Is rapid ART right for all?

Simon Collins
HIV i-Base

www.i-Base.info

Disclosure

No personal financial conflict of interest

Introduction

- Community perspective
- No personal link to this research
- Rapid = same-day, next day, within a week
- Right for all = right for *most* people (better definition with listed exceptions)
- Individual not population-based

Thank you to the BHIVA organising committee for the chance to speak

Talk is from a perspective of a community advocate for the last 20+ years.

If is not from my direct involvement in rapid-ART studies, although I am involved in the INSIGHT group responsible for the START study.

Always happy to bring a community perspective to BHIVA who decided the title of this talk

“Rapid ART” – same-day or within a week

Very little is ever “right for all” so better to define as right for most people – and perhaps list exceptions

Also, this is in the context of UK care

Individual vs population-based medicine

- Healthcare in the UK is still largely based on individualised medicine – even when economic costs govern access to treatment and care.
- Rapid-ART is different to public health policies: Test & Treat [1, 2] and Option B+ [3].
- Urgent ART: late pregnancy, newborns, late dx

1. Velasco-Hernandez et a. Lancet Inf Dis (2002); 2. Granich et al. Lancet (2008); 3. WHO (2012).

The last point is important to clarify.

- Healthcare in the UK is still largely based on individualised medicine – even when economics costs increasingly govern treatment and access to care

- Rapid-ART is different to public health policies like Test & Treat and Option B+

Test and Treat is a population-based approach to managing the HIV epidemic by treating HIV positive people on diagnosis to limit future transmission

Option B+ is a similar public health approach that recommended all HIV + pregnant women start ART during pregnancy and remain on it for life

HIV care is still complex enough to need a broad programme of care

1. US DHHS guidelines; archive at aidsinfo.nih.gov

Background

Treatment guidelines have varied over the last 20 years with thresholds linked to better ART. [1]

1998	2000	2002	2005	2009	2015
<500	<350	<200	<350	<500	All (any CD4)
					START study

More effective, convenient and safer ART.

Greater clinical concern for unsuppressed viral load.

The changes in guidelines recommendations for starting ART have varied considerably.

The move to earlier treatment is driven by having better treatment with fewer side effect.

In 2015, results from the START study changed WHO guidelines within a few weeks.

Driven by better and safer drugs and a greater concern for unsuppressed viral load.

San Francisco – 2015

Same-day ART vs historical control. Enrolled 2013–14.

- N=39 (92% men)
- Same day referral – compressing timeline for care.
- Complex issues: housing, drug use etc

Pilcher et al, IAS 2015

If treatment was as easy as taking a pill once a day, why wait?

Better and safer ART challenged the establish model of providing HIV care.

