REPORT TO CONGRESS

Infertility and Prevention of Sexually Transmitted Diseases
2000 - 2003

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Executive Summary

Section 318A(o)(2) of the Public Health Service (PHS) Act requires the Secretary to submit a Report to Congress on the implementation of a grant program for the prevention of sexually transmitted disease (STD)-related infertility. This is the fourth Report to Congress. It covers 2000 to 2003, and follows the report for 1997 to 1999.

Findings of the Report:

- To begin addressing STD-related infertility prevention, Congress appropriated funds in 1993 to support the development of an Infertility Prevention Program (IPP). Through a cooperative effort between the Centers for Disease Control and Prevention (CDC) and the Office of Population Affairs (OPA), the program supports collaboration among Title X family planning clinics, STD clinics, and public health laboratories.
- Since 1993, significant progress has been made where chlamydia screening programs have been in place for several years. For example, between 1988 and 2003, screening programs in Region X (Alaska, Idaho, Oregon, and Washington) have demonstrated a decline in chlamydia positivity* of 50% (from 13.0% to 6.5%) among 15 to 44 year-old women in participating family planning clinics. For women 15 to 24 years old, chlamydia positivity declined 52% from 15.1% to 7.2%.
- Since the inception of the IPP, there has been substantial expansion of chlamydia screening activities beyond family planning and STD clinics in an effort to reach additional high-risk women in other settings such as juvenile detention and other correctional facilities, adolescent health centers, community health centers, school-based programs, and Indian Health Service clinics.
- There has been substantial expansion of chlamydia screening in family planning and STD clinics since the inception of the program. Programs have also extended screening activities beyond family planning and STD clinics to high-risk women in juvenile detention and other correctional facilities, adolescent health centers, community health centers, school-based programs, and Indian Health Service clinics.
- In 2003, 877,478 cases of chlamydial infection were reported to CDC, more than twice the number of reported cases of gonorrhea. This represents a 5.1% increase over the number of chlamydia cases reported in 2002. The number of chlamydia cases will probably continue to increase as more women and men are screened, more sensitive test technologies are used, and reporting systems improve.

* Positivity is the number of women who test positive divided by the number of women who are tested (includes both positive and negative tests). For example, if 100 women are tested and 10 are positive, the positivity is 10%.

- The chlamydia prevalence monitoring system is well established and an important component of the surveillance system. Data from multiple sources on prevalence of chlamydial infection in defined populations have been useful in monitoring disease burden. In 2003, the median state-specific prevalence among women 15 to 24 years of age screened in family planning clinics was 5.9%. Data from other sites (prenatal, juvenile detention, correctional facilities, National Job Training Program) indicate a continuing high prevalence of infection especially among women less than 25 years of age.
- Progress in research and evaluation studies has been made, especially in evaluation of screening test performance. In 2002, CDC published new laboratory guidelines for gonorrhea and chlamydia testing that reflect the findings of the evaluation studies.
- Despite the CDC's 1993 recommendation to screen all sexually active women 15 to 19 years of age for chlamydia on an annual basis, national data from 2000 estimate the median state-specific proportion of sexually active females aged 15 to19 years screened was only 60%.
- Data from the 2002 Health Plan Employer Data and Information Set (HEDIS) also indicate that chlamydia screening of young (16 to 20), sexually active women in commercial managed care settings is even lower (27%) than estimates for the whole population of sexually active young women.
- Screening programs for men are limited. Recent research findings suggest that recurrent infections in women may be the result of reinfections from untreated male partners and that improved partner management strategies could reduce the high rate of reinfections and related consequences for women's health and fertility. CDC is evaluating whether screening men can prevent serious health consequences in women and whether screening men is feasible, cost-effective, and acceptable to men.
- Chlamydial and gonococcal infections remain the most frequently reported STDs in the United States. Women, especially young women, are disproportionately affected by these infections and their consequences. Access to chlamydia screening and treatment for chlamydia is the primary prevention strategy to reduce prevalence of this infection. Since 1993, the National IPP has made great strides in expanding chlamydia screening to young women in public sector settings. However, reported cases of chlamydial infections are expected to continue to rise as screening expands, more sensitive tests are used, and reporting practices improve.

