



## Editorial

### HIV prevention & treatment strategies - Current challenges & future prospects

On December 1, 2018, the 30<sup>th</sup> anniversary of World AIDS Day was marked and the theme for the year was 'Know Your Status', a pioneering global health campaign initiated by the World Health Organization (WHO) in 1988. The overall goal as outlined by the WHO was two-fold: (i) to 'urge people to know their HIV infection status through testing and to access HIV prevention, treatment and care services', (ii) to urge policymakers to promote a 'health for all' agenda for HIV and related health services, such as tuberculosis, hepatitis and non-communicable diseases<sup>1</sup>. While a substantial progress has been made in the management of individuals living with HIV/AIDS, as per UNAIDS data today<sup>2</sup>, globally, three out of four people living with HIV (PLHIV) know their status. In 2017, 79 per cent of PLHIV in India were aware of their status as per the report of India's National AIDS Control Organization (NACO) (<http://naco.gov.in/hiv-facts-figures>) and UNAIDS data (<http://aidsinfo.unaids.org/>). HIV-positive women are significantly more likely to be diagnosed, compared to HIV-positive men (87 vs. 68%)<sup>2</sup>. This is due to the number of women testing for HIV through preventing mother-to-child transmission services. Nonetheless, much is required to be done in reaching out to individuals who are living with HIV and who do not know their status and, as UNAIDS endorses<sup>2</sup>, it will be important to ensure access them with standard quality care and prevention services.

#### The 'Problem' and vulnerable 'Hotspots'

AIDS caused by HIV is one of the most complex health problems with devastating consequences. The rate of extraordinary diversifications of HIV both at population and individual levels upon contraction is stupendously significant than any other pathogenic organism seen yet. The unprecedented genetic divergence of HIV associated with its ability to

establish persistent infection quickly upon contraction and evading protecting immune responses in the course of natural infection has stymied scientists in their efforts to develop an effective vaccine. In 1991, the movement in fighting against HIV/AIDS for the first time was branded with the iconic red ribbon. This was the very first disease awareness ribbon, which was subsequently adopted by many other health causes<sup>1</sup>. As per UNAIDS data, at the end of 2017, East and South Africa (estimated to be 19.66 million) remained regions with the highest HIV prevalence, whereas regions in the Middle East and North Africa (estimated to be 220,000) were reported to have the least HIV prevalence ([AIDSinfo.unaids.org](http://aidsinfo.unaids.org)). Significant reduction in new HIV infections has been observed in East and South Africa, where new HIV infections have been reduced by 30 per cent since 2010 ([AIDSinfo.unaids.org](http://aidsinfo.unaids.org)). The majority of new HIV infections have been reported<sup>3,4</sup> in men who have sex with men, people who inject drugs, people in prisons, sex workers and/or transgenders, including the sexual partners of these individuals. Quite intriguingly, these groups have often been discriminated against and excluded from getting access to healthcare services. HIV also has been found to disproportionately affect adolescents and young people. As per the WHO estimates<sup>4</sup>, approximately one-third of new HIV infections have been observed in people aged between 15 and 25 yr. Additionally, globally, young women aged between 15 and 24 yr are estimated to be 3-5 times vulnerable than their male counterparts<sup>4</sup>. In sub-Saharan Africa, more than 70 per cent of new infections have been reported in adolescents<sup>4-6</sup>, a matter of great concern, which also indicates that, as these adolescents grow, particularly in countries with high disease burden, the high incidence among young people will pose significant threat in elevating the number of new infections globally.

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### **Interventional efforts associated with lowering burden of HIV incidence and prevalence**

With more than 30 years of the HIV epidemic, though there is still no cure or an effective vaccine, but with the extensive scale-up of HIV testing and treatment, there have been major advances in treating HIV<sup>7-9</sup>. The availability and rapid scale-up of antiretroviral therapy (ART) has transformed what was inevitably a fatal disease to a chronic, manageable condition, leading to notable declines in the worldwide rates of AIDS-related deaths and new infections. While this shift has resulted in tremendous progress towards controlling the epidemic, significant gaps remain. HIV testing is essential for expanding treatment and ensuring that all PLHIV can lead healthy and productive lives. Towards this, some ambitious plans have also been projected. For example, towards catalyzing the market for HIV self-testing, a large multicentric study led by the London School of Hygiene and Tropical Medicine (LSHTM) was conducted by Unitaid-funded HIV Self-Testing Africa (STAR) (<http://hivstar.lshtm.ac.uk/>) Initiative (between 2015 and 2017)<sup>10</sup>. The overall idea was to generate information to facilitate identification, selection and distribute self-test products effectively, ethically and efficiently with adequate post-test support services and answer key questions about the feasibility, acceptability and impact of this intervention. The data generated from this study will not only provide evidence in the WHO normative guidance, but also will ably support the development of national-level policy on HIV self-testing. In addition, the data will potentially support in moving towards achieving the UN's ambitious target of 90-90-90 target (<http://www.unaids.org/en/resources/909090>) that by 2020, 90 per cent of all PLHIV will know their HIV status, 90 per cent of all people diagnosed with HIV will receive sustained antiretroviral therapy and 90 per cent of all people receiving antiretroviral therapy will have durable suppression. While these are important steps towards potential elimination of the disease burden and its effective implementation, it is important to sustain our efforts towards strategically using socio-behavioural intervention to empower, vulnerable and affected population and enable them to battle the stigma and discrimination.

