HIVPA STUDY DAYS

CLINICAL SUMMARIES FROM THE SPEAKERS AT HIVPA STUDY DAYS

RPS

AN UPDATE ON WHAT YOU CAN EXPECT FROM THE NEW REVALIDATION PROCESS AND HOW THE RPS FACULTY CAN SUPPORT YOU WITH THIS

TRIAL SUMMARY

A SUMMARY OF TRIAL DATA RELEVANT TO THE NEW RAL-TEGRAVIR ONCE DAILY PREP-ARATION

HIVPA NEWS

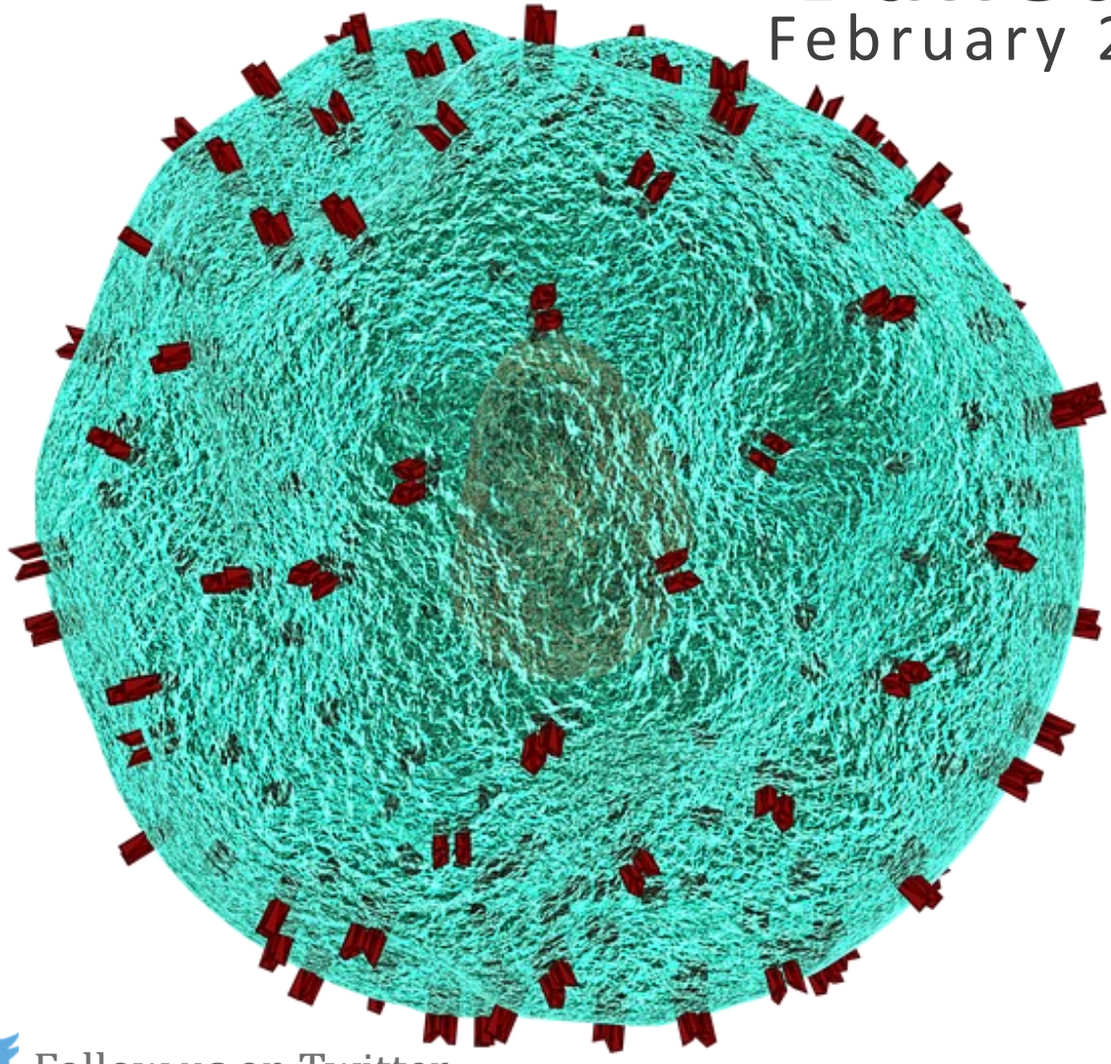
LATEST UPDATES FROM THE COMMITTEE

HIVPA

HIV Pharmacy Association

Bulletin

February 2018



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hivpaoffice@gmail.com

HIVPA News

Hello and welcome to the HIVPA bulletin! We have had some great contributions in this issue and I would like to sincerely thank all the authors. Please do not hesitate to contact me if you would like to make a contribution to the August 2018 issue. I am especially keen to include communications of any local initiatives, service evaluation or research projects. It is always really interesting to receive feedback on conferences or study events which others may not have been able to attend. I am also keen to encourage more junior members of the pharmacy team to submit reflective work or clinical summaries. Please email me directly at alexandra.lenko@uhl-tr.nhs.uk

Thank you, and I hope you enjoy this issue,

Alli Lenko (HIVPA Bulletin Lead)

Please be aware that any promotional content of this bulletin is not the responsibility of HIVPA

A SPECIAL THANK YOU You will all be aware by now that Sharon Byrne has stepped down as co-chair of HIVPA. Personally, and on behalf of the rest of the committee I would like to thank Sharon for all of her hard work and dedication. Sharon took over as HIVPA chair in 2010 with a strong vision for the future of the organisation. Her energy and enthusiasm have seen the HIVPA steering committee go from strength to strength, and Sharon's contributions have been pivotal in our success. Sharon was the regional winner of the HIVPA "Excellence in Pharmacy Practice Award" 2010 where her contributions to the specialty were recognised by both her local colleagues and the committee. In 2011 Sharon represented HIVPA at The Select Committee on HIV and AIDS in the UK at the House of Lords. Sharon, along with nursing, medical and psychologist colleagues, provided evidence on HIV and GUM care and services in the UK, and shared our achievements in multidisciplinary working as well as providing useful insights on where services could be improved. It has been a pleasure working with Sharon in our time as co-chairs together. Sharon has been incredibly supportive and inspirational to both myself and the rest of committee and we will miss working so closely with you. –Nadia Naous (HIVPA committee chair)

SPONSORS HIVPA would like to thank all of our sponsors for their continued support in 2018:

Gilead Sciences (UK) Ltd
Janssen—Cilag
Merck Sharpe and Dohme
Mylan
ViiV Healthcare

HIVPA would also like to welcome and thank our new sponsor:

Dr. Reddy's Laboratories (UK) Ltd

The support of our sponsors is essential to much of the work carried out by HIVPA including events like our study days and conference. Thank you!

REGIONAL REPS HIVPA currently have vacancies for Regional Representatives in the South East Coast and London, and North of England areas. If you are interested in filling the role of Regional Representative in either of the above regions, or would like to discuss in more detail what the role involves, HIVPA would be delighted to hear from you. Contact Portia Jackson, HIVPA Regional Representative Lead, via the HIVPA office at: hivpaoffice@gmail.com. Please send all expressions of interest by Friday 16th March 2018.

HIVPA COMMITTEE Silma Shah and Carol Wilkinson have stepped down from their roles on the committee. We would like to thank them for all their hard work and significant contributions during their time with HIVPA. The vacant posts will soon be advertised. Full details will be released shortly but we expect to welcome applications for the posts of technician representative, faculty lead and E-learning lead.

HIVPA Conference

HIVPA conference 2017 was filled with education, socialising and networking during which we heard from a range of expert speakers on topics including rheumatology and HIV, blood borne viruses, ageing and HIV. Beth Ward from the Royal Pharmaceutical Society (RPS) and Lucy Hedley provided an informative session on the RPS Faculty, General Pharmaceutical Council's revalidation requirements for pharmacy professionals and changes to the continuous professional development (CPD) recording system.

Personal highlights for me were the sessions on HIV-2 by Jane Deayton, CROI and BHIVA highlights by Dr Duncan Churchill and of course the annual HIVPA conference quiz conducted by our Brightonian hostess Dr Yvonne Gilleece.

HIVPA conference 2018 is shaping up to be even more exciting than last year and will be a great opportunity to get ahead on fulfilling the General Pharmaceutical Council's (GPhC) new requirements for the revalidation of pharmacy by meeting with other pharmacists and pharmacy technicians, consolidating and increasing knowledge through expert sessions whilst networking.

We will have sessions on cardiovascular disease and HIV, opportunistic infections and tuberculosis, transplants in HIV, commissioning for value, APTUK frameworks, RPS faculty, revalidation for both technicians and pharmacists and medication adherence. This will help everyone become revalidation ready and support professional development through the provision of learning opportunities for professional development at all career stages for generalist and specialist areas of practice.

We'd also like to encourage you to submit posters on audit/project posters you have been working on over the last year as this is a great chance to share with other colleagues the work being undertaken by pharmacist and technicians at your centre!

Reflection by **Ojali Negedu**
Imperial College Healthcare NHS Trust

SAVE THE DATE- HIVPA Conference 2018 will be held at the Crowne Plaza Hotel in Manchester on the 15th and 16th of June. The conference will start at lunchtime on Friday and will finish at 5.30pm on Saturday.

There are a wide variety of topics on offer over the two days, with some very experienced speakers that will cater for all our delegates, so book your place early to avoid disappointment. There will also be a poster exhibition at the conference which will display the best of HIV pharmacy practice and research. There will be a sponsors' exhibition open to our industry sponsors where information and updates will be available from our industry colleagues. Confirmed sessions so far include:

Cardiovascular disease and HIV Speaker: Scott Murray

Improving networks Speaker: Mas Chaponda

Ols and TB Speaker: Rob Miller

Adherence Speaker: Rob Horne

Treatment guidelines Speaker: Laura Waters

Commissioning for value Speaker: Sonali Sonecha

Virtual Clinic – Pharmacist cases Speaker: Adele Torkington

Transplant in HIV Speaker: Caroline Ashley

Isentress HD

The natural advantages of integrase inhibitors (INSTIs) compared with other third agents makes it easy to see why prominent guidelines are now recommending INSTIs as preferred initial therapy in the management of HIV. Large clinical trials and daily practice continue to show effective virological suppression with INSTIs combined with better tolerability, compared with protease inhibitors and non-nucleoside reverse transcriptase inhibitors (NNRTIs). In addition, transmitted INSTI resistance continues to remain low, particularly in developed countries, while the advent of dolutegravir has re-assured clinicians when it comes to patients with previous resistance and/or poor adherence.

