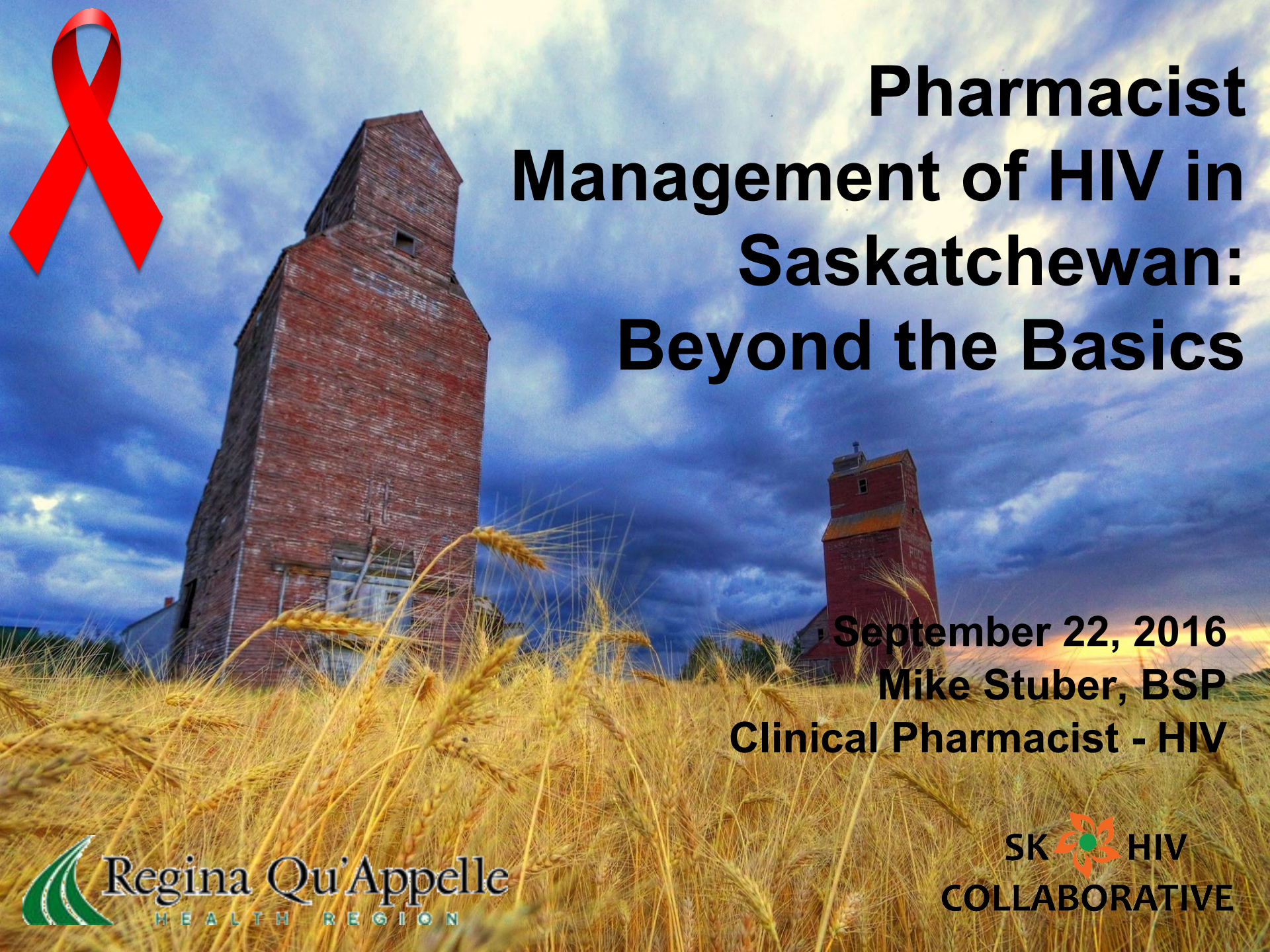


Pharmacist Management of HIV in Saskatchewan: Beyond the Basics

September 22, 2016

Mike Stuber, BSP

Clinical Pharmacist - HIV

Regina Qu'Appelle HEALTH REGION

SK HIV COLLABORATIVE

Disclosures

This learning program has been funded by Gilead Sciences Canada, Inc.

The presentation has been developed independently by Mike Stuber, BSP.

The opinions expressed in the learning program are those of the faculty and do not necessarily represent the views of Gilead Sciences Canada, Inc.

Please refer to the official prescribing information for each product for discussion of approved indication, contraindications, and warnings.

Disclosures

- I have received honoraria from the following companies:
  - Gilead Sciences, Bristol Myers Squibb, ViiV, Janssen
- If you detect **any** commercial bias, please let me know
  - Phone: 306.766.0717
  - Email: Michael.Stuber@rqhealth.ca

Objectives

1. Describe the indications for initiating ART based on recent guidelines and differences between recommended options
2. Understand the importance of adherence to ART and the consequences of poor adherence
3. Identify and manage drug interactions
4. Apply evolutions in ARVs to meeting unmet patient needs in managing HIV as a chronic disease

Deadly Record: Inside Saskatchewan's HIV crisis

CHARLES HAMILTON, SASKATOON STARPHOENIX, SASKATOON STARPHOENIX 09.16.2016 |

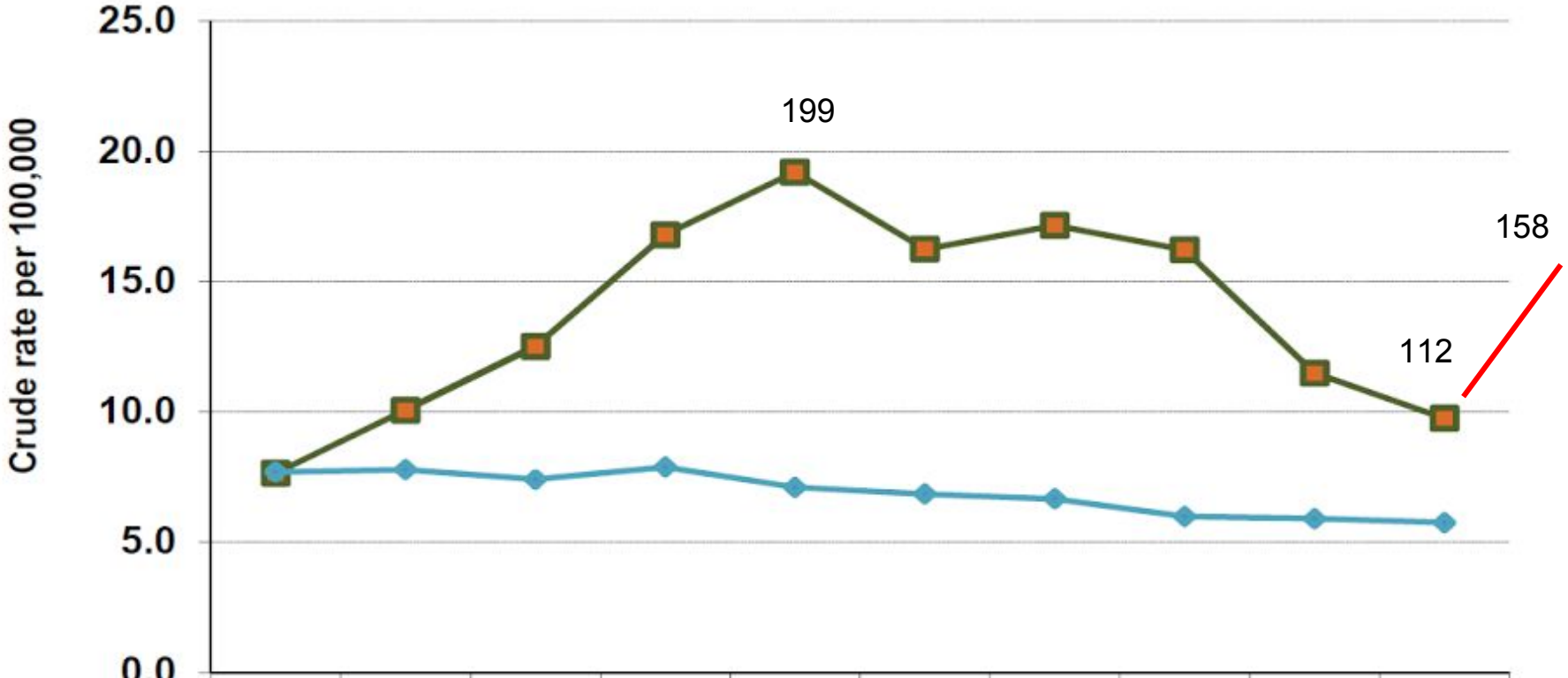
SHARE

Something as simple as the common cold could kill Lauren Cardinal.

