Research, Therapy, and Bioethical Hegemony: The Controversy over Perinatal AZT Trials in Africa

Claire L. Wendland

Abstract: Research on zidovudine (AZT) for pregnant women in Africa sparked worldwide debate in the late 1990s. The debate ultimately led to the rewriting of international ethics guidelines, in at least one case specifically to prohibit use of a placebo group (the most controversial aspect of the research) when known effective treatment is available. I draw upon clinical experience in Malawi and theoretical perspectives from anthropology to reframe the controversy. The dominant bioethical position constructed research and therapy as ethically distinct. This distinction ensured that inequalities of power and resources were perpetuated, not remedied, by the AZT debates.

International collaborative trials of short-course zidovudine (AZT) to reduce mother-to-child HIV transmission, conducted in nine African countries, sparked heated worldwide debate in the medical literature, the bioethics literature, and the popular press at the close of the twentieth century.[1] This debate has since led to revisions in ethical codes in the conduct of international clinical research, and to a fragile consensus prohibiting researchers from using placebo in conditions for which a known effective treatment is available. It has also reinforced a deep, if rarely articulated, distinction between the ethics of research and the ethics of therapy.

As a doctor who had spent time working in a Malawian hospital, confronted with the ramifications of AIDS and inadequate resources daily, I found certain emphases and omissions puzzling during the years this debate raged. As an anthropologist, I saw hegemony at work. That hegemony

African Studies Review, Volume 51, Number 3 (December 2008), pp. 1–23

Claire Wendland is an assistant professor at the University of Wisconsin-Madison in the Departments of Anthropology, Obstetrics and Gynecology, and Medical History and Bioethics. Her research explores how biomedical knowledges and practices are transformed when they are deployed in southeast Africa. Ongoing projects include a study of shifting ideas about maternal mortality among formal- and informal-sector health workers in Malawi.

has only grown stronger as this particular controversy recedes into the past. It is my intent in this article to open some of the bioethical considerations of the debate to a readership with deep knowledge of African ethics and philosophies. Challenging an America-centric "international bioethics" may lead to a more thoughtful search for solutions to problems of inequity in research and therapy alike.

A Time Line

1982: Public health officials in the United States first reported apparent mother-to-child transmission of an acquired immune deficiency complex (*Morbidity and Mortality Weekly Report* 1982). Meanwhile, doctors working in Central and East Africa began to see increasing numbers of patients suffering from the wasting syndrome Africans called "slim disease." North American and European researchers were beginning to call a similar syndrome AIDS, and soon it would become clear that the two were caused by the same virus (Iliffe 2006; Serwadda et al. 1985).

1990: In a large Malawi hospital, I watched at the bedside of a pale young woman who had just given birth and was now dying: her breathing was shallow, her heartbeat irregular, her consciousness waning. In the bay of the overcrowded postnatal ward reserved for acutely ill patients—the bay closest to the lone nurse who looked after the ward's sixty-odd patients—the dying woman was the only one not sharing her narrow metal cot with another patient. It was not because she had AIDS; many of the women in the ward did. (That year an estimated 60 percent of the nine million people living with HIV worldwide were Africans. One would not have guessed as much by perusing the medical literature, in which gay men and intravenous drug users in the West were still the major focus.[2]) But her thin body was covered with rotting lesions of Kaposi's sarcoma, and the terrible smell kept the others away.

At the hospital to which I would return in the United States, a drug that prolonged life in HIV-positive individuals had been available for three years. AZT was the first real success in a class of medications known as antiretrovirals, and it was having a miraculous impact on patients who not long before would have died quickly. In Malawi, AZT was not available.

Through the ward's open windows, we could just glimpse the stalls of the herbalists who hawked their medicines in the sycamore shade outside the hospital: roots and decoctions for tuberculosis, for infertility, for the relentless disease that made young healthy people waste away slowly. Inside the hospital we had nothing except a little pethidine to ease the dying woman's pain. That morning her child had slipped easily into this world. Not long after, weakened by illness, blood loss, and the exertion of labor, the young mother slipped out just as quietly. Her guardians, burdened with another orphan, wondered whether her newborn son would share her fate. There was no way to know, and nothing to be done about it in any case.

Table 1. Comparison of Standard 076 and Short-Course AZT (Zidovudine) Regimens

	076 AZT Regimen	Short-Course AZT Regimen
Medication doses	Oral AZT (100 mg 5x/day) starting at 14 weeks pregnancy Intravenous AZT (2 mg/kg over 1 hour, then 1 mg/kg/hour) in labor Oral AZT syrup for the newborn (2 mg/kg 4x/day) for 6 weeks	Oral AZT (300 mg 3x/day) starting at 36 weeks pregnancy Oral AZT (300 mg) at onset of labor and every 3 hours until delivery
Results	HIV transmission reduced from 25% to 8%	HIV transmission reduced from 25% to 15%
Costs	U.S. $800 per pregnancy	U.S. $80 per pregnancy

Note: Costs are in 1997 U.S. dollars. For both regimens, estimated costs are for medication alone and do not include clinic or hospital charges, pharmacist, nurse or physician fees, or costs of HIV testing.

Sources: Medication doses and results are from Connor and Sperling (1994) for the ACTG 076 regimen and Wiktor et al. (1999) for the short-course regimen. Costs are calculated based on wholesale price of medication in 1997, when the controversy over short-course AZT erupted. Some contemporary journalists gave the short-course cost as $50, some $80.

1994: Good news reached pregnant HIV-positive women and those who treated them in the wealthy parts of the world. The landmark AIDS Clinical Trial Group 076 study (often referred to simply as 076), conducted in the United States and France, showed dramatic reduction of HIV transmission between mother and infant with a lengthy course of AZT (Connor & Sperling 1994). Without treatment, an HIV-infected mother had about a 25 percent chance of passing the virusto her infant during pregnancy and birth. The 076 regimen reduced the maternal–child transmission rate to just 8 percent; AZT was the first medication that had been demonstrated convincingly to help *prevent* HIV infection, and it was very welcome news. How unfortunate, a few journalists commented, that the $800-per-pregnancy price tag of the 076 regimen kept it out of reach in the Third World.

1997: In the United States, an uproar over research ethics began in the pages of the *New England Journal of Medicine.* Peter Lurie and Sidney Wolfe, spokesmen for a watchdog organization called the U.S. Public Citizen's Health Research Group, wrote an article exposing a series of clinical trials in the Third World as unethical (Lurie & Wolfe 1997). In the same issue, Harold Varmus from the National Institutes of Health and David Satcher from the Centers for Disease Control and Prevention—organizations co-sponsoring some of the trials—defended the studies as ethically legitimate and scientifically essential (Varmus & Satcher 1997). Marcia Angell, the *Journal*'s editor,

https://doi.org/10.1353/arw.0.0084 Published online by Cambridge University Press

denounced the trials in an accompanying editorial (Angell 1997).

The controversial research, begun in 1994, had been designed to evaluate a shorter, simpler, and much cheaper regimen of AZT in pregnant women by comparing it to placebo (see table 1 for details of the two regimens). Pregnant women wishing to enroll in the study were tested for HIV. Those who were seropositive and gave consent were randomized to receive either AZT or placebo in the final weeks of pregnancy and during labor. Neither the woman nor any clinician caring for her knew whether she was receiving AZT or placebo. Her infant was then tested several times for HIV over a period of eighteen months. Since breast milk can also transmit the virus, mothers in some of the trials were instructed not to breastfeed in the months before newborn testing was complete, so as not to create additional opportunities for HIV transmission that could render the studies inconclusive. Neither mothers nor infants were offered any additional antiretroviral medications. They did receive free medical care for the duration of the research.

