In March 2013 a group of physician-researchers made the startling announcement that a baby in Mississippi had been ‘functionally cured’ of HIV (Persaud et al., 2013a). However, hopes that the discovery might indicate a pediatric cure for HIV were significantly tempered in July 2014, when doctors announced that the child had a detectable viral load. Nonetheless, the case remains unprecedented, and NIH-funded trials to build on the findings are in the planning stages (NIAID, 2014). Whether addressing HIV ‘cure’ or temporary ‘remission’, scrutiny of the ‘Mississippi baby’ case has focused largely on scientific and technical questions, with only introductory attention to ethical questions. By contrast, the social inequalities and gaps in care that made the discovery possible—and their ethical implications for pediatric HIV remission more globally—have gone largely unexamined. This paper describes the some of the structural inequalities surrounding the ‘Mississippi baby’ case and a parallel case of an HIV-infected infant in South Africa, where proof-of-concept studies of the approach used in Mississippi are in the early stages. We argue that an ethical program of research into infant HIV remission ought to be ‘structurally competent’, and not bracket the gaps in care that allow antenatal transmission to occur. To this end, we recommend that pediatric remission studies consider including a social science research component focused on social protection and barriers to care for HIV-positive pregnant women.

Keywords: ‘Mississippi baby’, HIV cure, HIV remission, ethics, inequality
Introduction

HIV/AIDS researchers have struggled with how to address problems of inequality since the advent of the epidemic over 30 years ago (Farmer, 1999; Parker, 2002). This struggle has been particularly acute in international HIV research, where issues of unequal access to antiretroviral treatment and differing standards of care between resource-rich and resource-poor countries have raised thorny ethical issues for scientists about the obligations of researchers to the patients and communities they study (Lurie and Wolfe, 1997; Angell, 1997; Bayer and Stryker, 1997; Wendland, 2008). The new field of HIV remission research (sometimes called ‘cure’ research) has recently entered into this arena. In this paper, we describe some of the unaddressed ethical issues raised by research examining sustained disease remission in HIV-infected infants.

In the first part of the paper, we outline the landmark Mississippi case that ignited research interest in infant HIV remission. We then compare this case to a typical case from the second author’s clinical practice in South Africa, a country with high rates of perinatal HIV infection where patients are currently being enrolled in proof-of-concept infant remission studies. In the second part of the paper, we argue that perinatal HIV transmission in both the U.S. and South African cases resulted from unequal, “structurally violent” conditions in which preventive health systems failed to reach socially and economically marginalized pregnant women (Farmer, 1996). In the third part of the paper, we advocate an ethical framework for pediatric remission research that would address, rather than bracket, the structural inequalities and health system failures that led to infant infection. We describe how a “structurally competent” (Metzel and Hansen, 2013) research agenda would pair biological remission studies with social science research focused on better understanding and preventing the perinatal infections upon which remission research depends. In doing so, we endorse an approach to pediatric HIV remission research that goes beyond procedural ethics and makes a commitment to reducing health disparities and improving community welfare (London, 2005; Benetar, 2013).

1. From Mississippi to South Africa

In 2010, a woman arrived at the emergency room of a rural Mississippi hospital in advanced labor. She was in her 35th week of pregnancy, and had received no prenatal care. Clinicians administered a rapid HIV test that revealed she was HIV-positive, and later testing showed that she also had a detectable viral load. Because labor was already in progress, the woman could not be given treatment to help prevent HIV transmission to her infant during birth. Her child was born vaginally. The rural hospital where she gave birth did not carry pediatric formulations of antiretroviral medications, and so at 30 hours of age, her newborn was transferred to the University Medical Center in Jackson, Mississippi, and placed under the care of pediatric HIV specialist Dr. Hannah Gay.

Because the newborn’s mother had received no prior HIV treatment and had delivered vaginally, Dr. Gay considered the infant to be at high risk for HIV infection. With the mother’s consent, she decided to immediately initiate an aggressive post-exposure prophylaxis (PEP) regimen of three antiretroviral drugs in hopes that this might prevent the infant from becoming infected (Oxford Union, 2013). Once testing confirmed that the newborn was, despite this preventive effort, HIV-positive, this triple combination of drugs was continued in order to treat the infant’s HIV infection. The mother also began combination antiretroviral therapy, and both mother and
child responded well to treatment. Within one month the baby’s HIV viral load became undetectable (Persaud et al., 2013b).

