

## Editorial

### **‘Getting to Zero’: are there grounds for optimism in the global fight against HIV?**

World AIDS Day has been observed on 1<sup>st</sup> December each year since 1988 and is one of the longest-running disease awareness and prevention initiatives of this kind in the history of public health. It is an opportunity to reflect on the global epidemic that has claimed 30 million lives over the past 30 years, to stake stock and to strategically move forward. For the 5-year period 2011-2015, World AIDS Day has adopted the bold theme: ‘Getting to Zero. Zero new infections, Zero discrimination, and Zero AIDS-related deaths.’ These words directly quote the United Nations Secretary-General Ban Ki-Moon in June 2011 which he prefaced with, “Today we have a chance to end this epidemic once and for all. That is our goal”.

The vision of a world with zero HIV infections, zero discrimination and zero HIV-related deaths has captured the imagination of diverse partners, stakeholders and people living with and affected by HIV. At the International AIDS Conference in Washington in July 2012, US Secretary of State Hillary Rodham Clinton called on Global AIDS Coordinator Eric Goosby to create a blueprint for the US government to achieve an AIDS-free generation. There is clearly a new era of optimism regarding the global response to HIV. Is this ill-founded or are their grounds for such optimism?

The scale of the epidemic is greater now than ever before, with an estimated 34.2 million people living with HIV in 2011, including 3.4 million children<sup>1</sup>. However, the continuing rise in the number of people living with HIV does not simply reflect ongoing new infections but is also a result of increasing survival associated with treatment (*i.e.* treatment success). The annual number of new infections each year has been slowly declining with 2.5 million infections in 2011 (a 20% reduction since 2001). This includes 330,000

new infections among children, which have reduced by 24 per cent within the preceding 2 year period<sup>1</sup>. The number of people dying from AIDS-related causes has decreased substantially from a peak of 2.2 million in 2005 to 1.7 million in 2011. Thus, despite the daunting reality of almost 7,000 new infections and 4,600 deaths across the world each day, there is growing evidence that the course of this epidemic is nevertheless changing and starting to head in the right direction.

Confidence is growing in the range of tools that we have at our disposal to address the HIV epidemic. The global scale-up of antiretroviral therapy (ART) has been an extraordinary success story. Implementation continues to accelerate, reaching more than 8 million people in low- and middle-income countries by 2011<sup>1</sup>. This represents a 20 per cent increase within the preceding year and a 20-fold increase over 8-years. Scale-up of ART is estimated to have averted 2.5 million deaths in low- and middle-income countries between 1995 and 2010<sup>2</sup>. Providing antiretroviral prophylaxis to pregnant women has prevented more than 350,000 children from acquiring HIV infection since 1995. These successes are to be celebrated and built on. There is still a long way to go, however, as coverage is just 54 per cent of the 14.8 million people estimated to be eligible for treatment. The fact remains, that for the 1.5 million people who started ART in 2011, there were 2.5 million new infections. We are neither keeping pace with those needing treatment nor effectively switching off the tap. A new era of effective HIV prevention is desperately needed.

In recent years, there has been a major shift in our understanding of the even greater potential role of ART in tackling this epidemic. The goals of ART are now expanding from simply preventing morbidity and

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death and mother to child transmission to also include prevention of sexual transmission. Natural history data originally showed that people living with HIV whose viral load is less than 1,500 copies/ml had a very low risk of heterosexual transmission<sup>3</sup>, suggesting that ART might also be effective for prevention. This was more recently confirmed by the HPTN052 study that demonstrated that ART reduces HIV transmission between discordant couples by 96 per cent<sup>4</sup>. These data strongly support a strategy of widespread use of early treatment as prevention (TasP).

The goal of TasP strategies is to diagnose and start ART early in as great a proportion of those living with HIV in a community as possible. Suppressing the overall 'community viral load' would be anticipated to switch off transmission and thereby help stem the epidemic<sup>5</sup>. The 2010 revision of the World Health Organization guidelines for ART was a step in the right direction towards this, recommending earlier treatment and use of less toxic drug regimens<sup>6</sup>. However, with increasing recognition of the preventive benefit of ART, future policy changes may push this agenda towards even earlier treatment. Many believe this to be the key strategy that is needed to make progress towards 'Getting to Zero'. In addition, this would potentially play a central role in tackling the HIV-associated tuberculosis epidemic<sup>7</sup>.

