Research Update

Rising reported rates of chlamydia among young women in Canada: What do they tell us about trends in the actual prevalence of the infection?

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Abstract: This article explores possible explanations for the rise in reported chlamydia rates among young women in Canada between 1997 and 2004 and considers whether rising rates can be used to infer a parallel increase in the actual prevalence of the infection. The transition to more sensitive testing methods is among the factors that could have contributed to the rise in reported rates. In contrast to Canada, the United States (US) monitors trends in the prevalence of chlamydia among young women as well as reported rates. The US data indicate that while reported rates of chlamydia among young women rose during the same time period, prevalence levels, when adjusted for increased use of more sensitive testing methods, remained relatively stable. While available data are insufficient to draw definitive conclusions about prevalence trends in Canada, existing studies do point to unacceptably high prevalence levels. The establishment of a sentinel chlamydia surveillance system would provide a mechanism to track prevalence trends and allocate resources for chlamydia prevention and control.

Background

Of the sexually transmitted infections (STI) reported to the Public Health Agency of Canada (PHAC), chlamydia is the most frequently reported with the highest rates being among 15- to 24-year-old females (PHAC, 2007a). Chlamydia, which is often asymptomatic, is of particular concern because, if left untreated, it can lead to pelvic inflammatory disease, ectopic pregnancy, tubal infertility, chronic pelvic pain and increased susceptibility to HIV infection (Cates & Wasserheit, 1991; Steban, 2004). Given its significance for the sexual and reproductive health of young Canadian women, it is important to track trends in the prevalence of chlamydia in this population in order to effectively target prevention and control strategies.

We have observed that reports about chlamydia rates by the health promotion community and the media often draw the conclusion that there has been an increase in chlamydia infection among Canadian young people in recent years (e.g., "Chlamydia in teens jumps 50%": Globe and Mail, Feb. 13, 2008; "Safe-sex complacency boosts STDs" Ottawa Citizen, April 30, 2008). The common assumption is that the rising trends seen in chlamydia rate data published by the PHAC and local jurisdictions are a valid reflection of trends in the percentage of young people in Canada who are actually infected with chlamydia. In other words, it is assumed that increases in reported chlamydia rates indicate parallel increases in the percentages of youth infected (i.e., that the prevalence of chlamydia is increasing). The rise in reported rates is thus taken as a sign that the sexual health of Canadian young people is being increasingly compromised. However, that assumption appears to conflate reported rates with prevalence and is questionable on a number of other important grounds as we will discuss below.

Calculating chlamydia rates

In Canada, the surveillance of chlamydia is primarily based on the tracking of newly diagnosed cases

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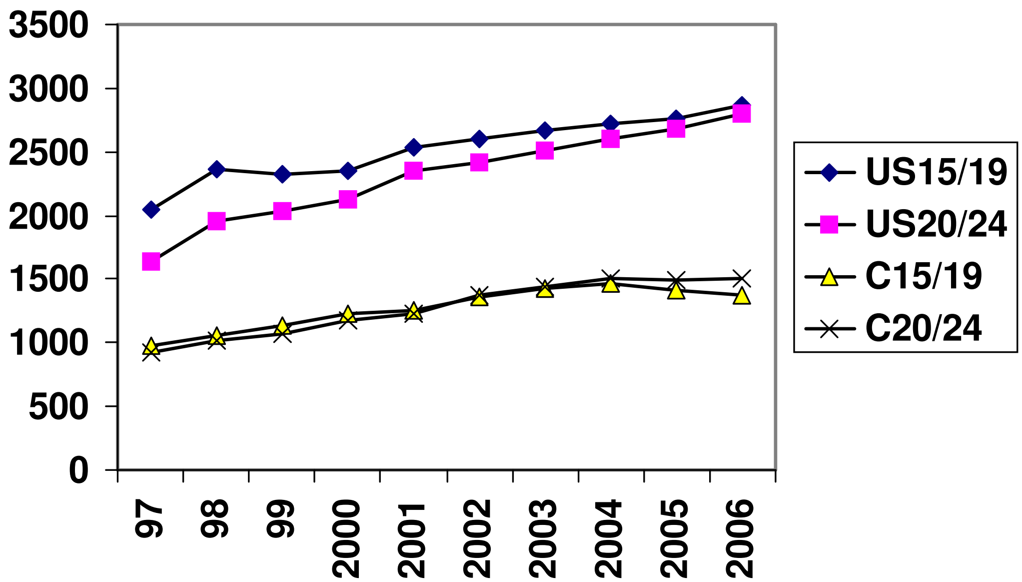
Figure 1 Reported chlamydia rates per 100,000 females aged 15-19, 20-24, Canada, USA



