A RESEARCH REVIEW™
CONFERENCE REVIEW

Making Education Easy

Virtual Meeting, November 16-20, 2020

In this issue:

Abbreviations used in this review

ART = antiretroviral therapy
ARV = antiretroviral
ESR = Institute of Environmental Science and Research
CDC = Centers for Disease Control and Prevention
HIV = human immunodeficiency virus
hs-CRP = high-sensitivity C-reactive protein
HSV = herpes simplex virus
LDL = low-density lipoprotein
MSM = men who have sex with men
PLWH = person living with HIV/AIDS
PrEP = pre-exposure prophylaxis
STI = sexually transmitted infection
TB = tuberculosis
TNF = tumour necrosis factor
UNAIDS = United Nations Programme on HIV/AIDS
VZV = varicella-zoster virus

Welcome to our review of the Australasian Society for HIV Medicine (ASHM) HIV & AIDS and Sexual Health joint virtual conferences,

held online this year in November. The annual meeting was held as a virtual meeting with both live and on-demand programmes. On this occasion sexual health and HIV streams were intertwined rather than overlapping. There was a single live stream accompanied by an on-demand forum including oral presentations and posters. Dr Anne Robertson has selected presentations of particular interest and provided associated commentary for inclusion in this review.

We hope you find this conference review stimulating reading, and I look forward to your feedback.

Kind regards

Dr Chris Tofield
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A selection of the presentations from the virtual meeting are available on demand and can be accessed here

Keynote presentation: Weight gain and new antiretrovirals

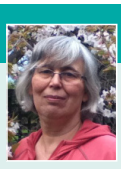
Presenter: Francois Venter

Summary: Professor Venter summarised the evidence linking weight gain to the use of newer antiretrovirals, particularly integrase inhibitors, in association with tenofovir alafenamide. He presented the data on weight gain from the South African ADVANCE trial, which included a high percentage of black people and women, with 351 participants in each study arm. The study was not designed to assess the impact of weight gain but the data was extracted following the findings of other integrase inhibitor studies. It was noted that women had a higher BMI at the start of the study. Over a 144 week period, the weight gain for women in the three arms (i) tenofovir alafenamide/emtricitabine/dolutegravir (ii) tenofovir disoproxil/emtricitabine/dolutegravir and (iii) tenofovir disoproxil/emtricitabine/efavirenz was 13.2 kg, 7.5 kg and 5.5 kg respectively. Men had smaller weight gains in the three arms of 7.2 kg, 5.5 kg and 2.6 kg. It was argued that although obesity has not been demonstrated to increase mortality there are significant adverse health outcomes, including in pregnancy. For late presenters the weight gain may be an indication of their return to health and for others the increase in weight may parallel the weight gain otherwise expected in the population. However, HIV clinics had become like diabetic clinics in a country where there are social pressures to avoid being thin because of the association with HIV and TB.

Comment: Weight gain in association with newer antiretrovirals has been a common theme at all HIV meetings this year. Prof. Venter presented the issue from a South African perspective where it had been hoped that roll out of a combined dolutegravir regimen, tenofovir alafenamide and emtricitabine, would be cost effective for a middle-income country because of the decreased need for regular renal and bone monitoring. For a country with major concerns about obesity, this was shown not to be a suitable option. For women, the adverse outcomes in pregnancy from obesity outweighed the possible small risk of fetal abnormalities associated with the use of an integrase inhibitor. In New Zealand, we do not have access to tenofovir alafenamide, but anecdotally, weight gain has been an issue for some patients switched to an integrase inhibitor for regimen simplification or reduction in other toxicities.

Session: Plenary – Clinical management and therapeutics

Independent commentary Dr Anne Robertson



Dr Anne Robertson is a Sexual Health Physician and lead of the MidCentral Health Sexual Health Service. She is the current President of the NZ Sexual Health Society and a previous President of the Australasian Chapter of Sexual Health Medicine (RACP).

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References: 1. Cahn P et al. *J Acquir Immune Defic Syndr;* 2020. **2.** GlaxoSmithKline New Zealand Tivicay Data Sheet. GSK NZ; 2019. Available at http://www.medsafe.co.nz/profs/datasheet/dsform.asp. **3.** GlaxoSmithKline New Zealand 3TC lamivudine 10 mg/mL oral solution Data Sheet. GSK NZ; 2018 Available at http://www.medsafe.co.nz/profs/datasheet/dsform.asp.