When the child was 18 months old, the mother and child stopped attending HIV care appointments in Jackson. For five months, the clinic was unable to reach the mother by phone, letter, or through the child’s grandparents, who did not know where the mother was. State public health officials eventually found the mother and child, and they returned to the Jackson clinic when the child was 23 months old. According to the mother, the child had stopped taking antiretroviral drugs at 18 months of age, and pharmacy records showed that no prescriptions had been collected after 15 months. Dr. Gay fully expected that the child would show evidence of viral rebound, and so was astounded when the child’s viral load test came back undetectable (Oxford Union, 2013). When ultra-sensitive follow-up tests found no evidence of ‘replication-competent’ HIV in the child, researchers made the startling findings public: the infant had been ‘functionally cured’ of HIV (Persaud et al., 2013b).

This was the second-ever documented case of likely cure of HIV, and the first to apparently result from antiretroviral therapy rather than much more invasive and expensive interventions.¹ Not surprisingly, the ‘Mississippi baby’ case was widely reported, and researchers moved rapidly to design international trials that would offer ‘proof of concept’ of this approach to pediatric HIV cure across a wide range of national and regional settings.

Following the announcement of the baby’s ‘functional cure,’ the Mississippi mother and child continued to be followed at the Jackson clinic. In July 2014, two years after discontinuing therapy, the child’s viral load test came back positive during a routine visit to Dr. Gay. Follow-up testing showed that the child, who had shown no detectable viral load while off antiretroviral therapy, was positive for HIV antibodies (National Institute of Allergy and Infectious Diseases [NIAID], 2014; Luzuriaga et al. 2015). Clinicians announced that the child’s HIV infection had returned, indicating that the HIV had not in fact been cured but perhaps induced into a state of ‘sustained remission’ through early aggressive treatment. The child was re-started on antiretroviral therapy and remains in the care of Dr. Gay. Although scientists were understandably disappointed by the failure to induce cure in the child, the child’s maintenance of an undetectable viral load for over two years without treatment was still ‘unprecedented.’ The development of international proof-of-concept studies continued, shifting from pediatric ‘cure’ to the study of pediatric ‘remission’ and the challenges of eradicating viral reservoirs (NIAID, 2014; Rainwater-Lovett, Luzuriaga, and Persaud, 2015).

¹ In 2008 the case of Timothy Brown, known as ‘the Berlin patient’, made international headlines when doctors announced that Brown had achieved ‘long term control’ of his HIV infection after receiving an allogeneic stem-cell transplant (intended to treat Brown’s leukemia) using a donor with a CCR5 Delta32 mutation that confers resistance to HIV acquisition (Hutter et al., 2009). Though researchers initially cautioned that this was not a ‘cure’ for HIV, the case was reported as such in the press and the term ‘functional cure’ was later used in the scientific literature when referring to this case (Levy, 2009; McNeil, 2008; Johnston and Barré-Sinoussi, 2012). The exact mechanism of the ‘cure’ is still speculative and it has been postulated that highly unique circumstances – e.g. the development of graft-versus-host disease – might have contributed to purging the patient’s HIV reservoir, and have seen efforts to duplicate this success frustrated (Henrich et al., 2013).
Whether addressing HIV ‘cure’ or ‘remission’,² scientific and media coverage of this case has focused largely on how remission occurred – in other words, on biological and technical questions regarding the infant’s infection status, the definition of ‘cure’, and, more recently, how such periods of apparent remission might be extended. By contrast, the structural inequalities that made what the press calls the ‘Mississippi baby’ case possible—specifically, how and why it happened that the mother received no prenatal or HIV care prior to her arrival at the hospital and why she later dropped out of HIV care for five months—have gone largely unexamined. Though the identity and thus the specific social background of the Mississippi mother and child are not public information, we can make some informed inferences based on existing demographic and epidemiological data. Mississippi has more counties with high child poverty rates than any other state in the United States, nearly all of which are black-majority counties in the rural Mississippi Delta area (O’Hare and Mather, 2008). In addition, three quarters of new HIV infections in Mississippi occur among African Americans, and in 2009, 57 of the estimated 77 infants born with HIV in the U.S. in 2009 were African American (Human Rights Watch 2011, p. 3; Centers for Disease Control [CDC], 2010). Thus, although we cannot know the specifics of this particular woman’s situation other than that she lived in rural Mississippi, received no prenatal care, and gave birth prematurely, it is likely that most women and infants in similar circumstances are poor and African American (McCullom, 2013).

