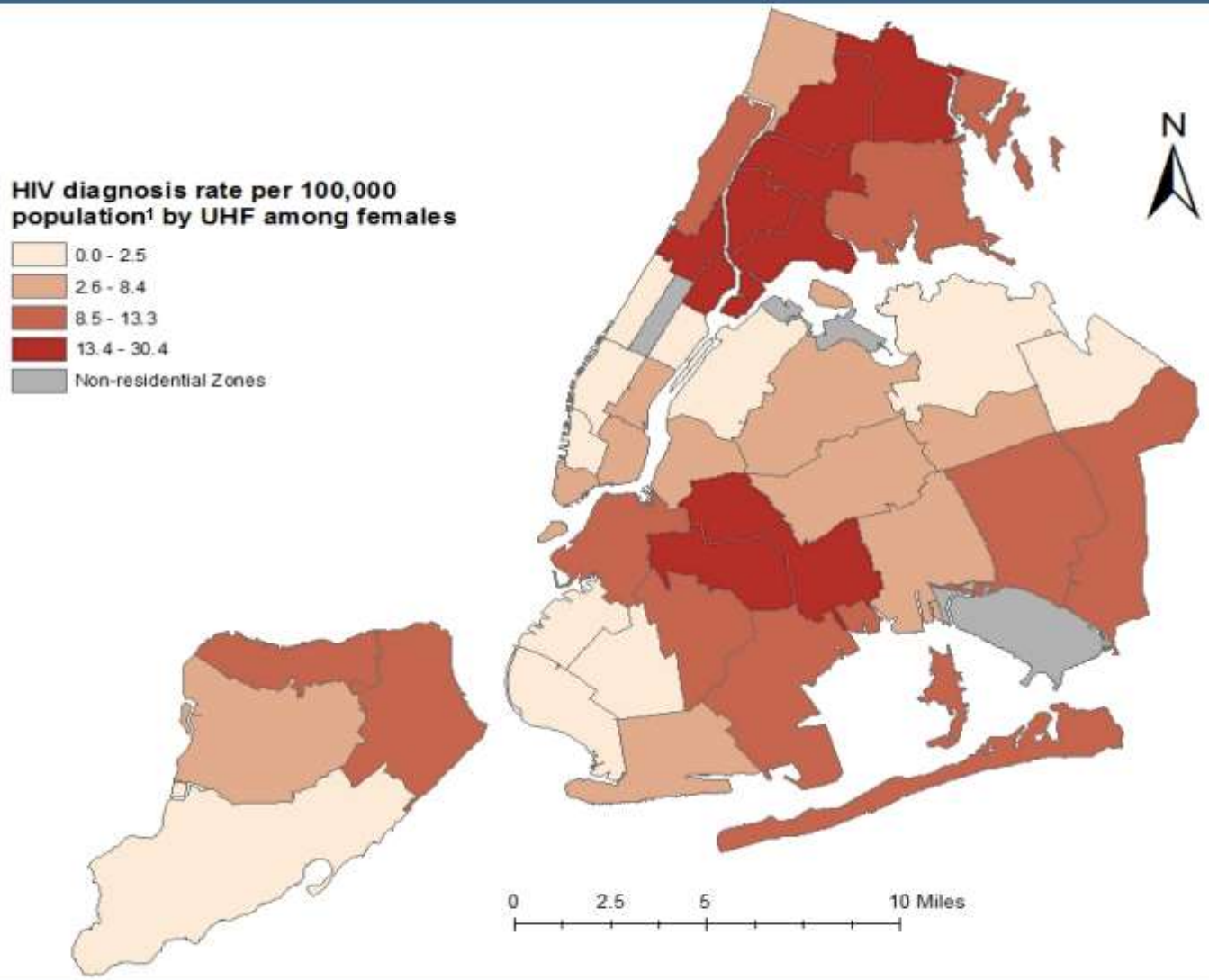
On Beyond Condoms: PreExposure Prophylaxis for Women

Maria Teresa Timoney CNM

Bronx Lebanon Hospital Center

June 8, 2017

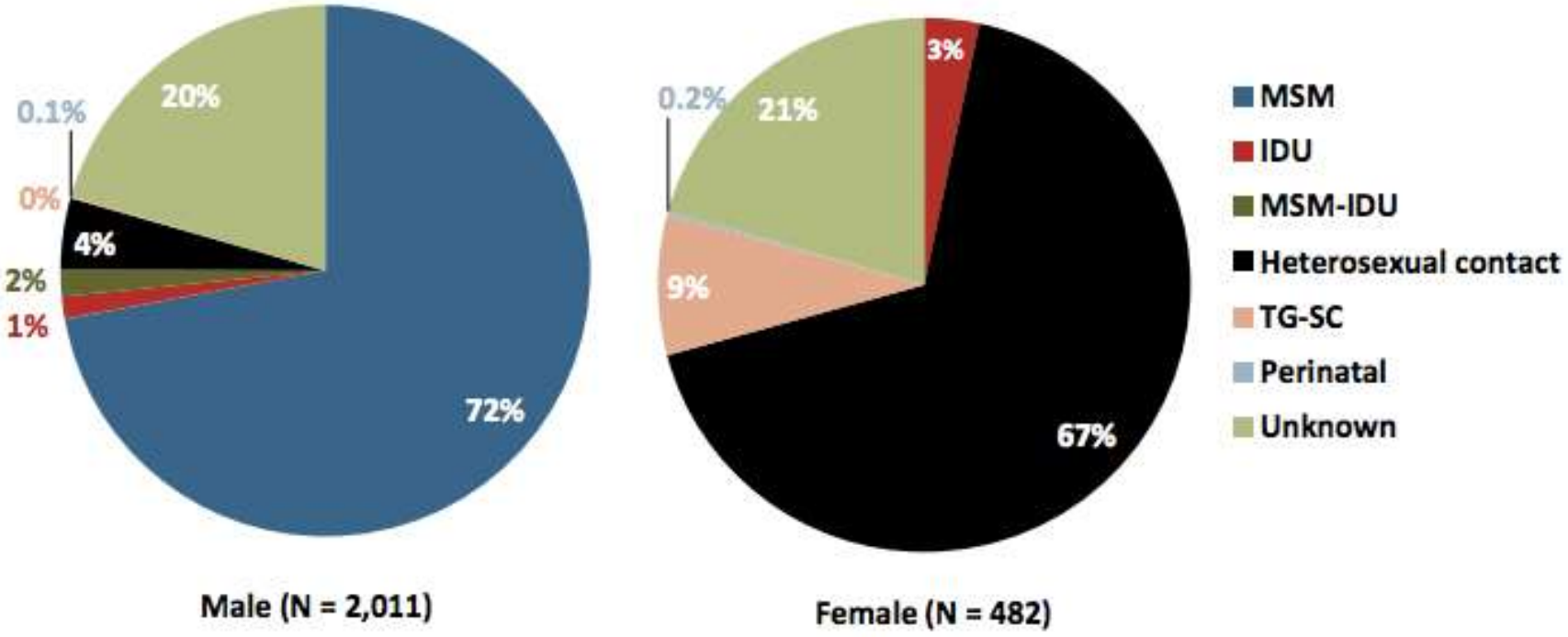
HIV DIAGNOSIS RATE BY UHF AMONG FEMALES IN NYC, 2015



Rates of new HIV diagnoses among females were highest in Hunts Point-Mott Haven, East New York, and Crotona-Tremont.

[1]Rates calculated using the intercensal 2015 NYC population.
Female includes transgender women.
As reported to the New York City Department of Health and Mental Hygiene by June 30, 2016.

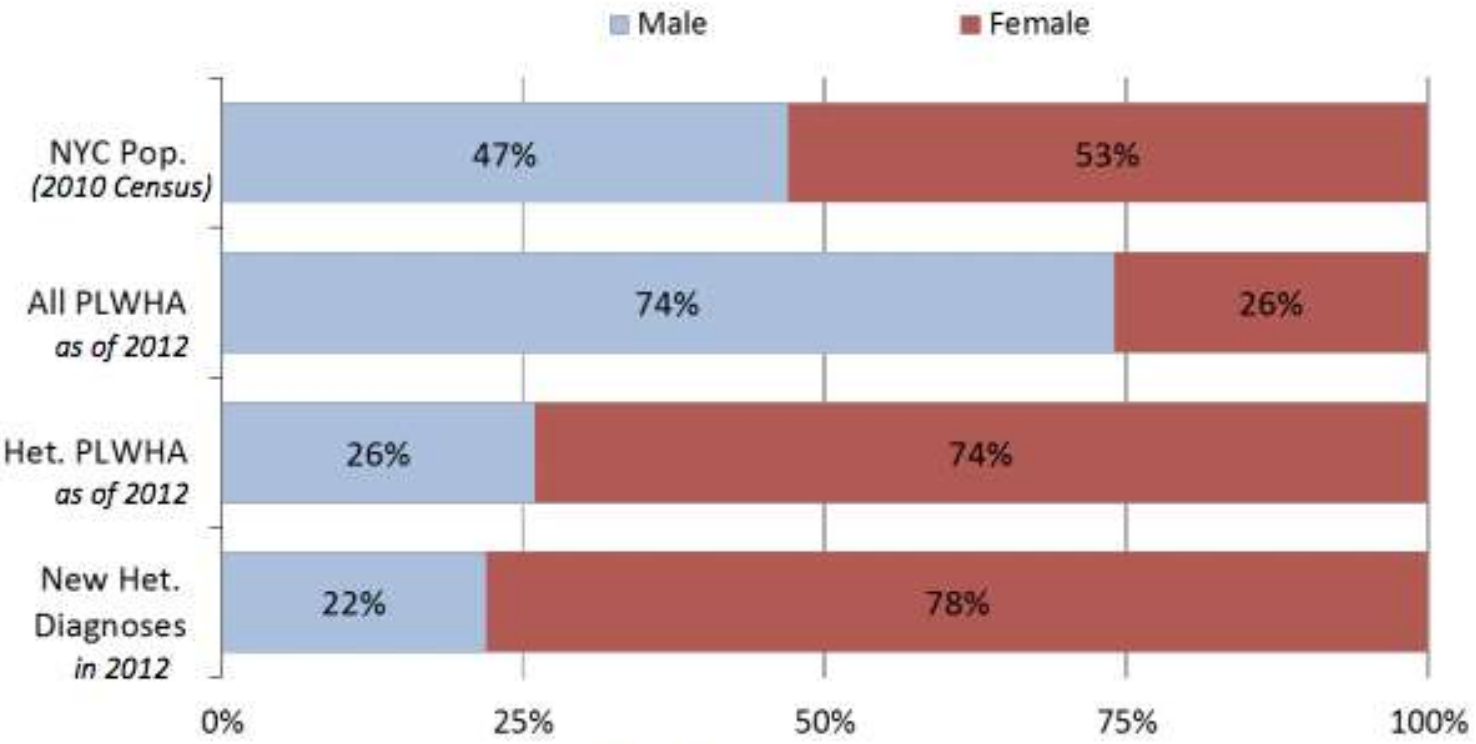
NEW HIV DIAGNOSES BY TRANSMISSION RISK AND GENDER IN NYC, 2015



MSM and those with heterosexual contact risk accounted for the majority of new HIV diagnoses among males and females, respectively, in NYC in 2015.