Most of the fifteen sites for the placebo-controlled trials were in nine sub-Saharan African countries; two were in Thailand and the Dominican Republic. (In this article I focus on the African cases, but the ethics in the other two situations were even more problematic: at the Thai and Dominican sites, antiretroviral medication became available for the general HIV-infected public during the course of the trials. In the African countries involved over the same time period, no antiretrovirals were available in the public sector outside of research protocols.) In all cases the studies had cleared the relevant national and institutional human-subjects research review boards. The U.S. government funded nine of the trials through either the Centers for Disease Control and Prevention or the National Institutes of Health (Resnik 1998).

Some critics questioned the consent procedure for enrollment of trial subjects at specific sites (French 1997). Opponents of the short-course AZT trials argued more generally that informed consent for participation in this type of research was difficult, if not impossible, in regions with low literacy rates or where enrollment in a clinical trial might be the only way to get any medical care (Tafesse & Murphy 1998). Ethicists were also concerned about who would benefit from the trials (Annas & Grodin 1998), and they had recent historical precedent to justify their concerns: the vaccine for hepatitis B, developed in Senegal, was unavailable there due to its high cost (Specter 1998).

By far the most contentious aspect of the trials, though, was the use of a placebo control group. Most of the ethical arguments over the AZT trials revolved around the interpretation of international human-subjects research guidelines that require *every* patient in a study to receive the best proven medical care available. With minor variations, this directive appears in the Nuremberg protocols, the World Medical Association's Declaration of Helsinki, and the widely used guidelines of the WHO-affiliated Coun-

cil for International Organizations of Medical Sciences.[3] Its interpretation turns on a fine point of emphasis: does it mandate *best* available medical care or best *available* medical care (i.e., best care available in a particular community)?

Opponents of the trials argued that this guideline clearly prohibited use of a placebo group, as a known effective therapy existed; short-course AZT should have been tested only against the demonstrated 076 regimen. In fact, since the short course was *expected* to be less effective than 076, some ethicists argued that according to the guidelines it should not have been tested at all (see Bayer 1998). Trial supporters responded that the 076 regimen, because of its cost, was not in practice available at any of the research sites, and thus could not possibly be considered the best proven medical care available in the countries involved (Levine 1998). They pointed to other international guidelines requiring research to be responsive to the health needs of the community in which it is carried out. Yes, a research protocol using the 076 regimen might be maximally advantageous to the individual subject. But it would be of no use to her community because of its cost, and because it would not answer the real question: is the experimental shorter course better than nothing? These guidelines, they suggested, practically *mandated* a placebo group because that was the current standard of care for women in Africa: nothing at all.

The *New England Journal* articles engendered a furor that reached the front page of the *New York Times* and spread worldwide. Premier medical journals devoted entire issues to the controversy. Accusations and counter-accusations flew: Angell (1997) invoked the notorious Tuskegee study; African researchers (Gambia Government 1998) countered with claims of Western ethical imperialism. When preliminary results of the Thai trial were reported the following year, the CDC suspended some of the remaining trials and modified others to remove the placebo group. Of all the U.S.-sponsored African trials, only the Côte d'Ivoire study was published (Wiktor et al. 1999).[4] To no one's surprise, the short course of AZT proved to be less effective than the 076 regimen—it reduced infections by about half instead of by two-thirds—but much better than nothing.[5]

2001: In the wake of the AZT controversy, bioethicists and researchers rewrote international research guidelines. A substantial revision of the Declaration of Helsinki, adopted in 2000 in Edinburgh, made clear that placebo control groups were unacceptable in cases where an effective treatment method was known. A major revision adopted by the Council for International Organizations of Medical Sciences (CIOMS) also restricted placebo use in international trials, though the language was murkier and the revision seemed to contradict portions of the Helsinki protocol it was intended to clarify (CIOMS 2002; Weijer & Anderson 2001).[6] Some ethicists seemed pleased with the changes they had wrought—no longer would researchers be able to defend exploitative research trials in the Third World—while others thought the revisions did not go far enough (Carlson et al. 2004).

Three years after the results of the trials were reported and remaining studies ended, no African government had adopted the short-course AZT protocol, not because it was less effective than 076, but because it was *still* too expensive. UNAIDS (2003) estimated that in 2001 less than 2 percent of the estimated 29 million Africans living with HIV/AIDS had access to any antiretroviral medications.

In Malawi, many years after AZT was proven to extend the lives of people living with HIV, the public sector still did not distribute any antiretrovirals outside research protocols. HIV prevalence among pregnant women attending urban hospitals remained at roughly 20 percent. AZT was not in use, but a significantly cheaper, slightly less effective antiretroviral medication called nevirapine was available during labor to pregnant women who enrolled in U.S.-sponsored HIV research protocols, and to those few women outside protocols who knew (and revealed) that they were HIV positive. In the hospitals, HIV testing was also frequently available only to people enrolled in transnational studies; the reagents were costly, and the public sector ran out of them on a regular basis.[7] Besides, there was little to be done about a positive test. Ongoing treatment for infected mothers was not a part of these transnational protocols. Women deciding whether to be tested had to weigh the chances of receiving medication that *might* prevent their newborns from getting AIDS against the heavy burden of a highly stigmatizing diagnosis for which few could afford treatment. Researchers' consciences might be eased by giving patients prescriptions or referring them to private clinics, but the expense of private medical care and of antiretrovirals meant treatment was out of reach for nearly all Malawian women. On the ground, most of the nurses, clinical officers, and doctors who watched helplessly over this carnage seemed more resigned than angry, wearily facing one more injustice in an unjust world. Clinicians at government hospitals told me that they gave moral support to these women, because there was nothing else to give.

More than a decade has passed since the initial flurry of statements, interviews, publications, denunciations, and exhortations over the perinatal AZT trials. The trials themselves have receded into the past, though they surface in the lists of historical ethical controversies presented in ethics classes and texts (see, e.g., Jecker et al. 2007; Macklin 1999). Life, death, and research go on. First-line antiretrovirals are increasingly available in Africa, thanks in large part to the relentless pressure put on drug companies, health ministries, and trade representatives by coalitions of African AIDS activists, medical humanitarian NGOs, and international human rights advocates. Second-line medications remain very difficult to access in most poor and middle-income countries and are the current battleground in the patent wars. Though the perinatal AZT controversy is no longer in the bioethics limelight, the underlying issues continue to rise again and again in debates over testing of other medications (Cohen 2000) or over transnational AIDS vaccine trials (Specter 2003).

Social Science and Ethics

Early work by social scientists interested in medical ethics often focused on the way ethical dilemmas, like other conflicts, could illuminate culture. As Peter Kunstadter explained, "Investigation and analysis of 'trouble cases' is important.... A thorough investigation not only indicates the nature of the value conflicts and identifies the parties to the conflicts, it also indicates the formal mechanisms for their resolution, thus giving information on social structure as well as value aspects of the problem" (1980:294). In the 1990s some social scientists began to expand the scope of inquiry in bioethics (see, e.g., Marshall 1992; Muller 1994; Weisz 1990). Not only could a careful analysis of bioethical problems elucidate social structure, some argued, but ethnographic methods could also be useful for understanding ethical quandaries. First, anthropologists and sociologists could look at bioethics itself as contingent. How might the origins, philosophical traditions, and social hierarchies of bioethics construct which types of problems count as "ethical dilemmas" and also construct—or constrict—the range of solutions considered? Whose interests do such constructions serve? Second, social scientists could reembed ethical problems themselves in historical, political, and cultural context.