The racial, economic, and health care inequalities surrounding the Mississippi case are especially important because the milestone discovery of sustained remission would not have been made had it not been for two significant health systems failures: first, to prevent infection to the infant; and, second, to maintain the mother and child on antiretroviral therapy. In this way, the biological reality of both the infection itself and its remission cannot be separated from the social reality of profound structural inequality (Lock and Nguyen, 2010). This makes the content and the context of the scientific discovery indivisible (Latour, 1987).

Existing research on the continuum of care in prevention of mother-to-child transmission (PMTCT) shows that such prevention failures are common, multi-causal, and context-specific (Sibanda et al., 2013; McNairy and El-Sadr, 2012; Sprague, Cherisch, and Black 2011). In order to see whether aggressive HIV treatment can induce remission in other high-risk or perinatally-infected infants, proof-of-concept studies will enroll many vulnerable women and babies who did not access preventive care that could have prevented mother-to-child transmission (IMPAACT P1115 protocol, 2014, p. 11). In this way, proof-of-concept studies will at times rely upon social inequalities and systemic failures akin to those experienced by the Mississippi mother and baby in order to find qualified research subjects. However, because mother-to-infant HIV transmission is relatively rare in the United States, many of the women and children enrolled in proof-of-concept studies will be from lower income countries with higher rates of perinatal transmission, including South Africa, the country with the greatest number of HIV-infected children in the world and significant health system weaknesses (Chopra et al. 2009; Sprague et al., 2011).

² We support the use of the term ‘remission’ (rather than ‘cure’) because ‘cure’ implies the complete elimination of disease with no chance of recurrence. ‘Remission’ more accurately reflects the combination of clinical improvement but sustained uncertainty seen in both the ‘Mississippi baby’ and the ‘Berlin patient’ (Tucker et al., 2014).
A typical case from the second author’s clinical practice in Pretoria provides a South African example of how structural inequalities and health system failures can contribute to perinatal infection: The patient, a black African woman in her twenties, was from a very poor family in rural South Africa, where she had left school at the age of twelve in order to care for her siblings. She moved to Pretoria in search of work, but her lack of schooling and the scarcity of jobs in the city left her unemployed and impoverished, living with her boyfriend in a corrugated iron shack in one of the several peri-urban informal settlements with neither electricity nor running water. She was diagnosed with HIV infection in 2007. After testing HIV-positive, she never returned to the clinic to get the results of her CD4 count test or access antiretroviral treatment. She gave birth to her first child—a son—in January 2011, having received no antenatal care. The infant was hospitalized shortly after birth and diagnosed with both HIV infection and congenital tuberculosis. Mother and son were referred for antiretroviral therapy, but never returned to the clinic despite numerous phone calls from the hospital social worker. The social worker sent a counselor to the mother’s house, but the family had moved and none of the neighbors could give a forwarding address. The patient eventually returned to the hospital a year later via ambulance, in labor with her second child. Her son was with her, as there was nobody to look after him at home. While his mother delivered his sister, he was assessed in the ward and found to have severe protein energy malnutrition (kwashiorkor). His infant sister was also found to be HIV-infected, and the mother was once again referred to the HIV clinic and encouraged to start her children on treatment. She had not disclosed her serostatus or the children’s status to her boyfriend for fear that he might abandon her.

Like this woman, many of the second author’s patients have specific social and economic circumstances that may impede their ability to access preventive care and put their infants at high risk for perinatal HIV infection. HIV researchers are both aware of and concerned about the ways in which social and economic inequalities impact their research participants. Yet, prevailing models of clinical research position structural inequality as separate from and outside the empirical questions posed by scientific investigation. Geissler (2013) has described this reticence to discuss obvious disparities as purposeful ‘unknowing’ that makes material inequalities something of a ‘public secret’ in global health research. Because infant HIV remission research necessitates perinatal HIV transmission (and thus the participation of women who have failed to access preventive care), we suggest that proof-of-concept studies consider including a rigorous social science component aimed at understanding and redressing the factors that put such women and their infants at risk. In doing so, we advocate for more open discussion of inequalities in research (Geissler and Okwaro, 2014) and endorse appeals to conceptualize global health in ways that go beyond biological and technological innovation to include “innovation in social action that could enhance health” (Benatar 2013, p. 304). Specifically, we propose that infant HIV cure research be paired with a rigorous structurally competent social science research agenda focused on social protection. Given the ‘global consensus that the world must strive towards elimination of new HIV infections among children by 2015,’ it is crucial that the factors leading to ongoing perinatal HIV transmission be examined in concert with efforts to understand HIV remission in infants (UNAIDS 2011, p. 6).

