

<b>Institution:</b> London School of Hygiene & Tropical Medicine (LSHTM)		
<b>Unit of Assessment:</b> 2		
<b>Title of case study:</b> Making HIV self-testing available to millions as a diagnostic strategy for low- and middle-income countries		
<b>Period when the underpinning research was undertaken:</b> 2008-2019		
<b>Details of staff conducting the underpinning research from the submitting unit:</b>		
<b>Name(s):</b> Elizabeth Corbett Fern Terris-Prestholt Katherine Fielding Helen Ayles & associated research teams	<b>Role(s) (e.g. job title):</b> Professor Assistant Professor; Associate Professor Associate Professor; Professor Clinical Professor	<b>Period(s) employed:</b> 01/12/2000-present 01/04/2000-present 24/01/2000-present 01/01/2003-present
<b>Period when the claimed impact occurred:</b> 2015-2020		
<b>Is this case study continued from a case study submitted in 2014?</b> No		
<b>1. Summary of the impact</b> (indicative maximum 100 words)  <p>People need to know their HIV status so they can seek treatment. LSHTM-led research — built up over decades of expertise in the field — showed self-testing kits were safe and effective, and could make a huge difference. This evidence led to the World Health Organization (WHO) developing policy and guidelines to support HIV self-testing and to the global health initiative Unitaids supporting rapid scale-up of the strategy. LSHTM also led implementation research to optimise delivery of self-testing kits, which made ethical, effective and efficient HIV testing widely available across the world, and influenced global and country-level policies. These activities allowed millions of people to learn their HIV status and access appropriate care, resulting in progress towards the UN 90-90-90 targets and the wider Sustainable Development Goal 3.3 to end AIDS by 2030.</p>		
<b>2. Underpinning research</b> (indicative maximum 500 words)  <p>The global HIV epidemic continues to expand, with 38 million people currently living with HIV and 1.8 million new infections each year, two-thirds of them in sub-Saharan Africa. The first of the UN 90-90-90 targets to end the HIV epidemic was for 90% of people with HIV to learn their HIV status by 2020. But, according to the WHO, 8.1 million, or 21% of people with HIV, remained unaware of their HIV status in 2019. As there is no effective vaccine or cure, early diagnosis and treatment remains the cornerstone of control efforts, and HIV testing is essential to this strategy. HIV self-testing has been considered since the 1990s, but concerns over accuracy and potential social harms (suicide, coercion and intimate partner violence) meant research and development stalled. This changed when LSHTM-led research in sub-Saharan Africa provided critical evidence to increase uptake of HIV testing.</p> <p><b>Making the case for focusing on HIV self-testing</b>          LSHTM-led studies from 2008 to 2010 showed that HIV self-testing was widely but informally used by African health workers, and that there was high uptake and accurate results from self-testing kits in urban Malawi (3.1). A community-based cluster randomised trial led by Corbett from 2011 to 2014 trained lay distributors to provide self-testing to neighbours; this was the first large-scale evaluation of self-testing globally, confirming high accuracy and uptake (3.2). 76.5% of 16,660 adult residents self-tested within one year with 44% of participants testing for the first time. A 'key informant' system identified and investigated all deaths, which confirmed there was no relationship to self-testing. New initiations of antiretroviral therapy increased significantly when self-testing was combined with optimal home-based initiation of HIV care. The combined results of these studies, coinciding with Food &amp; Drug Agency approval in 2012 of the OraSure In Home HIV test, prompted</p>		

WHO, UNAIDS, and the Bill & Melinda Gates Foundation to accelerate self-testing strategies for Africa.

### Increasing access to self-testing and analysing the data

The HIV Self-Testing Africa (STAR) Initiative — with the multi-partner research consortium led by LSHTM, and Population Services International (PSI) leading on implementation — represented the largest evaluation of HIV testing in Africa to date. STAR's first phase from 2015 to 2017 in Malawi, Zambia and Zimbabwe generated data on key delivery models (3.3-3.5) relating to usability, social harms, costs (3.6) and health impacts (3.3-3.5) to inform countries and WHO guidelines. It also evaluated models of distribution of self-tests including peer-distribution by female sex workers, and facility-based secondary-distribution (3.3) where kits were taken for sexual partners by antenatal and newly diagnosed HIV patients, and both community-based (3.4, 3.6) and community-led (3.5) models.

Building on evidence and experience gathered during the first phase, the next phase increased access to self-testing across sub-Saharan Africa and expanded implementation to 3 additional countries: Eswatini, Lesotho and South Africa. In total, 7 cluster-randomised trials funded by STAR investigated outcomes including population-level knowledge of HIV status, demand for antiretroviral therapy, and male circumcision. Economic evaluations defined preferences, and provider (3.6), societal (3.5) and projected scale-up costs, and informed cost-effectiveness modelling critical for policy-makers.