A friend of hers died because he refused to see a doctor and get an abscessed tooth

Fig 2

Rate of HIV cases by year
Saskatchewan and Canada, 2005-2014



	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
SK	7.7	10.1	12.5	16.8	19.2	16.3	17.2	16.2	11.5	9.8
Canada	7.7	7.8	7.4	7.9	7.1	6.9	6.7	6.0	5.9	5.8

Canadian rates from the Public Health Agency of Canada

The Numbers

- 9.8 new HIV infections/100k vs 5.8/100k in Canada
- ~2x national rate (down from 3x in 2009)
  - preliminary data show an increase in 2015/16 for Saskatchewan and a small decrease for rest of Canada
- 71% new HIV cases in Aboriginal peoples
  - 84% of women infected were Aboriginal
  - ~15% of SK population Aboriginal (~171,000)
    - rate of infection = 51/100k

The Numbers

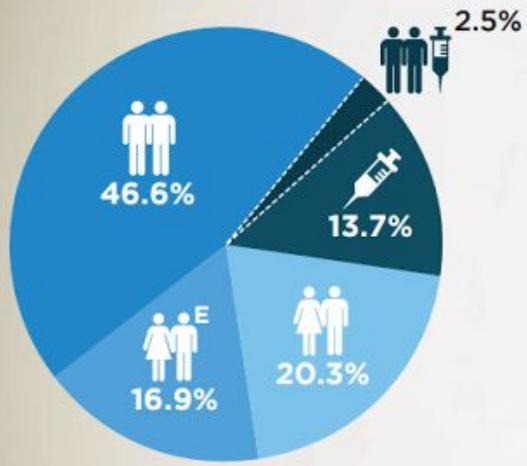
- 56% new HIV cases report IDU
  - 11% in rest of Canada(www.catie.ca)

- 5% prevalence rate of HIV in Regina (A-Track Pilot Survey)
  - Sub-Saharan Africa ~4.7% prevalence rate
  - 46% unaware of HIV + status
    - ~20% in rest of Canada(www.catie.ca)

NEW HIV INFECTIONS IN CANADA

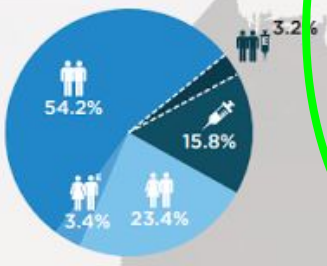
CATIE Canada's source for HIV and hepatitis C information | www.catie.ca

An estimated 3,175 new HIV infections in Canada in 2011 (9.5 per 100,000 population)



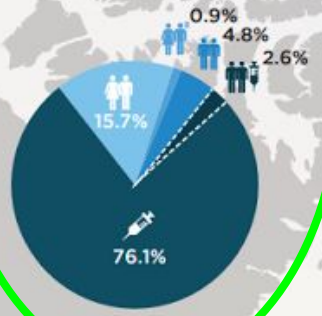
BRITISH COLUMBIA

An estimated 380 new HIV infections in 2011 (8.6 per 100,000 population)



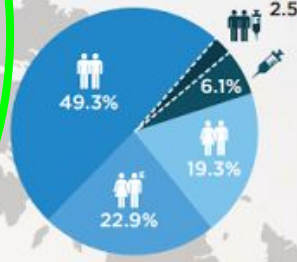
SASKATCHEWAN

An estimated 230 new HIV infections in 2011 (22.3 per 100,000 population)



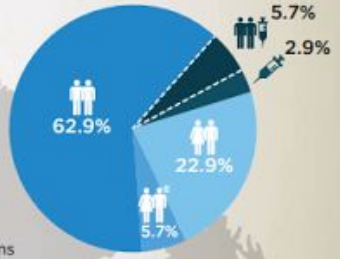
ONTARIO

An estimated 1,400 new HIV infections in 2011 (10.9 per 100,000 population)



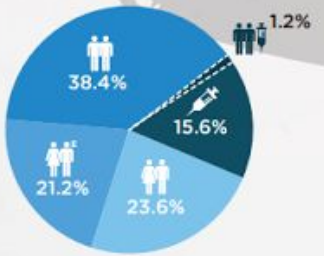
ATLANTIC CANADA

An estimated 35 new HIV infections in 2011 (1.5 per 100,000 population)



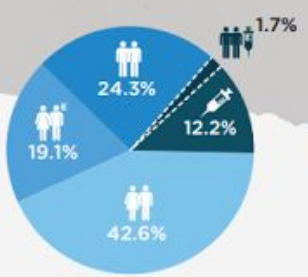
ALBERTA

An estimated 250 new HIV infections in 2011 (6.9 per 100,000 population)



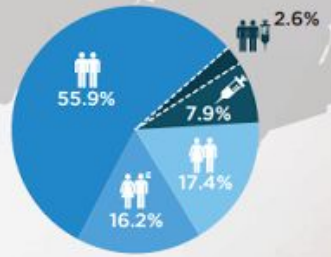
MANITOBA

An estimated 115 new HIV infections in 2011 (9.5 per 100,000 population)



QUEBEC

An estimated 760 new HIV infections in 2011 (9.6 per 100,000 population)



EXPOSURE CATEGORY

- Men who have sex with men
- Men who have sex with men and inject drugs
- People who inject drugs
- Heterosexual people, not including those born in countries where HIV is endemic
- Heterosexual people born in countries where HIV is endemic

Source: 2011 estimates from the Public Health Agency of Canada. Incidence rates have been calculated using 2011 census data from Statistics Canada. Exposure categories are based on a hierarchical classification at the time of diagnosis.

CATIE Ordering Centre Catalogue Number: ATI-40239

Saskatchewan's Situation

- Our epidemic is unique in Canada
  - MSM primary in rest of developed world
- Driven by injection drug use
- Heavily impacting women and indigenous peoples

Saskatchewan's Situation

- High prevalence in rural, northern and reserve communities where access to HIV specialized care is difficult
- Associated with groups who are marginalized and impacted heavily by stigma

Saskatchewan's Situation

- Multiple health, addiction and other concerns in HIV+ people (HCV, mental health, abuse, poverty, housing and food security)

- Very few resources exist for the unique challenges in Saskatchewan - we're on our own.

Saskatchewan's Situation

Saskatchewan should declare HIV-AIDS public health emergency

ANDRÉ PICARD
The Globe and Mail
Published Monday, Sep. 19, 2016 6:00AM EDT
Last updated Sunday, Sep. 18, 2016 8:55PM EDT

The rate of HIV-AIDS in Saskatchewan, particularly in First Nations communities, is so high that the province should declare a public-health state of emergency.

That's the view of a group of doctors in the province who, on Monday, are issuing a *cri de coeur* for action.

The ad hoc coalition, led by Dr. Ryan Meili of the West Side Community Clinic in Saskatoon, is comprised mostly of physicians who provide front-line HIV care, but they have some chilling data to justify sounding the alarm.

RELATED: Canada's Indigenous HIV treatment in the global spotlight

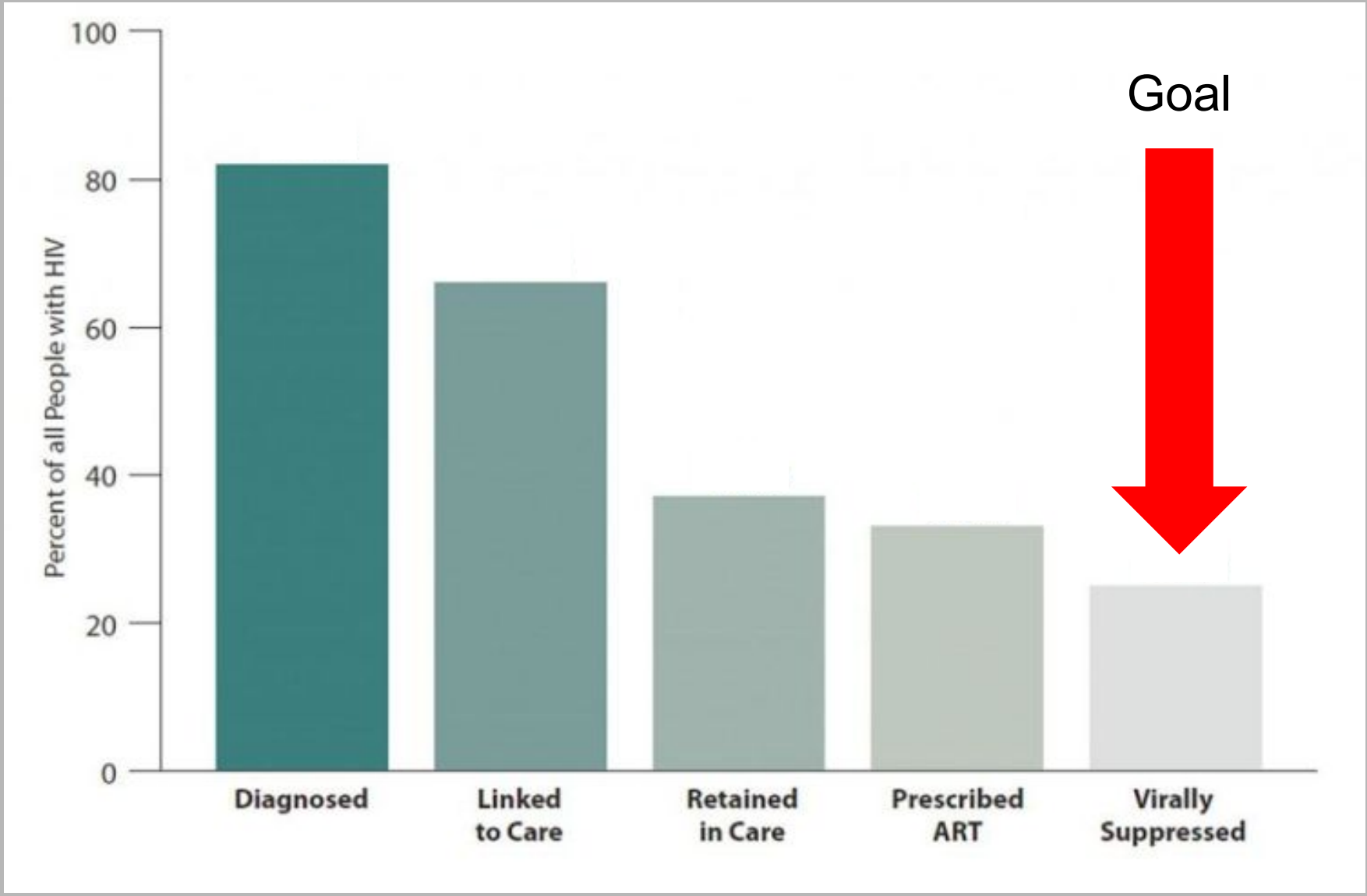
The HIV infection rate in Saskatchewan is 13.8 per 100,000 population, almost double the national average of 7.8 per 100,000.

