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A Midlife Crisis

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Editorial: AIDS at 35 a midlife crisis. By David Wilson, World Bank Global AIDS Program Director¹ and Alan Whiteside² AJAR Editor-in-Chief

AIDS was first publicly reported on 5th June 1981 in the *Morbidity and Mortality Weekly Report* (MMWR) of the US Centers for Disease Control (CDC). Doctors in New York and San Francisco were seeing clusters of previously extremely rare diseases such as *pneumocystis carinii*, and Kaposi's sarcoma. These infections manifested in exceptionally serious forms, initially, within a narrowly defined risk group—young, homosexual men, and lead to death with a short period. Soon it was clear these illnesses were occurring in other definable groups: haemophiliacs, blood transfusion recipients, and injecting drug users (IDUs). By 1982 cases were seen in the partners and infants of those infected.

There were reports of cases from Europe, Australia, New Zealand, a number of African countries, Brazil, and Mexico. In Zambia a significant rise in cases of Kaposi's sarcoma was recorded. In Kinshasa, Zaire there was an upsurge in patients with *cryptococcosis*, an unusual fungal infection. The Ugandan Ministry of Health was receiving reports of increased and unexpected deaths among young people in Lake Victoria fishing villages. The name 'Acquired Immunodeficiency Syndrome' (AIDS) was agreed in Washington in July 1982. Even when the syndrome had been identified and named it was not clear what its cause was, how it spread, and what treatments could be developed. In 1983 the virus was identified by the Institute Pasteur in France and called 'Lymphadenopathy-Associated Virus' or LAV. In 1987 the name 'Human Immunodeficiency Virus' (HIV) was confirmed by the International Committee on Taxonomy of Viruses.

The spread of diseases spread from animals to humans (and vice versa) is not unusual. This is called zoonosis. Recent examples include Severe Acute Respiratory Syndrome (SARS), tracked to civet cats, ; Avian Influenza (bird flu),); Middle East Respiratory Syndrome (MERS), linked to camels, ; the Ebola virus carried by fruit bats; and the Zika Virus which was first reported in monkeys in Uganda in 1947, but which is now spread by mosquitoes. HIV is, so far, the most deadly pathogen to have made the leap across the species barrier to humans. SARS was, fortunately, not as infectious; avian flu has not yet

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taken hold in humans; MERS outbreaks have been infrequent and controlled. The Ebola outbreak has requires constant monitoring but has not spread beyond control; and the full consequences of Zika are ll emerging.

This year marks the 35th since AIDS was first identified and the epidemic faces a ‘mid-life’ crisis. The opening lines from Charles Dicken’s from *A Tale of Two Cities* seem aptly appropriate to describe the AIDS epidemic at the end of 2016. “It was the best of times, it was the worst of times, it was the age of wisdom, it was the age of foolishness, it was the epoch of belief, it was the epoch of incredulity, it was the season of Light, it was the season of Darkness, it was the spring of hope, it was the winter of despair...” (*A Tale of Two Cities, Para.1, Line, 1*)

It seems to us it is time to take stock of both the successes we have meet and the challenges we face. In this editorial for the final issue of AJAR in 2016 we do this. Our credentials are we are both social scientists, from Southern Africa, Swaziland and South Africa in the case of Whiteside, and Zimbabwe for Wilson, who have been engaged with the epidemic since the late 1980s. We warned of the potential devastation AIDS would wreak across Africa, but this went unheard. We watched with dismay as colleagues and friends sickened and died, and the political leaders initially ignored what was to come. In this editorial we look at the best of times – where things went well; and the worst of times – where the challenges lie.

The Best of Times

Knowing the Epidemiological reality

It is clear AIDS is not a global threat as was initially feared. In most of the Americas, Europe, North Africa, the Middle East, Asia and the Pacific, it is located in specific groups, such as men who have sex with men, drug users and sex workers – and their immediate sexual partners. Here prevention efforts must continue, reinforced by epidemiological vigilance to understand evolving transmission patterns. It has become clear that the worst epidemics are in Southern, East and Central Africa. In this sub-region, especially the Southern cone, the epidemic is exceptionally serious. For example in South Africa in 2015 there were an estimated 7 million people living with HIV, and a 19.2% prevalence among the adult population. The small country of Lesotho (completely surrounded by South Africa) had an unbelievable adult prevalence of 22.7%, perhaps the highest in the world. Elsewhere in Africa Nigeria is noteworthy

because of the level of infection and the size of its population. The HIV prevalence rate is 3.1% among adults which translates into 3.5 million people living with HIV.

Advocacy and Evidence.

Because the early cases were located in the newly liberated and increasingly politically active gay population, there was massive mobilisation around the disease. Gay men particularly in the United States demanded action and answers and were not shy to call for this. AIDS was the first disease to have this level of engagement. It provides a model for patient activism and demanding accountability from both governments and the pharmaceutical industry. There was also a significant emphasis on understanding the science of the virus and the treatments that were available to patients. AIDS quickly became the most studied pathogen in history. In the west AIDS changed the medical discourse. In the rest of the world NGO's and patient advocacy groups sprang up and sought to educate themselves on the disease, treatments and prevention.