Report to Congress
Infertility and Sexually Transmitted Diseases

Introduction

More than 50% of all preventable infertility among women is a result of sexually transmitted diseases (STDs), primarily chlamydial infection and gonorrhea.[1] These STDs are caused by the bacterial organisms *Chlamydia trachomatis* and *Neisseria gonorrheae*. In 2003, 877,478 chlamydial infections were reported to the Centers for Disease Control and Prevention (CDC) – more than double the number of reported gonorrhea infections.[2] This makes chlamydia the most frequently reported bacterial STD in the United States. However, because most infected women, and at least one half of infected men, have no symptoms or have such mild symptoms that they do not seek medical care, many infections go undetected and are not reported or counted. In fact, it is estimated that 2.8 million new chlamydial infections occur each year in the United States.[3]

Untreated chlamydia can cause severe and costly reproductive and other adverse health consequences, including pelvic inflammatory disease (PID), which can lead to infertility. An estimated 10%-40% of women with untreated chlamydia will develop PID.[4] Of those with PID, it is estimated that 20% will become infertile; 18% will experience debilitating, chronic pelvic pain; and 9% will have a life-threatening ectopic pregnancy.[5] Chlamydia may also result in adverse outcomes for babies, including neonatal conjunctivitis and pneumonia.[6] Estimated tangible costs of *Chlamydia trachomatis* illness in the United States exceed $2.4 billion annually.[7] Data from a randomized controlled trial of chlamydia screening in a managed care setting suggest that screening programs can lead to a reduction in the incidence of PID by as much as 60%.[8] These data, combined with the asymptomatic nature of chlamydial infections, make routine screening in a variety of clinical and non-clinical settings the cornerstone of effective chlamydia prevention and control.

In addition to causing irreversible, adverse reproductive tract consequences in women, chlamydial infections are estimated to increase the risk of HIV transmission at least three to five fold among adults.[9] While genital ulcer infections have long been known to increase the risk of HIV transmission, more recent studies suggest that inflammatory STDs, such as chlamydia and gonorrhea, also increase risk for HIV acquisition and transmission.[10] The large number of chlamydial infections in the United States offers further rationale for implementing comprehensive chlamydia prevention and control efforts as a way to reduce the sexual spread of HIV infection.

The continuing high burden of infection and its silent nature make chlamydia a major public health concern that CDC is seeking to address through the National Infertility Prevention Program (IPP). The national program is based on the successful chlamydia screening demonstration project initiated in Health and Human Services (HHS) Region X (Alaska, Idaho, Oregon, Washington) in 1988. Based on the Preventive Health Amendments of 1992 which

authorized what is now known as the Infertility Prevention Program, the project expanded to include federal HHS Regions III (Delaware, Maryland, Pennsylvania, Virginia, West Virginia, and District of Columbia), VII (Iowa, Kansas, Missouri, and Nebraska), and VIII (Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming) in 1993. As funds expanded, CDC phased in the remaining HHS regions in 1995. IPP funds support screening and treatment of low-income and young sexually active women served in a variety of public health settings. In addition to providing screening and treatment services, CDC supports a chlamydia prevalence monitoring surveillance system to monitor trends in disease and to evaluate program impact. Laboratory, behavioral, and clinical research are also conducted to supplement the information gathered through the chlamydia prevalence monitoring surveillance system.

This Report to Congress highlights key activities of the National IPP undertaken by CDC and its partners during 2000-2003, and is divided into four sections: (I) Chlamydia Prevalence Monitoring and Surveillance Trends, (II) Service Delivery and Regional Infrastructure, (III) Promoting Chlamydia Screening in the Private Sector and (IV) Program Research and Evaluation Activities.

I. Chlamydia Prevalence Monitoring and Surveillance Trends

Chlamydia trachomatis infection is the most commonly reported notifiable disease in the United States.[11] It is among the most prevalent of all STDs and, since 1994, has comprised the largest proportion of all STDs reported to CDC.[12] The increase in reported chlamydial infections during the 1990s reflects the expansion of screening activities, increased use of the most sensitive diagnostic tests, an emphasis on case reporting from providers and laboratories, and improvements in reporting systems. Increases in reported chlamydial infections are likely to continue as screening expands to more public and private medical settings. In 2000, the Health Plan Employer Data and Information Set (HEDIS) introduced a measure for chlamydia screening of sexually active women, 16 through 26 years of age, who receive their medical care through managed care organizations. The promulgation of and adherence to this measure are also likely to increase screening and reporting practices in the private sector.[13]

