The Impact of a Comprehensive Chlamydia Prevention Program in Wisconsin

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An analysis using case reports, laboratory records of tests for C. trachomatis, *and Hospital Discharge Summary data shows that, following implementation of a chlamydia prevention program in Wisconsin in 1985, statewide declines were observed in prevalence, incidence and complications of infection. In 1990, prevalence rates among teenage women peaked at 2,794 infections per 100,000 15–19-year-old females. Between 1987 and 1991 (a period of stable testing volume), the proportion of positive tests decreased in all age-groups for females (by 29–41%) and males (by 10–14%), and the incidence of new infections in women decreased in clinic populations by 27%–50%. Between 1986 and 1991, hospitalization rates declined by 33% for pelvic inflammatory disease and by 20% for ectopic pregnancy.*

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The four million cases of genital *Chlamydia trachomatis* infection that occur every year in the United States incur an estimated $2.2 billion in direct and indirect costs.[1] More than 70% of this amount is attributable to serious, irreversible or potentially fatal complications of chlamydial infection in women, including pelvic inflammatory disease (PID), infertility, ectopic pregnancy and chronic pelvic pain.[2] Published estimates of health care costs may be too low because they fail to include costs of chlamydia-associated HIV infection in women: Evidence suggests that the risk of HIV seroconversion is three to five times as high among women infected with chlamydia as it is among uninfected women.[3]

Increased recognition of the high prevalence of chlamydial infections, more widespread availability of affordable diagnostic tests and a heightened emphasis on issues affecting women's health are leading to implementation of chlamydia prevention programs throughout the country. The Wisconsin chlamydia prevention program, one of the oldest in the United States, was initiated in 1985. The essential elements of this program, which have been described elsewhere,[4] include collaboration between public and private providers, the commitment of legislators to procure necessary funding, the availability of low-cost testing in centralized laboratories, selective screening in family planning clinics, universal screening in the largest sexually transmitted disease (STD) clinics, and computerized data systems that are used to identify persons at risk, focus public health resources and evaluate program effectiveness.[5]

A highly effective, comprehensive chlamydia prevention program should decrease the prevalence and incidence of infection and lead to declines in complications. The purposes of this analysis are: to compare two indicators of chlamydia prevalence in women and men—trends in reported rates of *C. trachomatis* and trends in the proportion of laboratory tests that were positive—since the initiation of Wisconsin's chlamydia prevention program; to examine trends in the incidence of chlamydial infections among women; and to describe trends in PID and ectopic pregnancy.

An evaluation of trends in the proportion of laboratory tests that are positive among routinely tested populations complements observed trends in rates of reported infections, because increases or decreases in population-based rates may merely reflect changes in testing practices. An evaluation of the potential impact of a comprehensive chlamydia prevention program is timely in light of the establishment of a national infertility prevention program in 1994, with a primary focus on the prevention of genital chlamydial infections.

Methods

Design and Data Sources

The scope of this analysis made it necessary to use four data systems. First, we used the Wisconsin Sexually Transmitted Disease Surveillance System, a computerized registry of all laboratory-confirmed cases of *C. trachomatis* infection[6] reported to the Wisconsin Division of Health since 1984, when reporting of chlamydial infections was legally mandated by the state legislature. Routinely collected information includes demographic characteristics, clinical characteristics of persons infected with *C. trachomatis,* and limited risk factor information.

Second, the Wisconsin State Laboratory of Hygiene Information System provided a computerized data base of all individuals testing either positive or negative for chlamydia at the laboratory between 1985 and 1991. The laboratory performs a high volume of chlamydia testing for the private sector, all testing for each of the state's 14 public STD clinics except the one located in Milwaukee and for the 59 public family planning clinics that provide testing services. The State Laboratory of Hygiene Information System includes unique identifiers, age, gender, source of health care, county where the test was performed, type of test and result of test.

The third data set was provided by the Milwaukee City Health Department Bureau of Laboratories, which performs all testing for the Milwaukee STD clinic, the largest such facility in the state. This data base includes the total number of laboratory tests, type of test, result of test, and gender of the individual tested.