Sources: CDC (2007a); PHAC (2007b)

reported to provincial ministries of health and then to the PHAC which compiles and publishes national statistics on notifiable STI (see PHAC, 2007a). In other words, when a person is tested for chlamydia and is found to be infected the result is reported to public health authorities. Public health authorities use the total number of newly diagnosed cases to calculate a rate per 100,000 of the population group in question. If the person is not infected, no report is made. It is important to note that the total number of tests done is not reported. Hence, we do not know the percent positive among those tested.

Reported rates of chlamydia in women aged 15-24 rose in Canada and the US from 1997 to 2004

Canada and the US, as well as most other Western countries, collect rate data on a number of STI including chlamydia. As indicated in Figure 1, the reported rate of chlamydia among young women has risen since 1997 in both Canada and the US. For example, in the US, the reported chlamydia rate among 15- to 19-year-old females rose from 2044 per 100,000 in 1997 to 2862 per 100,000 in 2006 while the reported rate among same aged females in Canada rose from 971 per 100,000 in 1997 to 1367 per 100,000 in 2006. (It is important to note that data for 2005 and preliminary statistics for 2006 [PHAC, 2007b] show that the reported rates among 15- to 19-year-old females were lower than in 2004). In sum, the reported rates of chlamydia among young women in both Canada and the US increased substantially from 1997 to 2004. It is on this basis that it is frequently noted and reported in Canada that "rates are rising" with the implicit inference that a rise in chlamydia rates logically implies increased prevalence and, by extension, that the sexual health of Canadian youth is increasingly compromised.

Do rising reported rates of chlamydia mean that the prevalence of chlamydia is also rising?

In order to understand and interpret reported STI rate data, it is important to clarify the distinction between a reported rate and prevalence. Prevalence statistics generally indicate the percentage of the population that has a particular condition or infection/disease at a given point in time. So, for example, the only completely accurate way to determine the prevalence of chlamydia in a given population (e.g., females aged 15-19) would be to test everyone in that population. The percentage positive would indicate prevalence.

Table 1 Seven hypotheses for explaining increasing chlamydia rates. Adapted from Rekart and Brunham (2008).

1. The highly sensitive and increasingly used nucleic acid amplification test (NAAT) results in more false positive tests than culture tests because of slightly lower specificity.
2. NAAT testing results in more true positive tests due to better sensitivity than non-NAAT tests.
3. NAAT testing of urine (as opposed to swab collection) is more acceptable to the patient leading to higher testing rates.
4. NAAT testing of urine and female self-collected specimens facilitate case finding and targeted screening among persons at high risk.
5. Decreasing chlamydia antimicrobial susceptibility may be leading to higher rates and prevalence.
6. Increasing high risk sexual behaviour may be leading to higher rates and prevalence.
7. Arrested immunity: When chlamydia is treated with antibiotics, the body's ability to respond immunologically to subsequent exposure is reduced, this increasing the likelihood of infection on subsequent exposure (i.e. increase in the rate of re-infection).

Given that testing everyone is not feasible, other methods are required in order to estimate prevalence within a population. In the US, the Centers for Disease Control and Prevention (CDC) uses several such strategies to estimate the prevalence of chlamydia among young women. However, prevalence monitoring as done in the US (discussed below) is not available in Canada. Thus we do not have a precise way to identify ongoing national trends in the percentage of the population infected with chlamydia. Without the benefit of complementary chlamydia surveillance mechanisms, such as prevalence monitoring, the reported rates are the default source of available trend data in Canada.

Hypotheses concerning increasing chlamydia rates

Can it be logically assumed that increasing reported rates of chlamydia among young women in Canada reflect an actual increase in the percentage of young women who are infected? To answer this question, it must be understood that numerous variables may be contributing to an increase in the number of positive chlamydia test reports and hence to increasing rates.

Rekart and Brunham (2008) offer seven different hypotheses as a guide to possible explanations for these increases in reported chlamydia rates. These hypotheses, adapted and abbreviated, appear in Table 1.

The first four hypotheses are related to the increasing adoption of more sensitive testing technologies, more frequent testing, and improved case finding. Each of these could lead to an increase in reported rates. The latter three hypotheses could indicate circumstances that would increase rates but also prevalence. We examine some of these hypotheses below in relation to rising chlamydia rates in Canada and the US with particular reference to young women.

