

the art of ART

2017 CONFERENCE REPORT

The 2017 Art of ART Meeting, held in Melbourne, Australia, was a series of plenary sessions and interactive workshops for S100 prescribers, nurses and pharmacists with a focus on the nuances of ART prescribing and contemporary HIV management in Australasia. This report provides a summary of key learnings.

Videos of the presentations are now available on the [art of ART program page](#).

Improving The HIV Care Cascade

Take Home Messages

1. Use of HIV rapid tests in 'other settings' can impact significantly on the HIV care cascade, especially when coupled with expedited treatment initiation.
2. Settings for routine HIV testing include primary care, obstetrics, Emergency Departments, community-based shop-fronts and peer-led testing centres.
3. Rapid treatment initiation strategies have been found to be safe, acceptable and effective, however they require a multidisciplinary approach and single point of contact.
4. Challenges include retention and contact tracing. System changes may be required.
5. Rapid nucleic acid tests are needed to identify and quickly treat acute HIV cases.

Overview

- Internationally, Australia performs best in HIV treatment cascade with 69% of all PLWH with an undetectable viral load. (2015)
- Potential threats exist which may hinder or even reverse this progress:
 - » Early indicators for 2017 show declining HIV rates in MSM but rising STI rates.
 - » MSM not testing as frequently as recommended ([see STIGMA testing guidelines](#)).
 - » 80% of newly acquired HIV notifications are in MSM and increases in risk behaviour are being reported.

Note: We advise right clicking on links and selecting 'open link in new tab' to facilitate easy reading of the report.

What can be done?

- More testing, especially for under-tested populations - those with poor healthcare access.
- Evaluation of home testing to engage 'hard to reach' populations in regular testing.
- More frequent testing.
- Quick confirmation of HIV status.
- Rapid entry to care and starting ART.
- Coordinated public health efforts as part of 'ring prevention':
 - » Acute case detection
 - » Partner services
 - » STD testing

Increase uptake in testing

Key Learnings

- Important to provide a range of testing options.
- Point of care testing or near patient testing improves HIV testing rates.
- Limits of rapid tests (acute infection detection) must be understood by operators.
- The quality of non-laboratory based testing must be maintained.
- Conventional laboratory testing needs to be efficient.
- Need to package full STI screening into lab tests with 24 hour turn around time and ideally within hours of testing.

Table: Point of care testing or near patient testing

TEST	PROS	CONS	AVAILABILITY	LINKS TO STUDIES
Peer-led testing in community-based settings	<ul style="list-style-type: none"> • Highly acceptable • Good sensitivity in detection of HIV in established infection. • Can be integrated with STI testing. 	<ul style="list-style-type: none"> • Challenge in identifying acute HIV infections: In one study tests failed to detect up to 50% acute infections. 	<p>Approx 100 PoCT services currently registered in Australia on the ASHM Testing Portal.</p>	<ul style="list-style-type: none"> • Study of Trinity Unigold HIV-1/2 antibody only test in 22 sites across NSW. • a[TEST] Oxford Street: A Successful Model of Community Rapid HIV Testing in Sydney
Home sampling	<ul style="list-style-type: none"> • Appeals to infrequent testers. • Involves conventional laboratory confirmation including nucleic acid tests. 	<ul style="list-style-type: none"> • Have to post sample and wait for result. • No integration with STI testing. 	<p>NSW pilot study of postal DBS programs launched. Priority populations can have kit sent to them at home for DBS collection.</p>	<p>Mail out DBS has been available in the US since 1996 and performed very well in the UK.</p>
Home testing/self-testing	<ul style="list-style-type: none"> • Rapid results • Convenient • Particularly suitable for people who may not feel connected to community, have limited access to services, or want to be discreet. 	<ul style="list-style-type: none"> • Challenge in identifying acute HIV infections. • Not integrated with STI testing. • No automatic link to care. 	<p>On its way. HIV self-testing devices can now be sold in AU but still lack TGA approval. Find out more.</p>	<ul style="list-style-type: none"> • In an Australian study, HIV self-testing resulted in a 2x increase in frequency of testing in MSM at high risk of infection, and nearly 4x increase in non-recent testers compared with standard care, without reducing the frequency of facility-based HIV testing. • BioSure HIV self test is an example of a self-test available in the UK that does not require lab testing. • Atomo is a test being developed in Australia and one to watch.