But the provincewide numbers hide the real problem: On reserves, the infection rate is 64 per 100,000.

Basics Review

- HIV has 2x+ national rate of HIV
- Primarily driven by injection drug use
  - Disproportionately affects indigenous people and women
- Rural, remote and reserve settings pose unique challenges to treating HIV in Saskatchewan

Cascade of Care

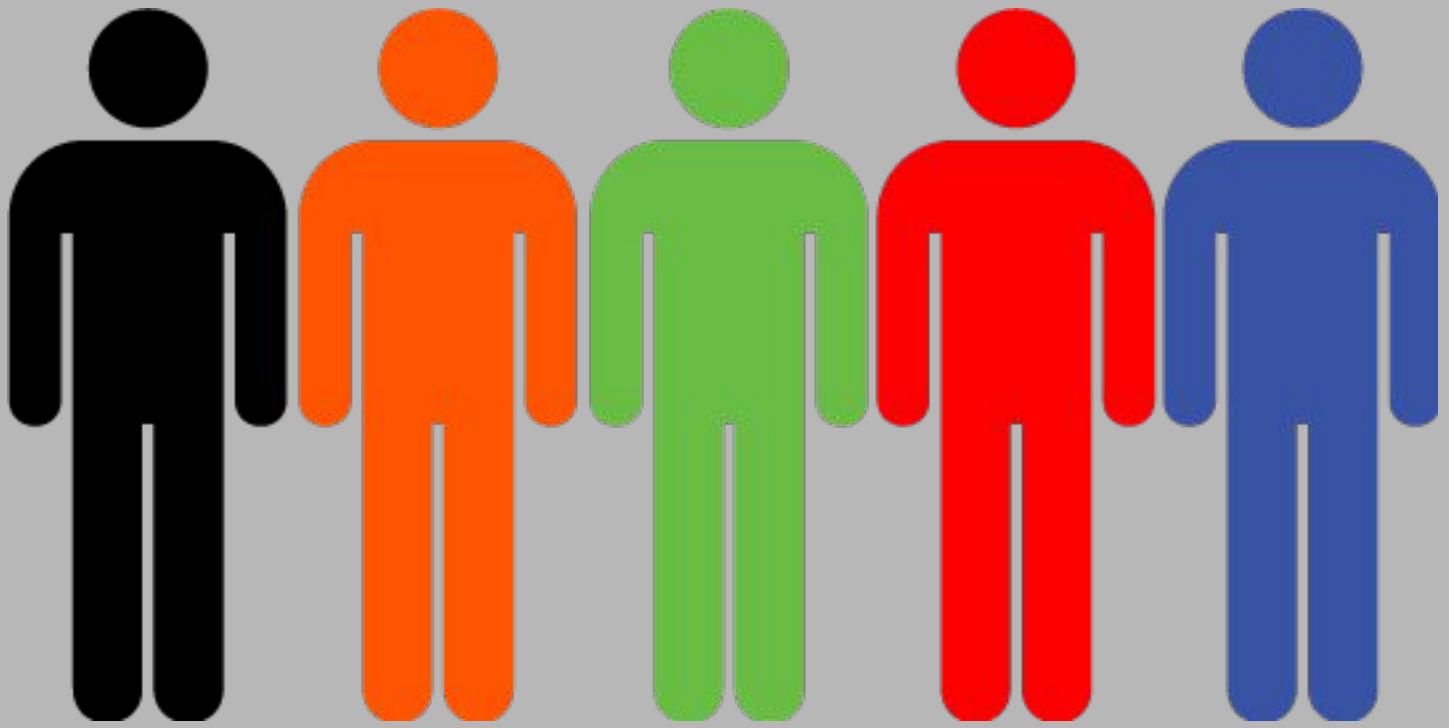


Undetectable = Untransmittable

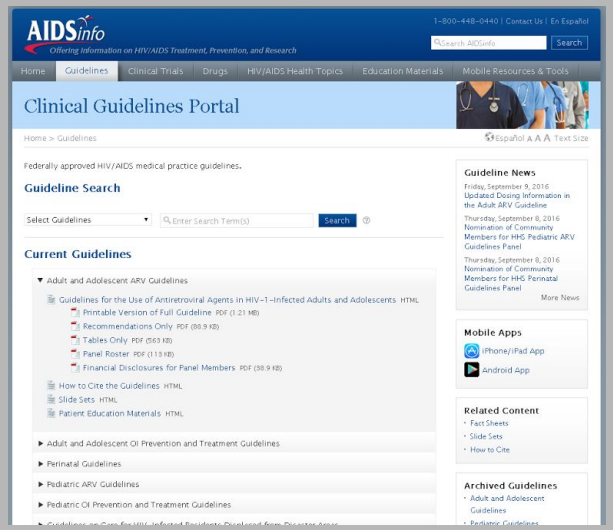
People living with HIV on antiretroviral therapy (ART) and virally suppressed "are **not capable of transmitting HIV to a sexual partner.** With successful ART, that individual is **no longer infectious."**

Dr. Carl Dieffenbach,
Director of the Division of AIDS, NIAID
National Institutes of Health
(August 26, 2016)

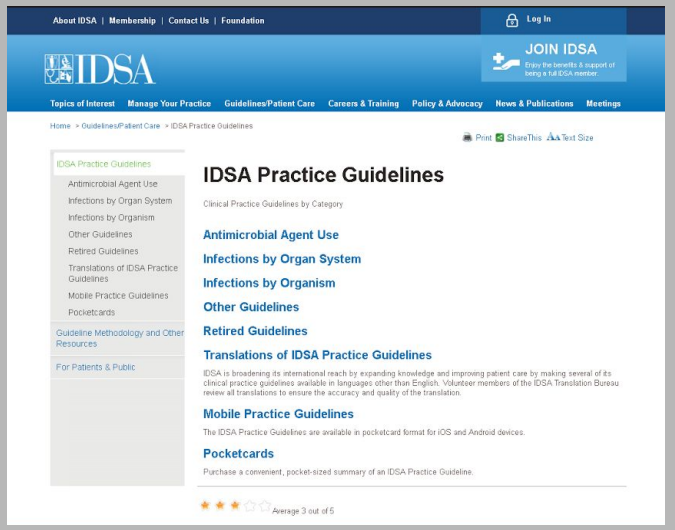
Who should be on ART?



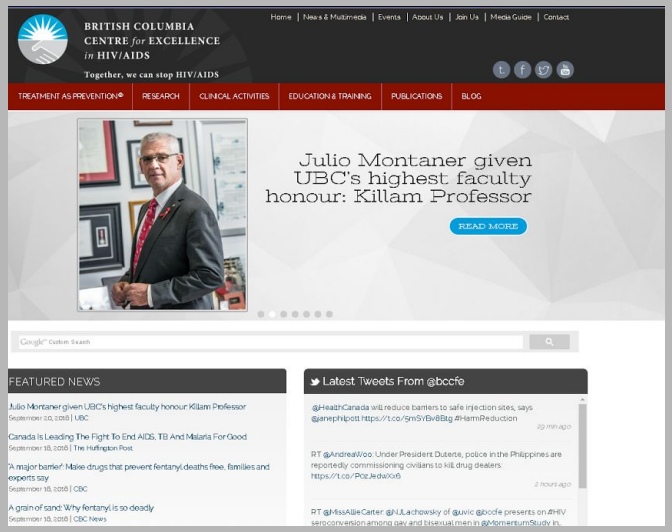
Who should be on ART?



https://aidsinfo.nih.gov/guidelines/



https://www.idsociety.org/IDSA_Practice_Guidelines/



http://www.cfenet.ubc.ca/

Who should be on ART?

Initiation of Antiretroviral Therapy (Last updated January 28, 2016; last reviewed January 28, 2016)

Panel's Recommendations
• Antiretroviral therapy (ART) is recommended for all HIV-infected individuals regardless of CD4 T lymphocyte cell count, to reduce the morbidity and mortality associated with HIV infection **(AI)**. • ART is also recommended for HIV-infected individuals to prevent HIV transmission **(AI)**. • When initiating ART, it is important to educate patients regarding the benefits and considerations regarding ART, and to address strategies to optimize adherence. On a case-by-case basis, ART may be deferred because of clinical and/or psychosocial factors, but therapy should be initiated as soon as possible.

