The Latest in HIV Treatment, Comorbidities & Prevention

Dr. Gordon Arbess, MD, CCFP

DFCM, St. Michael's Hospital

University of Toronto

November 6, 2015

St. Michael's
Inspired Care. Inspiring Science.

Northern Ontario School of Medicine

École de médecine du Nord de l'Ontario

ᑭᐧᐁᑎᓂᐧ ᐊᐢᑌᕮᐅ
ᒪᐧᐦᑭᐧ ᐃ ᐃᐧᑯᓂᐧᐃᐢ

CEPD continuing education and professional development

Faculty/Presenter Disclosure Slide 1

- **Faculty:** Gordon Arbess

- **Relationships with commercial interests:**
  - **Grants/Research Support:** None
  - **Speakers Bureau/Honoraria:** Merck, Gilead, Viiv
  - **Consulting Fees:** None
  - **Other:** None

Northern Ontario School of Medicine

École de médecine du Nord de l'Ontario

ᑭᐧᐁᑎᓂᐨ ᐊᐢᑌᕮᐅ
ᒪᐦᐢᑭᐧ ᐃ ᐃᐦᓂᓂᐧᐃᐢ

CEPD
continuing education and professional development

Disclosure of Commercial Support Slide 2

- **This program has received financial support from** N/A**in the form of** N/A
- **This program has received in-kind support from** *N/A* **in the form N/A**

- **<u>Potential for conflict(s) of interest</u>:**
  - None

Outline

- Treatment: When & How & Why
- Comorbidities/Paradigm Shift as Manageable Chronic Disease
- Prevention Issues

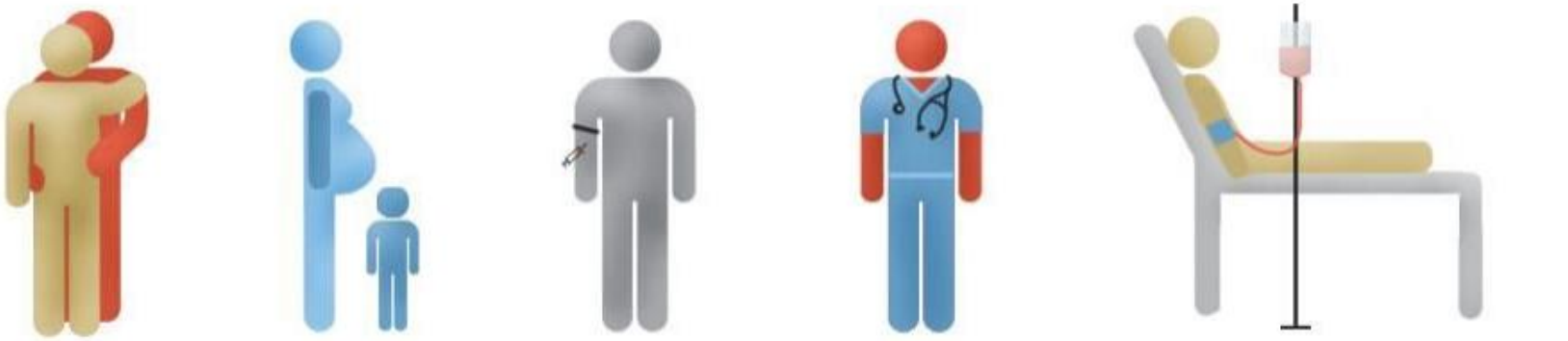
HIV/AIDS in the United States and Worldwide

- Approximately 1.1 million people are living with HIV/AIDS in the United States
  - An estimated 1 in 6 (15.8%) of those people are undiagnosed
  - Since the start of the epidemic, 636,000 people have died of AIDS
  - An estimated 50,000 new HIV infections occur in the US every yr
- More than 35 million people are living with HIV/AIDS worldwide, of whom 3.3 million are younger than 15 yrs of age
  - In 2012, an estimated 2.3 million people were newly infected with HIV

CDC. HIV Surveillance Report. 2013;18(no.5). CDC. HIV Surveillance Report, 2011; vol. 23.
UNAIDS Report On the Global AIDS Epidemic 2013.

71 300 new HIV diagnoses in Canada (2011)

HIV CAN BE TRANSMITTED THROUGH...



