The WelTel Trial in context and the importance of null findings

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The past decade has seen major advances in HIV care. Effective treatment exists, and drugs are becoming cheaper, more effective, and easier to tolerate. Thus, although most important clinical treatment questions have been answered, questions remain about how to get people into care earlier and remain on life-long treatment.

It is crucial to identify effective interventions to improve linkage to and retention in HIV care.[1] The recently WHO-endorsed test-and-treat[2] policy means that patients are eligible to start HIV treatment earlier than ever before.[3] In *The Lancet Public Health,* Mia van der Kop and colleagues[4] report the results of the WelTel study, in which they sought to identify whether a weekly two-way text-message check-in with patients in Kenya who were newly positive for HIV could improve one-year retention. Although it previously worked for those on treatment,[5] this randomised trial showed no benefit. Despite the absence of efficacy, the results provide crucial evidence for policy, for two reasons central to evidenced-based thinking: first, the importance of person, place, and time in interpreting results; and second, the importance of validly and precisely estimated null findings.

Regarding the first point, though we hoped the intervention would be effective, it was not guaranteed because the population studied was very different from the previous trial.[5] Text-messaging interventions are a popular approach in sub-Saharan Africa (and beyond) because mobile phone penetration is high and the cost of intervention is low. Although numerous trials have been done,[6] results have been mixed. This is expected since the effects of behavioural interventions are likely to vary depending on where and when they are used, to whom they are targeted, and how they are implemented. While the previous trial targeted participants already on HIV treatment, in the WelTel study participants had just tested HIV-positive and many might not have accepted the necessity of treatment.

Many factors determine whether an intervention like this will succeed. Is the text-messaging service free? Is the population highly motivated to seek care? Have the participants disclosed their HIV status? Do the participants know others who have sought treatment? We don't know the answers to these questions in the WelTel study, but we do know retention was high in this population, suggesting that the population might have been more motivated than the average person who tested HIV-positive. The authors found retention rates of 79% in the control group, by contrast with a much lower rate in most sub-Saharan African programmes.[7] Moreover, participants only answered texts 55% of the time, often because of problems with their phones, suggesting the intervention itself might need to be improved.

Regarding the second point on the importance of valid and precise findings, we appreciate that appropriate attention is being brought to null results.[8] The authors' finding didn't simply fail to demonstrate an effect of the intervention, they effectively showed lack of an effect through a strong design that minimised confounding and entailed appropriate measurement and good follow-up. The trial was not without its limitations, including the absence of blinding and the fact that only two-thirds of the participants completed the 12-month questionnaire.

The primary study finding was that there was no significant difference in 12-month retention between groups (79% for the intervention group *vs* 81% for the control group). Although the finding was null (risk ratio 0·98) the effect was precisely estimated (95% CI 0·91–1·05). This study therefore does not leave us wondering if a bigger study would have found meaningful effects. Instead, we have persuasive evidence that the intervention was not successful, at least as implemented. As Poole wrote nearly two decades ago,[9] we must take precise and highly informative estimates like these seriously, even if null.[9] Unfortunately, null findings are often difficult to publish or get little attention. Knowing there is no effect of an intervention is just as important as knowing there is one. Conversely, a wide confidence interval, even if statistically significant in that it excludes the null value, conveys substantially less information. Policy makers must base decisions on precise and valid estimates, meaning they are not threatened by random variation or systematic bias. The WelTel study appears to be quite informative in this respect, and will therefore have high impact for policy decisions. This approach is why the

outdated model in which results were prioritised only by their statistical significance is harmful for scientific progress and has been abandoned.[10] Still, with this trial, selection bias through loss to follow-up is probably the dominant form of error, and as such, should be taken into consideration when making decisions about the study results.[11]

With renewed attention being paid to patients newly testing positive for HIV under a test-and-treat strategy, it would have been exciting if the WelTel text-messaging intervention had improved retention and gotten more patients onto treatment. But knowing that it does not, at least as implemented, is an important advance as well, and one we should learn from as we seek new ways to improve retention in HIV care.

Matthew P Fox, Jay S Kaufman
Department of Epidemiology and Department of Global Health, Boston University School of Public Health, Boston, MA 02476, USA (MPF); Health Economics and Epidemiology Research Office, Department of Internal Medicine, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa (MPF); Department of Epidemiology, Biostatistics, & Occupational Health, McGill University, Montreal, QC, Canada (JSK)
mfox@bu.edu

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