2. Structural violence and structural competency
Structural competency refers to the ability to recognize symptoms, behaviors (such as ‘nonadherence’), and diseases as ‘the downstream implications of a number of upstream
decisions’ including housing and health care policy, food systems, infrastructures, racial and gender inequality, and disease definitions (Metzl and Hansen 2013, p. 128). These harmful socio-structural factors, sometimes framed as ‘structural violence’, intertwine with culture to form the stigmas and inequalities that lead to situations such as those faced by the ‘Mississippi baby’ and the Pretoria mother and her children (Farmer 1998, 2006). Research shows that a huge majority of primary care doctors and pediatricians in the United States believe that unmet social needs are directly responsible for their patients’ health problems, but feel unable to meet those needs and thus unable to provide adequate care (Harris Interactive 2011, in Metzl and Hansen, 2013). In low- and middle-income countries, failure to access PMTCT has been strongly linked to social and economic factors, suggesting a ‘critical’ need for women’s economic and social empowerment in many contexts in which PMTCT has failed (hlarlaithe et al., 2014; Painter et al. 2005). A ‘structurally competent’ research agenda would seek to understand how patients’ social and economic needs could be best addressed across a variety of diverse contexts.

What might a ‘structurally competent’ approach look like in relation to the two cases we have sketched here? Rather than abstracting these women and their infants from the social inequalities that put them at risk, a structurally competent approach would incorporate these inequalities into understanding and analyzing their cases. Granted, in many respects, the contexts inhabited by these women and their children are quite different. At 5.7 infections per 100,000 births in 2010, perinatal transmission has become quite rare in the United States (CDC, 2011). This is largely due to the wide availability of antiretroviral treatment, birth by caesarian section, and safe alternatives to breastfeeding. In contrast, perinatal transmission of HIV remains a significant public health issue in South Africa, where the mother-to-child transmission rate in 2011 was 2.7% (Goga et al., 2012). HIV is not an indication for caesarean section in South Africa, and HIV-infected mothers are encouraged to breastfeed. Due to the greater overall incidence of HIV infection in South Africa (particularly among women), this translates into approximately 17,000 new infant infections per year in contrast to the estimated 212 children infected with HIV perinatally in the US in 2010, the year the Mississippi baby was born (CDC, 2011). Thus, the Mississippi and South African cases differ significantly in their epidemiological context, mother-to-infant transmission rates, and access to preventative measures.

However, there are also some important similarities between these two cases. The United States and South Africa are both comparatively wealthy countries with very high levels of social and economic inequality. According to the Gini coefficient measurement of income inequality, South Africa, now Africa’s second wealthiest nation, is one of the most unequal countries in the world. The United States is the most unequal of all ‘developed’ nations (CIA, 2014; OECD, 2011). Both the United States and South Africa have long and troubled histories of state-sanctioned racial discrimination, and the AIDS epidemic has disproportionately impacted black communities compared to other racial and ethnic groups in both countries (Levenson, 2005; Inrig, 2012; Fassin 2007). In other words, they are both countries with high levels of structural violence: social inequalities that put people in harm’s way (Farmer, 2006). Seen through this lens, these two cases are in many ways emblematic of the forms of structural violence that define the AIDS epidemic in the United States and South Africa.
In the United States, structural inequalities have made poor African Americans in the South one of the communities hardest-hit by the HIV epidemic. Indeed, Mississippi is one of the poorest states in the country and has the lowest human development index (a measure of well-being and opportunity) of all fifty states (Measure of America/SSRC, 2014; American Human Development Project, 2009). It is located in the southern United States, the region of the country with the greatest burden of HIV and AIDS, accounting for 40% of Americans living with AIDS and 48% of AIDS deaths in 2009, and 45% of new AIDS diagnoses in the United States in 2010 (CDC, 2012, 2015). This burden of disease has fallen disproportionately upon African Americans, and in Mississippi three quarters of new HIV infections occur among African Americans (Human Rights Watch [HRW] 2011, p. 3). Moreover, a Human Rights Watch report on HIV/AIDS in the American south singled out the state of Mississippi as having especially poor services for individuals living with HIV (HRW 2010, 2011). In the period leading up to the birth of the ‘Mississippi baby’ in 2010, the state government actively resisted increased federal funding for HIV-related programs and services, even though it was estimated that at least half of Mississippians who tested HIV-positive were not receiving even basic HIV-related health care services (HRW 2011, p. 2, 15). More broadly, critics have charged that this ‘secret epidemic’ of HIV among African Americans has historically been ignored by American policymakers, and that African Americans have been ‘left behind’ by a national AIDS agenda more focused on HIV/AIDS abroad (Levenson, 2005; Black AIDS Institute, 2008; Inrig, 2012).

