Quality of life has been proposed as the fourth 90 to complement the UNAIDS 90-90-90 targets to monitor the global HIV response, highlighting a need to address the holistic needs of people living with HIV beyond viral suppression. This proposal has instigated a wider discussion about the use of patient-reported outcomes (PROs) to improve the treatment and care of an ageing HIV population with increasing comorbidities and a disproportionate burden of social problems. PROs can provide a first-hand assessment of the impact of HIV treatment and care on patients’ quality of life, including symptoms. The field of PRO measures is rapidly expanding but still no gold standard exists, raising concerns about tool selection. Challenges also remain in the collection, interpretation, and use of PRO data to improve the performance of the health system. An emerging concern is how to adapt PROs to different sociocultural and geographical settings.

Introduction
Global progress is being made towards achieving the UNAIDS 90-90-90 HIV targets: 90% of people with HIV diagnosed, 90% of those diagnosed on treatment, and 90% of those on treatment virally suppressed. As the HIV sector reviews the challenges and future priorities for optimal management of HIV, focus is slowly shifting away from a predominantly biomedical approach and the idea that viral suppression is the ultimate goal of HIV care. The concept of a fourth 90 has emerged, in which good health-related quality of life (HRQoL) is held to be of equal importance to the other 90-90-90 targets that health systems should aspire to achieve. This shift requires a holistic approach that addresses overall health, and the social and psychological aspects of HIV that can lead to poor health outcomes.

Person-centred health care is central to achieving this goal: delivering services that patients need, can access, and which address the wider determinants of poor health. To ensure that people living with HIV enjoy healthy ageing with sustained viral suppression, clinicians and health systems must respond to the lifelong needs of people living with HIV, from diagnosis until the end of life.

How can one know what patients need, unless we ask? Involvement of patients in designing health-care services has been shown to improve engagement and retention in care, increase resilience, and empower people to take a more active role in the management of their condition. Since the start of the HIV epidemic, the advocacy of the HIV community has been integral to how HIV prevention and treatment services have been designed. The prolonged life expectancy and the consequent rise of ageing HIV groups with unmet needs require a substantial change in how health systems provide care for HIV and age-related conditions.

One of the most efficient ways to ensure that care reflects patients’ needs and priorities is by collecting and using patient-reported outcome (PRO) data. Involving people with HIV in PRO development and adaptation can help to better identify HIV or treatment-related symptoms and detect stigmatising attitudes from the health system, which are among the main barriers to engagement in HIV care.

What are PROs?
A PRO can be defined as any report of the status of a patient’s health condition that comes directly from the patient, without interpretation by a clinician or anyone else. PROs capture a person’s experience as a patient in the healthcare system, which is central to achieving the fourth 90.

Key messages
- Patient-reported outcomes (PROs) provide vital information about a patient’s first-hand account of their experiences that cannot be directly measured and provide a more holistic view of their health and wellbeing.
- PROs can be used to instigate and support interventions at all levels (ie, clinical, institutional, and population) to ensure optimal HIV care and prevent ill health.
- Recent technological advances have made PROs more accessible to patients and investigators, streamlining data collection and analysis (ie, with electronic PROs and linkage to medical records).
- Further research is needed to show the utility of PROs in the field of HIV, making a clear link between improvements in PROs to improvements in health and clinical care.
- New PROs need to be developed and existing PROs cross-culturally adapted to populations with special attention to children and adolescents, the elderly, and settings in which key populations are highly stigmatised or criminalised.
- Patient involvement in the development of PROs is vital to ensure their usability and acceptability in the population of interest.
Use of PROs to improve HIV care quality and patients’ outcomes

People living with HIV report symptoms such as depression, anxiety, and pain more commonly than the general population, which can lead to worse clinical and PROs, such as poor adherence to treatment, poorer quality of life, mental health problems, sexual risk-taking, and viral rebound. PRO data can be used in a multitude of ways to improve care and patients’ outcomes at the patient, institution, and population levels.

