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# Correspondence

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## Strengthening universal HIV ‘test-and-treat’ approaches with social science research

The recent publication of new WHO guidelines, including a call for antiretroviral therapy for everyone diagnosed with HIV regardless of CD4<sup>+</sup> cell count and preexposure prophylaxis for people at substantial risk of HIV infection [1], marks an important moment for taking stock of what will be needed to take biomedical HIV prevention approaches to scale, and sustain them. As the author of a recent editorial in *The Lancet* [2] observes, these guidelines are ‘welcome but ambitious. [...] No studies exist that address how such a strategy can be executed on a global scale’ (p. 1420).

We, a multidisciplinary group of social scientists working as part of five large-scale ‘universal test-and-treat’ (UTT) trials being implemented across six African countries, would argue that successful large-scale expansion of treatment and preexposure prophylaxis will require an in-depth understanding of the heterogeneous community and health systems’ contexts of the rollout.

The Social Science of Universal Test and Treat Network group met in Kampala in October 2015 to critically reflect on the role social science plays in supporting the successful implementation of UTT in African contexts. These deliberations underlined the complexities of implementing the new era of treatment and prevention. Social science work to date and the experience of others implementing UTT already shows that UTT is not a biomedical ‘one-size-fits-all’ intervention. It includes multiple client journeys and repeated activities (such as testing and adherence) in diverse health systems and social contexts; moreover, diverse ‘models’ of UTT are currently being implemented. We cannot control for the very varied contexts in which antiretroviral therapy will be delivered, and the unanticipated factors in ‘real-life’ contexts that can mediate the effects of UTT on desired outcomes.

Among the early lessons from social science research in the trials are, for instance, that sex, age, and other social hierarchies matter, but so do attention to how taking treatment fits into an individual’s broader (and dynamic) life experience: addressing uptake, adherence, and retention will rely upon an understanding of why men and women delay, start, and stop treatment. Our UTT data are replete with examples of the dilemmas faced by individuals navigating each step in the care cascade, which are shaped, for example, by gendered power relations within couples. At a study site in Zambia, for instance, a 20-year-old HIV-positive woman

pregnant with her fourth child explained to study staff that she had not yet gone to the clinic to access HIV services because she was worried about her husband’s response to her status. She feared that he might divorce her if he found out she had HIV. The data we gather about real dilemmas among people making decisions about HIV care, in aggregate, inform a broad understanding of the ways in which individuals in different couples, families, and communities can be subject to pressures that may force them onto testing and treatment or delay access, as well as affect continued access to care. Certain populations, such as adolescents, are facing particularly severe pressures. We are also observing that migrant and highly mobile individuals, a key marginalized yet economically important population, need tailored interventions to support their access and sustenance in care, because those who move from place to place because of work or other factors will (continually) fall into each of the ‘10%’ not reached by the 90–90–90 targets. Social science research studies in the trials are investigating how forms of HIV-related stigma are changing as a result of UTT, and how these changes are in turn affecting the trials. Social scientists are examining how the history of delivery of HIV interventions in different places affects expectations and perceptions of HIV-care delivery, and how the delivery of prompt treatment is fitting within existing, often overstretched, health systems in Africa – both of which influence uptake and sustained use of treatment. We are learning that we need different ways to support people to accept prompt initiation of treatment if they do not feel unwell, or have concerns about side-effects or other factors that affect life and work.

In short, social and behavioral sciences provide crucial contextual evidence on how treatment and prevention is implemented and scaled up, and what social and behavioral consequences and impact of ‘universal’ access to testing, treatment, and prevention can be expected, and thus holds valuable lessons for the UTT rollout. We believe that now is a crucial time to set goals for the inclusion of social science in the implementation science research program for delivering high-quality prevention and treatment across Africa.

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### Conflicts of interest

There are no conflicts of interest.