Date of preparation: Aug 2019 TAPS DA2028AM-PM-NZ-DLM-ADVT-20AUG0001

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ELIMINATION OF HIV

What does elimination of HIV transmission mean for Australia, and how might we measure it?

Presenter: Skye McGregor

How does Australia compare to other countries?

Presenter: Jason Ong

Summary: The World Health Organization Global HIV Strategy has set a goal of ending AIDS as a public health threat by 2030. The UN 90:90:90 targets for the cascade of care are changing to 95:95:95 from 2021. Many countries have set more ambitious targets but what does elimination mean? Are these targets realistic? The 8th Australian HIV strategy runs through to 2022 and discusses "virtual elimination" which is not a clearly defined epidemiological term. Discussion focused on elimination terminology and, in the absence of being able to measure incidence, the concept of incidence prevalence ratio was introduced. Assuming a high testing rate, this is the number of new infections per year with the denominator being the number of people living with HIV. The elimination target benchmark (UNAIDS) is to not have more than one new diagnosis replace a PLWH during their estimated lifetime of 33 years after HIV diagnosis, i.e., a ratio of < 3.0. Australia is on target to achieve this at 2.6, but some fast-track cities in other countries are doing better. Australia has had a strong start supported by a strong community response and increasing use of PrEP. However, not everyone is benefiting, particularly those born overseas. It is important that interventions are maintained to prevent a rapid rebound in incidence if resources are diverted.

Session: HIV Symposium: Can Australia be the first country to eliminate HIV transmission?

A novel analysis of NSW HIV surveillance data to highlight HIV prevention program impact and gaps

Presenter: Phillip Keen

Summary: Based on the estimated concentrations of adult males who are gay in NSW, suburbs were divided into 3 groups, low (<5%), medium (5-19.9%) and high (>20%) concentration. Between 2014-2019 there was a 31% decrease in HIV new diagnoses for Australian-born men in NSW but the rate was static for overseas-born men. The decreases in new diagnosis by suburb groups were 57% for high concentration, 36% in medium concentration and 7% in low concentration suburbs.

Session: HIV Prevention, Epidemiology & Health Promotion Abstracts - General HIV prevention and GBM
Abstract

Declining HIV diagnoses and rising PrEP uptake in Auckland, New Zealand: Successes and challenges

Presenter: Peter Saxton

Summary: Traditionally, condom use has been high in MSM in Auckland and HIV testing levels moderate. Treatment for HIV regardless of CD4 count was introduced into Aotearoa NZ in 2017. PrEP was funded in NZ from 2018, although a demonstration project had been funded prior in 2017. Using epidemiological and behavioural data it was demonstrated that overall there was a 65% decrease in incident HIV infection with the reduction similar across all ages. Despite reduction in condom use, primary and secondary prevention was maintained with the use of PrEP and doubling of HIV testing. Both testing and PrEP uptake were higher in non-Māori. The percentage of men engaging in condomless anal sex and not testing was constant over the years at 29% in 2011 and 25% in 2019.

Session: Abstract Spotlight Session: HIV Epidemiology, Prevention & Health Promotion
Abstract

Cascade of care of people diagnosed with HIV in New Zealand between 2006 and 2017

Presenter: Sue McAllister

Summary: Of 2355 people diagnosed with HIV in NZ from 2006-2017, clinical data was available for 1490 people who were alive and living in NZ in 2017-2019. From notification, clinical, laboratory, pharmaceutical claims and hospitalisation data sources, anonymous linkage to ART and HIV viral loads demonstrated that 94.5% were on ART and 87.6% had a suppressed viral load. Of those diagnosed between 2014 and 2017, 91% had a suppressed viral load. NHI data linkage will decrease those for whom information was lacking and provide more complete data in the future.

Poster presentation #82
Abstract

Keynote presentation: Why are we not achieving control of the HIV pandemic?

Presenter: Chris Beyrer

Summary: HIV persists in women and girls in Eastern and Southern Africa despite a large role out of antiretroviral therapy. The ECHO contraception trial (Lancet 2019) showed no difference in acquisition of HIV between injectable, implantable and intrauterine contraceptive methods, but the rate of incident infections was 3.81% per year in a group of women not assessed for being at increased HIV risk. This rate was no different from that of 2001 at the time of an early vaccine trial and occurred despite study participants being offered individualised HIV intervention packages. The recent HVTN 702 vaccine trial was discontinued because of futility. The cumulative HIV acquisition rate for women was 4.2 per 100 person years compared to 1.2 for men. There is a disconnect between person and population intervention benefits of ARVs. Treatment rates are increasing but transmission is stable and is explained by late initiation of treatment when transmission occurs early and prevalence is driving incidence. Interventions have previously focused on mother-to-child transmission and there is a need to engage men. Globally there has been a slow roll out of PrEP and there is an ongoing need to target key populations who are defined as being at high risk of HIV acquisition AND have poor access to services.