Female includes transgender women and male includes transgender men.
As reported to the New York City Department of Health and Mental Hygiene by June 30, 2016.

Gender Disparities in Heterosexual HIV Transmission in New York City

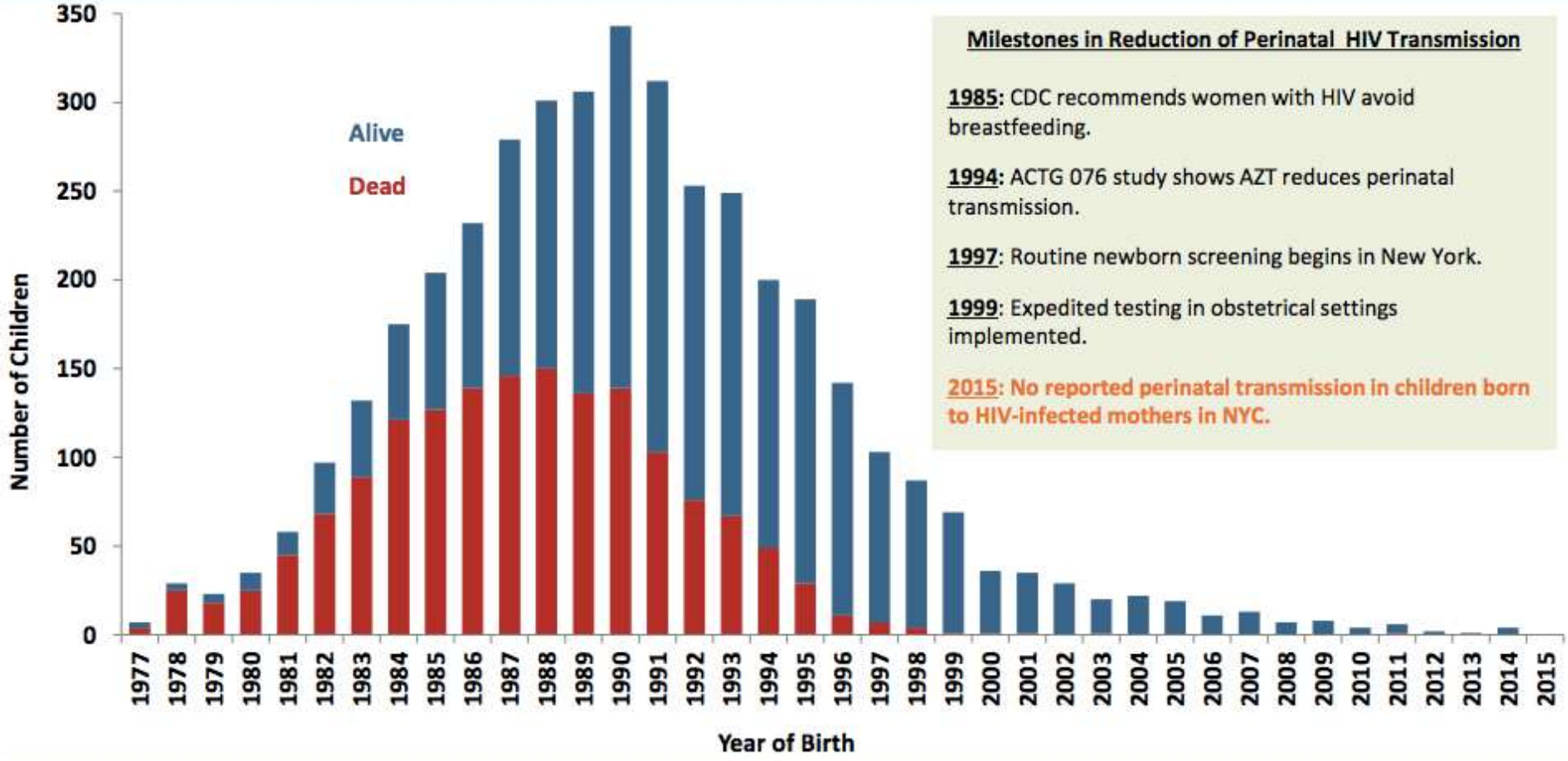


Heterosexual PLWHA and new heterosexual diagnoses are disproportionately female

NYC Health

JOHN JAY COLLEGE OF CRIMINAL JUSTICE

PERINATALLY HIV-INFECTED CHILDREN (N=4,042), BY YEAR OF BIRTH AND VITAL STATUS IN NYC, 1977-2015



Milestones in Reduction of Perinatal HIV Transmission

1985: CDC recommends women with HIV avoid breastfeeding.

1994: ACTG 076 study shows AZT reduces perinatal transmission.

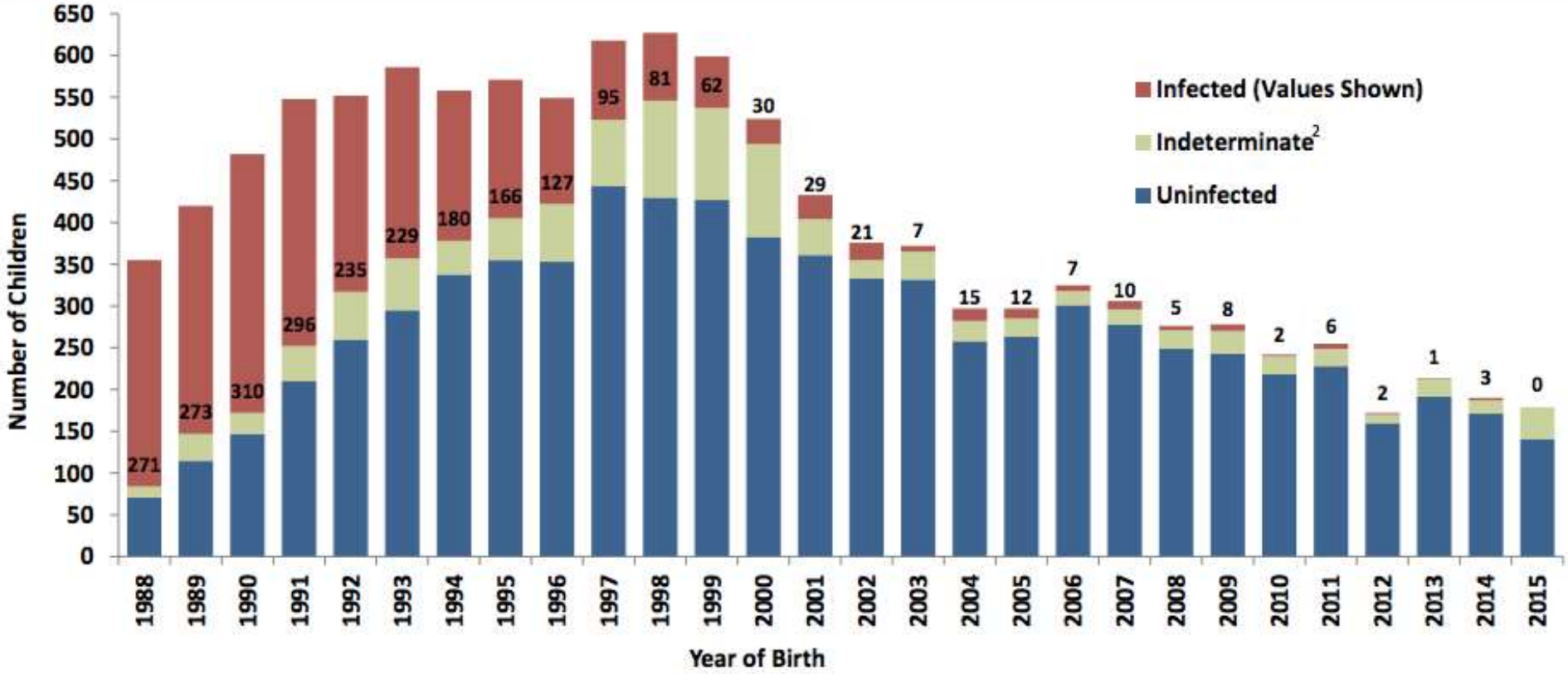
1997: Routine newborn screening begins in New York.

1999: Expedited testing in obstetrical settings implemented.

2015: No reported perinatal transmission in children born to HIV-infected mothers in NYC.

The number of HIV-infected infants born to HIV-infected mothers in NYC each year decreased dramatically from the peak in 1990. This decline followed the introduction of intensive perinatal prevention programs in NYC. During 2009-2014, there were 24 perinatally-infected infants born in NYC. In 2015, there were no reported infections among children born in NYC.