Since initial approval of Isentress (raltegravir) as the first in-class drug a decade ago, further integrases have been developed and become popular including elvitegravir and dolutegravir, soon to be followed by bictegravir later this year. As well as benefits in tolerability, INSTIs have the advantage of reducing viral loads more quickly than combinations including other third agents, generally have significantly less drug-drug interactions (DDIs) (excluding cobicistat-boosted elvitegravir) and can have a high genetic barrier to resistance (dolutegravir) while some are available as patient friendly single-pill combinations.

Although significant data supports the excellent tolerability profile of raltegravir, not just within the integrase class but across classes, and it's reassuring safety profile in pregnancy, it has the potentially significant disadvantage of requiring twice daily (BD) dosing, a particular concern in patients where adherence may already be an issue.

Although the BENCHMRK 1 & 2 trials demonstrated effective viral suppression with raltegravir in multi-drug resistant patients, there was also significant variability in raltegravir pharmacokinetics, potentially attributed to food intake or DDIs, but not necessarily. Despite this pharmacokinetic variability, raltegravir's half-life and long binding to the HIV integration complex convinced Merck-Sharp & Dohme (MSD) that it might be suitable for once-daily (QD/OD) administration. The QDMRK study demonstrated viral suppression after 48 weeks in 83.2% vs 88.9% when comparing once daily (2*400mg) with traditional 400mg BD dosing of raltegravir, with particularly poor rates in subgroups with high baseline viral loads (74%) and low baseline CD4 counts (71%). These results were at least partially attributed to once daily raltegravir trough concentrations being 5-6 times lower than that of twice daily dosing. Once-daily raltegravir was also associated with higher incidence of INSTI resistance, and although it could have a place in patients wishing to switch to once daily dosing once suppressed (still a contentious issue) it was not considered reliable in initial treatment, particularly for those with high viral loads. Overall, this initial attempt at once daily dosing was something of a flop.

MSD now seem to have made progress since their previous failures with the development of Isentress HD (high-dose). Their new once daily formulation of raltegravir is formulated as 2*600mg tablets. So how did they do it? While once daily dosing with different formulations (3*400mg and 2*600mg) demonstrates similar systemic pharmacokinetics, bioavailability of Isentress HD is greater as a result of improved absorption following from superior in vivo dissolution. Food seems to have a smaller effect on Isentress HD pharmacokinetics (42% vs 73% re-

Isentress HD

-duction in AUC). Smaller food effects were also seen with raltegravir 2*600mg when compared with raltegravir 2*400mg with low- and high-fat meals. Isentress HD is more rapidly absorbed in the fasted state with a higher Cmax and sharper absorption peak when compared with 400mg BD. As might be expected, the relative bioavailability of Isentress 2*600mg is higher than that of 2*400mg (66% vs 21%) as a result of greater dissolution.

Now that the ONCEMRK 96 week results are available we can translate theory in to practice when comparing once daily raltegravir with traditional dosing over the long term. The 96 week results were published in July 2017 and Isentress HD has now been commissioned by NHSE as a result.

Trial protocol randomly assigned treatment naïve individuals aged 18 years or older in a 2:1 ratio to either Isentress HD (n=531) or Isentress 400mg (n=266) while all received a TDF/FTC backbone. The majority of participants were white (60%) males (85%) with a mean age of 36 years (+/- 10.5). 12% of patients presented with AIDS and 3% with a hepatitis B or hepatitis C co-infection. The trial sought to establish non-inferiority, with a lower limit of -10%, with raltegravir twice daily where the primary endpoint was the proportion of patients in each arm achieving HIV-1 RNA levels <40 copies/ml while comparing safety and tolerability.

96 week data demonstrated non-inferiority with Isentress HD where 81.5% of patients taking once daily raltegravir (2*600mg) achieved viral suppression vs 80.1% with 400mg BD, treatment difference 1.4% (95% CI -4.4, 7.3). Immune reconstitution was also comparable with an increase in CD4+T-cell counts from baseline of 261.6 cells/ml vs 262.2 cells/ml with Isentress HD and Isentress BD respectively. Results were consistent across sub-groups including those with viral loads >100,000 copies/mL at baseline (28% of trial participants) with response rates of 85% vs 83%, treatment difference +1.8 (95% CI -4.2, 5.2). Any treatment-emergent drug resistance was detected in 0.8% of participants in both arms similar to findings of other INSTI trials in treatment-naïve individuals.

Considering the higher bioavailability and dose of Isentress HD it seems likely that adverse drug reactions would be more of a concern with the new formulation, but apparently not. Discontinuation from adverse events was minimal (0.9% vs 2.3%) compared with twice-daily Isentress while deaths were identical in each arm (0.4%) and were attributed to disease factors rather than treatment. The most common drug-related adverse effects were nausea (7.5 vs 7.5%), headache (3% vs 4.9%), dizziness (2.3% vs 3.4%), diarrhoea (2.4% vs 2.6%) and abdominal pain (3.0% vs 1.1%) when comparing Isentress HD with Isentress BD with both formulations being considered comparable in terms of tolerability. Bottom line numbers suggest that Isentress HD offers comparable viral suppression and tolerability to the 400mg formulation with the added convenience of once-daily dosing.

While MSD has competitively priced Isentress HD to match the original BD formulation, without any patent extension no less, a few caveats to once-daily dosing means that not everyone is eligible for a switch. There is no data available to support the use of Isentress HD in pregnancy and it may take some time for such information to accumulate. From a practical point of view Isentress HD is slightly larger in size which may be off-putting for some patients where frequency of administration is less of a concern than tablet size. As well as tablet size, tablet burden

Isentress HD

is also a sticking point for Isentress where any raltegravir regimen has to compete with the convenience of significantly smaller tablets and single-tablet regimens compared with other INSTIs.

In relation to interactions it has been advised that Isentress HD should not be co-administered with calcium, magnesium or aluminium containing compounds regardless of whether doses are separated, although it is difficult to know whether clinicians will heed this warning in practice. From a pharmacy perspective it is important we clearly communicate how the low trough levels with raltegravir OD, refer to the QDMRK data mentioned earlier, are relevant here. Other pertinent information includes the lack of data on dosing OD raltegravir alongside UGT1A1 inducers (ie rifampicin) where there is no data on the relevant pharmacokinetics, again in particular with regards to trough levels. It is likely that co-administration would require switching to BD raltegravir for re-assurance if twice-daily administration is an option. There is no data to suggest that less potent inducers such as efavirenz will cause clinically significant induction of Isentress HD. Conversely, inhibition of UGT1A1 by atazanavir causes clinically significant increases in raltegravir levels with the new once-daily formulation and concomitant use is not recommended; co-administration with tipranavir/ritonavir also results in increased exposure and is not recommended.

In conclusion it seems like treatment with raltegravir, with its advantageous tolerability profile, is back in contention for the treatment of patients requiring INSTIs where once-daily dosing is considered essential where patients are not pregnant and drug interactions are carefully considered.

Suggestions for further reading

Efficacy and safety of raltegravir for treatment of HIV for 5 years in the BENCHMRK studies: final results of two randomised, placebo-controlled trials. ***Original article : Lancet Infect Dis. 2013 Jul;13(7):587-96. doi: 10.1016/S1473-3099(13)70093-8. Epub 2013 May 7. JJ Eron***

http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(13)70093-8/fulltext

QDMRK Study: raltegravir QD vs BID, with TDF/FTC
Original article : Lancet Infect Dis. 2011 Dec;11 (12):907-15 - JJ Eron

http://www.arv-trials.com/first_line/eng/comp_INSTI-vs-INSTI/QDMRK.asp

ONCEMRK Study: raltegravir 1200 mg QD vs 400 mg BID, with TDF/FTC
Original article : Cahn P. Lancet HIV, 11 Sept 2017 (ePub ahead of print) ; Cahn P, IAS 2017, Abs. TUPLBEB20

http://www.arv-trials.com/first_line/eng/comp_INSTI-vs-INSTI/ONCEMRK.asp

Trial summary and reflection by **Richard Strang**
University Hospitals of Leicester NHS Trust

Your professional development; getting ready for revalidation

RPS Faculty

Why should I become a member of the Faculty?

Many pharmacists with an expertise in HIV are already considered specialists, however have you considered how you would demonstrate your advanced practice to your peers and other medical colleagues? Employers recognise the value of Faculty membership and some Chief Pharmacists are already including it as a requirement in job descriptions. The Royal Pharmaceutical Society (RPS) Faculty programme was established in 2013. In the five years that it has been supporting members; leaders from all sectors have commented on the development opportunities which are identified by completing and submitting the RPS Faculty portfolio. The Faculty programme is applicable to pharmacists from all sectors and can be used throughout your career and will support pharmacists to develop expertise as generalists or specialists.

What do I need to do?

The Faculty is structured around the Advanced Pharmacy Framework (APF). The APF identifies six key areas (which are also referred to as clusters) which are important for both development and in demonstrating advanced stages of practice:

Advanced Stage I,

Advanced Stage II,

Mastery.

You will need to submit for an assessment that demonstrates depth and breadth of advanced practice. You will need to build a portfolio of your practice, provide a CV of your career history, collect peer testimonials and undertake a record of expert professional practice assessment.

We have a number of resources to help you get started. Our 10-step programme supports members in building and preparing for their submission. The 10 step programme can be tailored to suit your individual requirements and needs. The benefit of this approach is that you are able to work through your submission at your own pace, 10 steps could mean 10 weeks or it could mean 10 months. These stepwise milestones have proven to help members complete their Faculty submission as it provides you with deadlines and keeps you on track.

Working in small groups with colleagues is another particularly successful way of completing and staying on track with the Faculty. Your peers and colleagues often are at the same stage of career development as you and by having small groups you are able to discuss clusters and record competencies in a clear and structured way. These working groups don't have to meet physically, but can meet over the phone or using email discussion platforms.

Your professional development; getting ready for revalidation

A mentor who has completed the Faculty programme and is working within your sector is again another useful resource that the RPS can offer members looking to complete their Faculty portfolios. Mentors may be able to review competencies that you have recorded and can discuss with you clusters which you are struggling to record. Mentors are accessible by email and telephone as well as meeting face-to-face with mentees. To find out more about mentorship and how a mentor can help you complete your faculty portfolio please visit the mentoring page on the RPS website - https://www.rpharms.com/network/mentoring

How does Faculty support revalidation?

Revalidation is coming. The General Pharmaceutical Council (GPhC) has announced that they are changing the way in which pharmacy professionals record their continuing professional development (CPD). We are working with the GPhC to ensure that Faculty can be used for revalidation, so you don't have to duplicate recording of your learning and development, and simply use what you've done for your Faculty submission.

What do I need to do for revalidation?

You will need to complete CPD records on an annual basis, which will include 4 CPD learning records, with a minimum of 2 records being planned and a maximum of 2 being unplanned. You will additionally need to complete one peer discussion and one reflective account.

