Prof James G. Hakim
University of Zimbabwe
Harare, Zimbabwe
Epidemiology

HIV incidence

- Southern Africa:
  - Temporal trends of HIV parameters including incidence, population viral load and viral load suppression were presented
  - Decline in HIV incidence in men but this is not consistent for women
- Zimbabwe, Zambia and Malawi:
  - every 1% increase in viral load suppression in decreased the predicted probability of one recent infection by 8%

![Graph showing incidence rates in different regions]
Epidemiology

HIV incidence

- Australia:
  - increased testing and declines in time from diagnosis to viral suppression were associated with reduced HIV incidence

- USA:
  - from 2008 to 2016 there were declines in the time to ART initiation and the duration in which individuals had elevated viral loads
  - not consistent across all populations (i.e. youth, African women, PWID)
Prevention interventions

Innovations

• Technology-based interventions prove to be acceptable to ‘hard to reach’ populations including young MSM and trans women
• Thailand: online time-based videos to deliver HIV/STI prevention sessions (vialogues)
  – Showed reductions in high risk behaviours and higher rates of condom usage
• Thailand: methods to provide counselling and testing to MSM and TGW
  – Result: those who access online had lower rates of linkage to ART compared to offline or mixed
Prevention interventions

Innovations

• USA: smart phone app to help with prep adherence among young MSM and young trans women who have sex with men
• Philippines: online campaign, offline and gay-networking apps to promote testing
  – Testing increased more than 60% after campaign
• China: internet-based self-testing model
  – Reached MSM never previously screened
• Vietnam: Facebook community that promoted HIV testing using influencers and offline lay testers
• Challenges remain in scale up of ART for treatment and PrEP worldwide to achieve elimination targets

Online to offline HIV testing cascade
March 2016 – March 2018 Vietnam

#client counselled #client got HIV tested #client having confirmed HIV+ #client enrolled into ARV

#client counselled 3626
#client got HIV tested 2808
#client having confirmed HIV+ 331 331
#client enrolled into ARV

Legrand WEPDC0103 Lomarda WEPDC0104 Jin WEPDC0105 Tran WEPDC0106
Prevention interventions

Key population-led services

• Barriers to care for PWID include repressive laws, lack of safety and confidentiality
• In Norway, providers understand to address not just the physical body but the whole being
• KP-led services in Thailand have increased outreach and yield better results
• KP-led interventions are appropriate, effective, sustainable, acceptable
• Brazil is ensuring the wellbeing and inclusion of trans people in decision-making through national policy
PrEP

ANRS Prévenir

- Ongoing prospective cohort study in Paris region enrolling high-risk individuals to take daily or on-demand prep
  - All tested for HIV at baseline, 1 month and every 3 months after
  - Daily sexual behaviour recorded and everyone counselled on adherence
  - 45.4% chose daily prep and 54.6% chose on demand
  - Both methods of taking prep are effective

n = 3,000

May 3rd 2017

TDF/FTC Daily

May 31st 2020

TDF/FTC On Demand

Show 15% reduction in new HIV diagnoses among MSM in the Paris Region

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Follow-Up Pts-years</th>
<th>HIV Incidence per 100 Pts-years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF/FTC (Daily)</td>
<td>443</td>
<td>0 (0-0.8)</td>
</tr>
<tr>
<td>TDF/FTC (On Demand)</td>
<td>506</td>
<td>0 (0-0.7)</td>
</tr>
</tbody>
</table>

Molina WEAE0406LB
PrEP Delivery

- Sub-Saharan Africa: integration with family planning clinics
  - Kenya and Zimbabwe show successful delivery alongside birth control and FP clinics could be key access points for women to obtain PrEP

**Facility Experience**
- Assess PrEP uptake trends
- Evaluate HCW readiness and attitudes on PrEP acceptability

**Client Experience**
- Understand client perspectives on PrEP regarding:
  - Uptake
  - Adherence and continuation
  - Risk compensation

Pintye TUAC0304  Gombe TUAC0307LB
PrEP

Real world use

- Sub-Saharan Africa: outcomes of PrEP funding include a significant uptake
- Thailand: iFACT study
  - 20 TGW who never underwent orchiectomy (removal of testicles) and had not received injectable feminizing hormone therapy (FHT) were enrolled within 6 months
  - Demonstrated lower plasma TFV exposure (13%) when daily oral feminizing hormones are used along with daily PrEP in the iFACT study

At pharmacokinetic day, plasma was collected at t=0 (pre-dose), 1, 2, 4, 6, 8, 10, 12, and 24 hours after directly observed medication ingestion with a standardized meal (a total of 9 samples)
Sexual health in the PrEP era

- Australia: STI incidence increased among MSM using PrEP in Australia
  - the majority of this increase was due to repeated STIs among a small proportion (13%) of participants
- Vietnam: commercial condom market to ensure sustainability
  - Successfully transitioned from free donor condoms to a robust commercial condom market
  - acceptable and affordable for key populations
- Zimbabwe: only 54.7% of FSW in the prevention cascade were covered by condoms and/or PrEP
  - Challenges with measurement, particularly structural factors, may limit the usefulness of the HIV prevention cascade as a tool
PrEP Delivery mechanisms