Sexual Contact

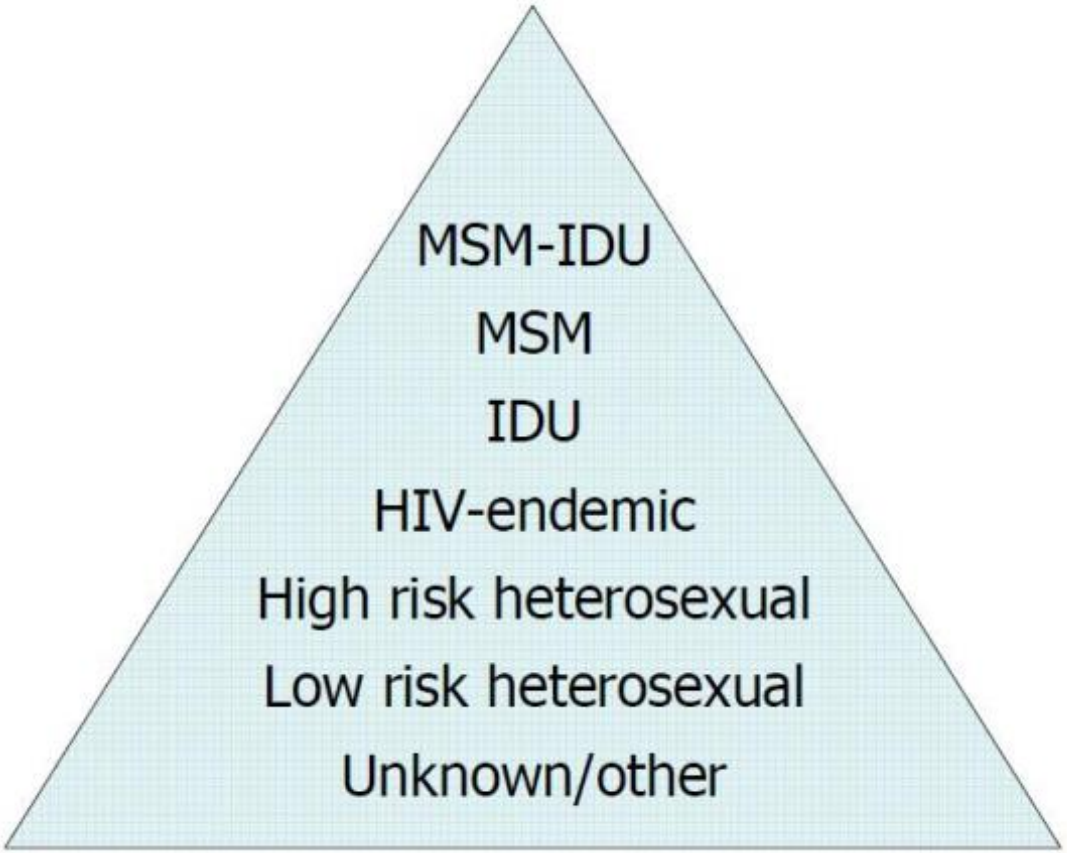
Pregnancy, Childbirth & Breast Feeding

Injection Drug Use

Occupational Exposure

and rarely,
Blood Transfusion/Organ Transplant

Exposure category hierarchy

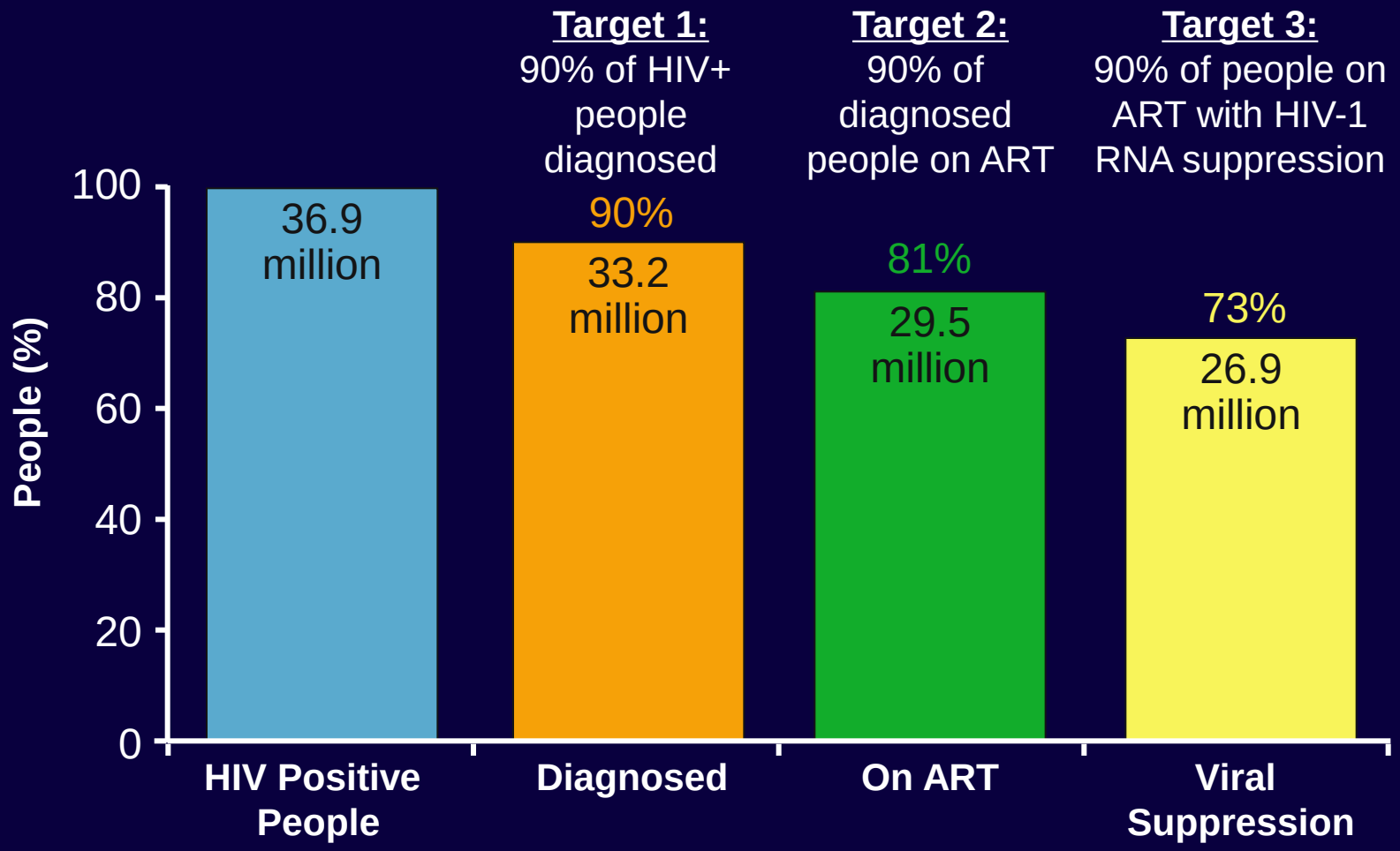


Ontario

PUBLIC HEALTH AGENCY of CANADA
AGENCE DE SANTÉ PUBLIQUE du CANADA

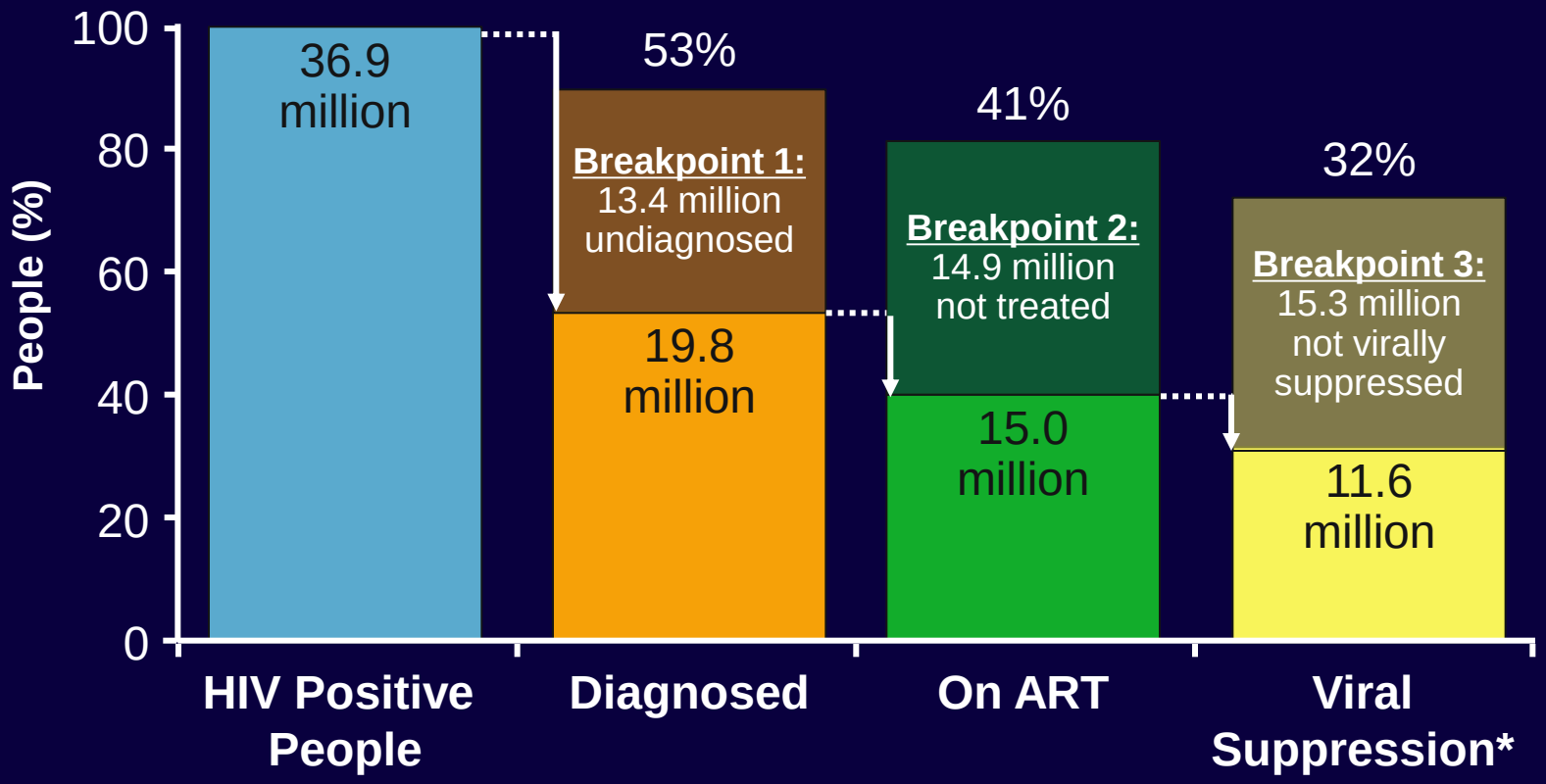
Sullivan A, Remis RS, Swantee C. Uptake and performance of HIV point-of-care testing in Ontario, 2007-2011 HIV Testing Conference, AIDS Bureau, Ontario Ministry of Health and Long-Term Care, Toronto, May 8, 2012. Available from: http://www.ohemu.utoronto.ca/Presentations.html

UNAIDS: 90-90-90 Treatment Targets



Levi J, et al. IAS 2015. Abstract MOAD0102. Reproduced with permission.

UNAIDS: 90-90-90 Global Estimated Gaps

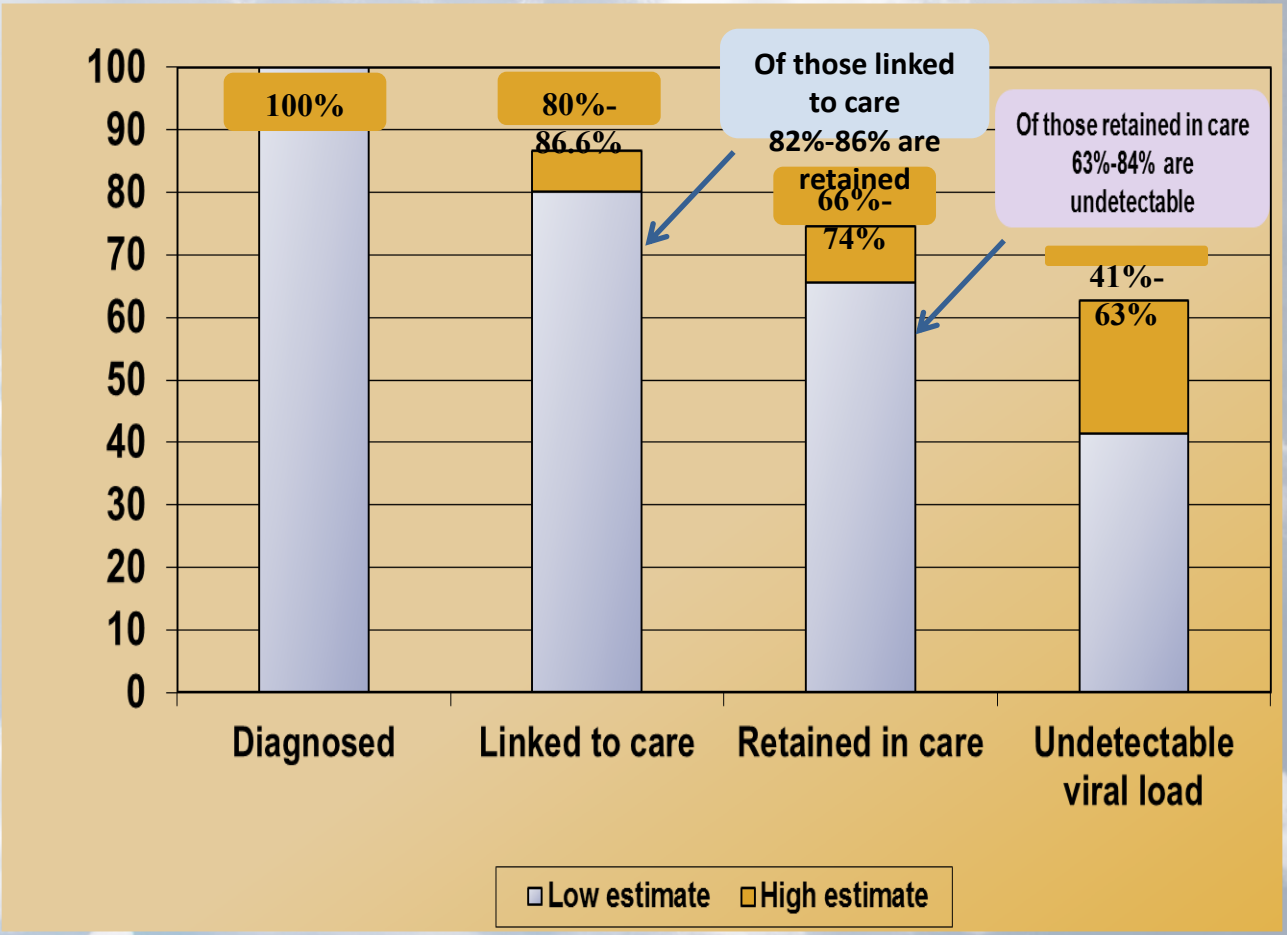


*HIV-1 RNA < 1000 copies/mL.

Levi J, et al. IAS 2015. Abstract MOAD0102. Reproduced with permission.

