

Folder eCC_00014424 is in stage Annual_Report_Due

Name of the University, Hospital, Research Institute, Academy or Ministry

London School of Hygiene and Tropical Medicine, LSHTM

Name of the Division, Department, Unit, Section or Area

Department of Clinical Research

City London **Reference Number** UNK-274

Title WHO Collaborating Centre for Sexually Transmitted Infections, STI

Report Year 05-2018 to 05-2019

- 1. Please briefly describe the progress made in the implementation of your agreed workplan as WHO collaborating centre during the past 12 months (or the reporting period listed above). Please report on how each workplan activity was implemented, if any outputs have been delivered, if any results have been achieved and if any difficulties have been encountered during this time. If an activity has previously been completed, has not started yet, or been placed on hold, please indicate this.**

The WHO Collaborating Centre for Sexually Transmitted Infections at the London School of Hygiene & Tropical Medicine (LSHTM) is based in the Clinical Research Department. Staff of the Department who work with WHO on STIs include Professors Rosanna Peeling, David Mabey, Philippe Mayaud, Rashida Ferrand and Deborah Watson-Jones; and Drs. Emma Harding-Esch, Kate Gallagher, Helen Kelly, Michael Marks, Jason Ong and Joe Tucker. Colleagues in other departments at LSHTM who also work with WHO on STIs include Drs. Suzanna Francis and Fern Terris-Prestholt.

In September 2018, we launched the Sexually Transmitted Infections Research Interest Group (STIRIG): <https://www.lshtm.ac.uk/research/centres-projects-groups/stirig>

STIRIG is co-directed by Dr Suzanna Francis (Faculty of Epidemiology and Population Health), Dr Emma Harding-Esch (Faculty of Infectious and Tropical Diseases) and Sarah Harman (Faculty of Epidemiology and Population Health).

STIRIG's aims are to:

- Raise awareness of STI-related research being conducted at LSHTM
- Increase cross-disciplinary and cross-Faculty work on STIs
- Develop internal and external collaborations
- Maximise funding opportunities

The steering committee has representatives from each of LSHTM's Faculties, as well as students and the MRC/UVRI & LSHTM Uganda Research Unit :

- Faculty of Epidemiology and Population Health: Richard Hayes, Aoife Doyle
- Faculty of Infectious and Tropical Diseases: Philippe Mayaud, Matthew Chico
- Faculty of Public Health and Policy: Peter Weatherburn, Matt Quaife
- MRC/UVRI & LSHTM Uganda Research Unit: Yunia Mayanja
- Students: Daniel McCartney (DrPH student), Caroline Gotsche (PhD student), Amanda Gabster (PhD student), Lauren Hall (MSc student)

STIRIG activities:

1. Website:

STIRIG's website (<https://www.lshtm.ac.uk/research/centres-projects-groups/stirig#welcome>) provides information on STIRIG structure and membership, events, newsletters, STI-related updates, research and collaborations, publications, and resources.

- STIRIG has over 67 members at LSHTM (<https://www.lshtm.ac.uk/research/centres-projects-groups/stirig#who-we-are>) and 116 members on its newsletter mailing list.

2. Seminars:

To date, STIRIG has hosted four seminars (<https://www.lshtm.ac.uk/research/centres-projects-groups/stirig#events>):

- “*Mycoplasma genitalium* - the 'silent' emerging super-bug”, Jason Ong (Monash University, Australia/LSHTM), Tuesday 11 December 2018
- “Pay-it-forward: a strategy for enhanced uptake of dual gonorrhoea and chlamydia testing among men who have sex with men in China”, Joe Tucker (LSHTM), Wednesday 30 January 2019
- “Epidemiology of oral HPV infection and HPV-related oropharyngeal cancer”, Marisa Mena (Bellvitge Biomedical Research Institute, Spain), Monday 25 March 2019
- “What drives adoption of innovations?”, Sebastian S Fuller (St George's, University of London), Monday 10 June 2019

3. Newsletters:

STIRIG also publishes a newsletter for internal and external colleagues. There have been 2 newsletters to date:

“STIRIG: What chlamydia research is happening at LSHTM?” November 2018 edition:
<https://us19.campaign-archive.com/?u=95833d08a96fe0a495c48e360&id=ccea0c1109>

- Gonorrhoea research at LSHTM” January 2019 edition: <https://us19.campaign-archive.com/?u=95833d08a96fe0a495c48e360&id=281fec55bb>
- The June 2019 newsletter focused on research degree students working on STIs: <https://us19.campaign-archive.com/?u=95833d08a96fe0a495c48e360&id=1a8b36d217>

Activity 1

Support the STI POCTs initiative (advise on research/validation, support normative work (guidelines), training on STI POCTs in LMICs).

Description:

- **Update the performance of commercially available POC STI tests**
- **Finalize TPPs and core protocols for evaluation of STI POC tests**
- **Technical advice on the road map for the evaluation and implementation of new STI POC tests**
- **Evaluation network for STI POC tests**
- **Investment cases for POC STI tests**

The ongoing evaluation of STI POCTs is a common priority shared by WHO RHR and the London School. Professors Peeling and Mabey have developed protocols for laboratory and clinic-based evaluation of POCTs for a variety of STIs in the past. In collaboration with Dr Igor Toskin, Prof Peeling has adapted those protocols into 9 core protocols that can be used for the independent clinic-based and clinic-utility validation of STIs POCTs in different populations and in different use case scenarios. Prof Peeling worked with Dr Toskin and other colleagues to finalise the site-specific protocols for independent clinic-based evaluation of dual HIV/syphilis POCT and POCT to detect NG/CT and TV in 12 countries and for the clinic-utility evaluation of dual HIV/syphilis tests in 5 countries, following feedback from the WHO ERC, and they have now been approved by the ERC.

