*Sexually Transmitted Diseases,* February 2005, Vol. 32, No. 2, p.78-83
DOI: 10.1097/01.olq.0000153574.38764.0e


# *Case-Finding Effectiveness of Partner Notification and Cluster Investigation for Sexually Transmitted Diseases/HIV*

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***Objective:*** **To assess the case-finding effectiveness of partner notification (PN) and cluster investigation for sexually transmitted disease (STD)/human immunodeficiency virus (HIV).**

***Study:*** **Literature review and quantitative summary.**

***Results:*** **Since 1975, the median case-finding yield for syphilis, gonorrhea, and chlamydia PN reported in the literature is about 1 new case found for every 4 or 5 cases interviewed. The yield from HIV PN is approximately half as large, although there is substantial variability in yield across reports for each disease. Published reports underline the central role provider referral plays in effective PN and case-finding. Successful PN is more likely with index cases who are of majority ethnicity and detected through screening or spontaneous presentation for care with symptoms and with partners with whom index cases have had sexual contact that is recent, frequent, and of long duration. The case-finding yield for HIV PN also is much higher when cases are diagnosed through confidential, rather than anonymous, testing. Cluster investigation and related strategies tend to have lower case-finding yields than PN but can play a very useful case-finding role, especially in settings with high disease incidence.**

***Conclusions:*** **STD/HIV PN and cluster investigation can contribute meaningfully to case finding. More research is needed to strengthen the empiric foundation of PN and related strategies, including the impact they have on disease transmission.**

Partner notification (PN), or contact tracing, has long been a cornerstone of efforts to control the spread of sexually transmitted diseases (STDs) and human immunodeficiency virus (HIV).[1–3] The PN process involves persons diagnosed with disease informing sexual partners (and drug-injection partners, in the case of HIV) about their exposure to infection and the need for medical examination and treatment. Often this process begins when a public health worker counsels a patient about PN and elicits his or her partners who may have been exposed to the infection. Typically, the patient and public health worker then make a plan about who—the patient and/or the public health worker—will notify particular partners and ensure their medical evaluation and treatment.

PN serves 3 main purposes: epidemiology, ethics, and case finding.[4] Epidemiology is a valuable function of PN,[5,6] as the process reveals the sociogeographic context and sexual/injection networks in which transmission takes place. PN also fulfills the ethical duty to warn persons exposed to serious infections. The third and original purpose of PN is case finding. The identification, examination, and treatment of contacts to disease are crucial for interrupting transmission of infectious diseases such as STD and HIV.

In this article, I review the empirical evidence on the case-finding effectiveness of PN and similar approaches for controlling STD/HIV. Various aspects of the literature on the effectiveness of PN have been reviewed many times over the past 20 years.[1–3,7–18] My review complements this prior work by providing a comprehensive update and an in-depth assessment of case-finding effectiveness. In addition, I also provide a review of research on the relative case-finding effectiveness of different PN referral strategies, factors associated with successful PN, innovative strategies for PN, coverage of PN, and impact of PN on disease transmission.

## Materials and Methods

I collected reports written in English that included results on the case-finding effectiveness of PN and/or cluster investigation for STD or HIV in developed nations. I identified potential reports to include from several sources; earlier reviews of this literature; my own library of several hundred published and unpublished reports on PN obtained from several systematic searches of MEDLINE between 1995 and 2003, with 4 pairs of key word combinations (contact tracing/PN × STD/HIV), as well as incidental discoveries of relevant reports; and selective systematic canvassing of the health science literature for relevant articles between May 2003 and May 2004. I also obtained pertinent articles cited in the reports that I inspected.

The focus of this review is on reports that describe activities conducted from 1975 to the present. In discussing the results, I also draw on selected reports from earlier eras to provide historical context. The identified reports likely constitute the large majority of published work on PN case-finding effectiveness from the last 28 years. Although there may be bias in which reports were ultimately published, it is not clear that the direction of any such

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This research was supported in part by an appointment to the Research Participation Program at the Centers for Disease Control and Prevention, National Centers for HIV, Sexually Transmitted Diseases and Tuberculosis Prevention administered by the Oak Ridge Institute for Science and Education through an interagency agreement between the US Department of Energy and CDC. I am grateful to Matthew Golden, Thomas Peterman, John Potterat, and Richard Rothenberg for their helpful comments on earlier drafts of this paper. An unabridged technical report that accompanies this article is available at http://www.interscientific.net/stdpnrep.pdf.

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Received for publication October 2, 2003, and accepted August 11, 2004.

TABLE 1. Summary of Measures of PN Case-Finding Yield, 1975–2004

| Disease | Number of Reports | Median Brought-to-Treatment Index (range) | Median Elicited/Initiated Partners Who Are Newly Diagnosed Cases (Range), % |
|---|---|---|---|
| Syphilis | 18 | 0.22 (0.05–0.46) | 8 (1–23) |
| Gonorrhea | 21 | 0.25 (0.09–0.58) | 18 (8–34) |
| Chlamydia | 14 | 0.22 (0.05–0.53) | 18 (7–30) |
| HIV | 38 | 0.13 (0.03–0.75) | 8 (0.2–48) |

bias would have been stable over time. The unpublished reports included in the review represent a small fraction of the PN data likely compiled in many areas.