ONTARIO HIV TREATMENT NETWORK

Ontario HIV treatment cascade from those diagnosed

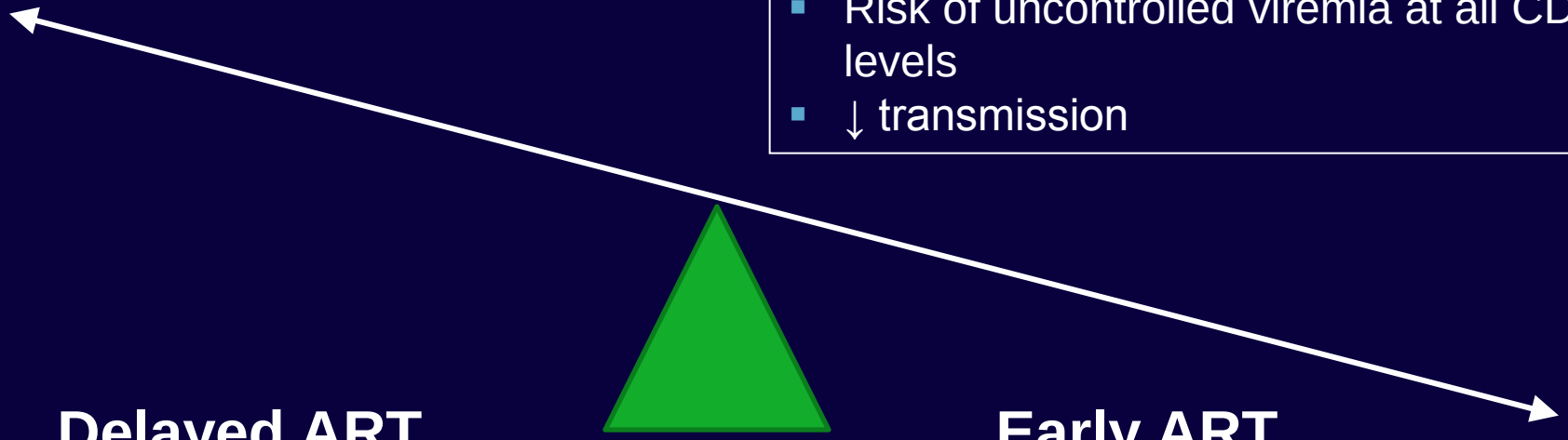


Source: personal communication, Ann Burchell & Sandra Gardner, July 15, 2014 based on reported data from PHAC, Robert Remis, and the OHTN Cohort Study. Note: Data is reported as current estimate, but lab data based on 2007/08, PHAC estimates from 2011, OCS from 2011 and Remis data from 2009, 2011, 2012.

When to Start Therapy: Balance Now Favors Early ART

- Drug toxicity
- Preservation of limited Rx options
- Risk of resistance (and transmission of resistant virus)

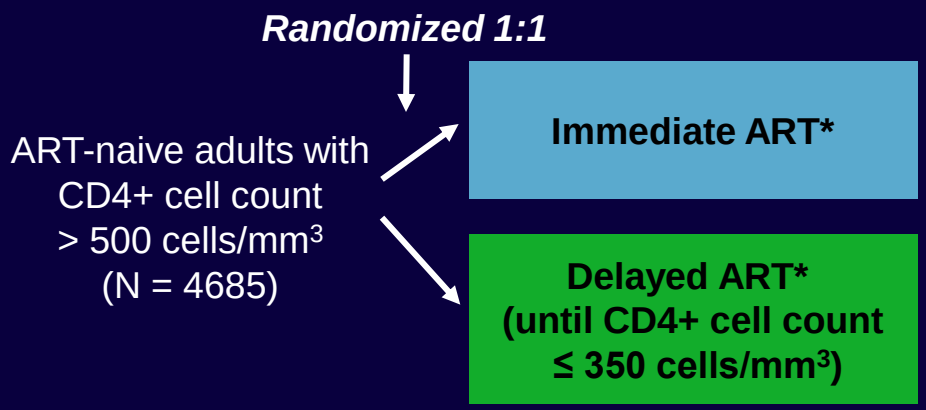
- ↑ potency, durability, simplicity, safety of current regimens
- ↓ emergence of resistance
- ↓ toxicity with earlier therapy
- ↑ subsequent treatment options
- Risk of uncontrolled viremia at all CD4 levels
- ↓ transmission



Delayed ART **Early ART**

START: Immediate vs Deferred ART

- International, randomized phase IV study
  - 215 sites in 35 countries



*Any licensed ART allowed, according to national guidelines.

- Study stopped by data and safety monitoring board following results of interim analysis
  - Risk of serious illness or death reduced by 53% with immediate ART
  - Rates of serious AIDS-related and non–AIDS-related events lower in immediate ART arm

ClinicalTrials.gov. NCT00867048. NIH Press Release, May 27, 2015.

Single Tablet Regimen (STR) Choices

DHHS Guidelines, April 2015: What to Start

Recommended Regimens	
INSTI based	DTG/ABC/3TC* DTG + TDF/FTC EVG/COBI/TDF/FTC† RAL + TDF/FTC
PI based	DRV/r + TDF/FTC

*Only for pts who are HLA-B*5701 negative. †Only for pts with pre-ART CrCl ≥ 70 mL/min.

- NNRTIs and ATV/r, previously classified as "recommended," are now "alternative regimens"

DHHS Guidelines. April 2015.

DHHS Guidelines, April 2015: What to Start

Alternative Regimens	
NNRTI based	EFV/TDF/FTC RPV/TDF/FTC*
PI based	ATV/COBI + TDF/FTC† ATV/r + TDF/FTC DRV/COBI + ABC/3TC‡ DRV/r + ABC/3TC‡ DRV/COBI + TDF/FTC†

*Only for pts with pre-ART HIV-1 RNA < 100,000 copies/mL and CD4+ > 200 cells mm^3.
†Only for pts with pre-ART CrCl ≥ 70 mL/min.
‡Only for pts who are HLA-B*5701 negative.

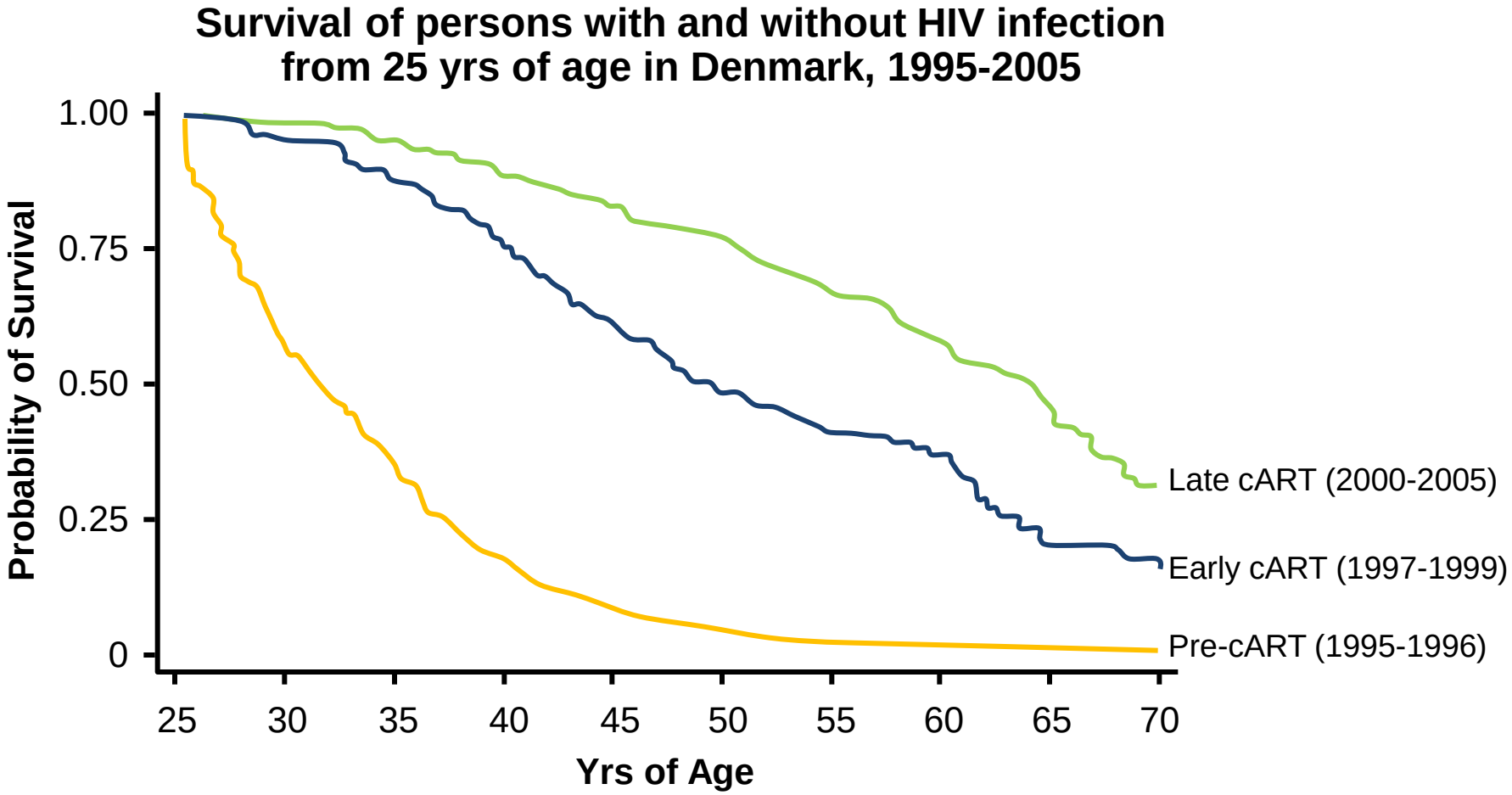
- An alternative regimen may be the preferred regimen for some pts

DHHS Guidelines. April 2015.