In South Africa, the HIV epidemic has been devastating, particularly among the poor. In 2014, an estimated 6.8 million South Africans were HIV-infected, including 340,000 children (aged 0 to 14 years of age). The adult (15-49) prevalence rate is 18.9% and approximately one-third of all deaths (an estimated 140,000 in 2013) are believed to be HIV-related (Statistics South Africa, 2013; UNAIDS, 2014). Although the situation has improved greatly over the last decade when AIDS denialism, the absence of a national treatment program, and open government support of false cures made South Africa the pariah of the HIV treatment world, the problem is unfortunately far from over (Fassin, 2007). Although HIV incidence has reached a plateau, the absolute number of people living with HIV (PLHIV) is on a steep increase of roughly 100,000 additional PLHIV each year. The social and economic relations of post-apartheid South Africa put women at particular risk, especially those who, like the mother described here, are poor, live in informal settlements, and are subject to very high rates of gender-based and sexual violence (Hunter, 2010; Wabiri and Taffa, 2013; Seesat et al., 2009; Jewkes et al., 2013). Of the approximate 1.1 million annual births (1,084,397) in the country, roughly one-third are to HIV-infected women. The social and economic barriers to care that poor women face are compounded by considerable weaknesses in HIV care service delivery (Sprague et al., 2011).

Thus, both the United States and South Africa exhibit social inequalities and forms of structural violence that are shaping HIV risk, including perinatal infection of infants, despite well-established means to prevent this. Were such failures not occurring, pediatric remission studies would not be possible, as such studies require neonates infected peri-natally. As a recent report from the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the Centre for the AIDS Programme of Research in South Africa (CAPRISA) noted, ‘the case of the “Mississippi baby” represents a paradox’: the discovery of viral remission in this infant resulted from a combination of health care excellence (aggressive, meticulous post-natal care by Dr. Gay and colleagues) and health care failures (the lack of prenatal care and failure to prevent mother-to-child transmission) (UNAIDS and CAPRISA 2013, p. 7). Because proof-of-concept trials will benefit from a similar
paradox (by recruiting many subjects whose infection resulted from health care failures), we suggest that such studies consider including a social science component aimed at understanding and preventing such failures in the future.

3. Ethical considerations and recommendations
Researchers have described a range of ethical considerations for HIV ‘cure’ and remission research, including risks associated with ARV treatment interruption, the possibility of therapeutic misconception, informed consent during labor, fair selection of participants and study sites, the impact of media representations of cure research, and the need for engagement with HIV-affected communities (Lo and Grady, 2013; Sugarman, 2013; Shah et al., 2014). However, current recommendations regarding the ethical conduct of cure and remission research have not addressed the paradoxical way in which ethics, structural inequalities, and scientific discovery interact in infant remission research. For example, the International AIDS Society’s Working Group on Ethics has suggested that participants with ‘conditions that could significantly compromise adherence, such as homelessness or substance abuse’ should be excluded from proof-of-concept studies and other pivotal trials (Lo and Grady 2013, p. 247). Yet, as the cases we have described above suggest, it is precisely women with barriers to adherence who are most likely to give birth without previous or with inadequate HIV treatment, and whose infants are most likely to benefit from research into pediatric remission.3

