NAAT identified chlamydial infections: Enhanced sensitivity, reduced transmissibility?

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C. trachomatis (Ct) infections present a significant public health risk

- Among most prevalent of all STIs
- Bacterial STI; Abx Rx
- Most common among young adults
- Many Ct infections are asymptomatic
- Untreated infection associated with significant morbidity

Nucleic acid amplification tests (NAAT)

- Provide powerful tools for evaluating the epidemiology of Ct
- Can be used with urine, self-administered vaginal swab specimens
- Enhanced sensitivity (>90%) in comparison to traditional assays, e.g. culture
- Ability to test asymptomatic patients

National surveys using NAAT

- National Longitudinal Study of Adolescent Health (Miller et al., 2005)
  - 4.7% U.S. females, 3.7% males aged 18-26 Ct+
  - 14% African American females, 11.1% AA males
  - Majority asymptomatic
- National Survey of Adolescent Males (Ku et al., 2002)
  - 3.1% U.S. males aged 18-19, 4.5% aged 20-26 Ct+

Regional studies using NAAT

- 1997-98 Baltimore STD and Behavior Survey (Turner et al., 2002) (Probability sample of household population)
  - 3% untreated infection (overall)
  - 8% ages 18-20
  - 6.4% African American;
  - >90% asymptomatic
- Other Findings:
  - Few reports of recent STI risk behaviors among NAAT+
  - Untreated infections exceeded no. of treated infections reported to Health Department

NAAT-identified Ct infections

- Are they clinically relevant?
- Are these infections transmissible?
- What is their public health significance?

Ct Transmissibility Study

- Evaluate whether the probabilities of infection transmission, as estimated by concordance of infection between partners, are equivalent for Ct infections that are detectable only by NAAT (N+) versus infections that are detectable by traditional assay (T+)

Hypothesis:

N+/T- are associated with *less* concordance than N+T+

Study design

- Screening and Index Subject Recruitment
  - JHH ED, Nov 2002-Feb 2005
  - 18-35, sexually active
  - Interview (ACASI)
  - NAAT for Ct (urine, vaginal swab)
- NAAT-positives identified, recruited for follow-up
  - Trained DIS (disease intervention specialists)
  - Referral to General Clinical Research Center (GCRC), JHH

Study design (cont)