Demand for HIV self-testing exceeded expectations, with high uptake among groups less likely to access traditional testing services (including men and young people). Distribution efforts achieved a high positive yield and increased uptake of antiretroviral therapy, suggesting newly-diagnosed people were linking up to care after self-testing.

STAR was headed by LSHTM, who designed and led the research, supported by the Liverpool School of Tropical Medicine (LSTM) and University College London. The large LSHTM team was led by Corbett, who headed the country team in Malawi. In-country HIV self-testing research activities were conducted by local research institutions: Malawi-Liverpool-Wellcome Trust Clinical Research programme (MLW), Zambart (Zambia), the Centre for Sexual Health and HIV/AIDS Research Zimbabwe, and the Wits Reproductive Health and HIV Institute (South Africa). The Initiative was funded by Unitaid, with implementation led by PSI, and WHO technical support for research.

### 3. References to the research (indicative maximum of six references)

**3.1** Choko AT, MacPherson P, **Webb EL, Willey BA**, Feasey H, Sambakunsi R, Mdolo A, Makombe SD, Desmond N, **Hayes RJ**, Maheswaran H, **Corbett EL**. 2015. Uptake, accuracy, safety, and linkage into care over two years of promoting annual self-testing for HIV in Blantyre, Malawi: a community-based prospective study. *PLoS Med*. 12(9):e1001873. doi: [10.1371/journal.pmed.1001873](https://doi.org/10.1371/journal.pmed.1001873).

**3.2** MacPherson P, Lalloo DG, Webb EL, Maheswaran H, Choko AT, Makombe SD, Butterworth AE, van Oosterhout JJ, Desmond N, Thindwa D, Squire SB, **Hayes RJ, Corbett, EL**. 2014. Effect of optional home initiation of HIV care following HIV self-testing on antiretroviral therapy initiation among adults in Malawi: a randomized clinical trial. *JAMA*. 312(4):372-9. doi: [10.1001/jama.2014.6493](https://doi.org/10.1001/jama.2014.6493).

**3.3** Choko AT, **Corbett EL**, Stallard N, Maheswaran H, Lepine A, **Johnson CC**, Sakala D, Kalua T, Kumwenda M, **Hayes R, Fielding K**. 2019. Effect of HIV self-testing alone or with additional interventions including financial incentives on linkage to care or prevention among male partners of antenatal care attendees in Malawi: An adaptive multi-arm multi-stage cluster randomised trial. *PLoS Med*. 2;16(1):e1002719. doi: [10.1371/journal.pmed.1002719](https://doi.org/10.1371/journal.pmed.1002719).

**3.4** Mulubwa C, **Hensen B**, Phiri MM, Shanaube K, Schaap AJ, Floyd S, Phiri CR, Bwalya C, Bond V, Simwinga M, Mwenge L, Fidler S, **Hayes R**, Mwinga A, **Ayles H**, HPTN 071 (PopART) Study

Team. 2019. Community based distribution of oral HIV self-testing kits in Zambia: a cluster-randomised trial nested in four HPTN 071 (PopART) intervention communities. *Lancet HIV*. 6:e81-e92. doi: [10.1016/S2352-3018\(18\)30258-3](https://doi.org/10.1016/S2352-3018(18)30258-3).

**3.5 Indravudh PP, Fielding K, Kumwenda MK, Nzawa R, Chilongosi R, Desmond N, Nyirenda R, Johnson CC, Baggaley RC, Hatzold K, Terris-Prestholt F, Corbett EL.** 2019. Community-led delivery of HIV self-testing to improve HIV testing, ART initiation and broader social outcomes in rural Malawi: study protocol for a cluster-randomised trial. *BMC Infectious Disease*. 19(1):814. doi: [10.1186/s12879-019-4430-4](https://doi.org/10.1186/s12879-019-4430-4).

**3.6 Mangenah C, Mwenge L, Sande L, Ahmed L, d'Elbée M, Chiwawa P, Chigwenah T, Kanema S, Mutseta M, Nalubamba M, Chilongosi R, Indravudh P, Sibanda E, Neuman M, Ncube G, Ong JJ, Mugurungi O, Hatzold K, Johnson C, Ayles H, Corbett EL, Cowan FM, Maheswaran H, Terris-Prestholt F.** 2019. Economic cost analysis of community-based distribution of HIV self-test kits in Malawi, Zambia and Zimbabwe. *Journal of the International AIDS Society*. 22 Suppl 1:e25255. doi: [10.1002/jia2.25255](https://doi.org/10.1002/jia2.25255).

