australia would have. Women and men who exchange sex for money, goods or favours may also have less control over the sex they have, including whether or not condoms are used. A trade-off between accepting more money for an unprotected sex act may appear a good deal to someone who is struggling to survive from day-to-day. The riposte to this point is that the researchers are not responsible for this inequity. This is true, but it is also true that they gain by it, because HIV prevention trials must instrumentalise the vulnerability of people who are at high risk of HIV to run successful trials. Weijer and Le Blanc argue that HIV prevention researchers are people 'already contributing importantly to redressing injustice'.⁶⁰ This contains an implicit claim that research is in itself a moral enterprise. Even if you take this claim to be uncontested (which it is not), it overlooks the fact the research is an industry – one that uses people as a raw material. This arguably creates an obligation on the part of researcher to provide a benefit that is commensurate with the risk, inconvenience and level of gratitude owed to those who participate in such significant research.

The assertion that HIV acquisition is not causally connected to experimental biomedical agents is problematised by the examples of two recent – and possibly three – prevention trials in which the experimental technologies specifically increased, rather than diminished, biological susceptibility to HIV infection. Three trials in the last decade have been stopped by their Data Safety and Monitoring Boards due to increased susceptibility to infection in the active treatment group, and in two of these cases it was found that the experimental agent increased the likelihood of seroconversion.⁶¹ These trials are an important reminder of the risk of participating in

clinical research and the possibility of unintended and unexpected effects when experimental products are used in the broader populations in efficacy trials.

However, to argue that the basis of an obligation is risk alone, underestimates the responsibilities of the physician/researcher and the inescapable obscenity that the success of HIV prevention trials depends upon recruiting people sufficiently vulnerable to HIV acquisition (due largely to structural factors beyond their control), and observing the rate at which they acquire this life-threatening infection.

Belsky and Richardson provide a moral framework for determining the care that should be provided to trial participants beyond that which is required for the successful conduct of a study.⁶² They argue that participants in clinical research entrust their health to researchers in a 'partial and limited' manner which creates a corresponding duty of care. Analysis of this, together with analysis of the strength of the claim, allows distinctions to be drawn.

Although the scope of this partial entrustment will vary, it is possible to generalise. As a participant typically gives permission for a disease under study to be monitored, the scope of the entrustment typically includes caring, as needed, for that disease. Since participants' permission is needed for doing tests or collecting confidential medical information, the scope of entrustment typically includes following up on any clinically relevant information or diagnoses generated.⁶³

The determination of obligation, they claim, depends upon a condition being within the scope of entrustment and the obligation being sufficiently strong. There are four tests of the strength of the claim. These are questions of the degree of the participant's vulnerability, the depth of the relationship between the participant and the researcher (meaning intensity and duration – is the study a one-off test or of an ongoing nature), the degree of gratitude the researcher owes the participant and consideration of whether there are important reasons against providing the care. They illustrate this with the example of a woman in a trial of a vaginal microbicide, who is found to have vaginal thrush, and who appears to have dental problems. The researcher is obliged to treat the first condition, as its diagnosis is made through an assay used in the research, and vaginal health is a significant factor in a trial that alters the vaginal environment. Her dental condition, however, falls outside the scope of entrustment because its diagnosis does not arise from 'exercising the permission participants grant on entering the study'.⁶⁴

⁵⁹ D. Zion. HIV/AIDS Clinical Research, and the Claims of Beneficence, Justice and Integrity. *Camb Q Health Ethics* 2004; 13: 404–413.

⁶⁰ C. Weijer & G.J. LeBlanc. *op. cit.* note 31.