There is an ongoing debate in the bioethics literature regarding the obligations of researchers to address inequalities and unmet needs within the communities they study, particularly those in low-income countries. Participants in the 2001 Conference on Ethical Aspects of Research in Developing Countries (2004) argued that research must offer ‘fair benefits’ to communities, as determined through a transparent process in which communities themselves determine the value of possible benefits. Others reject the fair benefits’ framework as ‘minimalist’, and accuse it of ‘screening out…morally relevant information’ because it does not ‘situate the health needs of individuals in the developing world within a broader social, political, and economic context’ – a criticism with which we agree (London 2005, p. 28). These authors propose a ‘human development approach’ to international research in which researchers have a ‘duty to aid people in the developing world’ in ways that ‘create and sustain social structures that secure individuals’ capacities for welfare and human agency’ (London 2005, p. 32, 34). Seeking a middle ground between these two poles, Lavery et al. promote the ‘relief of oppression’ framework, which, borrowing from the principle of harm reduction, argues that investigators have an obligation to reduce ‘barriers to freedom’ in host communities (Lavery et al., 2010). At the crux of these debates is the question of whether researchers have an ethical obligation to address the root causes of the health inequalities they study, or whether these inequalities may be separated or bracketed from scientific inquiry as what some call ‘background injustice.’

These debates over ethics and inequality have yet to be taken up in relation to pediatric remission research. Our intention here is not to re-hash or adjudicate these ethical arguments, but rather to sketch out how an infant remission research program might begin to address some of the social inequalities that perpetuate perinatal HIV infection. Because they will be enrolling infants whose mothers did not access successful preventive care, infant remission studies are extremely well positioned to investigate the reasons behind prevention failures and ways to improve outcomes.

3 In contrast to the IAS recommendations, Shah et al. advocate for the inclusion of vulnerable women and infants at high risk for HIV transmission in cure research (Shah et al. 2014).
Doing so would move social inequalities out of the ‘background’ of infant remission research and instead acknowledge the central role that they play in the generation of scientific knowledge.

There is a pressing need for such research. Existing data shows that at least a third of eligible women in sub-Saharan Africa do not access PMTCT prophylaxis (Wettstein et al., 2012). A recent meta-analysis attributed failure to access PMTCT in Africa primarily to inadequate health staffing and services, stigma, fear of disclosure, and lack of partner support (Gourlay et al. 2013, p. 1). Given the fact that these factors ‘have not changed over time and continue to plague PMTCT programmes more than 10 years after their introduction’ (ibid, p. 1), there is urgent need for research that goes beyond simply documenting impediments to PMTCT and instead investigates how obstacles to care might be overcome at both an individual and systemic level (Marcos, Phelps and Bachman 2012; Wettstein et al. 2012).

Specifically, we advocate a research agenda focused on social protection. Social protection refers to the ‘prevention, management and overcoming of situations that adversely affect people’s well-being’ (United Nations Research Institute for Social Development 2010, p. 135), often through initiatives and policies that provide income and other resources to the poor, protect the livelihoods of vulnerable people, and improve the rights and status of the socially marginalized (UNICEF, 2010). There is evidence that in some contexts social protection can help people overcome structural inequalities and barriers to health care, including HIV care (Miller and Samson, 2012). For example, research in Malawi has shown the effectiveness of cash transfers in supporting school attendance and reduced sexual risk among girls (Baird et al., 2010), and research in rural Uganda has shown that providing money for transportation increases adherence to HIV therapy and retention in care (Emenyonyu et al., 2010). Very recent results from a study in the Democratic Republic of Congo showed that cash transfers improved retention in PMTCT services (Thirumurthy et al., 2015), while researchers in Uganda observed that mothers’ access to education correlated with PMTCT success (Bajunirwe and Muzoora, 2005). In the United States, a program targeting chronically ill residents of the impoverished city of Camden, New Jersey, was able to improve access to care and clinical outcomes while reducing emergency room visits through the provision of coordinated, team-based, services that addressed not only medical needs but also social needs such as housing and food stability (Robert Wood Johnson Foundation, 2014; Gawande, 2011). Other studies have documented food insecurity among HIV-infected individuals in both the United States and in sub-Saharan Africa (Weiser et al. 2012, 2013; Kalofonos, 2010), and research suggests that social protection in the form of food assistance improves treatment adherence and outcomes (Hlarlaithe et al., 2014). To be clear, we are not claiming a proven causal link between such programs and the prevention of mother-to-child transmission. Rather, we are echoing calls to promote and study ‘HIV sensitive’ social protection programs that aim to curtail the forms of inequality that frequently structure HIV risk (UNAIDS, 2010; UNICEF, 2010). In doing so, we are attempting to amplify the voices of colleagues who have noted the urgent need for more research on the reasons behind—and possible solutions to—the failure of PMTCT programs to reach and retain many vulnerable

