PrEP Overview

Board of Health Presentation

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Outline

- Need for new preventions strategies
- What is PrEP?
- Data summary on PrEP
- PrEP guidelines
- Risk behaviors on PrEP
- Resistance

HIV Prevention: Toolbox for Success

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

Need for New Prevention Options

- Only 50% of MSM in Philadelphia used a condom the last time they had sex (50% for receptive anal sex and 53% for insertive anal sex)
- Over 25% of MSM in Philadelphia are infected with HIV (26.2%)
  - 35.3% in AA MSM
  - 26.9% in Latino MSM
  - 8.8% in White MSM

Data Source: PDPH/AACO National HIV Behavioral Surveillance among MSM4, 2014

What is pre-exposure prophylaxis?

- Breaking it down
  - Pre-exposure = before an exposure
    - Medication used before an exposure occurs
  - Prophylaxis = prevention
    - Medication used for prevention instead of treatment
- Putting it together
    - Medication used BEFORE an exposure in order to prevent a disease or condition
- Currently being used
  - Malaria (malarone, doxycycline)
  - Tuberculosis (isoniazid)
- HIV prevention
  - Antiretrovirals?

How does PrEP work?

- Steps leading to HIV infection
  1. An infected body fluid comes into contact with a mucous membrane such as the rectum, vagina, or penis
  2. HIV crosses the epithelial barrier and enters underlying tissue
  3. Replicates in the mucous membrane tissue (1-3 days)
  4. Enters the lymphatic and circulatory system and spreads throughout the body

- "Window of opportunity"
  - The time when the amount of virus is small and is replicating at the mucous membrane
  - Antiretrovirals could prevent HIV infection by helping the body clear the virus before it spreads

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.

Tenofovir/Emtricitabine FDA Approved for PrEP

FDA NEWS RELEASE

For Immediate Release: July 16, 2012
Media Inquiries: Erica Jefferson, 301-796-4988, erica.jefferson@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA approves first drug for reducing the risk of sexually acquired HIV infection

Evidence-based approach enhances existing prevention strategies

PrEP Trials

- PrEP Trials Have Shown Efficacy in MSM, Heterosexual Men and Women, and IDUs
  - Efficacy ranged from 44% to 75%[1-6]
- PrEP Works, but Adherence Is Critical
  - Efficacy ranged from 74% to 92% in persons who had detectable drug levels[1-6]
- In an implementation study mimicking the real world, efficacy was 86%[7]

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. 7. McCormack t al. CROI 2015. Abstract 22LB.

So How Many People Need to Take PrEP?

- Number needed to treat
  - the average number of patients who need to be treated to prevent one additional bad outcome
- PrEP = 13 to prevent 1 HIV infection
- Statins = 100 to prevent 1 cardiovascular event

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.

CDC Guideline: Follow-up and Monitoring

Follow-up	At Least Every 3 Mos	After 3 Mos and at Least Every 6 Mos Thereafter	At Least Every 6 Mos	At Least Every 12 Mos
All patients	▪ HIV test ▪ Medication adherence counseling ▪ Behavioral risk reduction support ▪ Adverse event assessment ▪ STI symptom assessment	▪ Assess renal function	▪ Test for bacterial STIs	▪ Evaluate need to continue PrEP
Women	▪ Pregnancy test (where appropriate)			
HBsAg+			▪ HBV DNA by quantitative assay*	

*Every 6-12 mos.

CDC. PrEP Guideline. 2014.

Unintended Consequences

- Resistance[1, 2]
  - To date, resistance has been identified in some of the individuals who were seroconverting around the time they started PrEP (5/8 persons in iPrex and Proud)
  - Highlights the need to rule out acute infection prior to starting PrEP in high risk populations
- Sexual Risk Behavior[3, 4]
  - Multiple studies have shown that there is no significant increase in HIV risk behaviors (STIs or condomless sex) in persons taking PrEP

1. McCormack t al. CROI 2015. Abstract 22LB. . 2. Liegler, T., et al. JID. 2014;210:1217-1227.
3. Grant RM, et al. N Engl J Med. 2010;363: 2587-2599. , 4. Baeten JM, et al. N Engl J Med. 2012;367:399-410.