In 2003, 877,478 chlamydial infections were reported to CDC from 50 states and the District of Columbia. The overall rate of chlamydial infection among women (466.9 cases per 100,000 females) was over three times the rate among men (134.3 cases per 100,000 males), reflecting in part the large number of women screened for this disease. However, with availability of nucleic acid amplification tests (NAAT) using urine specimens, men are increasingly being tested for chlamydial infection. From 1999-2003, the reported chlamydial infection rate in men increased by 46.6% (from 91.6 to 134.3 cases per 100,000 males) compared with an 18.2% increase in women over this period (from 395.1 to 466.9 cases per 100,000 females).[14]

The highest age-specific reported rates of chlamydia among women in 2003 occurred among 15 to19- year olds (2,687.3 per 100,000 females) and 20 to 24 years olds (2,564.4 per 100,000 females). Age-specific reported rates among men, while substantially lower than the rates in women, were highest in the 20 to 24 year-old age group (690.6 per 100,000).[15]

In 2003, the rate of chlamydia among African-American females in the United States was more than seven times higher than the rate among white females (1,633.1 and 217.9 per 100,000, respectively). The chlamydia rate among African-American males was 11 times higher than that among white males (584.2 and 52.9 per 100,000, respectively).

Case reports, however, are affected by screening and reporting practices and provide only part of the surveillance picture. To monitor trends in disease burden in defined populations, CDC initiated a chlamydia prevalence monitoring surveillance system in 1988. Data from multiple sources on prevalence of chlamydial infection in defined populations have been useful in monitoring disease burden and guiding chlamydia screening programs. Positivity∗ serves as a reasonable approximation of prevalence;[16] however, the increasing use of more sensitive laboratory tests that are able to detect more infections can result in apparent increases in positivity even when the underlying prevalence has not changed. The following table highlights chlamydia prevalence monitoring data for the years 2000 to 2003 for family planning clinics, prenatal clinics, and entrants to the National Job Training Program.

Table 1: Median Chlamydia Positivity in Selected Sites – 2000, 2001, 2002, 2003

Source of Data	2000 (Range)	2001 (Range)	2002 (Range)	2003 (Range)
Family Planning Clinics (Women Aged 15-24 Years)	5.2% (2.3% - 15.8%)	5.6% (2.7% - 13.9%)	5.6% (3% - 14.2%)	5.9% (2.8% to 18.9%)
Prenatal Clinics (Women Aged 15-24 Years)	5.9% (2.2% - 14.5%)	7.4% (3.7% - 13.5%)	7.4% (1.5% - 14.4%)	7.4% (2.4% - 19.7%)
National Job Training Program (Women Aged 15-24 Years)	11.9% (6.8% - 19.8%)	10.6% (5.1% - 18%)	10.1% (4.4% - 16.8%)	9.9% (3.4% - 16.0%)

Data from family planning and prenatal clinics indicate that positivity among young women 15 to 24 years of age screened in these settings increased over time. Because of the expanding use of more sensitive laboratory tests that detect more infections, increasing positivity trends may be attributable to differences in test types. Data from the National Job Training Program indicate a steady decline of positivity among these young women. Since the same test was used to screen this high-risk population between 2000 and 2003, the declining trends likely reflect a true decrease in prevalence of the population being screened.

∗ Positivity is the number of women who test positive divided by the number of women who are tested (includes both positive and negative tests). For example, if 100 women are tested and 10 are positive, the positivity is 10%.

In 2003, median state-specific chlamydia positivity among women 15 to 24 years of age screened in family planning clinics was 5.9%.[17] Despite the high prevalence observed in many states, data also indicate the effectiveness of large-scale screening and treatment programs in reducing chlamydia prevalence among women. For example, from 1988 to 2003, the screening programs in HHS Region X (Alaska, Idaho, Oregon, and Washington) family planning clinics demonstrated a 50% decline in chlamydia positivity from 13.0% to 6.5% among women 15 to 44 years of age. For women aged 15 to 24 years, chlamydia positivity declined 52% from 15.1% to 7.2%.

Across all 10 HHS regions, after adjusting trends to account for changes in laboratory tests and associated increases in test sensitivity, chlamydia test positivity decreased in four of 10 HHS regions, increased in five regions, and remained the same in one region from 2002 to 2003. Although chlamydia positivity has declined in some regions, increases in chlamydia positivity may be expected as programs expand to additional high-risk populations or settings.