Dr Harding-Esch is a member of the Public Health Applications of *Chlamydia trachomatis* Serology (PHACTS) group, with WHO leadership from Igor Toskin, which aims to develop Target Product Profiles for new diagnostics. In collaboration with colleagues at LSHTM (including STIRIG co-director Dr Suzanna Francis) and Public Health England, she is working on an ECDC-funded systematic literature review of novel testing technologies, strategies and approaches for testing high-risk populations for STIs in the EU/EEA.

Members of our centre have evaluated the performance of new POCTs for gonorrhoea and chlamydial infection as well as exploring the attitudes of patients and health care providers towards the use of POCTs and their implementation in health systems.

Prof Mayaud is developing proposals for setting up (and later evaluating) a fast track STI/HIV service provision model for key populations in Uganda with the MRC/UVRI & LSHTM Uganda Research Unit. The intervention will use existing POC or rapid tests (for HIV, syphilis, HBV, NG/CT GenXpert) to help orientate patients towards effective interventions: “Test and Treat”, Test

& vaccinate”, “Test and Prevent”. A first proposal has been submitted to evaluate the (cost)effectiveness of a fast tracking process for HBV vaccination among female sex workers in Kampala (both HIV-positive and negative) combining POC test for HBsAg and immediate short vaccination regimens (3 doses in 2 months) compared to standard serology (with one week delay for result) and starting standard regimens (3 doses in 6 months). Outcomes will include uptake, and sustained immunological response at 12 months).

Recent Publications on POC tests and testing

1. Aicken CRH, Sutcliffe LJ, Gibbs J, Tickle LJ, Hone K, Harding-Esch EM, Mercer CH, Sonnenberg P, Sadiq ST, Estcourt CS, Shahmanesh M. Using the eSexual Health Clinic to access chlamydia treatment and care via the internet: a qualitative interview study. *Sex Transm Infect.* 2018 Jun;94(4):241-247. doi: 10.1136/sextrans-2017-053227.
2. Dassah ET, Adu-Sarkodie Y, Mayaud P. Rollout of rapid point of care tests for antenatal syphilis screening in Ghana: healthcare provider perspectives and experiences. *BMC Health Serv Res.* 2018 ;18(1):130. doi: 10.1186/s12913-018-2935-y.
3. Harding-Esch EM, Fuller SS, Christine Chow SL, Nori AV, Harrison MA, Parker M, Piepenburg O, Forrest MS, Brooks DG, Patel R, Hay P, Fearnley N, Pond MJ, Kevin Dunbar J, Butcher PD, Planche T, Lowndes CM, Tariq Sadiq S. Diagnostic accuracy of a prototype rapid chlamydia and gonorrhoea recombinase polymerase amplification assay: a multi-centre cross-sectional pre-clinical evaluation. *Clin Microbiol Infect.* 2018. pii: S1198-743X(18)30462-2. doi: 10.1016/j.cmi.2018.06.003.
4. Harding-Esch EM, Cousins EC, Chow SC, Phillips LT, Hall CL, Cooper N, Fuller SS, Nori AV, Patel R, Thomas-William S, Whitlock G, Edwards SJE, Green M, Clarkson J, Arlett B, Dunbar JK, Lowndes CM, Sadiq ST. A 30-Min Nucleic Acid Amplification Point-of-Care Test for Genital *Chlamydia trachomatis* Infection in Women: A Prospective, Multi-center Study of Diagnostic Accuracy. *EBioMedicine.* 2018;28:120-127. doi: 10.1016/j.ebiom.2017.12.029.
5. Kerry-Barnard S, Fleming C, Reid F, Phillips R, Drennan VM, Adams EJ, Majewska W, Balendra A, Harding-Esch E, Cousins E, Tariq Sadiq S, Oakeshott P. 'Test n Treat (TnT)''- Rapid testing and same-day, on-site treatment to reduce rates of chlamydia in sexually active further education college students: study protocol for a cluster randomised feasibility trial. *Trials.* 2018 ;19(1):311. doi: 10.1186/s13063-018-2674-8.
6. Oakeshott P, Kerry-Barnard S, Fleming C, Phillips R, Drennan VM, Adams EJ, Majewska W, Harding-Esch EM, Cousins EC, Planche T, Green A, Bartholomew RI, Sadiq ST, Reid F. 'Test n Treat' (TnT): a cluster randomized feasibility trial of on-site rapid Chlamydia trachomatis tests and treatment in ethnically diverse, sexually active teenagers attending technical colleges. *Clin Microbiol Infect.* 2018 Nov 1. pii: S1198-743X(18)30724-9. doi: 10.1016/j.cmi.2018.10.019.

7. Huntington SE, Burns RM, Harding-Esch E, Harvey MJ, Hill-Tout R, Fuller SS, Adams EJ, Sadiq ST. Modelling-based evaluation of the costs, benefits and cost-effectiveness of multipathogen point-of-care tests for sexually transmitted infections in symptomatic genitourinary medicine clinic attendees. *BMJ Open*. 2018 Sep 10;8(9):e020394. doi: 10.1136/bmjopen-2017-020394.
8. Fuller, Sebastian S; Pacho, Agata; Broad, Claire E; Nori, Achyuta V; Harding-Esch, Emma M; Sadiq, Syed Tariq; (2019) "It's not a time spent issue, it's a 'what have you spent your time doing?' issue..." A qualitative study of UK patient opinions and expectations for implementation of Point of Care Tests for sexually transmitted infections and antimicrobial resistance. *PLOS ONE*, 14 (4).
9. Peelin R and Mabey D Point-of-care tests to reduce the burden of sexually transmitted infections. *Lancet Infect Dis*. 2019 Jun;19(6):570-571.