CURRENT HIV STATUS OF CHILDREN BORN TO HIV-INFECTED WOMEN AT SELECT NYC MEDICAL FACILITIES[1], BY YEAR OF BIRTH IN NYC, 1988-2015



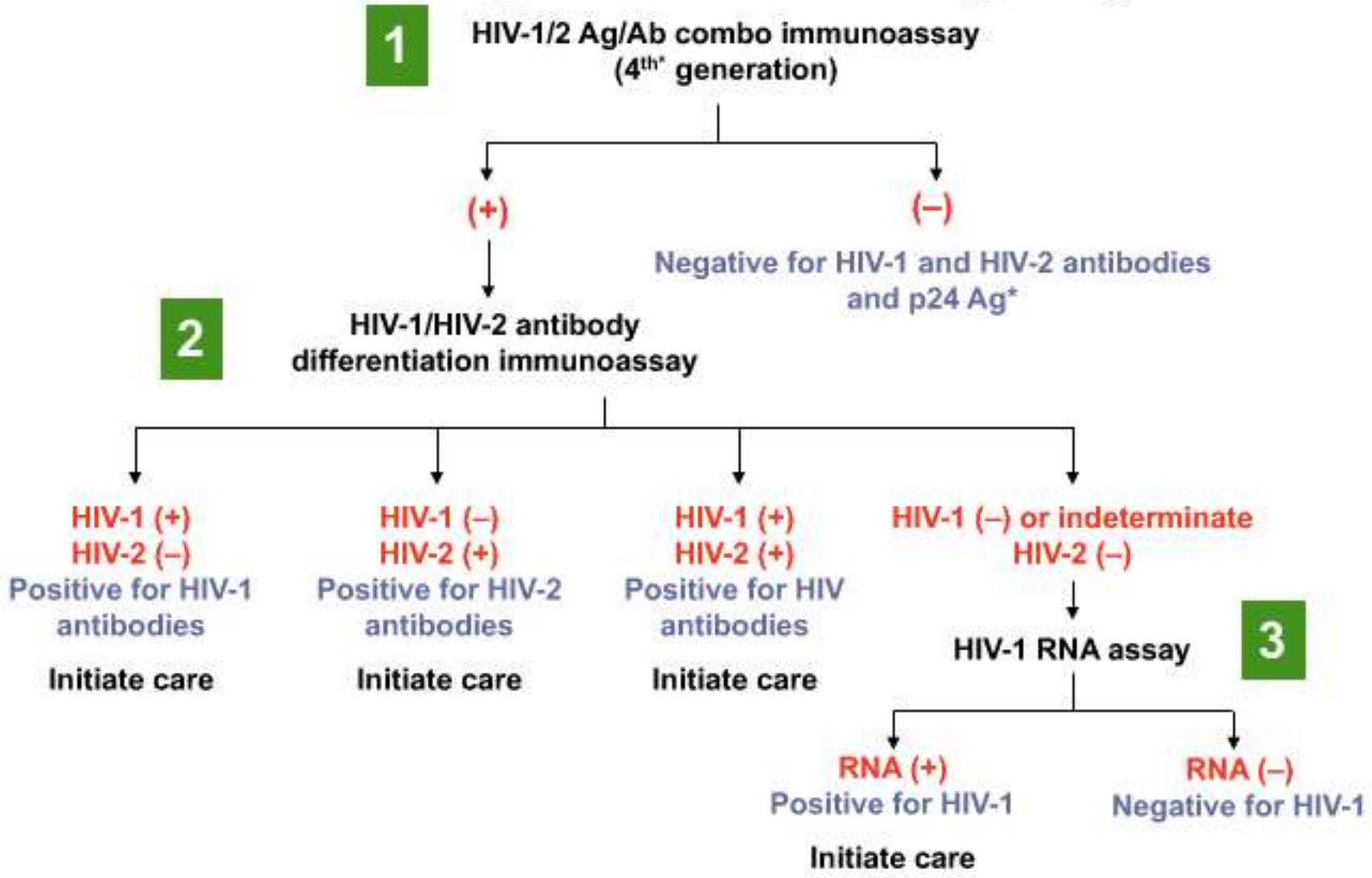
In 2015, for the first time since the epidemic began, there were no reported mother to child HIV transmissions among children born in NYC, reflecting the success of interventions to prevent perinatal HIV infection.

[1]Includes data collected at high-volume NYC medical facilities that care for the majority of HIV-exposed and infected children. Children born outside of NYC are not included in this figure.

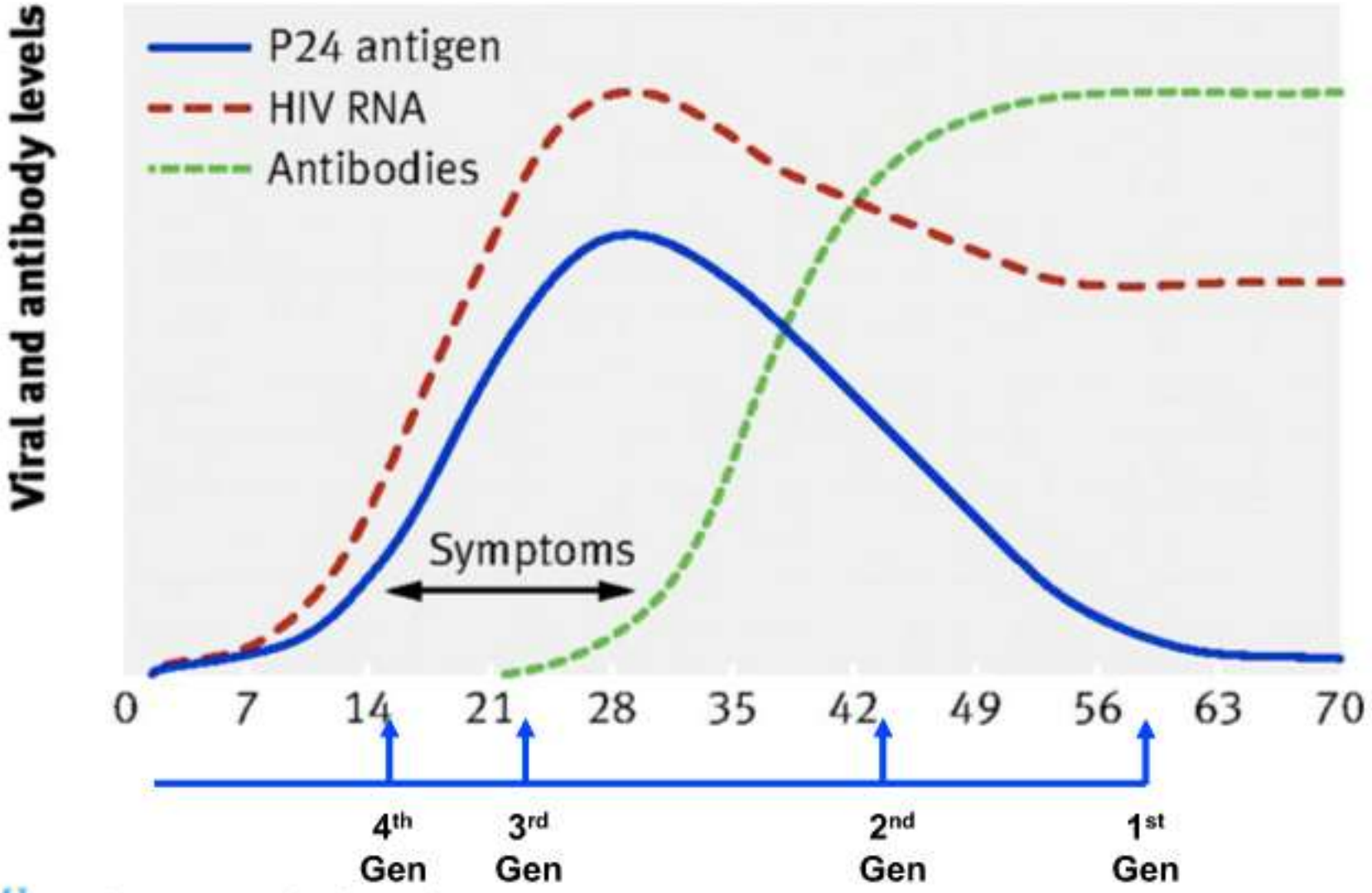
[2]Children born to HIV-infected mothers are followed for 2 years after birth to determine HIV status. HIV status is indeterminate if child is lost to follow-up.

As reported to the New York City Department of Health and Mental Hygiene by June 30, 2016

New HIV Diagnostic Testing Algorithm



Reduction of Window Period



BMJ Das G et al. BMJ 2010;341:bmj.c4583

E.B.

- 16 yo G1P0 39 6/7 admitted to L&D in active labor on 6/28/12
    - Complete PNC at Tremont
    - HIV negative at initial prenatal visit
    - HIV negative on 5/14/12
    - NSVD live baby boy, breastfed
- Alert from NYS DOH Newborn Screening of positive on 7/9/12
    - Mother and baby brought to Peds ID
    - FOB perinatally infected, off HAART
    - Stop Breastfeeding
    - AZT/NVP as post exposure prophylaxis for BF
- Baby boy HIV negative

Seroconversion in Pregnancy

Acquisition and transmission of HIV by women is higher during pregnancy

Studies of acute infection during pregnancy in the US include:

Birkhead et al (2010)[2] reported 13.8% (9/65) in New York City of perinatal infections occurred in maternal primary infection

Patterson et al (2007)[3] reported 50% (3/6) in North Carolina of perinatal infections occurred in maternal primary infection

Acute infection during pregnancy can lead to higher MCT due to increased viral load during acute infection[4]

[1]Mugo NR et al. AIDS 2011;25:1887-1895.

[2]Birkhead GS et al. Obstet Gynecol 2010;115:1247-55.

[3]Patterson KB et al. AIDS 2007;21:2303-2308.

[4]Marinda ET et al. Int J Epid 2011;40:945-954.

