

## Editorial

### What will it take to expand the pre-exposure prophylaxis to prevent new HIV infections in India?

Elimination of the human immunodeficiency virus (HIV) epidemic is not feasible without effective prevention. Preventive HIV strategy is built on two closely interlinked pillars: prevention of transmission of the virus from a person living with HIV, and prevention of the acquisition of HIV by a person at risk of HIV acquisition. Both preventive pillars are supported by the individualized combination of multiple non-pharmacologic interventions, which include behavioural and structural changes, use of barrier protection, voluntary medical male circumcision, and needle-syringe exchange among people who inject drugs. With the introduction of more efficacious, safer and better tolerated HIV antiretroviral drugs (ARVs) and their fixed dose oral combinations and, more recently, long-acting formulations, pharmacologic interventions have progressively gained a leading role in the preventive HIV strategy<sup>1</sup>. Treatment as prevention (TasP) approach utilizes virologic suppression in persons living with HIV adherent to antiretroviral treatment and data showing lack of HIV transmission from such persons as a prevention strategy, while pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) both involve persons at risk of HIV acquisition taking ARVs to prevent HIV infection. The concept of using ARVs for the prevention of the acquisition of HIV was first introduced in the 1980s with zidovudine (AZT) being used as a PEP in occupational HIV exposure<sup>2</sup>. The concept of using ARVs for PrEP was born within the paradigm of the prevention of the vertical transmission of HIV from mother to child<sup>3</sup> and progressed to PrEP for the prevention of horizontal HIV transmission based on animal and human studies in early 2000<sup>4</sup>. Oral PrEP with tenofovir disoproxil fumarate (TDF) plus emtricitabine (FTC) was approved by the Food and Drug Administration (FDA) in 2012 for persons of all genders<sup>5</sup>, followed by the approval of tenofovir alafenamide fumarate (TAF) plus FTC for persons assigned female at birth in 2019<sup>6</sup>.

It is estimated that globally, more than eight million people have been prescribed oral TDF/FTC since its approval<sup>7</sup>. Despite oral PrEP being implemented as an HIV prevention strategy globally, challenges with limited resources and healthcare capacity in low- and middle-income countries, low uptake, adherence and retention of oral PrEP have limited its impact on the global HIV epidemic. The 2022 approval of the long-acting injectable formulation of cabotegravir for people of all genders represents significant advancement in the options for medicamentous PrEP<sup>8</sup>. Furthermore, recent efficacy and safety data on twice-yearly lenacapavir for the prevention of HIV acquisition opens new horizons for more discreet PrEP choices to people globally<sup>9,10</sup>. To become an effective HIV prevention tool, both long-acting PrEP options will require substantial investment and commitment of global stakeholders.

In India, 2.5 million people are estimated to be living with HIV and ~68 thousand adults (15 yr of age and older) became newly infected with HIV in 2023<sup>11</sup>. The number of new infections has decreased by 44 per cent from 2010<sup>11</sup>, however, to achieve control of the epidemic in the country, preventive HIV strategy needs to be optimized. TDF/FTC has been approved as PrEP in India by the Drug Controller General of India since 2016<sup>12</sup>. Noted as a step towards reaching the 'last mile' in achieving HIV epidemic prevention and control the National Technical Guidelines for HIV PrEP in India have since been written under the oversight of the National AIDS control Organization of India (NACO). These guidelines were developed in close collaboration with the working and expert groups on PrEP and were validated by the Technical Resource Group on Antiretroviral Treatment. The national guidelines' main aim is 'to provide correct information around PrEP in India'<sup>12</sup>. The guidelines note the thoughtful approach, multistakeholder input and collaborative exercise that informed their development as well as an unequivocal acknowledgement of the value of PrEP and its inclusion as part of the 'existing basket of prevention strategies'

in India. NACO PrEP guidelines cite a World Health Organization (WHO) recommendation that people at substantial risk of HIV should be offered PrEP as an additional prevention choice and note substantial risk of HIV as an incidence of HIV typically considered to be higher than 3 per 100 person-years in the absence of PrEP<sup>13</sup>. Recognizing that an HIV incidence of over 3 per cent is rarely observed in India (except among people who inject drugs), NACO guidelines highlight the critical need to adopt and implement a case-based approach, wherein each case is assessed for PrEP suitability based on a risk-scoring system to maximize implementation and the cost-effectiveness of the PrEP programme<sup>12</sup>.