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4 We stress the importance of context in interpreting the results of these studies. An intervention found to be effective in one context may not be effective in all contexts. For example, in contrast to the Malawi results, a recent study of cash transfers in South Africa showed that cash transfers did not reduce HIV risk among young women, though the low rates of HIV risk overall in the study groups may have impacted the results (Pettifor et al., 2015; Miller, 2015).
women and children (Wettstein et al. 2012; Marcos, Phelps, and Bachman 2012; McNairy and El-Sadr 2012).

Our position shares some aspects of the ‘human development approach’ to international research ethics. This approach, grounded in the principle of social justice, argues that research programs should contribute to the building of health equity in host communities (London, 2005). We argue that pediatric remission research might do so by including both biological and social outcomes. Infant HIV remission research necessitates the collection of biological data from HIV-infected neonates. We advocate that remission research also collect social data on the structural inequalities that put such infants at risk, and how these inequalities might be remediated through social protection schemes. By pairing biological research with studies of social protection, pediatric remission studies could contribute to ‘expand[ing] the capacity of the basic social structures of that community to better serve the fundamental interests of that community’s members’ (London, 2005, p. 33). The onus of building such a research program ought not to fall solely on researchers. Funders should encourage and support schemes that would facilitate the integration of biological studies of infant remission with research into the social determinants of maternal and infant infection. In addition, scholars, advocates, and policymakers must apply research findings to affect concrete changes in the structural conditions that cause women to go untreated and babies to be born with HIV.

In advocating this approach to infant HIV remission research, we endorse international research frameworks that go beyond procedural ethics and insist upon an ethical commitment to reducing health disparities, promoting social justice, and openly confronting the inequalities that make global health science possible (Benatar and Singer, 2000, 2010; Benatar, 2013; Geissler, 2013; Crane, 2014). To this end, more research is needed to explain the causal pathways linking social protection to improved HIV prevention and care, and to understand how to best meet needs across a variety of diverse social contexts (UNICEF, 2010). In other words, while both the Pretoria mother and the mother of the ‘Mississippi baby’ appear to suffer from entrenched gender, racial, and economic inequalities, their specific needs are likely to differ. In addition, there is great social diversity across the African continent and this implies a diversity of unmet needs and barriers to PMTCT in African contexts. (For example, non-disclosure to male partners is often tied to poor ART adherence in Africa, but in at least one study in Kenya, non-disclosure was linked to better adherence as it allowed family units and social support networks to remain intact (Gourlay et al., 2013; Awiti et al., 2011)). For this reason, the research we propose should be conducted in collaboration with impacted communities, and should be aimed at developing context-specific, community-based solutions (Marcos, Phelps, and Bachman, 2012).

**Conclusion**

In 2011, UNAIDS launched the “Countdown to Zero” initiative, a global plan towards eliminating new HIV infections in children by the year 2015 (UNAIDS 2011). It is now 2016, and although significant progress was made towards this goal, the gains have been “uneven and fragile” (UNAIDS, 2014, p. 7). According to UNAIDS, between 2012 and 2013 the percentage of pregnant women with HIV receiving antiretrovirals grew by only 4%, with coverage actually declining in six countries (ibid). Simultaneously, investment in HIV cure research has grown, with over US $100 million going towards cure research, an increase of 16% from the previous year (International AIDS Society, 2014). Many of the study subjects for pediatric HIV remission
research will, by necessity, be infants whose mothers did not access preventive care. As the Mississippi and South African cases show, these are likely to be women and children living at the margins of extremely unequal societies. While research alone cannot undo these entrenched inequalities, it can make an important contribution by understanding the shortfalls of existing prevention programs and testing possible solutions. Because HIV infant remission research will include significant numbers of vulnerable women and children who were not able to access prevention services, we feel that remission studies are especially well positioned to explore and document ways in which women’s needs might be better met and their circumstances improved at both an individual and structural level. For this reason we advocate that the biological research agenda of understanding and prolonging HIV remission be paired with the social research agenda of reducing risk and improving access to effective prevention. The result, ideally, is a ‘win-win’ situation in which remission and prevention efforts can be improved synergistically in order to benefit the care of HIV-positive women and their children.

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