Where multiple reports existed for a particular program's PN activity during the same or overlapping time periods, I used the report with the more comprehensive coverage. In some circumstances, results could be presented for geographic areas at different levels of aggregation. The level I used for defining results was somewhat arbitrary, but my intent was to keep together those cases that were epidemiologically linked or worked by the same staff. If one report focused on an area (eg, a county) embedded in a larger area (eg, a state) for which another report is available, I used the report from the larger area only if the time periods coincided or overlapped. I treated reports pertaining to activities in a particular program for noncontiguous time periods as separate observations.

*Measures of Yield*

I used 2 key measures of case-finding effectiveness, or yield. The first is the brought-to-treatment index.[19] This index equals the number of newly diagnosed cases found (ie, "brought to treatment") in partners divided by the number of cases interviewed for PN. It indicates the mean number of newly diagnosed cases found from interviewing a case for PN. The inverse of this index indicates the mean number of cases that need to be interviewed for PN to discover a newly diagnosed case among partners. The second measure is the number of newly diagnosed cases in partners divided by the number of partners elicited or investigated ("initiated"). This measure indicates the proportion (or percentage if multiplied by 100) of elicited partners who are newly diagnosed cases.

If a report included information that allowed different calculations of yield, I used the most conservative result. In addition, when reports described overlapping samples of cases, I used the report based on the larger sample. Furthermore, wherever possible, I extracted results that were reported separately for women and men and for different diseases or conditions. To describe the distribution of each yield measure, I calculated the median and range by disease. I used only these minimal measures of central tendency and dispersion because some programs contributed multiple results to a summary (introducing nonindependence of results) and the somewhat problematic interpretation of the yield measures (outlined in the online technical report accompanying this article at http://www.interscientific.net/stdpnrep.pdf).

## Results

*Case-Finding Effectiveness of PN*

*Summary of Case-Finding Yield.* PN consistently results in the discovery of newly diagnosed cases of disease, although there is wide variation in yield across diseases and reports (Table 1). The appendix of the online unabridged technical report shows the critical information for each of the reports included in this summary.

There is a surprisingly similar level of yield across the bacterial STD, with median brought-to-treatment index values between 0.22 and 0.25. In other words, for the typical report, approximately 4 to 5 index cases were interviewed for PN to discover a newly diagnosed case of STD, on average. The median brought-to-treatment index for HIV is about half that for the bacterial STD. Despite the continuing controversy over the role of PN in HIV control, there are far more reports on HIV PN yield than for any other STD, even after excluding unpublished reports. In terms of the percentage of elicited partners who are newly diagnosed cases, PN for gonorrhea and chlamydia is approximately 2 to 3 times more productive than PN for syphilis and HIV. The yield from interviewing early latent syphilis cases may be less than that for primary and secondary cases, as indicated by one study in Louisiana[17] and a report on early latent cases[20] with the lowest yield of all syphilis reports.

The case-finding yield for syphilis has ebbed and flowed over the last 70 years. One of the earliest reports of PN for syphilis showed a brought-to-treatment index value of 0.10 for cases diagnosed in 1935 to 1937 in Buffalo, NY.[21] Between 1944 and 1948, the overall brought-to-treatment index for the states and cities monitored by the Centers for Disease Control and Prevention (including 26 states and 5 major cities by 1948) increased from 0.18 to 0.41.[22] In 1948, this index ranged from 0.10 to 0.84 across these areas. Also, in Norfolk, VA, in 1944, 15% of elicited partners of syphilis cases were newly diagnosed with syphilis.[23] The results in Table 1 and the appendix suggest a slide in PN yield for syphilis over the last 40 years, and this corresponds with the decline in the average number of partners elicited (contact index) in syphilis PN contact interviews in the US (from 4 in 1960 to 2 in 1983, as cited by Cates and colleagues[24]).

In contrast, the case-finding yield for gonorrhea PN overall seems to have remained relatively stable over the last few decades. The brought-to-treatment index for gonorrhea PN was 0.28 for 6 states (Alabama, Kentucky, Michigan, Ohio, Tennessee, Virginia) in 1970 to 1971.[25] In 1944, 10% of elicited partners of gonorrhea cases in Norfolk, VA, were newly diagnosed with gonorrhea.[23]

The highest case-finding yields for HIV PN tend to be from reports involving a relatively small number of interviewed cases. Although few reports included a comparison between interviewed cases and all cases diagnosed during the period of the report, it appears that HIV cases in men who have sex with men (MSM) may be underrepresented in many reports of PN yield. Golden and colleagues[26] surveyed the 39 local jurisdictions in the US with 200 or more reported AIDS cases in 2000 about their HIV PN activities. The survey results are consistent with those from my review. Twenty-two jurisdictions provided information on PN yield for 2001, with a median brought-to-treatment index of 0.08 (range = 0.01–1.03).