These tactics ran contrary to the most mainstream intellectual traditions of bioethics, those of moral philosophy. Moral philosophical approaches to ethical problems tend to take one of two tacks. According to the first, inductive methods are used to strip away contextual "distractions," in this way paring a problem down to the pure principles that in theory underlie it. The alternative (which is more common today) is a deductive approach, which applies principles derived rationally from analytic philosophy to messy human contexts. Both approaches have an august intellectual heritage. More than two centuries ago Immanuel Kant (cited in Marshall 1992:54) argued that it was "of the utmost necessity to construct a pure moral philosophy which is completely freed from everything which may be only empirical and thus anthropology." (Kant did not quite mean by *anthropology* what we do today, but his point is clear.)

The second, principles-based approach of analytic philosophy remains the mainstream in institutional bioethics worldwide. The version taught in most medical schools—often the only sort of bioethical thinking to which ordinary doctors and researchers are exposed—is that of the "four principles" of medical research and the physician–patient relationship first codified by American ethicists in the 1970s: autonomy, nonmaleficence (avoidance of harm), beneficence, and justice (see Beauchamp & Childress 2008). Though ostensibly the principles are equal in moral weight, many commentators have pointed out that in fact autonomy trumps the others, and concerns of justice get very short shrift (see, e.g., Kleinman 1995; Wolpe 1998). This approach, with its promise of objectivity and logical clarity, explains in part the fixation on international guidelines so noticeable in the

debate over the AZT trials. The AZT trials also demonstrate the weakness of such an approach: principles that seem clear on the printed page or in the classroom can be much more challenging when researchers institute them (or ethics boards review them) in the actual world.

Though the principles-based approach to ethics remains the most influential paradigm, its serious limitations have inspired many criticisms and modifications, both from within bioethics and from without. Within bioethics, many have attempted to transcend the limits of principlism with excursions into narrative ethics, casuistry, virtue ethics, and numerous other modifications. Outside bioethics, additional approaches include abandoning the principles framework altogether in favor of a human rights argument, or one that focuses on an ethical imperative to develop human capabilities.[8] Many of the critics insist that "moral dilemmas and the means to resolve them cannot be separated from the institutional, political economic, social and cultural contexts in which they are embedded" (Muller 1994:453).

In the case of the AZT trials, even a modest contextual analysis brings up new questions and provides a different perspective on some of the old answers. The remainder of this article explores three interlocking realms that surfaced in this debate: discursive power, definitions of agency, and the geographical boundaries of moral concern. Ultimately, I argue, all three of these realms relate to an underlying distinction between research and therapy that works in favor of the wealthy world in this and other contexts.

Rethinking the Controversy

The bioethical discourse surrounding the perinatal AZT trials is rich ground for an exploration of how power is constituted through discursive strategy, as it quickly became a battle over who had the right to judge which research was—or was not—ethical. Even before the *New England Journal* article appeared, the battle lines were drawn. The American authors of the *Journal*'s "exposé," Peter Lurie and Sidney Wolfe, had written an open letter six months earlier to Donna Shalala, then director of the U.S. Department of Health and Human Services. In this letter they urged withdrawal of support for the AZT trials, beginning with the following words: "Unless you act now, as many as 1002 newborn infants in Africa, Asia and the Caribbean will die from unnecessary HIV infections they will contract from their HIV-infected mothers in nine unethical research experiments funded by your Department."[9] The authors of the letter were physicians who had made their reputations as medical watchdogs, protectors of the public. They evidently were certain that no one could possibly have imagined such a research design to be ethical—so certain that they suggested that carelessness or corruption of host-country physician researchers was the likely explanation for their collaboration in the trials. Lurie and Wolfe toned down their rhetoric for the *New England Journal* publication, implying less

that the African physician researchers were rapacious elites exploiting their countrywomen and more that they were unwitting stooges of the American research industry.

African researchers, aware that they were being portrayed as incapable and corrupt, lashed back. Several responded by accusing the Americans of grandstanding for political purposes, and of ethical imperialism: "Stopping trials in Africa that are trying to help improve the health of poor people so that those in affluent countries can have peace of mind seems a tortured form of ethical logic" (Gambia Government 1998:287). African respondents, whatever their positions on the controversy—and Africans, like Americans and Europeans, took both sides—consistently argued that their own local ties established a superior authority. As two South African physicians commented pointedly in the *Washington Post*, "We are suspicious of those who claim to speak for our people, yet have never worked with them. Callous accusations may help sell newspapers and journals, but they demean the people here and the horrible tragedy that we live daily" (Bagenda & Musoke-Mudido 1997). Or, in the words of Edmund Katongole Mbidde, chair of Uganda's AIDS Research Committee, "If Ugandans cannot carry out research on their people for the good of their nation, applying ethical standards in their local circumstances, then who will?" (1998:837).

Virtually every major figure in American bioethics weighed in on the topic of the AZT trials. By using an unmodified "we," by speaking explicitly for "those of us in the research community" (Angell 1997:849), and by repeatedly invoking international research principles, these Americans positioned themselves as the global conscience. They allowed themselves what Thomas Nagel (1986) called "the view from nowhere," the authorized position of scientific objectivity. Africans addressing such research issues, by contrast, were sometimes specifically marked as nonuniversal spokespersons, with publications subtitled "A South African's Viewpoint" (Abdool Karim 1998) or "The Uganda Experience" (Yusuf 1998).[10] No one wrote: "Unethical AZT trials: Perspectives from Massachusetts."

When those most concerned with the trials hold the side marked as "local" (even a valorized local) in an implicit equation, the global credentials are silently ceded to the American physicians and ethicists. It is noteworthy in this context that in a generally thoughtful commentary on the AZT trials, the well-known public health ethicist and political scientist Ronald Bayer lamented what he called the "deep divide among the deeply committed" (1998:570) but dramatically limited his scope of inquiry: the so-called deeply committed were ten American ethicists and physicians. Not one of those listed, moreover, was actually involved in the research. No matter what the debate's outcome, its conduct—that is, who was considered a spokesperson for the world, who determined what was or was not a question of ethics—furthered the asymmetries of power already so notable in research ethics (Anya 2008).

Some of the grounding assumptions of this bioethical hegemony, and

its historical and cultural embeddedness, become clearer when we turn to a different aspect of the commentary over the AZT trials: the essential but relatively unexamined distinction between research and therapy.

Standards of medical treatment often vary among regions because of local conditions, including economic conditions. Whereas variation in standards of research sets off bioethical alarms, such variations in medical treatment are rarely seen as ethical problems. Two examples will serve to demonstrate the distinction. First, it has been known for years that breastfeeding increases maternal–infant transmission of HIV. Yet many international guidelines that recommend formula feeding for at-risk infants in the developed world continue to recommend breastfeeding in places where the water to mix formula is unsafe (and formula is prohibitively expensive) and where diarrheal diseases are even more deadly to infants than AIDS is.[11] Second, even among women given antiretrovirals, elective cesarean delivery reduces perinatal transmission of HIV (International Perinatal HIV Group 1999). Yet elective cesarean is not usually recommended in southern Africa, in part because the rare complication of uterine rupture for subsequent births is likely to be fatal, in part because postoperative infection rates are often so high that they pose an unacceptable level of risk to mothers and babies, and in part because in many regions there is not enough health-care infrastructure to test pregnant women and perform cesareans on those who are seropositive.[12] Though such guidelines can be controversial, no one castigates those who write them as unethical for espousing standards of care very different from those that prevail in the West. Whereas different standards of research are seen as egregious exploitation of the poor, different standards of therapy are seen as regrettable but necessary due to the realities of economic heterogeneity.