Comorbidities

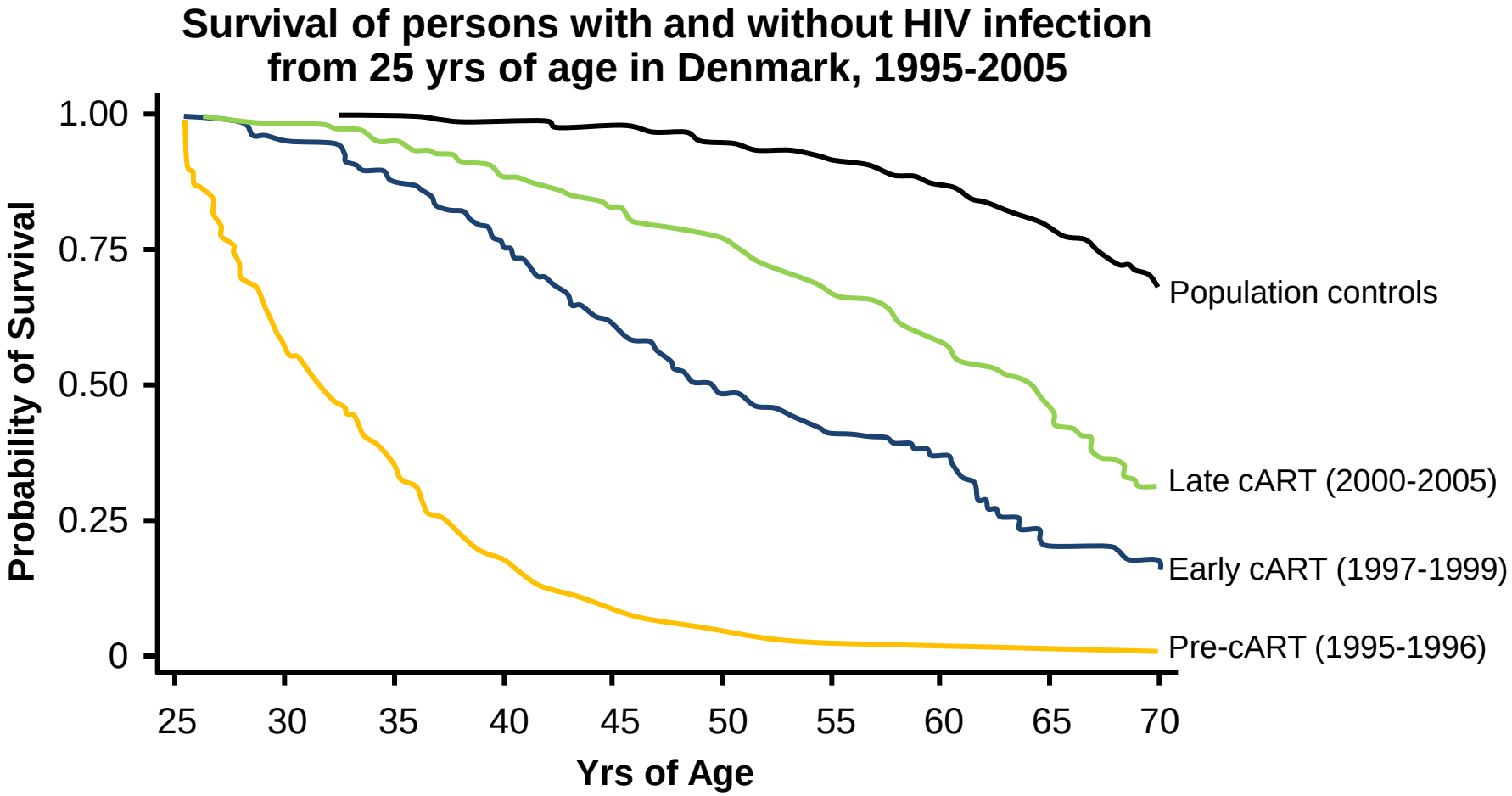
St. Michael's
Inspired Care. Inspiring Science.

Since Start of ART, Survival Rates Have Increased for People With HIV



Lohse N, et al. Ann Intern Med. 2007;146:87-95.

However, a Discrepancy Still Remains Compared With Uninfected Controls



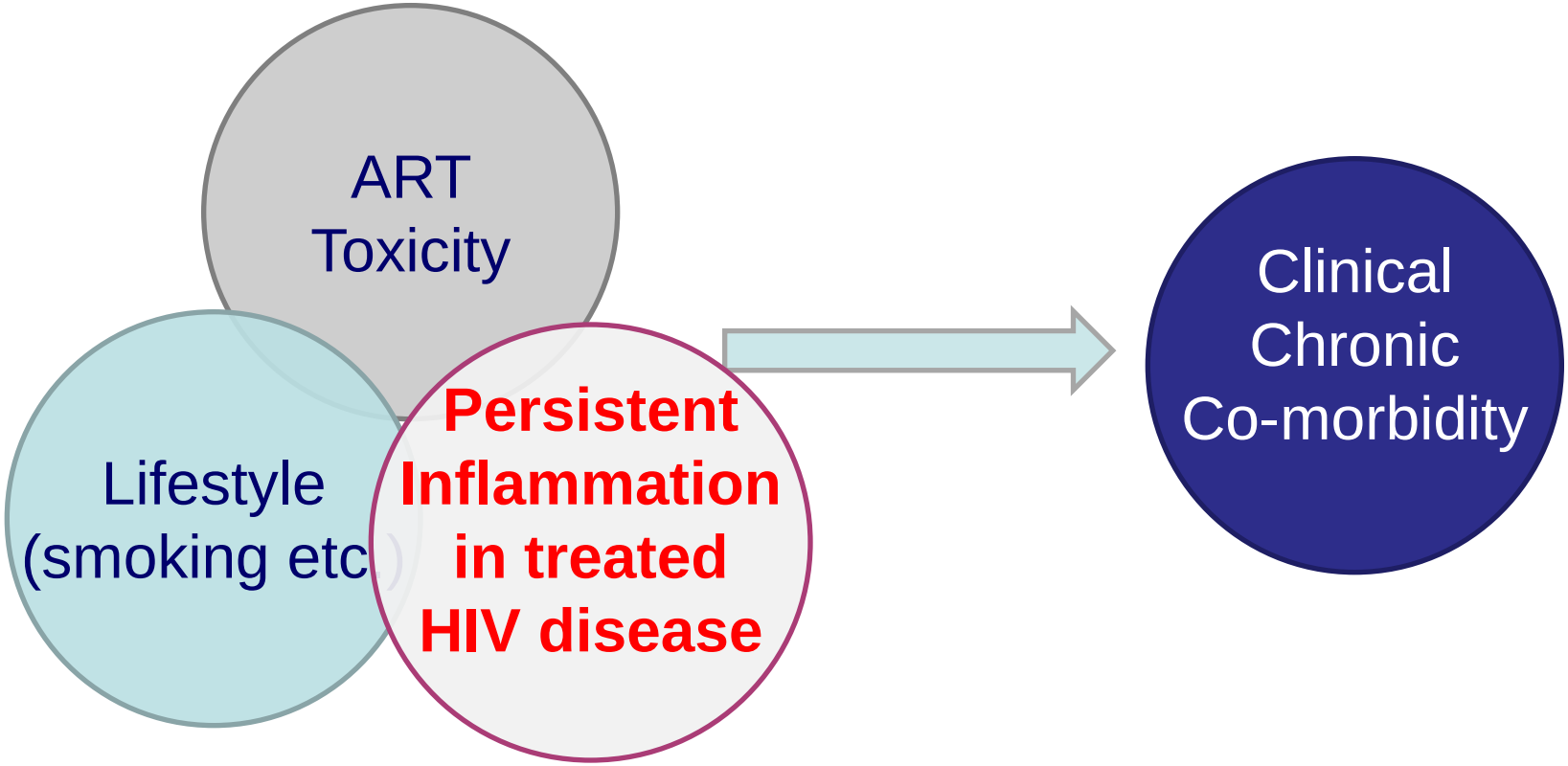
Lohse N, et al. Ann Intern Med. 2007;146:87-95.

HIV is now a chronic disease requiring treatment for many decades, which has raised a series of new problems

- Persistent inflammation/immune dysfunction
- Subtle but cumulative treatment toxicity
- Excess co-morbidity (non-AIDS events)
- Clinical aging
- Overburdened health care systems not designed or resourced to provide chronic care

Chronic disease drivers, known and suspected

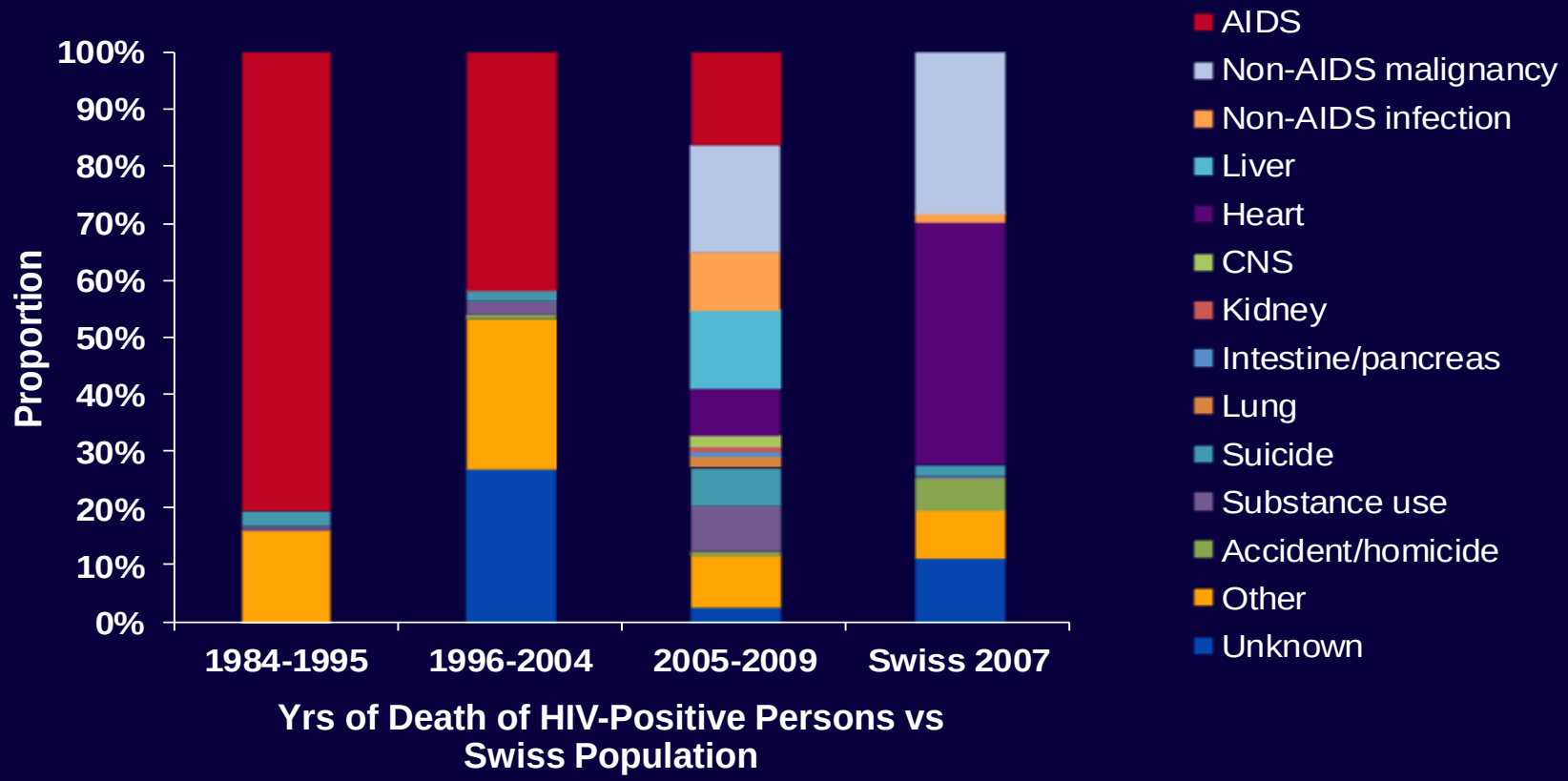
- Many chronic diseases of ageing are more common in those with HIV, even after adjustment for ART use and lifestyle factors