Initiating early treatment - From “universal ART” to “same-day ART”

- New HIV infections occur predominantly in HIV susceptible networks with low rates of condom use and high potential for chains of transmission.
- Heterosexual HIV transmission is 6 x more likely in acute HIV infection ([Wawer JID 2004](#); [Bellan PLoS Medicine 2015](#)). Risk may be 9 x higher in MSM. ([Hollingsworth, Pilcher et al. 2015](#))
- Tackling acute HIV is key to managing the epidemic.

Why same day ART?

1. Reduces reservoir/hyperinfectivity ([Jain et al. JID 2013](#); [Saez-Cirion et al., PLoS Pathog. 2013](#)),
 - » Dramatically improves time to viral suppression,
 - » Reduces transmission.
2. Enhances retention
 - » Avoids the delays in assessment and starting ART that can result in loss of patients from care ([S.Rosen et al CROI 2015 study](#)).
3. Improves health outcomes
 - » Improves morbidity and mortality in all stages of infection, ([START INSIGHT NEJM 2015](#))
 - » Improves durable suppression of viral load.
4. Because it's what patients want (see example of San Francisco).

Is it feasible?

- Feasible within existing health systems environment.
- Safe, acceptable, effective however needs multidisciplinary approach and single point of contact.
- Studies:
 - » The RAPID Initiative ([Pilcher et al. 8th IAS, Vancouver, 2015. abstract WEAD0105LB](#))
 - » Same-day HIV testing and antiretroviral therapy initiation results in higher rates of treatment initiation and retention in care ([Koeneg et al. AIDS, Durban, 2016. Abstract 8138](#))

Key findings from San Francisco RAPID Initiative

- Numbers were small (39 RAPIV participants vs. 188 for historical standard of care controls.)
- 70% of participants in the RAPID study had acute infection (infected within last 6 months).
- RAPID participants were a 'high needs' population e.g. 25% were homeless.
- Mean time from diagnosis to 1st dose of ART was 1 day vs. 37 days in the standard of care comparator group.
- Treatment was initiated in the clinic using a 5-day starter pack.
- At 24 weeks 95% of RAPID participants achieved complete viral suppression vs. 70% of the comparator group.
- Median time to viral suppression was 56 days vs. 119 in the standard of care comparator group.
- Multidisciplinary 'one-stop-shop' was integral to the program success.

Key Learnings

To be effective, Rapid ART initiation requires:

- Multidisciplinary team
- Ability to identify acute cases
- Single point of contact for referrals (phone number/pager)
- Flexible scheduling with flexible staff
- ART regimens preapproved before genotyping or lab testing available

Triple Therapy Might Not Be The Only Answer

Take Home Messages

1. Need to change the language of ART from 'triple' to 'optimal'.
2. Optimal ART will result from dual class drug combinations that are potent, tolerable, non-toxic and convenient.

Why explore other options?

- First principles - 'primum non nocere' - use only as much drug as you need.
- Spare drug classes and individual drugs for later.
- Maximise tolerability; minimise toxicity.
- Reduce costs globally.