Fourth, we obtained rates of hospitalization for PID and ectopic pregnancy from the Hospital Discharge Summary data base for patients hospitalized between 1982 (several years before implementation of the chlamydia prevention program) and 1991. Hospital participation in the discharge data base was voluntary in Wisconsin during 1982 and 1986 and became mandatory in 1989.

Population

Criteria for inclusion in the analyses varied for the four different data bases. From the Wisconsin Sexually Transmitted Disease Surveillance System (which included reports only on those testing positive for *C. trachomatis*), we included all 87,358 cases (69,961 among females; 17,297 among

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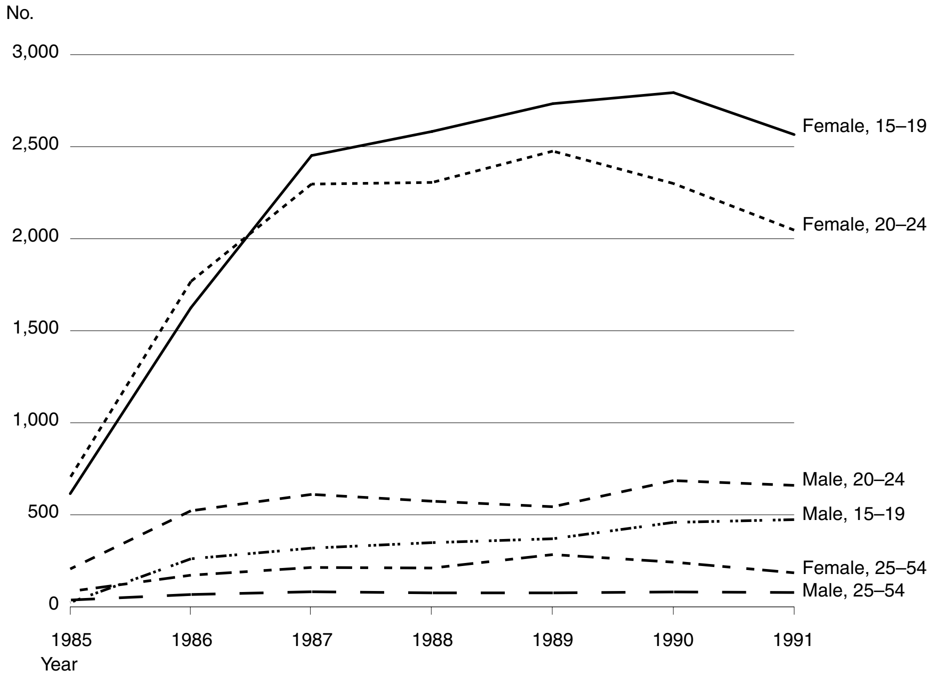
males) of *C. trachomatis* infection reported in Wisconsin residents between 1985 and 1991. These analyses were not age-restricted because 99% of the persons about whom age data were reported were within the sexually active age range (10–55 years). For the two laboratory-based data sets, we included all tests performed for *C. trachomatis* infection in either the State Laboratory of Hygiene (357,106 females; 50,346 males) or the Milwaukee City Health Department Bureau of Laboratories (14,478 females; 24,378 males) from 1985 through 1991. We restricted analyses of trends in hospitalized PID and ectopic pregnancy to women between the ages of 15 and 44.

Main Outcome Measures
We compared trends for two indicators of prevalence of *C. trachomatis* infection—number of reported cases per 100,000 population (1985 to 1991) and proportion of laboratory tests positive for *C. trachomatis* (1985 to 1991). To examine trends in the incidence of chlamydial infection, we calculated the proportion of women who tested positive during a given year among those who had had a negative test during the preceding year (365 days).[7] Finally, we measured trends in hospitalization rates for two of the most common chlamydia-associated sequelae in women—PID and ectopic pregnancy.*

Analyses
We analyzed the computerized data to produce contingency tables for the measures of prevalence and incidence. Because the volume of laboratory testing for chlamydia was fairly constant across all age, sex and source-of-care subgroups from 1987 through 1991, we calculated the reduction in disease incidence as the difference between 1987 and 1991 in the proportion of positive tests, divided by the proportion of tests that were positive in 1987.[8] We calculated annual age-specific and sex-specific rates for chlamydial infection, as well as annual rates for PID and ectopic pregnancy, using Bureau of Census population estimates for each year.[9]

Results
Trends in Prevalence
Analyses of rates of reported *C. trachomatis* infection by age for females and for males from 1985 through 1991 demonstrate that after an initial increase during the early years of the chlamydia prevention program (1985–1987), rates stabilized in females aged 20 or older and in males aged 25 or older (Figure 1). However, rates continued to increase among females younger than 20 and males younger than 25. Rates peaked at 2,794 cases per 100,000 females aged 15–19 in 1990, 686 cases per 100,000 males aged 20–24 in 1990, and 474 cases per 100,000 males aged 15–19 in 1991.