Impact of more sensitive chlamydia test methods

The introduction and increased use of NAAT testing would be a potential contributor to increases in reported rates of chlamydia. Since the 1990s, jurisdictions in Canada, the US and other Western countries have gradually moved away from using enzyme immunoassay (EIA) testing for chlamydia to more sensitive testing technologies. Among the effects of this transition to more effective test methods is that a greater percentage of tests done will be found to be positive with the new methods compared to the older EIA method. In other words, the increase in the reported chlamydia rates may be due, at least in part, to better tests, and need not indicate more people becoming infected (Burckhardt, Warner & Young, 2006; Van Dyck et al., 2001).

In Canada, women in the Capital Health Region of Nova Scotia tested before and after the rapid shift from EIA to the more sensitive polymerase chain reaction (PCR) tests showed a 46% increase in the percentage of tests that were positive (Forward, 2003). Forward concluded that the increased number of reported cases of chlamydia in Canada "….may be due in large part to more sensitive tests" (p. 229). A similar study in Glasgow, Scotland, found a 62% increase in the percentage of tests that were positive when new testing methods were implemented (Scouler et al., 2001). (For an exception where the transition to NAAT did not result in a higher percent positive see Lemstra et al., 2007.)

Although the extent to which NAAT has replaced EIA as the standard test for chlamydia in Canada has not been precisely documented, it is clear that the transition to more sensitive testing methods has been ongoing (e.g., Forward, 2003; Lemstra et al., 2007). *The Canadian Guidelines on Sexually Transmitted*

Infections (PHAC, 2006a) recommend NAAT testing for urine, urethral, or cervical specimens. Overall, the evidence would strongly suggest that the transition to NAAT for chlamydia screening in Canada has contributed to the rise in the reported chlamydia rates. It is also possible that as the transition to NAAT becomes complete, the effect of the overall incremental increases in the cumulative sensitivity of tests used with young Canadian women will have less impact in increasing the reported rates. This may provide some explanation for the apparent reversing of course of reported rates among 15- to 19-year-old women in Canada in 2005 and 2006 (see Fig. 1).

Impact of more frequent testing and of sampling methods that enhance case finding

Rekart and Brunham (2008) note that NAAT testing of urine samples may be more acceptable to patients and therefore serve to increase the total number of tests done. The PHAC (2006a) STI guidelines endorse the use of such testing in stating: "Due to its non-invasive nature a urine-based NAAT is ideal for screening asymptomatic persons when a pelvic examination is not warranted for other reasons" (p. 128). Increased testing frequency in-it-self can increase the number of positive test reports and thus increase the reported chlamydia rates. Case finding could be similarly enhanced by increased use of NAAT urine testing. Research from Ontario suggests that both young female patients and physicians prefer the more recently available patient-collected swabs for NAAT testing (Richardson et al., 2003). It is likely that the introduction of easier to use tests (e.g., Lemstra et al., 2007) as well as public health campaigns to encourage testing (e.g., Ottawa Citizen, April 30, 2008) have served to progressively increase the total number of chlamydia tests conducted in Canada. Collectively, the developments described here have the potential to raise reported chlamydia rates.

Although the PHAC has a sentinel surveillance system to track chlamydia prevalence in street youth (PHAC, 2006b), Canada does not gather prevalence data for the large general population of youth which makes difficult to ascertain with precision the extent to which the transition to NAAT and the apparent increase in tests being conducted contributed to the rise in reported rates of chlamydia. It is noteworthy, however, that in the US, the extent of their chlamydia surveillance data (see below) does allow for more definitive explanations for their increases in reported chlamydia rates among young women . In their annual chlamydia prevalence monitoring project report (CDC, 2007b), the US CDC notes the steady increase in the reported rates of chlamydia infection among women aged 15-24 from 1987 to 2006 and suggests that:

> These increases in the reported national chlamydia rates likely represent increased chlamydia screening, increased use of nucleic acid amplification tests, which are more sensitive than other types of screening tests, and improved reporting, as well as the continuing high burden of the disease (p. 6).

It is quite likely that the introduction of NAAT and increases in testing frequency have also contributed to the increasing reported rates of chlamydia in Canada.