Local PrEP Awareness Among MSM

- 32% of NHBS-MSM4 participants knew someone in Philadelphia who had taken PrEP
- 6% of HIV negative men had taken PrEP
- 59% of HIV negative MSM were willing to take PrEP
  - 62% of AA, 71% of Latino and 54% of whites
- Major reasons for not wanting to take PrEP
  - Low risk (37%), questions about side effects (35%), need to take daily (19%)

Data Source: PDPH/AACO National HIV Behavioral Surveillance among MSM4, 2014

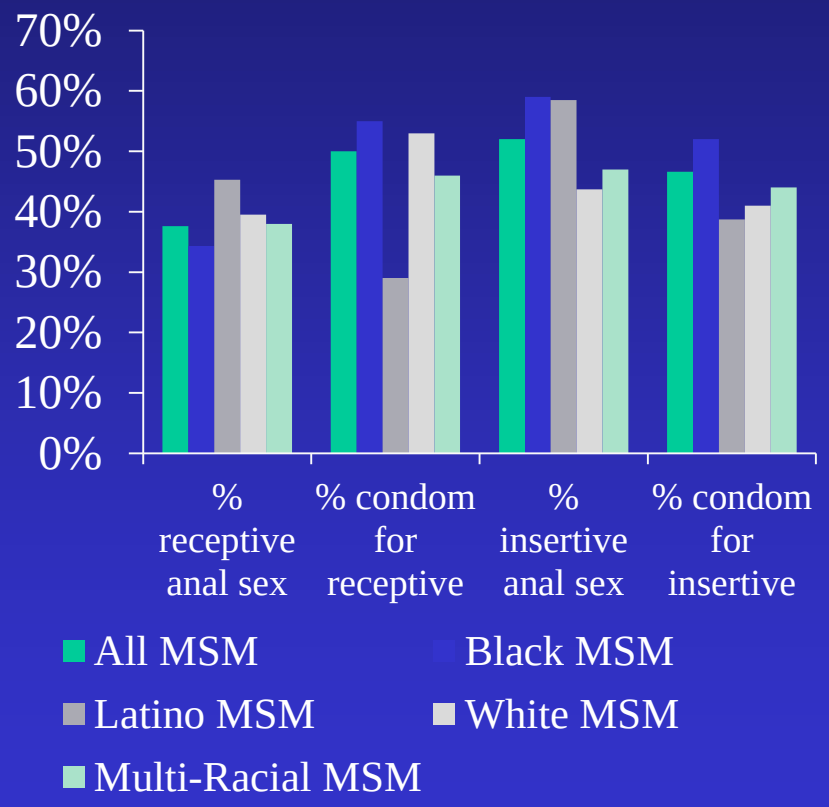
So who should know about PrEP?

- Everyone

Questions?

Need for New Prevention Options NHBS-MSM4, 2014

Condomless Sex



HIV Prevalence

Demographic Group	MSM4 % HIV Positive Tested n=693	MSM4 % New Positives
Total	26.2%	23.3%
Race		
Black	35.3%	23.3%
White	8.8%	18.8%
Latino	26.9%	22.2%
Multi-racial	25.9%	27.3%

Data Source: PDPH/AACO National HIV Behavioral Surveillance among MSM4, 2014

Potential PrEP strategies

Route of drug delivery	• Oral (pill) • Topical microbicide(gel) –Rectal –Vaginal • Injection • Intravaginal ring
Dosing schedule	• Daily • Intermittently • Coitally (before/sex)
Number of antiretroviral drugs	• Single • Combination
Choice of antiretroviral drug	• Over 25 available

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)

