Intensified research into the experiences of sexually-active MSM, how HIV risk is perceived, and the reasons for taking such risks would usefully complement analyses of incidence for informing effective public health strategies. The findings of Le Vu and colleagues call for well-funded, creative, and thoughtful approaches to improve the sexual health of MSM so that the devastation of HIV can be remedied.

We declare no conflicts of interest.

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Quantification of the role of discordant couples in driving incidence of HIV in sub-Saharan Africa

Data presented in the meta-analysis by Oghenowede Eyawo and colleagues3 sheds new light on the role of serodiscordant couples in driving the incidence of HIV in Africa. The HIV epidemic in Africa is driven by heterosexual transmission. Studies have shown transmission in stable discordant couples can be as low as 1-9 per 100 person-years to as high as 19-0 per 100 person-years; these couples are typically in stable relationships lasting at least a year. However, the extent to which they drive country-level incidence in sub-Saharan Africa is unknown. We use a mathematical model, parameterised with data from Eyawo and colleagues3 to quantify the role of stable discordant couples in driving country-level incidence in 14 countries: Burkina Faso, Cameroon, Côte d’Ivoire, Ethiopia, Ghana, Guinea, Kenya, Lesotho, Malawi, Niger, Rwanda, Senegal, Tanzania, and Zimbabwe. HIV prevalence in these countries ranges from 1% (Niger, Senegal) to 24% (Lesotho).3

Eyawo and colleagues’ data1 show that most couples in stable relationships in the 14 countries are concordant (ie, either both HIV-positive or both HIV-negative). Few couples are discordant, ranging from 1% (Senegal) to 14% (Lesotho). Our model shows that the role of stable discordant couples in driving incidence of HIV will be sensitive to the fraction of the population in stable relationships (webappendix). To assess the magnitude of this effect, we did a sensitivity analysis for each country by varying the fraction from 0 to 0·9 (figure).

Our results show stable discordant couples can be important in driving country-level incidence in sub-Saharan Africa. We find the higher the percentage of the population in stable relationships (regardless of whether they are in discordant or concordant couples), the more discordant couples drive incidence. Notably, their role in driving incidence is country-specific. For example, if 40% of the population in Ghana is in stable relationships, stable discordant couples could account for 34% of the country-level incidence. However, if the same percentage in Rwanda is in stable relationships, they could only account for 18% of the country-level incidence. Results from a previous study suggest transmission in stable discordant couples could account for about 50% of the country-level incidence.4 Our results show that such transmission is possible, but is more likely in some countries than in others; for example, it seems possible in Kenya but unlikely in Guinea (figure).

We agree that public health programmes aimed at preventing HIV infection in stable discordant couples could be very useful in reducing transmission. However, determination of the degree to which these couples drive incidence of HIV in specific countries is crucial, because this will determine the necessity and intensity of other interventions.
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Mouse viruses and human disease

Recent evidence claims to show that the link between xenotropic murine leukemia virus-related virus (XMRV) and chronic fatigue syndrome (CFS) and prostate cancer is probably a result of laboratory contamination.

A part of the research has focused on proving that the molecular approach (PCR) is sensitive but not specific, predisposing it to possible contamination. Another part of the research has shown that the virus is common even in human cell-lines and since it can be amplified easily, the possibility of contamination is high. Finally, the most interesting piece of evidence is the molecular evolution of the samples isolated from patients, cell-lines, and mice proving that XMRV has not been circulating between human beings.

Nevertheless, the paper by Lombardi and colleagues that began this debate provided solid evidence based not only on the molecular identification of the virus, but also on immunological responses of the host (virus-specific antibodies), viral expression in patients’ peripheral blood mononuclear cells (flow cytometry), and an infection model (infection of cultured human cells from patients’ samples). Recently, a model of rhesus macaques enforced the evidence for the infectious potential of XMRV. The immunological and infection evidence cannot be explained by nucleic acid contaminations. Thus, the only explanation for the molecular evolution data, from a study by Hue and colleagues, is that the patients have been infected by a common source of XMRV and not through human contact.

