

Common Questions Surrounding Common Infections in the Outpatient Setting

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General Internal Medicine Grand
Rounds

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Outline

- Urinary tract infections in women... Does my patient have one?
- Abscesses and cellulitis in the era of MRSA? Antibiotics and which ones?
- Anal pap smears for men having sex with men... Should I be doing them?
- Pre-exposure prophylaxis for HIV among men having sex with men?

Part 1

UTIs

Case 1

52 y/o female with 12 hours of urgency, frequency, dysuria and difficulty voiding. She is otherwise healthy. She is sexually active with her husband. She denies any vaginal discharge, itching or bleeding (history of hysterectomy).

POCT urinalysis: No leuk esterase, no nitrites, trace lysed blood.

Subsequent data not available at time of visit...

Laboratory urinalysis: No leuk esterase, no nitrites, no blood, few CaOxylate crystals.

Urine culture: 10^4 – 10^5 non-hemolytic strep

Question 1

Does she have a UTI?

Question 2

How did the laboratory criteria we used get established?

The 11th Commandment (almost)?

A woman with dysuria but who lacketh pyuria and $\geq 10^5$ CFU of bacteria shalt not have a UTI.



And the lord so hateth odd integers that he banished the 11th commandment into the wasteland of medical dogma.

Question 2

How did the laboratory criteria we use for UTI get established?

Leukocyte esterase and or nitrite test

•“Gold Standard” = Bacteriuria

Test, colony count	Performance characteristics				Reference(s)
	Sensitivity	Specificity	Predictive values		
			Positive	Negative	
Leukocyte esterase					
≥10 ⁵ cfu/mL	68–98	59–96	19–86	91–97	[35, 48, 49, 53, 54]
≥10 ⁴ cfu/mL	64–77	59–83	16–52	89–96	[47, 49, 53]
≥10 ³ cfu/mL	62–79	55–84	3–81	51–99	[49, 52, 53]
Nitrite					
≥10 ⁵ cfu/mL	19–45	95–98	50–78	82–89	[48, 49, 53, 54]
≥10 ⁴ cfu/mL	8–39	97–98	27–81	85–87	[49, 53]
≥10 ³ cfu/mL	0–50	48–98	0–82	37–99	[49, 52, 53]
Leukocyte esterase and nitrite					
≥10 ⁵ cfu/mL	35–84	98–100	84	98	[48, 53]
≥10 ³ cfu/mL	0–45	62–98	0–66	42–99	[52, 53]
Leukocyte esterase and/or nitrite					
≥10 ⁵ cfu/mL	67–100	67–98	40–95	84–96	[28, 38, 48–50]
≥10 ⁴ cfu/mL	74–79	66–82	42–54	91–92	[49, 50]
≥10 ³ cfu/mL	71–84	41–83	49–81	46–90	[49, 50, 52]

Question 2

How did the laboratory criteria we use for UTI get established?

Urine Culture

- “Gold Standard” = Pyelonephritis or repeatedly positive urine cultures yielding $\geq 10^5$ CFU in *asymptomatic women*.
- 30 – 50% of women with “acute urethral syndrome” will have $< 10^5$ CFU.

Question 3

Can I treat for UTI when diagnostic testing doesn't support the diagnosis?

Symptoms of dysuria and frequency

- “Gold standard” = Response to antibiotics
- RCT evaluating symptomatic response to therapy with TMP/SMX versus placebo in women with dysuria and frequency but negative dipstick urinalysis.

Outcome	Placebo	TMP/SMX	P-Value
Dysuria Day 3	20/27 (74%)	5/21 (24%)	0.0005
Dysuria Day 7	11/27 (41%)	2/21 (10%)	0.02

P = NS for frequency

Question 4

So if symptoms predict outcomes in the absence of diagnostic testing, why'd you order so many tests Koeppe?
Can symptom driven therapy be effective in the absence of diagnostic tests?

Question 4

Can symptom driven therapy be effective in the absence of diagnostic tests?

Pre and post Telephone Guideline for UTIs (n = 3,889):

- Decreased use of Urinalysis and Culture
- Increased use of guideline recommended antibiotics
- **No difference in return visit for UTI within 60 days**
- **No difference in incidence of pyelonephritis within 60 days**
- **Trend toward more office visits for STDs within 60 days**
- Did not look at total amount of antibiotics used

Am J Med 1999;106:636-641.

Question 4

Can symptom driven therapy be effective in the absence of diagnostic tests?

Telephone Group vs. Control Group:

- **No difference in symptomatic relief**
- **No difference in satisfaction with care**
- Two patients in control group did not get antibiotics (n = 36) whereas all patients in the telephone group did (n = 36).

J Fam Pract 2001;50(7):589-594.