Figure 1. Reported number of *C. trachomatis* cases per 100,000 people, by year, according to sex and age, 1985–1991, Wisconsin



In contrast with trends in reported rates of chlamydial infection, trends in the proportion of laboratory specimens that were positive decreased for women and men in all age-groups between 1987 and 1991 (Figure 2, page 110). During these years, the overall volume of tests remained stable, with a gradual increase in use of antigen detection methods (direct fluorescent antibody or enzyme-linked immunoassay) and a decrease in the use of tissue culture. It is unlikely that changes in testing practices account for observed downward trends, because tissue cultures made up a sizable proportion of all tests performed each year.

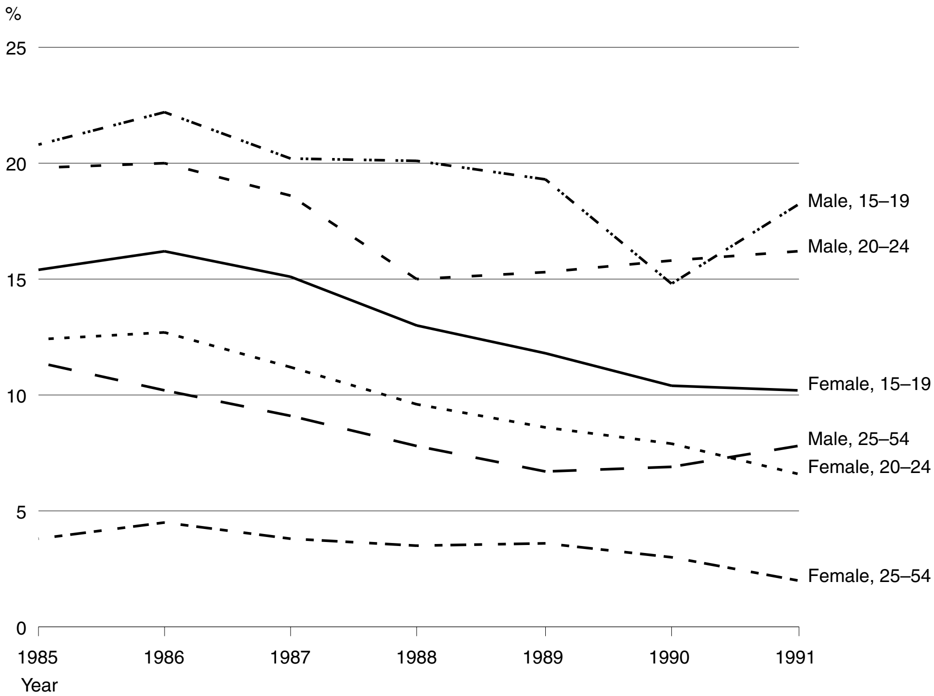
In the period between 1987 and 1991, the proportion of tests that were positive for *C. trachomatis* decreased by 32% (from 15.1% to 10.2%) among females aged 15–19 years, by 41% (from 11.2% to 6.6%) among females aged 20–24 years and by 29% (from 3.8% to 2.7%) among females aged 25–54 years. Among males, net decreases between 1987 and 1991 in the proportion of positive tests within age-groups ranged from 10% to 14% (from 20.2% to 18.2% among 15–19-year-olds, from 18.6% to 16.2% among 20–24-year-olds and from 9.1% to 7.8% among 25–54-year-olds).