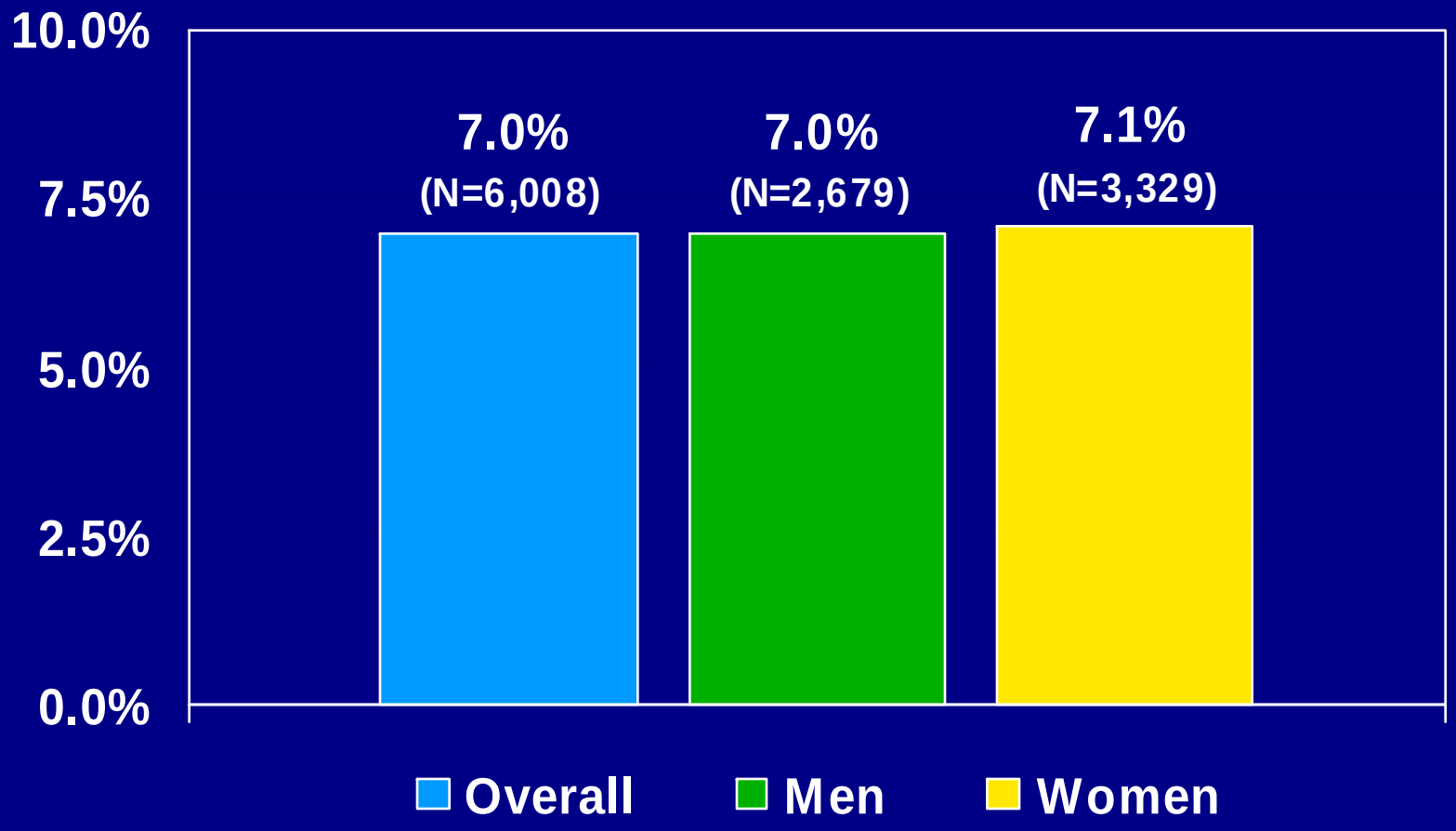
- Index Follow-up Visit
  - clinical exam and treatment
  - Interview (ACASI) on risk behaviors
  - NAATs: Urine/swab, clinician collected swab
  - Traditional assay: Culture/DFA for Ct
- Partner recruitment
  - Same as above

Results: Index subject recruitment

- 14,188 ED patients approached to determine eligibility

- 6,952 eligible
  - 6,094 (88%) consented to participate, provided a specimen for NAAT

