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Professor Solomon Benatar's legacy in transforming bioethics in global health research

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The HIV pandemic exposed, on a global scale, both our shared vulnerability and the profound inequities that defined access to innovation, clinical care, public health systems and regulatory and bioethics capacity between industrialised countries and low- and middle-income countries (LMICs).[1-4] These disparities were inseparable from colonial legacies, political oppression and structural violence, which shaped health systems and social resilience across the Global South.[5,6] Within this context, Prof. Solomon Benatar emerged as an important voice advocating a justice-oriented and context-sensitive response to global health research.

Sub-Saharan Africa (SSA), home to a disproportionate share of people living with HIV globally,[7-9] continues to bear approximately 50% of the global burden of the pandemic, particularly among young women (aged 15 - 24 years) and their infants.[10,11] During the 1990s, scientists working in Africa expanded HIV surveillance, undertook studies to enhance understanding of transmission dynamics and pathogenesis, and evaluated locally appropriate prevention and treatment strategies.[12-15] Although partnerships with institutions in industrialised countries accelerated the conduct of multicountry trials, they also exposed major differences between industrialised and LMICs in post-trial access to prevention and treatment interventions and in research capacity, including infrastructure. These inequities intensified debates regarding placebo use, appropriate comparator arms and sponsors' obligations to provide antiretroviral treatment to participants who acquired HIV during trials, particularly as combination antiretroviral therapy (cART) remained largely inaccessible in many LMICs.[1,16-20]

Importantly, as multicentre HIV prevention and treatment trials advanced knowledge that was implemented in industrialised countries, the standard of prevention and care in the comparator arm of proposed clinical trials in LMICs became increasingly contentious, pausing pivotal trials for several years.[21-23]

This manuscript revisits the ethical debates of the late 1990s and early 2000s to show how Prof. Benatar helped move the field beyond the impasse that paralysed HIV prevention and treatment research. His contributions consistently argued for a justice-centred, pragmatic and context-specific approach to global health ethics, together with stronger local scientific leadership and more equitable research partnerships.[24-29]

The ethical impasse of preventing mother-to-child transmission

In 1994, a major scientific breakthrough in preventing mother-to-child transmission (PMTCT) of HIV occurred in the United States of America (USA) through the Pediatric AIDS Clinical Trials Group Protocol 076 (PACTG 076). A prolonged zidovudine (AZT) regimen, initiated during pregnancy and continued throughout labour and the postpartum period, was shown to reduce vertical transmission by approximately 70%.[30] Although this rapidly became the standard of care – defined as the best available care – in industrialised countries, the regimen was unfeasible in much of the Global South owing to cost, complexity, late presentation for antenatal care, home deliveries and breastfeeding practices.[31-34]

At the time PACTG 076 was reported, SSA had become the epicentre of the HIV pandemic, and scientists in Africa and Asia were seeking simpler regimens that could be tested and implemented under local conditions.[35-38] Based on emerging pathogenesis data and real-world patterns of antenatal care use, investigators proposed shorter antiretroviral regimens initiated closer to delivery. Critics in the USA regarded placebo-controlled trials of such regimens as unethical because an effective intervention already existed, even if it was inaccessible or not feasible to implement in LMICs.[1,16,19]

The result was a deeply polarised debate that threatened to stall PMTCT and adult HIV prevention research. For some, anything short of the highest global standard was inherently exploitative.[39] For others, insisting on an unattainable standard risked denying women and infants access to interventions that were scientifically plausible, locally relevant and potentially life-saving.[18,19,40]

Amid these debates, Prof. Benatar was a prominent voice in global deliberations on HIV research, bioethics and human rights. Through peer-reviewed publications, conference interventions and collaborative work within the US Division of AIDS (DAIDS)-funded HIV/AIDS networks, and later at the Dalla Lana School of Public Health, University of Toronto, he helped shift the discourse from polarised positions toward equity-driven and action-oriented solutions.[41,42] He questioned whose interests research served, how ethical double standards operated in low-resource settings and how historical injustice shaped contemporary vulnerability, while retaining beneficence, non-maleficence, autonomy and justice as foundational ethical commitments.[43-45]

At the 2002 HIV Prevention Trials Network (HPTN) Annual Meeting, one of us (Quarraisha Abdool Karim (QAK)) organised and chaired a plenary session to confront the ethical disagreements that were paralysing the HIV prevention research agenda in SSA. Prof. Benatar was an invited speaker, based on his contributions to bioethics in South Africa. He received a standing ovation after his presentation – an unusual response at such meetings – because it articulated the moral core of the problem with unusual clarity. He emphasised that research ethics could not be separated from inequity, historical injustice and the realities of fragile health systems.

Shortly thereafter, HPTN leadership asked QAK to establish and chair the HPTN Ethics Working Group (EWG), a multidisciplinary group convened to advance these deliberations. This team included Jeremy Sugarman, Ronald Bayer, Solomon R. Benatar, Marge Chigwanda, Monica Ruiz, Deborah Donnell, Laura Guay, Stella Kirkendale, Bernard Lo, Kathleen MacQueen, Sophia Mukasa Monico, Vasantha Muthuswamy, Katharine Shapiro, Ronald Strauss, Steve Wakefield and Cynthia Woodsong.