⁶¹ Briefly, two experimental microbicides (topical agents designed to be used in the vagina to prevent infection) have caused an increased rate of HIV infection in women using the product in clinical trials testing their efficacy (see below); L. Van Damme et al. (on behalf of the COL-1492 study group). Effectiveness of COL-1492, a nonoxnol-9 Vaginal Gel, on HIV-1 Transmission in Female Sex Workers: A Randomized Controlled Trial. *Lancet* 2002; 360(9338): 971–977; L. Van Damme et al. Lack of Effectiveness of Cellulose Sulfate Gel for the Prevention of Vaginal HIV Transmission. *N Engl J Med* 2008; 359(5): 463–472; One vaccine trial has shown increased susceptibility to HIV associated with the product in certain populations; S.P. Buchbinder et al. Efficacy Assessment of a Cell-mediated Immunity HIV-1 Vaccine (the Step Study): A Double-blind, Randomised, Placebo-controlled, test-of-concept Trial. *Lancet* 2008; 372: 1881–1893.

⁶² L. Belsky & H. Richardson. Medical Researchers' Ancillary Clinical Care Responsibilities. *BMJ* 2004; 328: 1494–1496.

⁶³ *Ibid.*: 1495.

⁶⁴ *Ibid.*

Applying this framework to HIV prevention trials, randomised controlled trials (RCTs) require seroconversions in order to get results, and HIV testing occurs as part of the trial. As Richardson points out in his later article, this places treatment for HIV centrally within the scope of entrustment, and establishes a presumptive duty of care.⁶⁵ HIV prevention trials in developing countries involve people who are highly vulnerable, and they necessarily instrumentalise the socio-economic vulnerability of research subjects to HIV to produce a result. Trial participation requires long-term commitment with relatively frequent clinical contact. Participation involves risk due to the exposure to an agent that has been used in relatively few people and the seroconversion of a percentage of trial participants are foreseeable harms, necessary to the research and over-determined by circumstance. The participants' agreement to volunteer for the trial provides researchers with a significant opportunity. The researchers, science and society all benefit from successful HIV prevention trials, but unless ART is provided for seroconverters and appropriate general health care to all participants, no commensurate benefit is provided to the participant. The degree of dependence upon the researcher is likely to be high given poor health infrastructure. Hence, all the conditions for determining that there exists a strong claim are present.

Finally it needs to be considered whether there is an important reason not to provide ART. Prolonging the lives of otherwise healthy people who are in their most productive years provides a strong moral imperative for ART. The point that providing therapy for some members of a community but not others introduces a new level of advantage and disadvantage in an important one, because justice and equity are central aims of the enterprise.⁶⁶ It is not sufficient, however, to deny research participants a justifiable claim to life saving treatment. Some degree of priority-setting and rationing is unavoidable in ratcheting up universal ART programs in resource-poor areas. Prioritising research participants in government or donor-funded facilities is appropriate, as research participants remain citizens and human beings to whom both governments and aid organizations have responsibilities. However such prioritisation must involve the leveraging of research funds to increase the overall pool available, so that research participants do not merely displace other eligible people.

Using this model, contraception would fit into the 'scope of entrustment' for HIV prevention trials, along with testing for and treatment of sexually transmissible infections (which is standard practice) and compensation

for illness and/or disability arising from use of the experimental drug (which is what the Cambodian sex workers sought).

Stobie and Slack argue that taking the principle of reciprocal justice seriously would mean that both infected and uninfected participants deserve equal contribution of thanks, suggesting that ART provision would provide an unfair benefit to those who seroconvert.⁶⁷ This account fails to recognise that while risk is theoretically borne equally by the participants in a randomised trial, its outcome – harm – is experienced asymmetrically. It is unknown who will receive the experimental agent, it is unknown whether its effects will be beneficial or detrimental and it is unknown who will be exposed, and at what level, to HIV infection while on the trial. All bear the risk, but through the confluence of a range of factors, only some experience the burden of actually acquiring HIV. Providing compensatory care for those who are 'unlucky' – those who experience statistically predictable harm that affect some but not all individuals – is an equitable approach to off-setting the inequitable burdens.

In 2008, Macklin addresses the role of changing circumstances in creating obligation. She argues for ART provision as an act of beneficence and an exercise in justice-as-reciprocity neatly reversing 'ought implies can' to 'can implies ought'.