Activity 2

Title: Assist WHO in activities that aim to improve STI control and prevention in key populations, mainly MSM, as well as to improve SRH services in adolescents.

Research into social entrepreneurship and crowdsourcing approaches to enhance the uptake of STI testing in MSM

Prof Peeling, Dr. Jason Ong, and Dr. Joe Tucker have worked on organizational characteristics of HIV/syphilis testing services for men who have sex with men in South China since 2010 using social entrepreneurship and demonstrating that it is an effective service model. This work resulted in a "Practical Guide on Crowdsourcing in Health and Health Research" that was launched at a special session of the International AIDS Society Conference in Amsterdam, the Netherlands. In addition, a crowdsourced project called "pay-it-forward" was found to increase gonorrhoea/chlamydia test uptake among MSM in China. This was selected as one of the top ten innovations at the World Health Summit (Berlin, Germany) and also at the UNAIDS Health Innovation Exchange, a side event to the 72nd Annual World Health Assembly.

Research into STI epidemiology among users of pre-exposure prophylaxis (PrEP) for HIV

Drs. Philippe Mayaud, Jason Ong and Joseph Tucker led a systematic review and meta-analysis of the prevalence and incidence of STIs among PrEP users, in collaboration with the WHO HIV Department and WHO Department of Reproductive Health and Research. This work was presented at the WHO Think Tank Meeting in Montreux, Switzerland (March 2019) and is currently being prepared for publication.

Research on the epidemiology of sexually transmitted infections in a cohort of transgender women in São Paulo, Brazil

Prof Mayaud and Daniel McCartney set up a cohort study of transgender women in collaboration with the Santa Casa de São Paulo School of Medicine in Brazil, to assess the prevalence and incidence of STIs, including *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG),

Trichomonas vaginalis (TV), *Lymphogranuloma venereum* (LGV) and *Mycoplasma genitalium* (MG) through etiological diagnosis of self-collected samples from potential infection sites, including anorectal, oropharyngeal and neovaginal. A preliminary study was conducted to assess the acceptability of providing self-collected samples among a sample of transgender women. 23 participants completed an investigator-led survey, 16 of whom (69.6%) stated that they had never had an STI test that used a urine sample or STI swab in the past. All participants provided a positive response willing to give samples for screening of other STIs during a future visit, and all indicated that they would feel comfortable collecting samples by themselves if they received information on how to collect.

A STIRIG tweet during Joe Tucker's STIRIG seminar, lamenting the lack of STI research advocates and how no-one wanted to be the face of an STI, triggered responses from other STI researchers on Twitter, many posting pictures/artwork of their favourite organisms and giant microbe fluffy toys. Jackie Cassell, one of the editors for BMJ STI picked up on it and coined the hashtag #FaceOfAnSTI. The STI and HIV 2019 World Congress have also responded and will have a corner at their conference in Vancouver in July dedicated to #FaceOfAnSTI, to publicise the work of STI researchers and advocates. Giant Microbes will donate gigantic versions of STI microbes, as well as smaller versions to give away.

Recent Publications on STIs in key populations

1. TDR. (2018) Crowdsourcing in health and health research: a practical guide. Geneva: World Health Organization; 2018. TDR/STRA/18.4. Licence: CC BY-NC-SA 3.0 IGO.
2. Tang W., Wei C., Cao B., Tucker, J.D. (2018) Crowdsourcing to expand HIV testing among men who have sex with men in China: A closed cohort stepped wedge cluster randomized controlled trial. *PloS Medicine*. 15(8):e1002645. doi: 10.1371/journal.pmed.1002645
3. Li KT, Tang W, Wu D, ..., Tucker JD. (2019) Pay-it-forward strategy to enhance uptake of dual gonorrhoea and chlamydia testing among men who have sex with men in China: a pragmatic, quasi-experimental study. *Lancet Infect Dis*. 2019 Jan;19(1):76-82. doi:10.1016/S1473-3099(18)30556-5. PubMed PMID: 30587296.
4. Tucker JD, Day S, Tang W, Bayus B. Crowdsourcing in medical research: concepts and applications. *PeerJ*. 2019 Apr 12;7:e6762. doi: 10.7717/peerj.6762. eCollection 2019. PubMed PMID: 30997295; PubMed Central PMCID: PMC6463854.
5. Smith MK, Stein G, Cheng W, Miller WC, Tucker JD. Correction to: Identifying high risk subgroups of MSM: a latent class analysis using two samples. *BMC Infect Dis*. 2019 Mar 26;19(1):284. doi: 10.1186/s12879-019-3886-6. PubMed PMID: 30914046; PubMed Central PMCID: PMC6434628.
6. Zhao P, Liu L, Zhang Y, Cheng H, Cao B, Liu C, Wang C, Yang B, Wei C, Tucker JD, Tang W. The interaction between HIV testing social norms and self-efficacy on HIV testing among Chinese men who have sex with men: results from an online cross-sectional study. *BMC Infect Dis*. 2018 Oct 30;18(1):541. doi: 10.1186/s12879-018-3454-5. PubMed PMID: 30376818; PubMed Central PMCID: PMC6208016.