Why have research and therapy come to be seen in this way as subject to different ethical codes? Research is not inherently more dangerous than therapy. Indeed, because doctors may use unproven therapies freely without the oversight required in research protocols, at least one prominent ethicist has argued that research is safer (Fost 1998). Conflicts of interest for the researcher may be no greater than those for the clinician. Ethicists have been concerned that clinicians acting as researchers may bend clinical rules to get their patients enrolled, for the benefit of the research and to the detriment of their patients. Such violations are well documented. Any clinician working in a poor but research-saturated area has seen the opposite problem, however: in situations in which enrollment in a study is the only way to get patients access to therapy, doctors and nurses may bend research rules to get their patients enrolled, to the detriment of the research but the benefit of the patients.

The disproportionate focus on research in bioethical discourse, like the dominance of Americans in the field, is in part an artifact of the circumstances of the birth of bioethics as a profession.[13] The first modern formal codification of bioethical rules, the Nuremberg Protocol, was created in

the wake of the discovery of Nazi atrocities performed under the rubric of clinical research. Institutional oversight of research, and thus the bioethics industry, began in the United States with Henry Beecher's 1966 disclosure of clinical trials performed without appropriate consent. Institutional oversight expanded rapidly following the exposure of the Tuskegee experiment, in which U.S. Public Health Service physicians watched poor African American men suffer from syphilis long after effective treatment was available and used elsewhere. Despite later forays into problems of personhood and the boundaries of life, bioethicists have retained a strong preoccupation with human experimentation, the area in which their efforts have historically been most concentrated and most successfully institutionalized. Those writers arguing most vociferously against the perinatal AZT trials often invoked Tuskegee, Nuremberg, or other widely known examples of unethical human experimentation; Angell's (1997) editorial described the Tuskegee study in some detail before discussing the AZT trials. The mere mention of Tuskegee and Nuremberg, of course, lends great moral weight to whatever arguments follow.

The philosophical roots of Western bioethics in Kantian individualism may also produce a deep-seated discomfort with clinical research. As Renée Fox, who has compared American and Chinese ideas of medical ethics, notes: "From the outset, the conceptual framework of bioethics has accorded paramount status to the value-complex of individualism" (1990:206; see also Macklin 1999). The very concept of human subjects research can be seen as conflicting with this Western value complex, for human subjects research is inherently utilitarian. Benefit to the subject involved in a study may be an important side effect of research, but the intention of clinical trials is to learn something that might improve the well-being of the community, or some future group of people.

Many African cultures are said to be more collectivity-oriented than those of the West: according to the often-quoted isiZulu maxim, "umuntu ngumuntu ngabantu" (a person is a person through persons).[14] Perhaps reflecting a greater comfort with communal ideals, women enrolled in the AZT trials who were interviewed as the controversy broke tended to be very clear about the utilitarian purpose of the research. In the words of a participant from Côte d'Ivoire: "People are trying to help us, and if a bunch of people have to die first, I am ready to risk my life too, so that other women and their babies can survive. If I got the placebo, that will hurt, for sure. But there is no evil involved" (quoted in French 1997). American commentators were clearly less comfortable with such utilitarianism and condemned the doctors who allowed it: "Physicians, even those conducting research, must never abandon their principal duties as caretakers and advocates for the individual patient" (Kim 1998:838). A few American clinicians, taking this argument to its logical end, oppose all clinical research on this basis, holding that the good of the individual patient must always outweigh any possibility of benefits to real or hypothetical others (Markman 1992).

Historically and philosophically, then, American ethicists and clinicians see a sharp divide between research, with its purpose of communal good, and therapy, with its goal of maximizing individual agency and well-being. This conceptual divide becomes problematic, and concerns about agency become magnified, when individuals believe their own good may be maximized through research participation. In the West the AIDS crisis precipitated a shift in thinking about clinical research that caught many ethicists off guard, as gay men, pregnant women, intravenous drug users, and others argued successfully for expanded access to clinical trials (Levine 1996; Epstein 1996). For the first time the human subject, traditionally a passive object exposed to the burden of clinical research, became a real subject—an *active* subject—in a politicized process through which research came to be seen as a good, or even a right, and equitable access to the potential benefits of clinical research as a form of justice.

Concerns about the agency of human subjects seen as "vulnerable" arose again over the perinatal AZT trials. Was offering free medical care and the chance of a beneficial medication to poor pregnant African women unethically coercive? In published international research guidelines on avoiding exploitation in research involving vulnerable populations, one physician described the perfect example of a nonvulnerable population for AIDS research as "educated, middle-class males who are familiar with health care and medical research" and for whom there is "no problem with consent.... Most members [of this population] are fully capable of making a competent, voluntary, informed and understanding decision about becoming a research subject" (Mariner 1993:52–54). Other populations were more suspect. Some critics (Schüklenk 1998) argued that pregnant HIV-positive women could never really give informed consent, pressured as they were by worries about their pregnancies. Others (e.g., Tafesse & Murphy 1998) suggested that illiterate people (and perhaps impoverished people as well) could not give real consent.

These contentions hinge on a concept of the free-agent individual that is important in mainstream bioethics, but many observers—prominent among them social scientists and feminist ethicists—would challenge them. In an influential article comparing Chinese medical morality with American bioethics, Fox and Swazey describe the American concept of individualism: "Social and cultural factors are largely seen as external constraints that limit individuals. They are rarely presented as enabling and empowering forces, *inside* as well as outside of individuals, that are constituent, dynamic elements in making them human persons" (1984:354; emphasis in original). In this view of the individual, paradigmatic in bioethics, agency is maximized by the invisibility of social structures. This notion, however, has been criticized both by feminist ethicists and legal theorists, who see its basic premise—that the individual is defined by separation from others—as a questionable construct of white male liberal legalism. Perhaps, then, it is not surprising that the further a potential research subject deviates from an

imagined educated white middle-class male norm, the greater the doubt cast on her agency. Poor pregnant African women, burdened by connections with (and obligations to) family, fetus, or community, could not possibly make autonomous—and therefore ethically acceptable—decisions.

Colonialism, Neocolonialism, and Research

Although the origin of bioethics as a branch of moral philosophy may lead to a decontextualized, rule-driven approach, many of those who spoke out on the AZT trials insisted upon putting the trials into the historical and political context of colonialism. All but one of the African countries hosting the trials had been colonized by European nations. Notably, both commentators opposed to the trials and those supporting them made reference to colonialism to bolster their arguments. Trial critics viewed short-course AZT research using placebo controls as "safari research," an unacceptable resurrection of imperialist exploitation. According to a North Carolina physician-researcher, "Exploitation by industrialized countries of the human and natural resources of the developing world has a long and tragic history. It has never been difficult for economically wealthy countries to justify their acts by citing, for example, the supposed genetic or moral inferiority of those exploited. Substituting economic inferiority in these old arguments makes the enterprise no less offensive" (Kim 1998:838).