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

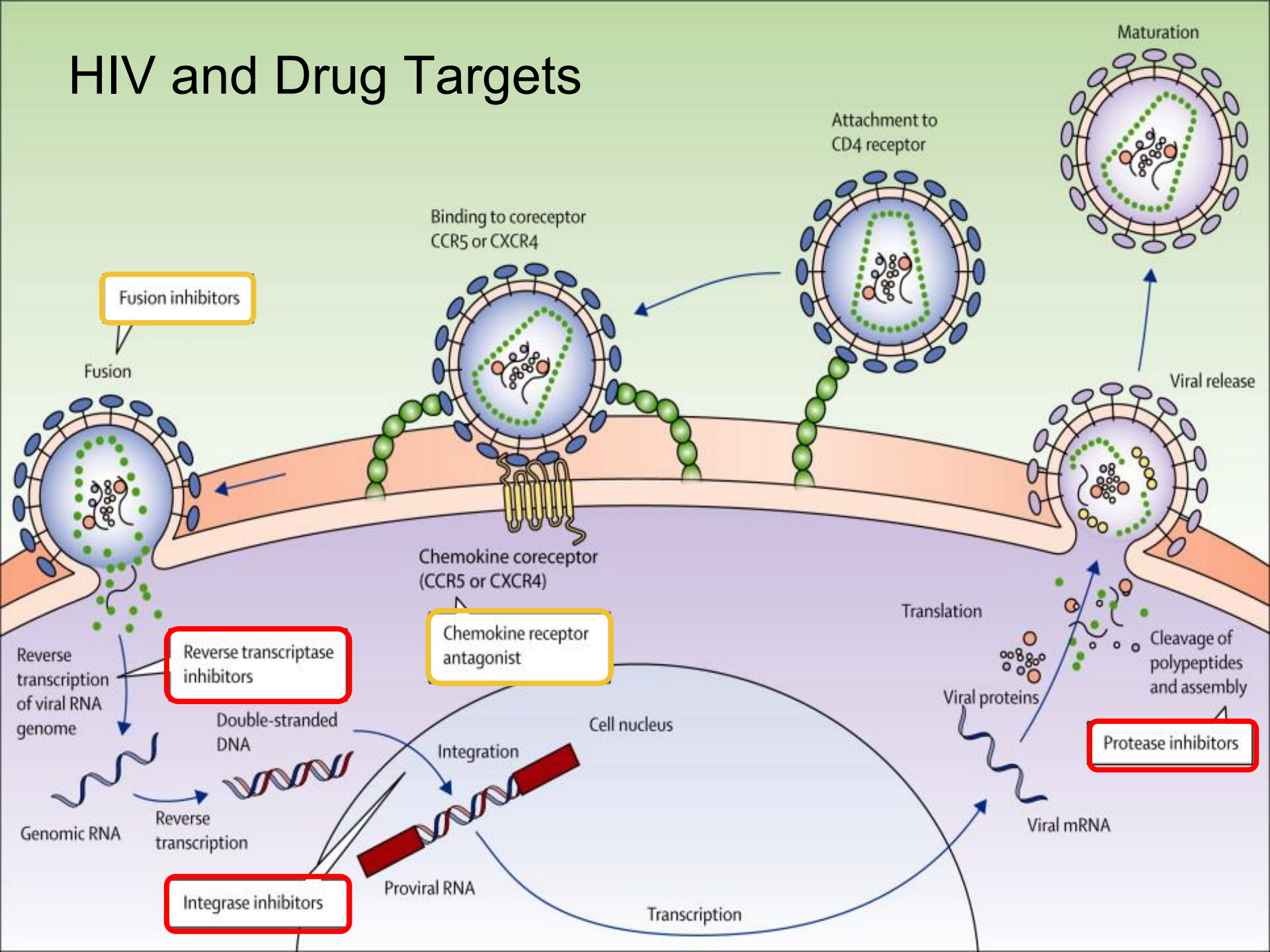
https://aidsinfo.nih.gov/contentfiles/lvguidelines/AA_Recommendations.pdf

Who should be on ART?

- Guidelines updated in 2012 to return to ‘hit hard, hit early’ approach to reflect the advances in ART
- Compelling indications:
  - Pregnancy to prevent MTCT
    - SK had 3 infants born with HIV in 2015
  - Advanced infection
    - AIDS defining illnesses
    - CD4+ count below 500, 350, 200 etc
  - Transmission risk
    - Serodiscordant relationship
    - Ongoing IDU


ARE
YOU
READY?

HIV and Drug Targets



Antiretrovirals

NRTI

- **Abacavir (ABC)**
- ~~Didanosine (ddI)~~
- **Emtricitabine (FTC)**
- **Lamivudine (3TC)**
- ~~Stavudine (d4T)~~
- **Tenofovir (TDF/TAF)**
- Zidovudine (AZT, ZDV)

NNRTI

- ~~Delavirdine (DLV)~~
- Efavirenz (EFV)
- Etravirine (ETR)
- Nevirapine (NVP)
- Rilpivirine(RPV)

PI

- **Atazanavir (ATV)**
- **Darunavir (DRV)**
- ~~Fosamprenavir (FPV)~~
- ~~Indinavir (IDV)~~
- Lopinavir (LPV)*
- ~~Nelfinavir (NFV)~~
- Ritonavir (RTV)
- ~~Saquinavir (SQV)~~
- ~~Tipranavir (TPV)~~

Pharmacokinetic Booster

- **Cobicistat (c)**
  - no anti-HIV activity
- **Ritonavir (r)**

Integrase Inhibitor (INSTI)

- Raltegravir (RAL)
- **Elvitegravir (EVG)****
- **Dolutegravir (DTG)**

Fusion Inhibitor

- ~~Enfuvirtide (T-20)~~

CCR5 Antagonists

- Maraviroc (MVC)

*LPV available only as coformulation with ritonavir

**EVG available only in fixed dose combination with cobicistat (c) and TAF/FTC or TDF/FTC

Fixed-Dose Combinations (FDC)

NRTI

- Truvada® (TDF+FTC)
- Descovy® (TAF+FTC)
  - Caution w/ 10mg vs 25mg
- Combivir® (AZT + 3TC)
- Kivexa® (ABC + 3TC)
  - Generic available

NNRTI

- Complera® (RPV+TDF/FTC)
- Odefsey® (RPV+TAF/FTC)
- Atripla® (EFV + TDF/FTC)

PI

- Kaletra® (LPV/r)
- Prezcobix® (DRV/c)

Integrase Inhibitors

- Stribild® (EVG/c/TDF/FTC)
- Genvoya® (EVG/c/TAF/FTC)
- Triumeq® (DTG/ABC/3TC)

What to Start?

- **<u>HIV is treated with at least 3 drugs from 2 different classes</u>**
  - This may change with future studies

2 NRTI + 1 PI or 1 NNRTI or 1 INSTI = Regimen

What to Start: Initial Combination Regimens for the Antiretroviral-Naive Patient (Last updated July 14, 2016; last reviewed July 14, 2016)

Panel's Recommendations

- An antiretroviral (ARV) regimen for a treatment-naive patient generally consists of two nucleoside reverse transcriptase inhibitors (NRTIs) in combination with a third active ARV drug from one of three drug classes: an integrase strand transfer inhibitor (INSTI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or a protease inhibitor (PI) with a pharmacokinetic (PK) enhancer (booster) (cobicistat or ritonavir).
- The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) classifies the following regimens as Recommended regimens for antiretroviral therapy (ART)-naive patients:

  Integrase Strand Transfer Inhibitor-Based Regimens:

  - Dolutegravir/abacavir/lamivudine[a]—**only** for patients who are HLA-B*5701 negative **(AI)**
  - Dolutegravir plus either tenofovir disoproxil fumarate/emtricitabine[a] **(AI)** or tenofovir alafenamide/emtricitabine **(AII)**
  - Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine **(AI)**
  - Elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine **(AI)**
  - Raltegravir plus either tenofovir disoproxil fumarate/emtricitabine[a] **(AI)** or tenofovir alafenamide/emtricitabine **(AII)**

  Protease Inhibitor-Based Regimens:

  - Darunavir/ritonavir plus either tenofovir disoproxil fumarate/emtricitabine[a] **(AI)** or tenofovir alafenamide/emtricitabine **(AII)**
- On the basis of individual patient characteristics and needs, an Alternative regimen or, less frequently, an Other regimen, may be the optimal regimen for a particular patient. A list of Alternative and Other regimens can be found in Table 6.
- Given the many excellent options for initial therapy, selection of a regimen for a particular patient should be guided by factors such as virologic efficacy, toxicity, pill burden, dosing frequency, drug-drug interaction potential, resistance testing results, comorbid conditions, and cost. Table 7 provides guidance on choosing an ARV regimen based on selected clinical case scenarios. Table 8 highlights the advantages and disadvantages of different components in a regimen.