Joseph Millum (2009) raises a problem with the claim that the obligation is there because it is now possible, through alliances with other parties, to provide ART with relatively little burden upon researchers.⁶⁸ Millum points out that the putative obligation is upon researchers and trial sponsors, not upon governments and international aid agencies, to provide ART for seroconverters in research trials. Governments and aid agencies, he contends, should have their own priorities for distribution of ART. Given that everyone who has HIV at a stage that requires treatment deserves it, and governments' obligations are to the citizenship and not to select groups thereof, Millum argues that it is not justified to shift resources from non-participants to participants. Recall that this was one of the issues in the Cameroon PrEP site – the demand for ART already outstripped supply and prioritising research participants would displace others. Millum writes:

The central problem with using either beneficence or justice to ground an obligation to supply ART to trial participants is that neither gives us reason to privilege

⁶⁵ H. Richardson. Gradations of Researchers' Obligation to provide Ancillary Care for HIV/AIDS in Developing Countries. *Am J Public Health* 2007; 97(11): 1958.

⁶⁶ B. Lo, N. Padian & M. Barnes. The Obligation to Provide Antiretroviral Treatment in HIV Prevention Trials, *AIDS* 2007; 21: 1229–1231.

⁶⁷ M. Stobie & C. Slack. Treatment Needs In HIV Prevention Trials: Using Beneficence To Clarify Sponsor-Investigator Responsibilities. *Developing World Bioethics*, no. doi: 10.1111/j.1471-8847.2009.00272.x

⁶⁸ J. Millum. Post-trial Access to Antiretrovirals: Who owes What to Whom? *Bioethics* 2009. doi: 10.1111/j.1467-8519.2009.01736.x. Available at: <http://onlinelibrary.wiley.com/doi/10.1111/j.1467-8519.2009.01736.x/full> [Accessed 13 Sept 2010].

trial participants over other equally needy people. Duties of beneficence and duties to rectify injustice are grounded in the unfortunate situation of the beneficiaries; they are not dependent on the beneficiaries participating in clinical trials.

The justification for special treatment of research participants rests upon reciprocity, according to Millum. Their participation in research is primarily of benefit to others, and hence they are owed ‘an appropriate response to the benefits received’.⁶⁹ Millum does not conclude that this obligation is necessarily that of life-long ART (recall that for the Cambodian sex workers, insurance against any long-term adverse effects of the trial drug was the key goal), but he is adamant that if ART is provided, it ought not to be at the expense of others.

Millum’s contention that the obligation is not necessarily to provide access to ART is based on arguments that the strength of the obligation can vary according to individual factors within trials. Firstly, the researcher/participant relationship may be brief and superficial; secondly, the duties of reciprocation depend on the benefits generated, and that these benefits vary between trials.

The first part of Millum’s argument pays too little attention to Belsky and Richardson’s ‘scope of entrustment’,⁷⁰ which for an HIV prevention trial clearly includes treatment for the condition under study. Regarding the strength of the claim, trials may vary somewhat in their requirements of participants, but ongoing, regular monitoring over a number of years is the expected obligation of participants, which is hardly an insignificant relationship.

The second aspect of Millum’s argument is grounded in a notion that only *some* HIV prevention trials provide the kinds of benefits (in terms of knowledge) that would justify ART provision as an appropriate response. While undoubtedly some trials produce generalisable knowledge that could transform the prevention of HIV, it would be a very crude analysis that rated participation in such a trial above a trial of a failed product, or a harmful product. Can Millum seriously imply that participants in the male circumcision trials which changed the landscape of HIV prevention are owed more than, say, participants in the Carraguard microbicide study, which showed safety but no efficacy? Clinical research is an iterative process and learning progresses at each stage. Learning what does not work is as important as learning what does.

