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Letter to the editor

Interrupting antiretroviral therapy in HIV cure trials during COVID-19: Adaptation to low transmission settings

To the editor

We read with great interest the viewpoint by Fidler et al.[1] published recently in The Journal of Virus Eradication. The Australian experience regarding COVID-19 is unique, considering the relatively small number of infections compared to many other countries. At the time of writing, 28,786 people have been diagnosed with COVID-19, with 909 deaths, out of a population of just over 25.5 million.[2] New infections peaked at 460 a day on March 28, 2020 in the first wave, and at 746 on the 20th July in our second wave, which was predominantly experienced in the state of Victoria, Australia's second most populous state. The city of Melbourne was placed in one of the longest and strictest lockdowns in the world in early August, which lasted 111 days, and restricted all non-essential movement and business. During this time, other states in Australia had closed borders, but with few new infections, activities continued almost as normal.

This led the Australian public health authorities to define areas of community transmission as "hotspots", which are then subjected to increased testing coupled with movement restrictions.[3] At the time of writing, Australia has essentially eliminated community transmission of SARS-CoV-2; international borders are tightly controlled and remain closed to non-essential international travel. Australia has experienced further short-lived outbreaks involving community transmission but there are currently no "hotspots" in Australia and the few infections that are diagnosed daily are in returned travellers in quarantine. A national vaccination program is scheduled to being in late February 2021. Clinical and research activities are now returning to pre-pandemic levels, and there is a critical need for trial management plans that are specific to settings with low or negligible SARS-CoV-2 transmission.

Based on work published recently by Peluso[4] and Fidler et al.,[1] a working group was convened comprising clinician researchers and representatives from community HIV advocacy organisations, in order to develop a COVID-19 risk mitigation plan for HIV cure clinical trials in low COVID-19 settings. Analytical treatment interruptions (ATI) of antiretroviral regimens are essential to understand if investigational interventions are able to control viral replication in the absence of antiretroviral therapy. In addition, the need for regular study visits during ATI for viral load monitoring and the risk, albeit extremely low, of contracting COVID-19 concurrently with HIV rebound viremia and potentially $CD4^+$ T cell decline, warrant careful consideration.

There was universal agreement amongst our convened working group that HIV cure research continues. This is also consistent with findings from an online survey of people living with HIV in the state of Victoria that found 91% of respondents were still willing or more willing than pre-pandemic to participate in research during the pandemic.[5]

Similar to Fidler et al., our plan introduces additional consent details, extra exclusion criteria, strategies to minimise study visits in the hospital setting, routine asymptomatic testing, and an active COVID-19 infection response plan. Vaccination strategies could also be included into study protocols as vaccines become available. Our plan will only be implemented at an established threshold determined to represent increased risk of community SARS-CoV-2 transmission. In the Australian context this was defined as more than 10 new cases of locally acquired infection in the preceding 3 days within the metropolitan region where the trial is conducted.

Research towards an HIV cure must continue during the COVID-19 pandemic but planning to mitigate the risk of SARS-CoV-2 transmission is critical. These plans can be tailored to each setting according to each level of transmission.

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Declaration of competing interest

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