Adolescent sexual risk behaviour has decreased as the reported rate of chlamydia has increased

It is anticipated that increasing high risk sexual behaviour would lead to rising reported rates of chlamydia and also to a true increase in prevalence. Although increases in risk behaviour have no doubt occurred in distinct sub-populations in Canada, this does not appear to be the case, in general, for young people. For example, the B.C. *Adolescent Health Survey* (McCreary Centre Society, 2004), a periodically conducted large-sample health survey of youth in British Columbia found that: the percentage of sexually active female respondents who reported using a condom at last intercourse increased from 52% in 1998 to 63% in 2003; the percentage of sexually active youth (both sexes) who reported having 3 or more lifetime sexual partners remained constant; and the percentage who reported having been diagnosed with an STI declined from 6% in 1998 to 4% in 2003. Using a sample of high school students from across Canada, Boyce, Doherty, Fortin and Mackinnon (2003) found that the percentage of sexually active Grade 11 females who reported having one lifetime sexual partner increased from 47% to 54% between 1988 and 2002 whereas the percentage reporting 6 or more lifetime partners decreased from 11% in 1988 to 9% in 2002. Although level of sexual risk behaviour is just one of a number of factors that determine STI prevalence, with respect to the general population of young women in Canada, the shift in sexual risk behaviour appears to be toward less risk.

Chlamydia among young women in the United States: Reported rates versus prevalence

As noted above (Figure 1), the trend to increasing reported chlamydia rates among young women in Canada is mirrored by a similar trend in the US. Because Canada lacks ongoing availability of chlamydia prevalence data, it is instructive to examine trends in chlamydia prevalence among young US women in the context of rising reported rates in that country. The US CDC employs several mechanisms for monitoring chlamydia prevalence trends among young women. These include: unadjusted state median positivity data collected from family planning clinics from each of the ten U.S. Health and Human Service (HHS) regions; adjusted data from each of the HHS regions; and prevalence data from entrants to the US National Jobs Training Program. Together, these sources of data suggest relatively stable chlamydia prevalence among young women in recent years despite consistently rising reported rates.

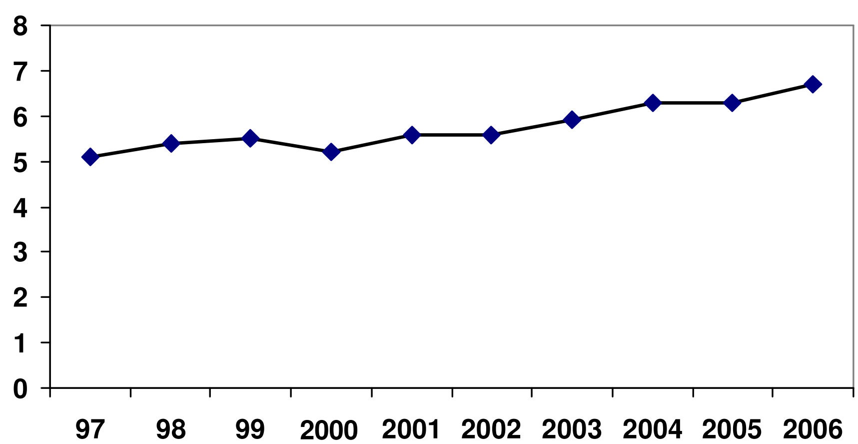
Chlamydia data from US family planning clinics: Unadjusted for test sensitivity

The CDC (2007b) uses "screening data to estimate chlamydia prevalence among selected populations" (p. 2). Young women aged 15-24 are screened for chlamydia at family clinics in all 10 HHS regions that, together, cover the US. This data is used to calculate median state-specific chlamydia test positivity. This measure is considered to be a reliable reflection of chlamydia prevalence in this sample population (Dicker, Webster, Mosure & Levine, 1998). As indicated in Figure 2, the median state positivity for women aged 15-24 gradually increased from 5.1% in 1997 to 6.7% in 2006. This trend appears to track rising chlamydia rates. However, it is very important to note that the national state-specific positivity data in Fig. 2 is not adjusted for the introduction over time of tests (e.g., NAAT) with increasing levels of sensitivity.