Thirdly, Millum’s contention that the obligation to seroconverters on a research trial is borne by the researcher alone is flawed. The responsibility of the researcher does not nullify the pre-existing obligations of a government to its citizens, nor of the international

humanitarian community to people in need. Hence a model of shared care, to which researchers contribute but are not solely responsible, is appropriate. This position is adopted by Lo and colleagues, who extend the argument to contend that ART provision should be community-wide, rather than limited to trial participants.⁷¹ Taking the obligation to provide ART to seroconverters as a given, the basis of their argument is social justice, and they advance two reasons for this position. Firstly, in a community where a major HIV prevention trial is being conducted it is possible that there will be participants from past trials in the area for whom ART was not provided. Secondly the research project should generally aim to reduce health disparities, not increase them by constructing a new level of privilege and disadvantage.

In accordance with the obligation to provide ART in resource-poor setting, they argue that if national programs are up and running, the sponsor/researcher should contribute to these programs in a way that facilitates the sustainability of the programs. Donor money should be used in strategic ways to reduce the structural barriers to accessing treatment for communities (such as distance from health facilities), not just individual participants. Providing a bus service, they argue, is a better intervention than simply transporting single participants to medical appointments. This concept fits neatly with Millum’s view that fulfilment of obligations to participants should maintain or increase the global provision of ART, though he disagrees that the researchers have any specific obligation to the wider population and that government and aid agencies have an obligation to research participants. It dovetails with the argument advanced by Shapiro and Benatar,⁷² that there is an obligation for researchers to ratchet up infrastructure and care so as to benefit the whole population, rather than limiting benefits to research participants.

The logistical problem that arises from the argument that researchers’ obligations ought not to be offset to other institutions nor be fulfilled at the expense of other needy people, is summed up by Macklin:

The NIH and the MRC have as their mission the conduct of research, not the provision of health benefits to research subjects or the developing countries from which they are drawn. It is in . . . the[ir] interest to conduct research efficiently and effectively, and that can only be done by sticking to their narrow mission.⁷³

⁷¹ Lo et al. *op. cit.* note 66.

⁷² K. Shapiro & S.R. Benatar. HIV Prevention Research and Global Inequality: Steps Towards Improved Standards of Care. *J Med Ethics* 2005; 31: 39–47.

⁷³ R. Macklin. 2004. Striving for a Single Standard. In *Double Standards in Medical Research in Developing Countries*. Cambridge, UK; Cambridge University Press: 101–102.

⁶⁹ Ibid: 7.

⁷⁰ Belsky & Richardson, *op. cit.* note 62.

Given that true universal access remains a dream, it is timely for research funders to revisit their mission, and recognise that their moral obligation requires that provision of benefits to participants (or at least facilitation of, and contribution towards, benefits) be considered as legitimate an expense as the salaries of research staff, or the costs of transporting blood samples to laboratories.

DISCUSSION

Why argue for the right for trial participants to access ART – and other necessary medical benefits, as required – when all people with HIV who require treatment have that right, grounded in human rights conventions?⁷⁴ Does this not privilege the rights of the few over that of the many? It is not, in my view, a question of placing the rights of some over others, but of articulating the responsibilities of different agencies toward different populations and individuals, with a view to creating a context that facilitates the goal of universal access.

The generalised right to health as articulated in human rights conventions, in particular the *International Covenant on Economic, Social and Cultural Rights*, places responsibilities upon governments and the international community. But other parties also bear specific responsibilities: for example, physicians have particular responsibilities to provide care for their patients, and the research community, as I have argued in the article, has a special responsibility towards research participants. Stressing both physician/patient responsibilities and researcher/participant responsibilities do not undermine the generalised claim for care by the needy, but they apportion that responsibility in specific ways. In my view, the delineation of responsibilities to provide care creates an enabling environment for universal access.