Those supporting the trials often depicted colonialism as an ongoing process, once political and now economic, and challenged wealthy countries to support appropriate research and therapy as recompense—however inadequate—for such exploitation (Stolberg 1997). Solomon Benatar, a South African physician, called Western neocolonialists to task for global health inequalities: "Whose industries benefit from continuing underdevelopment in the Third World? Whose consumers benefit from primary products that keep African producers just above the bread line? Whose bankers benefit from Third World indebtedness? Whose delicate consciences are soothed by the giving of modest gifts?" (1998:297). Thus in the struggle between those opposing and supporting the trials, research was framed discursively either as resurrection of a presumed-dead colonialism or as expiation for ongoing domination.

The African countries selected for the trials, with the single exception of South Africa, were among the poorest in a very poor region of the world. Table 2 shows selective economic and health indicators in 1994, when research began, both for the countries that hosted short-course AZT studies and for the United States, the funding source and technical advisor for nine trials.[15] These indicators give a general sense of the asymmetries of health and resources among those involved, and make clear that the disparities in health went well beyond HIV.

In many of these countries, deteriorating farmland, overpopulation, urbanization, chronic illness among productive-age workers, and in some

Table 2. Selected Economic and Health Indicators, 1994

Country	GNP per capita US$	Per capita annual health care spending US$	External debt ratio as % of GNP	Life expectancy from birth (years)	Under-5 mortality (deaths per 1000 live births)	HIV seropositivity in urban women seeking antenatal care (%)
Burkina Faso	300	17	37	46	186	8
Côte d'Ivoire	610	22	223	51	137	12
Ethiopia	100	3	77	50	170	20
Kenya	250	7	103	54	106	15
Malawi	170	4	87	41	212	21
South Africa	3,040	240	18 (1996)	65	73	6
Tanzania	89	2	218	51	144	—
Uganda	190	7	92	41	172	19
Zimbabwe	500	31	69	49	103	42
U.S.	25,880	3623	—	77	9	—

Note: Monetary figures are in 1994 U.S. dollars.

Sources: Per capita GNP, per capita health care expenditures, life expectancies, and under-5 mortality rates for all countries except Tanzania have been taken or calculated from the WHO's World Health Reports. (1994 data is primarily available in the 1996 report.) Health data for Tanzania, not a WHO member state, is from the Economist Intelligence Unit (1994). External debt ratios are from the World Bank (1996). Estimated HIV seropositivity rates in pregnant women are from epidemiological fact sheets available from UNAIDS. Where multiple studies were available I have used median values.

cases war or civic unrest had led to worsening problems with food production. Corrupt governments and military misadventures sometimes drained public funds. Debt restructuring policies mandated in the mid-1980s were arguably a more serious and widespread factor contributing to the general decline. "Structural adjustment" and its successor programs enforced currency deregulation—leading to rapid inflation—and ended price supports for food, health care, and education, leading to economic crisis. Those who could not grow food also could not buy it. Chronic malnutrition and vulnerability to disease increased. Health care infrastructure was destabilized by these programs just as the HIV/AIDS epidemic hit.[16] The epidemic itself worsened the situation, as health care providers died or fled and already overburdened health systems crumbled under the added numbers of seri-

https://doi.org/10.1353/arw.0.0084 Published online by Cambridge University Press

ously ill patients. Clinics went unstaffed, essential medicines unbought.

At least one question arises immediately from this contextualization: why was an $80 AZT regimen chosen for testing, in a region where annual per capita health care budgets were typically less than half (and often less than one-tenth) of that number? Cost-effectiveness analysis would not have supported pharmacologic prevention strategies; in fact, medical therapy for pregnant women ranked far below condom distribution, education, and treatment of other STDs as a cost-effective HIV prevention strategy. Some commentators (e.g., Schüklenk 1998) speculated that the choice of studies was related to expansion of market opportunities for Glaxo Wellcome, the maker of AZT.[17] In fact, though the short-course AZT regimen tested in the studies was never used in Africa's public sectors, it was used briefly in Thailand and elsewhere in Asia until the cheaper medication nevirapine became available. It also kept the public health focus tightly on pharmaceuticals.

Yet it was the high cost of AZT that *created* the "need" for investigation of cheaper therapies, and this cost was maintained by zealous enforcement of international patent laws. Parallel to the time line of the pandemic's progress at the beginning of this article one could write a time line of patent policy.[18] In the same decade that AIDS was beginning to appear on the public health radar in Africa and in the West, pharmaceutical industries mounted a global public relations campaign and pressured many Third World countries to pass legislation strengthening patent laws—with the assistance of bilateral trade sanctions from the U.S. government (Santoro 1992). The year after the 076 trial made clear that AZT could reduce transmission of HIV from mother to child, the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement was signed as part of the newly formed World Trade Organization (WTO). The agreement provided twenty-year international patent protection for all drugs and technologies, including AZT. In 1997, the year the controversy over the short-course AZT trials broke out, the South African government invoked an emergency clause in the TRIPS agreement and announced plans to manufacture or purchase inexpensive copies of various antiretroviral medications, including AZT. U.S. drug manufacturers brought a lawsuit, and the U.S. government authorized trade sanctions in retaliation.[19]

Many doctors, AIDS activists, and human rights advocates spoke up in opposition to the sanctions. Bioethicists, so vocal in opposing the AZT trials, were less in evidence. Criticism of this aggressive patent protection and its cost in human lives (Pecoul et al. 1999) did not alter the basic position of the pharmaceutical companies, though in the waning days of Clinton's presidency there was some softening of the government's stance on the matter. In 2003, two years after international research guidelines had been rewritten to prevent trials like the ones described here, one year after its own self-imposed deadline, and two years before the patent on AZT finally expired, the World Trade Organization's TRIPS Council clarified the Doha

Declaration (from the WTO 2001 meeting in Qatar) to give Third World countries the right to import generic drugs when public health concerns dictated. So many bureaucratic obstacles had to be overcome in order to activate this "right," however, that some observers questioned how meaningful the declaration was in practice.

To cite Solomon Benatar (1998:297) again, "whose delicate consciences are soothed by the giving of modest gifts?"

Conclusion

Where, then, are the boundaries of moral community, of moral concern? This question is a longstanding problem for philosophers and ethicists. If social scientists cannot answer it, perhaps we can at least demonstrate how those boundaries shift and in whose favor the shifts work.

In the controversy over African AZT trials, American ethicists spoke directly to an imagined worldwide biomedical research community, condemning research protocols designed to be responsive to local economic conditions very different from those in their home country. They denounced this research in terms that made them representatives of the global, while marking others (researchers and especially research subjects) as exploitable locals whose agency was in doubt. The U.S. government, meanwhile, represented matters such as human rights violations and social justice as bounded by the nation-state. This framing ensured that *transnational* policies—such as international patent protection for AZT and other basic medications—were not considered as possible sources of human rights violations.

The historically created split between research and therapy worked in the First World's favor here. The self-appointed guardians of medical morality, envisioning themselves as members of a world community, set moral standards based on Western philosophical constructs. But when it came time for the concrete realization of these standards—that is, when the findings of research needed to be made available in the form of therapies—the boundaries of community shrank to the borders of the nation-state. Third World peoples were left pinned between an unreachable standard and an inadequate set of resources. Researching the second-best is unethical, American bioethicists said to African doctors, nurses, patients, and policymakers; but paying for the best is up to you. It is this maneuvering, I would argue, and not the use of a placebo control group, that was the most serious ethical violation in the perinatal AZT controversy, and it remains a tragically underexamined problem in bioethics today.