As stated in the introduction, women disproportionately bear the long term consequences of STDs. Primary complications for women include PID and tubal scarring which can cause infertility, ectopic pregnancy, and chronic pelvic pain. Chlamydia screening and treatment have been shown to reduce the incidence of PID, the primary link to infertility.[18] However, Trend data for PID and tubal factor infertility resulting from either chlamydia or gonorrhea are difficult to obtain. Definitive diagnosis of these conditions is complex, and changes in medical management have occurred that further complicate this issue.

Hospitalizations for PID declined steadily throughout the 1980s and early 1990s, but remained relatively constant between 1995 and 2003.[19] These trends may reflect changes in the etiology of PID as well as changes in the clinical diagnosis and management of PID rather than true trends in disease. In the 1990s, a greater proportion of women diagnosed with PID were treated in outpatient instead of inpatient settings. Because of this change in PID clinical management, CDC uses data on the number of initial visits to physicians for PID as reported through the National Disease and Therapeutic Index to monitor disease trends. Between 2000 and 2003, the number of women 15 to 44 years of age with initial visits to physicians for PID declined from 254,000 to 123,000.[20]

Declines in hospitalizations for ectopic pregnancy have also occurred during this time frame, but as with PID, evidence suggests that health care practices associated with ectopic pregnancy changed in the late 1980s and early 1990s. Before that time, treatment of ectopic pregnancy usually required admission to a hospital; hospitalization statistics were therefore useful for monitoring trends in ectopic pregnancies. Beginning in 1989, hospitalizations for ectopic pregnancy have generally declined. Between 1998 and 2002, hospitalizations for ectopic pregnancy declined 25% from 41,200 to 30,800; however, data suggest that nearly half of all ectopic pregnancies are treated on an outpatient basis.[21]

II. Service Delivery and Regional Infrastructure

A. Service Delivery:

Between FY 2000 and FY 2003, CDC allocated IPP funding to public health departments in all 50 states, 5 directly-funded cities, Puerto Rico, Virgin Islands, and the following territories: American Samoa, Guam, Northern Mariana Islands, Marshall Islands, Micronesia, and Palau. Federal IPP funding allocations increased 53%, from $17.9 million to $27.3 million, during this period. CDC distributed awards ranging from $10,724 to $1.9 million. As directed by the Preventive Health Amendments of 1992 that authorized the program, IPP funds are used to provide chlamydia screening, treatment, and prevention counseling to low-income, young, sexually active women; screening and treatment for the partners of these women; public information and outreach about these services; and training to health care workers. At least 50% of these funds must support screening and treatment of women in Title X family planning programs. In 2002 (last data available), Title X family planning programs reached nearly 4.9 million women in 4,645 clinic sites. Most women (60%) were less than 25 years of age – the age group that is most vulnerable to this infection.[22] In addition, nearly two-thirds (65%) of Title X users have incomes at or below the poverty level. Through CDC's collaboration with the Office of Population Affairs (OPA) and the large network of Title X clinics, access to chlamydia screening for low-income, young, sexually active women has expanded. Information from the chlamydia prevalence monitoring surveillance system indicates that at least 1.4 million* women were tested at family planning clinics in 2003, among whom 75,029 cases of chlamydia infection were detected.

Screening has also expanded to new sites including juvenile detention centers, school-based clinics, community health centers, mobile van outreach sites, and Indian Health Service sites. The expansion of services to these non-traditional sites has been possible, in part, because of the advent of NAATs, which are less invasive (urine specimens are collected) and allow men and women to receive testing services without an exam.

With input from the National Coalition of STD Directors, regional IPP committee members, and the 10 regional IPP coordinators, in 1998 CDC created 23 quality indicators (QIs) for the five core IPP program areas (i.e., laboratory, surveillance and data management, program management, clinical services, and training). In 1999, performance measures for 10 of the 23 QIs were developed. The purpose of these measures is to guide program development toward optimum quality and consistency. In FY 2000, eight project areas were funded to

* Not all chlamydia tests conducted through the IPP are reported to the chlamydia prevalence monitoring surveillance system. Reporting tests and negative test results through this system is voluntary and not required by law as chlamydia case reports. In addition, some clinics and settings submit data to this surveillance system even though they do not receive any support through the IPP (e.g., National Job Training Program), enhancing CDC's ability to monitor disease trends in multiple settings.

evaluate the QIs and associated performance measures. These projects are highlighted below.