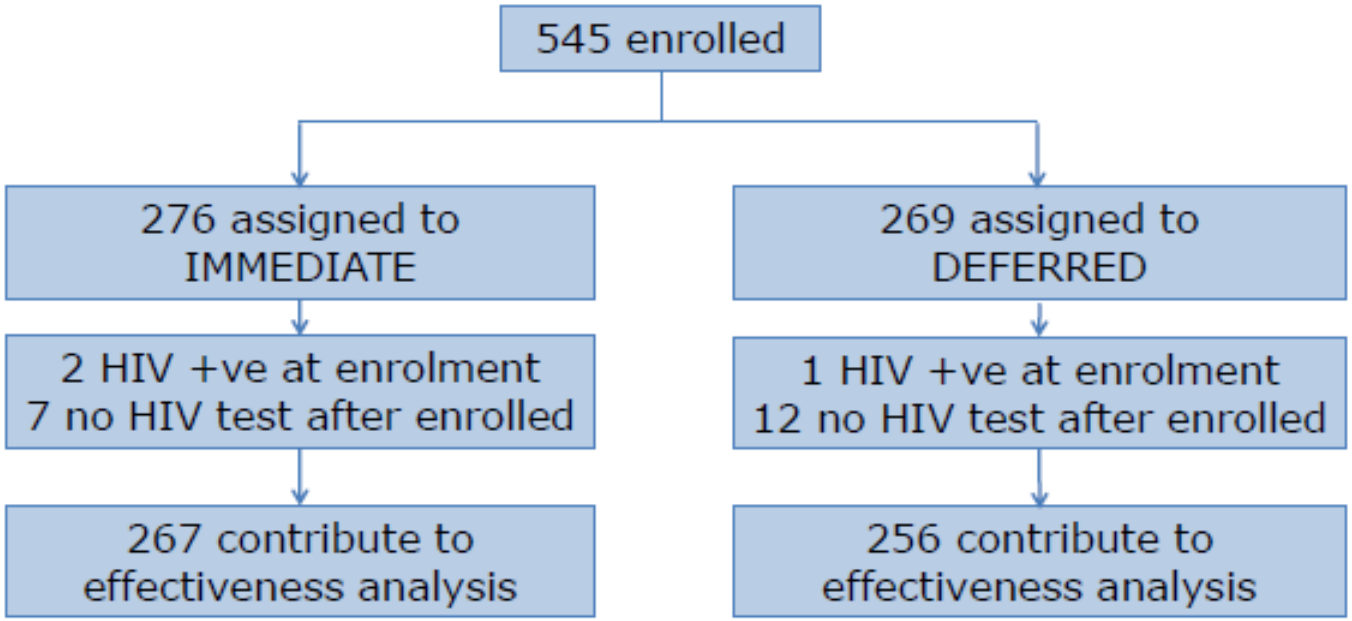
1. Grant RM, et al. N Engl J Med. 2010;363:2587-2599. 2. Baeten JM, et al. N Engl J Med. 2012;367:399-410. 3. Thigpen MC, et al. N Engl J Med. 2012;367:423-434. 4. Choopanya K, et al. Lancet. 2013;381:2083-2090. 5. Van Damme L, et al. N Engl J Med. 2012;367:411-422. 6. Marrazzo J, et al. CROI 2013. Abstract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

The Proud Study



Calculation of person-years:

From enrolment to the first of the following

- HIV test at m12, or
- HIV test at the time of access to PrEP, or
- diagnosis of HIV infection

McCormack t al. CROI 2015. Abstract 22LB.

The Proud Study

HIV Incidence

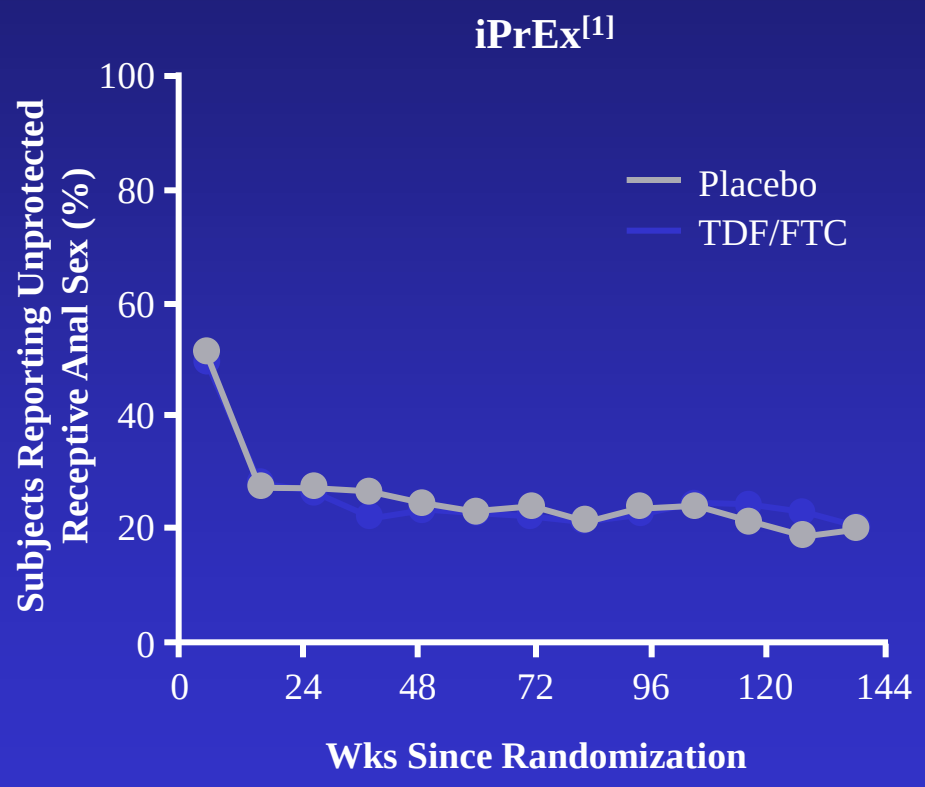
Group	No. of infections	Follow-up (PY)	Incidence (per 100 PY)	90% CI
Overall	22	453	4.9	3.4–6.8
Immediate	3	239	1.3	0.4–3.0
Deferred	19	214	8.9	6.0–12.7