7. Tang W, Mao J, Liu C, Mollan K, Zhang Y, Tang S, Hudgens M, Ma W, Kang D, Wei C, Tucker JD; SESH study group#. Reimagining Health Communication: A Non-Inferiority Randomized Controlled Trial of Crowdsourced intervention in China. *Sex Transm Dis.* 2018 Oct 22. doi: 10.1097/OLQ.0000000000000930. [Epub ahead of print] PubMed PMID: 30363026.
8. Day S, Blumberg M, Vu T, Zhao Y, Rennie S, Tucker JD. Stakeholder engagement to inform HIV clinical trials: a systematic review of the evidence. *J Int AIDS Soc.* 2018 Oct;21 Suppl 7:e25174. doi: 10.1002/jia2.25174. Review. PubMed PMID: 30334358; PubMed Central PMCID: PMC6192899.
9. Ong JJ, Liao M, Lee A, Fu H, Pan SW, Tang W, Wei C, Dan W, Yang B, Yang L, Wang C, Tucker JD*. Bridging the HIV-syphilis testing gap: dual testing among men who have sex with men living in China. *Sex Transm Infect.* 2018 Aug 20. pii:sextrans-2018-053527. doi: 10.1136/sextrans-2018-053527. [Epub ahead of print] PubMed PMID: 30126948.
10. Cao B, Zhao P, Bien C, Pan S, Tang W, Watson J, Mi G, Ding Y, Luo Z, Tucker JD. Linking young men who have sex with men (YMSM) to STI physicians: a nationwide cross-sectional survey in China. *BMC Infect Dis.* 2018 May 18;18(1):228. doi: 10.1186/s12879-018-3145-2. PubMed PMID: 29776395.
11. Ong JJ, Fu H, Pan S, Smith MK, Wu D, Wei C, Cao B, Ma W, Yang L, Tang W, Tucker JD. Missed Opportunities for Human Immunodeficiency Virus and Syphilis Testing Among Men Who Have Sex With Men in China: A Cross-Sectional Study. *Sex Transm Dis.* 2018 Jun;45(6):382-386. doi: 10.1002/jia2.25098
12. Ong JJ, Fu H, Smith MK, Tucker JD. Expanding syphilis testing: a scoping review of syphilis testing interventions among key populations. *Expert Rev Anti Infect Ther.* 2018;16(5):423-432. doi: 10.1080/14787210.2018.1463846.
13. Ong JJ, Wu D, Huang W, Fu H, Desmond N, Ma W, Kang D, Liao M, Marley G, Wei C, Tang W, Liu C, Zhang Y, Pan SW, Yang B, Yang L, Huang S, Tucker JD. Pressured HIV testing "in the name of love": a mixed methods analysis of pressured HIV testing among men who have sex with men in China. *J Int AIDS Soc.* 2018;21(3):e25098. doi: 10.1002/jia2.25098
14. Tucker JD, Pan SW, Mathews A, Stein G, Bayus B, Rennie S. Ethical Concerns of and Risk Mitigation Strategies for Crowdsourcing Contests and Innovation Challenges: Scoping Review. *J Med Internet Res.* 2018 ;20(3):e75. doi: 10.2196/jmir.8226
15. Watson J, Tang W, Pan S, Wu D, Zhao P, Cao B, Liu C, Bien C, Huang W, Luo Z, Tucker JD Out of the Closet, Into the Clinic: Opportunities for Expanding MSM-Competent Services in China. *Sex Transm Dis.* 2018. doi: 10.1097/OLQ.0000000000000808. [Epub ahead of print]
16. Wu D, Li KT, Tang W, Ong JJ, Huang W, Fu H, Lee A, Wei, Tucker JD. Low chlamydia and gonorrhoea testing rates among men who have sex with men in Guangdong and Shandong Provinces, China. *Sex Transm Dis.* 2018 Dec 7. doi: 10.1097/OLQ.0000000000000963.
17. Li KT, Tang W, Wu D, Huang W, Wu F, Lee A, Feng H, Pan SW, Han L, Mak V, Yang L, Tucker JD. Pay-it-forward strategy to enhance uptake of dual gonorrhoea and chlamydia testing among men who have sex with men in China: a pragmatic, quasi-

- experimental study. *Lancet Infect Dis.* 2019 Jan;19(1):76-82. doi: 10.1016/S1473-3099(18)30556-5.
18. Yang LG, Zhang XH, Zhao PZ, Chen ZY, Ke WJ, Ren XQ, Wang LY, Chen WY, Tucker JD. Gonorrhoea and chlamydia prevalence in different anatomical sites among men who have sex with men: a cross-sectional study in Guangzhou, China. *BMC Infect Dis.* 2018 Dec 18;18(1):675. doi: 10.1186/s12879-018-3579-6.
 19. Cao, B; Zhao, P; Bien-Gund, C; Tang, W; Ong, JJ; Fitzpatrick, T; Tucker, JD; Luo, Z; (2018) The Web-Based Physician is Ready to See You: A Nationwide Cross-Sectional Survey of Physicians Using a Mobile Medical App to Evaluate Patients With Sexually Transmitted Diseases in China. *JMIR mHealth and uHealth*, 6 (10). e10531. ISSN 2291-5222 DOI: <https://doi.org/10.2196/10531>
 20. Beksinska, A; Prakash, R; Isac, S; Mohan, HL; Platt, L; Blanchard, J; Moses, S; Beattie, TS; (2018) Violence experience by perpetrator and associations with HIV/STI risk and infection: a cross-sectional study among female sex workers in Karnataka, south India. *BMJ open*, 8 (9). e021389. ISSN 2044-6055 DOI: <https://doi.org/10.1136/bmjopen-2017-021389>
 21. M Kumi, Smith; Stein, Gabriella; Cheng, Weibin; Miller, William C; Tucker, Joseph D; (2019) Identifying high risk subgroups of MSM: a latent class analysis using two samples. *BMC infectious diseases*, 19 (1).213.
 22. Kohli, Manik; Hickson, Ford; Free, Caroline; Reid, David; Weatherburn, Peter; (2019) Cross-sectional analysis of chemsex drug use and gonorrhoea diagnosis among men who have sex with men in the UK. *SexualHealth*. DOI: <https://doi.org/10.1071/SH18159>
 23. Kuteesa, Monica O; Quaiife, Mathew; Biraro, Sam; Katumba, Kenneth R; Seeley, Janet; Kamali, Anatoli; Nakanjako, Damalie; (2019) Acceptability and predictors of uptake of anti-retroviral Pre-Exposure Prophylaxis (PrEP) among fishing communities in Uganda: a cross-sectional discrete choice experiment survey. *AIDS and behavior*. *AIDS Behav.* 2019 Feb 8.