Question 4

Can symptom driven therapy be effective in the absence of diagnostic tests?

Patient Initiated antibiotics...

- 159/169 (94%) women correctly diagnosed infection:
 - 1 Case of Chlamydia.
 - 9 No other diagnosis found. Symptoms resolved.
- 158/169 (93.5%) clinical success rate.

Ann Intern Med 2001;135:9-16.

Case 2

71 y/o female with h/o IBS and 11 days poor appetite, nausea and diarrhea with intermittent constipation. Had some urinary burning earlier but took some OTC “Azo” and is not c/o this at time of visit.

POCT urinalysis: Small leuk esterase, trace blood

Subsequent data not available at time of visit...

Urine culture:
10⁴ – 10⁵ Group B Strep
10⁴ – 10⁵ Gardenerella
10³ – 10⁴ Mixed Gram Positive Flora

Question 5

Does treating positive findings in the urine in the absence of symptoms improve outcome?

Asymptomatic Bacteriuria is Common

Population	Prevalence, %	Reference
Healthy, premenopausal women	1.0–5.0	[31]
Pregnant women	1.9–9.5	[31]
Postmenopausal women aged 50–70 years	2.8–8.6	[31]
Diabetic patients		
Women	9.0–27	[32]
Men	0.7–11	[32]
Elderly persons in the community ^a		
Women	10.8–16	[31]
Men	3.6–19	[31]
Elderly persons in a long-term care facility		
Women	25–50	[27]
Men	15–40	[27]
Patients with spinal cord injuries		
Intermittent catheter use	23–89	[33]
Sphincterotomy and condom catheter in place	57	[34]
Patients undergoing hemodialysis	28	[28]
Patients with indwelling catheter use		
Short-term	9–23	[35]
Long-term	100	[22]

^a Age, ≥70 years.

Pyuria

32% Premenopausal women
30 – 70% Pregnant women

70% Diabetic women

90% Elderly institutionalized

30 – 75% Short term catheters
50 – 100% Long term catheters

Treatment of Asymptomatic Bacteriuria Hasn't Shown Benefit

Population	Outcome	Antibiotics N (%)	No antibiotics N (%)	p-value
Non-catheterized institutionalized males (1)	Infectious morbidity (IM) Mortality (M)	IM = 8/16 (50) M = 5/16 (31)	IM = 11/20 (55) M = 5/20 (25)	NS NS
Non-catheterized institutionalized females (2)	Genitourinary morbidity (GM) Adverse drug events (AE)	GM = 17/26 (65) AE = 9/26 (35)	GM = 13/24 (54) AE = 1/24 (4)	NS 0.03
Ambulatory elderly women (3)	Symptomatic UTI (SU) Ongoing bacteriuria (OB)	SU = 5/63 (8) OB = 36/55 (65)	SU = 10/61 (16) OB = 20/55 (36)	NS 0.02
Non-catheterized institutionalized women (4)	Mortality (M)	M = 30/166 (18)	M = 39/192 (20)	NS
Incontinent institutionalized men and women (5)	Frequency of incontinence (N = 176) Pre-antibiotics (PreA) Post-antibiotics (PostA)	PreA = 34%	PostA = 35%	NS
Diabetic women (6)	UTI hospitalization (UH) Other hospitalization (OH) Adverse drug events (AE)	UH = 3/55 (5) OH = 17/55 (31) AE = 18/55 (33)	UH = 5/50 (10) OH = 15/50 (30) AE = 6/50 (12)	NS NS 0.05

- 1) Lindsay, et al. NEJM 1983;309:1420-1425. 2) Lindsay, et al. Am J Med 1987;83:27-33.
3) Boscia, et al. JAMA 1987;257(8):1067-1071. 4) Abrutyn, et al. Ann Intern Med 1994;120(10):827-833.
5) Ouslander, et al. Ann Intern Med 1995;122(10):749-753. 6) Harding, et al. NEJM 2002;347(20):1576-1583.

Question 6

But is my patient really asymptomatic? What about the patient without dysuria, but with other non-specific symptoms I can't explain and positive findings on urinalysis and/or culture?

“Asymptomatic” bacteriuria (N = 72) in the elderly (f/u = 6 months)

Symptom	Worse w bacteriuria	Worse w/o bacteriuria	No change	p-value
Incontinence—awake	13.9%	16.7%	69.4%	NS
Incontinence—asleep	5.6%	8.3%	86.1%	NS
Incontinence—Cough or sneeze	2.8%	2.8%	94.4%	NS
Frequency	2.8%	5.6%	91.7%	NS
Urgency	5.6%	4.2%	90.3%	NS
Difficulty falling asleep	37.5%	36.1%	26.4%	NS
Difficulty staying asleep	33.3%	38.9%	27.8%	NS
Fatigue	34.7%	40.3%	25.0%	NS
Malaise	36.1%	33.3%	30.6%	NS
Anorexia	40.3%	34.7%	25.0%	NS
Weakness	31.9%	34.7%	33.3%	NS

“Asymptomatic” bacteriuria

- 14 of 54 patients with delirium had a UTI.
- 40 of 54 patients with delirium did not have a UTI.
- 69 patients with a UTI did not have delirium.
- 284 patients had neither a UTI or delirium.