- Zimbabwe: higher uptake of PrEP in rural compared to urban clinics
  - village chiefs who mobilized stakeholders were involved in demand increase
- Brazil: encouraging data using three measures of adherence: pill count (returned bottles), self-report and medication possession ratio
  - All three measures were highly correlated and had good positive predictive value although rates of false negatives were relatively high
In the PrEP pipeline

- More than 12 clinical trials with 20,000+ participants across countries have shown that high PrEP adherence translates into high protection
- Open label studies demonstrated effectiveness and PrEP is being scaled up
- New in PrEP pipeline
  - long-acting injectable PrEP
  - subcutaneous PrEP implants
  - broadly neutralizing antibodies
- Pipeline of alternative PrEP delivery methods is exciting as they would provide people with different options at different times in their lives
Young people

- Strategies for improving adolescent engagement in health care services, improve HIV-related outcomes such as linkage to care and reducing risk factors for HIV include:
  - Malawi: integrated youth-friendly services lead to substantial improvements in uptake of HIV testing, condoms and contraception among adolescent girls and young women
  - USA: Multi-level interventions resulted in a dramatic decrease in days to reach care for youth diagnosed with HIV
  - Kenya: a child/caregiver intervention showed increased HIV disclosure to children living with HIV
Men

- The biggest gap in the treatment cascade is diagnosing men, particularly men aged 25-34
- Men are less likely to know their HIV-positive status than women in a number of sub-Saharan African countries
- How to reach men:
  - HIV self-testing and community-based HIV testing services
  - Geomapping to provide holistic package of services in appropriate locations
  - Reaching men where they gather
Test and treat

PARTNER2 study

- Estimate transmission risk in 972 gay male sero-discordant partnerships
- Zero phylogenetically-linked transmissions during 1600 couple-years of follow up
- Supports treatment as prevention and U=U
- Limitations relate to generalizability
  - 89% were white European males and heterosexuals and trans people only accounted for 1.1% of participants
Treatment Cascade

Strengthening the treatment cascade

- Five trials of universal test and treat reported impressive progress
  - PopART: home-based testing and support to linkage and retention delivered by lay health workers
  - SEARCH: “health fairs” delivered services and improved all aspects of the cascade
  - MaXART: early ART appeared to improve retention
  - BCPP: community based interventions to drive testing plus immediate ART
  - TasP: Home-based HIV testing and immediate ART

Orne-Gliemann TUBS0102 OkelloWEAX0102LB
Universal test and treat

Testing

- Malawi: facility-based HIV self-testing increased uptake of HIV testing among outpatients compared to provider-initiated HIV testing
- Strategies for uptake of HIV testing
  - performance-based incentives in health facilities
  - point-of-care early infant diagnosis
  - community-based index HIV-testing
  - health facility-based HIV self-testing

![Graph showing testing uptake by sex and age across arms (n=5,885) with AOR values and percentage increments.](image)
HIV testing

Self-testing

- Self-testing with friends among MSM and TGW
  - Training with a trusted friend and provision of HIVST kits made testing less stressful regardless of results
- HIVST kits to young women
  - Kenya: increased male partner and couples testing
- Pharmacists as partners in HIVST kit distribution
  - French pharmacists show interest but low sales and lack of discrete location for counselling
- Community distribution
  - Zambia: community-based oral HIVST distribution found no difference in time linked to care (64% in non-HIVST zone vs 65% in HIVST zone)
  - Malawi: increased likelihood of testing uptake for communities randomized to community-based HIVST v. clinic-based testing
HIV Treatment Updates
Track B: AIDS 2018 Highlights

Produced by the International AIDS Society
November 2018
Overview

ART
- Monotherapy
- GEMINI 1 & 2
- WHRI 052
- SWORD 1 & 2
- Switch to DTG

Pregnancy
- Tsepamo
- DolPHIN-1

TB Co-infection
- INSPIRING
Monotherapy

- France: MONCAY Study (non-inferiority study)
  - Open-label, randomized, controlled trial in 9 sites

  - Virological results at week 24: DTG was non-inferior to DTG/ABC/3TC but significantly more participants in the monotherapy arm developed virological failure before week 48
  - Monotherapy arm has stopped early according to safety monitoring board
  - Emphasized that dolutegravir is not recommended as monotherapy

Stable, efficient and well-tolerated DTG/ABC/3TC regimen*

Randomization 1:1 (n=158)

DTG 50 mg QD (n=78)

DTG/ABC/3TC single tablet QD (n=80)
Dolutegravir with 3TC

- An important treatment-naive study
- Compared dual therapy (dolutegravir plus lamivudine, DTG/3TC) to dolutegravir plus TDF/FTC
- This new two-drug approach is supported by the pharmacokinetic properties of DTG
  - high potency and showed high genetic barrier against drug resistance in phase 3 registrational studies
- Efficacy was >90% in all arms, including when stratified for high vs low viral load.
- regulatory approval has not yet been granted for the DTG/3TC by FDA/EMA
ART