As from Autumn 2018 or the time you are due to renew your registration with GPhC, you will need to submit your CPD records. In 2019 additional requirements will be introduced for the peer discussion and reflective account.

CPD will also now relate to your previous year of practice rather than a longer time frame.

What should I do now?

We are developing resources, services and products to support you with revalidation so you'll be ready for all the changes. Take a look at our dedicated revalidation webpage (https://www.rpharms.com/revalidation), which provides a summary of the key changes and a timeline of when you need to complete certain activities. We have a number of resources including exemplar records, FAQs, and pre-recorded webinars. We are also running a series of events across the country so join us if you can and take the opportunity to ask questions. Keep an eye on the webpage for details of dates.

I hope the above has helped answer some of the questions you may have around revalidation. For further information or support please get in touch directly with our revalidation support team on 0207 572 2737 or email revalidation@rpharms.com.

Contribution by **Aamir Shaikh** with Elizabeth Ward
Royal Pharmaceutical Society

HIVPA Study Days– To Sum It Up

HIVPA hold four study days during the year which are always popular with our members because we invite high profile speakers to address topical clinical issues. Here is a summary of the topics discussed at the most recent study days from the speakers themselves.

Dates and topics for 2018

An introduction to HIV **24th April 2018**

Research, cure, "How to": conduct critical appraisal, journal article review style session, fake news, advanced practice, posters **19th September 2018**

New treatment guidelines, resistance and switch **7th November 2018**

The study days are open to any pharmacy or healthcare staff especially those with a special interest in HIV, so please feel free to share information about these events with your colleagues. Attendance is free for HIVPA members. A small charge is required for non members, payable in advance.

The Study Days are held at the Pullman hotel, 100-110 Euston Road, London NW1 2AJ near Euston and Kings Cross train stations.

To reserve your space on any of our Study Days please email Yvonne on hivpaoffice@gmail.com

Recent feedback comments from study day attendees:

Very informative and highlights areas that may not be experienced in each clinic.

A very interesting and extremely informative meeting.

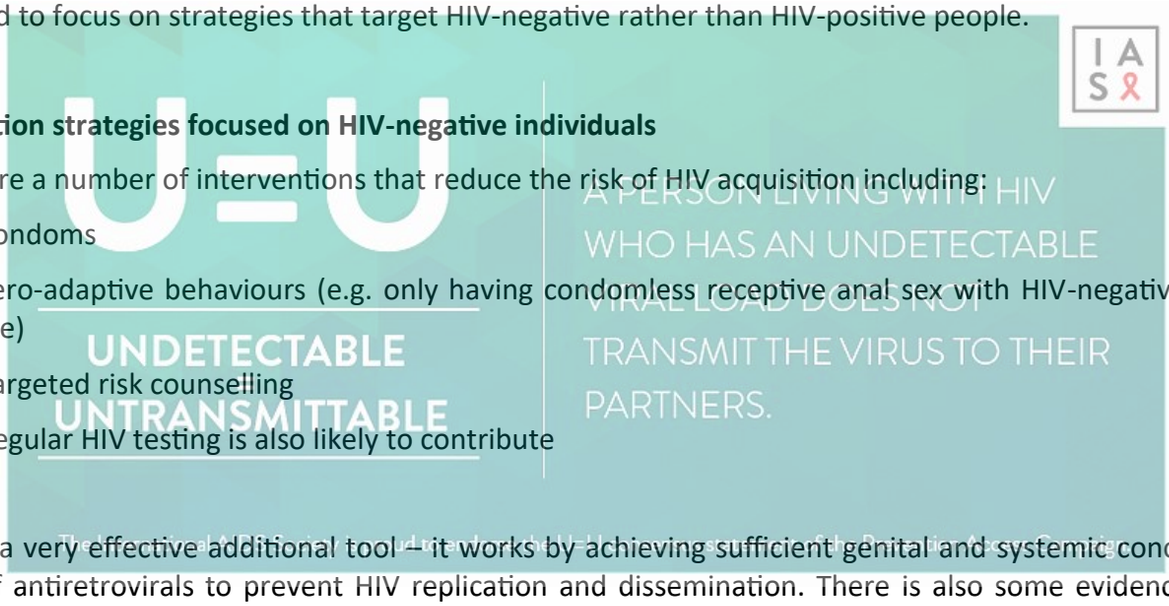
Very informative study day, lots of very useful information + some very impressive speakers. Starting later a good idea in terms of travel. Thanks!

HIV pre-exposure prophylaxis (PrEP)

Why do we need PrEP?

Until recently the annual number of new HIV diagnoses in the UK was rising (just over 6,000 cases in 2015), despite high levels of treatment and high rates of viral suppression. We know that effective antiretroviral therapy (ART) essentially eliminates the risk of onward HIV transmission; the randomised HPTN 052 trial and the observational PARTNER study demonstrated ZERO cases of transmission to an HIV -negative partner where the HIV-positive person had an undetectable viral load on ART. Further evidence was provided by OPPOSITES ATTRACT, an observational study in men who have sex with men (MSM) presented at the 2017 IAS conference; if we combine the MSM data from PARTNER with OPPOSITE ATTRACT there have been NO ONWARDS TRANSMISSIONS from suppressed MSM after around 40,000 condomless anal sex acts! Undetectable = untransmissible.

So, if so many people are on ART (96% of the diagnosed population in 2016) and undetectable (94% of the treated population in the same year) and treatment as prevention (TasP) is so effective why do we still see so many new HIV diagnoses? The impact of TasP will vary according to the nature of the epidemic in a given region – in the US most transmission is from people who are diagnosed but not on treatment so TasP has significant potential to reduce new infections. In UK MSM, however, most transmission (estimated over 80%) is from people with HIV that is **undiagnosed** – here TasP cannot have an impact and we need to focus on strategies that target HIV-negative rather than HIV-positive people.



Prevention strategies focused on HIV-negative individuals

There are a number of interventions that reduce the risk of HIV acquisition including:

- Condoms
- Sero-adaptive behaviours (e.g. only having condomless receptive anal sex with HIV-negative people)
- Targeted risk counselling
- Regular HIV testing is also likely to contribute

PrEP is a very effective additional tool – it works by achieving sufficient genital and systemic concentrations of antiretrovirals to prevent HIV replication and dissemination. There is also some evidence that tenofovir-DF/emtricitabine (TDF/FTC, the most studied and, currently, only licensed drug for PrEP) reduces T-cell activation which may contribute to it's protective effect.

Several studies have demonstrated the effectiveness of TDF/FTC PrEP in heterosexuals and MSM; there are more limited data support TDF alone in heterosexuals. IPERGAY and PROUD were the game changers for Europe: IPERGAY is a French study which investigated intermittent or 'event-based' TDF/FTC vs placebo (drug taken before/after sex) and PROUD is a UK study that investigated immediate vs deferred PrEP with daily TDF/FTC. Both trials showed an **86% reduction** in HIV incidence with PrEP. The intermittent regimen is best explained by this helpful community-led guide: http://i-base.info/guides/prep

HIVPA Study Days– To Sum It Up

Access to PrEP

Scotland is the only British country providing routine PrEP and they are doing so with generic TDF/FTC. Wales provide Truvada through a pilot scheme with no cap on numbers. England is providing generic PrEP via the PrEP IMPACT trial which is running in several GU clinics to provide PrEP to about 10,000 people. The decision to run a trial was the culmination of many months of policy writing, a court case (following a legal challenge form the National AIDS Trust) to determine whether or not NHSE are responsible for prevention (it ruled they are, NHSE appealed, and the original decision was upheld) and finally a decision by NHSE to not routinely commission PrEP but to invest £10 million in the trial. PrEP IMPACT is being led by PHE and managed by St Stephen's AIDS Trust.

The other route to access PrEP is to purchase it online and here the community have been instrumental in providing access to information including which generic sites have supplied drug that has been validated by measured drug levels. In England it is entirely legal to buy up to 3 months of generic drugs online (regardless of that drugs patent) for personal use – this is not the same across Europe, including Ireland.

A legal challenge in the UK between Gilead and generic companies was referred to the European Court and a ruling is pending – it is highly unlikely that NHS England would procure generic PrEP while that decision is awaiting. Scotland, as above, have gone ahead but there is a theoretical risk of legal challenge and in Ireland, Gilead blocked access to generic TDF/FTC for PrEP. It will be interesting to see how this all unfolds!

Other outcomes

The significant impact of PrEP on HIV acquisition risk is undoubted and the marked decline in new HIV diagnoses in England in 2016 (driven mainly by steep falls in some central London services) is likely driven, at least in part, by MSM at high risk of HIV acquisition using PrEP and by increased HIV testing frequency (which itself may be a consequence of people accessing services for PrEP monitoring and advice). Although most PrEP trials did not demonstrate any increase in rates of other sexually transmitted infections (STIs) and tended to show a reduction in risk behaviour (condom use, number of partners) the open -label extension of IPERGAY demonstrated a significant increase in condomless sex and increased STIs including syphilis. In the US, where Truvada has been licensed for PrEP since 2012, cohorts show high rates of STI in PrEP users but very low or zero new cases of HIV which, for most of us working in sexual health, is a 'pro' that far outweighs the 'cons'. Syphilis rates continue to rise in the UK, though this predates availability of PrEP and is more likely driven by changes in sexual behaviour in the light of the high efficacy of successful ART in preventing transmission. Interestingly rates of gonorrhoea have fallen MSM which may be a product of increased testing frequency.

Tenofovir-DF is associated with renal impairment and in PrEP trials, people receiving TDF/FTC experienced a small, non-progressive decline in estimated glomerular filtration rate (eGFR). In IPERGAY significantly more participants experienced creatinine rise (18% vs 10% on placebo, p=0.03), almost all grade 1. The US Kaiser Permanente cohort showed that eGFR decline in the 1st year of PrEP use is most frequent in individuals with a baseline eGFR <90, particularly those over 50. The iPrEX study measure bone mineral density in MSM receiving TDF/FTC PrEP and showed a reversible drop in BMD.

There are also benefits of PrEP beyond HIV prevention. In addition to the potential benefits of more frequent STI screening, qualitative interviews from PROUD eloquently describe the impact of PrEP on fear and anxiety related to sex.

Alternatives to TDF/FTC

There is a large trial underway in MSM, DISCOVER, comparing tenofovir-alafenamide (TAF)/FTC with TDF/FTC. TAF may not be suitable for PrEP in women as early data shows lower cervico-vaginal concentrations of drug compared with TDF. Topical TDF trials have shown moderate efficacy at best and this correlates with vaginal flora – women with non-lactobaccillus-dominant flora have lower drug levels.

