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- If you detect any commercial bias, please let me know
  - Phone: 306.766.0717
  - Email: Michael.Stuber@rqhealth.ca



## Objectives

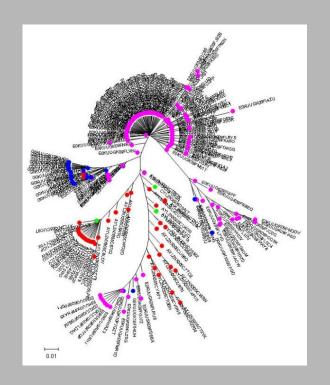
- 1. Understand the scope and complexity of SK's unique HIV epidemic
- Recognize and understand the importance of effective drug therapy in the treatment of HIV

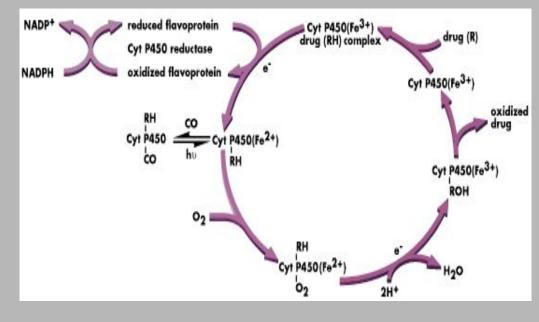
3. Explore the basics of HIV management in a community pharmacy setting





All the things pharmacists love!





## Putting a face to HIV treatment

We're not just treating HIV, we're treating people



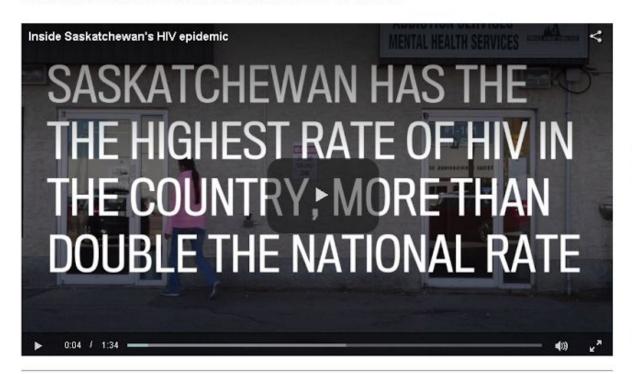


PROVINCIAL POLITICS FIRST NATIONS CITY HALL CRIME RIDERS

II secretario

# Deadly Record: Inside Saskatchewan's HIV crisis

CHARLES HAMILTON, SASKATOON STARPHOENIX, SASKATOON STARPHOENIX 09.16,2016 I







omething as simple as the common cold could kill Lauren Gardinal.



### 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.

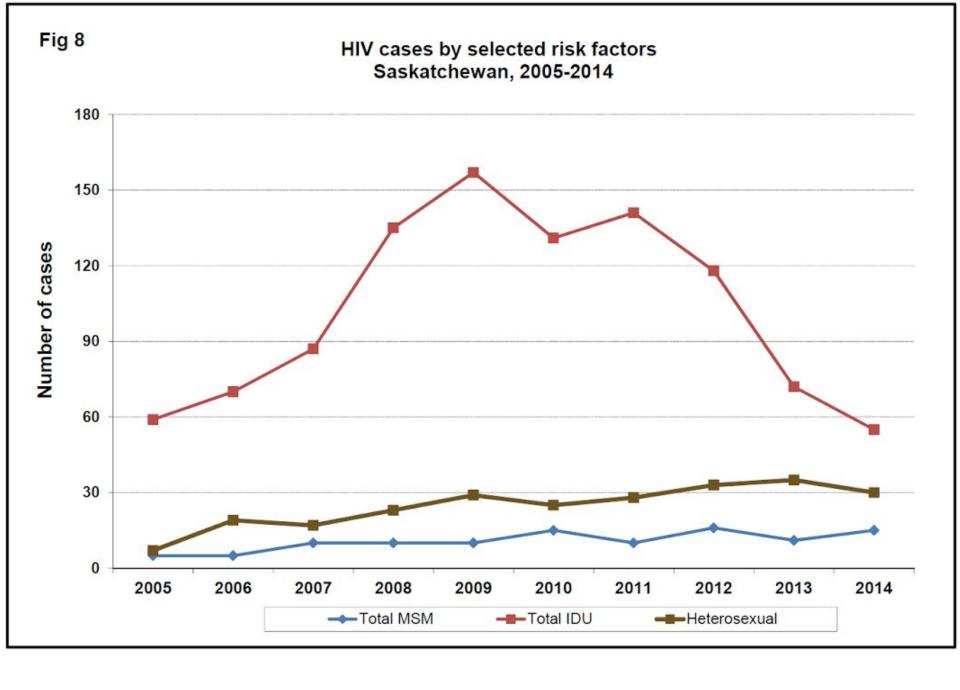
That's the view of a group of doctors in the province who, on Monday, are issuing a *cri de coeur* for action.