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion*

[a] Lamivudine may substitute for emtricitabine or vice versa.

https://aidsinfo.nih.gov/contentfiles/lvguidelines/AA_Recommendations.pdf

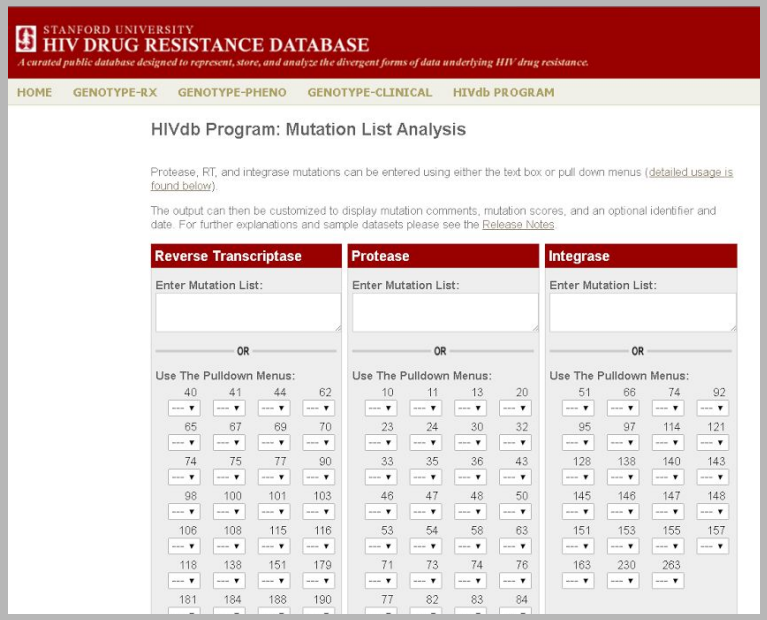
What to Start?

- Guidelines updated frequently
- Recent removal of NNRTI options and ATZ/r (Reyataz/Norvir) option
- Addition of TAF/FTC options

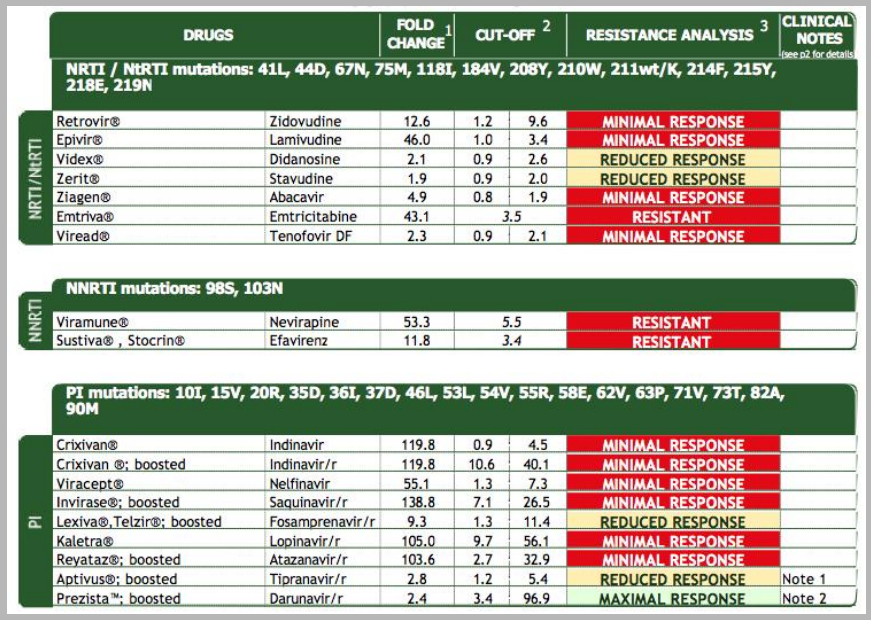
- Reflects release of newer agents that are effective in broader conditions (high VL, resistance) and ‘cleaner’ with respect to comorbid conditions, drug interactions, and adverse effects

What to Start?

- Lab values
  - Viral Load/CD4
    - Need OI prophylaxis? Certain ARVs avoid in high VL
  - Genotype
  - HLA B*5701
    - Excludes ABC use (Triumeq, Kivexa) due to HSR



http://sierra2.stanford.edu/sierra/servlet/JSierra



	DRUGS		FOLD CHANGE [1]	CUT-OFF [2]		RESISTANCE ANALYSIS [3]	CLINICAL NOTES (see p2 for details)
	NRTI / NtRTI mutations: 41L, 44D, 67N, 75M, 118I, 184V, 208Y, 210W, 211wt/K, 214F, 215Y, 218E, 219N						
NRTI/NtRTI	Retrovir®	Zidovudine	12.6	1.2	9.6	MINIMAL RESPONSE	
	Epivir®	Lamivudine	46.0	1.0	3.4	MINIMAL RESPONSE	
	Videx®	Didanosine	2.1	0.9	2.6	REDUCED RESPONSE	
	Zerit®	Stavudine	1.9	0.9	2.0	REDUCED RESPONSE	
	Ziagen®	Abacavir	4.9	0.8	1.9	MINIMAL RESPONSE	
	Emtriva®	Emtricitabine	43.1	3.5		RESISTANT	
	Viread®	Tenofovir DF	2.3	0.9	2.1	MINIMAL RESPONSE	
	NNRTI mutations: 98S, 103N						
NNRTI	Viramune®	Nevirapine	53.3	5.5		RESISTANT	
	Sustiva® , Stocrin®	Efavirenz	11.8	3.4		RESISTANT	
	PI mutations: 10I, 15V, 20R, 35D, 36I, 37D, 46L, 53L, 54V, 55R, 58E, 62V, 63P, 71V, 73T, 82A, 90M						
PI	Crixivan®	Indinavir	119.8	0.9	4.5	MINIMAL RESPONSE	
	Crixivan ®; boosted	Indinavir/r	119.8	10.6	40.1	MINIMAL RESPONSE	
	Viracept®	Nelfinavir	55.1	1.3	7.3	MINIMAL RESPONSE	
	Invirase®; boosted	Saquinavir/r	138.8	7.1	26.5	MINIMAL RESPONSE	
	Lexiva®,Telzir®; boosted	Fosamprenavir/r	9.3	1.3	11.4	REDUCED RESPONSE	
	Kaletra®	Lopinavir/r	105.0	9.7	56.1	MINIMAL RESPONSE	
	Reyataz®; boosted	Atazanavir/r	103.6	2.7	32.9	MINIMAL RESPONSE	
	Aptivus®; boosted	Tipranavir/r	2.8	1.2	5.4	REDUCED RESPONSE	Note 1
	Prezista™; boosted	Darunavir/r	2.4	3.4	96.9	MAXIMAL RESPONSE	Note 2

VircoTYPE - virtual phenotyping report

What to Start?

- Comorbidities
  - Renal function
    - CrCl <60 mL/min = avoid TDF regimens
      - TAF okay down to 30 mL/min
  - HBV
    - Tenofovir is a treatment for HBV so use caution when starting/stopping this medication. TAF and TDF both effective
  - Osteoporosis
    - TDF regimens not ideal
      - TAF appears to be okay
  - Depression/anxiety
    - May want to avoid EFV

What to Start?

- Comorbidities
  - Cardiovascular disease
    - ABC may be associated with increased MI risk
  - DM
    - PIs may impact blood sugar control/lipids
    - EFV can impact lipids
  - Viral Hepatitis
    - Caution with drug interactions and duplication of therapies
  - Osteoporosis
  - Psychiatric illness

What to Start?

- Cost
  - Very expensive
    - Triumeq = $1445/34 day supply (per SPDP website)
    - Genvoya = $1547.68/34 day supply
    - Prezcobix + Truvada = $1753.38/34 day supply
  - Different coverage for different patients
    - NIHB vs SPDP formularies
    - 3rd party coverage
    - Special Support Programs
    - Social Assistance Program/SAID
    - Manufacturer rebate programs

What to Start?

- Cost
  - Although meds are quite expensive they are mostly covered through insurance
    - Do not let cost be a barrier
      - Ensure Special Support up to date (if SPDP)
        - Changes in income can be addressed
      - EDS completed
      - Third party programs
      - Community based organization assistance
      - When in doubt - call HIV provider's clinic
    - Watch for transitions in care
      - Moving provinces
      - federal/provincial corrections

What to Start?

- Drug interactions
  - Major but progressively smaller obstacle
- Lifestyle
  - Work schedule
  - Adherence
  - Ongoing chaos
    - Housing, addictions, etc

- Chaos is not necessarily a good predictor of poor adherence but important to keep in mind - may opt for more robust regimen

Pharmacist Role

- Community pharmacists have access to eHealth portal/PIP to assess appropriateness and completeness of ARV regimen

- Regular monitoring of lab values helps assess treatment success and can pick up early signs of treatment failure, DIs or adverse effects
    - Patients see pharmacists more frequently than clinic staff

Pharmacist Role

- Be familiar with resources and guidelines to assess ART appropriateness

- Ensure regimen is affordable for patient
  - Do not let patient go without medication for cost related issues - call for help if needed

Adherence

Adherence

#1 cause of failure is poor adherence

- 90-95% adherence (<2-3 missed doses/month of QD regimen) ideal to maintain integrity of treatment
  - Lower adherence likely okay when drugs have higher genetic barrier to resistance (dolutegravir, protease inhibitors)
- Poor adherence leads to antiretroviral drug levels below the MIC in tissue/plasma
  - Selection of drug resistant HIV mutants

Barriers to Adherence

- Pill burden
- Adverse Effects
- Treatment fatigue
- Relative regimen complexity
- Navigation of health care system
- Drug Costs
- Swallowing difficulty
- Transitions in care

Barriers to Adherence

- Cultural differences
- Housing Stability/Transiency
  - Remote/Rural/Northern isolation
- Social chaos
- Addictions/Mental Health
- Access to Food

- STIGMA

Consequences

- HIV is heterogenous and there is a diverse group of viral mutants - retrovirus replication is error prone
  - Usually less ‘fit’ and make up small proportion of viral pool
  - Dominant viral population without drug present is ‘wild type’