Injectable rilpivirine was an exciting prospect for PrEP but further development has been terminated following studies showing suboptimal female genital tract drug concentrations and ex vivo viral suppression. Injectable rilpivirine continues to be developed as a therapeutic agent.

Injectable cabotegravir has been shown to be well tolerated and is under investigation in PrEP efficacy trials dosed every 8 weeks.

Finally a vaginal ring containing the investigation NNRTI dapivirine has shown moderate efficacy and, unlike topical tenofovir, levels are not impacted by differences in vaginal flora.

Conclusions

We have all the tools we need to eliminate HIV transmission and PrEP is a crucial one of those. Unfortunately the costs, drug and service-related, associated with providing PrEP are a significant barrier to PrEP in several European countries, including England. The down turn in new HIV diagnoses in England is really limited to a few central London centres and to MSM; we need to focus on better prevention and testing in order for all regions and all groups at risk to enjoy the benefits of HIV prevention.

Laura Waters Consultant GU/HIV Medicine, Mortimer Market Centre, CNWL

HIV and Dietary Management

Cardiovascular Disease

* CVD is the leading cause of non-AIDS morbidity & mortality in PLHIV. It is also the most frequent cause of death in PLHIV surviving > 10 years after starting ART (Tricky et al, 2016). Relative risk of CVD for PLHIV is 1.6 vs general population (Islam et al, 2012).
* Increased prevalence of surrogate markers for CVD in PLHIV - ART may not mitigate, and may exacerbate these markers.

HIVPA Study Days– To Sum It Up

* Assessment of CVD: NICE recommends QRISK2 (gen pop) BHIVA suggests added RR factor of 1.6 for HIV: https://www.qrisk.org/
* Poor diet and HIV can both increase CVD risk. Critical drivers of non-AIDS events are the metabolic and inflammatory consequences of excess adiposity Dietary factors can contribute to hypertension, dyslipidemia, obesity/ overweight, risk of T2DM which all increase risk

Dietary modification of CV risk

* Variety of similar evidence –based dietary approaches, paucity of evidence for their efficacy in HIV patient cohorts although there is some (Lazzaretti et al 2012)
* Cardioprotective diet: Basis for NICE recommendations - Low in saturated fat intake (<7% kcal), main fat sources are from monounsaturated fat , starchy food mainly wholegrain. low in sugar & refined sugars products including fructose, => 5 portions of fruit and vegetables per day , => 2 portions of fish / week, 1 to be oily, => 4 - 5 portions of unsalted nuts, seeds and legumes / week, wine in moderation
* Portfolio Diet: as above + addition of specific functional foods - Plant Stanols and/or Sterols: 2g daily +Almonds: 30g (about 23 almonds) daily + Soluble fibre: 20g daily + Soya protein: 50g daily

Overweight and Obesity in PLHIV

* Overweight and obesity and increasing issue in HIV populations
* Koethe et al, 2016: Cohort study in USA & Canada - ACCORD (HIV) vs NHANES (Non –HIV), ~ 14,000 people, 12 year period. Median BMI at ART initiation increased from 23.8 to 24.8 kg/m2 - 1998 and 2010 in NA-ACCORD, but the percentage of those obese (BMI ‡30 kg/m2) at ART initiation increased from 9% to 18%. Weight gain in the first 3 years after starting ART resulted in NA-ACCORD participants ‘‘catching up’’ to the average BMI of similarly aged members of the general population, and exceeding the general population in the case of HIV-infected white females.
* Analysis of data from DAD study showed short-term gain in BMI following ART initiation appeared to increase the longer term risk of CVD, but only in those with pre-ART BMI in the normal range. It was also associated with increased risk of diabetes regardless of pre-ART BMI (Acchra et al, 2015
* Obesity or lipohypertrophy? Lipohypertrophy - “accumulation of visceral and central fat in the abdomen, dorsocervical region (“buffalo hump”), or breasts - Assessment methods: clinical examination, self-report, anthropometry, bioelectrical impedance analysis (BIA) and imaging (DEXA/ MRI/).
* Ideally need baseline (pre ART) anthropometric data for comparison. Both generalised obesity and lipohypertrophy are prevalent among HIV-infected persons on ART

Weight Management – Key points

* Refer to a Dietitian if possible +/- weight management services via the GP

HIVPA Study Days– To Sum It Up

* Prevention of weight gain–consider when starting patients on ARVs, aim for -5-10% weight loss = positive benefits to health -more realistic than aiming for a normal BMI, avoid crash diets and yo-yo ing of weight, increase physical activity – e.g. 10,000 steps/ day, permanent dietary change – no quick fixes, behavioural change crucial, be aware that some PLHIV find concept of weight loss stigmatising , if BMI> 35 – consider requesting a bariatric referral
* Weight reduction medication:

  ⇒ Orlistat (Xenical): Co-admin with ARVs not studied, theoretical reduction in ARV absorption, Needs to be taken 1 hour either side of food to be effective– acts on the meal. If patient on lipophilic ARV could restrict Orlistat to meals taken > 2 hours pre/ post ARVs

  ⇒ Liraglutide (Saxenda): significantly more expensive but no known interactions with ARVs

  ⇒ OTC/ herbal supplements for weight reduction: Very limited double blinded RCTs evaluating efficacy, individual ingredients may demonstrate certain effects,, efficacy influenced by purity grade of supplement, lifestyle of pt, food-drug interactions, excessive dosing, side effects. See separate hand out for Summary of "New Dietary Supplements for Obesity: What We Currently Know – Rios-Hoyo et al 2016"

  ⇒ Advising on dietary supplements for weight loss: Is it safe commercially available or black market? What are the key ingredients/ rationale? Is there a risk of interactions with ARVs? Might it be beneficial even as a placebo?

Pro-biotics in HIV

* Alteration in the gut microbiota can influence diseases, in PLHIV (including those on ART), gut microbiome very different vs those not infected with HIV, suggestion that dysbiosis may lead to a breakdown in the gut's immunologic activity à systemic bacteria diffusion and inflammation
* No universal 'pro-biotic' – most commonly proposed organisms are *Lactobacillus* and *Bifidobacterium* strains
* Theoretical risk of bacteraemia, sepsis and multiple organ failure due to bacterial translocation, no reported cases in those studying immunocompromised groups incl PLHIV

Nina Lenton HIV Specialist Dietitian, St Mary's Hospital, Imperial College Healthcare NHS Trust

The following pages are a summary of new dietary supplements for obesity: What We Currently Know and my lay thoughts on potential ARV interactions

HIVPA Study Days– To Sum It Up

Supplement	Rationale	Evidence for	Evidence against/ adverse effects/ limitations	Bottom line
Bitter Orange (*Citrus aurantium*) -Citrus tree and its fruit -Extract used in traditional Chinese and South American folk medicine	-Contains multiple phytochemicals including alkaloids – especially synephrine. -May exert sympathomimetic effects that contribute to an oxidative metabolism (i.e. 'fat burning')	-Effect of bitter orange on wt loss reported in combination with other products positively. -Small clinical trial – positive effect of synephrine on BMR	-Most studies have not found significant weight loss effects from administration -Common adverse events included chest pain, tachycardia, anxiety, dyspnoea, and pain in the lower left quadrant	Currently not enough evidence to recommend as an adjuvant in weight loss management.
Hoodia gordonii -medicinal plant from Apocynacae family	-Appears to have anorexigenic effects -unclear which compound is responsible but likely Oxypregnane glycoside P57AS3 (also known as P57)	-Rat trials in vivo = decreased food intake	-Needs to be consumed in large quantities due to extensive gastric breakdown -1 RCT (dbl blinded, cross overtrial): 49 overweight women = no effect on body weight -side effects include- Headache, nausea, inc SBP, inc pulse, inc bili, inc ALP, decrease in BUN, ECG abnormalities	Not effective for weight loss management and that it may lead to significant adverse events.
African wild mango or African bush mango - *Irvingia gabonensis* -Seeds high in lipids, polyphenols and flavinoids	-Researchers have observed inhibition in the expression of peroxisome proliferator-activated receptor gamma (PPAR-γ) and leptin	-An RCT evaluating weight loss, was included in a systematic review by Onakpoya et al who reported that 200 to 3150 mg/day of an I. gabonensis	-The most common adverse events included headache, sleep difficulties, and flatulence; however, these events were not significantly different between	Based on available clinical trials & systematic review, represents a possible adjuvant in weight loss strategies but more research

Supplement	Rationale	Evidence for	Evidence against/ adverse effects/ limitations	Bottom line
	protein levels and up-regulation of adiponectin expression with supplementation	extract given for 4 and 10 weeks resulted in both statistically and clinically significant reductions in body weight and waist circumference compared with placebo.	the study groups. -All the clinical trials were performed in Black Africans and in relatively small study samples.	needed to evaluate the effect in a larger, more diverse population.
Forskolin -active compound of Coleus forskohlii, -used in Ayurvedic medicine	-Forskolin is a potent stimulator of cAMP, which activates the hormone-sensitive lipase, thus promoting the release of fatty acids from adipose tissue	-Small clinical trials have found different effects based on gender	-No significant adverse events were reported in this study. -Conflicting results in men vs women + small number of participants in the studies so conclusions cannot be drawn regarding the effects on weight loss management.	Might be helpful in the management of overweight although more evidence is needed.
Green Coffee Extract -From green unroasted coffee beans	-The mechanisms proposed include a lipolytic effect on adipocytes, a decrease in pancreatic lipase activity, inhibition of fatty acid synthase, h droxymethylglutaryl	-A meta-analysis reported a statistically significant weight loss of almost 2.5 kg after supplementation with green coffee extract in doses ranging from 180		Because of the moderate clinical magnitude and the significant heterogeneity of the reported clinical trials, the current evidence is insufficient to recommend green coffee as an adjuvant within weight management.

Supplement	Rationale	Evidence for	Evidence against/ adverse effects/ limitations	Bottom line
	CoA reductase, and acylCoAcholestero acyltransferase; an increase in β-oxidation; and promotion of PPAR-α expression in the liver	to 200 mg/day over a treatment period of 4 to 12 weeks. Given these results, though, green coffee extract should be studied in larger clinical trials to assess its effect.		**Potential decrease in pancreatic lipase activity therefore treat as orlistat i.e. kept separate from ARVs?**
<u>Fucoxanthin</u> -a carotenoid widely distributed in nature.	-Fucoxanthin reduces both plasmatic and hepatictriglyceride concentrations. It also decreases acetyl-CoA. -Studies have revealed that fucoxanthin down regulates the expression of the low-density lipoprotein receptor in the liver. -Moreover, fucoxanthin decreases the expression of PPAR-γ, CCAAT/ enhancer-binding protein-α (C/EBPα), and sterol regulatory element-binding protein 1c (SREBP-1c) during the intermediate	-In a double-blind, placebo-controlled clinical trial, 31 obese participants found no significant differences regarding weight loss or body fat between the groups. -Another study of 151 obese premenopausal women found that patients receiving 300 mg of pomegranate seed oil and 300 mg of seaweed extract containing 2.4 mg of fucoxanthin had a statistically significant reduction in body weight, body fat, and waist circumference.	-Few clinical trials have been conducted	Based on the results from these clinical trials, no recommendations can be made regarding the consumption of fucoxanthin in the treatment of obesity.