Session: Plenary – Epidemiology, Prevention & Health Promotion

Keynote presentation: Differentiated service delivery through key population-led health services

Presenter: Nittaya Phanuphak

Summary: Thailand has approved the use of PrEP to key populations but role out has been slow. A differentiated service delivery model employing trained lay key workers who are connected to targeted community groups has been initiated. A programme of increased testing, same day initiation of ART for those who are positive or initiation of PrEP in those who test negative has been achieved. This involves flexible service delivery in the community but with close links to hospital-based or community medical services. Lay workers complete formal training and the assessment process. The model is centrally led and there is an evaluation process to guide service delivery options.

Comment: These presentations demonstrate that some progress has been made towards elimination of HIV in easy-to-reach communities with good community support. There is little progress in those who are at risk of HIV but have poor service access. Concern has been raised that funding will be reduced in areas where there have been gains resulting in rebound of transmission when disparities exist and there is still significant community transmission. The failure of linkage of HIV prevention to reproductive health in Sub-Saharan Africa was disappointing, but the Thailand all-of-system approach demonstrated what could be potentially achieved with strong leadership and service coordination. There is a particular need for roll out of PrEP globally.

Session: Plenary – Epidemiology, Prevention & Health Promotion

Keynote presentation: eSexual Health – where do we go from here?

Presenter: Claudia Estcourt

Summary: There were several presentations in the conference programme on how services coped during COVID-19 lockdowns by using telehealth and remote consultations, but digital health had been of interest to the LUSTRUM (Limiting Undetected Sexually Transmitted Infections to Reduce Morbidity [2016-2021]) project in the UK research group led by Professor Estcourt prior to the arrival of a pandemic. The definition of digital health used was based on that of the World Health Organization: "Digital Health is the convergence of digital technologies with health, healthcare, living and society to enhance the efficiency of healthcare delivery and make medicine more personalised and precise." Digital technology has largely been studied in the management of long-term single conditions which differ significantly from STI management where a range of interventions are required for completion of treatment for patients and sexual contacts. There are challenges when consumer want does not equate with consumer need, particularly where there is psychosocial complexity and concerns about safety. Barriers to engagement in treatment include mild intellectual disability and low digital literacy. Cost effectiveness may be limited by lower treatment rates compared to face-to-face consultations. There is emerging evidence that digital technologies increase testing rates but not condom use and may be useful for maintenance of PrEP. Access to support and integration into physical clinical pathways was emphasised in contrast to "Amazonised" approaches to health care delivery with often poor online information. Digital health should be considered as a part of overall service development in conjunction with a codesign and evaluation process.

Comment: Slow roll out of digital technology and lack of availability of equipment during COVID-19 lockdown has led to implementation of digital processes and remote testing without much consideration of how digital technology integrates into overall service provision. This presentation allowed us to take a step back and look at the bigger picture. Scottish researchers who were referred to during the presentation have contributed to the webinar series offered by the NZ Telehealth Forum and Resource Centre and can be accessed at www.telehealth.org.nz/health-provider/webinars/

Session: Plenary – Clinical management and therapeutics

Keynote presentation: Control of gonorrhoea; not as simple as we thought

Presenter: Chris Fairley

Summary: Behavioural interventions such as the RESPECT trials are labour intensive and have a relatively small benefit on condom uptake and do not have any effect on number of partners. The biggest impact on disease transmission can be achieved by early testing and treatment. This requires good access to services. Jurisdictions with multiple entry points to services appear to do better in controlling transmission and a distinction was made between NSW with high MSM populations compared to Victoria which has higher infection rates despite smaller MSM populations. Victoria has one dedicated specialist service for the whole state compared to multiple geographically distributed services in NSW. The other area to target is reduction in stigma to encourage earlier presentation. STIs were contrasted with obesity. The latter has become a key focus of public health strategy unlike STIs which are considered to result from an individual's actions.

Comment: Unlike HIV, other STIs have no evidence-based biomedical interventions and multifaceted and multicomponent intervention packages are required. The PREVEN trials in Peru showed that the effect was modest and that funding gaps increasingly make delivery of behavioural interventions difficult. NSW in addition to having multiple specialist service entry points also has a dedicated STI Programmes Unit which offers resources and support to primary providers. As for HIV, an all-of-health system approach is required.