- Drug levels fall below MIC

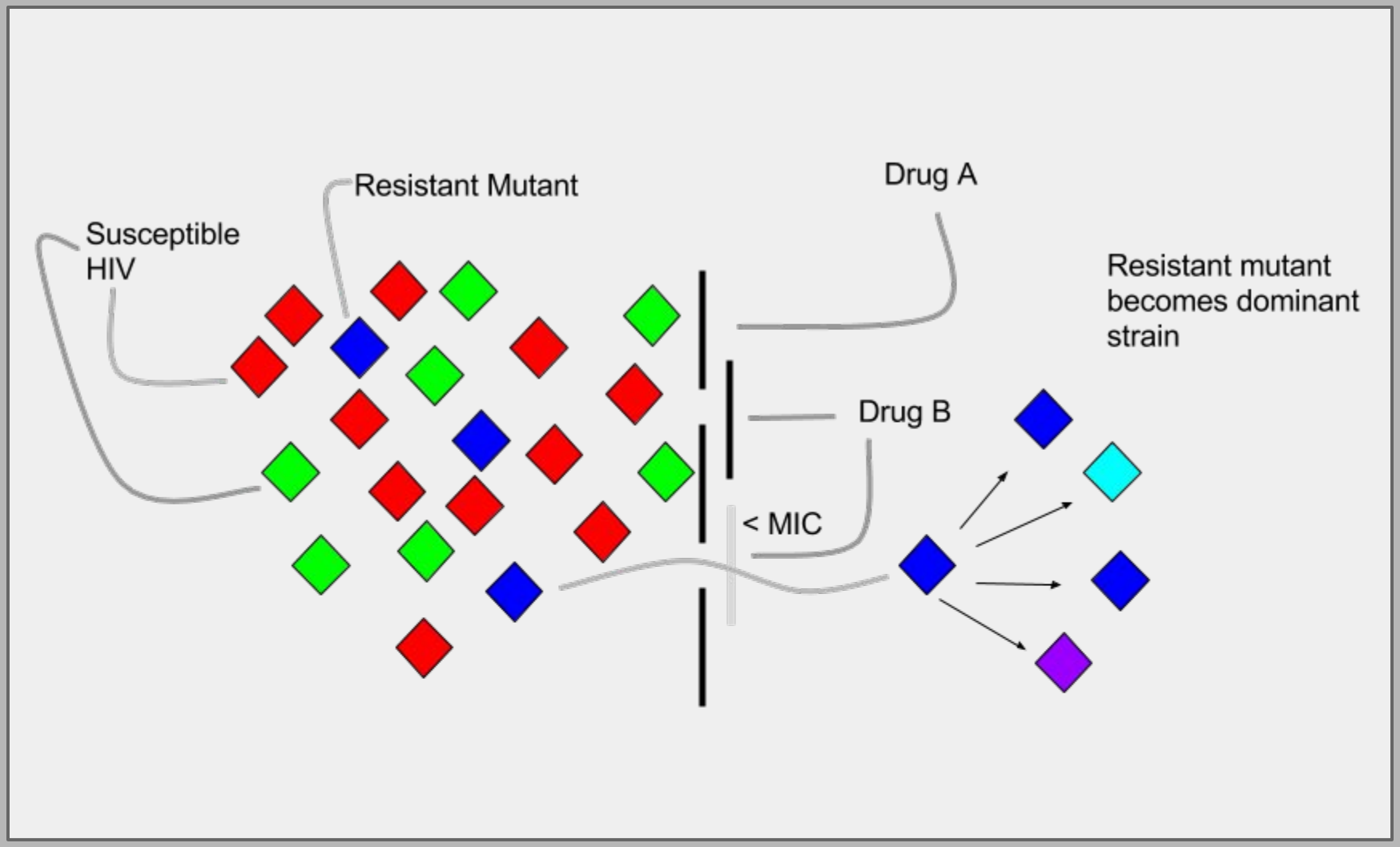
- Different drugs have different t 1/2, potentially leaving only one mechanism of action to prevent HIV replication

Consequences

- Certain mutants may have altered enzyme activity, bypassing or overcoming mechanism of drug activity
  - Lower genetic barrier drugs - may only require single base pair change to confer resistance (NNRTI)
  - Higher genetic barrier drugs - require multiple base pair changes to confer resistance (PIs)

- Drug resistant variant, in presence of drug, is most ‘fit’ and becomes dominant strain
  - VL increases

Consequences



Consequences

- If drugs removed there is no selection pressure for mutant; ‘wild type’ reappears within 2-4 weeks
  - Implications for genotypic testing
  - Mutant variant still present and ‘archived’ in tissue

- Requires different or additional medications to suppress drug resistant HIV

- Second and third line therapies may require more pills, dose times or have less desirable adverse effects/DIs

Consequences

- Drug resistant HIV can be transmitted

- G190A mutation which confers resistance to efavirenz, nevirapine and potentially to rilpivirine common amongst IDU in Regina area
  - Traced to a transmission network
  - Precluded use of only STR at the time, Atripla
  - Patients prescribed multi-tablet PI regimen instead

Adherence

- Important to maintain integrity of first line therapy
  - Three *active* drugs from at least two different classes
    - ritonavir/cobicistat are not active
- Patients who are highly adherent to and persistent with ART will not develop drug resistance
- Off/on adherence will lead to resistance sooner than just stopping medication

Adherence

- Recognize signs of poor adherence and act as soon as possible
  - PIP, patient interview at each visit, date of last/next clinic appointment
  - Refill dates different for each drug or consistently late

- Careful monitoring of VL can help identify if adherence is poor and there is risk of resistance
  - If VL not done in last 6 months this should be repeated
  - Contact clinic if blood work out of date or:
    - VL is not suppressed despite ongoing ART
      - <200 c/mL acceptable occasionally - ‘blip’
      - >500 c/mL send for resistance testing, ideally while patient still on ART

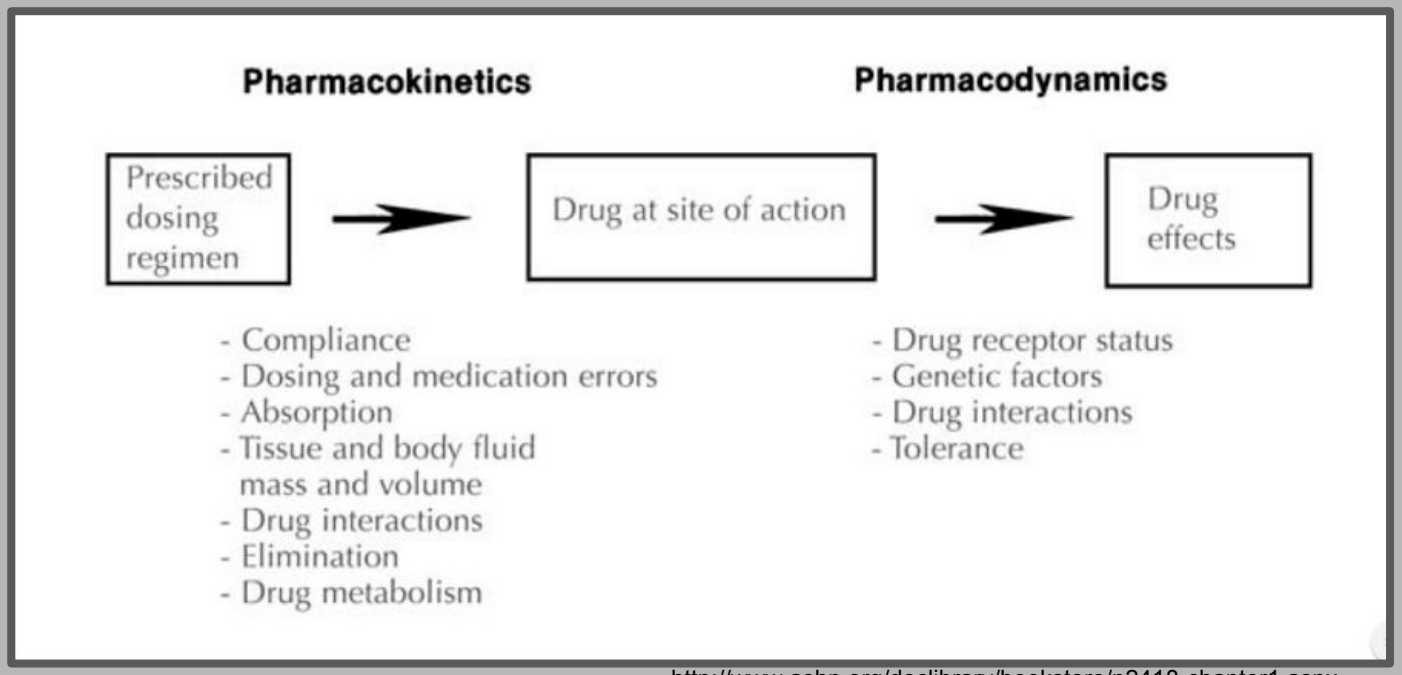
Adherence

- Pharmacists have a crucial role to play in optimizing adherence and persistence of ART

- Creative and patient focused solutions to poor adherence
  - DOT
  - Home Care
  - Blister packing/limited dispense
  - Pick up at another location