On an individual level, there is good evidence that the routine use of PROs such as quality of life and self-reported symptoms can improve clinical decision making, symptom recognition, patient–clinician communication, and help clinicians identify and address problems related to quality of life. The desire to improve PROs can drive choices in clinical care—for example, when reduced symptom burden is the primary reason for a joint patient–provider decision to switch HIV treatment. Research shows that patients’ experience with antiretroviral therapy (ART) is more accurately captured using PROs than by clinician documented side-effects alone, and that patient-reported symptoms more accurately predict clinical outcomes such as hospitalisation and mortality compared to provider-reported symptoms. PROs can be employed during routine clinical assessments as screening tools to help focus the consultation on current needs, to trigger specific clinical assessments for early detection of clinical conditions, and as the basis for follow-up to improve resource allocation and efficiency.

In clinical research trials, the 2013 Consolidated Standards of Reporting Trials PRO extension recommends promoting PROs to primary or secondary trial endpoints, particularly when interventions show similar clinical efficacy, and provides detailed guidance on the reporting of PROs to inform care of patients. This recommendation is not limited to pharmacological trials—for example, a randomised controlled trial from Kenya used HRQoL as the primary endpoint of a palliative care intervention for people living with HIV.

When used at the institutional level, PROs enable comparisons of providers’ performances to stimulate improvements in service. For example, in England’s National Health Service, quality dashboards monitor the quality of care for specialist services. Dashboards are produced at the institutional level and indicators are benchmarked. HRQoL is currently an indicator on the dashboards for cancer, specialised pain management, and pulmonary hypertension. This system of indicators is used by providers and policy makers to inform decisions about quality improvement. There is also potential for such dashboards to be used by patients to help select health-care providers.

At the population level, PROs can identify health disparities between different population groups and monitor the health system response to HIV. For example, in treatment as prevention trials in sub-Saharan Africa, patient-reported symptoms have been incorporated into algorithms to determine eligibility for immediate initiation of ART.

Despite their public health and clinical relevance, PROs are not well integrated in the routine HIV data collection. A lack of clear guidance on why, when, and how to collect these data is in part to blame. Current clinical treatment guidelines and national monitoring frameworks insufficiently address the use of PROs to monitor HIV care. Neither UNAIDS nor the major global funders of surveillance activities, such as the US President’s Emergency Plan for AIDS Relief and the Global Fund to Fight AIDS, Tuberculosis, and Malaria, include PRO indicators. Further evidence is needed to conclusively show the utility of PRO data in the field of HIV, linking improvements in PROs to improvements in health and clinical care.

A brief history of PROs in HIV

PROs have been used since the start of the epidemic to gain a better understanding of HIV transmission patterns and monitor behaviours. In the years before ART, PRO data were oriented towards HIV disclosure and sexual and injection risk behaviours and targeted specific risk groups such as people who inject drugs and men who have sex with men. PRO data on risk behaviours and access to opioid substitution therapy evidenced the protective role of opioid substitution therapy against HIV transmission and contributed to the revision of national and international guidelines.

The arrival of ART in the mid-1990s transformed HIV into a chronic disease for those accessing treatment and shifted the interest in PROs from risk behaviour to monitoring clinical treatment outcomes, such as ART adherence, symptom burden, and HRQoL. These PROs also affected major changes in clinical guidance and policy. For example, research on people with HIV and opioid use disorder found that buprenorphine use was...
associated with improved self-reported adherence to ART. These findings led to the availability of buprenorphine being incorporated into HIV treatment guidelines and its subsequent entry into the WHO list of essential medicines.

During the 2000s, PROs became progressively important tools in decision-making processes for the management of HIV infection, informing therapeutic choices in the presence of ART with similar efficacy. Access to ART alone does not fully address quality of life–HIV. The ageing of people living with HIV sheds light on new issues of interest for how HIV affects the ageing process, such as cognitive problems, memory loss, weight control, bone and joint problems, and sleep disorders.