Knowledge.

There have been unprecedented and exceptional scientific advances since the epidemic was first identified. Although it took a few years to identify the virus, once this was done, it quickly became apparent as to how HIV was spread, and what interventions could be put in place to prevent transmission. By 1996 there were drugs available. The accumulation of scientific knowledge has continued. We are aware of how complex it will be to bring an end to the epidemic through vaccines or treatment but the efforts continue. The work around HIV and AIDS has had huge impacts throughout the medical, virological, immunological, and social science research worlds.

Treatment.

In 1996 it became apparent that the most effective form of treatment was a combination of three different drugs. This breakthrough meant patients could recover. Initially patients had to take handfuls of tablets at specified times of the day, some with and some without food. The cost was immense, initially over \$10 000 per patient per year. In 2016 a person can take just one pill a day and treatment is delivered for less than \$100 per patient per year in some parts of the the developing world. In Kwazulu-Natal, South Africa, the global epicenter of the HIV epidemic AIDS treatment has increased community life expectancy by a full 11 years, reversing decades of decline -- life expectancy in Kwa-Zulu Natal is

higher today than before the HIV epidemic. This seems scarcely creditable to those who witnessed the early years of the epidemic and is indubitably one of the great successes of global health.

In the next few years a 'once a month' tablet will be available, within a decade, implants will be developed to deliver long acting medicines. However there is a caveat, while most people can live virtually normal lives both in terms of length and functionality, there is still no cure and the drugs have side-effects, some of which are significant and cumulative and may reduce the quality and quantity of lives.

The Worst of Times.

Prevention lags.

One of the fundamental tenants for public health is that prevention is cheaper and easier and better than having to treat the resulting condition. The global action against tobacco means that millions of people will not be faced with lung conditions including cancer and emphysema. Prevention of smoking will save trillions of dollars in expensive and ultimately often futile medical interventions. The same is true of making it mandatory for people to wear seatbelts in motor vehicles. A study in Nebraska found that in motor vehicle accidents, the mean hospital costs were \$7099 for those not using any type of seatbelt, as compared with \$2909 for motor vehicle occupants using a lap-shoulder seatbelt. The cost for a child in a seatbelt was \$1132.¹

The recent UNAIDS prevention gap report shows new HIV infections stagnating at 2.1 million annually, with many countries experiencing unexpected increases. IHME's independent estimates are even higher—74 countries with increased HIV incidence and 2.5 million new infections every year. Clearly prevention messages are not as effective as we would hope.

One of the earliest and most successful interventions with regard to HIV was blood and blood safety. It is rare, including in conflict and emergency situations, for blood not to be tested. This was the most efficient mode of transmission but was relatively uncommon. Prevention of mother to child transmission is cheap and effective provided the mothers can be reached. Across the world transmission rates have fallen from as high as 30 percent to zero or just a few percent. It is possible to prevent in vitro transmission and the infection of the infant through breastfeeding. The current thinking is that mothers should begin receiving ARVs as soon as they are identified as being HIV positive and this should continue for their lives.

The bulk of transmission takes place between sexually active people, both heterosexual and homosexual. The interventions have not changed dramatically: abstinence; fidelity; and condom use will all prevent HIV transmission. There is evidence to show that women who are uninfected are twice as likely to become infected through sexual intercourse and this highlights the gendered nature of the epidemic. An encouraging new development is a microbicide that would be female controlled. The issue of gender empowerment has been brought to the fore by the AIDS epidemic. There are a number of pilot interventions looking at giving girls greater power through cash transfers. These seem on the whole to show promise; the challenge is to find the resources to scale them up.

Transmission of HIV between injecting drug users can be addressed through the provision of clean needles or opioid substitution projects. However, such proven programs are lamentably small in number and reach.

Although the technology and knowledge is available, there are blocks in the face of the implementation. This includes the fact that homosexuality, drug use, and sex work is illegal and discriminated against in a number of countries.

No end to AIDS in sight.

The recent Durban 2016 AIDS Conference saw talk of the end of "ending the HIV epidemic" as a feasible goal with the tools we have. This is not the case, we need new and better tools. Talk of ending AIDS has led to a widespread perception in the broader health and development community that this crisis is over. It isn't and continued exhortations that we can end the AIDS epidemic with our existing armory may further undermine global recognition of and commitment to address this epidemic.