OR for delirium with a UTI: 1.44, $p = 0.37$

- 9/14 patients delirium improved with therapy for their UTI
- 2/14 improved with treatment of other medical conditions
- 3/14 did not improve

Summary of questions and their “answers”

1. Does my patient with dysuria and frequency but without typical laboratory findings have a UTI?

Answer: I don't know, but I suspect she does.

2. How were the laboratory criteria we use to diagnose UTIs developed.

Answer: Leukocyte esterase test and nitrite test were developed to predict bacteriuria. Culture criteria were developed from patients with pyelonephritis and asymptomatic bacteriuria but not cystitis. Bacteriuria itself doesn't predict outcome...

3. Is it reasonable to treat a patient with dysuria and frequency but w/o supportive diagnostic testing for UTI?

Answer: This is probably reasonable when a better alternative diagnosis isn't available.

Summary of questions and their “answers”

4. Can symptom driven therapy be appropriate in the absence of diagnostic testing?

Answer: In women w/o frequent or recurrent UTIs or concern or STDs, empiric therapy is appropriate.

5. Does treating asymptomatic bacteriuria improve outcomes?

Answer: No. *Note: This does not apply to pregnant women or those undergoing urologic procedures.*

6. Does treating patients with non-specific symptoms and positive urinalysis/urine culture findings (but w/o dysuria or frequency) improve outcome?

Answer: My opinion is that while occasionally frail elderly patients with little reserve may benefit from antibiotics; in most cases it's probably true, true, unrelated and antibiotics are not indicated.

Part 2
Superficial Skin and Soft Tissue
Infections

Case 3

43 y/o male presents with a erythematous lesion on left thigh (3 cm x 3 cm) with a central area of fluctuance. The lesion is drained with expression of 1 – 2 cc purulent drainage.

Question 1

Does my patient need an antibiotic after superficial abscess drainage?

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Does my patient need an antibiotic after superficial abscess drainage?

Study	Success with no antibiotics or inactive antibiotics		OR (C.I.)
Rajendran 2007	145/166 (87%)	--	--

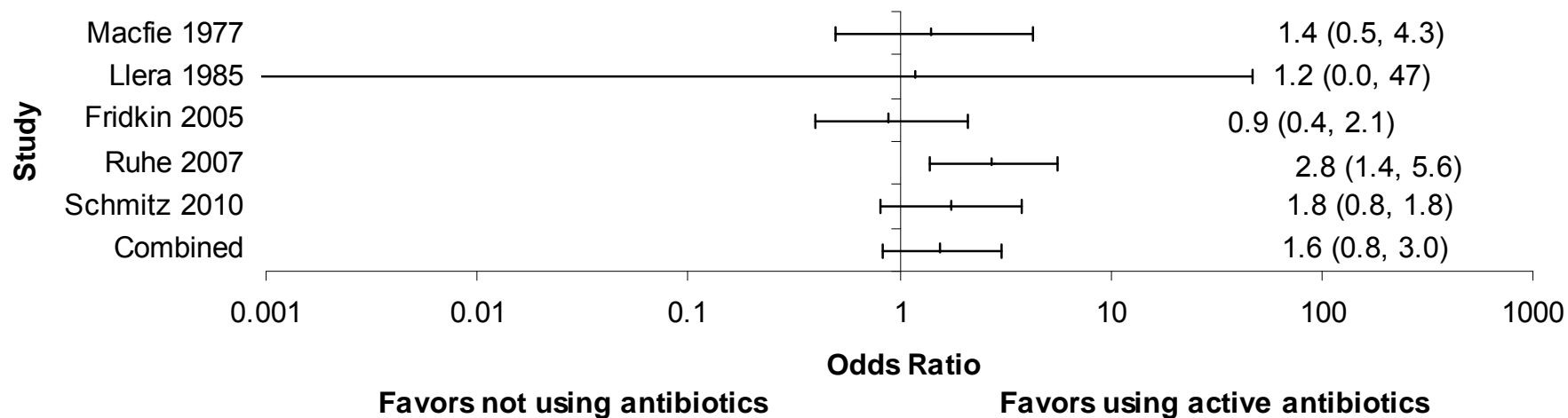
Study	Success with no antibiotics	Success with active antibiotics	OR (C.I.)
Schmitz 2010*	75/102 (74%)	73/88 (83%)	1.8 (0.82 – 3.78)
Llera 1985*	22/23 (96%)	26/27 (96%)	1.2 (0.0 – 46.5)
Macfie 1977*	77/85 (91%)	125/134 (93%)	1.4 (0.5 – 4.3)
Meislin 1977	100/100 (100%)	35/35 (100%)	NC