Carol S. Camlin<sup>a</sup>, Janet Seeley<sup>b</sup>, Lario Viljoen<sup>c</sup>, Eva Vernooij<sup>d</sup>, Musonda Simwina<sup>e</sup>, Lindsey Reynolds<sup>f</sup>, Ria Reis<sup>g,h,q</sup>, Rebeca Plank<sup>j</sup>, Joanna Orne-Gliemann<sup>k</sup>, Nuala McGrath<sup>l,r</sup>, Joseph Larmarange<sup>m</sup>, Graeme Hoddinott<sup>c</sup>, Monica Getahun<sup>n</sup>, Edwin D. Charlebois<sup>o</sup> and Virginia Bond<sup>b,p</sup>, <sup>a</sup>Department of Obstetrics, Gynaecology and Reproductive Sciences and Division of Prevention Science, University of California, San Francisco, California, USA, <sup>b</sup>Department of Global Health and Development, London School of Hygiene and Tropical Medicine, London, UK, <sup>c</sup>Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Stellenbosch University, Tygerberg, South Africa, <sup>d</sup>Amsterdam Institute for Social Science Research, Department of Anthropology, University of Amsterdam, Amsterdam, The Netherlands, <sup>e</sup>Zambart, University of Zambia, Ridgeway Campus, Lusaka, Zambia, <sup>f</sup>Population Studies and Training Center, Brown University, Providence, Rhode Island, USA, <sup>g</sup>Department of Anthropology, University of Amsterdam, Amsterdam, The Netherlands, <sup>h</sup>The Children's Institute, School of Child and Adolescent Health, University of Cape Town, Cape Town, South Africa, <sup>i</sup>Brigham and Women's Hospital, <sup>j</sup>Harvard School of Public Health, Boston, Massachusetts, USA, <sup>k</sup>INSERM Unité 897, Institut de Santé Publique Epidémiologie Développement, University of Bordeaux, Bordeaux, France, <sup>l</sup>Faculty of Medicine, University of Southampton, Southampton, UK, <sup>m</sup>CEPED (UMR 196 UPD

IRD), Institut de Recherche pour le Développement (IRD), Paris, France, <sup>n</sup>University of California at San Francisco, San Francisco, California, USA, <sup>o</sup>University of California, Center for AIDS Prevention Studies, San Francisco, California, USA, <sup>p</sup>Zambart, University of Zambia, Ridgeway Campus, Lusaka, Zambia, <sup>q</sup>Leiden University Medical Center, The Netherlands, and <sup>r</sup>Africa Centre for Population Health, University of KwaZulu-Natal, South Africa.

Correspondence to Carol S. Camlin, PhD, MPH, Department of Obstetrics, Gynaecology and Reproductive Sciences and Division of Prevention Science, University of California, San Francisco, California, USA.

E-mail: Carol.Camlin@ucsf.edu

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## Raltegravir is safely used with long-term viral suppression for HIV-infected patients on hemodialysis: a pharmacokinetic study

The number of HIV-infected patients receiving hemodialysis has been remarkably increasing because of the rise in the prevalence of chronic kidney disease [1]. Renal dysfunction and the hemodialysis procedure significantly affect the pharmacokinetics of antiretroviral drugs, and dose adjustment and/or change in the medication schedule are occasionally needed, which carry a risk of poor adherence and treatment failure. Raltegravir (RAL) is an integrase inhibitor of HIV. It is mainly metabolized by uridine diphosphate glucuronosyltransferase 1A1 in the liver, and urinary excretion is less than 10% [2]. Thus, RAL is considered a better choice of antiretroviral drug for HIV patients on hemodialysis.

In this study, we determined serum concentrations of RAL by high performance liquid chromatography in two HIV-infected patients undergoing maintenance hemodialysis. The patients received regular doses of RAL (400 mg) twice daily both on hemodialysis and nonhemodialysis days in combination with abacavir and etravirine. This study was approved by the Ethical Committee of Gunma University Faculty of Medicine, and written informed consent was obtained from each patient.

Patient 1 was a 64-year-old man who had been on maintenance hemodialysis thrice weekly from June 2011

because of idiopathic membranous nephropathy. He had been taking RAL for the previous 2 months before hemodialysis was initiated. During the year between June 2011 and June 2012, blood sampling was performed on nine different days: 3 days when hemodialysis was performed in the morning (a.m.-hemodialysis), 3 days in the afternoon (p.m.-hemodialysis), and 3 nonhemodialysis days. During each hemodialysis session, blood samples were collected from the indwelling dialysis catheter every 1 h. On nonhemodialysis days, venous blood was drawn at the same time intervals. The patient took RAL regularly at 08:00 and 20:00 regardless of whether hemodialysis was performed. Figure 1a shows the kinetics of RAL concentrations in patient 1. There was no difference in the RAL concentrations at each time point between a.m.-hemodialysis (solid line) and nonhemodialysis (dotted line) days. Peak values were reached 3.5 h after taking RAL at comparable levels on a.m.-hemodialysis and nonhemodialysis days (942.2 and 859.9 ng/ml, respectively). The kinetics of RAL on the p.m.-hemodialysis days (dashed line) also fitted with those obtained on a.m.-hemodialysis and nonhemodialysis days. These results indicated that hemodialysis had no impact on the pharmacokinetics of RAL in this patient.  $C_{\text{trough}}$  was 238.6 ng/ml, above the reference value (14 ng/ml) of  $IC_{95}$  reported previously [3].