Supplement	Rationale	Evidence for	Evidence against/ adverse effects/ limitations	Bottom line
	and late stages of adipocyte differentiation carboxylase expression, thus decreasing malonyl-CoA formation, as well as the expression of fatty acid synthase, decreasing the synthesis of long-chain saturated fatty acids	-Furthermore, the group receiving 8 mg of fucoxanthin showed an increase in resting energy expenditure, measured by indirect calorimetry		
Raspberry Ketone -is an aromatic substance used by the food industry for flavouring	-In vitro studies using adipocytes have observed an increase in fatty acid oxidation, suppression in lipid accumulation, and increased secretion of adiponectin. -Possible mechanisms of action include stimulation of the white and brown adipose tissues and inhibition of pancreatic lipase activity	-Molecular studies demonstrating pathway of action -In vivo in Rats, raspberry ketone prevented high-fat diet–induced increases in body weight and visceral adipose tissues.	-Nil human studies -Raspberry ketone has the potential adverse effect of cardiotoxicity as well as a teratogenic effect, as identified in silico	Raspberry ketone has the potential adverse effect of cardiotoxicity as well as a teratogenic effect, as identified in silico **Given potential mechanism of action includes inhibition of pancreatic lipase activity - ? should be treated as Orlistat i.e. kept separate from ARVs**
Glucomannan -a hydrocolloid polysaccharide of the mannan family, found in roots,	-Glucomannan can absorb up to 50 times its weight in water. It passes relatively unchanged	-Two meta-analyses evaluating efficacy of glucomannan. These studies analyzed nine clinical	-Both studies reported significant heterogeneity in their results, one found a statistically	Although statistically significant reduction in weight among study participants using glucomannan, this weight loss is not

Supplement	Rationale	Evidence for	Evidence against/ adverse effects/ limitations	Bottom line
tubers, and many plant bulbs -soluble fibre	into the colon, where it is fermented by the gut microbiota. -Different mechanisms have been proposed to explain the effects of glucomannan on weight loss, including promotion of satiety through increased mastication efforts, delayed gastric emptying, and reduced small bowel transit. Fecal energy loss also has been proposed as a mechanism, because soluble fibers reduce fat and protein absorption.	trials, six of which were included in both analyses.	significant reduction in weight, −0.79 kg, among participants receiving glucomannan for a mean of 5.2 weeks. The more recent meta-analysis revealed a non-statistically significant difference of −0.22 kg in weight loss between the glucomannan and placebo groups, contradicting the earlier meta-analysis	necessarily clinically significant; thus, the results should be interpreted carefully.
β-Glucans -Glucose polysaccharide -present in cereal grains in cell wall of endosperm or in mushrooms as major structural component of the cell walls.	-Glucans non- digestible fibre fermented in cecum/ colon (pre-biotic. -Weight loss effects derive from being a soluble fibre		Overall, most of these trials reported no or nonsignificant effects on weight loss from β-glucans administered at 3 to 10 g/ day for 4 to 12 weeks	Therefore, no conclusions can be drawn regarding the effects of β-glucan administration on satiety and/or appetite. Given these results, it may be concluded that β-glucan administration does not appear useful in treating overweight or obesity.

HIVPA Study Days– To Sum It Up

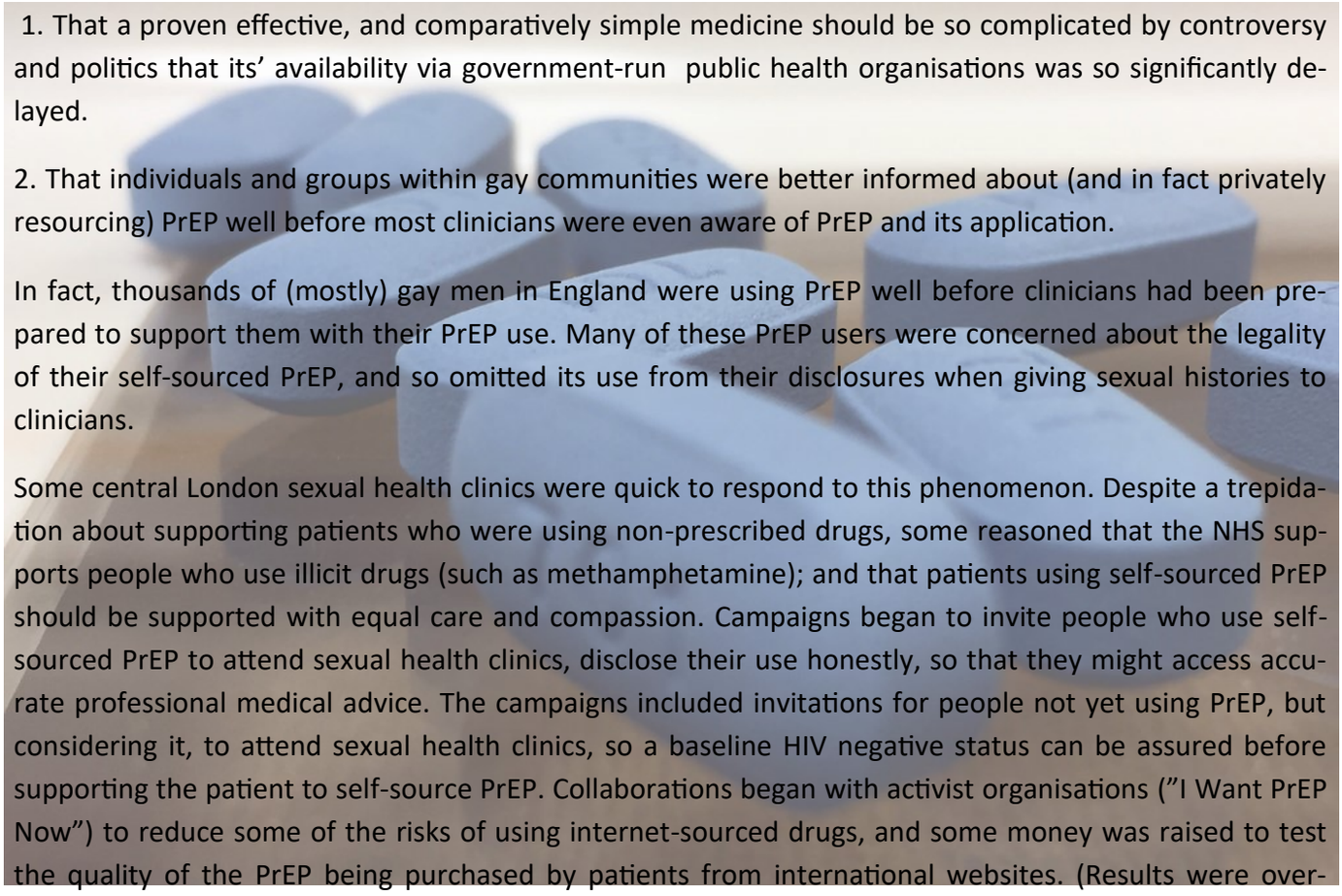
Supplement	Rationale	Evidence for	Evidence against/ adverse effects/ limitations	Bottom line
Guar Gum -from *Cyamopsistetragonoloba* plant -source of soluble fibre	-Source of soluble fiber and is used as an emulsifier and thickener in diverse foods -Bulking agent – therefore decreases food intake and increases satiety	-Meta-analysis of 11 RCTs (dbl blinded, placebo-controlled) guar gum 9-30g/day for 3 weeks-6 months – no signif differences. -Subsequent RCT in patients with T2DM – signif reduction in WC but not wt loss		Therefore, current evidence does not support the use of guar gum as a dietary supplement for treating overweight or obesity.
Chitosan -a family of deacetylated chitins	-The mechanism by which chitosan may exert a weight loss effect is by binding to negatively charged fat molecules within the intestinal lumen, thus preventing its absorption	-First published meta-analysis reported a statistically significant weight loss of 2.38 kg after 28 days of treatment; however, more recent meta-analyses and systematic reviews have not found the same results. -Cochrane meta-analysis including 13 clinical trials found a weighted mean difference in body weight of −1.7 kg after chitosan supplementation vs placebo, which was statistically significant.	-No mention of harm - One clinical trial compared the effects of orlistat (a pancreatic lipase inhibitor) vs chitosan on fecal fat excretion, finding that the latter did not inhibit dietary fat absorption.	**If preventing/ reducing fat absorption – potential for reduced absorption of lipophilic ARVS?**

Supplement	Rationale	Evidence for	Evidence against/ adverse effects/ limitations	Bottom line
		However, when the inclusion standards were increased and only high-quality trials were analyzed, the reduction in estimated weight loss was only −0.6 kg, which nevertheless was still statistically significant.		
White Kidney Bean *-Phaseolus vulgaris*	-"carbohydrate blocker" actions, phaseolamin inhibits pancreatic amylase and so theoretically digestion of dietary starches.	Small short-term studies - statistically significant decrease in fat mass but not weight.	-Poor quality trials -No long term safety reports	Accurate conclusions cannot be drawn - more robust clinical evidence, together with long-term safety report needed.
Garcinia cambogia -south east Asian tree	-Extracts of its exocarp have shown anorexigenic effects. G. cambogia contains high amounts of hydroxycitric acid— its proposed bioactive substance—whose mechanisms of action regarding weight loss include inhibition of extramitochondrial citrate lyase (thus, fatty acid and cholesterol synthesis)	-Results from RCTs have been controversial, with some studies failing to show significant differences versus control groups and others reporting significant weight loss	-in vivo experiments found an association of G. Cambogia and isolated hydroxycitric acid with significant adverse effects, the clinically most important of which is hepatotoxicity, but also testicular atrophy, epididym fat accumulation, hepatic collagen accumulation, lipid peroxidation, and increased hepatic transaminases	Little evidence exists to support its long-term effectiveness in weight management . Additionally its safety profile should be considered carefully (the plant has not been confirmed as the sole culprit when used in multicomponent formulations)

HIVPA Study Days– To Sum It Up

The Clinician's Experience of PrEP

The phenomenon of PrEP (Pre Exposure Prophylaxis for HIV) might be summarised by the following two points.



1. That a proven effective, and comparatively simple medicine should be so complicated by controversy and politics that its' availability via government-run public health organisations was so significantly delayed.

