nature portfolio

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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☒	☐ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☒	☐ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐ A description of all covariates tested
☐	☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☒	☐ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☐	☒ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	No software was used
Data analysis	R version 4.1 was used for analysis. Package adaptMCMC version 1.4 used for Markov Chain Monte Carlo

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The data underlying the results presented in the study are available from SCHARP data management center, HPTN-data-access@scharp.org

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	All data is from cisgender women
Reporting on race, ethnicity, or other socially relevant groupings	Calibration of efficacy curves did not use race and ethnicity information. Self-identification of African American was used to adjust TFV-DP ranges associated with 2, 4 and 7 pills per week, however that analysis was performed in a prior study which we cite.
Population characteristics	All subjects were cisgender women in sub-Saharan Africa, full information on their characteristics is given in the primary manuscripts for HPTN 082, VOICE, FEMPrEP and Partners PrEP.
Recruitment	Subjects were recruited to all studies based on factors associated elevated rates of HIV acquisition. Individuals in Partners PrEP had a primary partner known to be living with HIV. Individuals in HPTN 082 were recruited based on a VOICE risk score of five or more. This information is available in the primary manuscripts for all studies.
Ethics oversight	The study was reviewed and approved by the HIV Prevention Trials Network (HPTN).

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	There were no sample size calculations in this study
Data exclusions	There was no data excluded from this study
Replication	The study described is computational. The code has been preserved so that it is fully reproducible. It is no longer ethical to conduct placebo controlled, randomized PrEP efficacy trials so these studies cannot be repeated in the same manner.
Randomization	In the underlying studies FEM-PrEP, Partners PrEP, and VOICE, participants were randomized to either receive oral TDF/FTC or placebo. In HPTN 082, all participants received TDF/FTC.
Blinding	All studies were blinded during follow-up and analysis.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	VOICE: NCT00705679; FEMPrEP:NCT00625404; Partners PrEP: NCT00557245; HPTN 082: NCT02732730
Study protocol	VOICE: 10.1056/NEJMoa1402269; FEMPrEP: 10.1056/NEJMoa1202614; Partners PrEP: 10.1056/NEJMoa1108524; HPTN 082: doi.org/10.1371/journal.pmed.1003670
Data collection	VOICE: South Africa, Uganda, Zimbabwe 2009-2012; FEMPrEP: Kenya, South Africa, Tanzania 2009-2012; Partners PrEP: Kenya, Uganda 2008-2010; HPTN 082: South Africa, Zimbabwe 2016-2018
Outcomes	VOICE, FEMPrEP and Partners PrEP had HIV acquisition (as measured by seroconversion) as the primary outcome. They also collected data on adherence as plasma tenofovir quantifiability as a secondary outcome. The threshold of quantifiability in each study was slightly different as described in the manuscript. VOICE required >0.3 ng/ml at any follow-up visit, Partners PrEP >0.3 ng.ml at the time of seroconversion, and FEMPrEP >10ng/ml at time of seroconversion. In HPTN 082, TFV-DP concentration in DBS throughout followup was the primary endpoint and TFV concentration in plasma was the secondary endpoint.