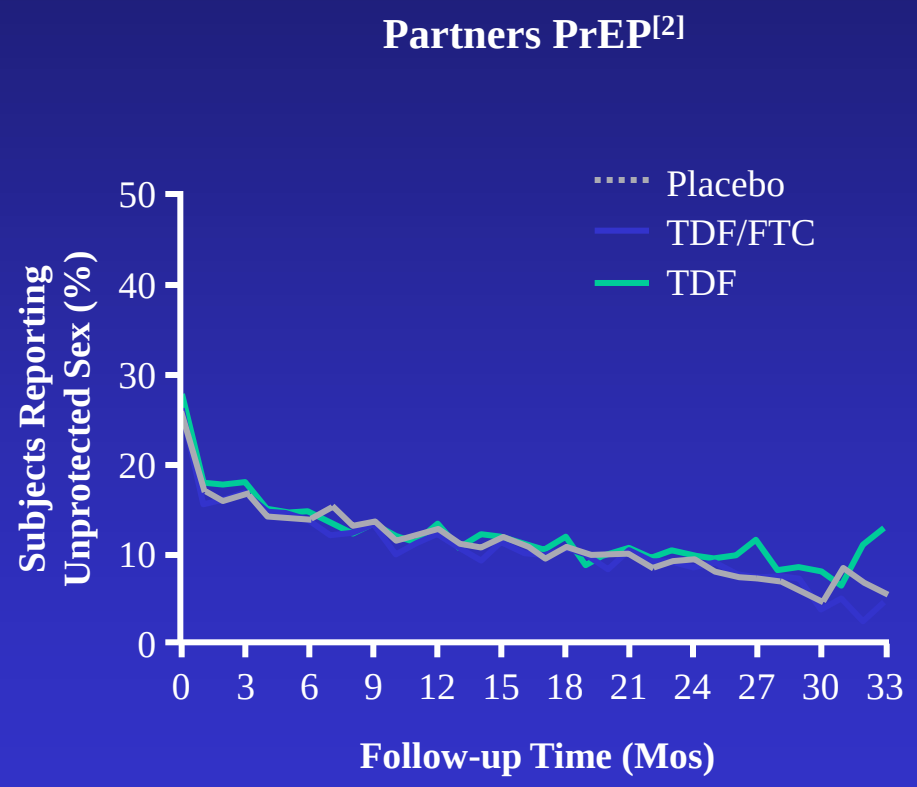
Efficacy =86% (90% CI: 58 – 96%)
P value =0.0002

Rate Difference =7.6 (90% CI: 4.1 – 11.2)
Number Needed to Treat =13 (90% CI: 9 – 25)

McCormack t al. CROI 2015. Abstract 22LB.

PrEP Trials Found *Decreasing* Risk Behavior Over Time





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Reported sexual behaviour (preliminary)

Anal sex partners in last 90 days **BASELINE n=539**	**Immediate** Median (IQR)	**Deferred** Median (IQR)
Total number of partners	10.5 (5-20)	10 (4-20)
Condomless partners, participant receptive	3 (1-5)	2 (1-5)
Condomless partners, participant insertive	2.5 (1-6)	3 (1-7)

Anal sex partners in last 90 days **MONTH 12 n=349**	**Immediate** Median (IQR)	**Deferred** Median (IQR)
Total number of partners	10 (3-24)	8 (3-15)
Condomless partners, participant receptive	3 (1-8)	2 (1-5)
Condomless partners, participant insertive	3 (1-8)	3 (1-6)

