Preparing for PrEP implementation

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Outline

• PrEP rationale

• Challenges ahead
Why PrEP

• In PrEP, an HIV uninfected individual takes antiretroviral medication(s) daily. By having these medications in the bloodstream, HIV may be unable to establish infection.

• Evidence that PrEP may work to prevent HIV
  • PMTCT
  • Animal studies
  • PEP
  • iPrex
Pre- and post-exposure ART prevents vertical HIV transmission

Prolonged nevirapine or nevirapine/zidovudine prophylaxis to breastfeeding infants from Malawi decreased postnatal HIV transmission by half

Kumwenda et al. NEJM 2008
Preclinical Evaluation of Tenofovir (TDF) and TDF-Emtricitabine (FTC) (N=40)

- Either FTC or TDF were protective
  - 70% to 100% Effective/expos
- Emtricitabine + Tenofovir
  - The combination was 100% effective
  - Even after repeated rectal exposures (14)
- The prophylactic activity probably reflects
  - Long intracellular half life
  - Activity in macrophages
  - High concentration in genital tissues
Macaque data indicating Intermittent PrEP may be feasible

Garcia-Lerma, Sci Trans Med 2010
Considerations re TDF & FTC/TDF for PrEP

POTENT:
✓ **Broad antiviral activity** (HIV-1 subtypes, HIV-1&-2)
✓ Active against virus types found both in early and late HIV infection (i.e., R5 & X4 viruses)
✓ Acts early in the life cycle of HIV (pre-integration) so it can **block initial infection**
✓ **Rapidly active** (suggesting even intermittent use might be possible)

SAFE:
✓ Favorable safety and tolerability
✓ High barrier to resistance, and limited cross-resistance

EASY:
✓ **Relative easy to use** (low pill burden, no food restrictions, no drug interactions with contraception/TB meds/antibiotics)

*Evaluation of both TDF and FTC/TDF because of potential for different cost, resistance, and efficacy*
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Reality check

• Experience of moving from trials to implementation
  – Real world effectiveness is usually less than trial efficacy
  – implementation usually more complicated than planned
  – pace of scale-up usually much longer than expected
• Thorny issues to be addressed include
  – cost of daily PrEP (possibly greater than treatment for national budgets?)
  – motivation for daily PrEP (why would uninfected take it?)
  – experience with other daily prevention like OCs
  – political challenge of advocating scarce resources for socially marginalized groups
    • sex workers, MSM, IDU
    • readily available drug
Reality check: Setting the tone

- PrEP will not be a ‘magic bullet’
  - PrEP integrated into current HIV prevention programs
- Regulatory approval and manufacturing capacity
- Potential for developing resistance
- Potential for adverse reactions
  - Renal dysfunction, hepatitis B flares
- Possibility of risk compensation or disinhibition
  - People on PrEP may have more sex, use condoms less
Challenges for PrEP implementation

• resistance, HIV testing & counselling, and re-testing
• resources constraints
• how best to provide PrEP, targeted or general distribution?
• Effective Targeting

For the same number of people starting PrEP, **effective targeting** to those at most risk can substantially **amplify impact**.
Thank you!