Overall, from 1987 to 1991, the proportion of tests showing positive results decreased by roughly one-third among female clients seeking care in family planning clinics (from 12.5% to 7.7%), in STD clinics (from 13.2% to 8.4%) and in private health care settings (from 7.6% to 5.1%). For males, the proportion of tests positive for *C. trachomatis* declined by 7–13% in family planning clinics (from 21.0% to 18.2%) and private provider clinics (from 12.9% to 12.0%), and by 18% in STD clinics (from 15.9% to 13.1%). Our findings were similar when analyses were restricted to the subgroup of individuals undergoing only one test for *C. trachomatis* infection during the study period.

Trends in Incidence
From 1987 to 1991, a 40% decrease in the incidence of new *C. trachomatis* infection occurred among women who had tested negative for *C. trachomatis* during the preceding year (Table 1, page 110). The sharpest declines were observed at private facilities (50%), followed by public family planning clinics (36%) and STD clinics (27%).

*The International Classification of Diseases, Ninth Revision, Clinical Modification (DHHS publication no. [PHS] 80–1260, U.S. Government Printing Office, Washington, D.C., 1980) was used to code discharge diagnoses. Diagnostic codes used for acute PID included 614.0–614.5, 614.7, 614.9, 098.10, 098.16, 098.17, 098.30, 098.36, 098.37, 098.39, 098.86, 615.0–615.5 and 615.9; those used for ectopic pregnancy were 633.0–633.9.

Figure 2. Proportion of laboratory tests that were positive for *C. trachomatis*, by year, according to sex and age



Trends in Complications

Rates of hospitalization for PID in Wisconsin decreased by 54% between 1982 and 1991, from 137.0 to 63.2 cases per 100,000 women aged 15–44 (Figure 3). Hospitalization rates for PID declined by 31% between 1982 and 1985 (the year the chlamydia prevention program was begun) and by 33% between 1986 and 1991. Rates of hospitalization for ectopic pregnancy increased by 14% before program initiation and fell by 20% after implementation. Rates decreased gradually between 1986 and 1990 (from 100 to 92.3 cases per 100,000 women) and then dropped sharply in 1991 (to 79.9 cases per 100,000 women).

Discussion

Following establishment of a comprehensive chlamydia prevention program, declines were observed in four of the five indicators evaluated—the proportion of tests positive among women and men, the incidence of new infections in women, the rate of hospitalization for PID and the rate of hospitalization for ectopic pregnancy. In contrast, net increases occurred in reported rates of chlamydial infection.

Our analysis demonstrates that reported rates of *C. trachomatis* infection have increased most markedly among adolescent females: In 1990, approximately 3% of adolescent females residing in Wisconsin were reported as infected. Rates of infection also increased among males younger than 25, although the increase was smaller than that observed in females. In contrast to trends in rates, trends in the proportion of laboratory tests that were positive decreased by roughly one-third among females in all age-groups. Among males, the proportion of laboratory tests that were positive also showed net declines, although these decreases were less marked and less consistent than those seen among females.

Although reported rates of *C. trachomatis* infection were five to 10 times higher in females than in males, the proportion of tests positive was consistently higher for males than for females. Under prevailing medical practice, large numbers of asymptomatic women are routinely screened for *C. trachomatis* infection, but testing of men has been limited primarily to those who are symptomatic. The net effect is to identify higher numbers of infected women, with an overall lower proportion of tests positive. Conclusions regarding variations in disease occurrence between men and women are most likely to be valid if they are drawn from populations in which all men and all women are screened. When the Milwaukee STD clinic screened all clients for *C. trachomatis* in 1990, 13% of tests for each sex were positive (data not shown).

For both males and females, we found a discrepancy between increasing or stable trends in reported rates of infection and decreasing trends in proportion of tests positive for *C. trachomatis*. However, trends in reported rates are an inaccurate measure of prevalence because they are unavoidably influenced by trends in testing practices. Observed increases in reported rates among some subgroups are likely to be related to increased testing by private health care providers, because both the number of cases of *C. trachomatis* reported by the private sector and the number of private laboratories reporting cases increased between 1987 and 1991 (data not shown). Thus, given the declines in the proportion of positive tests for all providers and all age-groups, the true prevalence of chlamydial infection in Wisconsin probably has decreased.