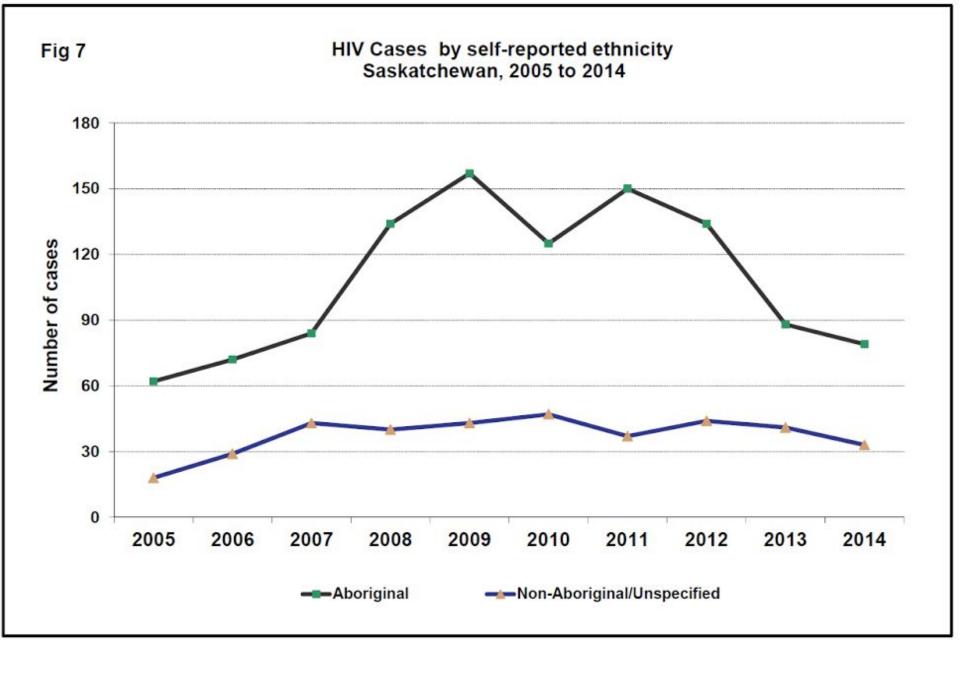
The ad hoc coalition, led by Dr. Ryan Meili of the West Side Community Clinic in Saskatoon, is comprised mostly of physicians who provide front-line HIV care, but they have some chilling data to justify sounding the alarm.

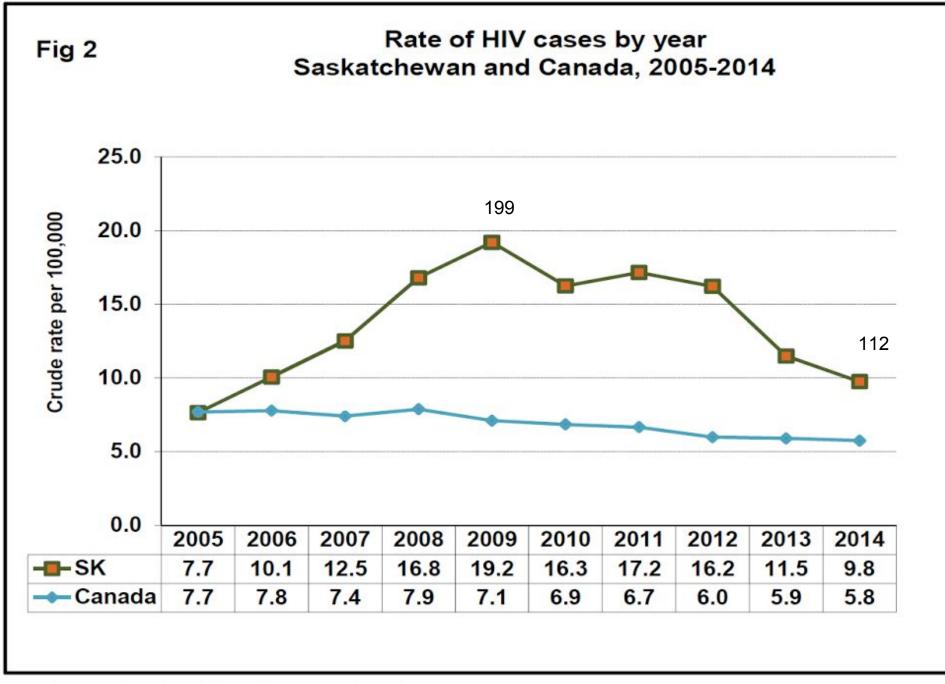
RELATED: Canada's Indigenous HIV treatment in the global spotlight

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.









### 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





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

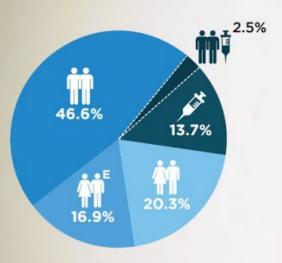
- 5% prevalence rate of HIV in Regina (A-Track Pilot Survey)
  - Sub-Saharan Africa ~4.7% prevalence rate
  - 46% unaware of HIV + status
    - ~20% in rest of Canada (www.catie.ca)

### **NEW HIV INFECTIONS IN CANADA**



www.catie.ca

An estimated 3.175 new HIV infections in Canada in 2011 (9.5 per 100,000 population)



### EXPOSURE CATEGORY



Men who have sex with men



Heterosexual people, not including those born in countries where HIV is endemic



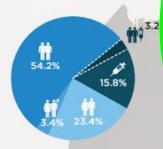
Heterosexual people born in countries where HIV is endemic

People who

inject drugs

#### BRITISH COLUMBIA

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



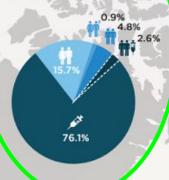
### ALBERTA

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



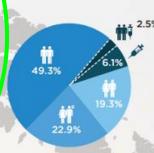
#### **SASKATCHEWAN**

An estimated 230 new HIV infections in 2011 (22,3 per 100,000 population)