HIV Seroconversions During Pregnancy and Prior-to-Pregnancy, EPS, 2005-2010

	2005 N (%)	2006 N (%)	2007 N (%)	2008 N (%)	2009 N (%)	2010 N (%)	2005-2010 N (%)
All Pregnancies	**2,064**	**1,975**	**1,814**	**1,720**	**1,543**	**1,192**	**10,308**
During Pregnancy	8 (0.4)	26 (1.3)	14 (0.8)	28 (1.6)	26 (1.7)	22 (1.9)	124 (1.2)*
Prior-to-Pregnancy	1,470 (71.2)	1,381(69.9)	1,283 (70.7)	1,204 (70.0)	1,061 (68.8)	836 (70.1)	7,235 (70.2)
Unclassifiable	586 (28.4)	568 (28.8)	517 (28.5)	488 (28.4)	456 (29.6)	334 (28.0)	2,949 (28.6)

*Estimated Annual Percent Change p<0.0001)

Perinatal HIV Transmission Among DP and PTP Seroconverting Women, EPS, 2005-2010

	2005 N (%)	2006 N (%)	2007 N (%)	2008 N (%)	2009 N (%)	2010 N (%)	2005-2010 N (%)
Perinatal HIV Transmission Among All Deliveries	56 (2.7)	35 (1.8)	42 (2.3)	29 (1.7)	26 (1.7)	22 (1.9)	210 (2.0)
Perinatal HIV Transmission Among DP Seroconverters	2 (25.0)	3 (11.5)	2 (14.3)	3 (10.7)	2 (7.7)	4 (18.2)	16 (12.9)
Perinatal HIV Transmission Among PTP Seroconverters	32 (2.2)	22 (1.6)	21 (1.6)	17 (1.4)	14 (1.3)	12 (1.4)	118 (1.6)

Rationale for PrEP during preconception, pregnancy & lactation

- Pregnancy is associated with ~2X increased risk of HIV acquisition
- Acute HIV during pregnancy associated with ~8X increased risk of perinatal transmission
- Acute HIV during breastfeeding associated with ~4X increased risk of neonatal transmission

Mugo AIDS 2011; Drake PLoS Med 2014; Humphrey BMJ 2010; Singh CROI 2013.

PrEP Studies:

HIV transmission risk lowest when participants took PrEP consistently

STUDY	**OVERALL** Reduction in risk of HIV infection	**Detectable level of medication in the blood** Reduction in risk of HIV infection
iPrEx	44%	>90%
TDF2	62%	---
Partners PrEP	75%	90%
BTS	49%	74%

Adapted from summary of research at http://www.cdc.gov/hiv/prevention/research/prep/

PROUD

- An open-label randomized trial done at 13 sexual health clinics in England
- 544 HIV -negative gay and other men who have sex with men who had had anal intercourse without a condom in the previous 90 days.
- Participants were randomly assigned (1:1) to receive daily combined tenofovir disoproxil fumarate (245 mg) and emtricitabine (200 mg) either immediately or after a deferral period of 1 year
- 3 HIV infections occurred in the immediate group (1·2/100 person-years) versus 20 in the deferred group (9·0/100 person-years) despite 174 prescriptions of post-exposure prophylaxis in the deferred group
- Based on early evidence of effectiveness, the trial steering committee recommended on Oct 13, 2014, that all deferred participants be offered PrEP.

Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial
McCormack, Sheena et al.
The Lancet , Volume 387 , Issue 10013 , 53 - 60

US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES - 2014

A CLINICAL PRACTICE GUIDELINE

Daily oral PrEP with TDF/FTC is recommended as one HIV prevention option for heterosexually-active men and women at substantial risk of HIV acquisition because these trials present evidence of its safety and 2 present evidence of efficacy in these populations, especially when medication adherence is high. (IA).

National HIV Behavioral Surveillance (NHBS)

- 25 cities throughout the United States
- Funded by CDC, designed collaboratively
- Ongoing, cyclical study of three risk groups: MSM, IDU, and high-risk heterosexuals (HET)
- NHBS-HET data collection in 2006-7
- Cross-sectional study design
- Interviewer-administered quantitative survey & HIV test
- Anonymous recruitment, survey & test

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What is a High-Risk Heterosexual?

Past Definitions

- Multiple sexual partners
  - But most women and many men recently infected report 1 sexual partner in past year
- Sexual partners' risks
  - But most did not accurately know partners' risks

Newer Ideas

- Geography
  - Heterosexual HIV is clustered in high-poverty neighborhoods
- Social networks
  - Some social and sexual networks have high HIV levels despite equal individual risks
  - Greater inter-network mixing may drive infections

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High-Risk Areas

1. Created high-risk area (HRA) index with:
   - New HIV diagnoses, 2001-6, NYC HIV surveillance
   - Household poverty, 2000, census
2. Explored index to identify:
   - Geographic clustering
   - Non-residential zip codes (for exclusion)
3. Selected top 30 zip codes as HRAs (top 20%)

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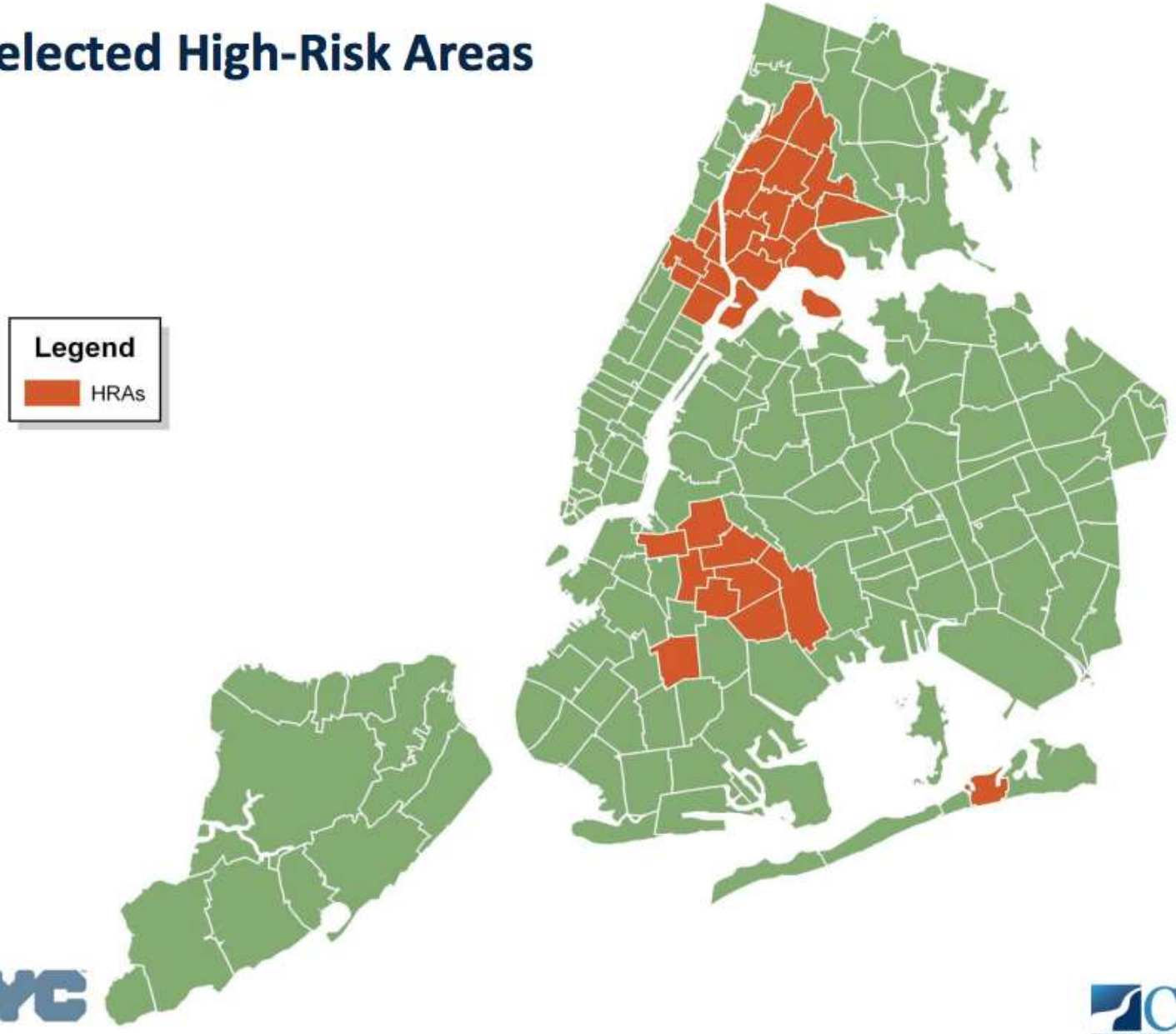
Selected High-Risk Areas



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High-Risk Heterosexual Definition

- Has a geographic or social connection to an HRA
  - Lives in HRA (geographic connection)
  - Recruited by someone who lives in HRA (social connection)
- A man or woman between 18-50 years old
- Vaginal or anal sex with opposite-sex partner in the past year
- Resident of NYC
- Speaks English or Spanish

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Ms N.K.