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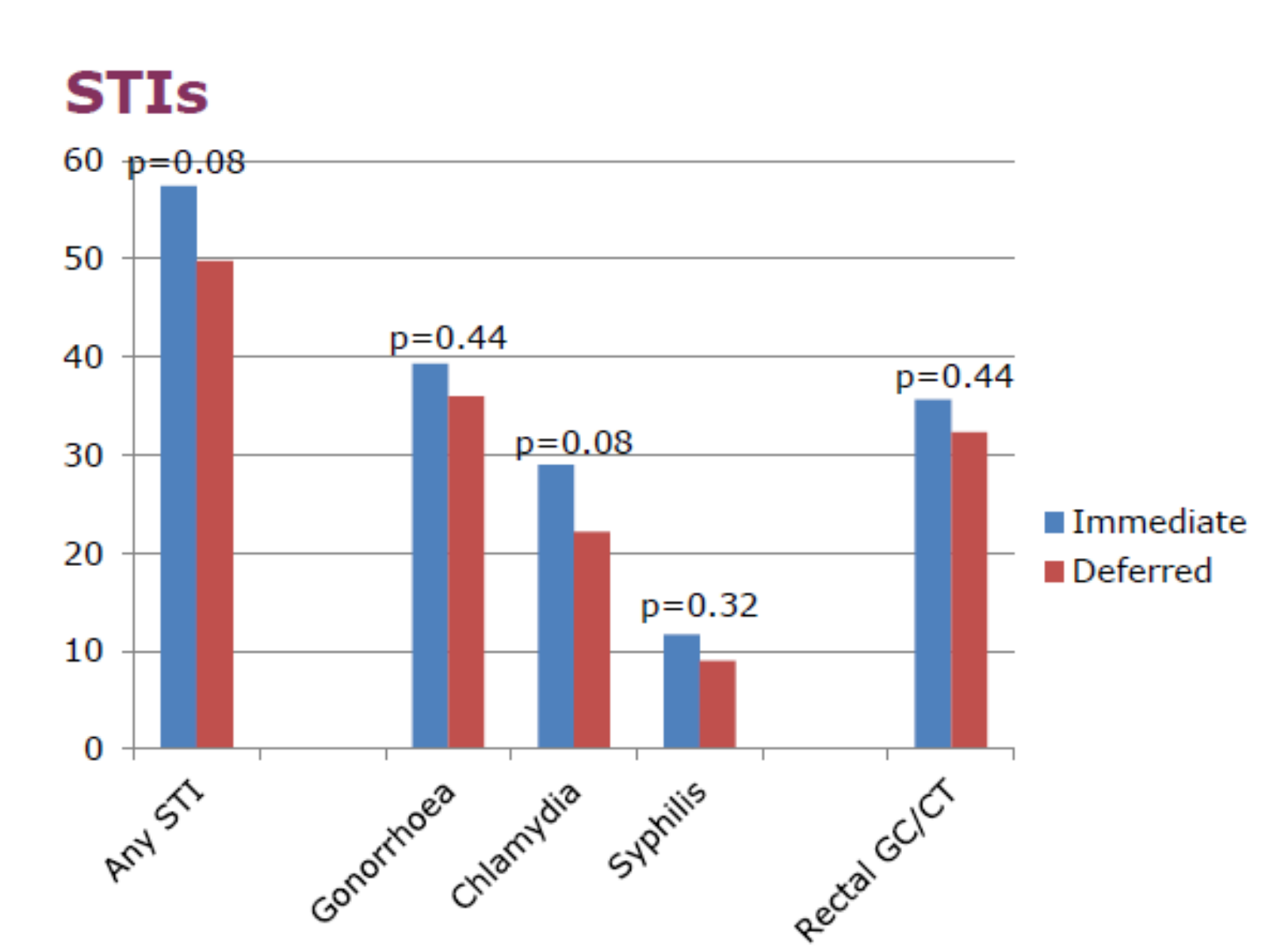

