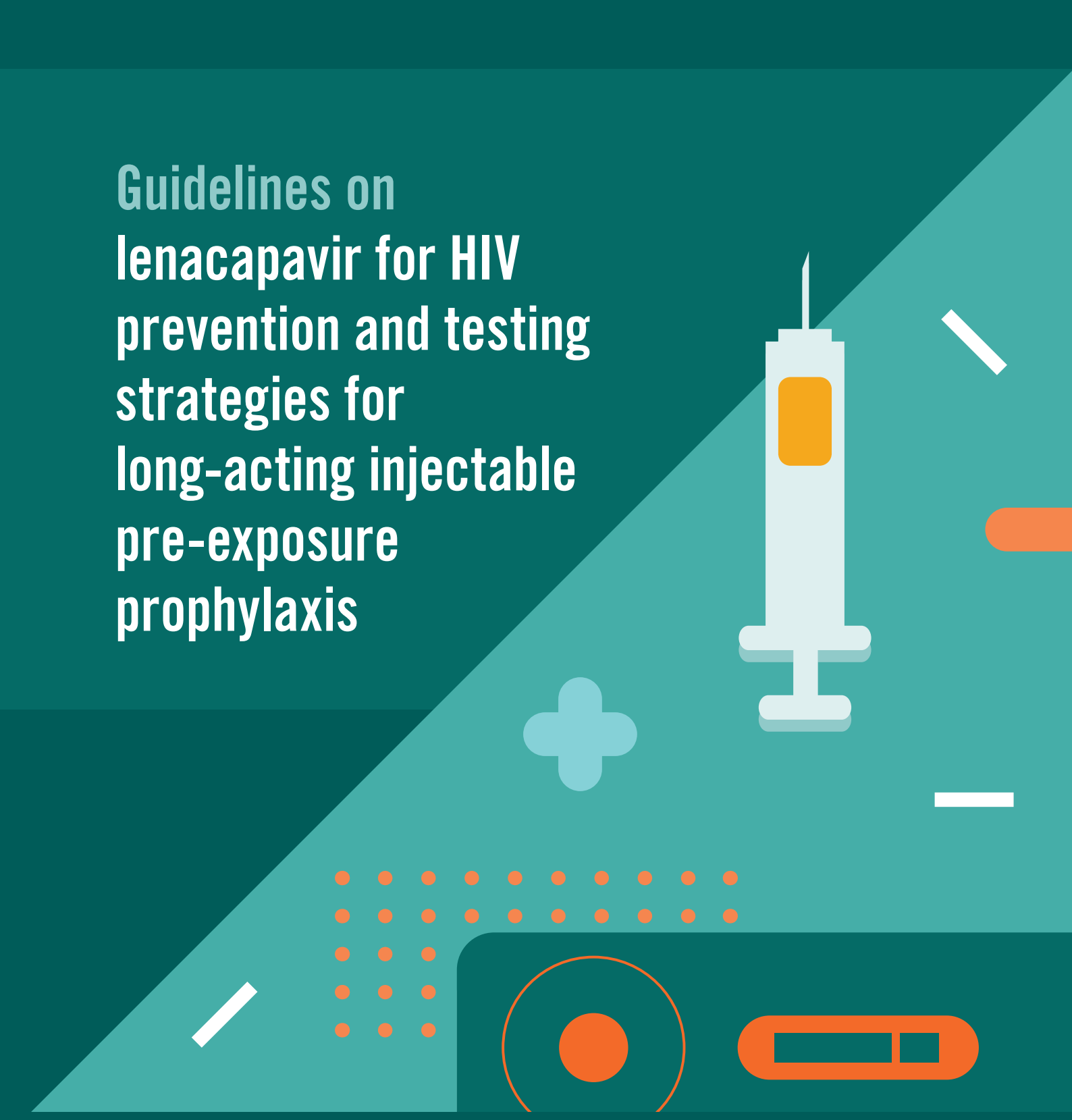
Guidelines on lenacapavir for HIV prevention and testing strategies for long-acting injectable pre-exposure prophylaxis



Web Annex E. Mathematical modelling of lenacapavir: landscaping review on impact and cost–effectiveness

World Health Organization

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Mathematical modelling of lenacapavir: landscaping review on impact and cost–effectiveness

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Abstract

Introduction. The twice-yearly injectable lenacapavir (LEN) is a promising intervention for HIV prevention, but the potential impact on HIV incidence and cost–effectiveness in different populations is unknown. Importantly, the cost of providing LEN in low- and middle-income countries is currently unknown. Mathematical modelling is a valuable tool for helping to estimate these outcomes. In this commentary we discuss the current state of evidence of modelling of LEN for prevention and we address research gaps.

Discussion. We conducted a landscaping review of published and unpublished modelling work on LEN for HIV prevention in support of the development of World Health Organization guidelines on lenacapavir for long-acting prevention of HIV. As of March 2025, four published HIV transmission models including LEN for prevention were identified in three settings in sub-Saharan Africa (South Africa, western Kenya and Zimbabwe). When used with high uptake, the models show that LEN could avert up to 41% of new HIV infections in all three settings, depending on time horizon and population coverage.

The studies found that LEN could be cost–effective at costs up to US$ 225 per person per year (PPPY) in South Africa, US$ 33 PPPY in western Kenya and US$ 42 PPPY in Zimbabwe. One study also found that long-acting PrEP such as LEN for female sex workers would be the most cost–effective PrEP implementation strategy in Zimbabwe. Cost–effectiveness was consistently higher across all four models if LEN coverage was targeted to those at highest risk of acquiring HIV, but such a strategy also limited overall impact. In some models LEN had higher impact than other PrEP methods due not only to higher efficacy, but also because of assumptions of increased uptake and persistence of use. Future research should address questions of impact and cost–effectiveness in other populations (for example, in concentrated epidemics), in settings other than sub-Saharan Africa and aligned with realistic programmatic implementation.

Conclusions. Models show that LEN could have a substantial impact in reducing HIV incidence across multiple settings in sub-Saharan Africa. However, to achieve cost–effectiveness, its cost PPPY must be relatively inexpensive, and uptake by key populations must be prioritized.

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