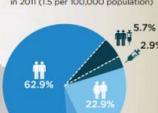
An estimated 1,400 new HIV infections in 2011 (10.9 per 100,000 population)

ONTARIO



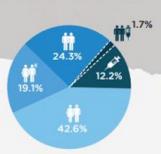
### ATLANTIC CANADA

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



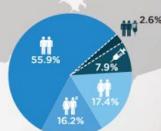
#### MANITOBA

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



#### **QUEBEC**

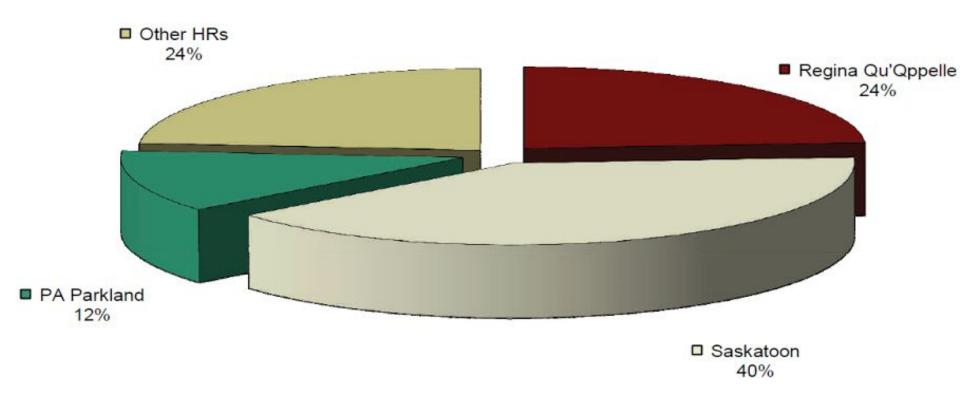
An estimated 760 new HIV infections in 2011 (9.6 per 100,000 population)



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

Fig 6 Proportion of HIV cases reported by selected health regions Saskatchewan, 2005-2014



In 2016 PAPHR makes up ~25% new infections

## Saskatchewan's Situation



- Our epidemic is unique in Canada
- Driven by injection drug use
- Heavily impacting women and indigenous peoples





- 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





- 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.





- Although there are calls for more funding and action this is unlikely to come in the near future
- Fragmented system of First Nations government, federal health and provincial funding
- Lack of infrastructure and coordination to solve complex problem
- Need to make better use of existing resources and maximize efficiency by building capacity to treat increasing numbers





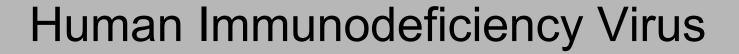
### VS



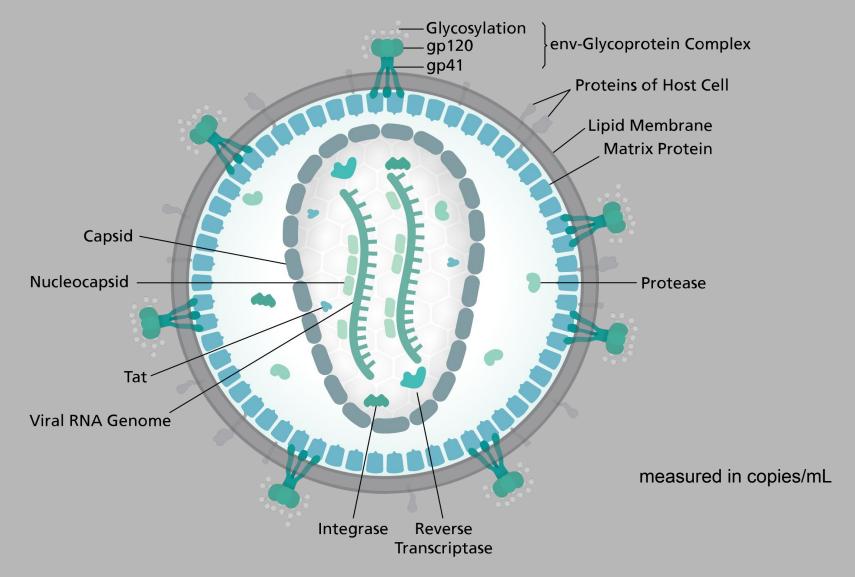




- HIV can infect and affect anyone regardless of ethnicity, income, drug use, location etc
- Treat the person with HIV, not just the HIV itself
  - Each person is an individual and as health care providers we need to assess patients as such
  - Do not let bias, past experiences or perceptions of their HIV status impact care
- Our own experiences and lives are not the same as our patients and seeing their life through our own lens can lead to problems