Drug Interactions

Drug Interactions



http://www.ashp.org/doclibrary/bookstore/p2418-chapter1.aspx

- May impact ART success
- May impact patient health

Drug Interactions

- Other ARVs
- OI medications
- Prescription
- Non-prescription
- Herbals
- Food
- Recreational/street

Drug Interactions

- Newer therapies are less prone to DIs than earlier therapies but caution should still be used whenever any medications changed
  - Check PIP for meds filled elsewhere
  - Ask patient if any changes

- Don’t assume HIV clinician has managed DIs

Drug Interactions

- Pay special attention to:
  - Inhaled corticosteroids (ritonavir/cobicistat)
  - PPIs (rilpivirine, atazanavir)
  - Polyvalent cation supplements - magnesium, calcium etc (integrase inhibitors
  - Hepatitis C therapies
  - Anticonvulsants
  - Rifampin (everything!)
  - Antiplatelet /coagulant drugs
  - Statins
  - Erectile dysfunction drugs
  - Psychotropics
  - Contraceptives
  - methadone

Drug Interactions

- Resources:
  - HIV InSite:
    - http://hivinsite.ucsf.edu/insite?page=ar-00-02
  - Toronto General Hospital Immunodeficiency Clinic
    - http://hivclinic.ca/drug-information/drug-interaction-tables/
  - HIV/HCV Drug Therapy Guide
    - http://app.hivclinic.ca/
  - RQHR HIV Clinic Pharmacist
    - 306-766-0717

Summary

- Drug interactions with antiretrovirals are becoming less difficult to manage
  - Given the implications of treatment failure extra attention is still warranted

- Be thorough and check all medications/OTCs patient takes (check full profile/patient history) periodically and when any medications stopped or started

- Many resources exist for interpreting DIs but when in doubt call HIV clinic pharmacist to help manage

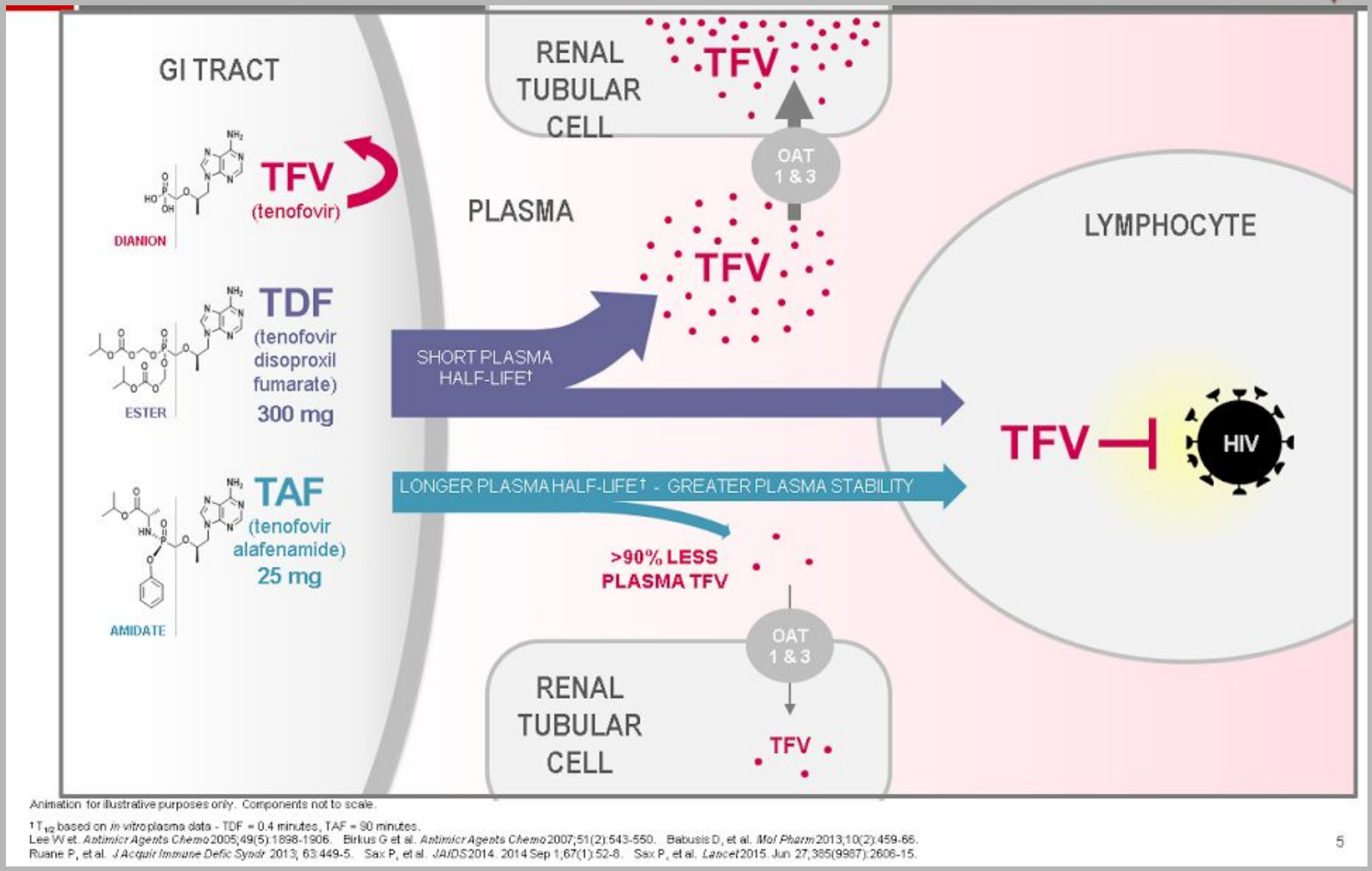
Evolutions in HIV Treatment

What's New?

New Tenofovir

- Tenofovir disoproxil fumarate (TDF) is found in Truvada, Atripla, Stribild, Complera
  - Very effective NRTI
  - May lead to renal problems and lower BMD
- Tenofovir alafenamide (TAF) is found in Descovy, Genvoya and Odefsy
  - Very effective NRTI
  - Has improved adverse effect profile with respect to renal function and BMD
  - Does not offer lipid lowering effect of TDF
  - Not indicated for PrEP
  - Dose is smaller (10-25mg vs 300mg) resulting in smaller tablet

New Tenofovir



Animation for illustrative purposes only. Components not to scale.

† $T_{1/2}$ based on *in vitro* plasma data - TDF = 0.4 minutes, TAF = 90 minutes.

Lee W et. *Antimicr Agents Chemo* 2005;49(5):1898-1906. Birkus G et al. *Antimicr Agents Chemo* 2007;51(2):543-550. Babusis D, et al. *Mol Pharm* 2013;10(2):459-66. Ruane P, et al. *J Acquir Immune Defic Syndr* 2013; 63:449-5. Sax P, et al. *JAIDS* 2014. 2014 Sep 1;67(1):52-8. Sax P, et al. *Lancet* 2015. Jun 27;385(9987):2606-15.

New Tenofovir

- Descovy (emtricitabine/TAF)
  - 200mg/25mg and 200mg/10mg strength
    - Use 10mg strength with cobicistat or ritonavir containing regimens (25mg without)
  - Currently reimbursed by manufacturer pending formulary approval
  - Possible to pursue switch for those who would benefit from switch to TAF
    - Older, declining creatinine clearance, fracture risk
- Genvoya (elvitegravir/cobicistat/emtricitabine/TAF)
  - TAF version of Stribild
  - Can likely make switch in Stribild patients who may benefit from TAF

Single Tablet Regimens

- Trend to fewer pills

- Triumeq (dolutegravir/abacavir/lamivudine)
  - Can replace dual tablet regimen (Tivicay+Kivexa)

- Prezcobix (darunavir/cobicistat) - *not STR*
  - Reduces PI regimen pill counts by eliminated Norvir (ritonavir)
  - Still requires NRTI backbone (Truvada, Descovy or Kivexa)

Single Tablet Regimens

- Usually a better option for patients
- Pharmacists can contact prescriber to have regimen switched to STR
- SPDP coverage pending for Genvoya/Descovy
- NIHB coverage pending for Genvoya/Descovy and Triumeq (prior approval needed)

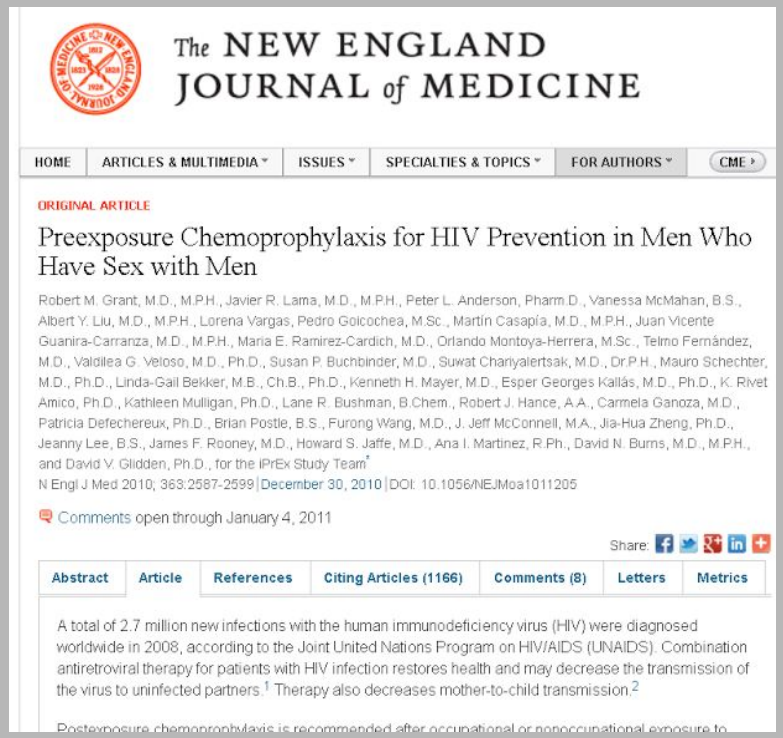
The Future

- Ongoing research into ‘cleaner’ agents
  - Focus on integrase inhibitors
- Injectable formulations
- Duotherapy or monotherapy vs triple therapy ART