Once a virus is endogenised, it is forced to follow the evolutionary rate of the host. Since XMRV is integrated in cell-lines, the virus evolution is restricted to the host’s pace of evolution, and viral descendants have none or minimum sequence diversity. Thus, if a contaminated product, previously cultured in cell-lines, is administered to people then the infections would provide the evolutionary patterns reported by Hue and colleagues. If the immunological data reported by Lombardi and colleagues are correct, then we need to trace the common source for these infections to prevent possible public health concerns. Products from cell-lines should be the first candidates.

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Simard and colleagues reported the most current and largest comprehensive assessment of cancer incidence in people with HIV on antiretroviral therapy. Whereas the incidence of AIDS-defining cancers, Hodgkin’s lymphoma, and many other non-AIDS-defining cancers was increased, a striking finding of this report was the nearly 50% reduction in the incidence of breast and prostate cancer. This paradoxical reduction in breast-cancer risk has been reported in the context of immune suppression. Researchers from several laboratories have identified DNA sequences highly homologous to the mouse mammary tumour virus (MMTV; a betaretrovirus of mice) in about 40% of human breast cancer specimens. Others have identified sequences related to the xenotropic murine leukemia virus -related virus (XMRV; a gammaretrovirus of mice) in human prostate cancer. In both malignancies, a retrovirus from mice has been associated, albeit association itself is not evidence for causality. Furthermore, not all laboratories have replicated these associations, and a retroviral cause in breast and prostate cancer remains controversial. Arguments that mouse sequences detected in human samples are proof of contamination can be equally interpreted as evidence for zoonosis—the transmission of mouse viruses to human beings—as we have suggested.

Antiretroviral drug treatment (ART) might inhibit retroviruses other than HIV. Should ART have an effect on putative oncoviral cancers of long clinical latency or late onset (such as breast and prostate cancer), because HIV is generally acquired during the
Supplementary webappendix

This webappendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Appendix

We use a mathematical model to quantify the role of stable discordant couples in driving incidence in Burkina Faso, Cameroon, Ethiopia, Ghana, Guinea, Côte d’Ivoire, Kenya, Lesotho, Malawi, Niger, Rwanda, Senegal, Tanzania, and Zimbabwe. We use data, provided by Ewayo et al.\(^1\), that identifies the proportion of stable relationships (i.e., sexual relationships that last a year or more) that are concordant positive and the proportion that are discordant; we denote these by \( \gamma_+ \) and \( \gamma_d \), respectively. These data are used to determine the HIV prevalence in stable relationships \( (a_c) \), where

\[
a_c = \frac{\gamma_+ + \gamma_d}{2}.
\]

To estimate the prevalence of HIV in couples with short-term sexual relationships \( (a_n) \), we use data\(^2\) on country-level prevalence \( (A) \) and the equation:

\[
A = qa_c + (1 - q)a_n,
\]

where \( q \) represents the proportion of the population that is in stable relationships. The proportion of country-level incidence due to transmission in SDCs \( (\Omega) \) can then be represented as a function of \( q \) by the following equation:

\[
\Omega(q) = \frac{q\gamma_d \phi_c / 2}{q\gamma_d \phi_c / 2 + (1 - q)(1 - a_n)\phi_n},
\]

where \( \phi_c \) and \( \phi_n \) represent the annual probability that an uninfected individual acquires HIV when in a SDC \( (\phi_c) \) or when in a short-term sexual relationship \( \phi_n \). We calculate \( \phi_c \) using the relationship \( \phi_c = 1 - (1 - \alpha)^N \), where \( \alpha \) represents the per act transmission probability and \( N \) is the annual number of sex acts. We estimate \( \phi_c = 0.10 \), assuming \( \alpha = 0.001 \) and \( N = 104 \). We estimate \( \phi_n \) using the same parameter values and a similar equation:

\[
\phi_n = 1 - (1 - \alpha)^{a_nN}.
\]

However, in this case we multiply the annual number of sex acts by the prevalence of HIV in couples with short-term sexual relationships to calculate the number of sex acts with an HIV-positive partner.
The value of $q$ is unknown for any sub-Saharan country. Therefore, we calculated the proportion of country-level incidence due to transmission in stable discordant couples ($\Omega$) by varying $q$ (i.e., the proportion of the population that is in stable relationships) over the range 0 to 0.9 (Figure in text).

References