Consider the real-world effects of short-course AZT trials, which proved that giving less of the drug to poor women produced a result that was less effective than best practice, but better than nothing. The short-course regimen was not then implemented in southern Africa. Proving that short-course AZT was better than nothing for vertical transmission did not create momentum for significant price reductions and improved access. Those results supported the indecent pricing of the drug, by establishing a regimen that encouraged giving less drug for less effect in poor populations (resulting in more HIV

positive babies), rather than fuelling arguments for reasonable, affordable drug prices for all.⁷⁵

Putting the public health goals of a developing nation above the protection of the individual research subject, by allowing researchers to discount standards of care, places a lower value on the life of that subject, and this process supports, rather than challenges, global inequities. Access schemes created to support research projects, on the other hand, build capacity to scale up for broader provision of essential health services.

Protecting the rights of the individual research participants and requiring those who have a responsibility to honour them, prevents exploitation and upholds a notion of global equity. The alternative is the perpetuation of double standards which support an assumption that inequity is inevitable (and implicitly acceptable).

SUMMARY AND CONCLUSIONS

The devastation caused by HIV/AIDS in the developing world spawns two very different responses: one, which I characterise as relativist, a movement to work within the contextual constraints to research appropriate interventions; the other, universalist in scope, is an outcry against exploitation, and a desire to police the obligations that the researcher has to protect the research participant. The basic question being asked was: do research participants everywhere have the same rights? The answer to this, *a priori*, is that they do (or should).

Where the relativists and the universalists part company is on the reasoning about how to best protect the interests of those participants. The universalists argue that this means importing standards of care and post-trial care from the developed world, against which to test more context-appropriate interventions, as the protection of the individual research participant is the primary obligation of the researcher. The relativists argue that research participants are part of a community, and that community interests are best served by acknowledging the reality of local circumstance. Therefore, context-appropriate interventions should be tested against the baseline therapy currently available in the community, even if that is nothing.

While this debate raged, in the resource-rich world, the control of HIV-related diseases using combination antiretroviral therapy became the good news story of the late 1990s. The ascendancy of ART and reframing of HIV as a chronically manageable infection catalysed a struggle

⁷⁴ United Nations General Assembly. *International Covenant on Economic, Social and Cultural Rights*, 16 December 1966, 993 UNTS 3 at Article 12 (entered into force 3 January 1976). Available at: <http://www2.ohchr.org/english/law/ceschr.htm> [Accessed 3 Mar 2010]. Note that the US has never ratified this, as it appears to mandate universal access to healthcare.

⁷⁵ While there were, and are, substantial logistical problems with providing optimal treatment and prophylaxis to pregnant HIV positive women who present late for care, the short course AZT trials focused on giving less drug to poor women, rather than exploring optimal dosing within logistical constraints. The high price of the drug was taken as given, rather than a possible variable.

for equity in global health: the treatment access movement. This movement sought to displace the assumptions of unaffordability and excessive complexity, and replace it with the simple demand for equity, for recognition that access to life saving treatment had to be seen as a necessity and a right, not a privilege reserved for the affluent.

The stark disparity in access to life-saving drugs rekindled the question of what was owed to research participants in HIV prevention trials. The populations needed to test new prevention technologies were precisely those that lacked assured access to life saving treatment for those who seroconverted.

The PrEP trials discussed in this article represent a great social failure of institutionalised clinical research. These trials are important, because the views of the potential participants are brought to the fore, and they are insistent and compelling in their demands for what they consider to be reciprocal justice in research.

The experience of the PrEP trials, particularly in Cambodia, and the example of the treatment access movement, shows that people in the developing world want justice. This is to say that they want access to health care and treatment, and that they do not accept profit – even

the putative future profit for humanity – being placed over their lives and well being. The argument that researchers have a duty of care – indeed, a moral obligation – to ensure that therapy for the disease under study in prevention trials is available, is significant because it broadens the role of research in the developing world. Rather than functioning as a dislocated, disinterested machine for the production of knowledge, this obligation creates a new role for research as part of a capacity building project that can help to redress health disparities.

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Biography

Bridget G. Haire is a PhD student at the Centre for Values, Ethics and the Law in Medicine at the University of Sydney. She has a Masters (hons) in Bioethics from the University of Sydney and has worked as an HIV community advocate for more than 15 years.