

Institution: London School of Hygiene & Tropical Medicine		
Unit of Assessment: 2		
Title of case study: Uncovering and addressing gaps in care for adolescents with HIV		
Period when the underpinning research was undertaken: 2007-2019		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Rashida Ferrand Elizabeth Corbett Helen Weiss Richard Hayes Joanna Busza	Role(s) (e.g. job title): Clinical Associate Professor, Clinical Professor Clinical Reader; Clinical Professor Professor Professor Associate Professor	Period(s) employed: 01/04/2011-present 01/12/2000-present 01/01/1997-present 01/10/1978-present 01/12/2001-present
Period when the claimed impact occurred: 2013-2019		
Is this case study continued from a case study submitted in 2014? No		
1. Summary of the impact (indicative maximum 100 words) LSHTM researchers highlighted significant gaps in HIV testing and coverage of antiretroviral therapy (ART), and poorer outcomes, for older children and the adolescent age group. They identified barriers to HIV testing, such as the fact that children needed to have consent from their guardians. The research directly influenced both the World Health Organization and national governments in Africa to include adolescents in their HIV-related policies – marking a shift change from the previous focus on testing and care for infants and younger children only. As a result, HIV testing and care strategies were tailored to address the clinical and psychosocial circumstances of adolescents who had been infected with HIV from birth.		
2. Underpinning research (indicative maximum 500 words) A key role of HIV/AIDS research is to identify at-risk population groups and demographics, and LSHTM teams transformed understanding of how adolescents were affected and could be helped. Between 2007 and 2010, research from LSHTM found that children born with HIV lived without any treatment for much longer than anticipated. Nearly a third of untreated children with perinatally-acquired HIV had a median survival of at least 16 years. Studies led by Ferrand and Corbett showed that substantial numbers of children born when HIV prevalence among pregnant women peaked in the late 1990s were seeking medical help as adolescents (age 10 to 18), and that HIV was the leading cause of death in adolescents in sub-Saharan Africa (3.1). Before this, the understanding was that survival beyond 5 years of age with untreated HIV was exceptional. Due to the lack of recognition of the problem, HIV programmes had focused little attention on testing and treatment of older children and adolescents. The multidisciplinary ZENITH Project from 2012 to 2016 evaluated innovative HIV testing models to tackle the problem of undiagnosed HIV in adolescents. Ferrand and colleagues at LSHTM including Hayes and Weiss led the project, which also involved colleagues at the University of Zimbabwe and the Biomedical Research and Training Institute, and the Harare City Health Department. ZENITH evaluated strategies including: 1) opt-out HIV testing in primary care clinics for older children and adolescents, where tests were carried out routinely during appointments and patients had to actively decline if they did not want the test. This increased the provision and uptake of HIV testing by children aged 6 to 16 years by 20% and 30% respectively and increased HIV diagnoses by 55%. 2) a screening tool to identify adolescents at risk of HIV, for targeted testing. This was found to be a potentially more cost-efficient approach than universal HIV testing as it halved the numbers		

needed to screen to identify one HIV-positive child, thereby reducing time required for counselling and conducting HIV tests and the cost of test kits (3.2).

3) economic incentives to caregivers to have their children tested. These were found to increase uptake of HIV testing three-fold (3.3).

The research also demonstrated that clinic-based HIV testing was unlikely to be sufficient and community-based strategies were required to reduce the prevalence of undiagnosed HIV. As a result, ZENITH included a trial of an intervention delivered by lay workers to support caregivers to improve adherence to HIV treatment in children and adolescents. This was the first trial ever to demonstrate an impact on viral suppression, with a 33% reduction in odds of HIV virological failure (3.4). The few previous studies to address adherence among older children and adolescents in Africa had measured self-reported adherence only, an unreliable measure.

Ferrand's research showed that a high proportion of children growing up with HIV suffered from multisystem chronic comorbidities, despite taking ART (3.1, 3.5). Clinical studies in Zimbabwe and Malawi defined a previously unrecognised form of chronic lung disease which affected the small airways (constrictive obliterative bronchiolitis). This affected more than 15% of children with HIV, including those taking ART, and caused severe morbidity (3.6). A prospective cohort study (INHALE) conducted by her group from 2014 to 2016 also showed a high prevalence and incidence of sub-clinical cardiac disease in children with HIV taking ART. Most HIV programmes focus exclusively on ART delivery. This research further highlighted the need to focus on HIV-associated morbidities as part of HIV care.

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

3.1 Ferrand RA, Bandason T, Musvaire P, Larke N, Nathoo K, Mujuru H, Ndhlovu C, Munyati SS, Cowan FM, Gibb DM, **Corbett EL**. 2010. Causes of acute hospitalisation in adolescence: burden and spectrum of HIV-related morbidity in a country with an early-onset and severe HIV epidemic. *PLoS Med*. 7(2):e1000178. doi: [10.1371/journal.pmed.1000178](https://doi.org/10.1371/journal.pmed.1000178).