Chlamydia data from family planning clinics adjusted for test sensitivity

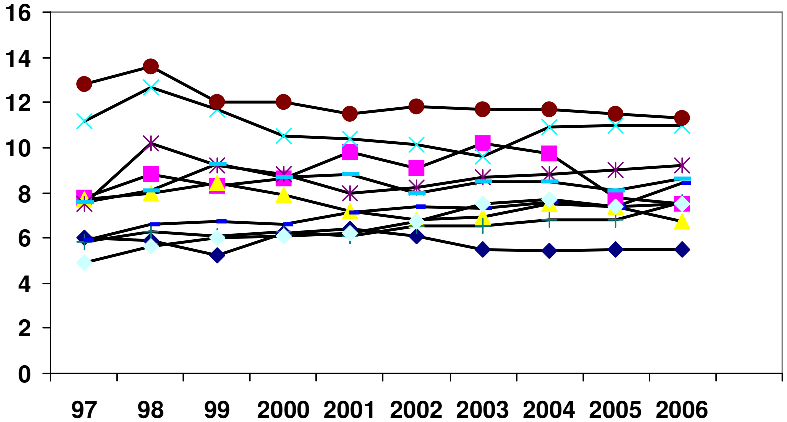
The CDC (2007b) does provide data for each of the HHS regions adjusted for changes in laboratory test methods and associated increases in test sensitivity. The adjusted percent positivity findings from 1997 to 2006 for each of the US HHS regions are provided in Figure 3. There are several important observations that can be made about this data. First, it should be noted that from 1997 to 2006, the adjusted chlamydia

Figure 2 **Unadjusted median state-specific positivity for chlamydia among women aged 15-24 attending family planning clinics in the US, 1997-2006.**



Source: CDC (2007b)

Figure 3 **Adjusted positivity for chlamydia among women aged 15-24 attending family planning clinics in each of the 10 HHS Regions.**



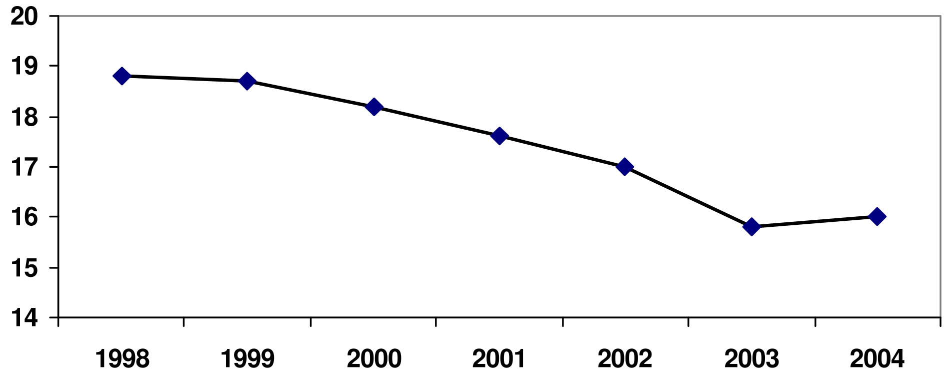
Source: CDC (2007b)

positivity decreased in five regions and increased in five regions. For example, in region III (Pennsylvania, District of Columbia, Maryland, Delaware, Virginia, West Virginia) the chlamydia adjusted positivity declined from 7.6% in 1997 to 6.7% in 2006 whereas, in Region X (Alaska, Washington, Oregon, Idaho) the adjusted rate increased from 4.9% in 1997 to 7.5 in 2006. Based on their comprehensive analysis of the data from region X, Fine, Dicker, Mosure and Berman (2008) concluded that there had been a true increase in chlamydia positivity in that region. In this case, breaking the data down by region clearly demonstrates that quite different prevalence trends can occur within different geographic regions and that these important differences, with significant public health implications, can be masked by larger national statistics. Second, in the case of the US, adjusting data to account for changes in testing technology produces a more refined picture of prevalence trends. After adjusting their estimates of chlamydia positivity to account for increases in test sensitivity, the CDC (2007b) concluded with respect to women aged 15-24 and the subgroup aged 15-19, that "Over time, positivity in both age groups has remained fairly stable, with small fluctuations from year to year" (p. 7). In sum, the rising reported rates of chlamydia do not, overall, seem to have been accompanied by a similar rise in prevalence among the young US women attending these family planning clinics.

Chlamydia data from the US National Jobs Training Program adjusted for test sensitivity

The foregoing CDC observation is buttressed by annual prevalence data drawn from the US National Job Training Program (NJTP), an occupational jobs training program for socioeconomically disadvantaged youth aged 16 to 24 (CDC, 2007b). About 20,000 young women from across the US enter the program each year and a chlamydia screening test is part of a required physical examination. Joesoef and Mosure (2006) assessed positivity data from women in the NJTP from 1998 to 2004 adjusting for a number of variables, including increased test sensitivity. Adjustment for test sensitivity resulted in a higher chlamydia prevalence for all years consistent with the expectation that the transition to more sensitive tests would have this effect. As indicated in Figure 4, the adjusted prevalence for this group of young women declined from 18.8% in 1998 to 16.0% in 2004 (Joesoef & Mosure). In other words, among this cross section of the US population of socioeconomically disadvantaged young women, the prevalence of chlamydia remained relatively stable between 1998 and 2004, albeit at much higher levels than seen in the family planning clinic attendees of comparable age.