Pre Exposure Prophylaxis (PrEP)

- Prevention of HIV-1 infection is possible through daily medication
- Truvada (TDF/FTC) but not Descovy (TAF/FTC) taken daily (alternate “on demand” regimen: ii tabs 2-24 hours before exposure, i QD until 48 hours post last exposure)
- Does not protect against other STIs or pregnancy
- Not for everyone

Pre Exposure Prophylaxis (PrEP)



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ORIGINAL ARTICLE

Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

Robert M. Grant, M.D., M.P.H., Javier R. Lama, M.D., M.P.H., Peter L. Anderson, Pharm.D., Vanessa McMahan, B.S., Albert Y. Liu, M.D., M.P.H., Lorena Vargas, Pedro Goicochea, M.Sc., Martín Casapía, M.D., M.P.H., Juan Vicente Guanira-Carranza, M.D., M.P.H., Maria E. Ramirez-Cardich, M.D., Orlando Montoya-Herrera, M.Sc., Telmo Fernández, M.D., Valdilea G. Veloso, M.D., Ph.D., Susan P. Buchbinder, M.D., Suwat Chariyalertsak, M.D., Dr.P.H., Mauro Schechter, M.D., Ph.D., Linda-Gail Bekker, M.B., Ch.B., Ph.D., Kenneth H. Mayer, M.D., Esper Georges Kallás, M.D., Ph.D., K. Rivet Amico, Ph.D., Kathleen Mulligan, Ph.D., Lane R. Bushman, B.Chem., Robert J. Hance, A.A., Carmela Ganoza, M.D., Patricia Defechereux, Ph.D., Brian Postle, B.S., Furong Wang, M.D., J. Jeff McConnell, M.A., Jia-Hua Zheng, Ph.D., Jeanny Lee, B.S., James F. Rooney, M.D., Howard S. Jaffe, M.D., Ana I. Martinez, R.Ph., David N. Burns, M.D., M.P.H., and David V. Glidden, Ph.D., for the iPrEx Study Team*

N Engl J Med 2010; 363:2587-2599 | December 30, 2010 | DOI: 10.1056/NEJMoa1011205

Comments open through January 4, 2011

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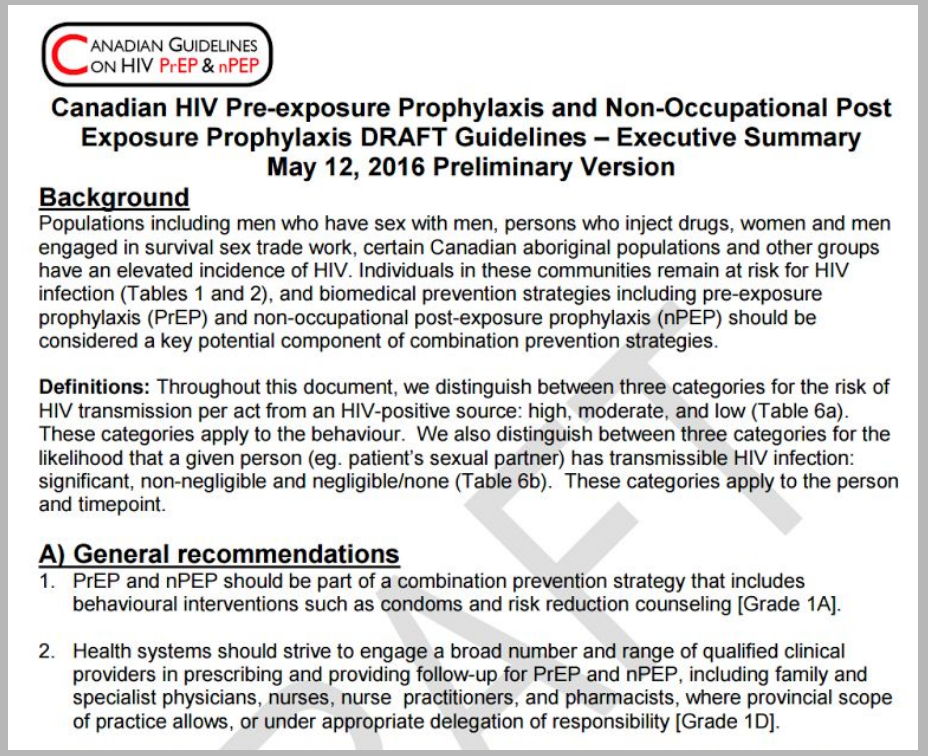
Abstract | Article | References | Citing Articles (1166) | Comments (8) | Letters | Metrics

A total of 2.7 million new infections with the human immunodeficiency virus (HIV) were diagnosed worldwide in 2008, according to the Joint United Nations Program on HIV/AIDS (UNAIDS). Combination antiretroviral therapy for patients with HIV infection restores health and may decrease the transmission of the virus to uninfected partners.[1] Therapy also decreases mother-to-child transmission.[2]

Postexposure chemoprophylaxis is recommended after occupational or nonoccupational exposure to

iPrex Study



CANADIAN GUIDELINES ON HIV PrEP & nPEP

Canadian HIV Pre-exposure Prophylaxis and Non-Occupational Post Exposure Prophylaxis DRAFT Guidelines – Executive Summary May 12, 2016 Preliminary Version

Background

Populations including men who have sex with men, persons who inject drugs, women and men engaged in survival sex trade work, certain Canadian aboriginal populations and other groups have an elevated incidence of HIV. Individuals in these communities remain at risk for HIV infection (Tables 1 and 2), and biomedical prevention strategies including pre-exposure prophylaxis (PrEP) and non-occupational post-exposure prophylaxis (nPEP) should be considered a key potential component of combination prevention strategies.

Definitions: Throughout this document, we distinguish between three categories for the risk of HIV transmission per act from an HIV-positive source: high, moderate, and low (Table 6a). These categories apply to the behaviour. We also distinguish between three categories for the likelihood that a given person (eg. patient's sexual partner) has transmissible HIV infection: significant, non-negligible and negligible/none (Table 6b). These categories apply to the person and timepoint.

A) General recommendations

1. PrEP and nPEP should be part of a combination prevention strategy that includes behavioural interventions such as condoms and risk reduction counseling [Grade 1A].

2. Health systems should strive to engage a broad number and range of qualified clinical providers in prescribing and providing follow-up for PrEP and nPEP, including family and specialist physicians, nurses, nurse practitioners, and pharmacists, where provincial scope of practice allows, or under appropriate delegation of responsibility [Grade 1D].

Draft Canadian Guidelines on HIV PrEP & nPEP -
http://www.catie.ca/sites/default/files/Canadian%20PrEP%20and%20nPEP%20Guidelines%20Executive%20Summary%20for%20circulation%20v0-5%20May%2012%202016.pdf

Pre Exposure Prophylaxis (PrEP)

- HIV negative MSM/TGW reporting condomless sex in last six months
  - Compelling if bacterial STI in last year or use of nPEP or
  - ongoing sex with HIV+ with high risk of transmission
  - Not recommended for stable/closed serodiscordant relationships where risk is negligible
- Heterosexual couples with high risk of HIV transmission
- May be considered for PWID after harm reduction systems in place
- Monitor q30d x 3 months then q3months thereafter for HIV infection, STIs, lab values

Pre Exposure Prophylaxis (PrEP)

Canadian Agency for Drugs and Technologies in Health

COMMON DRUG REVIEW

CADTH CANADIAN DRUG EXPERT COMMITTEE
FINAL RECOMMENDATION

EMTRICITABINE/TENOFOVIR DISOPROXIL FUMARATE
(Truvada — Gilead Sciences Canada, Inc.)
Indication: Pre-exposure Prophylaxis of HIV-1 Infection

Recommendation:
The CADTH Canadian Drug Expert Committee (CDEC) recommends that emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) be reimbursed for use as pre-exposure prophylaxis (PrEP) of human immunodeficiency virus type 1 (HIV-1) in combination with safer sex practices to reduce the risk of sexually acquired HIV-1 infection in adults at high risk for infection, if the following conditions are met:

Conditions:
1. Provided in the context of a sexual health program by a prescriber experienced in the treatment and prevention of HIV-1 infection.
2. Reduced price.

Reasons for the Recommendation:
1. Three double-blind, randomized, placebo-controlled trials (iPrEx [N = 2,499], Partners

Truvada = $941.90

-per 34 day supply base cost SPDP

Summary

- HIV treatment has advanced rapidly since first treatments released in 1990s
- Most patients diagnosed today will be treated with a single tablet regimen with very few long term adverse effects or drug interactions
- Future research may lead to injectables or a vaccine
- PrEP is indicated for prevention of HIV but unavailable to large groups of the population due to cost

Questions?

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