Findings

- Monotherapy has been shown to be ineffective in several studies.
- 2 drugs are ineffective if:
 - » From a single class or
 - » Include MVR
 - » NNRTI + 1N(t)RTI - AZT/NVP, ddi/NVP (INCAS) - TDF/EFV (COOL)
- 2 drugs from different classes show potential. Further investigation of the following warranted:
 - » Boosted PI + 1N(t)RTI
 - » Boosted PI + InSTI
 - » Boosted PI + NNRTI
 - » InSTI + NNRTI
 - » InSTI + N(t)RTI

STUDY	DRUGS	DESCRIPTION/OUTCOMES	KEY LEARNINGS
SWORD	Dolutegravir Ralpivirine	Comparable efficacy to three or four-drug regimens in virologically suppressed patients.	SWORD studies provide compelling data that suppression may be maintained with a two-drug regimen of dolutegravir and rilpivirine. Regulatory submissions for this two-drug regimen as a single tablet are being planned for 2017.
PADDLE	Dolutegravir Lamivudine	Viral load declined rapidly after starting therapy, similar to declines seen with standard three-drug ART.	In this pilot, proof of concept study , dual therapy with dolutegravir plus lamivudine induced rapid virologic suppression with a favourable safety/tolerability profile in HIV-1 infected, treatment-naive individuals. Needs confirmation in randomized clinical trial. This could be a simple, potent, well tolerated and potentially cheap strategy for HIV treatment initiation.
PI Monotherapy	Boosted PI Monotherapy Atazanavir Darunavir Lopinavir/ritonavir	Even though the overall efficacy was inferior to HAART, the numbers improved when the analysis was limited to those who had suppressed viral load on HAART for at least 6 months prior to the switch to monotherapy.	Arguments for this approach include regimen simplification, lower cost, and the avoidance of NRTI/NNRTI side-effects and resistance. http://www.aidsmap.com/Boosted-PI-monotherapy/page/1729863/
PIVOT		Trial in HIV-positive adults taking a stable NNRTI or PI-based regimen who had no previous VL failure and had VL < 50 c/ml for ≥ 6 months at trial entry.	PI monotherapy, w prompt reintroduction of NRTIs for VL rebound , was a successful long-term management strategy, preserved future treatment options, was safe and well tolerated, and may be considered for more widespread use in long-term HIV care.

STUDY	DRUGS	DESCRIPTION/OUTCOMES	KEY LEARNINGS
Dolutegravir monotherapy		Study stopped early	Dolutegravir used alone without other antiretrovirals was unable to keep viral load suppressed in some people who switched from a standard three-drug combination regimen. But evidence continues to show that dolutegravir plus a single other drug can work well as maintenance therapy.
MOBIDIP		<p>This study randomised 265 participants (between March 2014 to January 2015) who were on stable second-line boosted-PI treatment (either darunavir/r or lopinavir/r) to switch to either boosted PI monotherapy or dual therapy with additional 3TC.</p> <p>Recommended stopping the monotherapy arm due to higher rate of virological failure compared to the dual therapy arm.</p>	Simplifying HIV treatment: dual therapy works but monotherapy with either boosted-PIs or dolutegravir does not
INCAS	Various combinations of Nevirapine, Didanosine, and Zidovudine		<p>Triple drug therapy with zidovudine, didanosine, and nevirapine led to a substantially greater and sustained decrease in plasma viral load than the 2-drug regimens studied.</p> <p>https://www.ncbi.nlm.nih.gov/pubmed/9544767</p>
ACTG 5095	Triple-Nucleoside Regimens versus Efavirenz-Containing Regimens for the Initial Treatment of HIV-1 Infection		<p>Gulick RM, et al. 4 N Engl J Med 2004;350:1850-1861.</p> <p>Triple-nucleoside-analogue regimen of abacavir, zidovudine, and lamivudine found to be virologically inferior to a regimen containing efavirenz and two or three nucleoside analogues. This difference was observed regardless of the pretreatment viral load or the CD4-cell-count stratum.</p>
ACTG 5142			Riddler SA, et al. N Engl J Med 2008;358:2095-106
GEMINI study	Dolutegravir/Lamivudine		Study ongoing
ATLAS study	Long acting Cabotegravir/long acting Rilpivirine	Switch to long acting Cabotegravir/long acting Rilpivirine from current ART in HIV 1 infected, virologically suppressed adults	Study ongoing

Crystal Methamphetamine (CMA) Use in HIV Negative and HIV Positive GBM (Chemsex)

Take Home Messages

1. CMA differs from traditional recreational drug use and is associated with a high risk for HIV acquisition and transmission.
2. Party drugs can have toxic, potentially fatal, interactions with some ART and are associated with poor ART adherence.
3. Clinicians need to be better informed about risks, appropriate language and referral pathways, including for psychological support.