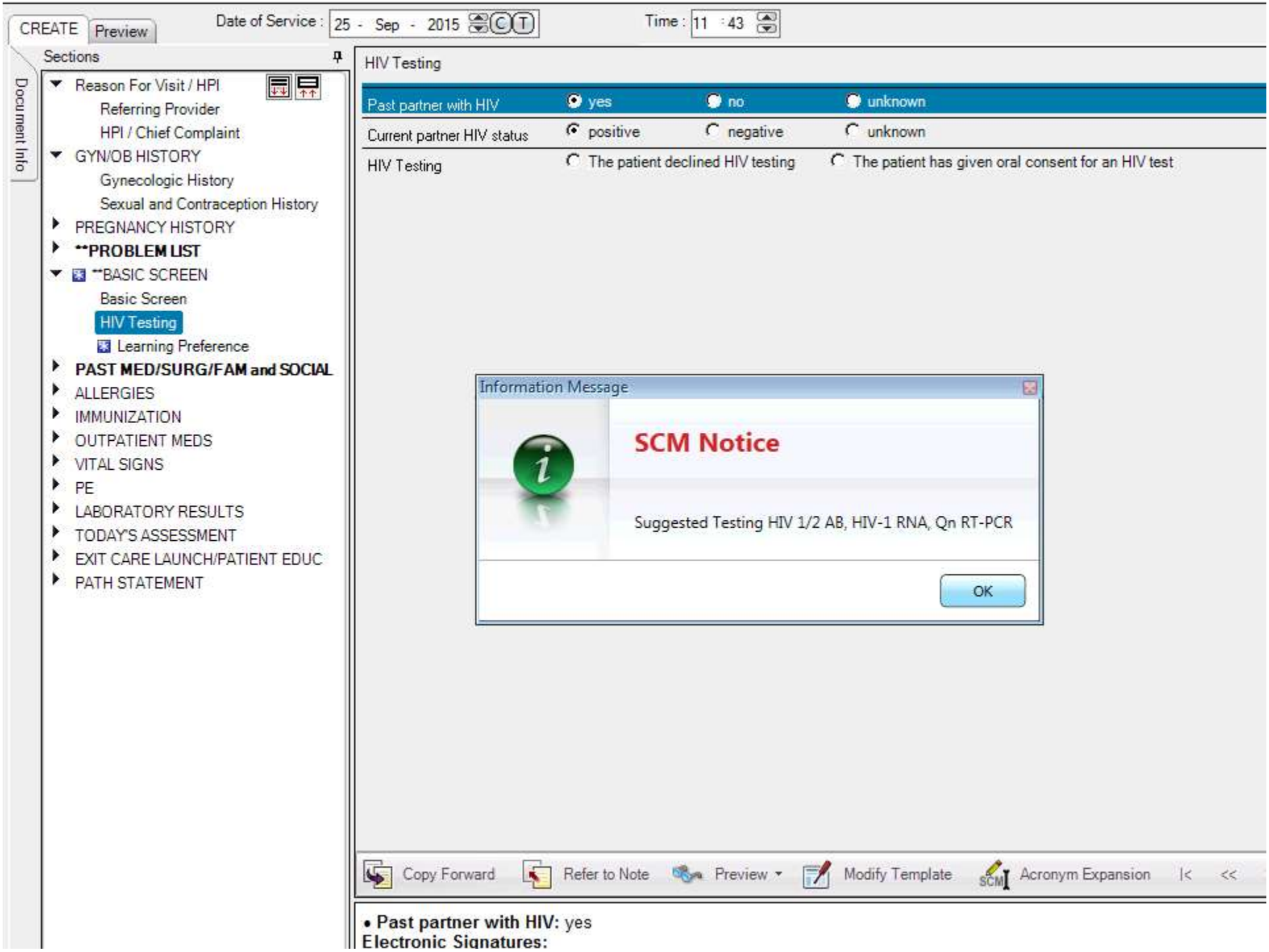
- 35 yo G2P1001, American of Guinean descent, at 8 6/7 by LMP and sono . HIV negative on 11/25/12
- Did not return for new OB because of travel. Returns with husband and 2 yo daughter in 3/2013
- On 3/14/13 FOB admitted to BLHC with fever, diffuse vesicular rash.
  - HIV positive. VL>500k, CD4 23
- Alert from ER counseling team to PRSW re pregnant wife
- NK is HIV negative w pcr <20
- Counseled abstinence, rx Truvada 1 tab po daily
- Adherence, repeated testing
- 7/8/13 C/S baby girl, HIV negative
- After extensive counseling, breastfeeding
- 10/2014 HIV ab negative pcr <20 intermittent PrEP
- 11/15/14 FOB VL 179, cd4 260 on HAART

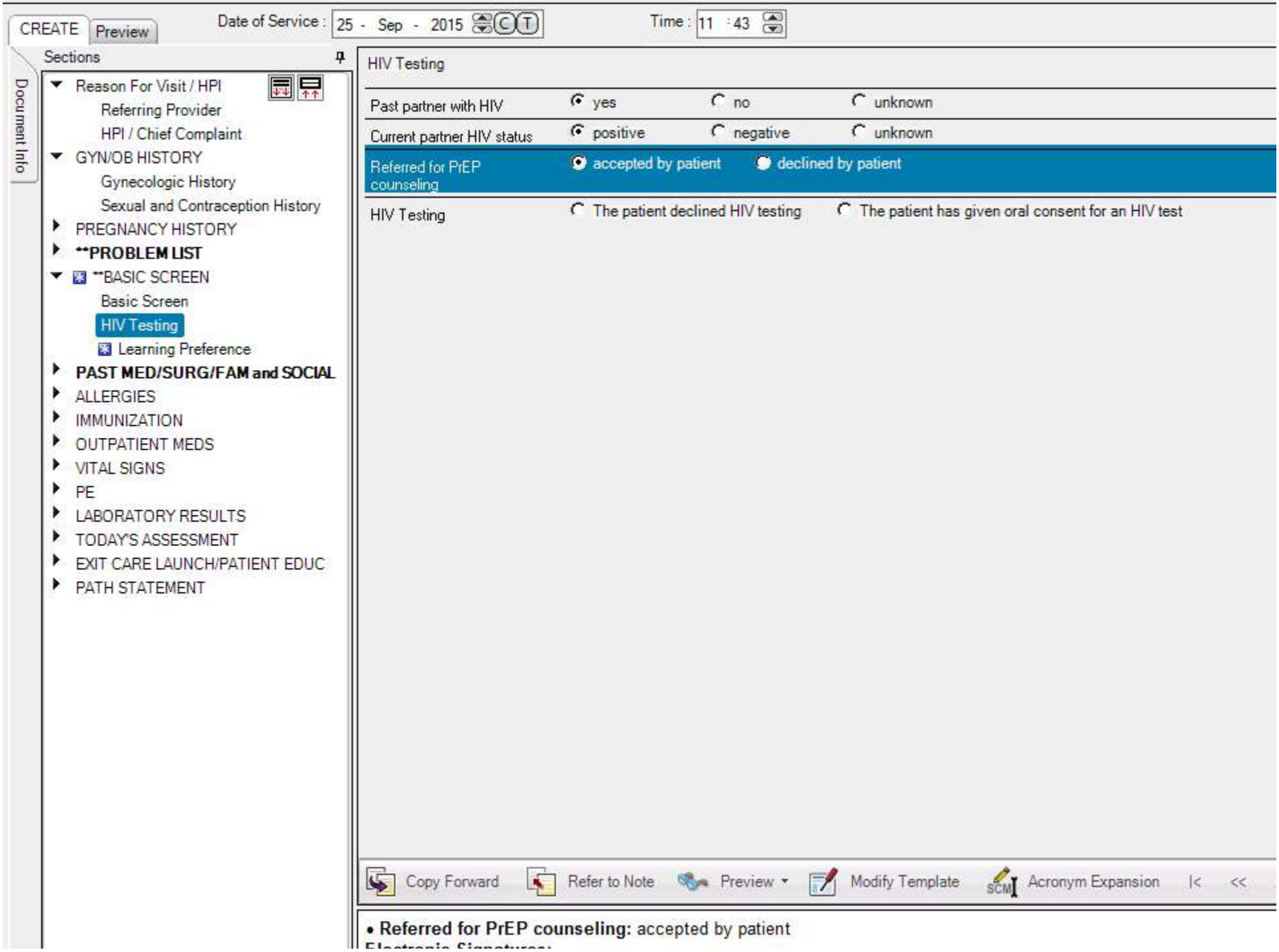
FOR AN HIV-NEGATIVE WOMAN PLANNING PREGNANCY WITH AN HIV-POSITIVE MALE PARTNER

- Options Reducing the risk of HIV acquisition by an HIV-negative woman during conception can be achieved by use of the following, singly or ideally in combination
- Antiretroviral treatment of the HIV-positive male partner to achieve an undetectable viral load
- STI diagnosis and any indicated treatment for both partners before conception attempts
- Daily, oral doses of TDF/FTC beginning 1 month before a conception attempt and continuing for 1 month after a conception attempt
- Intravaginal or intrauterine insemination, or intracytoplasmic sperm injection with a semen sample processed by “sperm washing” and confirmed to have a negative test result for the presence of remnant HIV9 OR
- Limit sex without a condom (natural conception) to peak fertility times identified by home or laboratory tests for ovulation in the female partner10 .

Breastfeeding

- The safety of PrEP with TDF/FTC or TDF alone for infants exposed during lactation has not been adequately studied. However, data from studies of infants born to HIV-infected mothers and exposed to TDF or FTC through breast milk suggest limited drug exposure.
- Additionally, the World Health Organization has recommended the use of TDF/FTC or 3TC/efavirenz for all pregnant and breastfeeding women for the prevention of perinatal and postpartum mother-to-child transmission of HIV.
- Therefore, providers should discuss current evidence about the potential risks and benefits of beginning or continuing PrEP during breastfeeding so that an informed decision can be made.


CREATE
Preview
Date of Service : 25 - Sep - 2015
Time : 11 : 43
Document Info
Sections
Reason For Visit / HPI
Referring Provider
HPI / Chief Complaint
GYN/OB HISTORY
Gynecologic History
Sexual and Contraception History
PREGNANCY HISTORY
**PROBLEM LIST
**BASIC SCREEN
Basic Screen
HIV Testing
Learning Preference
PAST MED/SURG/FAM and SOCIAL
ALLERGIES
IMMUNIZATION
OUTPATIENT MEDS
VITAL SIGNS
PE
LABORATORY RESULTS
TODAY'S ASSESSMENT
EXIT CARE LAUNCH/PATIENT EDUC
PATH STATEMENT
HIV Testing
Past partner with HIV
yes
no
unknown
Current partner HIV status
positive
negative
unknown
HIV Testing
The patient declined HIV testing
The patient has given oral consent for an HIV test
Information Message
SCM Notice
Suggested Testing HIV 1/2 AB, HIV-1 RNA, Qn RT-PCR
OK
Copy Forward
Refer to Note
Preview
Modify Template
Acronym Expansion
• Past partner with HIV: yes
Electronic Signatures:


CREATE
Preview
Date of Service : 25 - Sep - 2015
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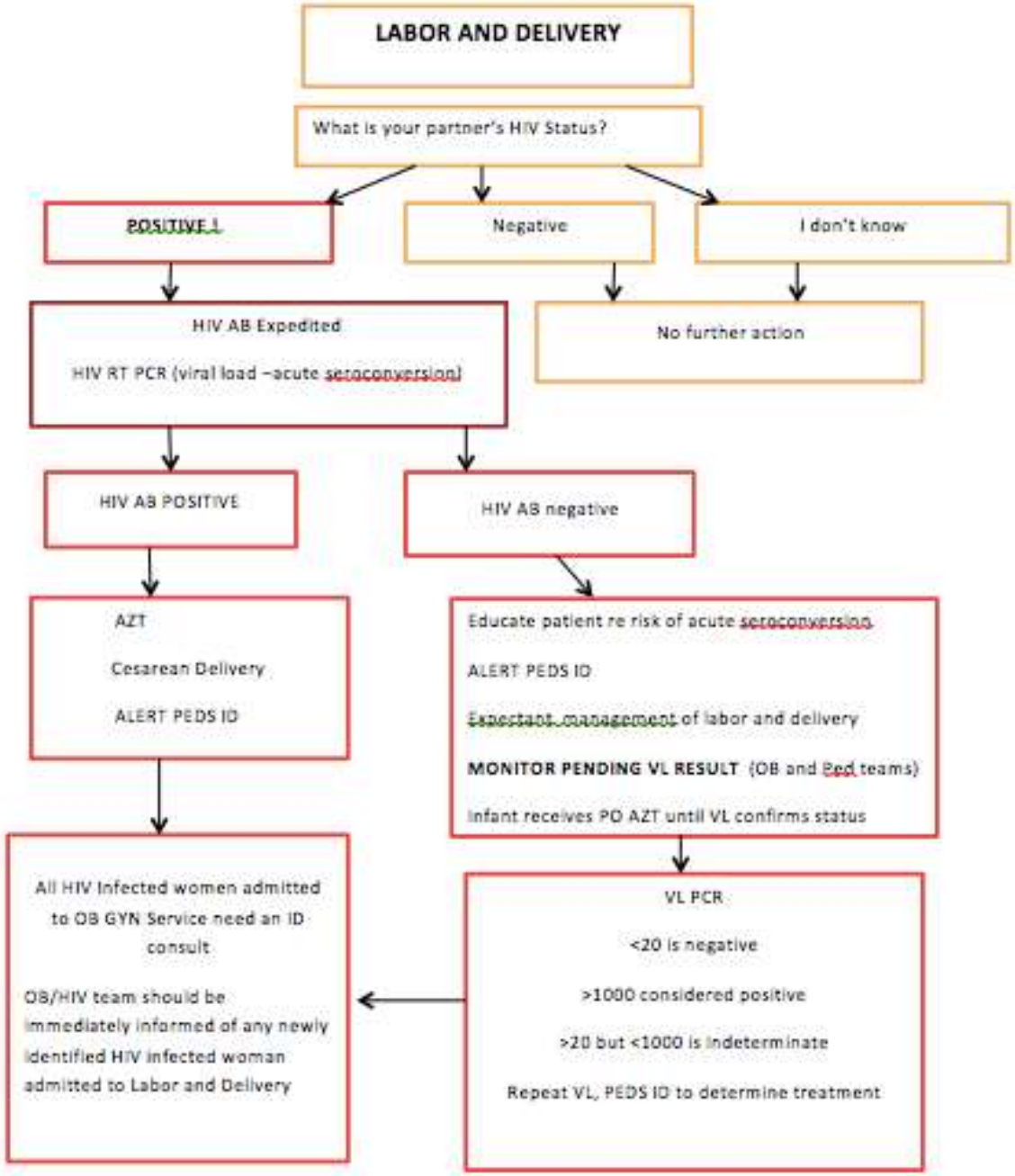
Referred for PrEP counseling
accepted by patient
declined by patient
HIV Testing
The patient declined HIV testing
The patient has given oral consent for an HIV test
Copy Forward
Refer to Note
Preview
Modify Template
Acronym Expansion
• Referred for PrEP counseling: accepted by patient


LABOR AND DELIVERY
What is your partner's HIV Status?
POSITIVE !
Negative
I don't know
HIV AB Expedited
HIV RT PCR (viral load –acute seroconversion)
No further action
HIV AB POSITIVE
HIV AB negative
AZT
Cesarean Delivery
ALERT PEDS ID
Educate patient re risk of acute seroconversion
ALERT PEDS ID
Expectant management of labor and delivery
MONITOR PENDING VL RESULT (OB and Ped teams)
Infant receives PO AZT until VL confirms status
All HIV Infected women admitted to OB GYN Service need an ID consult
OB/HIV team should be immediately informed of any newly identified HIV infected woman admitted to Labor and Delivery
VL PCR
<20 is negative
>1000 considered positive
>20 but <1000 is indeterminate
Repeat VL, PEDS ID to determine treatment

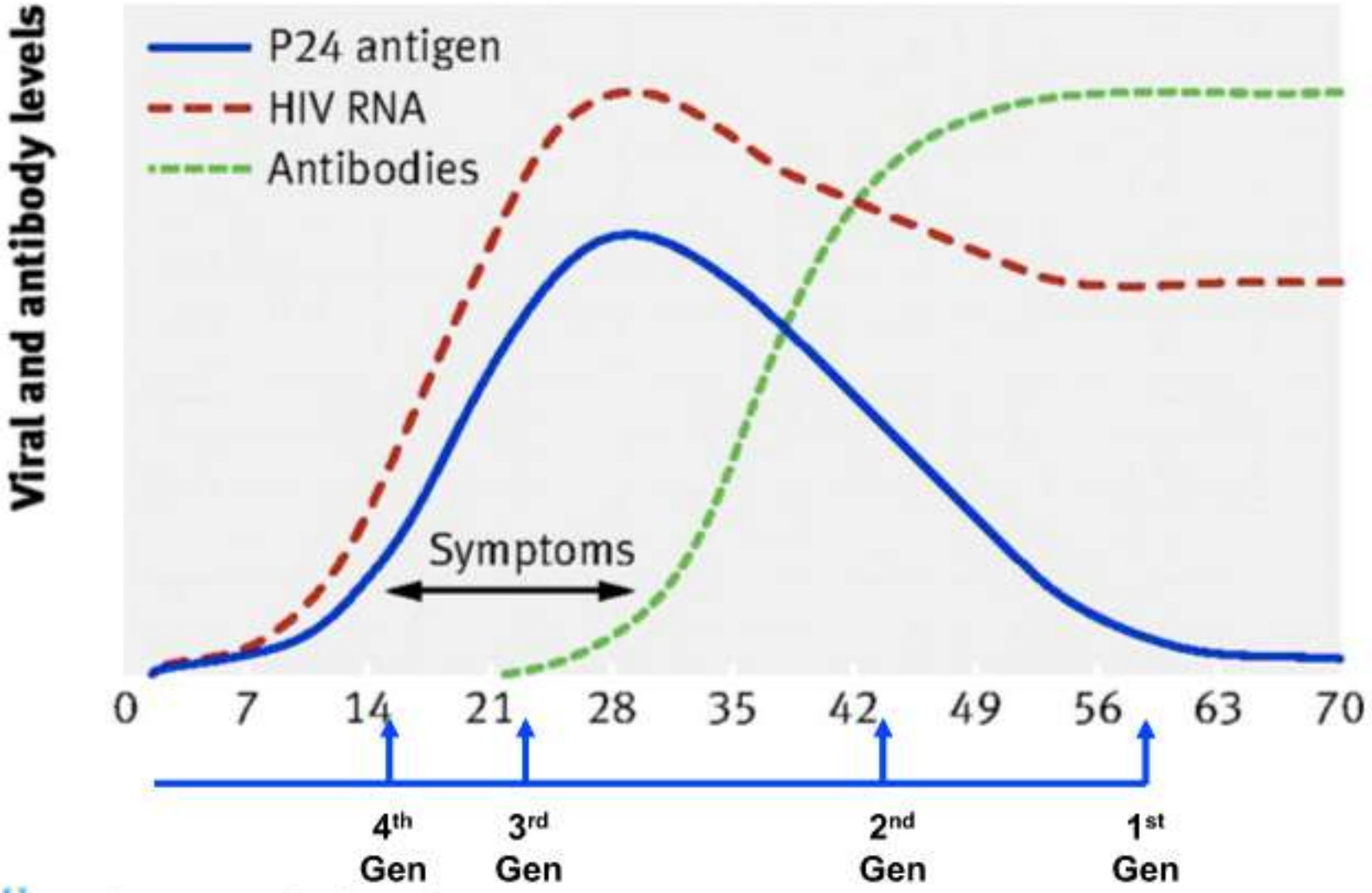
Ms CS

- 32 yo Caucasian G7P2 admitted on 2/18/14, 30 3/7 EGA febrile, PPROM x3 d
  - Hepatitis C, polysubstance abuse: cocaine, marijuana, etoh
  - Prior admission at Lincoln for pyelo 1/2014
  - 1/24/14 HIV negative Lincoln, 2/5/14 HIV negative BOOM
  - Incarceration 9/2-10/8/13
  - Records from FLA show 2 ER evaluations after assaults
  - C/S 2/21/14 baby girl 840 g LBW, respiratory distress, suspect sepsis
  - ACS: baby to foster care

Baby S

- Born 2/21/14
- Peds ID consult for Hep C exposure
- Discharged from NICU on 4/28/14, 65 days, 39 2/7
- 5/1/14 evaluated CCC for Hep C exposure
- 5/6/14 call from Newborn Screening “specimen problem”
  - 4 newborn screens sent, 3/4 negative, 4 is positive
- 5/7/14 Rapid test positive, EIA positive, VL sent
  - Too late for prophylaxis
  - ZDV, Epivir, Kaletra
- 5/29/14 Reevaluation at Wadsworth of 3 initial blood spots
  - Birth negative pcr
  - Day 5 positive pcr
  - 1 month positive pcr
- Baby adopted, in care at CCC, doing well.