The 2016 conference also underscored the limitations of Treatment-as-Prevention (TasP) the idea that people on treatment do not infect others so all infected people should be on drugs, treating all for the public health benefit of reducing further transmission, a magic bullet to end the epidemic. In a cluster randomized trial in KwaZulu-Natal, TasP did not reduce new HIV infections. Without decrying the transformative effects of treatment in reducing AIDS illness and death and slowing HIV transmission, we won't end this epidemic with tablets. We have never ended a global epidemic without a cure or vaccine and HIV is no exception.

Funding and political commitment.

For the first 30 years of the epidemic money was not generally the binding constraint. The international community stepped forward and made billions of dollars available. HIV funding from the international community has fallen from \$8.6 billion in 2014 to \$7.5 billion in 2015. Moreover, international financing is perilously reliant on one donor, the United States, which provides two-thirds of all international HIV financing. Financing fell in 13 out of 14 international HIV funders surveyed. US government funding fell from US\$5.6 billion to US\$5 billion, but this was largely a timing issue as the US moved funding to 2016 while planning new programs. Without including the US\$411 million reduction in U.S. funding, which is expected in 2016, total funding declined overall by 8 percent. The reliance on one major global funder – the US is not prudent and broader, more diversified international and domestic financing would mitigate the risks of such concentration.

Alongside funding declines, political commitment has waned and is moving from power to symbolism, as starkly attested by the 2016 Durban International AIDS Conference, where we welcomed the role that princes, princesses, film and rock stars played to raise the visibility of the conference, but wished more heads of government, senior legislators, development and finance ministers had participated.

The way forward.

We need to move beyond advocacy to a remorseless focus on complex reality. 90-90-90 has been an effective rallying cry, but its implied progression towards herd coverage and immunity does not capture the complexity of HIV transmission dynamics, which require us to first reach - and then retain - those with early, acute infection, high viral load and high rates of partner change or needle sharing - many of whom face multiple overlapping health and social vulnerabilities. We need a more targeted, nuanced, differentiated and comprehensive approach to epidemiological, implementation and social complexity.

We need to sustain international HIV financing – countries are not prepared for an abrupt transition. However, we must redouble our efforts to integrate HIV into the wider architecture of development assistance for health. We must focus on greater domestic financing and tackle displacement. Too many countries responded to increased global health financing by curbing domestic investment – this cannot continue. We must accelerate the progression from a short-term, emergency response to a sustained development response, where HIV is on-budget and integrated into national plans and budgets and

universal health coverage (UHC) and health systems. We need to sustain international commitment, while building national vehicles that will endure - the HIV response will be a long journey not a sprint. Ideally, international HIV support should provide the turbochargers and boosters of the global response, not the wheels and chassis^[a1]. [SS2]

We need to strengthen our focus on social and structural determinants of HIV transmission. Secondary education, income, greater economic opportunity and shared, inclusive growth reinforce HIV prevention.

We must find new ways of reengaging heads of government and finance and development ministers, who may think the HIV crisis has ended and may not understand the long-term developmental and financial implications of an epidemic where new HIV infections remain stubbornly high and treatment costs rise inexorably.

We must reconceive HIV prevention - there are no good outcomes without turning off the tap of new HIV infections. We need to revitalize comprehensive prevention, including ART-based prevention, key population prevention and male circumcision in Eastern and Southern Africa, reinforced by wider education, social protection and structural interventions led by other sectors. There is no magic bullet but we do have a quiver of partially effective arrows, which if targeted, deployed and implemented at-scale together will slow new infections. As we embrace the undoubted promise of PREP, we must heed the lessons of TasP and resist the false blandishments of a new magic bullet. We need more differentiated prevention implementation priorities that reflect HIV transmission dynamics - and concomitant implementation complexities and the realities of partial, uneven, mixed, variable and sometimes slow implementation. We also need to redouble our investment in new prevention technologies, including the vaginal ring, long-acting and implantable ARVs and above all a vaccine.

We face a lone, sinewy generational battle against a dogged virus. The good news is the remarkable success of AIDS treatment continues to buy time to implement comprehensive, scaled prevention and seek the new scientific tools we need to glimpse an ultimate end to AIDS - we must seize this opportunity with renewed urgency, purpose and apprehension of the enormity of the ground still uncovered – and the duration of the battle till before us.

Conclusion.

The African Journal of AIDS Research is undergoing changes. Editorials give us the opportunity to identify key issues. We are planning to include book reviews and commentaries. In the last issue we published, for the first time, Lucey Wilmott's response to an earlier article. We will not compromise our standards of scientific rigour and articles will continue to always go through peer review. However we want to lead the debate as well as follow it. This editorial recognises areas where the response has done well and some of the unfinished business. Unfortunately the number of infections continues to rise which means, as Southern Africans said 'A luta continua'.

ⁱ Int Emerg Nurs. 2016 May 10. pii: S1755-599X(16)30029-5. doi: 10.1016/j.ienj.2016.04.004. [Epub ahead of print] Seatbelt use to save money: Impact on hospital costs of occupants who are involved in motor vehicle crashes. Han GM, Newmyer A, Qu M.