Deeks SG, *et al*. *BMJ* 2009; **338**:a3172

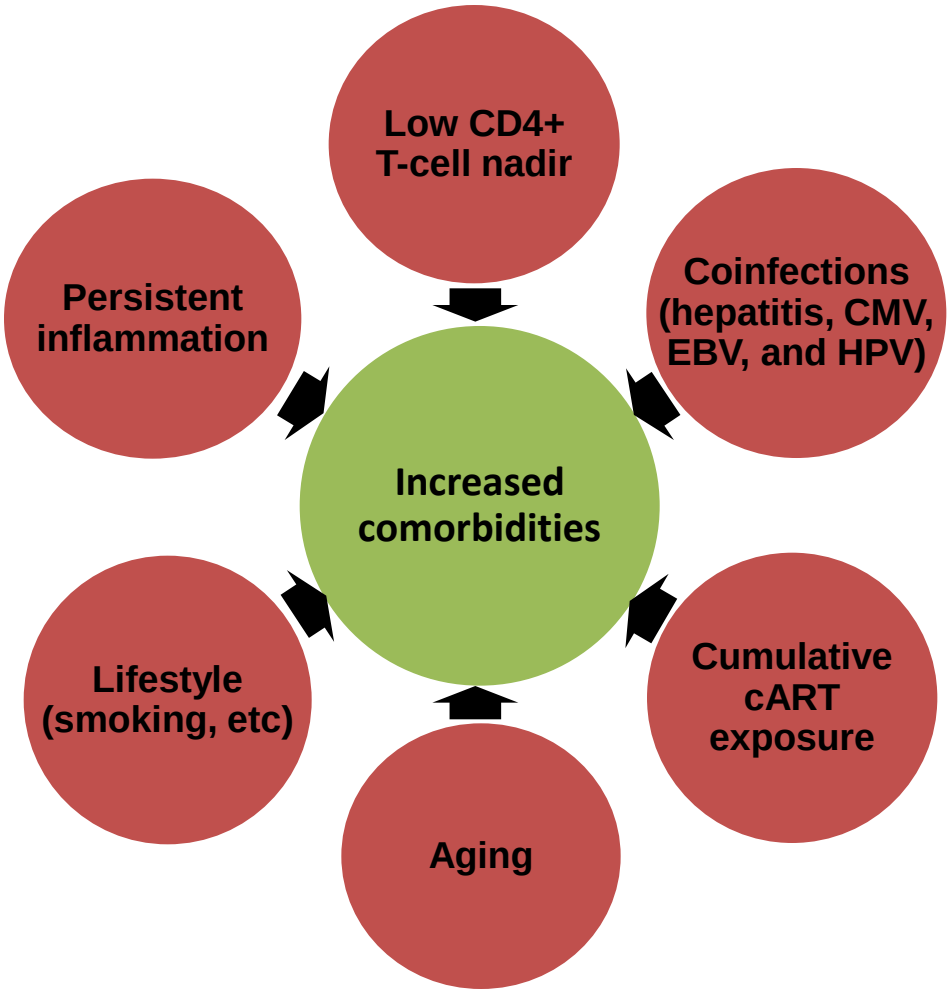
Changing Patterns of the Causes of Death in the Swiss HIV Cohort

Causes of Death in Participants in the Swiss HIV Cohort Study in 3 Different Time Periods, and in the Swiss Population in 2007



Weber R, et al. HIV Med. 2013;14:195-207.

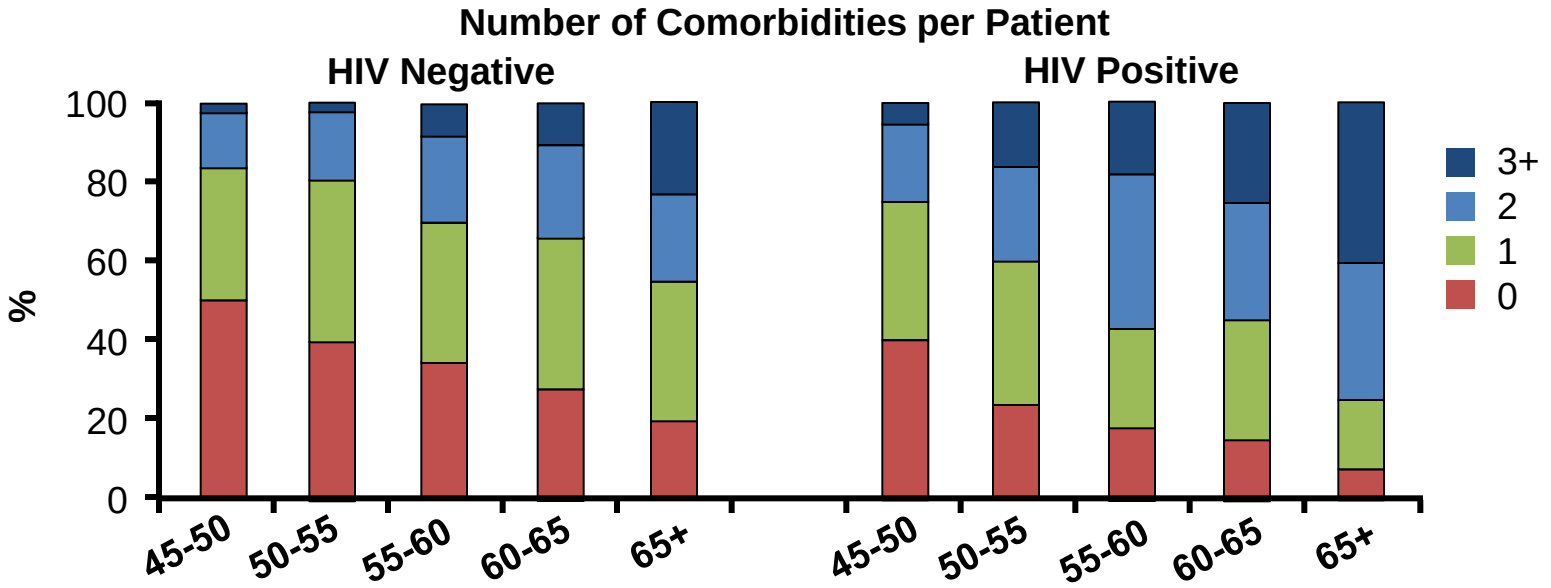
HIV Disease Contributes to Non-AIDS Events



Adapted from Deeks SG, et al. BMJ. 2009;338:a3172. Operskalski EA. Curr HIV/AIDS Rep. 2011;8:12-22.

HIV and Aging

- Cohort study of HIV and comorbidities in the Netherlands (N = 452 HIV-negative and 489 HIV-positive persons)
- Significantly more HTN, angina, MI, PVD, liver dx, CRF, and CA in HIV+



Mean Number of Age-Associated Noncommunicable Comorbidities

0.68	0.80	1.03	1.15	1.47	0.89	1.35	1.52	1.65	2.04

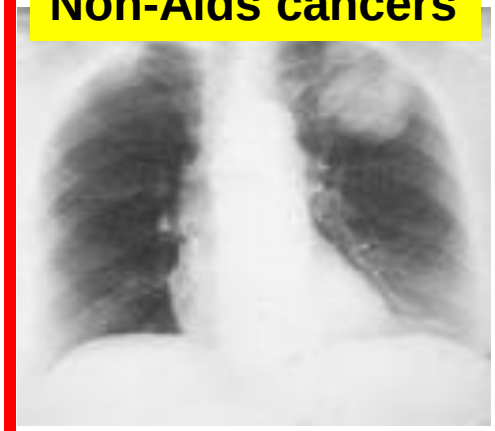
Number of Participants

166	108	70	53	34	159	111	86	62	52

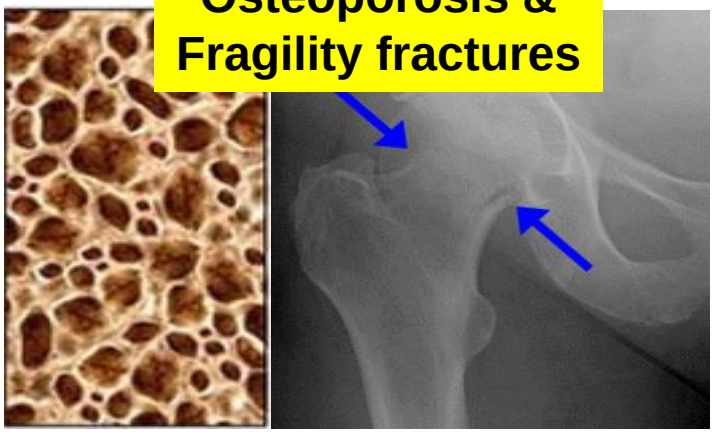
Schouten J, et al. AIDS 2012. Abstract THAB0205.