### **India's role in prevention and treatment efforts**

The HIV epidemic in India is predominantly driven by sexual transmission and accounts for about 86 per cent of new infections<sup>2,11</sup>. HIV prevalence in India is only 0.3 per cent as per the National AIDS

Control Organization (NACO)<sup>11</sup> and UNAIDS estimates<sup>2</sup>, but because of size, this approximately equates to over 2.1 million people currently living with HIV. Between 2010 and 2017, new infections declined by 27 per cent and AIDS-related deaths more than halved, falling by 56 per cent. However, in 2017, new infections increased to 88,000 from 80,000 and AIDS-related deaths increased to 69,000 from 62,000<sup>2</sup>. In compliance with the 90-90-90 target, the National AIDS Control Programme IV (NACP-IV, 2012-2017, extended to 2018), launched by the NACO (<http://naco.gov.in/nacp>), aims to reduce annual HIV incidence by at least 50 per cent through building comprehensive targeted interventions *via* antiretroviral therapy, education, care and support for the general population and building targeted interventions for key population who are at high risk of HIV transmission. According to the UNAIDS data<sup>2</sup>, by the end of 2017, about 79 per cent of PLHIV were aware of their status, of whom 56 per cent were on ART; however, the data on the effect of therapy on the quantum of virological suppression are not known. The treatment efforts, primarily through ART, helped PLHIV to manage their infection as a chronic condition rather than a life-threatening illness. With the introduction of 'test-and-treat' policy irrespective of the CD4 counts and clinical stage of the disease<sup>12</sup>, it is believed that there will be further reductions in the rates of death and infections with a potent ARV regimen, particularly in the early stages of the disease. In India, the Ministry of Health & Family Welfare, Government of India launched the 'test and treat policy for HIV' on April 2017 with a vision towards improving the longevity, quality of life and protecting from opportunistic infections of people infected with HIV.

In line with the global efforts, India is also contributing an important role in accelerating the discovery of an AIDS vaccine. One of the important achievements in this regard is the identification of individuals via screening a large number of HIV-infected individuals and who have demonstrated natural protective immunity towards HIV-1. These include people who can contain them from progression to AIDS for a number of years and maintain stable CD4 counts in the absence of antiretroviral therapy and also individuals who have been exposed to HIV but not contracted with the viral infection. This information will help not only to understand process that will delineate the basis of natural protection, but also to isolate and characterize the broadly neutralizing

monoclonal antibodies (bNAbs) that can compensate the shortcomings of ART in treating infected people and designing strategies for preventing HIV by improved immunogen via reverse engineering and pre-exposure prophylaxis<sup>13-18</sup>. Two preventive vaccine immunogens [BG505-SOSIP.664 (<https://clinicaltrials.gov/ct2/show/NCT03699241>) and eOD-GT8 60 mer (<https://clinicaltrials.gov/ct2/show/NCT03547245>)] that have been designed following this principle have now entered the Phase I human clinical trials. Trial data will inform to what extent these improved immunogens will provide immunogenicity in humans. If successful, it will inform vaccine discovery efforts for other diseases too. In addition to the currently existing different scaled intervention options, an effective vaccine, even if it is not fully efficacious, could prevent several millions of HIV infections, significantly avert disease burden and will help reduce long-term treatment costs to a great extent. A vaccine offers several advantages over existing intervention methodologies - for example, it can be delivered before virus acquisition, provide long-lasting protection, can be distributed widely and confidentially within broader public health programmes and potentially overcome challenges of socio-behavioural aspects associated with stigma and adherence. Although the challenges associated with vaccine discovery and development are lengthy with uncertain time, lengthy phased safety and efficacy trials, yet given that vaccines are the most effective and cost-effective tool for prevention, it is worth the wait.

### The way forward

HIV is a difficult virus to tackle. Despite the WHO's recommendation of 'test-and-treat' policy in 2015 regardless of the CD4 counts and stage of disease which has subsequently been implemented by national bodies (such as NACO in India), the rate of new infections and deaths is not falling rapidly enough in meeting the 90-90-90 target. So, what needs to happen? First and foremost, in line with the theme of this World AIDS Day, knowing the status for all is important<sup>1</sup>. As per the recommendation of the WHO<sup>1</sup>, this can be achieved by making the tests available that can diagnose HIV rapidly which can be then readily linked with prevention and/or treatment services. For example, the WHO first recommended HIV self-testing in 2016, which has been taken up by more than 50 countries<sup>3</sup>. Towards this endeavour, it is important to comprehensively map key populations and their partners and urgently need to act on priority to reach and cater to these populations who

are at the greatest risk of contraction of the virus. The future vision towards ending the incidence of HIV will require looking beyond care and bringing institutions, industries, non-governmental organizations and different partners to a common point with the help of government and health policymakers to ensure that the disease response is embedded within the universal health coverage. It is unlikely that elimination of HIV/AIDS is possible without putting in place strategic partnerships in bringing and rolling out comprehensive prevention and treatment through universal integrated health system that will provide HIV prevention, diagnosis and treatment. This should also offer services to cater to combat other co-morbidities associated with HIV/AIDS. Finally, in line with the sustainable development goals as recommended by the United Nations in 2015, it is important to put in place a comprehensive algorithm to integrate indicators to map the ongoing monitoring efforts to comprehensively assess the state of their national response and their progress in achieving national HIV targets in real time. This is important as such exercise will help improve the quality and consistency of data collected at the regional and global levels and will facilitate in enhancing the accuracy of the conclusions drawn at the national, regional and global levels<sup>19</sup>.

**Conflicts of Interest:** None.

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