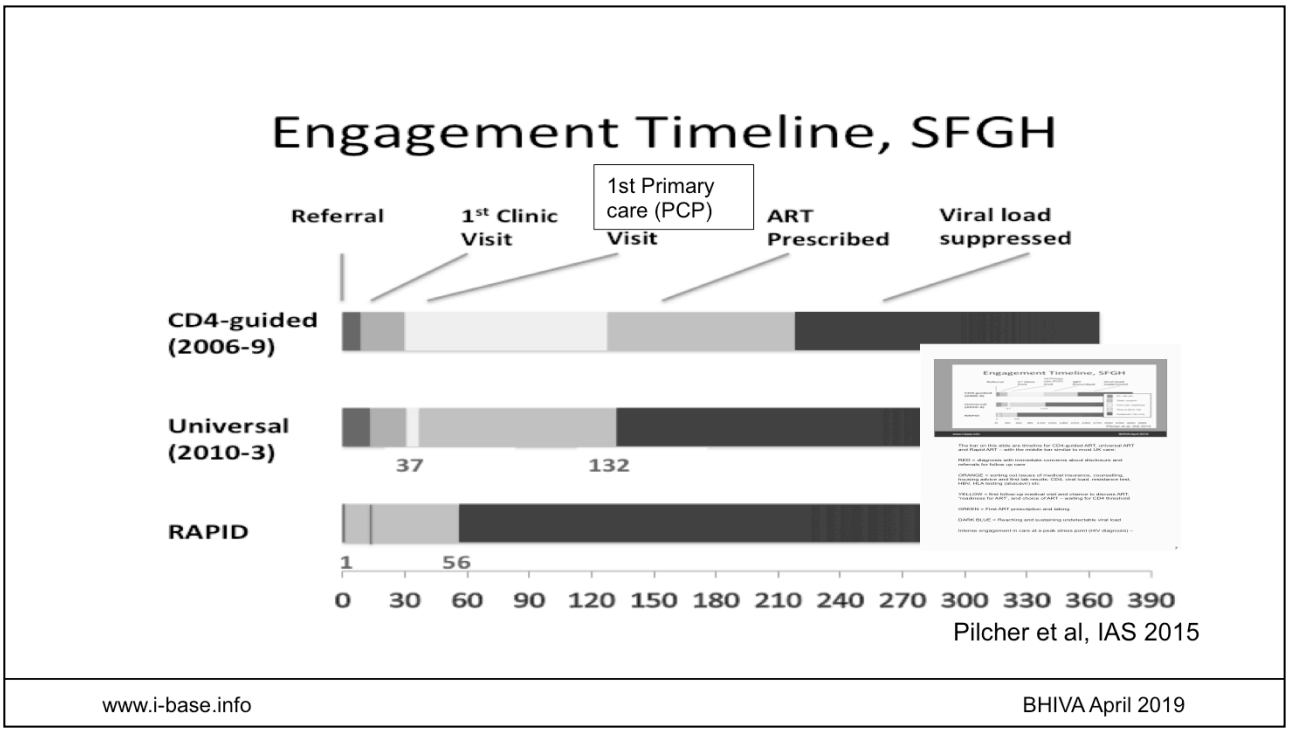
- counseling routine
- laboratory tests
- social support - including housing and medical insurance
- initial medical consultation
- prescribing using a multidisciplinary team.

Focus in same-day link to care, changing order of support, DOT first pill etc, then visit in a week assesed ART

For the intervention group this care was predominantly took place on the same day or shortly after the referral. For the SoC group these were spread over many visits

sometimes taking weeks or months before starting ART.

Complex cases in terms of substance use, housing etc.



The bar on this slide are timeline for CD4-guided ART, universal ART and Rapid ART – with the middle bar similar to most UK care:

RED = diagnosis with immediate concerns about disclosure and referrals for follow up care

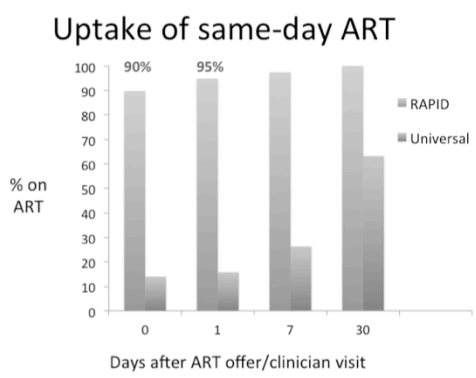
ORANGE = sorting out issues of medical insurance, counselling, housing advice and first lab results: CD4, viral load, resistance test, HBV, HLA testing (abacavir) etc

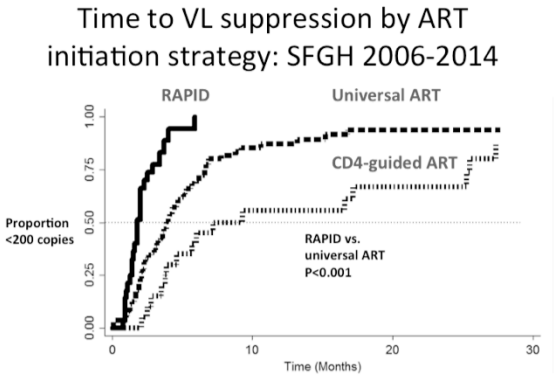
YELLOW = first follow-up medical visit and chance to discuss ART, "readiness for ART', and choice of ART – waiting for CD4 threshold

GREEN = First ART prescription and taking

DARK BLUE = Reaching and sustaining undetectable viral load

Intense engagement in care at a peak stress point (HIV diagnosis) –





High engagement and acceptance. Integrase-based ART.