News

A survey of HIV-positive patients attending 30 HIV clinics in England and Wales, presented at the [Conference on Retroviruses and Opportunistic Infections \(CROI 2016\)](#), found that nearly a third (29%) of gay male patients reported engaging in 'chemsex' in the past year and that one in ten reported 'slamming' (injecting – or being injected with – the drugs). Both chemsex and slamming were associated with a sixfold increase in the odds of condomless anal sex. [Reported by aidsmap](#)

Epidemiology of CMA use

- True prevalence not known.
- [AU study of 2250 GBM](#): 50% had used illicit drugs and 28% had used party drugs in the previous 6 months: 12% crystal methamphetamine, 21% EDM (erectile dysfunction medication), 32% amyl nitrite (poppers). Appears to be less use of mephedrone and GHB/GBL than in UK and more of EDM.
- [Study: Increasing use of 'party drugs' in people living with HIV on antiretrovirals: a concern for patient safety.](#)

The link between CMA use and HIV infection

- Associated with high risk practices but almost no data showing causal association
- HIV-positive gay bisexual and other men who have sex with men were more likely to disclose chemsex
- HIV negative GBM: Chemsex associated with acquisition of HCV
- [Study: Chemsex and the city: sexualised substance use in gay bisexual and other men who have sex with men attending sexual health clinics](#)

The impact of CMA use on engagement in care and adherence to treatment (HIV or PrEP)

- CMA use in HIV+ men associated with [reduced HIV ART adherence](#).
- No data that reduced adherence causes treatment failure.

Interaction of CMA with antiretroviral drugs

- No DDI PK/dose-effect relationship data: Risk evaluation based on case reports/ cohort studies. Shows DDIs can be significant.
- Not all recreational drug and ARV interactions are toxic:
 - » Choose non interacting ARVs – raltegravir; dolutegravir, NNRTIs
 - » Consider avoiding ritonavir and cobicistat

Strategies to initiate and sustain engagement in care in GBM who use CMA

Case Study: [56 Dean St](#), a sexual health clinic in London

- Walk in 1-2-1 chats
- Chemsex care plan where individuals identify their own goal
- Clinicians to provide medical assessment, STI screen, PEP, PrEP
- Substance use support – one to one with counsellor
- Risk reduction advice
- Online resources

The effectiveness of programs specifically targeting CMA use

No clear outcome data for Chemsex support however clear that multidisciplinary team essential

- Sexual health/HIV medical team
- Chemsex advisers
- Traditional drug support workers

Table: Pharmacological management of addiction to CMA

DRUG	SYMPTOMS	WHAT TO DO
Crystal Meth/mephedrone	If patients present with what appears to be drug-induced psychosis:	<p>Re-assure them that they are safe</p> <ul style="list-style-type: none"> • Do they have a friend to look after them? • Diazepam 5 mg twice daily for 2 days may be useful • Pharmacotherapy (olanzapine, antipsychotics)
Crystal Meth/mephedrone	If looks like an overdose, classified as medical emergency. Look for: hot, sweaty; chest pain; hallucinations; unsteady gait; tremors; rigidity; confusion/disorientation; agitation/panic; difficulty breathing	Call ambulance
GHB/GBL	Confusion, shaking, agitation, headaches, chest pain	<ul style="list-style-type: none"> • Check if using every day (for 4 consecutive days or more). If so, advise not to stop using without medical advice • If they have no more supply of GHB/GBL, refer immediately to A&E. Call ahead to ensure the A&E duty staff are aware of the dangers of GHB/GBL withdrawal • Detox involves high dose benzodiazepine and baclofen usually over 5 days; usually as inpatient, but can be outpatient-based with careful supervision