Study	Success inactive antibiotics	Success with active antibiotics	OR (C.I.)
Ruhe 2007	190/219 (87%)	296/312 (95%)	2.8 (1.4 – 5.6)
Fridkin 2005	44/59 (75%)	46/64 (72%)	0.9 (0.4 – 2.1)
Lee 2004	57/62 (92%)	5/5 (100%)	NC
Young 2004	44/44 (100%)	105/105 (100%)	NC

Question 1

Does my patient need an antibiotic after superficial abscess drainage?

Effect of Antibiotics Excluding Rajendran '07 (and Lee '04, Young '04 and Meislin '77)



Case 4

54 y/o female with DM presents with a 2 week h/o right ear lobe swelling. On exam ear lobe is swollen but without significant erythema or warmth. No drainable focus is noted. Given a diagnosis of cellulitis.

Question 2

Does my patient need MRSA coverage for her cellulitis?

Question 2

Does my patient need an MRSA coverage?

422 patients with skin and soft tissues prospectively studied at ERs in 11 different U.S. cities during August 2004.

- MRSA 59% (15% - 68%)
- MSSA 17% (0% - 40%)
- Other bacteria 15% (7% - 32%)
- Culture Negative 9% (0 - 20%).

Question 2

Does my patient need MRSA coverage?

Study Population	Outcome
Retrospective case-control study of children 0 – 21 with soft tissue infections (cellulitis, abscesses, other), n = 584 (1)	OR Treatment Failure (TMP/SMX)/(β-Lactam) = 2.4 (1.3–4.3)
Retrospective cohort study of adults ≥ 18 y/o with skin and soft tissue infection (subgroup with cellulitis only), n = 117 (2)	OR Treatment Success (TMP/SMX)/(Cephalexin) = 5.7 (1.4–23.2) (79% Cephalexin; 96% TMP/SMX)
Prospective observational study of adults ≥ 18 y/o with cellulitis only, n = 179. All received Beta-lactam therapy (3).	(131/179) 73.2% evidence of β-hemolytic strep (BHS) (serology or blood culture). 96% success rate overall 91% success rate in patients w/o evidence of BHS

1) Pediatrics 2009;123(6):e959-e966. 2) Am J Med 2010;123:942-950. 3) Medicine 2010;89(4):217-226.

Summary of questions and their “answers”

1. Does my patient need an antibiotic after superficial abscess drainage?

Answer: Most patients do not need antibiotics if adequate drainage has been obtained.

2. Does my patient need MRSA coverage for her/his cellulitis?

Answer: Most cases of cellulitis without drainable source appear to still be responsive to β -lactam therapy (therapy directed at Strep and MSSA).

