PREP WILL WORK

A. The pharmacology of PREP makes sense

1. The concept of once-daily dosing using drugs with long half-lives that act prior to integration has considerable merit.
2. This being said, we should perhaps not rule out the use in PREP of well-tolerated PIs that have a high genetic barrier re resistance. Who really knows whether the success of post-exposure prophylaxis is not really due to PREP?

B. The issue of drug resistance should not be exaggerated:

1. Relatively few potential transmitters are likely to harbour drug-resistant viruses. A more realistic concern is the selection of resistance in recipients of PREP who may not realize that they are actually HIV-positive. However, the use of two drugs in combination will guard against the selection of resistant variants.

2. Levels of virus that are commonly involved in transmission are far below those found in blood at peak viremia. Drugs used in PREP may still work even if they would not be active in therapy.
3. Viruses containing mutations associated with TDF/FTC are not as fit and may also not be as easily transmitted as wild-type viruses or viruses containing NNRTI mutations or TAMs
4. The advent of new drug classes such as CCR5 inhibitors and integrase inhibitors provides additional support for the concept of PREP.
5. Animal data support the use of TDF in PREP. Even though infections did occur, relative protection was achieved in high proportions of cases under conditions in which viral challenge involved extremely high doses of viruses and routes of transmission that are far more likely to establish infection than heterosexual intercourse.
6. Both TDF and 3TC/FTC retain reduced levels of direct antiviral activity despite the presence of relevant mutations, e.g K65R, M184V. This level of ARV activity may suffice to protect against viruses containing the aforesaid mutations.