SWORD 1 & 2

• These international phase 3 studies randomised 1024 participants on stable ART (>6 months) to either switch to open-label oral dolutegravir + rilpivirine (DTG/RPV) or continue on their current ART

• After week-48, all participants were able to switch to dual-ART with DTG/RPV
Results

- Viral response rates <50 copies/mL at week 48:

  - Non-inferiority was met
  - Safety was generally good and consistent with known side-effect profiles of individual drugs
  - One person with virological failure included drug resistance to RPV, but also had NNRTI resistance at baseline
  - No cases of DTG resistance were reported
ART

Switch to DTG

- Brazil DTG roll-out after guidelines changed to dolutegravir (DTG)-based ART as first-line treatment in 2017, compared to efavirenz (EFV) or PI-based ART (lopinavir/r or atazanavir/r).
- A study compared the observed effectiveness of different regimens in the initial response to ART using real world Ministry of Health data.
- 103,240 patients included in the analysis
  - 67.6% were male; median values of age =34 years old
  - baseline CD4 =394 cells/mm³
  - baseline VL= 38,057 copies/mL
  - adherence= 96.2%
- Overall, 76.9% achieved a VL< 50 copies/mL
- With 3TC+TDF+EFV as the reference, adjusted OR (95%CI) of achieving viral suppression in alternative combination were significantly lower.

<table>
<thead>
<tr>
<th>Combination</th>
<th>aOR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>3TC+TDF+DTG</td>
<td>1.42</td>
<td>1.32-1.52</td>
</tr>
<tr>
<td>3TC+AZT+EFZ</td>
<td>0.94</td>
<td>0.87-1.02</td>
</tr>
<tr>
<td>3TC+TDF+ATV/r</td>
<td>0.67</td>
<td>0.63-0.72</td>
</tr>
<tr>
<td>3TC+AZT+LPV/r</td>
<td>0.59</td>
<td>0.55-0.63</td>
</tr>
<tr>
<td>3TC+TDF+LPV/r</td>
<td>0.54</td>
<td>0.49-0.60</td>
</tr>
</tbody>
</table>
Pregnancy

Tsepamo

- May 2018, a potential signal of neural tube defects was reported in babies born to women who had conceived while using a dolutegravir (DTG)-based ART, leading to communications from WHO and other guidelines.
- The unexpected initial data were reported in four pregnancies from a registry in Botswana, where DTG-based ART was already being rolled-out.
- This initial incidence of neural tube defects was 0.94% - (4/426 pregnancies) compared to an expected background rate of 0.1%.
- The updated data since 1 May reported no additional DTG cases.

Zash TUSY15
Pregnancy

Tsepmamo

- Next formal analysis will occur after 31 March 2019 and will include women already exposed to DTG from conception before the recent change in guidance
- WHO guidelines released at AIDS 2018 still recommended DTG widely, and that women of childbearing potential using DTG are provided contraception
- Until further data is provided, country level guidelines may vary
Pregnancy

**DolPHIN-1**

- Randomised controlled trial of dolutegravir or a control arm using efavirenz (current standard of care) in women who were starting ART late in pregnancy (third trimester)
  - 60 HIV positive women in Uganda and South Africa
  - included intensive pharmacokinetic sampling including maternal plasma and cord blood, breast milk and infant plasma.

*To comply with guidelines, all subjects start EFV pending randomisation*
Results

- There was no significant pre-ART differences between arms in maternal age, gestation at treatment initiation (30.8 weeks), weight, obstetric history, VL (log 4 copies) and CD4 count (394 cells/mm$^3$)
- The dolutegravir arm reported significantly better virological responses
- Shows DTG was non-inferior vs EFV in late pregnancy

<table>
<thead>
<tr>
<th>HIV-1 RNA level at PP visit</th>
<th>ITT (M=F) DTG (N = 29)</th>
<th>EFV (N = 31)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50 copies/mL *</td>
<td>20 (69.0%)</td>
<td>12 (38.7%)</td>
<td>0.02</td>
</tr>
<tr>
<td>≥50 copies/mL</td>
<td>9 (31%)</td>
<td>19 (61.3%)</td>
<td></td>
</tr>
</tbody>
</table>
TB Co-infection

INSPIRING

- Study on the safety and efficacy of dolutegravir-based ART in TB/HIV co-infected adults at week 48
- Phase 3b randomised, open-label, multi-centre, non-comparative, active-controlled, parallel-group
Results

- Viral response rates <50 copies/mL at week 48 (ITT-E) were similar between arms:
- Non-responders in the DTG were largely driven by non-treatment related discontinuations
- Shows that DTG was not associated with an increased risk of IRIS.
- TB-associated IRIS rates were low with four cases in each arm (DTG 6%, EFV 9%)
- These data support the use of DTG based regimen in HIV/TB co-infection.