Part 3
HPV Screening among MSM

Case 5

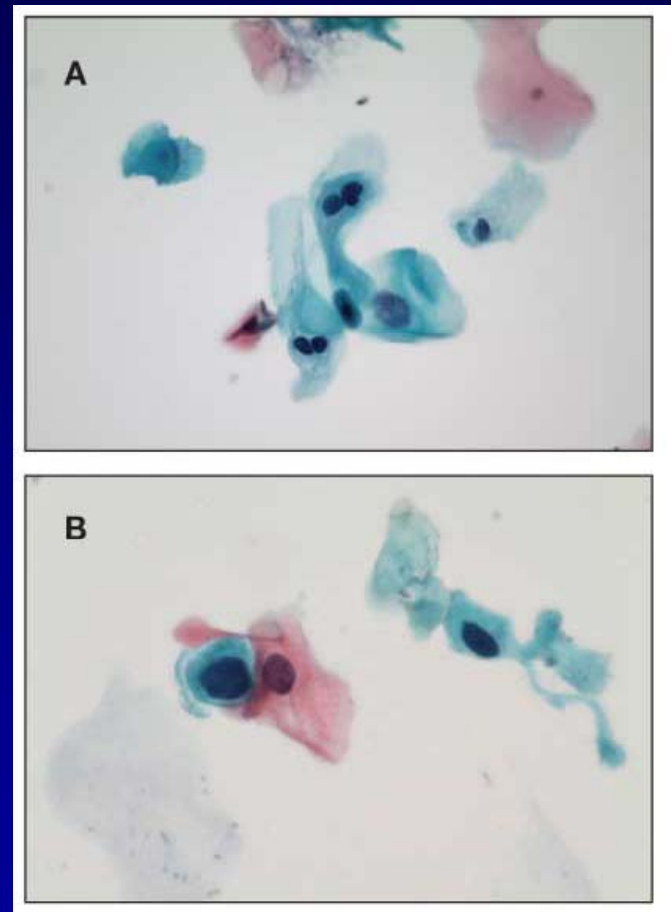
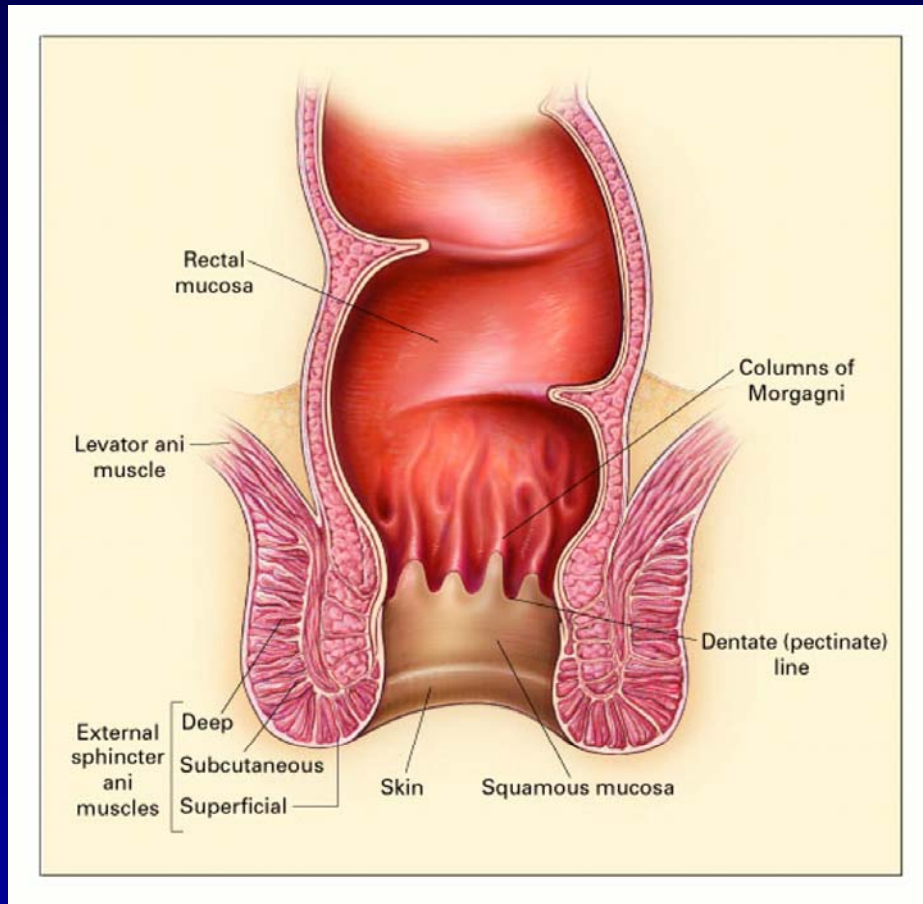
32 y/o gay male in for routine care. In monogamous relationship but he and partner are planning to move into an open sexual relationship. He was tested for HIV 6 months ago and was negative at that time.

Question

Should I perform an anal pap smear to look for HPV related disease?

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NEJM 2000;342:792-800.

AIDS Reader 2009;19(5):178-186.

Question

Should I perform an anal pap smear to look for HPV related disease?

Parameter	HIV Negative MSM	HIV Positive MSM
High Risk HPV Positive	34 – 42% (1,2)	56 – 95% (3)
Atypia on cytology (Anal pap)	31 – 62% (1,2)	41 – 97% (3)

1) Ann Intern Med 2008;149:300-306. 2) Dis Colon Rectum 2009;52:239-247. 3) CID 2006;43:223-233.

Question

Should I perform an anal pap smear to look for HPV related disease? How often does this become anal cancer?

Anal cancer incidence among persons with HIV

- 19.0 cases / 100,000 person years 1992 – 1995
- 48.3 cases / 100,000 person years 1996 – 1999
- 78.2 cases / 100,000 person years 2000 – 2003

~ Prevalence anal dysplasia among MSM with HIV

- 40,000 – 95,000 years dysplasia / 100,000 person years

Cases of carcinoma per cases of dysplasia

- Around 1 case anal carcinoma per 1000 persons years of dysplasia among persons with HIV?

Question

Should I perform an anal pap smear to look for HPV related disease?

What do guidelines recommend?