Session: Plenary: Epidemiology, Prevention & Health Promotion

Impact of rosuvastatin on progression of atherosclerosis in people with HIV at moderate cardiovascular risk

Presenter: Janine Trevillyan

Summary: The study aimed to investigate the effect of rosuvastain on atherosclerotic plaque progression as estimated by a change in carotid intima media thickness (cIMT) in people with 10-15% Framingham risk score but in whom a statin was not recommended. Participants were randomised to rosuvastatin 20 mg (or 10 mg if on a protease inhibitor) or placebo for 96 weeks. Recruitment was slow and there were 84 participants, which was short of the planned target of 102. Rosuvastatin led to the predicted reductions in cholesterol and LDL. There was no difference in cIMT progression between the 2 arms, although progression in the placebo arm was less than expected. There was a slightly lower hs-CRP in the rosuvastatin arm but no difference in interleukin 6. There was a significant rate of Grade 1 and 2 side effects in the rosuvastatin arm with discontinuation and such events may limit the benefits of a statin in those of low-to-moderate risk of atherosclerosis.

Comment: This was one of the few clinical HIV presentations in the conference programme which in the year of a pandemic had a public health focus. A lower threshold for commencing statins in people living with HIV is recommended compared to the general population, but the threshold has not been well defined. Many patients are reluctant to add yet another medication and this study does not support the use of statins in those with borderline clinical indications. Further information will become available from the large REPRIEVE trial which stopped recruiting in 2019.

Session: Abstract Spotlight Session: Clinical Management & Therapeutics
Abstract

Enteric and sexually acquired pathogens in men who have sex with men with clinical proctitis

Presenter: Eric Chow

Summary: Men presenting to sexual health clinics with proctitis complain of anorectal pain, discharge, bleeding and tenesmus. Previous research has shown that about 23% of men will be positive for chlamydia and 12% for Neisseria gonorrhoeae. The aim of this study was to elucidate other pathogens. Diagnosis was based on symptoms +/- proctoscopy. 499 specimens from symptomatic men (Group 1) were evaluated using the Speedex multiplex PCR assay (HSV-1, HSV-2, VCZV *Treponema pallidum*, *Trichomonas vaginalis* and *Mycoplasma genitalium*) and the AusDiagnostics Faecal pathogen M 16-well assay. Testing was also undertaken in 506 specimens stored from a previous study of asymptomatic MSM (Group 2). The HIV positivity rate was 16.0% in Group 1 and 14.8% in Group 2. *T. pallidum* (3.6 vs 0%), *Shigella* (2.8 vs 1%) and *M. genitalium* (9.4 vs 5.1%) were reported more frequently in men with symptomatic proctitis compared to asymptomatic men. Using PCR testing, *T. pallidum* was diagnosed more frequently than in previous studies where dark ground microscopy was used and not all men had positive serology. Most of the men with shigella did not report diarrhoea and testing should be considered in men with proctitis without diarrhoea.

Comment: Many men with sexually acquired proctitis will present to providers other than sexual health clinics. Until recently, management of anorectal syndromes have not been included in many STI guidelines. The current NZ Sexual Health Society Guidelines are in the process of being updated in conjunction with the Australian ASHM guidelines and will include management of anorectal syndromes.

Session: Abstract Spotlight Session: Clinical Management & Therapeutics
Abstract

THE SYPHILIS EPIDEMIC

An update on the epidemiology of syphilis in Australia with a particular focus on the changing epidemiology among women

Presenter: Belinda Hengel

Summary: Syphilis case notification data was presented for Australia, noting the high indigenous/non-indigenous ratio for infectious syphilis.

Session: The Syphilis Epidemic – what's happening and what's new?

Syphilis in remote Aboriginal communities

Presenter: James Ward

Summary: An enhanced response has been successful in slowing the rate of rise in new infections, but needs to be maintained. Cases of congenital syphilis are still occurring in Australia.

Session: The Syphilis Epidemic – what's happening and what's new?