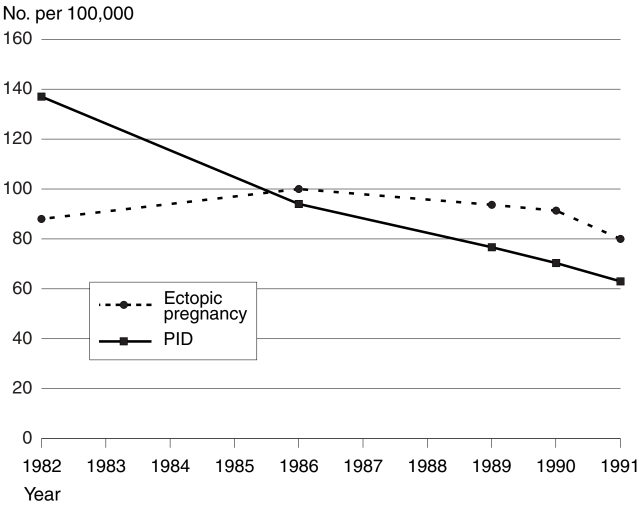
Our analysis is the first to demonstrate that a reduction in incidence has accompanied a widespread chlamydia prevention program. Following establishment of the prevention program, the incidence of new infection was reduced by 50% among patients receiving care from private providers, by 36% among women receiving care in family planning clinics, and by 27% among women receiving care in STD clinics, a pattern of incidence reduction that may foreshadow a shift in distribution of chlamydial infections from the population at large to high-risk core groups.

In addition to declines in the proportion of positive laboratory tests and the incidence of new cervical chlamydial infections, the declines occurred in rates of hospitalization for PID and ectopic pregnancy. Conclusive interpretation of all downward trends is influenced by several important limitations. First, the lack of data for a comparison group that did not participate in the chlamydia prevention program rules out absolute causal inferences. Further-

Table 1. Among women who tested negative for *C. trachomatis* during the preceding year, percentage (and number) with a positive second test, by year, according to source of care

Year	All	Family planning clinic	STD clinic	Private provider
1987	10.7 (844)	11.4 (467)	10.5 (24)	10.0 (353)
1988	9.2 (1,057)	10.1 (632)	10.6 (53)	7.9 (372)
1989	8.0 (1,026)	8.7 (636)	9.5 (66)	6.7 (324)
1990	7.2 (1,013)	8.0 (641)	7.1 (45)	6.0 (327)
1991	6.4 (901)	7.3 (569)	7.7 (44)	5.0 (288)
% change	–40.2	–36.0	–26.6	–50.0

Figure 3. Hospitalization rates for pelvic inflammatory disease and ectopic pregnancy among women aged 15–44, by year



more, changes observed in rates of hospitalization for chlamydia-associated PID are difficult to interpret for four reasons: 1) declines observed before implementation of the program were similar to those observed after implementation of the program; 2) the absence of a specific diagnostic code for chlamydia-associated PID makes it difficult to distinguish trends in chlamydial PID from those in gonococcal PID; 3) observed declines may reflect merely a shift from inpatient to outpatient treatment of PID; 4) changes observed in Wisconsin were similar to those observed throughout the country, although there was no national chlamydia prevention program during the study period.

In contrast with rates of PID, rates of ectopic pregnancy in Wisconsin increased before initiation of the chlamydia prevention program and began to decrease after implementation; this decline was most marked five years after the program began. This interval between program implementation and the decrease in the incidence of hospitalization for ectopic pregnancy may be related to the fact that the majority of women with genital *C. trachomatis* infections are young and are, therefore, not yet actively seeking to bear children.[10] Other factors that may have contributed to observed declines in ectopic pregnancy include decreases in gonorrhea,[11] adoption of safer sexual practices by at-risk groups[12] and increased ambulatory nonsurgical treatment of ectopic pregnancy. Unfortunately, it is not possible to control for these factors in analyses of aggregate data.[13]

In light of the difficulties involved in interpretation of trends in complications, trends in the proportion of tests positive and incidence of chlamydial infection are more accurate programmatic indicators at present. The marked and consistent declines in the proportion of tests positive and incidence of new infection that coincided with the prevention program probably reflect the effectiveness of widespread secondary prevention strategies that promote early diagnosis and treatment. In the future, the availability of single-dose therapy for both infected women and their male partners, the increased use of noninvasive urine tests in male and female populations, an increased emphasis on behavioral interventions in training of health care providers, and broader public health education should make important contributions to the prevention of chlamydial infection.

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