2. That individuals and groups within gay communities were better informed about (and in fact privately resourcing) PrEP well before most clinicians were even aware of PrEP and its application.

In fact, thousands of (mostly) gay men in England were using PrEP well before clinicians had been prepared to support them with their PrEP use. Many of these PrEP users were concerned about the legality of their self-sourced PrEP, and so omitted its use from their disclosures when giving sexual histories to clinicians.

Some central London sexual health clinics were quick to respond to this phenomenon. Despite a trepidation about supporting patients who were using non-prescribed drugs, some reasoned that the NHS supports people who use illicit drugs (such as methamphetamine); and that patients using self-sourced PrEP should be supported with equal care and compassion. Campaigns began to invite people who use self-sourced PrEP to attend sexual health clinics, disclose their use honestly, so that they might access accurate professional medical advice. The campaigns included invitations for people not yet using PrEP, but considering it, to attend sexual health clinics, so a baseline HIV negative status can be assured before supporting the patient to self-source PrEP. Collaborations began with activist organisations ("I Want PrEP Now") to reduce some of the risks of using internet-sourced drugs, and some money was raised to test the quality of the PrEP being purchased by patients from international websites. (Results were overwhelmingly positive, in regard to the quality.)

In late 2017, the PrEP Impact trial was launched offering PrEP to 10,000 HIV negative people in England, via a network of participating sexual health clinics. This is not to test the effectiveness of PrEP (which has already been established) but to assess the interest in PrEP before considering making it available freely on the NHS. (Some activists will argue that there are more politics at play here, such as Big Pharma contracts and monopolies in regard to purchase pricing for NHS England, as well as potential bigotry and stigma about promiscuity, and concerns about a reduction in condom use. I mention these arguments, because clinicians in sexual health services are likely to find themselves responding to questions and concerns regarding these politics from their patients.)

PrEP is effective, but it is not right for everyone. Clinicians can find themselves supporting patients to make decisions about whether PrEP is right for them. Factors that can play into this complex decision include;

⇒ HIV anxiety versus actual HIV risk

- ⇒ Authentic desire to use condoms consistently, versus real life use of condoms in varying complex sexual scenarios
- ⇒ In-bed pressures from community and sexual partners about changing condom politics in a new PrEP world
- ⇒ Differing community & individual concepts of STIs being problematic or upsetting, when negotiating necessity for condoms in a PrEP world.
- ⇒ Pressures and stigmas/bigotry re PrEP and condom use when hooking-up online

David Stuart 56 Dean Street, Chelsea and Westminster Hospital

The Role of the Hepatitis C Pharmacist

I was delighted to be invited again by HIVPA to present on a very exciting topic for me which is the role of the hepatitis C pharmacist. In North Manchester, we are the regional Infectious Diseases unit and so are blessed to have a very varied cohort and very wide ranging consultant specialities. We therefore not only treat HIV/HCV co-infections but also HCV mono infections.

During the study day we talked about the different clinic settings that can be used to provide hepatitis C treatment to ensure patient acceptability and continued adherence with therapy and follow up. We are very lucky to have very comprehensive community clinics including prisons, drug services, GP surgeries and voluntary sector clinics that we can provide care from, and we discussed how different individuals access these clinics, and benefit from the community services available.

We discussed the treatment options available within 2017 for hepatitis C and their mechanisms of action; we always love a bit of pharmacology! We are very thankful to have great treatments available that have very few side effects, very easy to take, however many drug-drug interactions which is why HIV pharmacists are best placed to advise, especially in our HIV/HCV co-infections.

We talked through some very complex patients including HIV/HCV co-infections in MSMs who use chems. A transgender patient with liver cirrhosis, we also discussed a vulnerable psychiatric inpatient with hepatitis C where the hepatitis C was the lowest priority for treating.

We were able to get down to the business of medicines optimisation strategies for hepatitis C pharmacy teams and how we can work with our CCG colleagues and really improve health outcomes for these individuals.

We moaned a little about all the admin and spreadsheets that has come with hepatitis C therapy, but were very thankful for CQUIN money that has allowed many units to hire pharmacists to manage these hepatitis C patients, rather than tagging onto the HIV pharmacist's never ending jobs list.

Adele Torkington North West ID unit @NMGH
HIVPA Expert Panel Member, Co-chair British Hepatology Pharmacist Group

My Research Journey

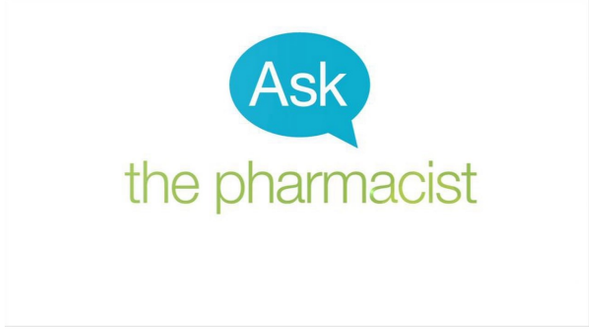
I was asked to write about my motivation for doing research. When I was a boy, I used to take apart redundant car parts to find out how they worked. I think I have always been curious. My father probably hoped I would follow his footsteps and become an engineer, however, in school holidays I was sitting in dispensaries in the Old Town of Edinburgh with my mother who was a locum pharmacist. At that time, I became fascinated by dispensing from prescriptions and wanted to know about how a written order, in Latin, could be interpreted as an instruction to dispense medicine. Now, I want to describe how the care we provide, as pharmacists, is perceived by the interprofessional team. Just like the cogs in the car parts, the interprofessional team works together and does something exceptional that improves a patient's quality of life. How does that work? So yes, I've always been curious. To study it, though, you have to ask the right question.

It was in 2012 when I realised the importance of asking the right question. I was a member of the HIVPA Research and Audit Committee. We believed we needed to prove our worth, and we wanted to survey our membership. We couldn't agree what we wanted to do, or what the question was. I reflected on that experience and decided to address what I believed was a deficiency in my knowledge and skills around research. I already knew that 'Research' is in most clinical pharmacist job descriptions in English hospitals. How could I achieve Mastery at Consultant Pharmacist level in Research? Certainly, Mastery level requires that you initiate and develop your own area of clinical practice research.

In 2014, I became aware that the National Institute for Health Research (NIHR) was offering fully-funded Master of Research in Clinical Practice (MResCP) studentships in England. I leapt at the chance and was lucky to get on the course at St. George's University of London (SGUL). I was thankful that St. George's University Hospitals NHS Foundation Trust supported this and gave me time away to study.

Uniquely, SGUL demanded that all students bring a research idea from their own clinical practice. This seemed to me to align better with my development needs. I knew I wanted to know more about what pharmaceutical care looks like in HIV treatment and care, so it was easy to think of what to study. How to do it though? During the course, we had modules on Research Methods, Statistics, Critical Appraisal, Research Project Planning and Management and Applied Research. We first learned how to differentiate between Audit, Service Evaluation and Research. The modules were timed to enable us to prepare a research protocol by Christmas of 2014 which was also a Summative Assessment. Although I passed that module, I had yet to submit the research design with an appropriate theoretical basis.

The question was clear enough: How do healthcare professionals perceive pharmaceutical care? Using the feedback from the Protocol Assessment, I was able to improve it and resubmit it for Ethics Committee and local Research & Development Approvals. This led to me choosing a qualitative research theoretical framework, specifically Hermeneutic Phenomenology. It is an inductive approach where the researcher, interprets the responses from participants to semi-structured questioning. The thematic analysis of the transcribed responses is a scientific method, and this is how new knowledge can be created. Consequently, I used Interpretative Phenomenological Analysis as the technique to describe the phenomenon, in this case, pharmaceutical care. Themes emerge in three categories: Descriptive, Linguistic and Conceptual.



My Research Journey

So how is this new knowledge? In the UK, we haven't fully described pharmacist activities in the specialty. Qualitative methodology allows us to describe in rich detail the sort of care issues we deal with. Qualitative interview data is typically nuanced and able to offer a viewpoint on clinical practice that can't be found in quantitative studies as they focus on specific answers based on a hypothesis.

Did I create new knowledge? I need to publish the study which I aim to do. Validity and rigour of qualitative methods are best evidenced in publication. Such research can inform practice guidelines for HIV specialist pharmacists in England, or the UK. Of note, Canada and the USA have practice guidelines for HIV clinical pharmacist practice. However, my research may not be generalisable, as there was only one site. Therefore it is an exploratory study and could be used to develop a broader research design including more centres. Interview-based studies commonly inform the design of a questionnaire which can then be quantitative and confirm or deny themes in clinical practice. A question may be about to what extent do HIV clinical pharmacists engage in drug-drug interaction queries each week? Responses need not be Y/N, but could be Likert scale (e.g. Not at all, Some Weeks, Most Weeks, Every Week, More than Once a Week).

There are a lot of research questions I have now that I would like to answer. It is necessary to prioritise these questions, and we are fortunate to have organisations like Pharmacy Research UK, that offer excellent guidance on the research journey, as well as research awards. Right now, I am lucky to be joining Professor Rob Horne's team at the School of Pharmacy, Department of Behavioural Medicine. There, I am acting as a research assistant on the SUPA programme, an NIHR-funded study, exploring whether an intervention in the clinic can improve uptake and adherence to antiretroviral therapy. I still have a foothold in clinical care part-time which I feel is important and informs the quality of research.

Now though, I have a chance to be a part of the creation of new knowledge, so I am excited about the next few years on my own research journey. I hope that I might be able to inspire others to consider a clinical academic career, as it is crucial for the NHS to become more research active especially at a time of immense challenge.

David Ogden GPhC, MSc, MRes

David Ogden won 2nd poster prize at the HIVPA conference 2017 with 'An exploratory study: Healthcare professionals' perceptions of pharmaceutical care in human immunodeficiency virus (HIV) and hepatitis C (HCV) management'.

Pharmacy Research UK

http://pharmacyresearchuk.org/

NHS National Institute for Health Research

https://www.nihr.ac.uk/

Kingston University London | St George's University of London

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An exploratory study: healthcare professionals' perceptions of pharmaceutical care in HIV and Hepatitis C management

Ogden DA [a], **Leake Date HA** [b], **Reeves S** [c] @daveinlond72

[a] formerly St. George's University Hospitals NHS Foundation Trust
[b] Brighton and Sussex University Hospitals NHS Trust
[c] Faculty of Health, Social Care and Education, Kingston University & St. George's University of London

Background

Pharmaceutical care (PC) is a philosophy of patient-centred care focussed on achieving best outcomes that improve a patient's quality of life[1]. Pharmacists who practice PC resolve drug-related problems (DRPs) among other processes[2]. Successful PC also relies on the integration of pharmacists into interprofessional healthcare teams[3]. Increased communication has been seen where pharmacists are located within healthcare environments[4].