A national surveillance system for congenital syphilis in New Zealand

Presenter: Tony Walls

Summary: Mother-to child syphilis transmission data from 2018 to 2020 from the NZ Paediatric Surveillance Unit were presented. There were 32 reported cases consistent with mother-to-child transmission of syphilis including 6 probable cases and 12 babies with clinical signs of congenital syphilis. The incidence of mother-to-child transmission of syphilis in NZ was high at 9 per 100,000 compared to a rate of 1.2 per 100,000 by the European CDC, with rates of 0.3 in the UK and 0.4 in Germany. There was over-representation of Maori at 41% and Pacific at 28%. The Paediatric Surveillance Unit data was compared with that reported to ESR. The latter included additional stillbirths and there is a need to combine the two data sources to obtain a full picture of mother-to-child transmission of syphilis in NZ. Factors associated with transmission included lack of antenatal care resulting in a diagnosis being made after delivery and failure to follow-up post treatment. First trimester antenatal screening was negative in some cases and follow-up third trimester testing was discussed.

Session: The Syphilis Epidemic – what's happening and what's new?

Syphilis diagnostics and laboratory surveillance in the 21st Century

Presenter: Deborah Williamson

Summary: There has been increasing use of *T. pallidum* DNA PCR on samples from lesions but there is no current standardisation of testing. There have been several gene targets used although recently these have been largely polA (tp0105), tpp47 (tp0574). Specificity is high but sensitivity differs across specimens and stage of disease with use of different comparators in studies. Multiplex PCR including testing for HSV 1 and 2, VZV and *T. pallidum* is being used for investigation of genital ulcers. There has been successful *in vitro* culture of *T. pallidum* (Edmonson DG et al., mBio 2018) with evidence of infectivity demonstrated on re-inoculation of a rabbit. However, this has been following rabbit passage rather than from direct lesion culture. It has been used to demonstrate the *in vitro* susceptibility of *T. pallidum* to doxycycline. Identification of a marker to distinguish between active and treated syphilis is work in progress. Two cytokines, brain-derived neurotrophic factor and TNF-β look promising as markers for active infection in addition to serology on a platform which is used in many labs (Kojima N et al., JID 2020). Molecular epidemiology is technically difficult for *T. pallidum* requiring metagenomics and whole genome sequencing (WGS). A new lineage associated with macrolide resistance, SS14, has emerged in the mid 20th century which differs from the Nichol strain which has driven many of the syphilis epidemics earlier in the last century. Analysis of the OMP TP0548 gene has been found useful to differentiate strains into broad lineages and has demonstrated that there has been a recent reappearance of Nichols lineages alongside the more dominant SS14 lineages in Victoria. Subsequent WGS has demonstrated the presence of a large number of different lineages circulating in Melbourne and is being correlated with clinical epidemiology.

Session: The Syphilis Epidemic – what's happening and what's new?

Oral and anal *T. pallidum* detection in men who have sex with men with early infectious syphilis

Presenter: Janet Towns

Summary: Janet Towns (Melbourne Sexual Health Service) presented her research on the careful clinical documentation, photography and swabbing of lesions in 200 MSM with syphilis. In addition, oral rinse, oral cavity, anal canal, first pass urine and semen samples were tested using *T. pallidum* polA PCR (the standard clinic test) and 47kDa PCR. 24% of oral specimens were positive on PCR but lesions were only identified in 50%. Positivity peaked at 44% in secondary syphilis compared to 7% in early and latent syphilis combined and was associated with high RPR titres. The positivity rate for anal samples was 23% (1/4 with no anal lesions), 6% in urine and 12% in semen. Only 3 patients had positive dry skin swabs and all had florid skin lesions. 50% of signs overall were unnoticed by patients. There was multisite positivity in 7% of primary syphilis and 25% in secondary syphilis. No patient with early latent syphilis had positive testing in more than one site. 74% of patients with secondary syphilis had positive testing in at least one site. There was a wide range in appearance of lesions and these were illustrated by clinical photographs. Secondary syphilis is likely to be the most infectious stage and may be driving transmission.

Comment: The syphilis symposium was one of the highlights of the conference. Anecdotally there here have been 7 cases of mother-to-child transmission of syphilis this year in Aotearoa, New Zealand including stillbirths reflecting the need to enhance our public health response and national syphilis action plan. The introduction of an enhanced syphilis response in Australia appears to be having some effect with the levelling of case notifications particularly in North Queensland. The management of syphilis is an art particularly in the assessment of serofast titres where there can be challenges in differentiating between serofast and reinfection status. The unexpected resurgence of an old disease has meant that we have had to manage clinical scenarios with the use of old diagnostic technology. New developments are therefore eagerly awaited. Janet Towns' study has been accepted for publication by Lancet Infectious Diseases including her wonderful library of clinical images.

Session: The Syphilis Epidemic – what's happening and what's new?

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