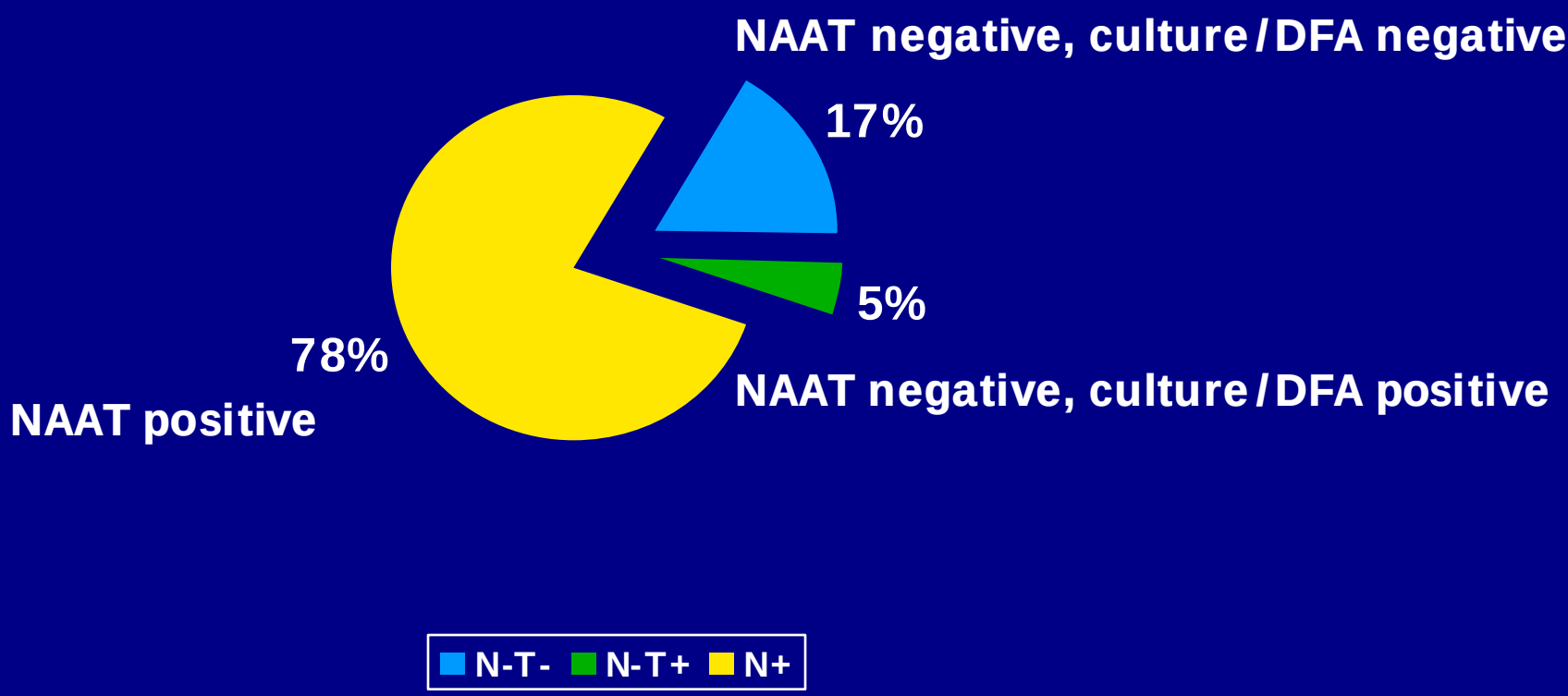
Results: ED Screening for Ct



Index follow-up and evaluation

- 419 Ct+ subjects
  - 81 (19%) Abx treatment
  - 338 Ct+ eligible for follow-up
- 166 (49%) enrolled
  - Enrolled subjects younger, female
  - Median time to follow-up: 21 days

Persistence of NAAT-identified infections at follow-up



Persistence of NAAT-identified infections

- Negative NAAT at follow-up associated with:
  - Female (RR=3.6, 95% CI 1.3, 9.9)
  - Antibiotic use in 3 months prior to ED screening (RR=2.6, 95% CI 1.2, 5.5)

Partner Evaluation

175 partners identified

152 contacted by disease intervention specialists

50 partners not enrolled

102 partners of CT+ index subjects enrolled

19 partnerships excluded

83 partnerships with NAAT and traditional assays results

Evidence of Ct transmission

- Transmission defined by concordance within partnerships

- Concordance definition:

  Positive NAAT (N+) or traditional assay (T+) for *C. trachomatis* among partners of Ct(+) index subjects

Ct concordance within partnerships

	Partner		
Index	Concordant	Non-concord.	
N+T+	**39 (75%)**	13 (25%)	52
N+T-	**14 (45%)**	17 (55%)	31
	53 (64%)	30 (36%)	

Prevalence ratio= 1.7 95% CI 1.1, 2.5

Infection concordance within partnerships

- Associated with timing of partner visit
- Persistent infections positively associated with partner concordance
  - 70% of partners of Ct+ index at follow-up vs. 11% of partners of Ct- index at follow-up

What is the meaning of a NAAT positive/culture negative Ct infection?

- 'True' infection
- Low organism burden from enhanced NAAT sensitivity
- Infection clearance
  - Lack of persistence among women
  - Non-persistent NAAT and reduced partner concordance
- Residual DNA from controlled or treated infection
  - Non-persistent NAAT and antibiotic use
- Measurement error
  - Sampling variation
- False positive result?

Summary

- NAAT-only infections are less transmissible, as measured by partner concordance
- 45% NAAT-only infections detected in partners
- 21% of NAAT-positive had no evidence of infection at follow-up (median=21 days)

Other considerations

- Cannot determine direction of infection transmission
- Recruitment of partnerships difficult and costly

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