Currently, PrEP uptake in India is estimated to be low at slightly over seven thousand people who initiated PrEP since 2017<sup>7</sup>. Published data and data from the publicly available domains suggest the low overall awareness of HIV PrEP in India and limited access to PrEP available mainly from private healthcare providers and selected non-government organizations (NGO) driven by end-user factors such as education status and ability to purchase medications<sup>14,15</sup>. While overall awareness of PrEP in subpopulations in survey studies to date remains relatively low, once informed about PrEP, most respondents expressed interest in and desire to take PrEP<sup>14,16</sup>. In addition to the growing use of PrEP outside of clinical trials around the globe, demonstration projects such as the one in Female Sex Workers in Kolkata, India, show the successful integration of PrEP into an existing community-based HIV prevention programme<sup>17</sup>. The government-supported national transformative programme 'Digital India' presents a unique opportunity to understand virtual sexual networks and create an HIV prevention platform that includes PrEP education and awareness while continuing the traditional and critical field-based approaches for HIV prevention by government and NGOs<sup>18,19</sup>.

Most of data on HIV risk assessment, awareness, eligibility and access to PrEP in India have been reported in adults, highlighting a striking paucity of information for adolescents under 18 yr of age<sup>20</sup>. As reported by the NACO HIV India Estimates 2023, adolescents under 15 yr of age are grouped under the category of children, and those 15 and older are grouped either in the 15+ adult categories or the 15 to 24 yr young people category<sup>21</sup>. While the 'young people' category is an important category to not let this vulnerable age

group get lost in adult data and addressed with adult-centric intervention approaches, understanding gaps in data and HIV risk and prevention including awareness and access to PrEP in minors is needed. Identification of the adolescent category for the persons aged 10 to 18 yr within the national HIV databases will allow to effectively address the existing data gaps and inform the development of the anticipatory guidance and best practices for PrEP among this vulnerable population.

Today, many parts of the world are moving into the era of PrEP practice where people can get to choose for HIV PrEP the best fit for their needs. In India, the majority of those who could benefit from PrEP, however, remain unaware of PrEP and/or cannot access or afford already available oral PrEP medications. In a country with a well-established track record of successful national programmes for the prevention of vertical transmission of HIV (since 2002) and free access to treatment for those living with HIV (since 2004), what will it take to provide facilitated access to cost-effective HIV PrEP to key populations most at risk?

A powerful tool in preventing HIV infection, PrEP has not yet reached its full potential in most regions of the world including India and the United States. While there is a growing use of PrEP in the United States paid for by insurers, a national PrEP programme does not exist, and gaps in PrEP awareness and access remain. Implementation research, strong public education, and awareness campaigns are needed to improve access to PrEP for the populations in need. The success of PrEP programmes will be measured not only by the number of people who are at risk for HIV initiating and retaining PrEP but also by the overall impact on the HIV epidemic<sup>3</sup>. With new and exciting options for long-acting injectable PrEP, the uptake and sustainability of PrEP adherence have been projected to improve and lead to reduced AIDS death and HIV incidence. Greater investment in and prioritization of PrEP in India is needed and will potentially accelerate the Nation's path to HIV elimination.

**Financial support & sponsorship:** None.

**Conflicts of Interest:** None.

**Use of Artificial Intelligence (AI)-Assisted Technology for manuscript preparation:** The authors confirm that there was no use of AI-assisted technology for assisting in the writing of the manuscript and no images were manipulated using AI.

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Received December 16, 2024; Accepted December 18, 2024;  
Ahead of print January 7, 2025; Published January 22, 2025

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