Cardiovascular disease

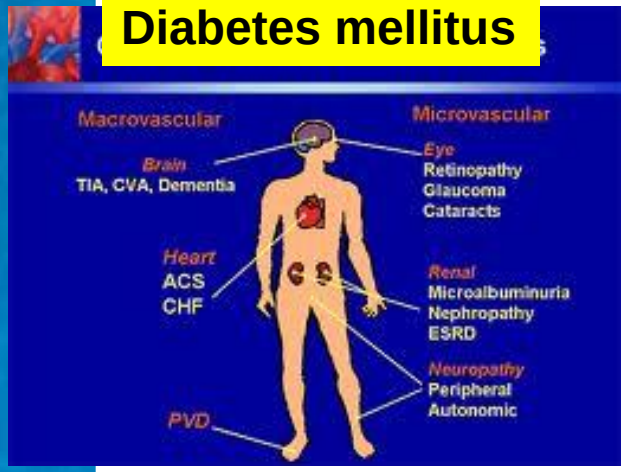
Non-Aids cancers



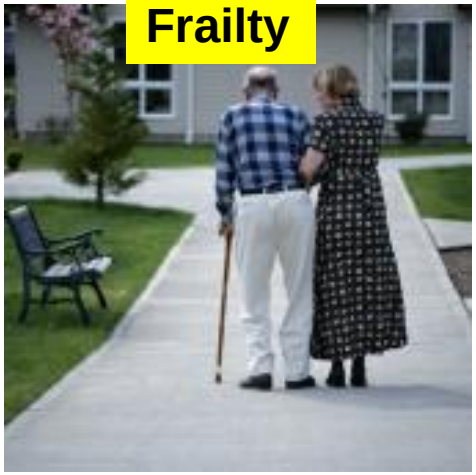
Osteoporosis & Fragility fractures



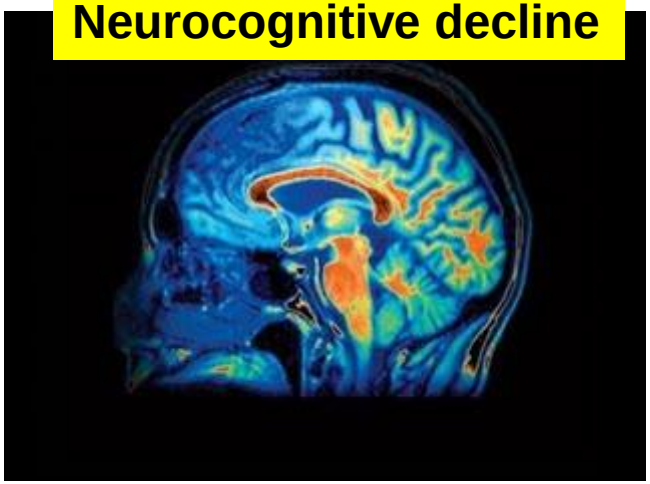
Diabetes mellitus



Frailty



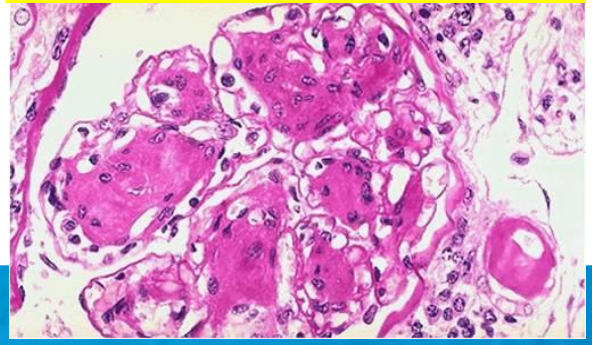
Neurocognitive decline



Chronic liver disease

Chronic obstructive pulmonary disease

Chronic kidney disease



My Patient

- 61 year old HIV + since 1989
- Has been on 15 different HIV meds
- Smoker
- Obese
- Osteoporosis
- Depression
- Hypertension
- Diabetes
- Heart attack-had stent
- Low testosterone, erectile dysfunction
- Claudication (pain in legs due to poor

Multiple Medications

- Aspirin
- Etravirine
- Darunavir
- Norvir
- Truvada
- Ramipril
- Norvasc
- Viagra
- Fosamax
- Lipitor
- Citalopram
- Metformin
- Januvia
- Metoprolol
- Wellbutrin
- Gabapentin
- Androgel

My patient

- Lives on own in unsafe apartment (bed bugs, noise, crack use)
- On ODSP
- Very little funds
- Bored, not working, lonely (partner died 2009)
- Feels Nobody really helping him

The Good News

- Has found clean, safe place in co-op
- Starting to volunteer at ACT, thinking of going back to school
- Has found new partner
- Joined gym, regular exercise regime
- Has quit smoking
- Naturopath
- Has lost 35 pounds
- Nutritionist-much healthier eating
- Cholesterol and Blood sugar more normal

Need for Teamwork

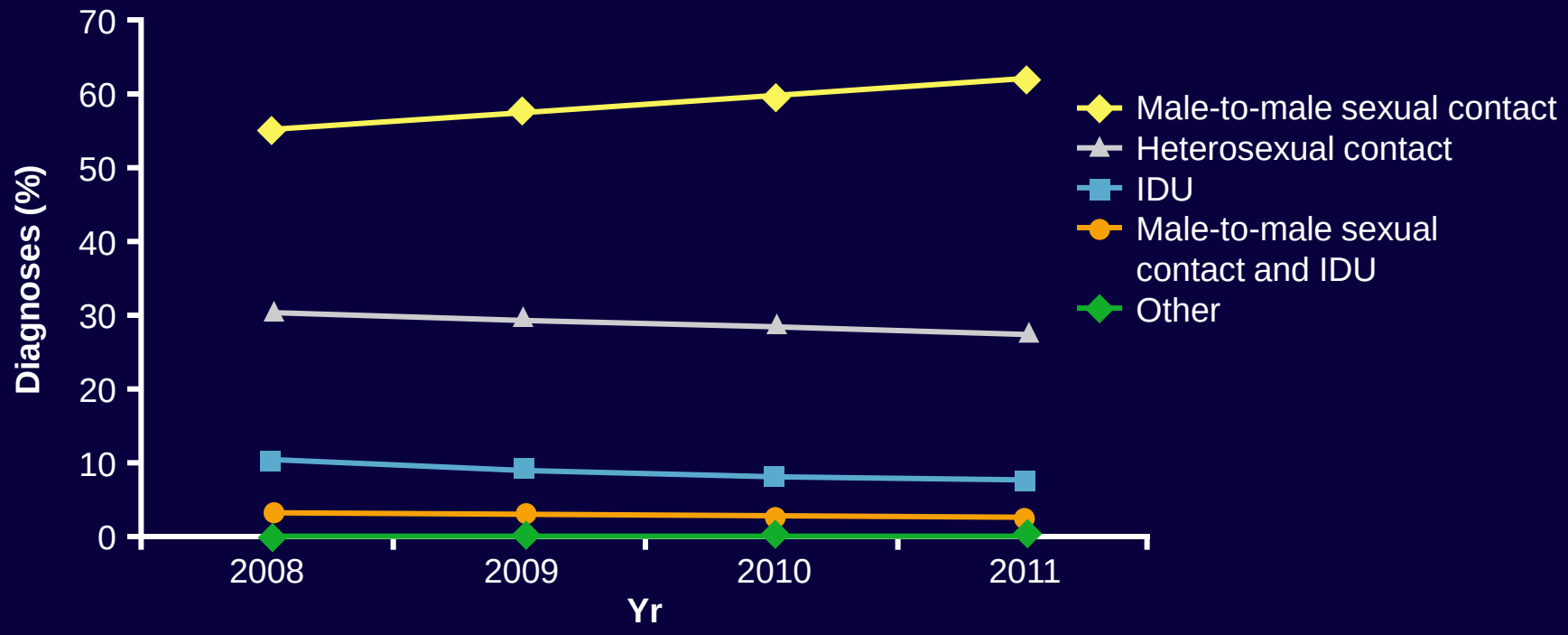
- A Holistic Doctor
- Nurse
- Dietician
- Social Worker
- Psychiatrist
- Addictions Counsellor
- Housing Worker
- Physiotherapist/OT
- Pharmacist
- Employment Counsellor
- ODSP Worker
- Geriatrics Team
- Various Specialists:
  - Cardiologist
  - Nephrologist
  - Endocrinologist

Prevention

St. Michael's
Inspired Care. Inspiring Science.

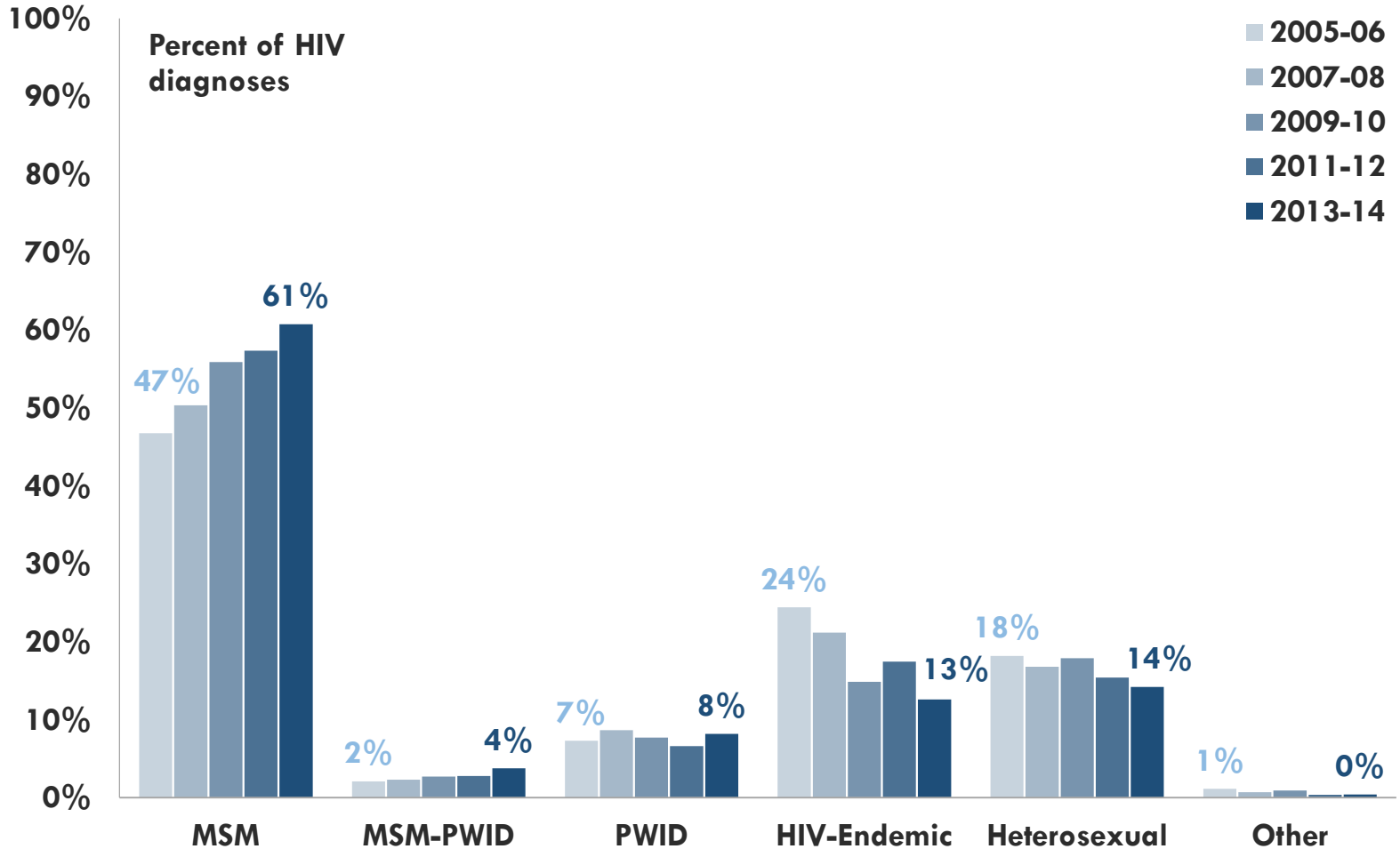
The Need for HIV Prevention: Continued HIV Risk in the US

- Estimated new HIV infections in the United States for the most affected subpopulations, 2008-2011



CDC. HIV in the United States: 2013.