There are other reasons for optimism. Recent years have also seen other significant scientific breakthroughs in HIV prevention. A randomized trial of oral chemoprophylaxis using a combination of two oral antiretroviral drugs (tenofovir and emtricitabine) among men who have sex with men<sup>8</sup> and a randomized trial of a vaginal tenofovir gel among women in South Africa<sup>9</sup> both showed partial efficacy. In July 2012, the WHO issued its first recommendations on use of pre-exposure oral prophylaxis (PrEP)<sup>10</sup>. The first evidence of efficacy for an HIV vaccine candidate has also been found in recent years<sup>11</sup>, restoring a little confidence in the hitherto demoralized HIV vaccine field. Meanwhile global scale-up of established prevention interventions such as prevention of mother to child transmission, condom distribution and male circumcision continues to grow. The first ever possible 'cure' of a patient living with HIV has been reported after receiving a stem cell transplant from a donor who was homozygous for CCR5 delta32 as treatment for acute myeloid leukaemia<sup>12</sup>. In July 2012, the International AIDS Society also published a document entitled 'Towards a cure' that outlines a global strategy towards finding a

cure for HIV infection<sup>13</sup>. Thus, the past few years have seen huge progress in the overall scientific agenda.

Despite this progress, are we being over-optimistic or simplistic in thinking we can tackle this epidemic that has ruled as the leading infectious cause of death for so many years? Can we sustainably scale up the needed interventions to levels of coverage sufficient to make a real impact on new infections? We should reflect on World AIDS Day in 2003 when the WHO and UNAIDS launched the '3 by 5' initiative, which was met with not a small amount of pessimism in some quarters. This target of providing treatment for 3 million people in low- and middle-income countries by the end of 2005 required a fundamental shift in thinking. Despite the daunting challenges of feasibility, funding and delivery, this goal provided a much-needed focus and vision to galvanize concerted international action to tackling the enormous challenge of AIDS. Ultimately the '3 by 5' goal was only met in 2007 and yet this provided huge momentum that has seen continued expansion of ART access to reach more than 8 million people by 2011<sup>1</sup>.

The world now has a choice between maintaining current efforts in scale-up of treatment and prevention and seeing incremental progress over time, or investing more smartly in the shorter term to achieve far greater gains. We are at a pivotal moment in the global response where we have the opportunity to grasp UNAIDS 2011-2015 strategy for 'Getting to Zero'<sup>14</sup>. This, of course, requires substantial international investment of resources. Since 2008, budgetary constraints and ongoing uncertainty resulting from the global recession have conspired to threaten existing hard-won gains. Global resources made available to HIV programmes in low- and middle-income countries decreased in real terms in 2009 and 2010<sup>2</sup> and this was compounded by the Global Fund's cancellation of the 11<sup>th</sup> round of funding in November 2011. The global investment in HIV was \$16.8 billion in 2011, falling short of the \$22-24 billion projected to be needed annually for the global response to HIV up to 2015<sup>1</sup>. However, this shortfall of around \$7 billion per year is only a small fraction of the estimated clean-up costs of Hurricane Sandy which hit the east coast of the USA in October 2012.

These financial challenges require that not only must the efficiency of HIV programmes be maximized, but also that the investment is recognised as being 'smart'. There are much wider health benefits of HIV care and prevention, including positive impacts on the HIV-associated TB epidemic, maternal and child health

and strengthening of the health system. The human and social benefits must also be understood, with the economic gains of improved health substantially offsetting the costs of treatment<sup>15</sup>. Simplistic and artificial debates regarding the competition between HIV and other global health needs are unhelpful in this regard. The challenges to scale-up are not only financial and logistical, however. Achieving high levels of coverage of interventions will also require a societal change in thinking. ‘Zero discrimination’ is a critical goal since stigma and discrimination are major barriers to uptake and utilization of services.

The call to ‘Get to Zero’ is a global call, involving the whole international community of nations. This includes India, with 2.4 million people (39% female) living with HIV in 2009 - the third highest number of any country after South Africa and Nigeria<sup>16</sup>. This represents 7 per cent of the global burden of HIV and half of Asia’s epidemic. There are around 140,000 new infection each year and 172,000 deaths. Incidence is estimated to have decreased by 50 per cent between 2000 and 2009, which is a laudable achievement and yet these are not grounds for complacency. Although HIV prevalence among female sex workers declined to less than 5 per cent, prevalence remains high among men who have sex with men (7.3%) and people who inject drugs (9.2%)<sup>16</sup>. Just less than half a million people in India were reported to be alive and receiving ART at the beginning of 2012<sup>17</sup>. This represents about 20 per cent of all those living with HIV and much greater ART coverage could contribute significantly to HIV prevention. Investments have increased substantially to \$2.5 billion during the National AIDS Control Programme III (2007-2012) and the domestic contribution increased to 25 per cent in 2011. There has been significant scale-up in coverage of focussed programmes among key populations at higher risk. However, further progress in coverage is needed as well as measures to reduce stigma and discrimination.

The story of AIDS over the past 30 years has been a truly remarkable one. There is a sense that at long last we are in a season of opportunity when real progress can be made. But this will require unity of purpose with scientists, policymakers, implementers, civil society, the community and international donors pulling together like never before with the unshakable belief that one day we can get to Zero.

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