We believe this body of research meets the 'at least 2\*' definition given its reach, significance and rigour.

#### 4. Details of the impact (indicative maximum 750 words)

Evidence from the above projects directly enabled millions of people to know their HIV status via international guidelines and test distribution; a crucial first step towards treatment and prevention, and a healthy life. The LSHTM-led research informed programmes and policies implemented by international organisations and national governments. It also created the right environment and global market for development and procurement of innovative HIV testing products. Through STAR's supporting evidence, HIV self-testing increased dramatically, from negligible volumes in 2015, when there was no supportive policy or quality-assured kits for use in low and middle income countries (LMICs). There are now 4 WHO pre-qualified products, with 5.5 million HIV self-testing kits used in 2018 (5.1).

#### Securing funding to fill the evidence gap and make an impact

The LSHTM team presented their Wellcome-funded HIV self-testing data to the 20<sup>th</sup> Conference on Retroviruses and Opportunistic Infections in 2013. Later that year, a UNAIDS technical update on HIV self-testing was released for resource-limited settings, encouraging development of frameworks to support HIV self-testing in national guidelines but stressing that the evidence base was not yet sufficient to support full guidance (5.2). This technical update was prominently influenced by the research done by LSHTM, LSTM and the MLW, showing HIV self-testing led to increased uptake of HIV treatment. The Malawi data was the only data on HIV self-testing from general LMIC populations.

In September 2013, the STAR Consortium was awarded USD72 million for 2015 to 2020 (lead organisation Population Services International, including USD13.7 million for the LSHTM-led research consortium) to catalyse the market for HIV self-testing, with specific aims of i) providing multi-country evidence to inform WHO guidelines to address this evidence gap, ii) supporting full integration of self-testing into national HIV policy and practice, iii) supporting manufacturers to develop and seek WHO pre-qualification for products for LMICs, and iv) negotiating price reductions for LMICs.

#### Kit development and distribution to increase access to tests

STAR created an enabling environment for HIV self-testing by generating diverse demand and financing, and accelerating entry to market for self-testing kits. This rapid progress was underpinned by LSHTM-led research, with 650,000 tests distributed prior to WHO prequalification under the research protocols approved by the LSHTM Ethics Committee. In July 2017, the WHO prequalified the first LMIC HIV self-testing kit (OraSure HIV Self-test) which was offered to LMICs for USD2 per kit following investment from the Bill and Melinda Gates Foundation (5.3). By the end of 2020, several quality-assured HIV self-testing products were registered, and the WHO had

prequalified 4 tests. 4 STAR Initiative countries (Malawi, South Africa, Zambia and Zimbabwe) drafted regulations governing *in vitro* diagnostics, including HIV self-test kits. With enabling policies and regulations in place, the number of kits bought by donors increased rapidly, and market forecasting estimated 16 million kits were procured by 2020 (5.4, 5.5). 10 million kits were bought for 2018-19 in the 6 STAR countries alone (Malawi, South Africa, Zambia, Zimbabwe, Lesotho and Eswatini).

Recognising the need to fund and scale-up HIV self-testing beyond the STAR Initiative countries, Unitaid, together with PSI and their partners, engaged ministries of health, the Global Fund and the US President's Emergency Fund for AIDS Relief (PEPFAR). They encouraged integration of self-testing into plans and budgets. In 2018, PEPFAR included HIV self-testing in its own right in its country guidance as a dedicated testing strategy, and increased funding for HIVST. By 2019, 99 countries had included self-testing in national procurement plans, funded by PEPFAR and the Global Fund (5.6).

### **Guidelines shaped by STAR evidence**

In parallel to scaling up access to self-testing kits, the evidence and experience produced by the STAR Initiative directly led to the development of policy and regulations that made HIV self-testing more widely available. In their capacity as experts on HIV testing and treatment, Corbett was a member of the Guideline Development Group for the 2015 WHO-consolidated guidelines on HIV testing services, and Ayles and Hensen served as external peer reviewers (5.7).

Phase 1 of STAR produced public evidence to inform WHO guidelines on HIV self-testing and partner notification in 2016, which strongly recommended HIV self-testing as an additional testing approach (5.8). This was followed by the WHO prequalification of the first HIV self-test, OraSure, in 2017 (5.3). STAR also provided evidence underpinning the WHO 2019 Consolidated Guidelines on HIV Testing Services revision, notably regarding delivery models and the link to HIV prevention, with Corbett and others listed as external contributors to the supporting evidence, and as part of the external review group (5.9). The results of the trial on community-led delivery of HIV self-testing (3.5), currently in press, were shared at the 10<sup>th</sup> International AIDS Society Conference on HIV Science in July 2019 (5.10) in advance of the published paper, and also underpinned the 2019 Consolidated Guidelines.