Pilcher et al, IAS 2015

This slide the results:

The slide on the left shows time to starting ART – with 95% people of the group starting on the first day of diagnosis or the following day and everyone stating within a month. It shows rapid up-take and acceptance or ART – and when first presented the researchers we surprised at how many wanted immediate treatment.

The slide on the right shows the significantly raster time to becoming undetectable

56 Dean St – Pilot 2017

- <48 hours for first apt (vs 14 day)
- Offer same day ART - before CD4, VL, resistance, HLA, RITA, STI/HBV etc.
- PI/b + TDF/FTC but switch away from PI/b asap.

Whitlock G et al, BHIVA 2017

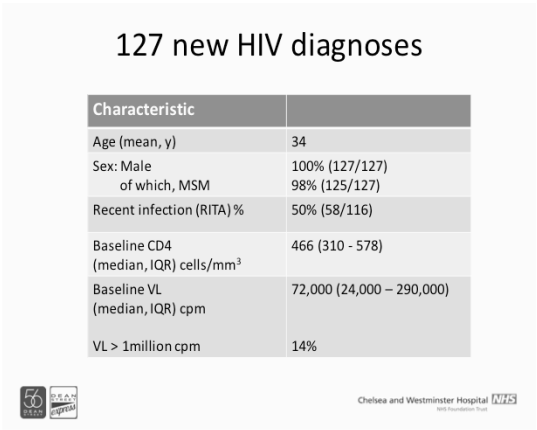
Similar approaches are now running in the UK.

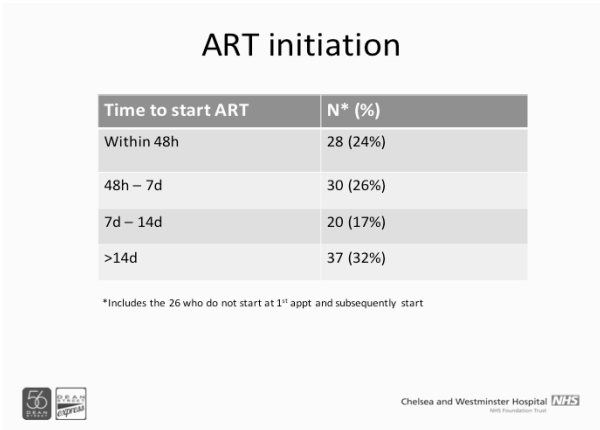
Results from the 56 Dean Street clinic were presented at BHIVA a couple of years ago.

ART was offered on the same day that someone was diagnosed. This required restructuring services within the clinic.

The initial ART was chosen based on avoiding or minimising the risk from drug resistance with an emphasis to change to easier and more appropriate ART when lab results were back

56 Dean St - 2017





Whitlock G et al, BHIVA 2017

This was larger cohort – n=127 new diagnoses over 5 months

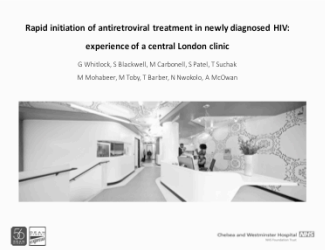
High percentage of recent infections, with high viral load

Rearranged clinic resources to include offer of same day ART

The 48 hours is to cover when early referrals can't be made because the clinic is closed at the weekend

56 Dean St - 2017

75% (89/118) started ART at first apt.
26/28 deferrals started within 1 month
ART: 24% <48 h and 28% <7 days
54% - PI/b, 29% INSTI; 10% NNRTI
But 28/118 - ≥ 1 primary resistance
54/55 (with 3 mo data) - <200 c/mL
Med. 61 days (44-117) to undetectable.


Rapid initiation of antiretroviral treatment in newly diagnosed HIV: experience of a central London clinic

G Whitlock, S Blackwell, M Carbonell, S Patel, T Suchak
M Mohabeer, M Toby, T Barber, N Nwokolo, A McOwan

Whitlock G et al, BHIVA 2017

This slide summarises the results.