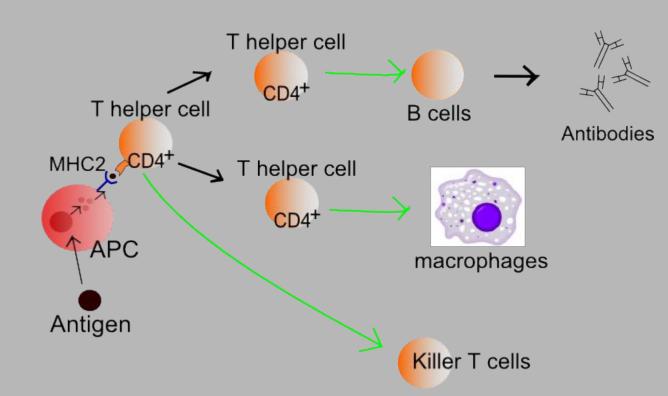


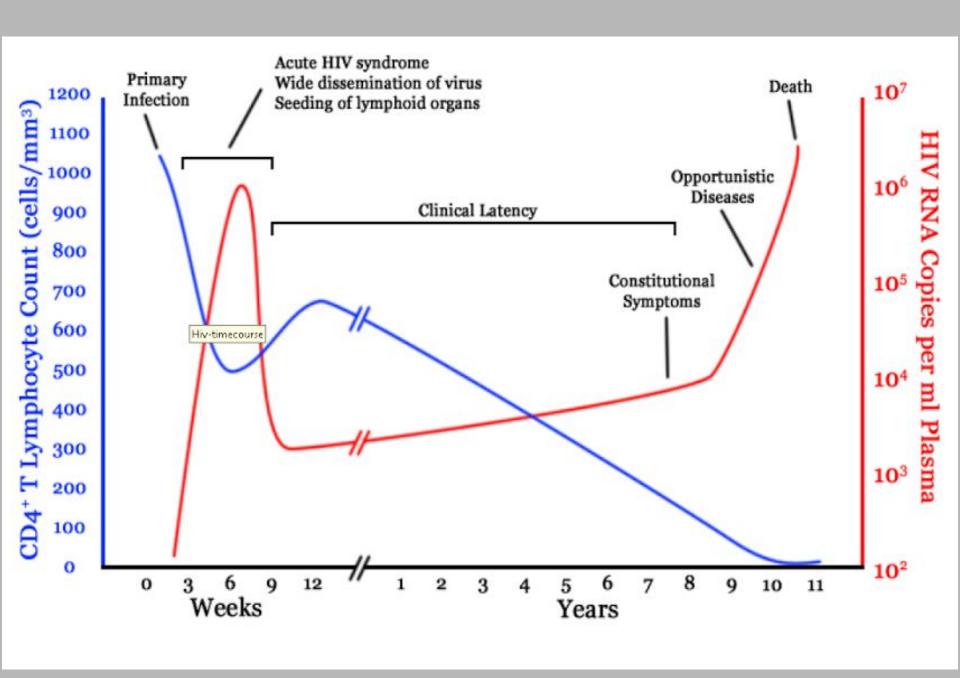


### CD4+ Cells

 Also known as T-cells are white blood cells that help protect the body from infection via activation of the immune response when they detect pathogens such as viruses or bacteria

measured in cells per cubic millimetre (mm³)