HIV diagnoses by exposure category (where known), 2005-2014

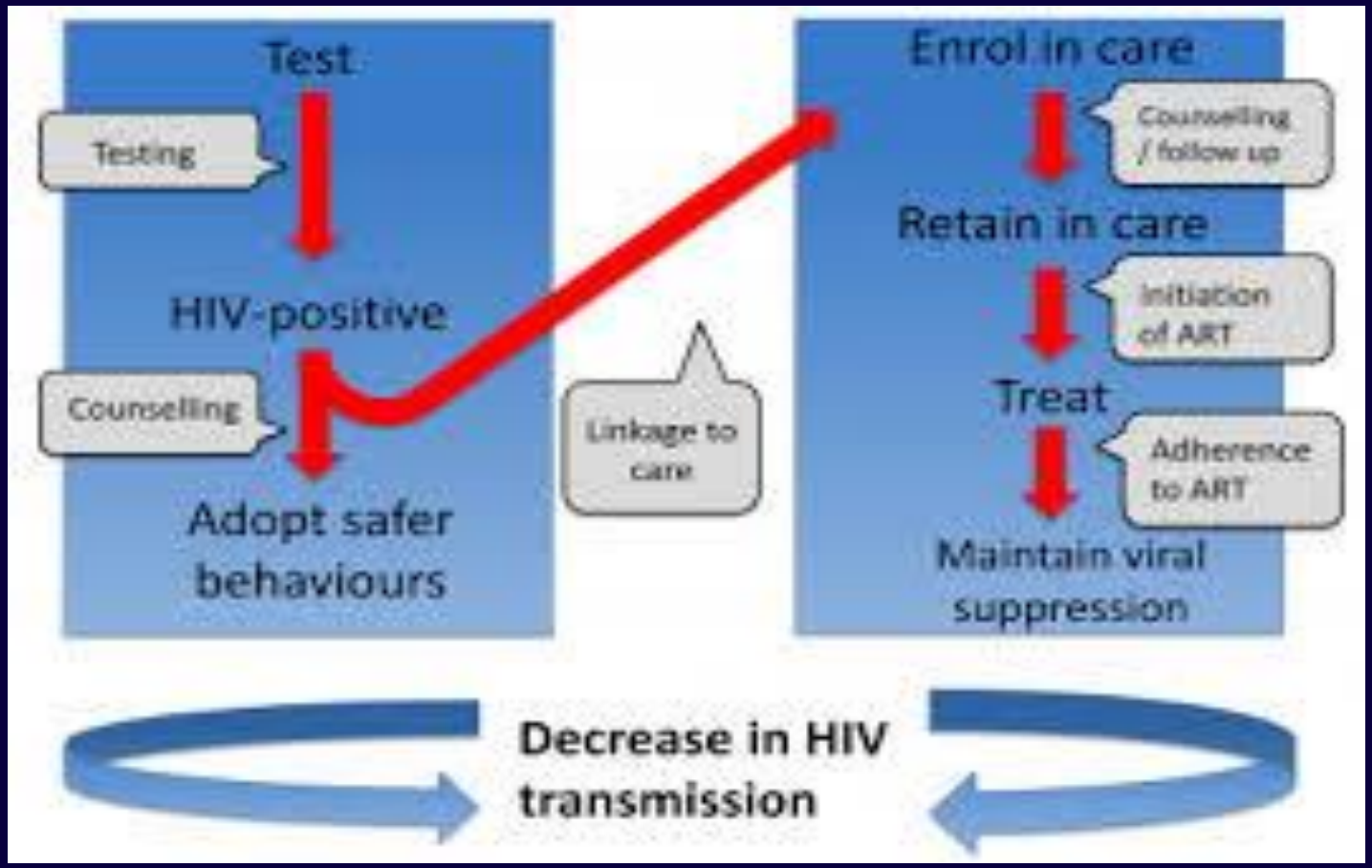


Data provided by Public Health Ontario Laboratory

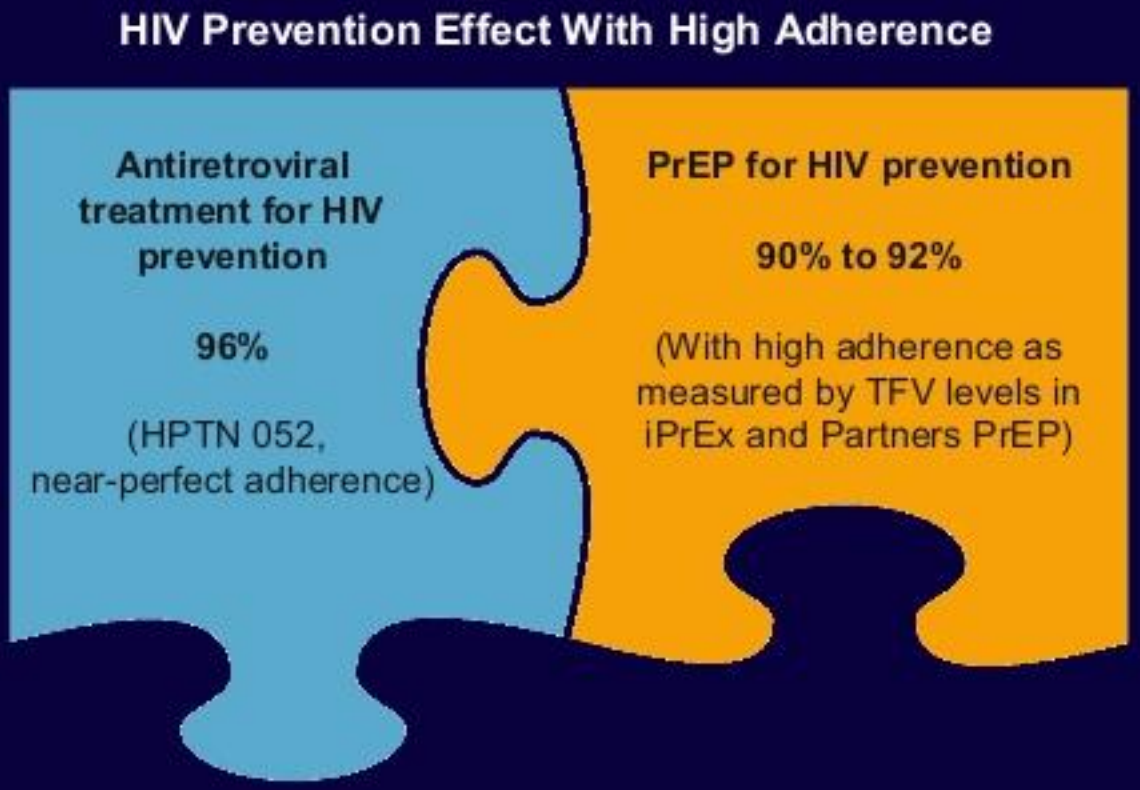
HIV Prevention: Toolbox for Success

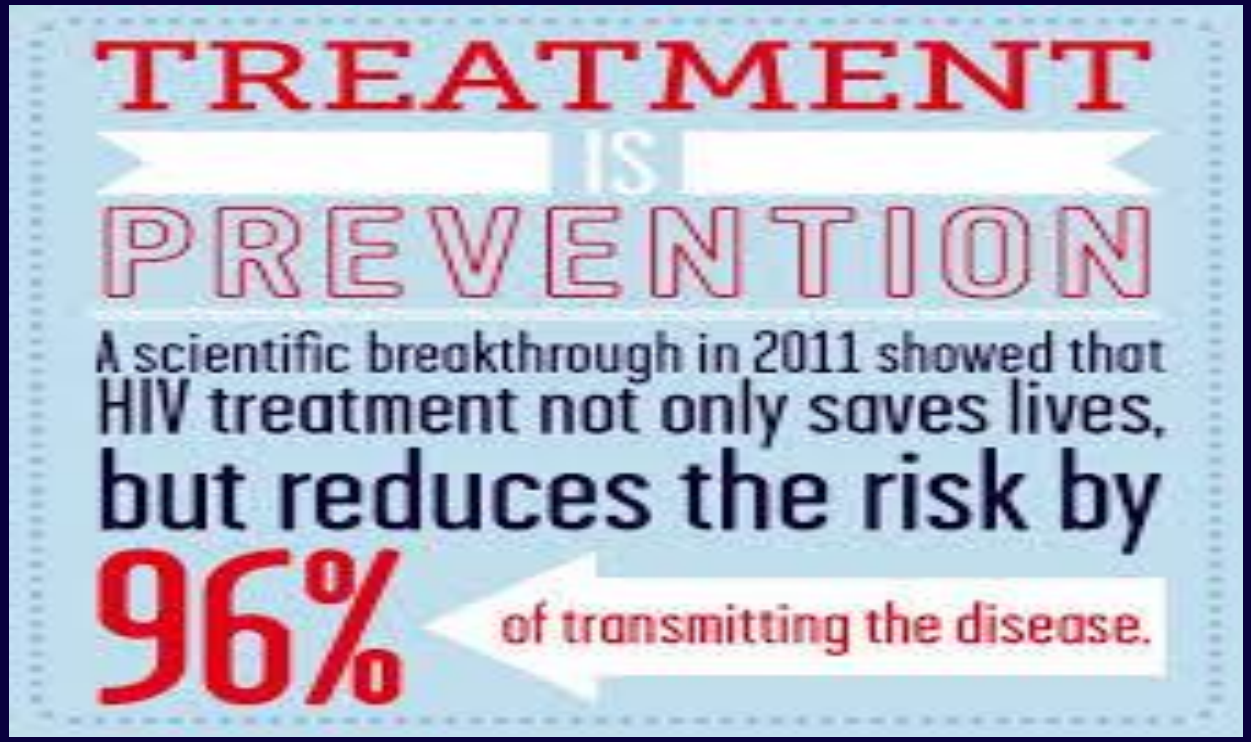
- Safer-sex counseling: understanding risk
- Condoms and lubricant
- Sterile syringes and avoiding sharing “works”
- HIV testing
- STI testing and treatment
- PEP (postexposure prophylaxis)
- PrEP (pre-exposure prophylaxis)

In November 2012, the U.S. Preventive Services Task Force recommended one-time HIV screening for all Americans aged 15 to 65


Test
Testing
HIV-positive
Counselling
Adopt safer behaviours
Linkage to care
Enrol in care
Counselling / follow up
Retain in care
Initiation of ART
Treat
Adherence to ART
Maintain viral suppression
Decrease in HIV transmission

Putting This Together




TREATMENT
IS
PREVENTION
A scientific breakthrough in 2011 showed that
HIV treatment not only saves lives,
but reduces the risk by
96%
of transmitting the disease.