3.2 Bandason T, McHugh G, Dauya E, Mungofa S, Munyati S, Weiss HA, Mujuru H, Kranzer K, **Ferrand RA**. 2016. Validation of a screening tool to identify older children living with HIV in primary care facilities in high HIV prevalence settings. *AIDS*. 30(5):779-85. doi: [10.1097/QAD.0000000000000959](https://doi.org/10.1097/QAD.0000000000000959)

3.3 Kranzer K, Simms V, Bandason T, Dauya E, McHugh G, Shungu M, Chonzi P, Dakshina A, Mujuru H, **Weiss H, Ferrand RA**. 2017. Economic incentives for HIV testing by adolescents in Zimbabwe: a randomised controlled trial. *The Lancet HIV*. doi: [10.1016/S2352-3018\(17\)30176-5](https://doi.org/10.1016/S2352-3018(17)30176-5)

3.4 Ferrand RA, Simms V, Dauya E, Bandason T, Mchugh G, Mujuru H, Chonzi P, **Busza J**, Kranzer K, Munyati S, **Weiss HA, Hayes RJ**. 2017. The effect of community-based support for caregivers on the risk of virological failure in children and adolescents with HIV in Harare, Zimbabwe (ZENITH): an open-label, randomised controlled trial. *Lancet Child and Adolescent Health*. 1:175-183. doi: [10.1016/S2352-4642\(17\)30051-2](https://doi.org/10.1016/S2352-4642(17)30051-2).

3.5 McHugh G, Rylance J, Mujuru H, Nathoo K, Chonzi P, Dauya E, Bandason T, Simms V, Kranzer K, **Ferrand RA**. 2016. Chronic morbidity among older children and adolescents at diagnosis of HIV infection. *Journal of Acquired Immune Deficiency Syndrome*. 73:275-281. doi: [10.1097/QAI.0000000000001073](https://doi.org/10.1097/QAI.0000000000001073).

3.6 Ferrand RA, Desai SR, Hopkins C, Elston CM, Copley SJ, Nathoo K, Ndhlovu CE, Munyati S, Barker RD, Miller RF, Bandason T, Wells AU, **Corbett EL**. 2012. Chronic Lung Disease in adolescents with delayed diagnosis of vertically-acquired HIV. *Clinical Infectious Diseases*. 55(1):145-52. doi: [10.1093/cid/cis271](https://doi.org/10.1093/cid/cis271).

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)

Before LSHTM research, HIV programmes tended to leave adolescents out of the picture for testing and treatment because there was little awareness that children infected by their mothers could survive untreated for so long. The studies by LSHTM stimulated a change of focus to include increased testing and coverage of ART in these age groups. Researchers from LSHTM brought international attention to this issue by actively engaging with national and global policy makers to influence policy. As a result, their findings on effective HIV testing and care strategies for adolescents have been widely implemented.

Changing guidelines for HIV testing and care

Ferrand was part of the group informing the guidelines for HIV testing and care of adolescents developed by the World Health Organization (WHO) in 2013 and 2014 (5.1, 5.2). The WHO then convened a technical consultation to inform the updating of HIV treatment guidelines for adolescents. This involved commissioning two systematic reviews (conducted by Ferrand and colleagues) to review evidence on service delivery and clinical outcomes for adolescents, for inclusion in the 2015 Consolidated ARV Guidelines revisions (5.2). These revised guidelines included new recommendations on ART in adolescents.

Findings by Ferrand and colleagues that lack of guardian consent was a key barrier to HIV testing in older children and adolescents led to the Zimbabwe national HIV testing guidelines changing in 2014 to enable healthcare workers to give consent for children to be tested when parental/guardian consent was not available. They also strengthened recommendations for universal testing of children and adolescents (5.3).

Ferrand was a member of two WHO global consultations on addressing illness associated with HIV in 2014 and 2019 (5.4), and presented reviews of evidence on HIV-related comorbidities in children and adolescents. The results of the 2019 review were used to revise the 2020 WHO HIV treatment guidelines including recommending disaggregated indicators for adolescent HIV care and treatment.

Using evidence from the clinical studies, The Center for Disease Control and Prevention (CDC) USA launched an Epidemiologic Assistance (Epi-Aid) investigation in Malawi and Zimbabwe in 2013 in collaboration with LSHTM researchers. An Epi-Aid is a rapid and short-term investigation of an urgent public health problem by the US CDC. The focus of an Epi-Aid investigation is to assist partners in making rapid, practical decisions for actions to prevent and control the public health problem. It reinforced the findings of high prevalence of chronic respiratory morbidity among children with HIV taking ART, feeding into the WHO recommendation on the need to focus on HIV-related comorbidities, specifically lung disease.