As a member of the HPTN EWG, Prof. Benatar, together with colleagues, helped shift deliberations beyond rigid readings of international bioethical guidance toward a more inclusive, practical and responsive framework for multicountry research.[46]

Prof. Benatar's role in the HPTN EWG was especially important. He contributed to the development and refinement of the Network's ethics framework, including the 2003 and 2009 HPTN Ethics Guidance for Research.[46,47] These collectively authored documents, arising from extensive deliberation, set out a structured approach to ethics oversight in multicountry prevention trials, including stakeholder consultation, protocol-level review, a comprehensive prevention package and transparent justification of control arms. This approach formalised expectations regarding background prevention, control-arm justification and access to effective interventions during and after trials.[48] The emphasis on transparent deliberation and responsiveness to local context closely reflected themes central to Prof. Benatar's scholarship.

Prof. Benatar's contributions within HPTN formed part of a broader international engagement with ethics forums and policy processes, through which he both shaped and refined emerging approaches to multinational HIV research.[46,47,49,50]

Beyond the guidance documents, the HPTN EWG addressed informed consent, standards of care and trial design in a series of publications that clarified the ethical reasoning underpinning global HIV research and, crucially, helped break the impasse that had paralysed PMTCT and other biomedical prevention studies.[45,46,50,51]

These and related deliberations on global health research contributed to revisions of the Declaration of Helsinki in 2013 and the CIOMS guidelines in 2016. Although these revisions cannot be attributed to any single individual, Prof. Benatar's scholarship on justice, standards of care, sponsor responsibilities and contextual interpretation formed part of the wider literature informing them.[28,41-43,52-57] In particular, the Declaration of Helsinki sharpened guidance on placebo use in clinical trials, specifically the use of 'best proven' standards, and on post-trial access to successful interventions, while the CIOMS guidelines placed greater emphasis on responsiveness to host-country needs, equitable partnerships and capacity strengthening.[41-43,53-57]

From principlism to global justice

Prof. Benatar's wider scholarship located HIV/AIDS within a complex global system marked by widening disparities and fragile public health infrastructures, particularly in Africa.[41] He argued that bioethics would remain limited unless it engaged with the global political economy of health, the ethics of power and the structural determinants of vulnerability.[43,49,52] In this account, beneficence could not mean simply offering the best intervention available anywhere; it also required identifying the best achievable and sustainable intervention within a given context. Non-maleficence and autonomy likewise had to be interpreted in settings where structural inequality constrained meaningful choice. Justice, in turn, required explicit attention to the forces that reproduced global health disparities.

Applied in this way, the principlist approach became a rational means of overcoming this impasse. Prof. Benatar repeatedly emphasised that ethical guidelines are living instruments rather than immutable texts and therefore must be interpreted thoughtfully in relation to context, feasibility and evolving evidence.[58] This position did not weaken ethical standards; it made their application more honest, practical and just.

A further strength of Prof. Benatar's approach was his emphasis that ethical research in the Global South required more than adapted guidance: it required local leadership, community engagement and stronger governance. He argued that research in Africa should be led by African scientists, shaped by local communities and designed to address local priorities.[29] This commitment was also evident in research ethics capacity-building initiatives in SSA, including Fogarty International Center-supported programmes that helped develop sustainable expertise in ethics review, governance and academic leadership.[59] This orientation helped normalise more equitable partnerships and strengthen local ownership within HPTN and related research platforms.[60]

The scientific and programmatic consequences were substantial. Simplified PMTCT regimens, and later biomedical prevention interventions, were developed, evaluated and translated into policy partly because this ethical stalemate was overcome.[7,36,61-64] These advances saved millions of infant and adult lives and provided a model for integrating bioethics, human rights and public health pragmatism in global health research.

The PMTCT debates of the mid-1990s were among the first major global health crises to expose the challenges of applying bioethical guidance in a rigid and universal manner amid profound inequality. Prof. Benatar's leadership helped lay the foundation for a more just, inclusive, reasonable and context-sensitive approach to knowledge generation – one that continues to shape the design of vaccine trials, HIV prevention research and responses to emerging pandemics. He also argued that ethical guidance should be continuously revisited as evidence evolves and access to interventions changes, with attention not only to individual participants but also to the structural determinants of health that shape communities and health systems.

Persistent inequities in access to COVID-19 vaccines and to pre-exposure prophylaxis (PrEP), despite the participation of LMICs in the research that enabled licensure, underscore the continuing relevance of his call to align bioethics with justice, human dignity and the right to health.

For those working on the frontlines of epidemics in SSA, his legacy remains both a moral compass and a practical challenge: rigorous science must be socially responsive, grounded in solidarity and of clear benefit to the communities most affected by global health threats.

Data availability statement. None.

Declaration. None.

Author contributions. QAK conceptualised and wrote the first draft of this manuscript. JM assisted with the literature review and editing.

Acknowledgements. The authors thank Jeremy Sugarman and Sharana Mahomed for their valuable feedback on the earlier version of this manuscript.

Conflicts of interest. None.

Funding. None.

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Submitted 30 June 2025; accepted 14 April 2026.

S Afr Med J 2026;116(6b):e3843. https://doi.org/10.7196/SAMJ.2026.v116i6b.3843