Reduction of Window Period



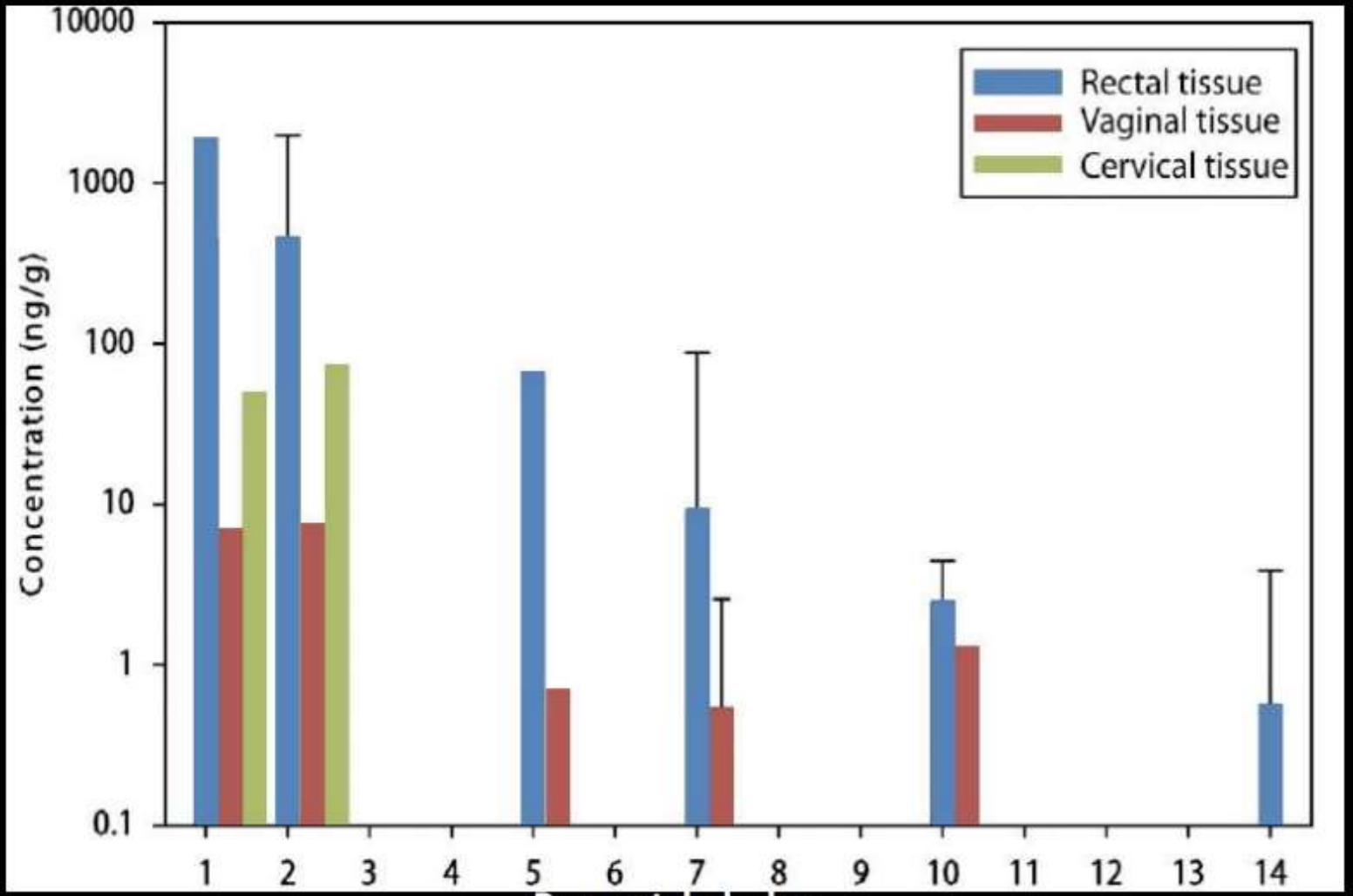
BMJ Das G et al. BMJ 2010;341:bmj.c4583

Table 1: Summary of Guidance for PrEP Use

	Men Who Have Sex with Men	Heterosexual Women and Men	Injection Drug Users
Detecting 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)
Clinically eligible	Documented negative HIV test result before prescribing PrEP No signs/symptoms of acute HIV infection Normal renal function; no contraindicated medications Documented hepatitis B virus infection and vaccination status		
Prescription	Daily, continuing, oral doses of TDF/FTC (Truvada), ≤90-day supply		
Other services	Follow-up visits at least every 3 months to provide the following: HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment At 3 months and every 6 months thereafter, assess renal function Every 6 months, test for bacterial STIs		
	Do oral/rectal STI testing	Assess pregnancy intent Pregnancy test every 3 months	Access to clean needles/syringes and drug treatment services

STI: sexually transmitted infection

TDF Concentrates 10-100x More in Rectal Tissue than in Cervico-vaginal Tissues

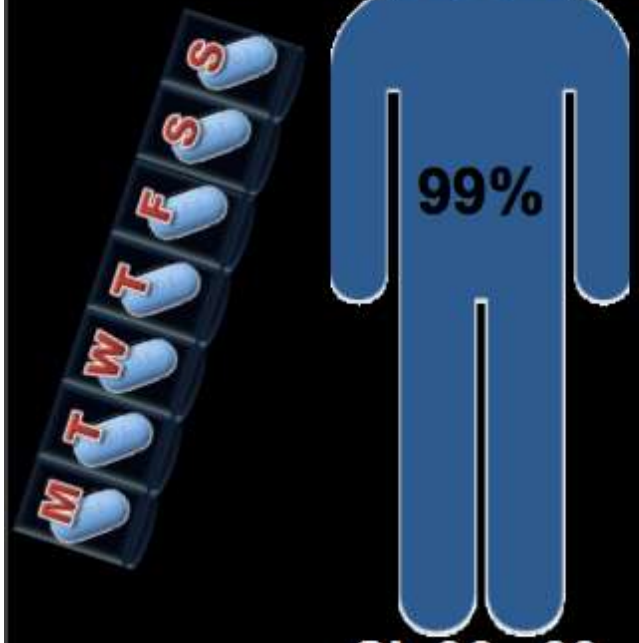


Slide courtesy Landovitz

Patterson KB *et al.* Sci Transl Med. 2011.

Maximizing the Potential Effectiveness

TDF/FTC (7x/week)

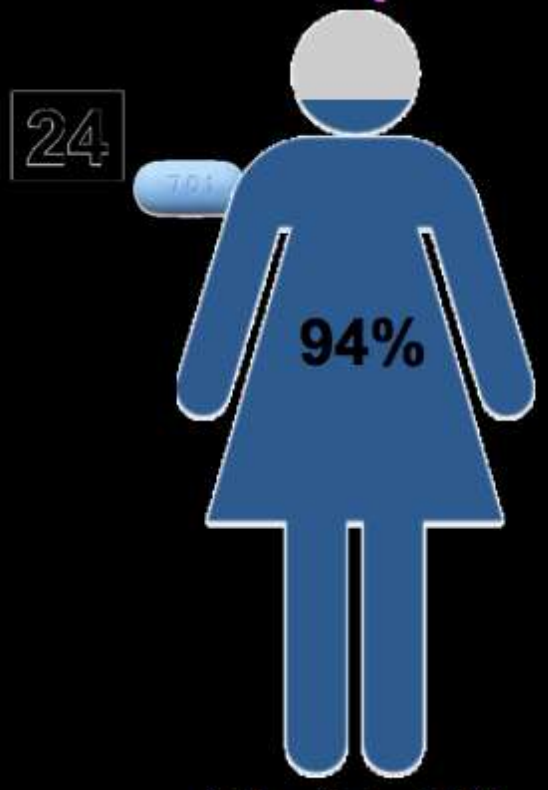


CI: 96 - 99

Some adherence forgiveness with retained protection

Anderson P *et al*, Sci Transl Med. 2012.

TDF/FTC (~1x/24°)



CI: -17 - 100

6-7 doses per week likely required

Donnell D *et al*, JAIDS. 2014.
Cottrell ML *et al*, R4P, 2014.

Slide courtesy Landovitz

March 23, 2016

Dear New York City and New York State PrEP Providers,

Last month, the first reported case of a breakthrough HIV infection in a patient consistently taking oral tenofovir disoproxil fumarate and emtricitabine (TDF/FTC, or Truvada®) as pre-exposure prophylaxis (PrEP) to prevent HIV was reported at the 2016 Conference on Retroviruses and Opportunistic Infections (CROI) in Boston [1]. The patient was infected with a strain of HIV resistant to both TDF and FTC. While such viruses are extremely rare, the case demonstrates that PrEP, like other preventive medications and behavioral interventions, does not provide 100% protection against HIV infection. Nevertheless, the body of scientific and clinical data previously presented about the efficacy of PrEP confirms the critical role of this intervention in reducing new HIV infections in New York City (NYC), and New York State (NYS).

As such, the New York City and New York State Departments of Health (DOH) continue to fully support the use of TDF/FTC as PrEP for individuals at risk of HIV infection. The rare event reported at this conference provides an opportunity to revisit NYSDOH AIDS Institute guidance for PrEP and to clarify the importance of communicating with patients about PrEP and the risk of HIV and other sexually transmitted infections (STIs).