Studies on sexual and reproductive health in adolescents

Professor Ferrand is leading a cluster randomised trial in Zimbabwe (the CHIEDZA trial) evaluating the impact of a multicomponent package of SRH and HIV services offered to 16-24 year olds in a community-based setting on population level HIV and SRH outcomes. The CHIEDZA package will be offered to all clients aged 16-24 year olds living in the intervention clusters (a geographically defined area that includes a community venue and a primary care clinic). A additional study will investigate the uptake, acceptability, prevalence and yield of STI screening using the GC/CT Genexpert assay is embedded within the CHIEDZA trial. STI screening will be offered to all clients attending the CHIEDZA service, including those who present with STI symptoms. The outcomes will be:

- 1) Uptake of STI screening
- 2) Prevalence and yield of chlamydia and gonorrhoea infection
- 3) % of symptomatic clients who are GC and/or chlamydia positive
- 4) % of partners that attend for screening and treatment

She will also conduct a qualitative assessment of KAP and acceptability of STI screening.

Prof Mayaud is working with two PhD students in Panama (Amanda Gabster) and Tanzania (Ruby Mcharo) on adolescent STI epidemiology, and developing STI testing programmes with adolescent accessing PREP in Uganda. In Panama, among indigenous populations, rates of Chlamydia and syphilis were found to be very high (syphilis particularly in boys) and STI were related to forced and transactional sex.

Recent Publications on SRH in adolescents

1. Morhason-Bello I, Kabakama S, Baisley K, Francis SC, Watson-Jones D. Reported oral and anal sex among heterosexual adolescents and adults in sub-Saharan Africa: A systematic review. *Reprod. Health* **16**, 48 (2019).
2. Francis SC, Miro G, Nakuya K, Rutakumwa R, Nakiyingi-Miro J, Nabaggala G, Musoke S, Namakula J, Tanton C, Torondel T, Ross DA, Weiss HA. Self-collection of vaginal swabs among adolescent girls in a school-setting in East Africa. *Sexually Transmitted Diseases*, 2019 May 5; 46 (5).
3. Baisley, Kathy; Andreasen, Aura; Irani, Julia; Nnko, Soori; Changalucha, John; Crucitti, Tanya; Francis, Suzanna Carter; Hansen, Christian; Hayes, Richard; Buve, Anne; +1 more... (2019) HPV prevalence around the time of sexual debut in adolescent girls in Tanzania. *Sexually Transmitted Infections*. (In Press)
4. Francis, Suzanna C; Holm Hansen, Christian; Irani, Julia; Andreasen, Aura; Baisley, Kathy; Jaspers, Vicky; Crucitti, Tania; Changalucha, John; Hayes, Richard J; Nnko, Soori; +2 more... (2018) Results from a cross-sectional sexual and reproductive health study among school girls in Tanzania: high prevalence of bacterial vaginosis. *Sexually transmitted infections*. ISSN 1368-4973 DOI: <https://doi.org/10.1136/sextrans-2018-053680>
5. Gabster A, Pascal JM, Cislighi B, Francis S, Weiss HA, Martinez A, Ortiz A, Herrera HM, Gantes C, Quiel Y, Ríos, Campbell E, Mayaud P. High prevalence of sexually transmitted infections, and high-risk sexual behaviors among indigenous adolescents of the Comarca Ngäbe-Buglé, Panama. Submitted.
6. Gabster A, Mayaud P, Pascale JM, Cislighi B. How Gender Norms affect indigenous adolescents' sex related choices and actions: a qualitative study in Panama. Submitted.

Activity 3

Title: Assist WHO in activities that aim to improve women's and children's health particularly in the area of dual elimination of mother to child transmission of HIV and Syphilis (eMTCT) and prevention of cervical cancer.

Description:

- **Update dashboard for eMTCT of HIV and Syphilis**
- **Update toolkit development for eMTCT of HIV and Syphilis**
- **Conduct epidemiological studies of HPV and related disease in various population groups**
- **Evaluate the efficacy of HPV vaccination for the prevention of cervical cancer**
- **Produce systematic reviews, clinical validation studies and health economic evaluations for HPV**

Studies on eMTCT of HIV and syphilis

Prof Peeling is a member of the WHO/UNAIDS Global Validation Advisory Committee (GVAC) for the dual elimination of the Mother to Child Transmission of HIV and Syphilis. She participated in the review of dossiers submitted to GVAC from countries claiming to have achieved elimination of HIV and Syphilis. She also contributed to the revision of the dual elimination handbook. In particular, she developed diagnostic quality standards that countries need to meet when they submit data to prove that they have achieved elimination. The International Diagnostics centre has created a dashboard to help countries track their progress with dual elimination. Prof Peeling worked with WHO RHR on a systematic review of the accuracy of dual rapid HIV-syphilis syphilis test.