Region I:

Multi-state – Connecticut, Maine, and Vermont – Quality Indicator: Clinical Services
This project developed a system to measure adherence to the Region I chlamydia screening criteria. A data collection tool was developed that collected age, occurrence of risk factors that meet regional screening criteria, chlamydia test results, and reasons for not screening. Overall, 67% of women who were screened for chlamydia met the screening criteria. However, only 57% of women who should have been screened were actually tested. The most common reasons for not testing women who met the screening criteria were patient refusal, no change in sex partner, or recently tested.

Region III:

Delaware - Quality Indicators: Clinical Services and Training
This project developed an integrated STD/family planning patient form to improve documentation of risk reduction counseling and partner referral and treatment. In addition, a needs assessment was developed to assess technical assistance and training needs related to these areas. The major finding from the assessment was that a clear, written policy at the institutional level was needed to assure appropriate and consistent documentation.

Maryland – Quality Indicator: Program Management
The newer and more sensitive NAAT technologies are also more costly, which has limited their use for routine chlamydia testing. This project evaluated pooling of urine samples to determine if laboratory costs could be reduced and to evaluate diagnostic sensitivity. Test costs may be reduced by pooling (combining multiple specimens into a single specimen) and retesting of individual samples only from positive pools. In this project, pooled specimens were found to have high diagnostic sensitivity. Cost data were inconclusive. A survey of clinicians was also conducted to determine the acceptability of pooling patient specimens. Most clinicians (61%) supported specimen pooling.

Region VI

Arkansas – Quality Indicator: Laboratory
This project assessed the quality of endocervical specimens collected for chlamydia in participating IPP clinic sites throughout Region VI. Clinicians submitted slides to the Arkansas Department of Health Laboratory that examined them for specimen adequacy. Of 110 participating clinicians, only one required additional training.

Region VII

Iowa – Quality Indicator: Laboratory
For non-amplified chlamydia tests, adequate specimen quality is necessary to assure high diagnostic sensitivity. This project evaluated whether the sensitivity of a NAAT for chlamydia was also influenced by the quality of female endocervical specimens. Results

indicate that test sensitivity is still linked to specimen quality. Based on these findings, criteria were developed defining an adequate specimen. The Iowa laboratory staff is using the criteria to monitor specimen quality and provide feedback and training to clinicians.

Region IX

California – Quality Indicator: Clinical Services
This project developed a system to determine the quality of chlamydia screening and treatment in family planning clinics by linking existing data sources. Laboratory and family planning clinic data were successfully merged to generate provider-specific chlamydia positivity by age group and to identify providers with low testing percentages. The median screening coverage among these providers was found to be 66.4%.

Region X

Multi-State - Idaho, Alaska, Oregon, Washington – Quality Indicator: Training
This project successfully implemented a specimen adequacy training protocol developed by the IPP laboratory committee. The target groups for this training were new clinicians and clinicians collecting inadequate specimens.

Washington State – Quality Indicator: Program Management
This project developed an administrative structure for the public health laboratory to bill (and receive payment from) clinics for chlamydia tests not meeting screening criteria. Procedures were also identified to obtain reimbursement from clients who met the screening criteria and who had private insurance or Medicaid.

In 2002, additional project funds were awarded to support innovative service expansion projects that included expanding screening to adolescents in teen health clinics, juvenile detention centers, and community health centers. One project was also funded to implement and evaluate partner-delivered therapy. These projects ended in 2003, and results will be available in late 2004.

B. Regional Infrastructure Support and Training

One important aspect in the replication of the 1988 CDC and OPA chlamydia screening demonstration project in HHS Region X (Alaska, Idaho, Oregon, and Washington) was developing a regional collaboration among family planning clinics, STD clinics, and public health laboratories. The goals of this regional collaboration were to (1) develop standards for consistent chlamydia screening and testing activities among all federally funded family planning clinics and STD clinics; and (2) develop consistent quality assurance and testing procedures among public health laboratories. As the program expanded to all 10 HHS regions, the regional collaboration model was also replicated. Each region has an established committee composed of state STD, family planning, and public health laboratory program representatives. Through an interagency agreement with OPA, CDC provides funding to support a regional coordinating agency in each of the 10 HHS regions. The 10 coordinating

agencies are funded to provide regional project administration, data management and analysis, technical assistance, and quality assurance activities. The regional approach has been instrumental in creating efficient ways to enhance monitoring and accountability of the local projects. In addition, as programs have developed screening protocols, policies, and quality assurance mechanisms, the regional infrastructure has served as an important conduit to assure timely distribution of products developed in other regions. By bringing together local expertise from a variety of disciplines, regional and locally-driven solutions to problems, which complement and extend national directions, are developed in an effective manner. This approach substantially enhances local buy-in to what is essentially a "grass roots" development of issue identification and problem solving with appropriate technical support from CDC.

