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From START to finish: implications of the START study

How best to use antiretroviral therapy (ART) has been a topic of debate for almost three decades. The landmark START trial[1] settled one question that should have been resolved long ago—when to initiate ART in people with HIV. Findings of START showed a 57% reduction in AIDS, severe non-AIDS events, or deaths in people with a CD4 count higher than 500 cells/μL who were randomly assigned to immediate versus deferred treatment.[2] This finding supports conclusions from observational studies and the recently completed west African TEMPRANO trial[3] (which also favoured early treatment), and has profound implications for public health.

START should also be regarded in the context of the HPTN 052 trial,[4] which showed a 96% reduction in HIV transmission in serodiscordant couples when the HIV-infected partner was taking ART. HPTN 052 complemented findings from modelling exercises[5] and ecological studies that noted a decrease in new HIV infections in association with treatment scale-up at the population level.[6] Synthesising these findings, early treatment of HIV is beneficial for individual as well as population health, ART is the most potent HIV prevention intervention,[7] and universal access to ART is absolutely central to the global HIV response.

Despite success in ART scale-up, HIV-related stigma and discrimination remain high. For a long time HIV/AIDS was dealt with differently from other infectious diseases, which protected the vulnerable, but might have constrained prevention and therapeutic benefit, especially early on in the epidemic.[8] With findings showing HIV prevention benefit from treatment, the pendulum has swung back to more traditional ideas about infectious disease control. Ways need to be found to enhance the protection and rights of people with or at risk of HIV while achieving as close to universal uptake of diagnosis and treatment as possible.

HIV testing needs to be expanded in clinical and community settings, and contact tracing and active case finding should be promoted. Immediate, active linkage to treatment could lessen loss to follow up that characterises delays in ART initiation based on a CD4 cell count threshold. Tuberculosis programmes offer relevant experience with emphasis on diagnosis, immediate treatment and adherence, cohort analysis, contact investigation, and standardised reporting with monitoring of response to treatment. A comprehensive approach is needed that accounts for all individuals identified with HIV and follows them up through the care continuum to its ultimate goal of viral suppression.[9] And even as the test-and-treat approach becomes the face of the HIV response, other modalities of combination prevention, especially voluntary medical male circumcision, condom use, and harm reduction interventions should not be neglected.

Challenges to expansion of treatment include stigma, fear, denial, reticence to disclose, and difficulty accessing HIV services, especially for men, young people, and key populations. Focus on numbers has detracted from attention to quality of services throughout the continuum of care.[9] Retention has been constrained by distance from clinical settings, shortage of health workers, unfriendly or judgmental services, stock outs of commodities, and inability to track patients in the community. Even in generalised epidemics, attention is required to the special needs of hard-to-reach populations such as men who have sex with men, sex workers, people who use drugs, migrant workers, east African fisher folk, and young people.

Acting on START and HPTN 052, WHO has recommended immediate treatment for all people with HIV,[10] requiring that almost 22 million additional people access ART now, not considering continued HIV

incidence.[11] The UNAIDS-Lancet Commission estimated that HIV/AIDS funding will need to increase from the current $19 billion annually to $36 billion per year.[12] Failure to contain the HIV epidemic now will result in an eventually unmanageable global disease burden; the challenge is to pay now or pay a lot more later.

With the issue of when to start treatment resolved, how best to use pre-exposure antiretroviral prophylaxis (PrEP) and in what formulation rises in importance as an operational question, especially for young African women. WHO recommended PrEP as an additional intervention for groups with an annual HIV incidence of 3% or greater.[10] Experience with preventive treatment in other infectious diseases such as malaria and tuberculosis has been mixed, but PrEP offers potent protection against HIV if adhered to. Science drives formulation of guidelines, yet the benefit of guidelines depends on social and political will to implement them.

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Camels, MERS-CoV, and other emerging infections in east Africa

Although human Middle-East respiratory syndrome coronavirus (MERS-CoV) infection seems to be associated with exposure to animals, including camels, identification of the animal reservoir remains challenging.[1-3] We believe that this gap results from the fact that surveillance systems for diseases in both human beings and animals remain fragmented and fail to take into account the social and ecological contexts within which diseases emerge. Additionally, there is a paucity of data for emerging infectious diseases in animals, especially camels in east Africa. For example, most MERS-CoV cases have been identified in the Arabian Peninsula, in places with robust health care, veterinary care, and disease surveillance. Although preliminary data link some cases of human MERS-CoV to exposure to dromedary camels or their products,[1,2] reliable health records of both human beings and animals cannot confirm a causal relationship. At the same time, many of the camels in the Arabian Peninsula derive from herds in east Africa, where both human and animal health systems, including surveillance, remain inadequate.

To understand the potential reservoirs and prevalence of MERS-CoV, and in the absence of surveillance and clinical data in east Africa, some researchers have tapped into banked animal and human biological specimen repositories as a proxy for baseline data.[3] Findings of retrospective serosurveys done between 1983 to 1997 in east Africa showed that most (up to 81%) camels were exposed or infected as early as 1980.[3] However, these findings do not consider exposure to other viruses or the potential sources of exposure. Indeed, although not recognised until now, MERS-CoV infection seems likely among east African camels, but the lack of surveillance delays its detection.

Further, in human and camel populations, MERS-CoV infections might be masked by other common co-