What Is PrEP?

- For PrEP, an HIV-uninfected individual takes antiretroviral medication(s) ***before*** potential HIV exposure
- The idea of providing a medication as prophylaxis against an infectious disease is well established, eg:
  - Use of antimalarials before traveling to malarial zones
  - Use of antibiotics prior to dental procedures
- Oral contraceptives are also used prophylactically to prevent pregnancy

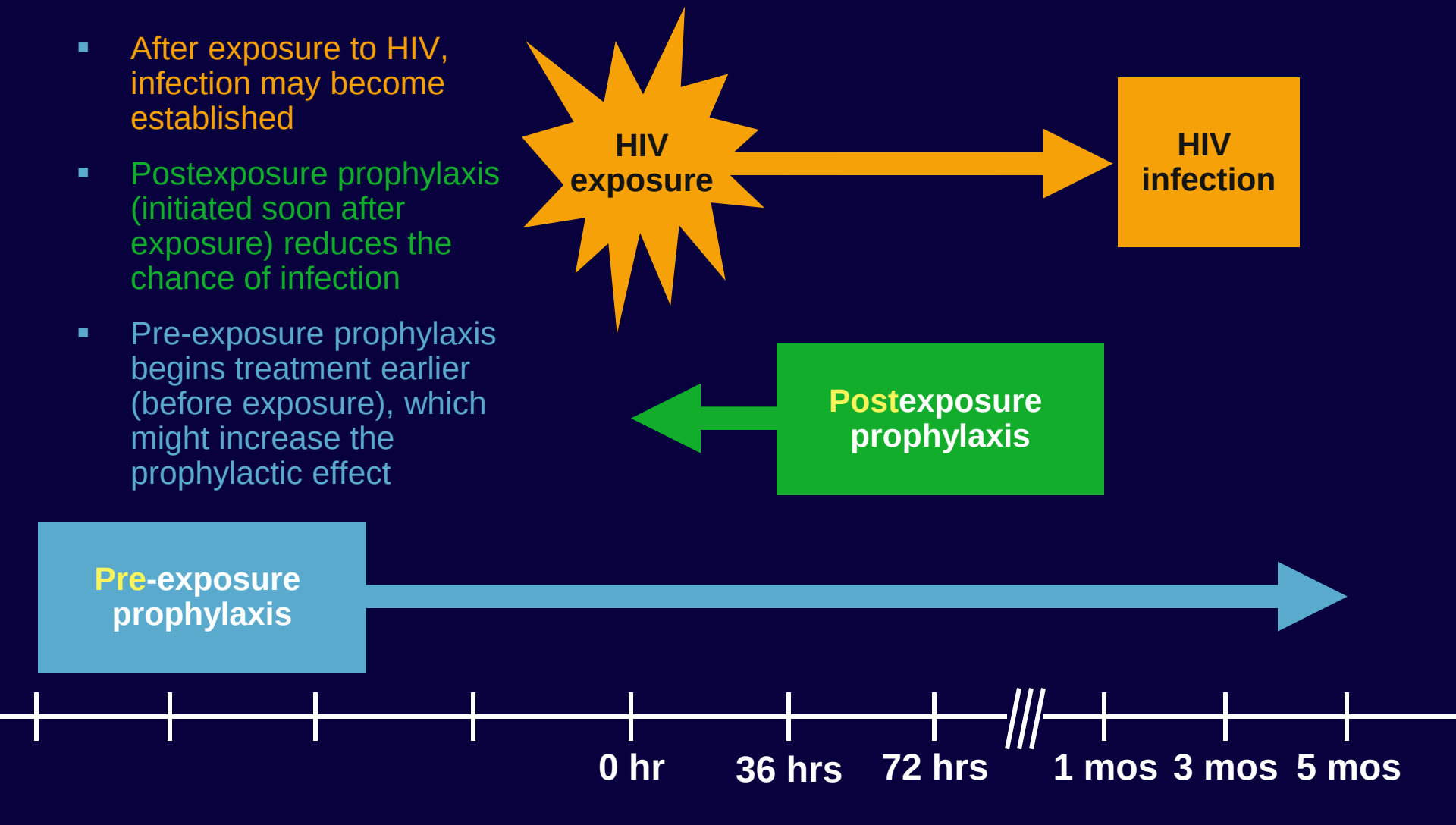
Antiretrovirals Used in HIV Prevention: The Foundation for PrEP

- Prevention of mother-to-child transmission
  - Antiretrovirals given to the mother during pregnancy, labor, and delivery and to the infant postpartum[1]
  - PMTCT has virtually eliminated perinatal HIV infection in the US and other developed countries
- Postexposure prophylaxis
  - Antiretrovirals given within hrs of a known or suspected HIV exposure (eg, needle stick injury, rape)
  - US public health guidance for PEP is available for both occupational[2] and nonoccupational[3] exposure to HIV

1. DHHS. Perinatal Guidelines. 2014. 2. Kuhar DT, et al. Infect Control Hosp Epidemiol. 2013;34:875-892. 3. MMWR. 2005;54(RR-2):1-20.

Pre- vs Postexposure Prophylaxis

- After exposure to HIV, infection may become established
- Postexposure prophylaxis (initiated soon after exposure) reduces the chance of infection
- Pre-exposure prophylaxis begins treatment earlier (before exposure), which might increase the prophylactic effect



PrEP Trials Have Shown Efficacy in MSM, Heterosexual Men and Women, and IDUs

Trial	Population/Setting	Intervention	HIV Infections, n		Reduction in HIV Infection Rate, % (95% CI)
			PrEP	Placebo	
iPrEX[1] (N = 2499)	MSM, transgender women, 11 sites in US, South America, Africa, Thailand	TDF/FTC	36	64	44 (15-63)
Partners PrEP[2] (N = 4747)	Serodiscordant couples in Africa	TDF	17	52	67 (44-81)
		TDF/FTC	13		75 (55-87)
TDF2[3] (N = 1219)	Heterosexual males and females in Botswana	TDF/FTC	9	24	62 (21-83)
Thai IDU[4] (N = 2413)	Volunteers from 17 drug Thai treatment centers	TDF	17	33	49 (10-72)

- 2 additional trials of PrEP (FEM-PrEP[5] and VOICE[6]), both conducted among high-risk African women, did not demonstrate protection against HIV; in both trials, PrEP adherence was very low

1. Grant RM, et al. N Engl J Med. 2010;363:2587-2599. 2. Baeten JM, et al. N Engl J Med. 2012;367:399-410. 3. Thigpen MC, et al. N Engl J Med. 2012;367:423-434. 4. Choopanya K, et al. Lancet. 2013;381:2083-2090. 5. Van Damme L, et al. N Engl J Med. 2012;367:411-422. 6. Marrazzo J, et al. CROI 2013. Abstract 26LB.

PrEP Works, but Adherence Is Critical

Study	Efficacy Overall, %	Blood Samples With TFV Detected, %	Efficacy By Blood Detection of TFV, %
iPrEx[1]	44	51	92
iPrEx OLE[2]	49	71	NR
Partners PrEP[3]	67 (TDF) 75 (TDF/FTC)	81	86 (TDF) 90 (TDF/FTC)
TDF2[4]	62	80	85
Thai IDU[5]	49	67	74
Fem-PrEP[6]	No efficacy	< 30	NR
VOICE[7]	No efficacy	< 30	NR

1. Grant RM, et al. N Engl J Med. 2010;363:2587-2599. 2. Grant RM, et al. Lancet Infect Dis. 2014; 14:820-829. 3. Baeten JM, et al. N Engl J Med. 2012;367:399-410. 4. Thigpen MC, et al. N Engl J Med. 2012;367:423-434. 5. Choopanya K, et al. Lancet. 2013;381:2083-2090. 6. Van Damme L, et al. N Engl J Med. 2012;367:411-422. 7. Marrazzo J, et al. CROI 2013. Abstract 26LB.

PrEP in Clinical Practice: What Are the Barriers to PrEP Uptake?

- Users
  - Unaware of HIV risk, PrEP availability, or how to access it
  - No or delayed access to clinical preventive care
  - Uninsured or unable to pay
  - Adherence challenges
  - Concern about disclosure and stigma
- Providers
  - Unaware of intervention
  - Uncertain how to deliver the intervention
  - Wary of complexity and time involved
  - Discomfort with assessing candidacy
  - Uncertain how to bill for intervention

CDC PrEP Guideline: For Which Patients Is PrEP Recommended?

- PrEP is recommended as one prevention option for the following adults at substantial risk of HIV acquisition
  - Sexually active MSM
  - Heterosexually active men and women
  - Injection drug users

	MSM	Heterosexual Women and Men	Injection Drug Users
Potential indicators of substantial risk of acquiring HIV infection	▪ HIV-positive sexual partner ▪ Recent bacterial STI ▪ High number of sex partners ▪ History of inconsistent or no condom use ▪ Commercial sex work	▪ HIV-positive sexual partner ▪ Recent bacterial STI ▪ High number of sex partners ▪ History of inconsistent or no condom use ▪ Commercial sex work ▪ In high-prevalence area or network	▪ HIV-positive injecting partner ▪ Sharing injection equipment ▪ Recent drug treatment (but currently injecting)

CDC. PrEP Guideline. 2014.

Thank You!