Figure 4 Chlamydia prevalence among women aged 16-24 entering the US National Jobs Training Program



Source: Joesoef & Mosure, (2006)

Conclusions

At the beginning of this article, we noted a frequent and persistent assumption in Canada that the secular rise in the reported rate of chlamydia in young women is synonymous with or equivalent to a rise in the actual prevalence of chlamydia in this population. This assumption often underlies a more general assumption that adolescent sexual health in general is increasingly threatened. We suggest that the data and literature presented in this article call these assumptions into question. In the absence of an ongoing, regular collection of test-positivity data in Canadian settings, assumptions about trends in the actual prevalence of chlamydia among Canadian young people remain speculative. Taken together, the circumstantial evidence from both Canada (e.g., transition to more sensitive tests, data suggesting stable to reduced sexual risk among young people) and the US (stable prevalence in the context of rising rates) suggest that the extent to which the prevalence of chlamydia among young women in Canada has increased, decreased or remained relatively stable cannot be definitively ascertained based on currently available published data. It follows that we should exercise greater caution when commenting on chlamydia rates to ensure that they are not misunderstood, by media and the pubic, to mean prevalence.

Even if, as in the US, the actual prevalence of chlamydia among young women in Canada has not increased in concert with rising rates, this should not be taken as an indication that chlamydia is not a significant threat to the health and well-being of Canadian young people. The few published chlamydia prevalence studies that have been conducted in Canada suggest that the infection is common. For example, Richardson, Sellors, Mackinnon, Woodcox et al. (2003) in a prevalence study of young women in Ontario found an overall prevalence of 6.0% with lower prevalence found at family physician's offices (3.4%) and student health centres (2.8%) and higher prevalence at street health centres (18.2%). In a study of street youth living in seven urban centres across Canada, Shields, Wong, Mann et al. (2004) found that 10.9% of females were infected with chlamydia. Combined with the data from large scale and up-to-date prevalence studies from the US, there can be little question that chlamydia infection among Canadian young people is common and has resulted in substantial negative health outcomes for individuals and costs for the health care system.

With respect to the consequences of chlamydia infection, it is of interest to consider the conclusion by Rekart and Brunham (2008) after they had reviewed research on the seven hypotheses presented in Table 1. They concluded that we are not losing ground in our efforts to control sexually transmitted *Chlamydia trachomatis* infection "because we are achieving the primary objective of chlamydia control, to improve reproductive health" (p. 90). In their view, chlamydia prevalence is increasing driven by re-infections associated with greater susceptibility due to arrested immunity. They also argue that the primary goal of reducing complications is being realized, i.e., chlamydia complications are declining in spite of increasing incident cases of chlamydia (M. Rekart, personal communication, May 28, 2008) (for a discussion of arrested immunity see Brunham & Rekart, 2008; Brunham et al., 2005).

Whether chlamydia prevalence is stable or rising, prevalence is likely to be at unacceptably high levels. Chlamydia prevention and control strategies should thus be a priority for public health programming. Many Canadian young people lack important information about chlamydia such as that the infection is common, usually asymptomatic, potentially highly damaging to reproductive health, and that consistent condom use significantly reduces the risk of infection. Youth also require easy access to STI testing and treatment.

It is apparent from existing data in both Canada and the US that chlamydia prevalence is higher among socially and economically disadvantaged youth. It is also the case that reported rates of chlamydia infection among Canadian youth differ considerably between geographic regions with northern communities being disproportionately affected (PHAC, 2007a). Given a high prevalence of chlamydia among youth in Canada and significant regional disparity in reported infection rates, the establishment of a sentinel chlamydia prevalence monitoring system for Canadian youth could greatly assist in effectively targeting prevention and control strategies. Canada does have a sentinel surveillance system that tracks chlamydia prevalence among street youth (PHAC, 2006b), but a broader collection of test positivity data from youth at appropriate sites across Canada would help in identifying trends both regionally and nationally. The regular collection and dissemination of such data would provide a mechanism to guide allocation of resources for chlamydia prevention and control.

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