Prof Mayaud has continued to publish on an evaluation of utilisation of Syphilis POC test in Ghana and obstacles in implementation. He is starting new studies at MRC/UVRI/LSHTM Uganda on charting the progress towards eMTCT of syphilis and HIV with an evaluation of the implementation of the new (Oct 2018) Ugandan guidelines of dual testing using HIV and Syphilis Duo test to determine if there is any improvement in testing (and treatment) rates for both infections and the overall cure rates (the WHO 95-95-90 criteria) comparing the period of 9 months before and 9 months after implementation. The study will start in summer 2019.

Recent publications on eMTCT of HIV and syphilis

1. Dassah ET, Adu-Sarkodie Y, Mayaud P. Rollout of rapid point of care tests for antenatal syphilis screening in Ghana: Health care provider perspectives and experiences. *BMC Health Services Research*. 2018;18(1):130.
2. Perez F, Mayaud P. One step in the right direction: improving syphilis screening and treatment in pregnant women in Africa. *Lancet Global Health*. 2019. pii: S2214-109X(19)30064-6.
3. Liu H, Chen N, Yu J, Tang W, He J, Xiao H, Lin S, Hu F, Feng Q, Tucker JD, Xia H, Qiu X. Syphilis-attributable adverse pregnancy outcomes in China: a retrospective cohort analysis of 1187 pregnant women with different syphilis treatment. *BMC Infect Dis*. 2019;19(1):292. doi: 10.1186/s12879-019-3896-4. PubMed PMID: 30925908; PubMed Central PMCID: PMC6439997.

Epidemiological studies on HPV and related diseases

Profs. Mayaud and Watson-Jones and Drs Kelly and Gallagher have completed studies on the epidemiology and prevention of HPV infection in Tanzania, Ghana, Burkina Faso and South Africa and published their results. The studied populations have included general populations of young women, HIV-negative and HIV-positive women and men.

Recent Publications on HPV epidemiology and risk factors

1. Chikandiwa A, Kelly H, Sawadogo B, Ngou J, Pisa PT, Gibson L, Didelot MN, Meda N, Weiss HA, Segondy M, Mayaud P, Delany-Moretlwe S; HARP Study Group. Prevalence, incidence and correlates of low risk HPV infection and anogenital warts in a cohort of women living with HIV in Burkina Faso and South Africa. *PLoS One*. 2018 May 1;13(5):e0196018. doi: 0.1371/journal.pone.0196018
2. Chikandiwa A, Pisa PT, Chersich MF, Muller EE, Mayaud P, Delany-Moretlwe S. Oropharyngeal HPV infection: prevalence and sampling methods among HIV-infected men in South Africa. *Int J STD AIDS*. 2018 Jul;29(8):776-780. doi: 10.1177/0956462418755882.
3. Chikandiwa A, Chimoyi L, Pisa PT, Chersich MF, Muller EE, Michelow P, Mayaud P, Delany-Moretlwe S. Prevalence of anogenital HPV infection, related disease and risk factors among HIV-infected men in inner-city Johannesburg, South Africa: baseline findings from a cohort study. *BMC Public Health*. 2017 Jul 4;17(Suppl 3):425. doi: 10.1186/s12889-017-4354-0.
4. Doutre S, Omar T, Goubri-Lompo O, Kelly H, Clavero O, Zan S, Chikandiwa A, Sawadogo B, Delany-Moretlwe S, Costes V, Mayaud P, Segondy M; HARP Study Group. Cervical intraepithelial neoplasia (CIN) in African women living with HIV: role and effect of rigorous histopathological review by a panel of pathologists in the HARP study endpoint determination. *J Clin Pathol*. 2018 Jan;71(1):40-45. doi: 10.1136/jclinpath-2017-204512. Epub 2017
5. Gallagher KE, Erio T, Baisley K, Lees S, Watson-Jones D. The impact of a human papillomavirus (HPV) vaccination campaign on routine primary health service provision and health workers in Tanzania: a controlled before and after study. *BMC Health Serv Res*. 2018 Mar 12;18(1):173. doi: 10.1186/s12913-018-2976-2.
6. Kelly H, Faust H, Chikandiwa A, Ngou J, Weiss HA, Segondy M, Dillner J, Delany-Moretlwe S, Mayaud P. Human Papillomavirus Serology Among Women Living With HIV: Type-Specific Seroprevalence, Seroconversion, and Risk of Cervical Reinfection. *J Infect Dis*. 2018 . doi: 10.1093/infdis/jiy252.
7. Segondy M, Ngou J, Kelly H, Omar T, Goubri-Lompo O, Doutre S, Mayaud P, Didelot MN. Diagnostic value of human papillomavirus (HPV) 16 and HPV18 viral loads for the

detection of high-grade cervical intraepithelial neoplasia (CIN2+) in a cohort of African women living with HIV. *J Clin Virol.* 2018;99-100:79-83. doi: 10.1016/j.jcv.2018.01.006.