During the reporting period, 7 of the 10 regional IPP committees began a long-term strategic planning process to review regional IPP committee activities. This planning work led to the recognition that the regional committees had expanded efforts beyond development of screening standards and laboratory quality assurance activities. To keep pace with these developments and maximize results at the regional level, new priority areas were created in collaboration with the regional IPP committee members.

These priority areas will be used in the development of regional plans for 2004. The priority areas include:

- Targeting and expanding chlamydia screening in public and private settings to young, sexually active women and men at risk for infection.
- Incorporating analysis of regional prevalence monitoring data for regional and local data-directed program planning.
- Improving appropriate and timely treatment for persons diagnosed with chlamydial infection and their partners.
- Promoting the use of high quality diagnostic tests for chlamydia.
- Increasing adoption of "best practice" prevention strategies to reduce chlamydia transmission.

III. Promoting Chlamydia Screening in the Private Sector

A significant proportion of individuals seeking medical care for STDs access care through the private sector.[23] Recognizing this, CDC has focused attention on improving access, utilization, and quality of STD prevention services in the private sector through several approaches in conjunction with regional IPPs as well as more directly. The following are highlights of significant activities that CDC conducted between 2000 and 2003.

Since the Federal Employees Health Benefit plan is often considered a model for other employers, CDC successfully collaborated with the Office of Personal Management to recommend the inclusion of chlamydia screening as a covered service. In cooperation with

George Washington University, written purchasing specifications for STD prevention services were developed that employers can use when they are negotiating the scope of services for employee health plans. In 2002, CDC also collaborated with the National Business Group on Health to develop an issue brief for employers to raise their awareness of the prevalence of STDs and the health and financial cost consequences.[24]

In addition, CDC has funded two projects to demonstrate the level of chlamydial infection in the private sector and to determine how to improve chlamydia screening rates in managed care organizations. Using rapid cycle quality improvement techniques, one project increased screening rates by over 40%.[25] Prevalence in the population screened in the 10 pediatric clinics participating in this study ranged from 5.8% to 7.6%. The second project increased screening rates from 61% to 83% by coupling chlamydia screening with screening for cervical cancer.[26]

Of potentially greatest importance, CDC has worked with the National Committee for Quality Assurance (NCQA) to initiate a Health Plan Employer Data and Information Set (HEDIS) performance improvement measure focused on screening of young women for chlamydial infection. CDC continues to work with NCQA on the chlamydia HEDIS measure; over the three years that it has been in place, rates of chlamydia screening have slowly risen. The chlamydia screening rate in commercial managed care settings increased two percentage points between 2001 and 2002. The screening rate for women ages 16 to 26 was 25.4% in 2002 as compared with 23.1 in 2001.[27] Since 2000, NCQA has also tracked screening rates in Medicaid managed care plans. In 2002, the average rate of screening in Medicaid managed care plans for the same age group was 41.3%, an increase of nearly 2% from 2001 (39.6%).

Most recently, in 2003, CDC compiled information about relevant STD guidelines, tools, and resources and sent this information to major health plans and trade organizations, professional medical organizations, employer health purchasing coalitions, and government partner agencies. The two page-briefing document outlined the magnitude of chlamydial infection in the United States, provided the most up-to-date information on recommendations for chlamydia screening, and discussed technical assistance resources available from CDC and its partners.

IV. Program Research and Evaluation Activities

The IPP Research Program continues to research and evaluate issues to prevent STD-related infertility. The research and evaluation activities are closely linked with the service delivery component. The goals of the research projects are to (1) assess the performance of new diagnostic tests, and (2) conduct research related to the epidemiology of chlamydia reinfection and preventing recurrence in women. The following provides an update of the outcomes of studies initiated or continued during the reporting period.