Related Research

- [Desai et al. A systematic review of interventions to decrease the prevalence of ‘chemsex’](#)
- [Bracchi et al. Increasing use of ‘party drugs’ in people living with HIV on antiretrovirals](#)
- [Lea et al. Methamphetamine treatment outcomes among gay men](#)
- [Laurent Karila et al Synthetic Cathionics: A New Public Health Problem](#)
- [Hammoud et al: Following Lives Undergoing Change \(Flux\) Study](#)
- [CL Moore et al. Patterns of Drug Use and Drug-Related Hospital Admissions in HIV-positive](#)

STI Challenges in the Era of HIV Biomedical Prevention

Take Home Messages

1. Bacterial STI are increasing among gay men.
2. Azithromycin still effective for Chlamydia trachomatis. Note: rectal infections require test of cure.
3. Outbreaks of azithromycin-resistant *N. gonorrhoeae* occurring.
4. Ceftriaxone remains effective for *N. gonorrhoeae* but oral alternatives are running out.
5. Beware azithromycin resistance in syphilis and *M. genitalium* in MSM.
6. *M. genitalium* treatment is fraught, with no guidelines re screening asymptomatic individuals.
7. Doxycycline pre or post exposure prophylaxis is likely to reduce Chlamydia and syphilis but not *N. gonorrhoeae* and will likely increase the prevalence of resistant *N. gonorrhoeae*

The increased incidence of STIs in GBM on PrEP – actual or artifact?

- Challenge: PrEP involves regular STI/HIV testing. More testing = more diagnoses.
- [Mathematical modelling study](#): Found if PrEP became widespread among gay men in the US, STI diagnoses would rise in the first year, but would fall thereafter.
- Study: [STI rates in PrEP users very high, but evidence that PrEP increases them is inconclusive](#).

Drug resistant *N. gonorrhoeae* – the Australian perspective and future treatment options

- Rates of *N. gonorrhoeae* in Australia are highest in men aged 25-29 years and are increasing.
- 2016 outbreak of azithromycin-resistant *N. gonorrhoeae* in South Australia resulted in [changes to Treatment Guidelines](#):
 - » Single agent azithromycin removed from SA gonococcal treatment guidelines
 - » 1st line regimen: Ceftriaxone with concomitant azithromycin (1 g)
 - » 2nd line regimen: Gentamicin concomitant with increased dose of 2g oral azithromycin
 - » Test of cure crucial for all patients treated with 2nd line regimens.
- Treatment failures with Ceftriaxone rare but have been reported in Australia.
- Some new drugs in the pipeline along with novel combinations of old ones.
- Read the [2016 GONORRHOEA EXPERT MEETING](#) Report from WHO and DNDi.
- For *N. gonorrhoeae* contact tracing refer to the [Australian STI Management Guidelines](#) or the [Australasian Contact Tracing Guidelines](#).

Mycoplasma Genitalium – An Update

- Has similar clinical features to Chlamydia, and is increasing in incidence.
- Challenging to treat, and may be associated with ≥50% treatment failure.
- From June 20, 2016, *M. genitalium* detection is performed using an assay which enables simultaneous reporting of a macrolide resistance marker (MRM) should *M. genitalium* be detected.
- Azithromycin 1g failing more over time. MRM strongest predictor of azithromycin outcome.
- Alternatives: Azithromycin 1.5g, Moxifloxacin, Pristinamycin, (prior to use, consider decreasing bacterial load with Doxycycline).
- For *M. genitalium* contact tracing refer to the [Australian STI Management Guidelines](#) or the [Australasian Contact Tracing Guidelines](#).