8. Chikandiwa A, Pisa PT, Muller EE, Tamalet C, Mayaud P, Chersich MF, Delany-Moretlwe S. Incidence, persistence, clearance, and correlates of genital human papillomavirus infection and anogenital warts in a cohort of men living with Human Immunodeficiency Virus in South Africa. *Sexually Transmitted Diseases* 2019; Feb 20. doi: 10.1097/OLQ.0000000000000979
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11. Wang, Q; Ma, X; Zhang, X; Ong, JJ; Jing, J; Zhang, L; Wang, LH; (2018) Human papillomavirus infection and associated factors for cervical intraepithelial neoplasia in women living with HIV in China: a cross-sectional study. *Sexually transmitted infections.* ISSN 1368-4973 DOI: <https://doi.org/10.1136/sextrans-2018-053636>

Studies on HPV vaccination and the prevention of cervical cancer

Profs Mayaud and Watson-Jones and colleagues published a number of papers on systematic reviews of HPV and HIV, of screening strategies for cervical cancer among women living with HIV, and on strategies for improving the uptake of HPV vaccination in LMICs.

Prof Mayaud and Dr Kelly with colleagues at Queen Mary University London (QMUL) have evaluated the potential usefulness of additional triage test such as DNA methylation of human genes to improve cervical cancer screening among women living with HIV in Africa. The encouraging results (high specificity for more severe lesions CIN3) have led to the development of a proposal to test a range of methylation assays (commercial and in house) targeting human genes as well as HPV genes on the already collected HARP samples and possibly other specimens as a collaboration between LSHTM, QMUL and ICO (Catalan institute of Oncology in Barcelona) (Marie Curie Fellowship obtained by Dr Kelly). The work has included a systematic review of the performance of existing methylation assays, confirming the high specificity of the QMUL in-house assay. A manuscript will soon be submitted. Prof Mayaud and Dr Kelly have also conducted a systematic review of the effect of antiretroviral therapy (ART) on the natural history of anal HPV lesions.

Recent Publications on HPV screening and vaccination

1. Gallagher KE, LaMontagne DS, Watson-Jones D. Status of HPV vaccine introduction and barriers to country uptake. *Vaccine*. 2018 Mar 23. pii: S0264-410X(18)30167-1. doi: 10.1016/j.vaccine.2018.02.003. [Epub ahead of print]
2. Kelly H, Weiss HA, Benavente Y, de Sanjose S, Mayaud P; ART and HPV Review Group. Association of antiretroviral therapy with high-risk human papillomavirus, cervical intraepithelial neoplasia, and invasive cervical cancer in women living with HIV: a systematic review and meta-analysis. *Lancet HIV*. 2018;5(1):e45-e58. doi: 10.1016/S2352-3018(17)30149-2.
3. Looker KJ, Rönn MM, Brock PM, Brisson M, Drolet M, Mayaud P, Boily MC. Evidence of synergistic relationships between HIV and Human Papillomavirus (HPV): systematic reviews and meta-analyses of longitudinal studies of HPV acquisition and clearance by HIV status, and of HIV acquisition by HPV status. *J Int AIDS Soc*. 2018 Jun;21(6):e25110. doi: 10.1002/jia2.25110.
4. Kelly H, Chikandiwa A, Warman R, Segondy M, Sawadogo B, Vasiljevic N, Didelot MN, Meda N, Weiss HA, Delany-Moretlwe S, Mayaud P, Lorincz A: Associations of human tumour suppressor gene *EPB41L3* DNA methylation and cervical intraepithelial neoplasia in women living with HIV-1 in Africa. *AIDS* 2018 Sep 24; 32(15): 2227-2236.
5. Kelly H, Chikandiwa A, Alemany Vilches L, Palefsky J, deSanjose S, Mayaud P. Effective antiretroviral therapy, anal high-risk human papillomavirus, anal intraepithelial neoplasia and anal cancer: a systematic review and meta-analysis. (submitted)
6. Gallagher, KE; Kelly, H; Cocks, N; Dixon, S; Mounier-Jack, S; Howard, N; Watson-Jones, D; (2018) Vaccine programme stakeholder perspectives on a hypothetical single-dose human papillomavirus (HPV) vaccine schedule in low and middle-income countries. *Papillomavirus research* (Amsterdam, Netherlands). ISSN 2405-8521
DOI: <https://doi.org/10.1016/j.pvr.2018.10.004>

2. Please briefly describe your collaboration with WHO with regards to the activities of the WHO collaborating centre during the past 12 months (e.g. means of communication, frequency of contact, visits to or from WHO). Please feel free to mention any difficulties encountered (if any) and to provide suggestions for increased or improved communication (if applicable).

Profs Peeling and Mayaud have made frequent visits to WHO in the past year to discuss our collaboration in the field of STI/SRH. Prof Mabey was a member of the committee which reviewed target product profiles for POC tests for the diagnosis of gonococcal infections and for identifying antimicrobial susceptibility of *Neisseria gonorrhoeae* in 2019 . Prof Peeling is a member of the

WHO/UNAIDS Global Validation Advisory Committee (GVAC) for the dual elimination of the Mother to Child.

Prof. Peeling and Dr. Tucker have visited the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases several times in the past year to discuss the Social Innovation in Health Initiative, a program that supports several STD-related projects. Both Dr. Peeling and Dr. Tucker are members of the TDR Global Working Group. In addition, Dr. Tucker has organized three open challenge contests in partnership with the TDR related to infectious diseases.

Prof Mayaud is a member of the committee reviewing the burden of STI, of the committee reviewing the management of STIs and Syndromic management guidelines. Prof Mayaud has been nominated by Dr James Kiarie (WHO/RRH) as an STI expert to the International Health Regulations (IHR) Roster of Experts. Dr Harding-Esch is a member of the Public Health Applications of *Chlamydia trachomatis* Serology (PHACTS) group, with WHO leadership from Igor Toskin, which aims to develop Target Product Profiles for new diagnostics. In collaboration with colleagues at LSHTM and Public Health England, she is working on an ECDC-funded systematic literature review of novel testing technologies, strategies and approaches for testing high-risk populations for STIs in the EU/EEA.