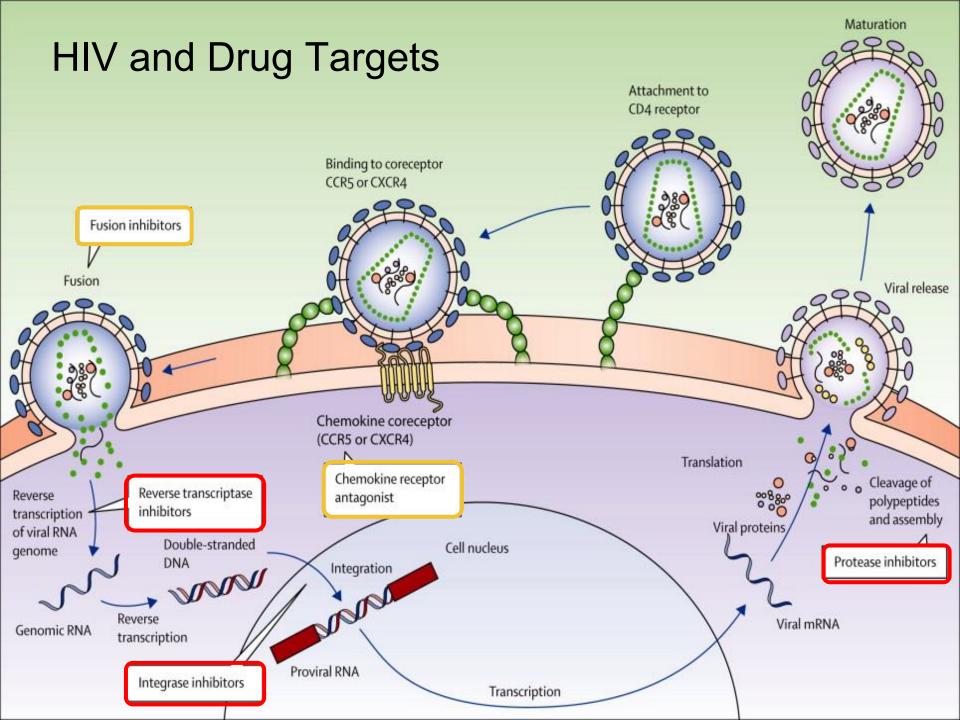














### Anti-RetroVirals



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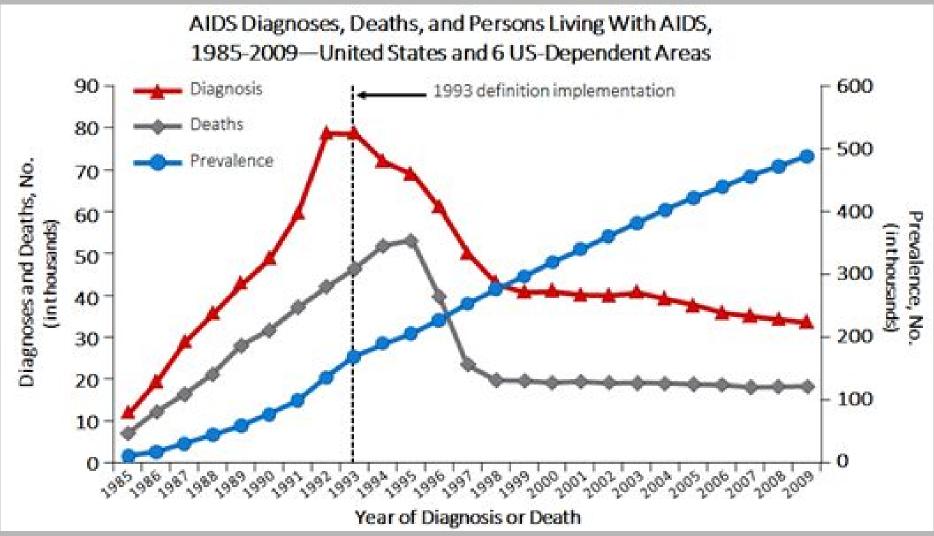


- Effective ART:
  - Suppresses Viral Replication
    - "undetectable" viral load

- Improves Immune Systems
  - Improved CD4+ counts
  - Avoidance of Ols and AIDS defining illnesses
  - Prevention of death
- Reduces Inflammation
  - End-organ damage, cancers



## **Mortality Benefit**





- Individual
  - Longer lifespan than pre-HAART era
    - Near normal
  - Reduced morbidity and mortality
    - Associated hospitalizations
  - Reduced incidence of non-AIDS comorbidities
    - CVD, DM, CKD, non-AIDS cancers
    - Still higher than HIV- cohorts



Societal:

Reduced health care costs

Improved productivity

- Societal:
  - ZERO TRANSMISSIONS
    - Treatment as Prevention (TasP)
    - 90-90-90 Approach

Less transmissions saves countless dollars



## We Can End HIV Epidemic



The NEW ENGLAND JOURNAL of MEDICINE

#### ORIGINAL ARTICLE

### Antiretroviral Therapy for the Prevention of HIV-1 Transmission

M.S. Cohen, Y.Q. Chen, M. McCauley, T. Gamble, M.C. Hosseinipour, N. Kumarasamy, J.G. Hakim, J. Kumwenda, B. Grinsztejn, J.H.S. Pilotto, S.V. Godbole, S. Chariyalertsak, B.R. Santos, K.H. Mayer, I.F. Hoffman, S.H. Eshleman, E. Piwowar-Manning, L. Cottle, X.C. Zhang, J. Makhema, L.A. Mills, R. Panchia, S. Faesen, J. Eron, J. Gallant, D. Havlir, S. Swindells, V. Elharrar, D. Burns, T.E. Taha, K. Nielsen-Saines, D.D. Celentano, M. Essex, S.E. Hudelson, A.D. Redd, and T.R. Fleming, for the HPTN 052 Study Team\*

#### ABSTRACT

#### BACKGROUND

An interim analysis of data from the HIV Prevention Trials Network (HPTN) 052 trial showed that antiretroviral therapy (ART) prevented more than 96% of genetically linked infections caused by human immunodeficiency virus type 1 (HIV-1) in serodiscordant couples. ART was then offered to all patients with HIV-1 infection (index participants). The study included more than 5 years of follow-up to assess the durability of such therapy for the prevention of HIV-1 transmission.

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We randomly assigned 1763 index participants to receive either early or delayed ART. In the early-ART group, 886 participants started therapy at enrollment (CD4+ count, 350 to 550 cells per cubic millimeter). In the delayed-ART group, 877 participants started therapy after two consecutive CD4+ counts fell below 250 cells per cubic millimeter or if an illness indicative of the acquired immunodeficiency syndrome (i.e., an AIDS-defining illness) developed. The primary study end point