STAR was decentralised to allow each country to submit protocols around common research questions and to progress at their own pace. WHO reported as of 2019 that 59 countries had policies which allowed HIV self-testing, and 28 countries, across high and low income settings, were actively implementing HIV self-testing (5.4, 5.6). This was in contrast to 2015, when only 3 countries (all of which were high-income) were actively implementing self-testing services as part of their public health HIV response.

## **5. Sources to corroborate the impact** (indicative maximum of 10 references)

**5.1** World Health Organization. HIV/AIDS. HIV self-testing. Accessed at:

<https://www.who.int/hiv/topics/self-testing/en/>

- Status of HIV self-testing (HIVST) in national policies (situation as of July 2019). Global AIDS Monitoring (UNAIDS/WHO/UNICEF) and WHO HIV Country Intelligence Tool, 2019. Accessed at: [https://www.who.int/hiv/topics/self-testing/HIVST-policy\\_map-jul2019-a.png?ua=1](https://www.who.int/hiv/topics/self-testing/HIVST-policy_map-jul2019-a.png?ua=1)

**5.2** Joint United Nations Programme on HIV/AIDS (UNAIDS). A short technical update on self-testing for HIV. Geneva, Switzerland (2013).

**5.3** OraSure Technologies. OraSure Technologies enters agreement with Bill & Melinda Gates Foundation to reduce price of rapid, point-of-care HIV self-test in 50 developing countries (Press Release). July 2017. Accessed at:

<https://www.globenewswire.com/news-release/2017/06/27/1029393/0/en/OraSure-Technologies-to-Drive-Accelerated-Adoption-of-OraQuick-HIV-Self-Test.html>

**5.4** Unitaid, World Health Organization. Market & Technology Landscape: HIV rapid diagnostic tests for self-testing, 4<sup>th</sup> edition. Geneva: Unitaid, 2018.

- Details on scale up and procurement

**5.5** Unitaid, STAR and World Health Organization. 'Knowing your status – then and now: realising the potential of HIV self-testing'. 30<sup>th</sup> World AIDS Day Report. December 2018.

- contains information on distribution of HIVST kits, and market impact information (as of 2018)

**5.6** World Health Organization. Ingold H, Mwerinde O, Ross AL, Corbett E, Hatzold K, Johnson C, Baggaley R, Ncube G, Nyirenda R. Accelerating global access and scale-up of HIV self-testing: a call for action. *Journal of the International AIDS Society* 2019 Mar;22 Suppl 1:e25249. doi: [10.1002/jia2.25249](https://doi.org/10.1002/jia2.25249).

**5.7** World Health Organization. Consolidated guidelines on HIV testing services. 5Cs: Consent, confidentiality, counselling, correct results and connection. July 2015.

- Corbett on Guideline Development Group, Ayles and Hensen external peer reviewers

**5.8** World Health Organization. Guidelines on HIV self-testing and partner notification. Supplement to consolidated guidelines on HIV testing services. December 2016.

- STAR research referenced

**5.9** World Health Organization. 2019 Consolidated guidelines on HIV testing services for a changing epidemic.

- Corbett and others listed as external contributors to supporting evidence, and as part of the external review group
- Chapters 3 & 5 reference lists, main STAR LSHTM authors (staff or PhD student) – Ayles, d'Elbee, Corbett, Fielding, Hensen, Indravudh, Johnson (WHO and LSHTM PhD student), Neuman, Sande, Terris-Prestholt, Webb, Witzel

**5.10** Indravudh P, Fielding K, Kumwenda M, Nzawa R, Chilongosi R, Desmond N, Nyirenda R, Johnson C, Baggaley R, Hatzold K, Terris-Prestholt F, Corbett E. Community-led delivery of HIV self-testing targeting adolescents and men in rural Malawi: a cluster-randomised trial. Late breaker oral presentation. A-1077-0240-04874. *10th IAS Conference on HIV Science (IAS 2019)*, Mexico City, Mexico.

- Results of research output 3.5 shared and included in WHO 2019 Consolidated Guidelines (5.9). Journal publication in press as: **Indravudh PP, Fielding K**, Kumwenda MK, Nzawa R, Chilongosi R, Desmond N, Nyirenda R, Neuman M, **Johnson CC**, Baggaley R, Hatzold K, **Terris-Prestholt F, Corbett EL**. Effect of community-led delivery of HIV self-testing on uptake of HIV testing and antiretroviral therapy in rural Malawi: A cluster-randomized clinical trial. *PLoS Med* (in press)