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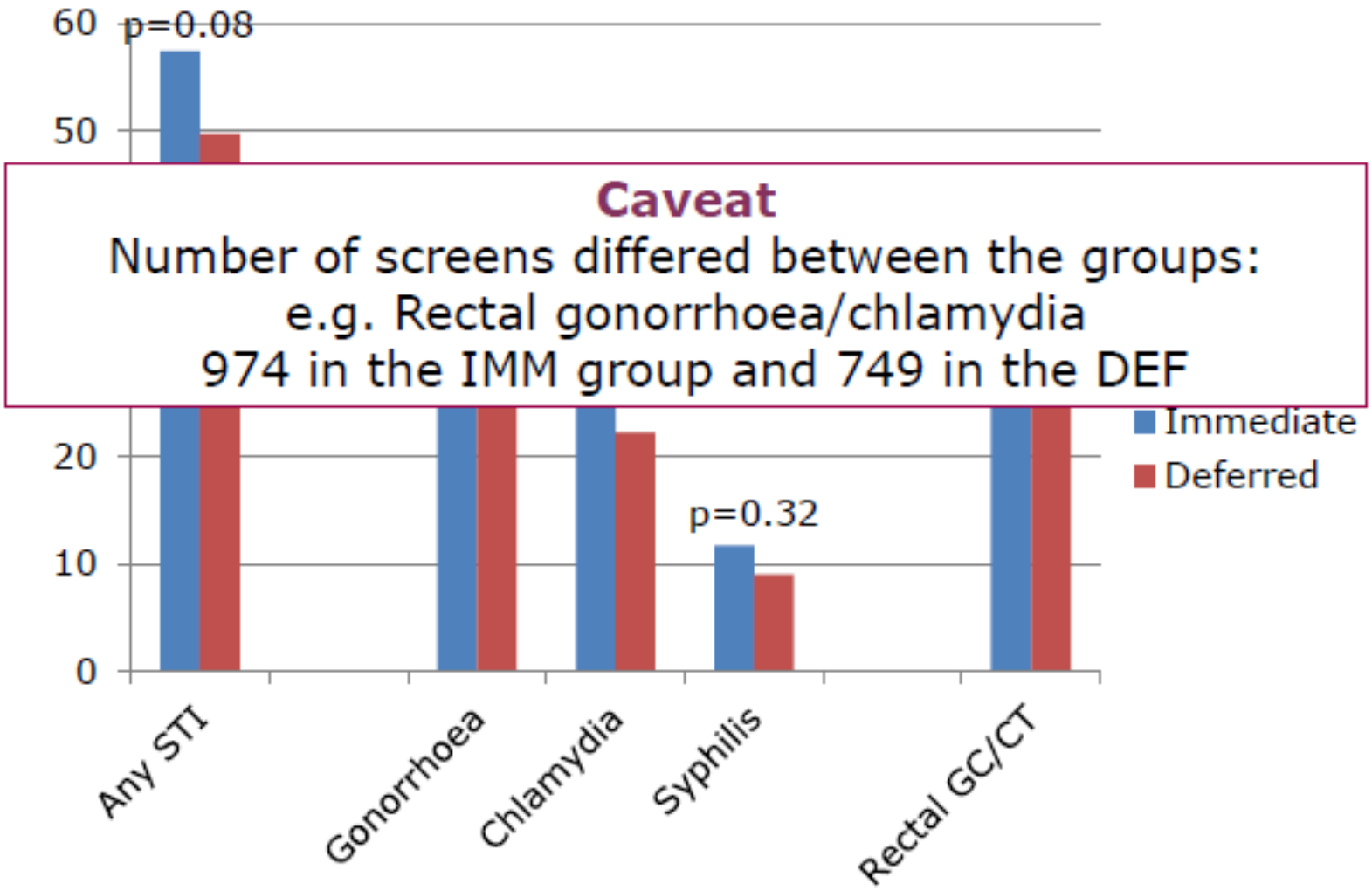
STIs



Caveat

Number of screens differed between the groups:
e.g. Rectal gonorrhoea/chlamydia
974 in the IMM group and 749 in the DEF

McCormack t al. CROI 2015. Abstract 22LB.

Pregnancy

- PrEP use at conception and during pregnancy by the uninfected partner may offer an additional tool to reduce the risk of sexual HIV acquisition[1]
- Data directly related to the safety of PrEP use for a developing fetus are limited
- Potential risks and limited information should be discussed
- TDF and FTC are classified as FDA Pregnancy Category B medications[2]

1. CDC. PrEP Guideline. 2014. 2. DHHS. HIV Perinatal Guideline. 2014.

Resistance

- Data from the Proud study[1]
  - 3 of 6 individuals who were seroconverting around the time they started PrEP developed resistance with a M184V/I (resistance to one component in Truvada)
- Data from iPrex[2]
  - 2 of 2 individuals who were seroconverting around the time they started PrEP developed resistance with a M184V/I (resistance to one component in Truvada)
- Highlights the need to rule out acute infection prior to starting PrEP in high risk populations

1. McCormack t al. CROI 2015. Abstract 22LB. . 2. Liegler, T., et al. JID. 2014;210:1217-1227.