HPTN 052 - published in NEJM July 18, 2016





Press conference at CROI 2014. Photo by Liz Highleyman,

PARTNER Study presented at CROI - 2014

# 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)



## We Can End HIV Epidemic

90%

of all



living with HIV will know their HIV status 90%

of all



living with HIV will receive sustained antiretroviral therapy

90%

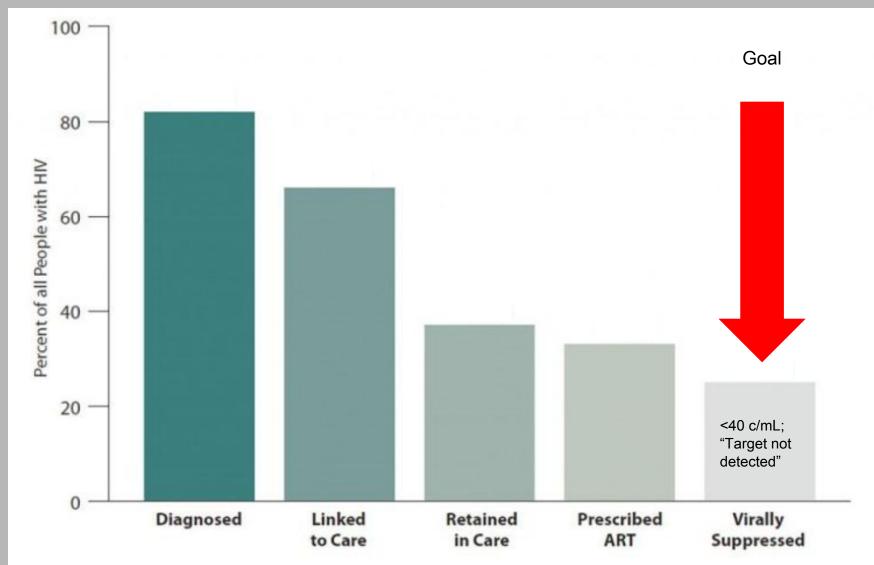
of all



receiving antiretroviral therapy will have durable viral suppression



### Cascade of Care



## **HIV Basics**



- Lots of support needed
  - At ALL stages of cascade
  - Fragmented system

- Many steps to achieve goal of Cascade
  - Not always linear progression
  - Different barriers for different patients at different times



## Pharmacist Roles in Cascade

"My pharmacists (clinical and community) are very important to me! They're the final part of my healthcare team – like the final piece of a puzzle that shows the complete picture.

As an individual that has to visit many different doctors and specialists, it is my pharmacists that do not change. So they are the ones who truly know my entire medication regiment. I trust them with my life! I trust them to recognize any potential problems with my drugs and to let me and my doctors know about it."

-Dom





- Diagnosis
  - Testing for HIV/HCV
    - Being done by some pharmacies in Saskatchewan; pilot projects across Canada
  - Harm reduction
    - Who is at risk for HIV/HCV and when was their last test?







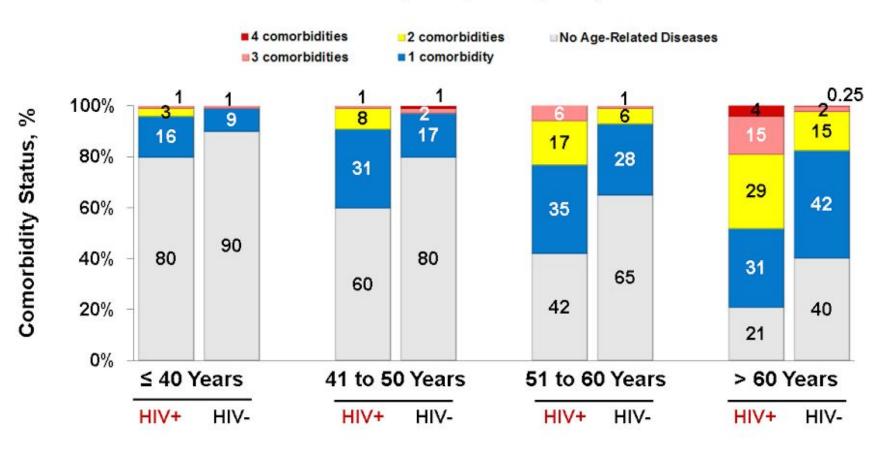
- Diagnosis
  - Comorbidity Managers
    - Cardiovascular
    - renal
    - Bone
    - smoking cessation
    - Addictions
    - Gastrointestinal
    - viral hepatitis
  - Premature aging

#### #

#### HIV+ vs HIV-Onset of Age-Related Comorbidities

#### Prevalence of Individual Noninfectious Comorbidities

HIV+ (N=2854) vs HIV- (N=8562)



HIV+ individuals vs age-matched HIV- controls have more individual noninfectious comorbidities and at an earlier age (all P < 0.001)





- Linked/Retained in Care
  - Coordinators/intermediaries between HIV team, community workers and patients
  - Community support linkage
    - CBOs
  - Appointments
  - Laboratory tests & monitoring
    - eHealth portal to stay up to date on lab values





#### Things you can do in *my*eHealth

- » Register a new account
- Reset my password
- » Retrieve my user ID
- » Add or change an Organization/Facility

### myeHealth Login

User ID

Secure Login A

- » Register a new account
- » Reset my password
- » Retrieve my user ID

#### Welcome to myeHealth

eHealth Saskatchewan is responsible for developing and implementing the Electronic Health Record (EHR) for Saskatchewan. The EHR makes important information available to support improved patient care. eHealth also coordinates, implements and maintains key electronic health information systems in many public healthcare organizations.

## Pharmacist Roles in Cascade



- Prescribed ART
  - Drug therapy experts
    - Ensure right drug/regimen
      - Ensure <u>entire regimen</u> is dispensed at each visit common drug error
    - DDIs ongoing basis
    - Coverage in place
      - This can change be cautious!
      - Patients may be embarrassed to seek help
    - Adverse effects
      - Minor to major can all impact adherence



Inquiries to: Richard Harrigan BC Centre for Excellence in HIV/AIDS 603-1081 Burrard Street Tel: 1-800-517-1119 Vancouver, BC, V6Z 1Y6 Fax: 1-604-806-9463

Resistance Analysis of HIV-1 Protease and Reverse Transcriptase

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NRTI/NtRTI Drugs	Fold Change <sup>1</sup>	Cut-off <sup>2</sup>		Resistance Analysis <sup>3</sup>	
Zidovudine (Retrovir)		1.5	11.4	SUSCEPTIBLE	
Lamívudine (Epivír)	1.3	2.1	4.6	SUSCEPTIBLE	
Didanosine (Videx)	0.8	0.9	2.6	SUSCEPTIBLE	
Stavudine (Zerit)	1.0	1.0	2.3	SUSCEPTIBLE	
Abacavir (Ziagen)	1.0	0.9	3.5	REDUCED RESPONSE	
Emtricitabine (Emtriva)	1.0	3	.1	SUSCEPTIBLE	
Tenofovir DF (Viread)	0.8	1.0	2.3	SUSCEPTIBLE	