A. Efficacy of New Screening Tests for Chlamydia

The development and marketing of semi-automated tests for *C. trachomatis* in the late 1980s has made large-scale chlamydia screening feasible. A large number of such tests, including

enzyme immunoassays and a nucleic acid hybridization test, were on the market in 1993. The initial research and evaluation task for the IPP was to develop evidence-based recommendations regarding selection and use of these tests. These recommendations were published as the laboratory testing section of CDC's *1993 Recommendations for the Prevention and Management of Chlamydia trachomatis Infections* (MMWR 1993; 42(No RR-12)12-24).

Preparation of the 1993 *Recommendations* identified that the principal impediments to selecting the most cost-effective screening tests were a lack of (1) evaluation studies in which commercial tests were compared directly with each other; (2) statistical methodology for carrying out such multiple-test-comparison studies; and (3) confirmation procedures to ensure that a positive screening test was not falsely positive. To address these shortcomings, CDC, in collaboration with the Region X IPP, conducted a comparative evaluation of five screening tests. The results demonstrated that the five tests fell into three distinct groups with respect to performance, enabling screening programs to consider performance as well as cost when purchasing tests.[28] A CDC statistician and an external expert also developed statistical modeling methods to reduce the bias in performance estimates associated with application of usual statistical methods to studies evaluating multiple tests.[29 30]

Between the mid-1990s and the present, a second generation of chlamydia screening tests, NAATs, has been marketed that can also detect *N. gonorrhoeae* infections. These tests employ enzymes that replicate chlamydial and gonococcal nucleic acid and are inherently more sensitive than the first generation tests, but also more costly and difficult to perform. CDC, with the assistance of external experts, published updated recommendations to address the second generation tests in the MMWR report *2002 Screening Tests to Detect Chlamydia trachomatis and Neisseria gonorrhoeae Infections* (MMWR 2002;51(No. RR-15)).

The IPP research program also conducted a multi-center study that directly compared the first and second-generation chlamydia screening tests. The results quantified an increase in the detection rate of infections in women for the second-generation tests compared to the older tests, which will permit local programs to assess the cost-effectiveness of the more expensive second-generation tests.[31] In addition to increased sensitivity, a benefit of the second-generation tests is the ability to use them with urine as well as traditional cervical samples. This is of tremendous operational importance because it makes it possible to screen women without requiring a pelvic examination and allows screening to be conducted in a broader variety of settings. It is also a more acceptable screening test for men and can be used to expand screening to men.

B. Risk Factors for Recurrent Infection and Preventing Recurrence of Chlamydial Infection in Women

Recurrent chlamydial infections are linked to increased risks of pelvic inflammatory disease and subsequent ectopic pregnancy.[32] The following studies were implemented to determine risk factors associated with recurrent infection and strategies to prevent recurrent infections through patient delivered partner therapy.

Risk Factors for Recurrent Infections in Adolescent and Young Adult Women
This study component was designed to identify risk factors for early recurrent chlamydial infections in women. In addition, important epidemiologic, clinical, behavioral, and biologic risk factors associated with recurrent chlamydial infections in women and their sex partner(s) were described. The study was conducted between 1995 and 1996, and suggested that young age and incomplete therapy increase the risk for a persistent/recurrent infection. The study also suggested that women's current male sex partners were not receiving treatment for chlamydia and that women were getting reinfected by resuming sex with these infected (and untreated) sex partners.[33]

Preventing Recurrence of Chlamydial Infection in Adolescent and Young Women: A Randomized Trial Evaluating Patient-provided Therapy
This study follows the study described above. It was initiated in 1996 and completed in 2001. The primary goal of this study was to determine whether the substantial risk for early recurrent chlamydial infection among young women (14 to 34 years of age) could be reduced by using an alternative method of providing treatment to their male partner(s). This alternative approach involves providing female patients who have chlamydial infection with single-dose therapy for them to provide to their male sex partner(s). This was compared to the usual approach to partner treatment, in which young women are advised to refer their male partner(s) to the health department for examination and treatment. The study found that the risk for reinfection was 20% lower in women who were provided treatment to give to their male partners. Although not statistically significant, patient-delivered therapy was found to be at least as effective at reducing risk for reinfection as the standard practice of referring male partners to the health department, and may be an appropriate option for some patients.[34]

C. Male Screening Research Project

This project, initiated in September 1999, includes three components: (1) a screening demonstration project, (2) a longitudinal study, and (3) a cost-effectiveness analysis. Data collection for all three components of the research project was completed in early 2004 and is currently in the analysis phase.