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In 2015, WHO published guidelines for the use of test-and-treat strategies to reduce the rate of new HIV infections. This policy, which has become a cornerstone of the UNAIDS 90-90-90 HIV targets, brought to light...
hrqol is a particularly versatile pro with several validated generic and hiv-specific adaptations. multidimensional hrqol measures can be helpful by giving a global score for the overall health and wellbeing, provided that the scales have good psychometric properties (in line with current guidance, such as cosmin guidance for health outcome measure generation and validation, and the rothrock protocol for item generation). results should also be easily interpretable and allow comparisons within or between hiv populations. the challenge is to use hrqol scales that are not overly complex but sensitive enough to capture patients’ experience with hiv and treatments. generic hrqol tools should be pre-validated in hiv populations, and hiv-specific hrqol tools should be complemented by an assessment of the specific physical and mental symptom burden for a comprehensive quality-of-life assessment.

selecting the right pro: considerations and principles of use

the choice of the right prom must be guided by the nature and objectives of the study. users should consider factors such as setting, population, and resources to guide decisions on sampling method, questionnaire length, interview format, use of incentives, and whether to use generic or hiv-specific proms (table 2). for example, when measuring adherence to assist hiv care providers with treatment choices, the use of a short, simple measure of adherence is sufficient, whereas a more complex and comprehensive measure might be needed when investigating dimensions associated with non-adherence or the impact of an intervention to improve adherence.

to retain the psychometric properties of a validated pro, it must be used in the exact format with identical wording, ordering, and, where applicable, scored per the instructions. it is good practice to pre-test the questionnaire using cognitive interviews with a few patients from the population of interest prior to use.

wherever possible, it is important to ensure that the pro of interest has a documented or plausible association with the hiv clinical or health outcome of interest, to inform effective interventions for the proximal and distal determinants—for example, the causal pathway from depression to poor adherence to poor immunological status and hiv-related morbidity. we have summarised some popular topics in hiv research alongside the pros associated with the interconnected topic that a researcher should consider measuring (table 3).

where the aim is to understand inequalities in the area of health and social needs of people living with hiv, selection of generic scales allows comparisons with the general population or other populations to compare quality of life. additionally, hiv-specific proms address the issues of hiv-specific symptoms and problems such as art side-effects and stigma.

<table>
<thead>
<tr>
<th>Considerations</th>
<th>Population-level prevalence or surveillance</th>
<th>Cohort research (including nested interventions)</th>
<th>Clinical use (patient level)</th>
<th>Clinical trial research</th>
<th>Multicountry monitoring</th>
</tr>
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<tbody>
<tr>
<td>Ability to compare with general population surveys, use of probability sampling to ensure representativeness, and extra resources, long-term investment, or incentives that might be required due to population size and frequency of collection</td>
<td>Causal pathway to clinical outcomes and other measures and focused research question</td>
<td>Measurement of symptoms and side-effects, short-forms that can be easily collected and scored, and developmental age for child respondents</td>
<td>Cost-effectiveness studies to derive utility (qaly, dalys) and measures responsive over a relatively short period of time, given the limited duration of hiv clinical trials</td>
<td>Brief, multidimensional tools that can be easily collected in routine monitoring and cross-cultural validation and adaptation</td>
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considerations include sampling, length, mode, format, generic versus hiv-specific outcome measures. qaly=quality-adjusted life-year. dalys=disability-adjusted life-year.
A further consideration is specific issues facing the population of interest. Most PROs have been developed in adult populations. Tools to measure HRQoL and other PROs in children and adolescents are less frequently reported; however, few generic and HIV-specific tools exist that address the specific needs and experiences of young people with HIV. Youth adaptations of adult-validated instruments generally aim to shorten and simplify language while retaining psychometric properties.62-64 Recent efforts to develop measures of health-related quality of life in young people with HIV tend to include stigma or HIV disclosure due to their relationship with health outcomes.65,66

Older people with HIV also have specific considerations for PRO development and selection. For example, those diagnosed in the 1980s and 1990s are likely to have experienced traumatic loss of partners, friends, family, and community members to HIV, bringing an added layer of complexity to the measurement of PROs, such as social support, mental health, and feelings of loneliness and isolation as people age.