Prof Peeling has interacted with WHO regional offices in Europe, Africa, Western Pacific, South East Asia and South America to discuss the evaluation and implementation of improved diagnostic tests for syphilis and other STIs, including Zika virus. Dr Natalie Broutet (WHO RHR) convened two meeting of experts in Geneva to discuss the sexual transmission of zika virus, and to develop research protocols that would lead to a better understanding of this phenomenon; Prof Mayaud was invited to present at those meetings his work with colleagues from EU funded Horizon 2020 ZIKAlliance.

STIRIG launched on 18th September 2018 (<https://www.lshtm.ac.uk/newsevents/events/lshtms-sti-research-interest-group-stirig-launch>). The keynote address was by Dr Teodora Wi (Medical Officer, Human Reproduction, World Health Organisation): “End the silence! Research, Sex and STIs”. Following the success of the launch, a symposium is being planned for late-2019/early 2020, focusing on “Antimicrobial resistance and sexually transmitted infections”. This will be co-hosted with LSHTM’s AMR Centre (<https://amr.lshtm.ac.uk/>) and the Bristol Sexual Health Improvement Programme (SHIP; <http://www.bristolhealthpartners.org.uk/health-integration-teams/sexual-health-improvement-hit/more-about-shipp/>) who hosted the first AMR-STI symposium in September 2018 (<http://www.bristolhealthpartners.org.uk/events/view/2018/09/21/preparing-sexual-health-services-for-the-challenge-of-antimicrobial-resistant-bacteria/331>). STIRIG has been in discussions with Dr Wi to develop the symposium’s programme, including having international speakers to enable lessons learned between the UK and other countries. The current symposium themes are: Surveillance; STI prevention and control; Treatment guidelines; New treatment initiatives; Antibiotic stewardship; New diagnostic initiatives (point of care tests); Vaccines; Bring it all together and future plans.

Please briefly describe any interactions or collaborations with other WHO collaborating centres in the context of the implementation of the above activities (if any). If you are part of a network of WHO collaborating centres, please also mention the name of the network, and describe any involvement in the network during the last 12 months.

Prof Mayaud has collaborated with colleagues from Europe, Brazil and other Latin American countries in the large ZIKAlliance Consortium. The main aims of the Consortium are to quantify the incidence, transmission and impact of Zikavirus among humans (maternal and sexual transmission). In Brazil, they were able to demonstrate a moderate impact of Zikavirus on fertility among infected males. The Consortium has also submitted its research study design and a review of maternal diagnosis of TORCH infections including Zika showing the disparity of quality of diagnosis of these infections which for many have not been standardised or improved for decades leading to a general neglect or poor testing practices in resource constrained environments.

Publications on maternal and sexual transmission of Zika virus

1. Avelino-Silva V, Alvarenga C, Tozetto-Mendoza T, Canto CL, Manuli E, Abreu C, Mendes-Correa MC, Sabino EC, Figueiredo WM, Pannuti CS, Segurado AC, **Mayaud P**. Potential effect of Zika virus infection on human male fertility. *Revista do Instituto de Medicina Tropical de São Paulo*. 2018 Oct 25; 60:e64.
2. Avelino-Silva VI, **Mayaud P**, Rosenberger KD, et al... [...], Jaenisch T, and the ZIKAlliance Clinical Study Group. Multicentric cohorts to study Zika virus infection in pregnant women, infants and acute clinical cases in Latin America and the Caribbean: the ZIKAlliance Consortium. *BMC Infect Dis*. (under review).
3. Voordouw ACG, Rockx B, Jaenisch TJ, Fraaij P, **Mayaud P**, Vossen ACTM, Koopmans M. TORCH diagnostic practice analysis to improve pre- and postnatal testing of Zika virus infection. *Clinical Microbiological Reviews* (under review).
4. Kim CR, Counotte M, Bernstein K, Deal C, Mayaud P, Low N, Broutet N; Investigating the sexual transmission of Zika virus. Transmission of Zika virus Expert Meeting participants. *Lancet Glob Health*. 2018 Jan;6(1):e24-e25. doi: 10.1016/S2214-109X(17)30419-9.
5. WHO. Sexual transmission of Zika Virus: Current status, challenges and research priorities. WHO: Geneva, Dec 2017. WHO/RHR/17.23.

3. Please briefly describe any type of technical, programmatic, advisory or other support received from WHO during the past 12 months for the implementation of the agreed activities listed above (if any).

Prof Mayaud has received two grants from WHO's recent RFPs, as part of Consortia looking at estimating the burden of non-sexual HSV1-related disease (Project 1 led by University of Bristol – PI: K Looker) and modelling the interactions between HSV-2 and HIV to estimate the burden of HSV2 associated HIV infections to predict the impact of HSV2 vaccines (Project 2 led by Imperial

College London - PI: MC Boily). The WHO is seeking to reinvigorate efforts in the research of HSV1 and HSV2 vaccines for global use. Manuscripts on the global burden of HSV-1 ophthalmic and neurologic diseases are being prepared. The work on HSV2 vaccine is ongoing. A systematic review of the impact of ART on HSV2 outcomes (genital shedding and disease manifestations) is being conducted. Prof Mayaud has also received a RFP from WHO to conduct a systematic review of STI prevalence and incidence among HIV PREP users and models of STI care within PREP services. The work was done with Dr Jason Ong and presented at the PREP STI Think Tank group in March 2019 in Montreux. A manuscript and a report are being developed and results will be presented in a satellite workshop at the upcoming IAS Conference in Mexico (July 2019).