Today, someone who walks from the northwest toward the Malawi hospital ward where I watched a young woman die long ago may still pass the herbalists selling their medicines. Those approaching from the east or south must make their way between the gleaming buildings of the transnational research projects. Gates, Wellcome, the CDC, Johns Hopkins are all

represented: all the big guns in international research, plus many smaller guns. The studies conducted within have been carefully vetted, stamped, and approved as ethical; there will be no more research on second-best therapies, though this restriction sometimes means the projects are not very relevant to the local clinical world. Climate controlled, well equipped, stuffed with staff and microscopes and laboratory reagents and automated specimen processors, the research buildings make for a striking contrast with the hospital they surround. It is sometimes hard not to see them as parasites feeding on an emaciated host.

Wenzel Geissler and colleagues recently argued that formal bioethics can have an anesthetic effect, freeing one from the need for ethical reflection or from a bad conscience. Their study of malaria researchers in The Gambia led them to conclude that "by reducing research ethics to a choice between global principles or local conscience, the political-economic order, within which overseas medical research is inevitably situated, is excluded from ethical scrutiny" (2008:11). Analysis of one important bioethical controversy compels me to agree. Transnational bioethics is too important to leave to the experts. Clinicians, scholars, and others concerned with health in Africa and justice in the world must continue to challenge the hegemonic discourse of formal "international" bioethics and contribute to a search for new solutions.

Acknowledgments

My analysis is strongly influenced by fieldwork on two other research projects conducted in Malawi between 2001 and 2007. I am grateful for fieldwork funding from the Social Science Research Council International Field Research Dissertation Fellowship, two Graduate Fellowships from the University of Massachusetts Amherst, and an award from the University of Wisconsin-Madison Graduate School. I am also grateful to colleagues in Malawi and in the United States who have discussed maternal-to-child HIV transmission research and its attendant controversies. Three anonymous reviewers for *ASR* provided me with extensive and thought-provoking feedback. This is not the article they would have preferred me to write, but thinking seriously about their arguments has helped me make it a far better piece than it was.

References

Abdool Karim, Salim S. 1998. "Placebo Controls in HIV Perinatal Transmission Trials: A South African's Viewpoint." *American Journal of Public Health* 88 (4): 564–66.

Angell, Marcia. 1997. "The Ethics of Clinical Research in the Third World." *New England Journal of Medicine* 337: 847–49.

Annas, George, and Michael Grodin. 1998. "Human Rights and Maternal-Fetal HIV Transmission Prevention Trials in Africa." *American Journal of Public Health* 88

(4): 560–63.
Anya, Ike. 2008. "Ethical Issues in Health-Care Practice and Research in Sub-Saharan Africa." In *Health Knowledge and Belief Systems in Africa*, edited by Toyin Falola and Matthew Heaton, 205–11. Durham, N.C.: Carolina Academic Press.
Bagenda, Danstan, and Philippa Musoke-Mudido. 1997. "We're Trying to Help Our Sickest People, Not Exploit Them." *Washington Post*, September 28.
Bandawe, Chiwoza R. 2005. "Psychology Brewed in an African Pot: Indigenous Philosophies and the Quest for Relevance." *Higher Education Policy* 18: 289–300.
Bayer, Ronald. 1998. "The Debate over Maternal-Fetal HIV Transmission Prevention Trials in Africa, Asia and the Caribbean: Racist Exploitation or Exploitation of Racism?" *American Journal of Public Health* 88 (4): 567–70.
Beauchamp, Tom L., and James F. Childress. 2008. *Principles of Biomedical Ethics.* 6th edition. New York: Oxford University Press.
Beecher, Henry. 1966. "Ethics and Clinical Research." *New England Journal of Medicine* 274: 1354–60.
Benatar, Solomon R. 1998. "Global Disparities in Health and Human Rights: A Critical Commentary." *American Journal of Public Health* 88 (2): 295–300.
Buchanan, David R. 2008. "Autonomy, Paternalism, and Justice: Ethical Priorities in Public Health." *American Journal of Public Health* 98 (1): 15–21.
Cambrosio, Alberto, et al. 2006. "Regulatory Objectivity and the Generation and Management of Evidence in Medicine." *Social Science and Medicine* 63: 189–99.
Carlson, Robert V., Kenneth M. Boyd, and David J. Webb. 2004. "The Revision of the Declaration of Helsinki: Past, Present and Future." *British Journal of Clinical Pharmacology* 57 (6): 695–713.
Chin, James. 1990. "Global Estimates of AIDS and HIV Infections: 1990." *AIDS* 4 (Supplement 1): S277–83.
CIOMS (Council for International Organizations of Medical Sciences). 2002. *International Ethical Guidelines for Biomedical Research Involving Human Subjects.* Prepared by the Council for International Organizations of Medical Sciences (CIOMS) in Collaboration With the World Health Organization (WHO). Geneva: CIOMS.
Cohen, Mike. 2000. "AIDS Drug Controversial in S. Africa." *Associated Press*, April 7.
Connor, Edward, and Rhoda Sperling. 1994. "Reduction of Maternal-Infant Transmission of Human Immunodeficiency Virus Type 1 With Zidovudine Treatment." *New England Journal of Medicine* 331: 1173–80.
Coovadia, H. M., et al. 2007. "Mother-to-Child Transmission of HIV-1 Infection during Exclusive Breastfeeding in the First Six Months of Life: An Intervention Cohort Study." *Lancet* 369 (9567): 1107–16.
DeVries, Raymond, et al. 2007. *The View From Here: Bioethics and the Social Sciences.* Oxford: Blackwell Publishing.
Economist Intelligence Unit. 1994. *Country Profile: Tanzania, Comoros.* London: The Unit.
Epstein, Steven. 1996. *Impure Science: AIDS, Activism, and the Politics of Knowledge.* Berkeley: University of California Press.
Ferriman, Annabel. 2001. "World Medical Association Clarifies Rules on Placebo Controlled Trials." *BMJ: The British Medical Journal* 323 (7317): 825.
Fost, Norman. 1998. "Ethical Dilemmas in Medical Innovation and Research: Distinguishing Experimentation from Practice." *Seminars in Perinatology* 22 (3): 223–32.

Fox, Renée C. 1990. "The Evolution of American Bioethics." In *Social Science Perspectives on Medical Ethics*, edited by George Weisz, 201–17. Dordrecht: Kluwer Academic Press.

Fox, Renée C., and Judith P. Swazey. 1984. "Medical Morality Is Not Bioethics: Medical Ethics in China and the United States." *Perspectives in Biology and Medicine* 27: 336–40.

French, Howard. 1997. "AIDS Research in Africa: Juggling Risks and Hopes." *New York Times*, October 9.

Gambia Government/Medical Research Council Joint Ethical Committee. 1998. "Ethical Issues Facing Medical Research in Developing Countries." *Lancet* 351 (9098): 286–87.

Gathii, James T. 2005. "Third World Perspectives on Global Pharmaceutical Access." In *Ethics and the Pharmaceutical Industry*, edited by Michael A. Santoro and Thomas M. Gorrie, 336–51. New York: Cambridge University Press.

Geissler, P. W., et al. 2008. "'He Is Now Like a Brother, I Can Even Give Him Some Blood': Relational Ethics and Material Exchanges in a Malaria Vaccine 'Trial Community' in The Gambia." *Social Science and Medicine* 67 (5): 696–707.