This population is also likely to have been exposed to early, toxic HIV treatments and have experienced AIDS-defining illness giving them a unique symptom, side-effect, and treatment profile (ie, lipoatrophy, neuropathy, treatment fatigue, and ART resistance). Such states coexist with geriatric conditions, which include multimorbidity and polypharmacy, frailty, and cognitive impairment. These features indicate the need for PROMs that can capture and measure such a complex pattern of effects and needs. In summary, developing specific tools to measure PROs in children and adolescents and in the elderly living with HIV is vital for accurate measurement but remains challenging.57,67

**Methods to collect PRO data**

There are three main modes of collecting PRO data: interviewer-administered surveys, self-administered paper questionnaires, and self-administered electronic questionnaires. Interviewer-administered surveys are useful for short questionnaires in routine clinical practice. However, a high volume of patients can limit the amount and quality of data captured.68 Additionally, interviewer time is costly, so lengthy questionnaires are often limited to well-resourced studies. Interviewer-administered questionnaires are also subject to social desirability bias, wherein sensitive or potentially embarrassing questions such as sexual behaviour, drug use, or domestic violence, are systematically misreported.

When surveys are administered by clinicians, patients might not provide honest answers to avoid repercussions.69 One example comes from a study of people co-infected with HIV and hepatitis C; when patients were asked the same questions on alcohol use by their HIV clinician and their hepatologist, participants routinely under-reported their alcohol intake to their hepatologist compared to their HIV clinician.44 Conversely, patients might over-report certain problems or behaviours to induce a response or to access additional care.

Paper questionnaires are most commonly used for research and clinical practice, and have the benefit of minimal participant burden, ease and speed of administration, and flexibility in terms of mode of administration and timing of assessment. However, this approach can be costly and labour intensive, requiring data entry and a phase of data cleaning and reconciliation. The larger the survey, the more burdensome this becomes, usually resulting in a considerable time-lag to report results.

Electronic data collection of PROs, or ePROs, is increasingly popular, particularly in large-scale application of PROs. Electronic data capture decreases human resource burden, minimises errors, and enables sophisticated survey administration.69-70 ePROs can be captured using computers, tablets, or smartphones; accessed via apps, online webtools, or in kiosks located at the point of care; and adapted for single or serial use (eg, using electronic reminders for follow-up surveys or electronic diaries). Well-designed ePRO systems can also present automated, user-friendly reports that score multidimensional tools and interpret results in real-time, with options to aggregate data at an organisation or clinic level or disaggregate data for individual patient–clinician use.70 Data linkage into registries can present this data alongside laboratory results or across attendances at multiple health-care settings.

There is great potential to capitalise on recent technological advances and widespread adoption of electronic hospital records and data collection systems. Linking PROs to electronic clinical records allows clinicians to prescribe ePROs, which are sent to the patient via email or text alert.71 Free-standing electronic applications and software designed to collect ePROs are available for clinical and research use.65 Modern data-mining techniques could enable ePROs to analyse natural language data in free text with scores from a questionnaire of PROMs, to evaluate PROs both qualitatively and quantitatively.72 ePROs are acceptable and time-saving for
both people living with HIV and researchers provided that they ensure confidentiality, are not lengthy, and present results in a concise manner.6 A French pilot study (NCT03296202) is underway to pilot the integration of an ePRO system into routine HIV care.7

Despite all their promise, ePROs present challenges for integration into routine practice.6 Modifications to existing health record systems are usually costly and time-consuming. Providing patients with devices to collect data entails substantial upfront and maintenance cost. If patients are to use their own device, there is a risk of excluding patients without access to a suitable device, or the internet, introducing bias. Use of ePROs might not be appropriate in all cultures and settings, particularly where widespread mistrust in technology or the government exists, and people are concerned about how their data will be stored and used.

Finally, certain groups of patients continue to exhibit strong preferences for paper-based PRO surveys, particularly older people.7,8 In a large-scale survey of people living with HIV in the UK in 2017, when given a choice of a paper-based or web-based questionnaire, 87% of respondents chose to complete the paper questionnaire.7,9 Data collection approaches that support the use of ePROs in health care are rapidly developing, but enthusiasm for technological advances should be balanced with a need to carefully test and evaluate their use.

Strategies to minimise bias and optimise response rates

Ensuring representative and complete data is an important consideration for PROs to increase their validity and generalisability. Antiparticipation and reduction of potential source bias are essential as missing data and dropout might be associated with the PRO of interest.10

In recent years, so-called survey fatigue has been blamed for reduced survey response. Long or poorly written or constructed surveys, repetitive questions, and lack of information about the usefulness of the survey might all result in non-response or incomplete surveys.