NRTI/NtRTI Mutations\*: 69N

NNRTI Drugs	Fold Change	Cut-	off <sup>2</sup>	Resistance Analysis <sup>3</sup>
Nevirapine (Viramune)	40.0	6.0		RESISTANT
Efavirenz (Sustiva, Stocrin)	10.1	3	1.3	RESISTANT
Etravirine (Intelence)	1.0	3.2	27.6	SUSCEPTIBLE
Rilpivirine (Endurant)	1.1	3	.1	SUSCEPTIBLE

NNRTI Mutations4: 190A

PI Drugs	Fold Change <sup>1</sup>	Cut-off <sup>2</sup>		Resistance Analysis <sup>3</sup>	
Indinavir/r (Crixivan)		2.3	27.2	SUSCEPTIBLE	
Nelfinavir (Viracept)	2.0	2.2	9.4	SUSCEPTIBLE	
Saquinavir/r (Invirase)	0.7	3.1	22.6	SUSCEPTIBLE	
Fosamprenavir/r (Lexiva, Telzir)	0.6	1.5	19.5	SUSCEPTIBLE	
Lopinavir/r (Kaletra)	0.9	6.1	51.2	SUSCEPTIBLE	
Atazanavir/r (Reyataz)	0.8	2.5	32.5	SUSCEPTIBLE	
Tipranavir/r (Aptivus)	0.9	1.5	7.0	SUSCEPTIBLE	
Darunavir/r (Prezista)	0.5	10.0	106.9	SUSCEPTIBLE	
PI Mutations4:					

This nucleic acid amplification, sequence-based test was developed and its performance characteristics determined by the BCCEE Research Laboratory. US Clients only: This test does not require premarket review by the US Food and Drug Administration and has not been approved by the FDA. The laboratory is certified under CLIA '88 to perform high complexity clinical Laboratory testing. This test is used for clinical purposes.

Predicted Fold Change in SOS inhibitory Concentration (ICSO), relative to susceptible reference virus.
 Cut-off values for maximal and minimal clinical response (Clinical Cut-Off) or for normal susceptibility range in vitro (Biological Cut-Off).
 Biological Cut-Offs are printed in Italic.
 Resistance Analysis based on the magnitude of the Fold Change relative to the Clinical or the Biological Cut-Offs.
 Mustations indicated are those reported on public lists (ANRS, Stanford, IAS-USA) or by drug development sponsors.

For more information on these results and their interpretation, or to suggest how to improve this report please contact the lab at (800) 517-1119 or email prharrigan@cfenet.ubc.ca

#### Genotyping

 Are the prescribed drugs effective in this patient?



- HLA B\*5701 status
  - Are they on a abacavir containing regimen

## **Drug Interactions**

- Varies by drug class and individual agents
  - Beware of the classic high risk medications
    - Antidepressants
    - Anticonvulsants
    - Methadone
    - Oral contraceptives
    - Antibiotics
    - Natural products/supplements
  - HCV drugs are becoming more common
    - Dls with Harvoni, Holkira etc use caution
  - http://hivclinic.ca/drug-information/ excellent Canadian resource!
  - http://hivinsite.ucsf.edu/insite?page=ar-00-02
- Check entire profile often and call if need help interpreting the interaction
- Illicit drugs (cocaine, opioids, methylphenidate, benzo's) may have altered effect







- Viral Suppression
  - Overcoming Adherence Barriers
    - Coverage
    - Adverse effects managment
    - Convenience packaging
    - Transitions in Care
    - Creative solutions to barriers in care
  - Adherence is notoriously difficult to assess
  - Persistence vs adherence

<40 c/mL or TARGET NOT DETECTED

#### HIV 1 RNA; PCR/NAAT (HIV-1 Viral Load NAAT) New Cumulative Results

Time Collected
Time Reported
Ordering Provide
Specimen Sourc
Copied To
Comments

REGINA SK S4PØWS

Test Result Ref. Range (Units) Abnormality Status
HIV 1 RNA; PCR/NAAT (HIV-1 Viral Load NAAT) a 131 (Copies/mL) Final

\* Abnormal \*\*\* Critically Abnormal

RNA detected.

Test Method: HIV-1 Abbott RealTime NAAT (Nucleic Acid Amplification Test) Dynamic Range: 40 - 10,000,000 Copies/mL based on 0.6 mL sample input. This test product is only validated/licensed to monitor HIV-1 antibody postive patients receiving anti-retroviral drug therapy. Use of this product for screening or diagnosis is neither licensed nor validated.

Test	Result	Ref. Range (Units)	Abnormality	Status
CD3 Cells/100 Cells (CD3 (%))	84	59-84 (%)		Final
CD3 Cells (CD3 (ABSOLUTE))	975	887-2331 (x10e6/L)		Final
CD3+CD4+ Cells/100 Cells (CD4 (%))	* 10	33-59 (%)	L	Final
CD3+ CD4+ Cells (CD4 (ABSOLUTE))	* 120	689-1566 (x10e6/L)	L	Final
CD3+CD8+ Cells/100 Cells (CD8 (%))	* 55	15-39 (%)	Н	Final
CD3+ CD8+ Cells (CD8 (ABSOLUTE))	635	262-1066 (x10e6/L)		Final
CD3+CD4+ Cells/CD3+CD8+ Cells (CD4/CD8 RATIO)	a * 0.19	0.92-3.80	L	Final

\* Abnormal \*\* Critically Abnormal

Interpretation(s):

PLEASE NOTE: THE REFERENCE RANGES USED ARE TAKEN FROM A STUDY BY THE NEW JERSEY MEDICAL SCHOOL.