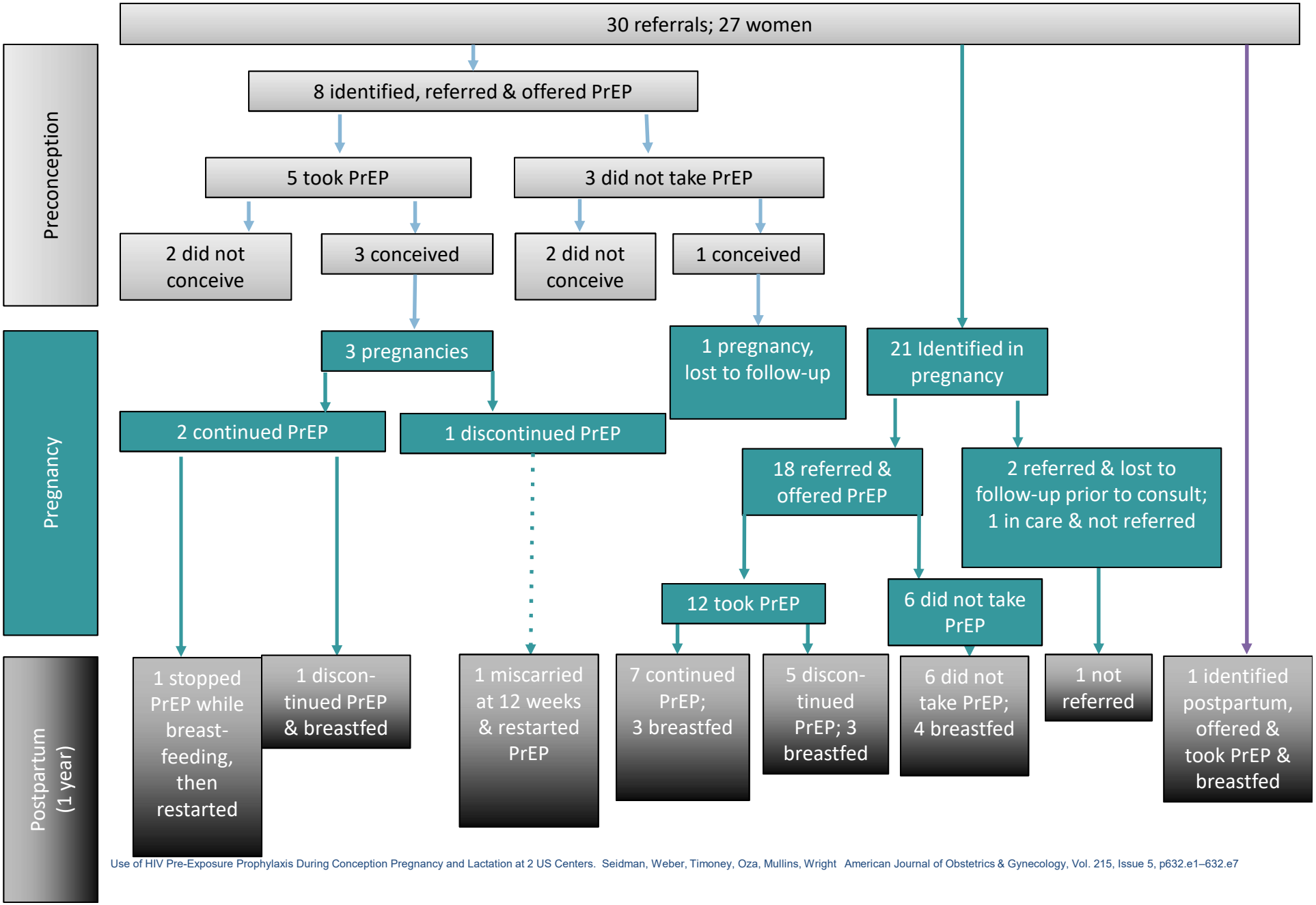
We urge providers to adhere to CDC and NYSDOH AIDS Institute PrEP guidance with their patients on PrEP by:

1. Testing for HIV every three months using a laboratory-based, ideally 4th generation, HIV test;
2. Assessing for signs of acute HIV infection at every visit;
3. Having a low threshold for testing for acute HIV and other STIs; and
4. Encouraging patients on PrEP (or on HIV treatment) to use condoms as often as possible.

THE CASE REPORTED AT CROI 2016

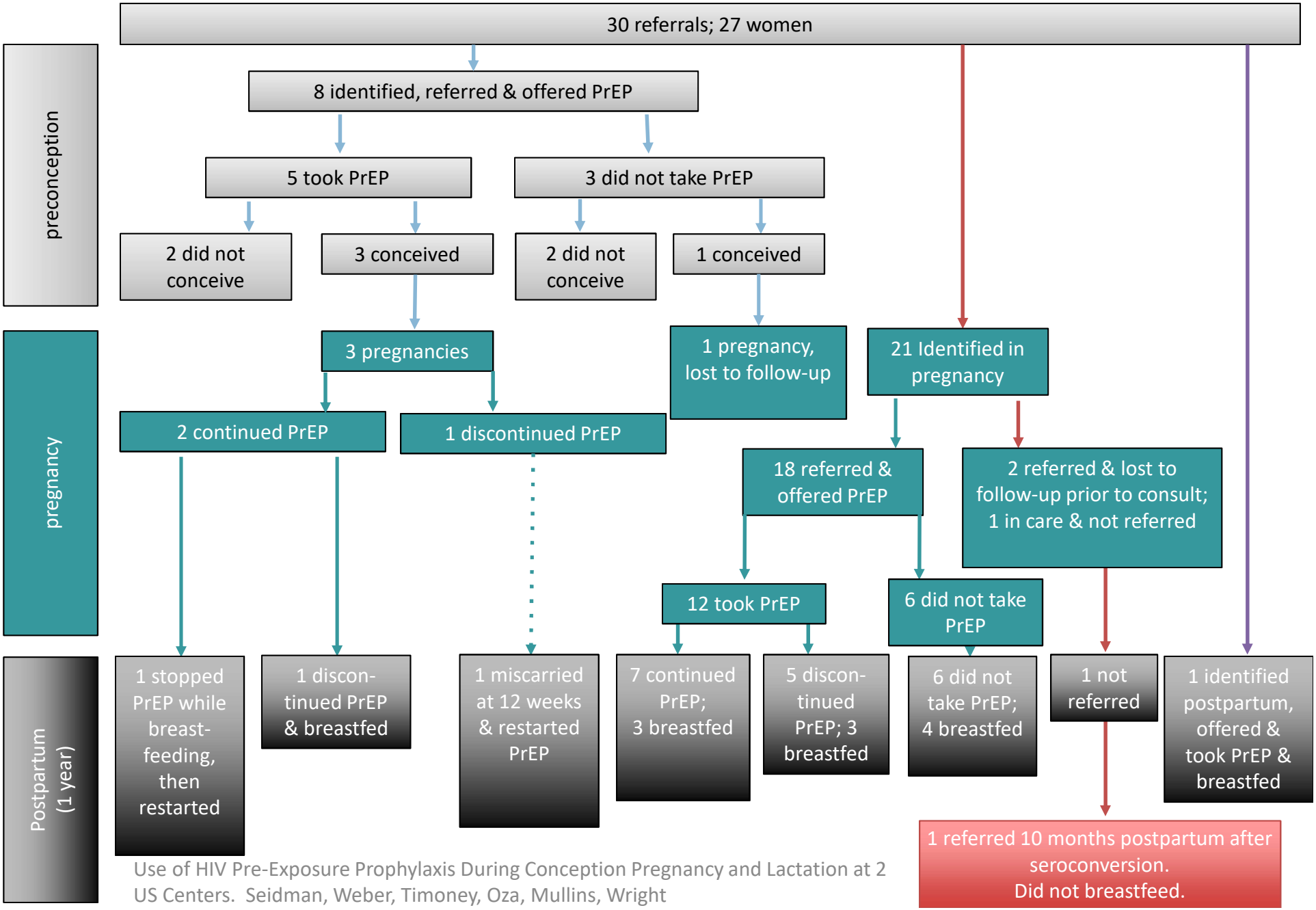
A 43-year-old man in Toronto, Canada, was diagnosed with acute HIV infection after taking PrEP for 24 months, during which time he tested negative for HIV 7 times. Patient self-report, pharmacy data and laboratory analysis indicated the patient had long-term adherence to PrEP and a high concentration of TDF/FTC in his blood at the time of seroconversion. The patient was diagnosed with acute HIV infection when visiting an emergency room with severe abdominal pain and a high fever; he reported receptive anal sex without condoms with multiple male partners in the 2 to 6 weeks before diagnosis. Subsequent viral sequencing determined that the patient was infected with a strain of HIV-1 that demonstrated genotypic evidence of high-level resistance to emtricitabine and low-level resistance to tenofovir disoproxil fumarate, the two antiretroviral (ART) drugs in PrEP. The transmitted virus also demonstrated resistance to integrase inhibitors, medications used in first-line HIV treatment and post-exposure prophylaxis (PEP) regimens. The patient immediately began HIV treatment and achieved an undetectable viral load by taking a combination of dolutegravir (Tivicay®), darunavir/cobicistat (Prezcobix®) and rilpivirine (Edurant®).

Women identified as at substantial risk of HIV acquisition pre-conception, during pregnancy and postpartum at 2 U.S. centers



Use of HIV Pre-Exposure Prophylaxis During Conception Pregnancy and Lactation at 2 US Centers. Seidman, Weber, Timoney, Oza, Mullins, Wright American Journal of Obstetrics & Gynecology, Vol. 215, Issue 5, p632.e1–632.e7

Who was missed?



Use of HIV Pre-Exposure Prophylaxis During Conception Pregnancy and Lactation at 2 US Centers. Seidman, Weber, Timoney, Oza, Mullins, Wright

3 women not offered PrEP

Presented to ED s/p assault, 27 weeks pregnant. Disclosed partner living with HIV and not on meds. Not offered PEP or PrEP. Lost to follow-up.

Diagnosed with syphilis, 32 weeks pregnant. Reported many partners, some of whom living with HIV. Homeless, engaging in exchange sex, active meth use. Treated for syphilis, multiple brief OB triage visits, never offered PEP/PrEP & lost to follow-up.

Late presentation to care, diagnosed with significant fetal anomalies at 30 weeks. Disclosed partner living with HIV, treated at same institution, at first visit. Seen twice weekly until delivery. Never referred for consult but had frequent HIV testing. Viral load negative at delivery. Infant died postpartum and patient lost to follow-up. Represented 10 months postpartum, positive HIV test, referred for care.

Use of HIV Pre-Exposure Prophylaxis During Conception Pregnancy and Lactation at 2 US Centers. Seidman, Weber, Timoney, Oza, Mullins, Wright . American Journal of Obstetrics & Gynecology, Vol. 215, Issue 5, p632.e1–632

LC

- 27 yo G3P2012 HIV **negative** w positive partner who is in care, adherent to atripla
  - Planned pregnancy (PrEP prior to IUD removal)
  - Repeated negative Ab and pcr, weekly pcr before delivery.
  - Planned breastfeeding, endorsed by Peds ID
  - NSVD, no need for NN AZT, stopped truvada after delivery
  - Breastfed 1 month
  - Restarted PrEP prior to mirena and resumption of sexual activity

Assess risk in ALL women, not just pregnant women.

Thank you!

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