There was high uptake or early ART 75% vs 25% deferring ART.

Of those who initially deferred almost almost all went on to start ART.

About half were started on PI-based ART, with just under a third using integrase inhibitor-based ART.

Of those with VL data at the time of the presentation, all except one did start ART.

Baseline drug resistance was higher than expected.

Community views 1

- HIV still has a life-changing impact.
- Most calls to i-Base – even in 2015 want ART – esp in primary HIV infection.
- ART can normalise HIV – single pill.
- Experience with PrEP and PEP is common.
- U=U reduces worry about risk to partners.

So these two examples are from public health clinics and the results should already be widely known.

But the perspective of someone who is newly diagnosed, HIV is still a life-changing event.

Most calls to the i-Base phoneline – even in 2015 – were from people who already knew they wanted treatment – and from people who more-often being told they were fine and would have to wait.

The stress associated with becoming positive meant that returning to normal life was often very difficult – taking years – still pre-occupied with risk to their lives, limited sex and early death

In 2019, ART is more widely accepted, including PEP, PrEP and U=U

Community views 2

- Shock of diagnoses – high engagement.
- Period of stress.
- High level of interest and motivation.
- Reduce viral load >1 log in 2 days.
- Options to change and modify.
- Clinical benefits at all HIV stages.

- Shock of diagnoses – often high engagement with care.
- Period of stress.
- High level of interest and motivation.

Ata time when people are acutely worried about their health, they can proactively do the one this that will help their health.

San Francisco – 2013-2017

N=216 (92% men)

CD4: 441 (3 to 1905)

VL: 37,000 (0 to >10 million)

51% with substance use

48% major mental health dx

30% homeless or unstable housing

Coffey et al, CROI 2019

www.i-base.info BHIVA April 2019

This year at CROI, longer follow-up was reported from the San Francisco study, With similar complexities to the pilot study from 2015.

The population in this study was notable for being more complex cases

Although the control arm was matched for most criteria, the RAPID ART group were diagnosed earlier in infection

-There was higher proportion of people with:

active substance use,

mental health issues

and who were homeless

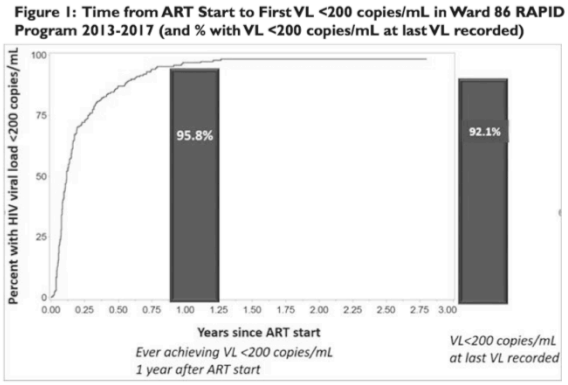
San Francisco – 2013-2017

Med, 1 year f/u (0 to 3.9)

92% <200 c/mL at 1 year

96% <200 c/mL over time

14% rebound >200 c/mL but most (78%) resuppressed.



Coffey et al, CROI 2019

It is reassuring to see that longer term follow up is till showing this to be effective.

Cautions

- Both examples restructured services.
- BHIVA standards include comprehensive assessment with referral to other services.
- HIV nurse, HIV health advisor, doctor and peer support.
- Sexual health and mental health.
- Latent TB, CVD, BMI, fracture risk etc.

BHIVA Standards (2016) and BHIVA Monitoring Guidelines (2019 update).