New tools for HIV risk screening

The HIV screening tool algorithm which came out of the ZENITH study used a set of questions to identify adolescents at risk of being HIV positive. It was adapted and implemented widely in a number of PEPFAR (The President's Emergency Plan for AIDS Relief) supported countries for at-risk groups of adults, children (age 0 to 10) and adolescents (age 10 to 19). Ferrand chaired a symposium at the 2018 International AIDS Society meeting which showcased how the HIV screening tool could be used in primary care settings, as well as other strategies to encourage increased HIV testing (such as the economic incentives developed by Ferrand and colleagues) (5.5). The HIV screening tool was recognised as a best practice tool as part of the UNICEF 'Field Lessons' initiative to strengthen health services and outcomes among adolescents living with HIV (5.6).

According to a WHO scoping review, as of 2018, tools and questionnaires (either Ferrand's or as adapted by Bandason et al) were implemented in Zimbabwe, Zambia, Malawi, Uganda and Nigeria to screen adolescents for HIV, and regularly demonstrated high performance (5.7). In Zimbabwe, the algorithm was adapted and implemented among orphans and vulnerable children. In particular, Ferrand provided technical expertise to the Zimbabwe Ministry of Health/ CDC and the Elizabeth

Glaser Pediatric AIDS Foundation (EGPAF) to adapt the screening tool for use in primary care services.

Raising awareness and creative influence

To help address stigma and other issues faced by adolescents with HIV, Ferrand developed a film, 'Chiedza's Song', and open access educational materials which facilitated discussions in communities and schools (5.8). The film, which premiered at the International AIDS Conference in Durban in 2016, was adapted in partnership with the Ministry of Education and shown in schools in Zimbabwe. Ferrand was also involved in a 'Let Youth Lead' roundtable held at LSHTM in 2017, convened by Sentebale (a charity focused on providing psychosocial support to children and adolescents with HIV) and chaired by Prince Harry, the Duke of Sussex (Sentebale's co-founding patron). This led to a policy brief in 2017 (co-drafted by Ferrand) to support organisations working with adolescents with HIV in Africa to implement evidence-based programmes. The brief provided a snapshot of promising interventions in sub-Saharan Africa to improve outcomes among such groups (5.9).

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

5.1 World Health Organisation. 2013. HIV and adolescents: guidance for HIV testing and counselling and care for adolescents living with HIV: recommendations for a public health approach and considerations for policy-makers and managers.

- Ferrand on guideline development group (pg iii), research showcased (pg 69). References 14-16, 28, 42, 131.

5.2 World Health Organisation 2014. Report of the consultation on the treatment of HIV among adolescents. Meeting report 22-13 September 2014. Accessed at:

<https://www.who.int/hiv/pub/arv/consultation-hiv-treatment-adolescents/en/>

- Ferrand listed in Annex 2: list of participants

World Health Organisation. Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV. September 2015.

- Annex 2: evidence to decision-making tables and supporting evidence. Includes report of the consultation on the treatment guideline update (Annex 2.2.6) and Ferrand research referenced (reference list pg 321 & pg 70)

5.3 Zimbabwe Ministry of Health and Child Care 2014. Zimbabwe National guidelines on HIV testing and counselling

- Guidelines updated so that healthcare worker can give consent if parent or caregiver cannot, pg 6

5.4 WHO 2014. Scoping consultation on chronic comorbidities in people living with HIV. Accessed at: <https://www.who.int/hiv/pub/arv/consultation-comorbidities-plhiv/en/>

- Ferrand listed as participant in section 8

Invitation from Dr Gottfried Hirnschall, Director, Department of HIV and Global Hepatitis Programme, WHO, to Dr Rashida Ferrand to the Scoping Consultation: Integration of non-communicable disease prevention, assessment and treatment into HIV treatment programme (WHO) 9-10 April 2019.

5.5 IAS Symposium 2018 Session: "Getting to the first 95 for children and adolescents: Innovative approaches for pediatric case finding." Accessed at:

<http://programme.aids2018.org/Programme/Session/1166>

- Symposium session co-chaired by Ferrand to showcase use of HIV screening tool and other strategies, presentation by US Agency for International Development contains country implementation details

5.6 UNICEF 2013. Field Lessons: Strengthening Health Services and Outcomes for Adolescents Living with HIV.

- Research showcased pg 38

5.7 Quinn C, Wong V, Jamil MS, Baggaley RC, Johnson CC. Web Annex L. Symptom and risk-based screening to optimize HIV testing services: a scoping review. In: Consolidated guidelines on HIV testing services, 2019. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.

Duffy M, Sharer M, Berhan A, et al. HIV risk screening for high-yield community testing services for orphans and vulnerable children: a literature review. *Vulnerable Children and Youth Studies* 2018; **13**(2): 95-115. doi: [10.1080/17450128.2017.1332399](https://doi.org/10.1080/17450128.2017.1332399)

5.8 Chiedza's Song. Video and resources for schools. Accessed at: <https://mesh.tghn.org/articles/chiedzas-song-growing-hiv-zimbabwe/>

5.9 London School of Hygiene & Tropical Medicine and Sentebale, The Prince's Foundation for Children in Africa. Policy Brief: "Addressing challenges facing adolescents in knowing and managing their HIV status in sub-Saharan Africa". 2017.