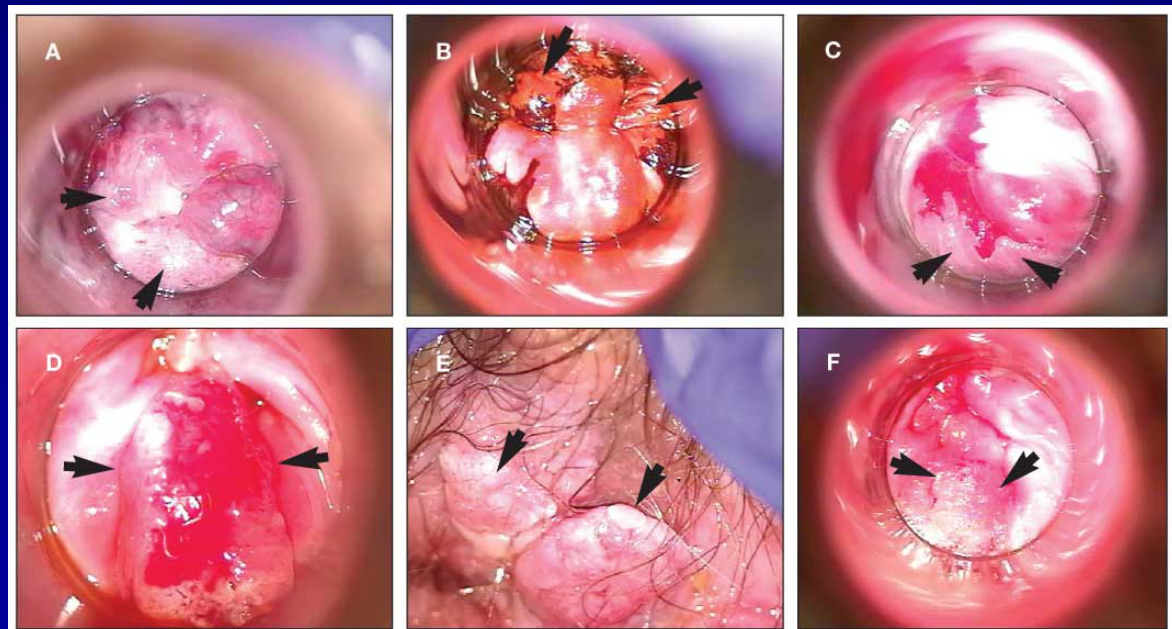
- Digital Rectal Exam (B III)
- Anal pap smear (C III)
- No recommendation to do HPV DNA testing

Question

Should I perform an anal pap smear to look for HPV related disease?

So I did a anal pap smear and it came back positive... Now what?

- Guidelines recommend referral for high resolution anoscopy (HRA) (B III)



Question

Should I perform an anal pap smear to look for HPV related disease?

- Guidelines give anal pap smears a grade C III recommendation... Thus your right if you do and your right if you don't...
- I perform DRE on my patients and only do anal pap smear if I feel anything abnormal.
- If I find atypia (I almost always do) I then refer to HRA. To my knowledge only Craig Nielsen in the ID Clinic is doing these at UCH.

