EDITORIAL

Growing Evidence Supports an Implementation Shift Toward Vaginal Sampling for *Chlamydia trachomatis, Neisseria gonorrhoeae,* and *Trichomonas vaginalis* Screening

Sarah M. Wood, MD, MSHP[1,2,3]

Alexander G. Fiks, MD, MSCE[1,3,4]

[1]Department of Pediatrics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

[2]Division of Adolescent Medicine, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania

[3]Clinical Futures, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania

[4]Division of General Pediatrics, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania

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In the first article in an ongoing series on sexual and reproductive health in the *Annals of Family Medicine*, Dr Kristal Aaron and colleagues present a rigorous meta-analysis on the comparative efficacy of vaginal—compared with urine—samples for molecular detection of sexually transmitted infections in female-sex-at-birth individuals.[1] Their findings, from 28 rigorous studies, yielded pooled sensitivity estimates for urine, compared with vaginal specimens, that were 7.2%, 5.8%, and 4.9% lower for *Chlamydia trachomatis*, *Neisseria gonorrhoeae,* and *Trichomonas vaginalis*, respectively, with statistically significant odds ratios for chlamydia and gonorrhea. Since 2014, guidelines from the Centers for Disease Control and Prevention (CDC) recommend self- or clinician-collected vaginal swabs as the preferred specimen for nucleic acid amplification testing (NAAT) in female-sex-at-birth patients.[2] However, clinical practice has lagged. Urine continues to be the common sample type across settings, if screening occurs at all.[3]

Although these sensitivity differences may seem small, they must be considered in the context of widespread and rising chlamydia and gonorrhea prevalence and associated morbidities.[4] Given that chlamydia is the most common reportable bacterial infection in the United States, the population health impact of this sensitivity gap is substantial. In their Discussion section, the authors note that continued urine sampling could lead to >400,000 missed cases of chlamydia and gonorrhea annually.

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CORRESPONDING AUTHOR

Sarah M. Wood
Children's Hospital of Philadelphia
Roberts Center for Pediatric Research
2716 South Street, Suite 11212
Philadelphia, PA 19146
WOODSA@email.chop.edu

As clinicians caring for adolescents, we interpret these findings, which represent the first head-to-head comparison of pooled data from commercially available NAATs on simultaneously collected urine and vaginal samples, as necessitating a shift in practice. Over one-half of sexually transmitted infections (STIs) occur in female-sex-at-birth individuals aged 15-24 years, who also bear a high probability of infection recurrence.[5] Transitioning to vaginal, rather than urine, specimens in our patients could have critical population health impact by increasing early treatment and reducing downstream transmission. Chlamydia screening reduces the risk of pelvic inflammatory disease and its complications, including infertility, chronic pelvic pain, and ectopic pregnancy. Thus, adopting more sensitive screening strategies also supports 2 key tenets of reproductive justice for patients entering their peak reproductive years[6]—maintaining personal bodily autonomy and preserving the right to have children when desired.[7]

Unfortunately, chlamydia screening rates for US adolescents are already far below targets, even using noninvasive urine testing. The CDC, American Academy of Pediatrics, and US Preventive Services Task Force (USPSTF) recommend annual chlamydia screening in sexually active adolescent female-sex-at-birth individuals.[8-10] Yet only 53% of sexually active such individuals aged 16-24 years are screened,[11] and screening is often inequitable, with lower screening rates in White and privately insured patients.[12,13] Multifactorial determinants of insufficient screening include limited visit time, confidentiality concerns, implicit bias, and clinician discomfort around discussing sexual health with adolescents. Unfortunately, these screening barriers also translate to barriers to adopting vaginal sampling. In settings serving pediatric patients, vaginal sampling likely requires new workflows for teaching patients self-sampling techniques or for clinicians explaining and collecting specimens. Obtaining vaginal swabs confidentially also presents challenges. Most parents are acculturated to urine collection, which typically

does not raise a "red flag" about sexual activity. Vaginal sampling, however, is less discreet and not a common pediatric procedure. Chlamydia screening quality improvement interventions have benefited from "sample first" strategies where urine is obtained at visit intake.[14] Introducing vaginal sampling early in visits, without sufficient discussion, may have unintended consequences of alienating patients or families. Lastly, clinicians may insert their own biases about perceived lack of acceptability for vaginal swabs for adolescents, and be less likely to offer the procedure than a urine screen.