People living with HIV (PLWHIV) require many PC processes to achieve best outcomes, because antiretrovirals (medicines that suppress the virus) are taken lifelong, have significant DRPs that if unresolved can result in toxicity or treatment failure[5].

Hepatitis C (HCV) infected individuals also share a need for PC similar to PLWHIV. The new Direct-Acting Antivirals (DAAs) have extensive DRPs and demand for PC is increasing rapidly[6]. There is very little research looking at how interprofessional teams perceive PC and none comparing the need for PC in these two specialties.

This study was completed in partial fulfilment of Master of Research in Clinical Practice.

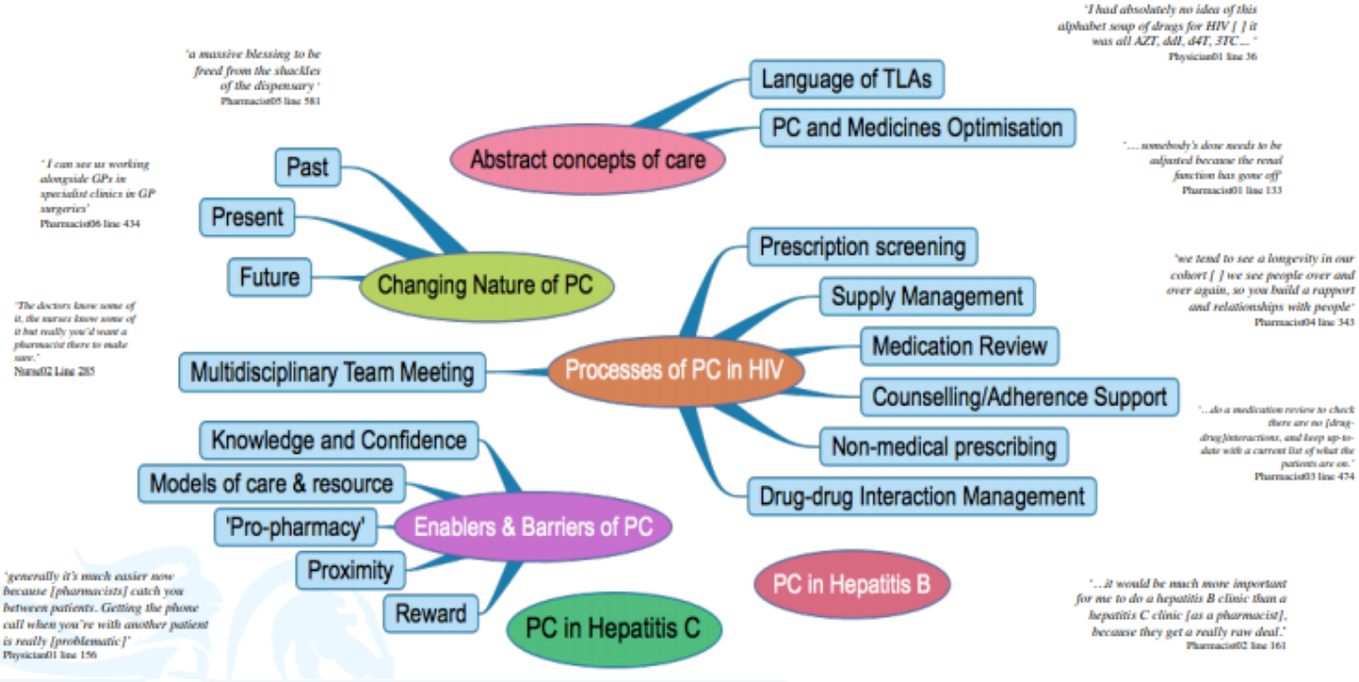
Method

- Ethical and R&D approvals were obtained for this study
- Hermeneutic phenomenology case study design
- Purposive sampling (n=8) with semi-structured interviews
- Six clinical pharmacists (5 HIV, 1 HCV), one HIV nurse and one consultant HIV/HCV physician
- NHS teaching hospital with HIV and HCV outpatient clinics.
- Verbatim transcripts analysed using Interpretative Phenomenological Analysis[7]
- Descriptive, linguistic and conceptual themes extracted

AIM: To explore healthcare professionals perceptions of current and desired PC in HIV and HCV management

OBJECTIVES:

1. To explore how healthcare professionals perceive the currently provided pharmaceutical care in HIV and HCV infection management
2. To investigate the demands and feelings of the above healthcare professionals in relation to future changes for improving the provided pharmaceutical care



Research findings

Six main themes and 17 subthemes emerged from the analysis (see Figure 1).

Non-pharmacist participants perceive PC as an abstract concept of medicines providing care. HIV medicines are marked by the use of three-letter acronyms (TLAs) that pharmacists help to translate. Pharmacists have difficulty discriminating between the new concept, Medicines Optimisation (MO), and PC possibly because MO has not been operationalised with processes.

Change in PC was prevalent with a sense of loss and ambivalence in relation to a recent outsourcing of the HIV outpatient dispensing service and closure of the satellite dispensary. Conceptually, the satellite dispensary was viewed as a prison, as it needed resourced, yet giving up control of dispensing was likened to torture.

'Prescreening' is a new process in PC in HIV arising from the outsourcing of outpatient dispensing.

Limitations

Perceptions of PC in hepatitis was limited by the predominance of HIV specialist participants. A multicentre study would enable more generalisable phenomena and improve validity.

Contribution to practice

Quality and extent of communication improved with the establishment of a pharmacist presence in clinic.

Prescreening is a new PC process that has been developed to manage workflow but has benefits in patient communication and in speeding up the screening process of prescriptions. This could benefit from publication as an advance in pharmacy practice.

PC opportunities exist in the Hepatitis specialties, in non-medical prescribing and running follow-up clinics for Hepatitis B patients.

Future work needs to explore patients' perceptions of PC in relation to outsourcing, and future models of care in community-based settings for HIV, HCV and Hepatitis B.

Disclaimer: The research was funded by the NIHR School for Public Health Research (SPHR). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

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Changing Times and Changing Approaches

I've always found HIV a fascinating area of medicine for many reasons aside from the mainstay of treatment being pharmaceuticals. As a disease it changed the way we manage medical problems, as unlike many other diseases all sectors of society were forced to work together to solve the problems it presented. The disease and the challenges it presented transcended international borders and in some ways marked the beginning of a 'Global Health Agenda'. Society was forced to address inequalities in class, gender, race and sexuality in order to tackle the disease.

Veterans in the field testify of how hard it was as a healthcare professional to watch patients die helplessly. Such veterans have been fortunate to see the evolution of treatment such that a patient diagnosed with HIV now has a much greater chance of living with a good quality of life to 'old' age. This is quite unlike a number of other chronic conditions where once diagnosed, patients live counting the days they have left. Unfortunately, the same cannot be said in less developed places like Africa where millions are still unable to gain access to treatment. In many places sustainable treatment is a challenge as patients are started on treatment but may be forced to miss doses due to budgetary constraints within their health system.

There is I believe the need for a new generation of advocates and health professionals who have grown up in an era with access to a wide range of treatment options. If the 90-90-90 target set by the UN in 2016 is to be a reality then a new generation of advocates and health professionals must step up to confront old and new challenges presented by the disease.1 This will require better and more efficient use of tried and tested tools, as well as the creation of novel tools with alternative methods of engagement.

You see, 36 years after the term AIDS (acquired immunodeficiency disorder) was officially coined, we risk allowing the old foes of the disease coming to the forefront again. This is because where-as we now have enough knowledge to be the generation that ends AIDS current strategies may be inadequate in the current climate where HIV is now competing with many other diseases within struggling health care systems. This may hinder us from reaching our ultimate goal of elimination.

HIV was previously recognised as a global epidemic requiring a global approach to fight the various it presented. These pertained to drug development, fair and affordable access to treatment, associated stigma and societal inequalities. It seems as though many have forgotten this as the present-day fight seems to lack lustre with the older advocates and health professionals starting to fade away. Tremendous efforts have been made over the last 36 years but there is a risk this will all be in vain if we are unable to achieve the UN 90-90-90 target by maintaining the momentum that got us this far.

We must continue to use tried and tested tools more effectively and creatively. For instance, there should be more mass prevention and awareness campaigns which are relevant to a generation fortunate to have grown up in an era without gruesome and hopeless images on their television screens. We must remember that 'we are the world' hence cannot turn a blind eye to the issues preventing millions in Africa from accessing treatment. If we do this, then we only give ourselves a false sense of security, as it is only a matter of time before increased drug resistance arising from inequities in access to consistent treatment in a borderless world reach our shores.

Old foes like gender inequality and poverty are still massive drivers of the epidemic in Africa so more innovative initiatives are required to address these. Such initiatives will need to address cultural influences on gender inequality, drivers of poverty and make better use of social media to effect change and ensure a downward trend in diagnoses.

Changing Times and Changing Approaches

Prevention is key here and not with preventative drugs per se which are likely to be a privilege in the developed world only but rather tried, tested, affordable and sustainable methods which include engagement tools and increased testing. Key to this is outreach work, pharmacists should also get more involved in this as giving people a holistic overview of alternatives to PREP, which present with challenges in itself is still key.

Contribution by **FE Adeniji**
Chelsea and Westminster Hospital
NHS Foundation Trust

The writer has recently published a book- 'Truth About Health Exposed' with a dedicated section on HIV geared towards enlightening the public. Proceeds from the book will go towards the Women Elite Sports Empowerment Initiative (WESIE) which uses sports as a community health and wellbeing tool.

References:

http://www.unaids.org/en/resources/documents/2017/90-90-90

HIVPA Benchmarking Exercise

In September 2009 HIVPA undertook a survey to investigate the range of activities carried out by hospital pharmacy staff specialising in HIV to establish a baseline. The survey aimed to describe the level of service provided for PLWH by hospital specialist pharmacy staff throughout the UK. Electronic questionnaires were sent to all pharmacists and technicians registered with HIVPA. Replies were collated to ensure that only one response was included per service within a designated trust. 34 responses were received (from 34 centres) within a six-month period. Data collected included number of patients registered with each service, number of patients on treatment, number of services with a designated satellite pharmacy, the breakdown of pharmacy staff in each service, number with Pharmacist-led clinics and a breakdown of activities undertaken such as ward rounds, financial reporting etc.

(HIVPA Bulletin 2011)

HIVPA are planning a follow up survey to the work carried out in 2009/10. In addition to repeating data collection for comparison, HIVPA also intend to collect additional data in line with current NHSE service specifications as well as the new BHIVA standards of care. More formal communication will follow when the data collection tool is finalised but we would like to encourage all centres to engage with this work. Please raise awareness amongst your colleagues in the hope of obtaining data from as many services as possible. Watch this space!