Sensitive topics might impact on response. The criminalisation of groups such as men who have sex with men, people who inject drugs, and sex workers can complicate PRO data collection and affect validity of data. Community involvement in the survey design, use of community-based locations as a neutral environment, or anonymous online surveys might improve response rates and reliability of PRO data.11 Incentives are an effective method of improving response rates, even of low or nominal value, with unconditional incentives (given prior to survey completion) resulting in the highest response rates.12

Use of appropriate statistical methods can reduce the bias introduced by non-response and sampling error. Survey weights can be applied to make the data more representative of the population, such as sampling weights and post-stratification. However, weighting generally cannot adjust for missing or biased data on the outcome of interest. Missing data in PROs occur when patients do not answer all the questions or only fill in certain subsections, and bias occurs when those who do not respond to the survey have different PROs compared with those who do respond. When missing data directly relate to the outcome, multiple imputation, propensity score approaches, or selection models (eg, Heckman model) are needed.13 These methods (multiple imputation in particular) require careful use as each has its own limitations and conditions under which the results remain valid.14

Linear regression models are often used to analyse continuous outcomes. However, when the distribution of data is skewed, normalisation of scores or more robust modelling approaches, such as generalised linear modelling, might be needed. One example to avoid the scoring system and simply rely on the analysis of the set of data is to use item response theory or structural equations modelling.15 These approaches can manage intermittent missing data and are more powerful than classic methods for comparing PROs.

Current interest and challenges

Many opportunities and challenges in the use of PROs in HIV exist. Opportunities exist to collect PROs to more fully evaluate interventions like test-and-treat strategies, the development and scheduling of novel drugs and formulations, and the measurement and reduction of stigma. With ageing HIV populations, new and adapted PROs can provide insight into the impact of longevity on HIV infection such as the emergence of complex co-morbidities, polypharmacy, menopause, and cognitive decline. These data can help to inform interventions that ensure long-term retention in care and maintenance of good physical and emotional health.

With the high efficacy of today’s HIV drugs, PROs have become increasingly important to inform therapeutic choices between ART regimens with otherwise similar virological response.16 To fulfil the need for durable ART, current drug development efforts aim to simplify administration schedules (eg, single-tablet regimens and long-acting injectable ARTs) to maintain virological response with minimal toxicity.17 Benefit to the patient, through improvement in PROs such as adherence to treatment, quality of life, and symptoms such as nausea, fatigue, mood, and sleep quality, is often the deciding factor for the use of one ART regimen over another. Clinical non-inferiority trials have increasingly looked to tolerability and side-effect profiles to show the utility of new HIV drugs.18 PROs are likely to become the main discriminant criterion and endpoints in HIV clinical trials, as is already the case in fields such as cancer.19

A key concern for expanded use of PROs is the validity for and transferability of existing PROs for use between different geographies, cultural contexts, and risk populations. Whereas using existing PROs enables direct
Comparisons between studied populations using the same scale and saves time needed to create a new scale. However, a PRO developed in one setting or population will not necessarily work in another setting. Understanding of concepts such as depression and quality of life vary hugely across cultures, global regions, genders, ages, and socioeconomic strata.89,90

Cross-cultural differences mean that using psychometric scales in different languages is not a simple matter of translating items. We have summarised several scenarios where cross-cultural adaptation or translation of an existing PRO questionnaire might be necessary, if an adaptation does not already exist (table 4). In HIV, cultural adaptation might be necessary when using instruments in different HIV risk populations. For example, a questionnaire developed in Australia where the HIV population is predominately white men who have sex with men, might require a phase of cross-cultural adaptation for use in the UK where the HIV population comprises a great deal more migrants from sub-Saharan Africa and women.

Comprehensive cross-cultural adaptation consists of four key steps. First, one must understand the priority issues of the outcome of interest in the target population through discussion groups and careful forward–backward translation. This step is crucial when moving from a high-income setting to limited-resource settings, in which structural barriers might compete or interact with individual barriers—for example, measuring adherence in a setting where ART shortages occur. Second, one must translate and adapt the questionnaire items, and scales, to ensure constructs and items are meaningful and interpretable.