Given these barriers, we are left with a key question: Is the "best" STI test for this highly vulnerable population simply the test we can easily obtain? This argument has long supported use of urine-based screening, allowing clinicians to accept pragmatic tradeoffs between screening effectiveness (using the most sensitive sample) and screening reach (screening the widest and most equitable sample). However, Dr Aaron et al provide sufficient data to demonstrate that defaulting to urine simply isn't enough. As the authors note, "We cannot continue to justify the use of urine except for women for whom collection of a vaginal sample is not acceptable."[1] With the need to curb rising STI rates and preserve patient fertility and quality of life, how should clinicians caring for adolescents proceed?

In addressing evidence-to-implementation gaps, the answer is never simple. We can turn to implementation science, however, to elicit the barriers and harness the facilitators of this practice shift among patients, clinicians, clinics, and health systems. The authors ask in their Discussion section, "What will it take to convince health care clinicians to change their STI testing patterns?" While this critical question needs addressing, placing the onus of change on clinicians alone will be insufficient to move the needle. Rather, improvement frameworks must also engage adolescents in youth-centered research to explore message framing to maximize acceptability of a more invasive and sensitive sampling type in primary care settings. Most acceptability research has compared vaginal sampling to pelvic exams, or compares vaginal and urine samples in STI clinics or detention facilities.[15,16] We also need to consider parents and guardians as stakeholders, as parental involvement in sexual health discussions, when acceptable to adolescents, can improve sexual health outcomes.[17] Successful programs will need to operationalize vaginal sampling within the clinic context, considering time limitations, multi-disciplinary staffing structures including nurses and medical assistants, supply chain, and workflows. Finally, the culture shift to vaginal sampling may be best disseminated through learning health systems, quality improvement collaboratives, or professional associations, which can track sample source as a quality metric.[18]

So where does this leave the urine sample? Although vaginal sampling for chlamydia and gonorrhea has higher efficacy than urine, the clinical effectiveness of adolescent STI screening programs will likely continue to utilize urine sampling when vaginal swab procurement is unacceptable to the patient or infeasible for the setting. Urine testing thus arguably still has a role, particularly as more community-based programs shift from targeted screening of sexually active teens to universal opt-out screening irrespective of sexual history.[19] These programs will need to balance substantially broadening the reach of screening and simplifying screening processes. In targeted screening programs of sexually active female-sex-at-birth individuals, which is the current CDC and USPSTF-recommended practice, the first offer should be for vaginal sampling, and if declined, always be followed by offering urine testing. In these cases, an inferior test will certainly be better than absence of screening. And critically, we should engage patients in shared decision making about testing methods that considers both method efficacy and the adolescent's bodily autonomy. Rather than making biased assumptions about adolescent preferences, framing the vaginal sample as more accurate may shift some reluctant adolescents toward acceptance of self- or clinician-collected vaginal sampling.

The data from Dr Aarons and colleagues has given us a strong push to change our testing practices. Family practitioners, pediatricians, and health systems will need to rise to this implementation challenge. As testing technologies advance, this pressure will only grow. Nearly all point-of-care STI testing devices, which are beginning to come to market, have validated their platforms on vaginal, rather than urine, samples.[20,21] By engaging now in implementation and quality improvement efforts with patients, clinicians, clinic staff, and health systems, we can improve the quality, sensitivity, and reach of testing for adolescents and meaningfully improve adolescent health.

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Key words: adolescent health; women's health; *Chlamydia trachomatis*; *Neisseria gonorrhoeae*, *Trichomonas*

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