Gisselquist, David, et al. 2003. "Let It Be Sexual: How Health Care Transmission of AIDS in Africa Was Ignored." *International Journal of STD and AIDS* 14: 148–61.

Iliffe, John. 2006. *The African AIDS Epidemic: A History*. Oxford: James Currey.

International Perinatal HIV Group. 1999. "The Mode of Delivery and the Risk of Vertical Transmission of Human Immunodeficiency Virus Type 1: A Meta-Analysis of 15 Prospective Cohort Studies." *New England Journal of Medicine* 340: 977–87.

Jecker, Nancy S., Albert R. Jonsen, and Robert A. Pearlman. 2007. *Bioethics: An Introduction to the History, Methods, and Practice*. 2nd edition. Sudbury, Mass.: Jones and Bartlett Publishers.

Kim, Roy. 1998. "Ethics of Placebo-Controlled Trials of Zidovudine to Prevent the Perinatal Transmission of HIV in the Third World." *New England Journal of Medicine* 338 (12): 837.

Kleinman, Arthur. 1995. *Writing at the Margin: Discourse Between Anthropology and Medicine*. Berkeley: University of California Press.

Kunstadter, Peter. 1980. "Medical Ethics in Cross-cultural and Multi-cultural Perspective." *Social Science and Medicine* 14(b): 289–96.

Levine, Carol. 1996. "Changing Views of Justice after Belmont: AIDS and the Inclusion of Vulnerable Subjects." In *The Ethics of Research Involving Human Subjects: Facing the 21st Century*, edited by Harold Y. Vanderpool, 105–26. Frederick, Md.: University Publishing Group.

Levine, Robert. 1998. "The 'Best Proven Therapeutic Method' Standard in Clinical Trials in Technologically Developing Countries." *IRB: A Review of Human Subjects Research* 20 (1): 6.

Louis, J., M. B. Landon, and R. J. Gersnoviez. 2007. "Perioperative Morbidity and Mortality among Human Immunodeficiency Virus-Infected Women Undergoing Cesarean Delivery." *Obstetrics and Gynecology* 110 (2): 385–90.

Lurie, P., P. Hintzen, and R. A. Lowe. 1995. "Socioeconomic Obstacles to HIV Prevention and Treatment in Developing Countries: The Roles of the International Monetary Fund and the World Bank." *AIDS* 9 (6): 539–46.

Lurie, Peter, and Sidney Wolfe. 1997. "Unethical Trials of Interventions to Reduce Perinatal Transmission of the Human Immunodeficiency Virus in Developing

Countries." *New England Journal of Medicine* 337: 853–56.
Macklin, Ruth. 1999. *Against Relativism: Cultural Diversity and the Search for Ethical Universals in Medicine.* Oxford: Oxford University Press.
Mann, Jonathan M. 1997. "Medicine and Public Health, Ethics and Human Rights." *Hastings Center Report* 27 (3): 6–13.
Mariner, W. K. 1993. "Distinguishing 'Exploitable' From 'Vulnerable' Populations: When Consent Is Not the Issue." In *Ethics and Research on Human Subjects: International Guidelines,* edited by Zenon Bankowski and R. J. Levine, 44–55. Geneva: CIOMS.
Markman, Maurie. 1992. "Ethical Difficulties with Randomized Clinical Trials Involving Cancer Patients: Examples from the Field of Gynecologic Oncology." *Journal of Clinical Ethics* 3 (3): 193–95.
Marshall, Patricia. 1992. "Anthropology and Bioethics." *Medical Anthropology Quarterly* 6 (1): 49–73.
Mbidde, Edward K. 1998. "Ethics of Placebo-Controlled Trials of Zidovudine to Prevent the Perinatal Transmission of HIV in the Third World." *New England Journal of Medicine* 338 (12): 837.
Morbidity and Mortality Weekly Report. 1982. "Unexplained Immunodeficiency and Opportunistic Infections in Infants: New York, New Jersey, California." *Morbidity and Mortality Weekly Report* 31 (49): 665–67.
Muller, Jessica. 1994. "Anthropology, Bioethics, and Medicine: A Provocative Trilogy." *Medical Anthropology Quarterly* 8 (4): 448–67.
Nagel, Thomas. 1986. *The View From Nowhere.* New York: Oxford University Press.
Pecoul, Bernard, et al. 1999. "Access to Essential Drugs in Poor Countries: A Lost Battle?" *JAMA: Journal of the American Medical Association* 281: 361–67.
Resnik, David. 1998. "The Ethics of HIV Research in Developing Nations." *Bioethics* 12 (4): 286–306.
Rothman, David. 1991. *Strangers at the Bedside: A History of How Law and Bioethics Transformed Medical Decision Making.* New York: Aldine.
Schoepf, Brooke G., Claude Schoepf, and Joyce V. Millen. 2000. "Theoretical Therapies, Remote Remedies: SAPs and the Political Ecology of Poverty and Health in Africa." In *Dying for Growth: Global Inequality and the Health of the Poor,* edited by Jim Y. Kim et al., 90–126. Monroe, Me.: Common Courage Press.
Schüklenk, Udo. 1998. "Unethical Perinatal HIV Transmission Trials Establish Bad Precedent." *Bioethics* 12 (4): 312–19.
Serwadda, D., et al. 1985. "Slim Disease: A New Disease in Uganda and Its Association With HTLV-III Infection." *Lancet* 2 (8460): 849–52.
Specter, Michael. 1998. "Uganda AIDS Vaccine Test: Urgency Affects Ethics Rules." *New York Times,* October 1.
_____. 2003. "The Vaccine: Has the Race to Save Africa from AIDS Put Western Science at Odds With Western Ethics?" *The New Yorker* (February 3), pp. 54–65.
Stolberg, Sheryl G. 1997. "U.S. AIDS Research Abroad Sets Off Outcry over Ethics." *New York Times,* September 18.
Tafesse, Eskinder, and Timothy Murphy. 1998. "Ethics of Placebo-Controlled Trials of Zidovudine to Prevent the Perinatal Transmission of HIV in the Third World." *New England Journal of Medicine* 338 (12): 838.
Turshen, Meredeth. 1999. *Privatizing Health Services in Africa.* New Brunswick, N.J.: Rutgers University Press.
UNAIDS (United Nations/WHO Joint Taskforce on HIV/AIDS). 2003. *Report on the*

Global HIV/AIDS Epidemic 2002. Geneva: UNAIDS.
Varmus, Harold, and David Satcher. 1997. "Ethical Complexities of Conducting Research in Developing Countries." *New England Journal of Medicine* 337: 1000–1005.
Volmink, J., et al. 2007. "Antiretrovirals for Reducing the Risk of Mother-to-Child Transmission of HIV Infection." *Cochrane Database of Systematic Reviews* (1): CD003510.
Weijer, Charles, and James A. Anderson. 2001. "The Ethics Wars: Disputes over International Research." *Hastings Center Report* 31 (3): 18–20.
Weisz, George, ed. 1990. *Social Science Perspectives on Medical Ethics.* Dordrecht: Kluwer Academic Publishers.
Wiktor, Stefan, Ehounou Ekpini, and John Karon. 1999. "Short-Course Oral Zidovudine for Prevention of Mother-to-Child Transmission of HIV-1 in Abidjan, Côte D'Ivoire: A Randomised Trial." *Lancet* 353 (9155): 781–85.
Wolpe, Paul R. 1998. "The Triumph of Autonomy in American Bioethics: A Sociological View." In *Bioethics and Society: Constructing the Ethical Enterprise,* edited by Raymond DeVries and Janardan Subedi, 38–59. Upper Saddle River, N.J.: Prentice Hall.
World Bank. 1996. *1996 World Debt Tables, Volume 2: Country Tables.* Washington, D.C.: The World Bank.
Yusuf, N. K. 1998. "Bio-ethical and Legal Issues in Relation to HIV/AIDS: The Uganda Experience." *Medicine and Law* 17 (4): 619–24.