- Check for VL and CD4+
- Look at date
  - Is it recent or should it be repeated?
- VL
  - o Is it suppressed?
- CD4+ above OI cutoffs
  - <50 MAC proph</p>
  - < 100 toxo proph</p>
  - o <200 PCP proph

# Managing Adverse Effects



- Try non-pharm strategies first (play with dose timing, food, etc)
- Maintain support and encouragement for patients considering going off therapy
  - use eHealth to show patient their VL or CD4 progress
- Nausea
  - dimenhydrinate, metoclopramide, ondansetron
- Diarrhea
  - loperamide

# Managing Adverse Effects



- Headache
  - acetaminophen (caution in HCV+ or heavy alcohol users); NSAIDs (use caution if patient on TDF)
- Rash
  - return to clinic for assessment ASAP
  - hydroxyzine, diphenhydramine
- Sleeping difficulty
  - change dose time, ?sedative such as diphenhydramine or zopiclone
- Lipids
  - low dose statin if indicated

## Managing Adverse Effects



- Abacavir Hypersensitivity
  - Onset within 7-8 days on average
    - Fever, influenza like symptoms, GI involvement, rash
  - Highly correlates with presence of HLA B\*5701 allele
    - Tested for before treatment started <u>can find on</u> <u>eHealth portal</u>
  - Immediately stop drug!
    - Symptoms may resolve quickly
    - Never rechallenge as this can result in rapid and severe onset of symptoms with potential death
  - Abacavir (Kivexa & generics, Triumeq)





- Viral Suppression
  - Maintaining Viral Suppression
    - Lifelong, chronic illness
    - encouragement/feedback
    - Ongoing monitoring lab values and clinic checkups
  - Intervene when necessary
  - Treat person with HIV as any other patient; build strong relationships
    - Better outcomes



#### Barriers to Adherence

Perspective



## 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



# <u>Stigma</u>

- Diabetes vs HIV outcomes
- Both chronic and treatable why do we see them differently?
- Stigma:
  - Nature of disease
  - Characteristics of HIV+ people
  - Community support (urban setting vs rural; cultural differences)

# **Stigma**

- Privilege and our perspective of HIV treatment can be a barrier
- Imperative to be aware that our experience is different than that of the patients
- Be empathetic (put yourself in their shoes) vs sympathetic (pity)
- Confidentiality patient's status must be kept confidential
  - Includes medication names, etc

## **HIV Basics**



- ART is the key to getting to 'viral suppression'
  - Pharmacists are experts in drug therapy provision
    - Under/poorly utilized in Saskatchewan
    - Unique opportunities vs other provinces
      - Community vs central ARV dispensaries
  - Pharmacists can be valuable resources at other steps of the cascade





- AIDS cases aren't decreasing
  - 22/28 AIDS cases in 2014 alive
- Provision of ART to hard to reach populations
  - Does it go far enough?
- Reduced HIV incidence
  - True incidence?
  - Northern/Remote communities

## Success and Failure



- Adherence Supports
  - DOT/EA approaches
    - Documented success in chaotic populations
    - System barriers to implementation
  - Home care
  - Case Management

## The Future



- Integration of community pharmacists into HIV team
  - Use of EMRs
  - Lower threshold for feedback to clinic team
    - Improved communications mechanisms
  - HIV testing and follow up
  - Care coordination
  - Case management involvement

## The Future



- Building capacity
  - Targeted education
  - Intra/Interdisciplinary collaboration
  - Strategies for overcoming adherence barriers

- Research
  - Data needed
  - Projects

## The Future



- Pharmacist compensation
- Community Practice Guidelines
  - Certifications
  - Internships
- 100% ARV reimbursement for all Saskatchewan people
- SK HIV Pharmacists Interest Group/Network
  - Sharing of information
  - Collaboration
  - Data collection

### Resources

- SK HIV Collaborative
  - http://www.skhiv.ca/
- Canadian HIV/AIDS Pharmacists Group (CHAP)
  - http://hivclinic.ca/chap/
- AIDSInfo Guidelines
  - https://aidsinfo.nih.gov/guidelines
- BC Centre for Excellence
  - http://www.cfenet.ubc.ca/
- Drug Interactions
  - http://hivclinic.ca/main/drugs\_interact.html
- Clinical Pharmacists
  - Regina 306.766.0717
  - Saskatoon 306,655,0688







- HIV is a chronic illness easily treated with ART
- People living with HIV are individuals and are more than their infection
- Myriad challenges and barriers to effective HIV diagnosis, engagement and treatment in Saskatchewan
  - Exacerbated by fragmented system
- As gatekeepers of ARVs and drug therapy experts, pharmacists are key players in guiding patients through the HIV Care Cascade



## Conclusions

- Active involvement of pharmacists in HIV care results in better outcomes
- Opportunities exist to increase capacity for pharmacist lead HIV interventions
- Ongoing educational opportunities and collaboration will produce novel ways of overcoming barriers to HIV care