Part 4

Pharmacotherapy for HIV Prevention

Case 5

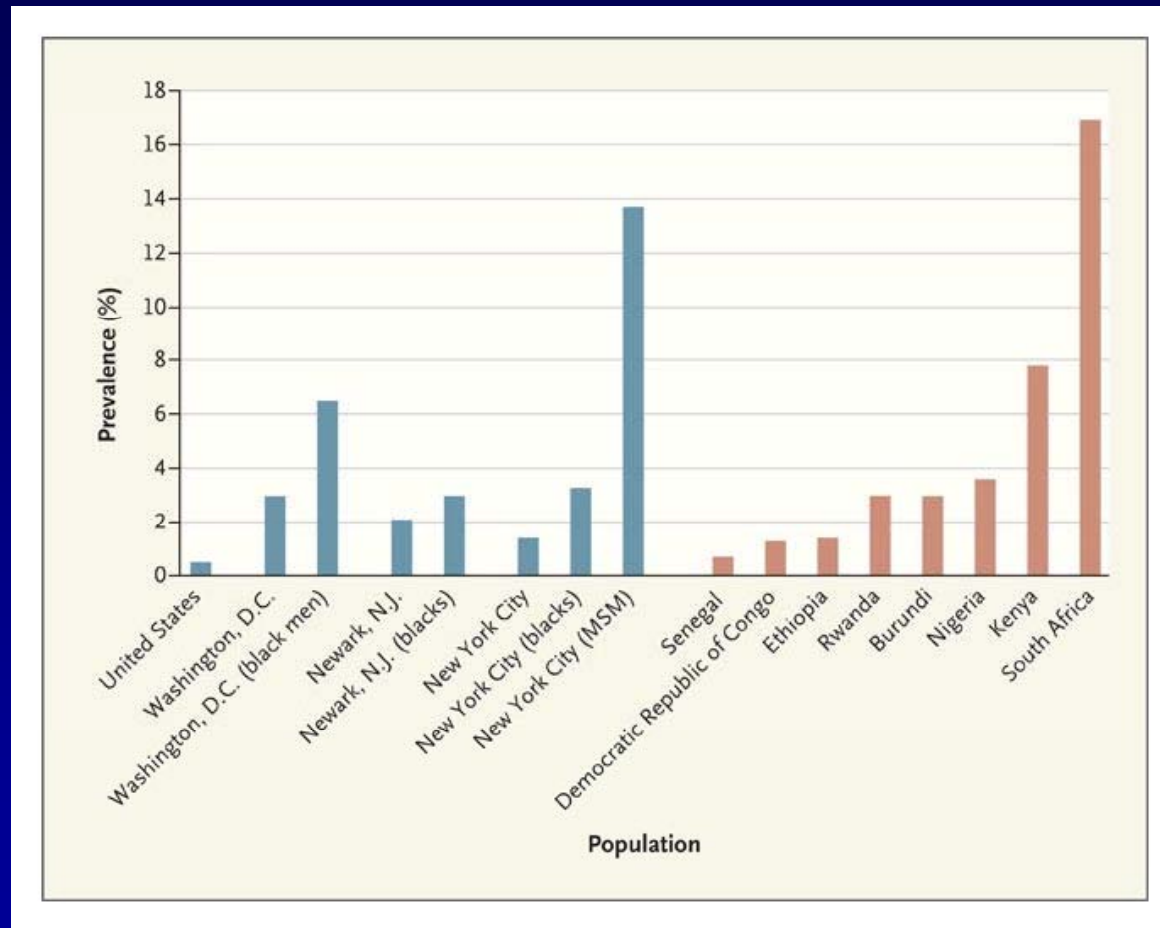
32 y/o gay male in for routine care. In monogamous relationship but he and partner are planning to move into an open sexual relationship. He was tested for HIV 6 months ago and was negative at that time.

Question

Should I recommend medication to prevent HIV, in addition to condoms?

Question

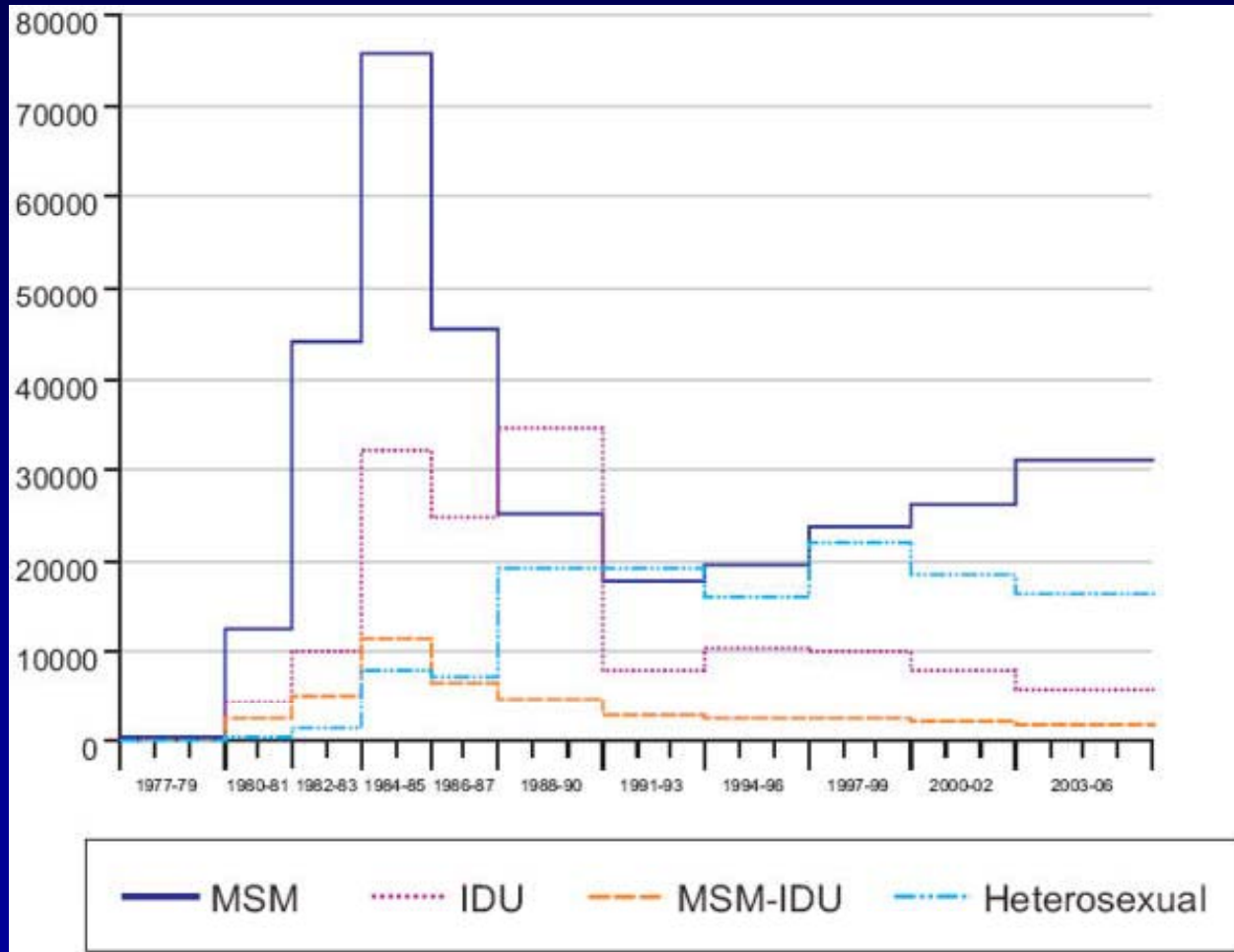
Should I recommend medication to prevent HIV, in addition to condoms?