Dates for your diary

8th International Workshop of HIV & Women 2nd-3rd March 2018, Boston www.virology-education.com

Conference on Retroviruses and Opportunistic Infections (CROI 2018) 4-7th March 2018, Boston www.croiconference.org

4th Joint BHIVA/BASHH Spring Conference 17-20th April 2018, Edinburgh www.bhiva.org

International Workshop on Clinical Pharmacology of Antiviral Therapy 22nd-24th May 2018, Baltimore www.virology-education.com

HIVPA Annual Conference 15-16th June 2018, Manchester www.hivpa.org/hivpa-conference-2018

22nd International AIDS Conference (AIDS 2018) 23rd-27th July 2018, Amsterdam www.aids2018.org

International Workshop on HIV & Ageing 13-14th September 2018, New York www.virology-education.org

HIV Glasgow 2018 28th-31st October 2018, Glasgow www.hivglasgow.org

12th INTEREST Workshop 29th May– 1st June 2018, Kigali www.interestworkshop.org

BHIVA 'Best of CROI' Feedback meetings 2018
Monday 19th March, London
Tuesday 20th March Birmingham
Wednesday 21st March, Haydock
Tuesday 27th March, Cardiff
Wednesday 28th March, Wakefield
Thursday 29th March, Edinburgh www.bhiva.org/BestofCROI2018.asp

The Clinical Pharmacy Congress 27-28th April 2018, London www.pharmacycongress.co.uk

HIVPA's Deputy Chair, Education Lead and Conference 2018 Lead, Lucy Hedley will be presenting two sessions at the CPC.

HIVPA
HIV Pharmacy Association

DESCOVY®▼-BASED HIV THERAPY

ZERO cases of tubulopathy in >3300 patients taking the Descovy® backbone with different 3rd agents in clinical trials at weeks 48 (n=3327)[1–7], 96 (n=1895)[7,8] and 144 (n=889)[7,9]

Descovy® is indicated in combination with other antiretroviral agents for the treatment of adults and adolescents (aged 12 years and older with body weight at least 35 kg) infected with human immunodeficiency virus type-1 (HIV-1).[10]

TRUSTED TRIPLE THERAPY[11,12]

Building on 20 years of a successful treatment approach

DESCOVY® PRESCRIBING INFORMATION

Consult the Summary of Product Characteristics (SPC) before prescribing.

Descovy®▼ emtricitabine 200mg/tenofovir alafenamide 10mg or 25mg film coated tablets.

Indication: In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults & adolescents (aged 12 years & older weighing at least 35 kg). **Dosage:** Adults & adolescents (aged ≥ 12 years, weighing at least 35 kg): One tablet, once daily, orally with or without food. The dose of Descovy should be administered according to the third agent in the HIV treatment regimen. Please consult the SPC for further information. Children (< 12 years or weighing < 35kg): Safety & efficacy has not been established. Elderly: No dose adjustment is required. Renal: No dose adjustment is required in adult or adolescent patients (aged ≥ 12 years, weighing at least 35 kg) with estimated creatinine clearance (CrCl) ≥ 30 mL/min. In patients with CrCl < 30 mL/min: not recommended. Should be discontinued in patients whose CrCl declines to < 30 mL/min during treatment. Hepatic: no dose adjustment required. **Contraindications:** Hypersensitivity to the active substances or to any excipients. **Warnings & Precautions:** Safety & efficacy in HCV co-infection has not been established. Tenofovir alafenamide is active against HBV. Co-infected HIV/HBV patients should be closely monitored for at least several months following discontinuation for symptoms of severe acute exacerbations of hepatitis. Descovy should be avoided in antiretroviral patients with HIV-1 harbouring the K65R mutation. Risks of mitochondrial dysfunction, immune reactivation syndrome, opportunistic infections, osteonecrosis with CART therapy. **Interactions:** Co-administration with certain anticonvulsants (eg. carbamazepine, oxcarbazepine, phenobarbital & phenytoin), antimycobacterials (eg. rifampicin, rifabutin & rifapentine), boceprevir, St. John's wort and HIV PIs other than atazanavir, lopinavir and darunavir is not recommended. Should not be administered concomitantly with medicines containing tenofovir alafenamide, tenofovir disoproxil, emtricitabine, lamivudine or adefovir dipivoxil. Co-administration of emtricitabine with medicinal products that are eliminated by active tubular secretion may increase concentrations of emtricitabine. Medicinal products that decrease renal function may increase concentrations of emtricitabine. Medicinal products that induce P-glycoprotein (P-gp) are expected to decrease the absorption of tenofovir alafenamide, resulting in decreased plasma concentration of tenofovir alafenamide, which may lead to loss of therapeutic effect of Descovy and development of resistance. Co-administration with medicinal products that inhibit P-gp and breast cancer resistance protein activity is expected to increase the absorption and plasma concentration of tenofovir alafenamide. Tenofovir alafenamide is a substrate of OATP1B1 and OATP1B3 *in vitro*. The distribution of tenofovir alafenamide in the body may be affected by the activity of OATP1B1 and OATP1B3. **Pregnancy & lactation:** Use in pregnancy only if potential benefit justifies the potential risk to the foetus. Breast-feeding; not recommended. **Side effects:** Refer to SPC for full information regarding side effects. Very common (≥1/10): Nausea. Common (≥1/100 to <1/10): Headache, dizziness, diarrhoea, vomiting, abdominal pain, flatulence, abnormal dreams, rash & fatigue. Uncommon (≥1/1000 to <1/100): anaemia, arthralgia, dyspepsia, angioedema & pruritus. **Legal Category:** POM. **Pack:** Bottle of 30 film-coated tablets. **Price:** UK NHS List Price – £355.73; Eire/Ireland – POA. **Marketing Authorisation Number:** EU/1/16/1099/001; EU/1/16/1099/003. Further information is available from Gilead Sciences Ltd, 280 High Holborn, London, WC1V 7EE, UK; Telephone:+44 (0) 8000 113700, For Ireland: +353 214 825 999. E-mail: ukmedinfo@gilead.com. Descovy is a trademark. **Date of approval:** August 2017; DVY/UK/17-08/MM/1194

▼ This medicinal product is currently subject to additional monitoring. Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse reactions to Descovy should be reported to Gilead via email to Safety_FC@gilead.com or by telephone +44 (0) 1223 897500.

Adverse events should be reported. For the UK, reporting forms and information can be found at www.mhra.gov.uk/yellowcard.

For Ireland, suspected adverse reactions should be reported to the HPRA Pharmacovigilance using a Yellow Card obtained either from the HPRA, or electronically via the website at www.hpra.ie. Adverse reactions can also be reported to the HPRA by calling +353 1 6764971.

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GILEAD

Descovy®▼
emtricitabine/tenofovir alafenamide
200/10mg and 200/25mg tablets

DVY/UK/17-11/MI/1258 Date of preparation: December 2017

TRIUMEQ is indicated for the treatment of HIV-infected adults and adolescents above 12 years of age weighing at least 40 kg.

Before initiating treatment with abacavir-containing products, HLA-B*5701 status must always be documented. Abacavir should not be used in patients known to carry the HLA-B*5701 allele due to the risk of hypersensitivity reaction.

Prescribing Information

Triumeq▼ dolutegravir 50mg/abacavir 600mg/lamivudine 300mg tablets
See Summary of Product Characteristics before prescribing.
Indication: HIV in over 12 years and ≥ *40kg*. Screen for HLA-B*5701 prior to use. Do not use if HLA-B*5701 positive. **Dose:** one tablet once daily with or without food. *Elderly:* Limited data in 65+ yrs. *Creatinine clearance <50ml/min* or *moderate/severe hepatic impairment:* Not recommended. Monitor closely in mild hepatic impairment. **Contraindications:** Hypersensitivity to any ingredient. Co-administration with dofetilide. **Warnings/precautions:** Both abacavir and dolutegravir are associated with risk of hypersensitivity reactions (HSR). Do not initiate in HLA-B*5701+ or previous suspected abacavir HSR. Stop Triumeq without delay if HSR suspected. Never reintroduce any dolutegravir- or abacavir-containing product after suspected HSR. Risks of immune reactivation syndrome, osteonecrosis, increased weight, lipids, glucose. Monitor LFTs in Hepatitis B/C co-infection. Inconclusive data on relationship between abacavir and MI; minimise all modifiable CV risk factors (e.g. smoking, hypertension, hyperlipidaemia). Not recommended if dolutegravir required b.d. (with etravirine (without boosted PI), efavirenz, nevirapine, rifampicin, boosted tipranavir, carbamazepine, oxcarbazepine, phenytoin, phenobarbital and St John's Wort). Use with cladribine not recommended. Use with Mg/Al-containing antacids, calcium, multivitamins or iron requires dosage separation. Caution with metformin: monitor renal function and consider metformin dose adjustment. **Pregnancy/lactation:** Not recommended. Avoid breast-feeding. **Side effects:** See SPC for details. Headache, insomnia, sleep/dream disorders, GI disturbance, fatigue, hypersensitivity, anorexia, depression, dizziness, somnolence, lethargy, malaise, cough, nasal symptoms, rash, pruritus, alopecia, arthralgia, myalgia, asthenia, fever, elevations of ALT, AST and CPK, blood dyscrasias, suicidal ideation or suicide attempt, rhabdomyolysis, lactic acidosis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis. **Basic NHS costs:** 30 tablets: £798.16
EU/1/14/940/001. MA holder: ViiV Healthcare UK Ltd, 980 Great West Road, Brentford, Middlesex TW8 9GS. Further information is available from Customer Contact Centre, GlaxoSmithKline UK Ltd, Stockley Park West, Uxbridge, Middlesex UB11 1BT.

POM S1A

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Date of approval: July 2017 Zinc code: UK/TRIM/0037/14(8)

Adverse events should be reported. For the UK, reporting forms and information can be found at *www.mhra.gov.uk/yellowcard*. Adverse events should also be reported to GlaxoSmithKline on 0800 221 441.

Adverse events should be reported. For Ireland, adverse events should be reported directly to the HPRA; Freepost, Pharmacovigilance Section, Health Products Regulatory Authority, Earlsfort Terrace, Dublin 2, Tel: +353 1 676 4971, *medsafety@hpra.ie*. Adverse events should also be reported to GlaxoSmithKline on 1800 244 255.

References: 1. Walmsley S et al. *J Acquir Immune Defic Syndr.* 2015;70:515-519. **2.** Orrell C et al. Published online July 17, 2017. *Lancet HIV.* doi: 10.1016/S2352-3018(17)30095-4. **3.** TRIUMEQ Summary of Product Characteristics. January 2017.

UK/TRIM/0001/18 | January 2018