The purpose of the demonstration project was to determine the prevalence of asymptomatic chlamydial infection in men, the feasibility and acceptability of screening asymptomatic males for chlamydia in multiple venues, and the risk factors for infection. Study sites included Baltimore, Maryland; Denver, Colorado; San Francisco, California; and Seattle, Washington. Project sites included school-based clinics, youth detention facilities, street outreach settings, and primary care clinics. The sex partners of infected males were contacted and offered treatment using urine-based screening tests. Men 15 to 35 years of age were targeted for screening, and more than 36,000 men were enrolled in the demonstration project from October 1999 through April 2003. Prevalence of chlamydia infection in males from the demonstration project ranged from 3%-16%, with the highest prevalence in adolescent primary care settings.

The purpose of the longitudinal study was to measure the rate and predictors of repeat infection. Infected males were treated and followed at one and four-month intervals. At each follow-up visit, urine testing was performed for chlamydial infection. A total of 363 males were enrolled in the longitudinal study, and repeat infection occurred in approximately 11% of men with a follow-up visit.

The economic analysis will evaluate the cost-effectiveness of screening men for chlamydia infection to decrease sequelae in women. Data from the demonstration project, longitudinal study, and published literature will be used for the cost-effectiveness analysis.

D. Transmission of Incident* and Prevalent† Chlamydial Infection

This study is examining biologic and behavioral determinants of chlamydia transmission. The project began in early 1999, and enrolled men, women, and their partners. A total of 130 sexual partnerships were sought, and approximately 110 have been enrolled. Data collection finished in September 2003; final analysis will be completed and results will be released in late 2004.

E. Chlamydia Screening Coverage of Sexually Active Adolescent Women in the United States, 2000

Since 1993, CDC has recommended screening all 15 to 19 year-old sexually active females at least annually. Estimates of screening coverage are important measures for evaluating programs, managing program resource allocation, and interpreting surveillance data.

To estimate state and regional chlamydia screening coverage of sexually active 15 to19 year-old women in the United States, in 2000 CDC used information from the chlamydia prevalence monitoring surveillance system, case reporting data, sexual activity estimates, and census information to develop a mathematical model for determining the percentage of sexually active women between the ages of 15 and 19 who were screened during 2000. Based on this model, estimated median state-specific screening coverage for 15 to 19 year-old sexually active females was only 60%. This does not meet the 1993 CDC recommendation to screen all sexually active women in this age group on an annual basis. It also indicates that existing public and private sector screening activities are not sufficiently identifying chlamydial infections in this high-risk population. These estimates can be compared with local information on screening coverage to guide the expansion of chlamydia screening and prevention programs.[35]

F. Laboratory Test Technology

* Incident infections are new infections occurring in a designated population during a specified period of time.
† Prevalent infections are the total number of infections within a specified population at a designated time.

Limited information is available on the volume and type of chlamydia and gonorrhea testing being performed in the United States. In 2002, CDC asked the Association of Public Health Laboratories to assess the types of tests used at 132 public health and 8 private laboratories. Overall, 57% of chlamydia tests and 60% of gonorrhea tests were non-amplified probe technology. Approximately 30% of chlamydia tests and 18% of gonorrhea tests were NAAT. Although 75% of laboratories reported capacity to perform gonorrhea cultures, only 16% of all gonorrhea tests performed were culture technology.[36]

Five major manufacturers of chlamydia and gonorrhea tests were also asked to provide the number of tests sold in the United States in 2001. They reported that an estimated 24 million chlamydia tests and 24.8 million gonorrhea tests were sold in the United States in 2001; less than 25% were sold to public health laboratories underscoring the important role of private sector testing.[37]

As laboratory technology evolves, continued monitoring of chlamydia and gonorrhea testing practices will become increasingly important to determine the amount of resources needed for chlamydia and gonorrhea screening and surveillance programs and to monitor the capacity to appropriately test for these diseases.

V. Summary

Chlamydial and gonococcal infections remain the most frequently reported STDs in the United States. Women, especially young women, are disproportionately affected by these infections and their consequences. Access to chlamydia screening and treatment is the primary prevention strategy to reduce prevalence of this infection. Since 1993, the National IPP has made great strides in expanding chlamydia screening to young women in public sector settings. However, reported cases of chlamydial infections are expected to continue to rise as screening expands, more sensitive tests are used, and reporting practices improve.

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