MSM represent 2% of US population but 53% of those living with HIV (CDC, NEJM 2010;362:967-970.)

Question

Should I recommend medication to prevent HIV, in addition to condoms?



Question

Should I recommend medication to prevent HIV, in addition to condoms?

Study Design	Baseline Risk	New HIV Infections
RCT comparing Truvada (TNF/FTC) daily with placebo, N = 2,499	<u>High risk MSM</u> # Partners / 12 weeks: 18 (+/- 35) Truvada 18 (+/- 43) Placebo Unprotect anal intercourse with person of HIV+ or HIV unknown / 6 months: 79% Truvada 81% Placebo	Placebo = 64 3.85 / 100 pt yrs TNF/FTC = 36 2.16 / 100 pt yrs P = 0.005

Question

Should I recommend medication to prevent HIV, in addition to condoms?

Concerns I have:

1. Toxicity
 - Median F/U 1.2 years
 - Does lack of AE over 1.2 years translate into longer periods of taking these medications?

Question

Should I recommend medication to prevent HIV, in addition to condoms?

Concerns I have:

2. Cost

- NNT ~ 59
- Cost per 1 year Truvada \$14,783.35
- Cost per case of HIV prevented ~ \$ 872,218

Question

Should I recommend medication to prevent HIV, in addition to condoms?

Concerns I have:

3. Will taking pill that “prevents HIV” really have an effect on risk taking behavior?
 - Self reported high risk sexual behavior decreased in both groups (NEJM 2010;363(27):2587-2599.).
 - Studies of counseling have consistently shown self reported high risk sexual behavior decreases with counseling (J AIDS 2002;30:177-186. AIDS 2005;19 Suppl 1. J AIDS 2007;44:569-577. PLoS Med. 2010 Aug 24;7(8):e1000329.)
 - But incidence of HIV and syphilis are increasing among MSM in the US... (JAMA 2008;300(5):520-529. Ann Intern Med 2011;155(3):145-151. <http://www.cdc.gov/nchstp/newsroom/HIVIncidencePressRelease.html>.)

Question

Should I recommend medication to prevent HIV, in addition to condoms?

Concerns I have:

3. Will taking pill that “prevents HIV” really have an effect on risk taking behavior?

Study Design	Questions and Odds Ratio for testing HIV + with positive answers to questions
Questionnaire regarding HAART and HIV among MSM who had never been tested for HIV or previously tested negative. Correlates with subsequent HIV tests. N = 1575	HAART mitigates HIV susceptibility = 1.83 (1.29–2.59) HAART mitigates HIV severity = 1.65 (1.17–2.33) HAART reduces my concern about HIV = 2.94 (2.12 – 4.07)

Question

Should I recommend medication to prevent HIV, in addition to condoms?

Concerns I have:

4. Recent FEM-PrEP trial (identical design except in sero-discordant heterosexual couples) halted early due to no evidence of protection in women taking Truvada compared to men

(<http://aids-clinical-care.jwatch.org/cgi/content/full/2011/425/1>).

Question

Should I recommend medication to prevent HIV, in addition to condoms?

What I would do... Counsel to wear condoms but not prescribe.

- Best approach to counseling?

**Questions, Comments, Rebuttals on any of
this???**