Cognitive interviewing ensures cultural equivalence of items and that interpretation is in the spirit of the item’s intended meaning. Third, revalidation must occur to ensure that the concepts measured are the same and to provide equivalent scales that allow comparisons of responses between different populations.91 Survey delivery methods and response format should also be appraised considering resources, literacy levels, and cultural norms. For example, a hand scoring system has been validated for patients with lower literacy levels in sub-Saharan Africa.92 Finally, in cultures that are less individualistic, participants might prefer to complete their PROM with another member of their family or community.

The involvement of people living with HIV in every stage of the development of PROs, from conceptualisation to publication, is crucial to build instruments that capture patients’ perspective. Furthermore, the interpretation of PRO data is immeasurably aided through post-survey group discussions of the findings to inform the next steps needed to improve PROs for the target groups. However, the extent to which this happens still varies considerably and is often limited to certain steps of the development of scales, such as item selection.93,94 Standards for the involvement of people living with HIV in PROs are needed to provide guidance and support for those working in this area. Therefore, we propose a list of recommendations for expanding the use of PROs in HIV (panel).

### Conclusions

Safeguarding and promoting the health and wellbeing of people living with HIV is much more than disbursing medications and viral load results. Measures and methods to collect and use PRO data offer new opportunities to

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**Panel: Recommendations for the use of patient-reported outcomes (PROs) in HIV research and clinical management**

- People living with HIV must be involved in every stage of PRO development and adaptation
- In an era of HIV treatment strategies and biomedical prevention interventions showing similar effectiveness, PROs should become the main discriminant criterion of treatment choice
- PROs need to be developed or cross-culturally adapted to populations with special attention to children and adolescents, the elderly, and settings where key populations are highly stigmatised or criminalised
- PROs measuring stigma can provide valuable information about the effectiveness of treatment interventions and campaigns, the extent of discrimination in health-care settings, and reasons for gaps in the HIV cascade of care
- Minimising the effect of biased and missing data in PROs can be achieved during the design stage through the choice of adequate PRO and, in the analysis stage, through selection models that control possible biases
- Novel PROs are needed in clinical practice and research, targeting people who are ageing with HIV to direct and monitor the effectiveness of comprehensive comorbidity prevention, and to inform future models of long-term HIV treatment and care

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**Table 4: Decision-making chart for cross-cultural adaptation of existing PRO instruments**

<table>
<thead>
<tr>
<th>Affects</th>
<th>Requires</th>
</tr>
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<tbody>
<tr>
<td>Culture</td>
<td>Language</td>
</tr>
<tr>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Use in same population</td>
<td></td>
</tr>
<tr>
<td>Use in new country with the same language</td>
<td>X</td>
</tr>
<tr>
<td>Use in another country with a different language</td>
<td>X</td>
</tr>
<tr>
<td>Use in new immigrants with different language but same source country</td>
<td>X</td>
</tr>
<tr>
<td>Use in a minority population with major cultural differences (eg, established ethnic minorities, LGBT populations, adolescents, and young people) in same source country</td>
<td>(as needed)</td>
</tr>
</tbody>
</table>
ensure that the patients’ voice is at the heart of health-care models worldwide. Such models need to be adapted to the changing reality, in which people living with HIV will suppress the virus and age with it and thus the patients’ perspective, captured in PROs, should have a central role in improving health-care design, monitoring, and evaluation.

Widespread use of PROs in HIV requires additional research to conclusively link improvements in PROs to improvements in health and clinical care. In addition, there is a need to better identify potential health-care provider-related barriers to the use of PROs in clinical practice and to increase providers’ training in collecting and interpreting PROs. Finally, it remains particularly challenging to use and adapt PROs across different geographies and risk populations, and fully involve people living with HIV in this work. However, doing so will help to build interventions to reduce stigma towards people living with HIV, improve their engagement in care, and identify models of care to better address unmet needs of the HIV population.

**Contributors**
MK and JVL conceived of the article. MK and PC developed the preliminary outline. MK prepared the first draft, and integrated and edited co-authors revisions. All authors contributed to specific sections of the article, reviewed the draft and subsequent revisions, and approved the final manuscript.

**Declaration of interests**
JVL reports grants from French National Agency for Research on AIDS, during the conduct of the study and grants from Merck Sharp & Dohme, outside the submitted work. PC reports research grants from French National Agency for Research on AIDS, outside the submitted work. All other authors declare no competing interests.

**References**
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