Notes

1. In recent medical literature readers will find that zidovudine is now more commonly abbreviated ZDV. At the time of the controversy over these trials, however, AZT (for the chemical name azidothymidine) was the standard abbreviation, and that is the one I use here.
2. In a PubMed search done in June 2008, 188 (<5%) of 4195 articles on HIV or AIDS published in 1990 were related to Africa or Africans, though years had passed since the first alarms had sounded from Uganda over the scale of the epidemic in Africa. The estimate for HIV infection in Africans is from Chin (1990).
3. Relevant portions of the Nuremberg Code can be found at www.hhs.gov/ohrp/references/nurcode.htm. The World Medical Association's Declaration of Helsinki is at www.wma.net/e/policy/b3.htm. The CIOMS guidelines, written in collaboration with the World Health Organization, are available at www.cioms.ch/frame_guidelines_nov_2002.htm. The 1979 Belmont Report of the United States National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research is also relevant, in that this report contains influential guidelines that apply to all federally funded research; it is available at www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm.
4. It appeared in the *Lancet* instead of the *New England Journal,* where there is a policy against publishing research considered by the editors to be ethically questionable.
5. Precise efficacy depends on whether prophylaxis is being used in a breastfeeding or non-breastfeeding population. Readers interested in detailed results are referred to Volmink et al. (2007). This lengthy article provides a useful current

summary analysis of all published trials looking at the use of antiretrovirals to reduce maternal-to-child transmission of HIV, including the placebo trials discussed here, from a medical—not ethical—perspective. Current multimedication protocols used in the United States are estimated to reduce maternal-to-child transmission rates to 1–2 percent.

6. For that matter, amendments to the Declaration of Helsinki revision adopted in 2001 under pressure from international researchers also made the issue murkier (Ferriman 2001), softening but not eliminating the language proscribing placebo.
7. HIV tests were available for two of the ten months in which I worked at one of the country's largest public referral hospitals in 2002 and 2003. Availability of testing, and of antiretrovirals, has improved significantly since that time, and especially after a national antiretroviral program began in 2005.
8. The literature expanding and critically evaluating the field of bioethics is vast, and the boundaries around the profession of bioethics much blurrier than I have space to discuss here. For useful starting points consider the edited volume by Jecker et al. (2007), most of it by contributors who would likely consider themselves bioethicists, or the recent collection by DeVries et al. (2007), most of whom would likely consider themselves as critics from outside bioethics. Much interesting work now comes under the rubric of public health ethics (see, e.g., Buchanan 2008; Mann 1997). The persistent failure of traditional bioethics to address issues of justice and inequality is one major factor pushing public health toward new conceptual frameworks for ethics.
9. From Public Citizen News Release, open letter to Secretary Donna Shalala, April 22, 1997 (available at www.citizen.org). The 1002 infants mentioned represent the one-quarter or so of newborns in the placebo arm of the trials who would inevitably become infected by HIV. The authors' calculation of excess death requires one to conceptualize the trials as *withholding* available therapy from half the mothers involved in the trials, while the researchers involved saw their studies instead as *providing* antiretrovirals—on a research basis—to half the women involved, women who otherwise had no access to antiretroviral medications. To put this calculation in a larger context: universal use of the 076 AZT regimen in sub-Saharan Africa at the time of these trials would have been expected to reduce the number of early childhood deaths from AIDS by two-thirds, from 500,000 to 170,000 per year.
10. An important exception to the unconscious ceding of the global was the protest from the "Gambia Government," actually a multidisciplinary ethical review board. Though The Gambia was not one of the countries involved in the trials, committee members specifically addressed the ownership of ethics, claiming "ethics cannot be owned by affluent countries alone" (Gambia Government 1998:287).
11. See www.unicef.org/programme/breastfeeding/feeding.htm for current guidelines; a recent publication by Coovadia et al. (2007) gives a useful summary of the relevant evidence.
12. Recent data on complications of cesarean section among HIV-positive women in the United States may force a rethinking of this strategy for HIV prevention in the wealthier parts of the world as well (Louis et al. 2007).
13. It is only fair to point out that not everyone would agree on the trajectory for the bioethics profession I am giving here, and certainly the intellectual history

of bioethics long predates Nuremberg. Most ethics histories, however, see congressional requirements for institutional oversight of research in the wake of Beecher's exposé and the outrage over the Tuskegee trials as hugely influential in the creation of bioethics as a *profession* (see, e.g., Rothman 1991). Some go so far as to see bioethical problems, and by implication bioethics, as "the historically contingent products of the clinical research enterprise itself" (Cambrosio et al. 2006:196).

14. Thanks to my colleague and friend Chiwoza Bandawe, who first introduced me to this now-famous saying, and who discusses some of its implications for medicine in Bandawe (2005).
15. A caveat about these statistics is important. They are usually presented as they are here, as if they were facts, but many are little more than educated guesses, and different estimates often differ wildly. Think back to the dying Malawian woman I watched in 1990. What did she die of? AIDS? Anemia? Malnutrition? Childbirth? All of them? If you had to pick just one, into which category would you place her? She was never tested for HIV. The test was unavailable, and no one needed to test her—she had lesions that looked like those of Kaposi's sarcoma, though there was no histopathological confirmation by biopsy. Besides, what difference would a positive test have made? Families in Malawi rarely acknowledged then that a loved one had died of AIDS; clinicians often felt sure of the diagnosis with little or no supporting evidence. There are many causes of wasting, fever, skin rashes, diarrhea, anemia, premature death. These uncertainties fueled the debates over AIDS in Africa, where some parties dismissed the uncomfortable topic of AIDS in favor of a focus on economic inequality, while others used statistics to paint Africans as victims of their sexual practices, ignoring issues of regional and international politics—or indeed, of other significant routes of HIV transmission (Gisselquist et al. 2003).
16. Many scholars and activists have drawn attention to the connection between international economic policies and poor health, including HIV/AIDS, in Africa (see, e.g., Schoepf et al. 2000; Turshen 1999). Peter Lurie, who later initiated the controversy over the perinatal AZT trials, is the co-author of one of the earlier analyses to appear in a medical journal (Lurie et al. 1995).
17. The company was Glaxo Wellcome at the time of Schüklenk's critique, Burroughs-Wellcome when AZT was patented, and GlaxoSmithKline by the time the patent finally expired (the first patent of any antiretroviral to do so) in 2005. Major headquarters are in the United Kingdom and the United States.
18. Space does not permit the full development of such a time line. Readers interested in a useful and exceptionally well-documented analysis of the interplay between international patent law and Africa's HIV pandemic are referred to Gathii (2005).
19. Sanctions were made under a special category of the U.S. Trade Act called Section 301, for the most "onerous or egregious" trade violators. Gathii (2005) reports that the South African government's support of a proposal to add HIV/AIDS drugs to the World Health Organization's essential medicines list was also an important factor in the U.S. section 301 listing.