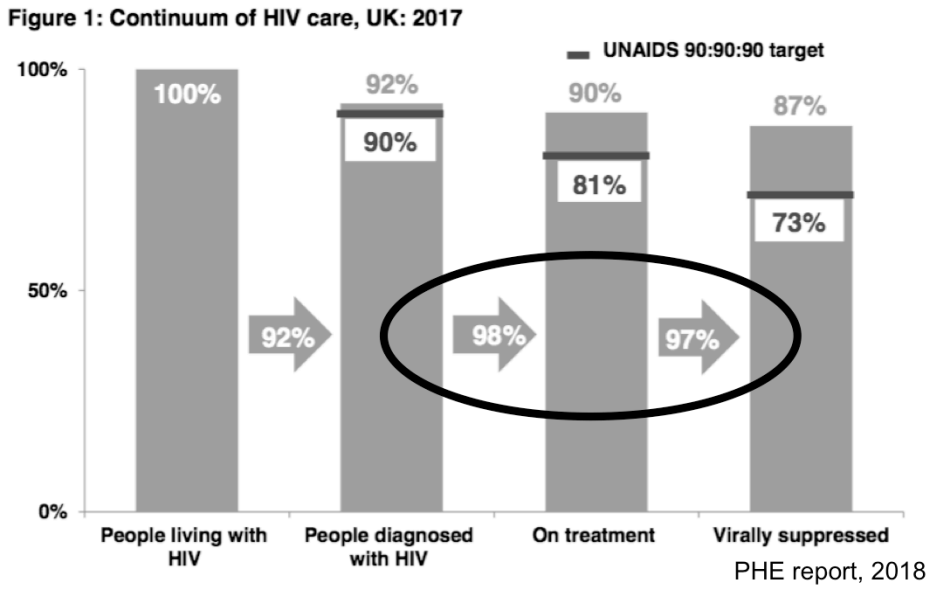
Both examples are small clinic numbers but with promising results.

Both clinics restructured services to offer the same care but in a different timeframe

BHIVA standards for this care are still just as important

Access to a team for support

Assessments for sexual and mental health, and clinical complications



PHE report, 2018

Luckily, the UK has high rates of viral suppression after starting ART – and high retention rates – 98% and 97% respectively.

Exceptions to uptake

- Very few – perhaps side effects with a high CD4 count (pipeline - injections, BNAbs ?)
- Perhaps other serious complications? (TB)
- Perhaps social circumstances: time to process information, discuss with partners, fear of negative reactions.
- Benefits: signposting to support services

At the start I suggested that rapid ART for all should more specifically be rapid ART for most – with a list of exceptions.

- Very few – I can't think of any.

Occasionally the i-Base phoneline gets calls from people who had real difficulties on oral ART. Potentially, injectable ART might overcome these difficulties, especially if adherence is a concern. But need lead-in oral dosing to ensure hypersensitivity would not be an issue – given the extremely long half-live.

Another option in the future might be option to be ART-free for six months based on early results with bNAbs.

- Perhaps other serious complications?
- Perhaps social circumstances

Other circumstances/barriersrs can include:

Insufficient time to process information, for both newly diagnosed and women diagnosed in pregnancy.

Limited time to share status with significant others, especially if they live with them and are likely to see meds.

Linked to the general fear of negative repercussions if sharing status does not go well.

Informed choice

- Personal choice – but an informed choice?
- Clinic as point of care for accurate info
- Treatment literacy.
- Uptake linked to community knowledge.
- Access to peer support
- Who is left out? [1]

1. Lee MJ et al. Int J STD AIDS (2019)

Personal choice – but then a question of whether this is informed choice?

Clinci will be a point of contact for accurate information

Uptake of rapid ART seems higher when population awareness of ART is higher.

Recent paper from St Marys showed those people lost to care are vulnerable people with mental health issues and drug and alcohol addictions. 13% didn't start within 3 months.

Conclusion

- Rapid ART can be an option for all.
- Acceptable and feasible in a high-income country with public health.
- ART is just part of care – other services are still essential.
- Integrase inhibitors overcome drug resistance and can have fewer side effects.

The conclusions is that while Rapid ART wont solve all problems – still just a componant of comprehensive care – it should be a universal choice.

Only possible with tolerable ART – for example US guidelines recommend INSTIs as first-line ARt

Thanks

Polly Clayden
Angelina Namiba
Michelle Ross
Roy Trevelion
Julie Fox
Sarah Fidler
Nneka Nwokolo
Gary Whitlock

Questions?

Back-up slides