*Partner Referral Strategies.* Prior reviews consistently showed that when a public health worker or clinical provider takes responsibility for notifying partners (provider and contract referral[18]), more partners are examined than when the patient alone is responsible for notifying partners (patient referral).[7,9,14] There may be a significant proportion of HIV-positive persons who cannot be persuaded to notify any of their sexual partners.[27] For instance, Perry and colleagues[28] found that 30% of their sample of 129 HIV-positive persons had not notified any of their past sexual partners by more than 2 years after diagnosis, despite receiving intensive and repeated counseling to do so.

In some studies, bacterial STD cases have notified a majority of their partners on their own.[29,30] However, most reports indicate that provider referral, when implemented, accounts for a greater percentage of partners actually notified than patient referral[31–36] (also Dandridge et al., unpublished data). Other research shows that simple forms of assistance from public health staff, such as reminder calls to index cases about PN, do increase the number of partners examined through patient referral.[7]

*Case and Partnership Correlates of Successful PN.* Case correlates of partner referral success for gonorrhea and chlamydia include multiple contacts with a disease control worker,[37] majority ethnicity[37,38] (also Phippard et al. and Whittington et al., unpublished data), having only 1 partner (Phippard et al. and Whittington et al., unpublished data), and older age at sexual debut (Phippard et al., unpublished data). Cases detected through screening or spontaneous presentation for care with symptoms produce a higher case-finding yield than those detected through PN.[39,40] However, PN for syphilis in Louisiana between 1993 and 1996 showed essentially uniform yields across different age groups of index cases.[17] Cases' sex also had no relation to yield for STD or HIV PN: the brought-to-treatment index was higher for females in 6 of 12 studies that allowed such comparisons (appendix in online technical report).

In 5 of 7 reports since 1975 that compared MSM and other cases directly, case-finding yields were as high or higher for MSM than for some other categories of cases.[39,41–46] However, the lowest reported case-finding yields for syphilis and HIV PN occurred in samples of cases where MSM overwhelmingly predominate or in areas where the majority of diagnosed cases are in MSM[26] (also see appendix in online technical report). Interestingly, in the 1950s and 1960s, MSM in many US communities (e.g., Dallas, Los Angeles, and Richmond) cooperated extensively with contact investigations for syphilis and gonorrhea, resulting in successful PN, despite the illegality of homosexual behavior at the time in all of those areas.[47–50]

For HIV PN, 2 to 3 times more partners are notified when index cases tested confidentially rather than anonymously,[51,52] even among MSM. One multisite European study[16] demonstrated that PN interviews of recent HIV seroconverters produced a higher brought-to-treatment index (0.16) and percentage of elicited partners who were newly diagnosed as a result of PN (16%) than interviews of other HIV cases (brought-to-treatment index = 0.09; 12% of elicited partners newly diagnosed through PN). Other index case characteristics associated with notifying and testing of partners in HIV PN include younger age,[45,46] minority ethnicity (not controlled for exposure category),[45,46] and diagnosis at a public clinic.[46]

Partners with whom an index case has had sexual contact that is recent, frequent, of a noncommercial nature, and of long duration are more likely to be notified and/or examined than other partners[21,37,38,53] (also Phippard et al., Whittington et al., and Willard et al., unpublished data). This might indicate cases are more prone to notify partners to whom they have a significant emotional commitment or who require less effort to notify. Partners with whom chlamydia cases had recent sexual contact are also more likely to be newly diagnosed with disease than those with whom sexual contact was less recent.[35]

*Innovative Strategies for PN.* In 2 randomized trials in Denmark, chlamydia cases were asked either to give urine sample collection kits to their sexual partners (who would then mail samples to the laboratory in prepaid envelopes) or refer their partners to examination (with a package containing a urethral swab and prepaid envelope for mailing to the laboratory).[54,55] The case-finding yields from cases in the urine collection kits arms were approximately twice as large as that for cases in the standard patient referral arms. A substantially and significantly higher proportion of partners was tested in the urine collection kits arm, and partners in this arm were tested 5 days earlier than those in the standard patient referral arm. An unknown number of partners in the patient referral arm may have been examined but not recorded as such if they did not bring the swab to their examinations. Patient-delivered testing for PN also has proved feasible and successful in general practices in Amsterdam, The Netherlands.[56]

Patient-delivered therapy (PDT) represents another innovative approach to PN. PDT entails diagnosed cases delivering medications (typically for gonorrhea, chlamydia, urethritis, and/or trichomonas) directly or arranging for such delivery to their partners. Observational studies showed that female chlamydia cases in Sweden and New Orleans who received PDT experienced lower rates of reinfection than cases who notified their partners through patient referral.[57,58] Recent randomized trials in the United States comparing PDT and patient referral PN demonstrated that PDT reduced index cases' reinfection with chlamydia by 18% to 20% and reinfection with gonorrhea by 68%[59] (also Golden et al., unpublished data). From a case-finding perspective, there are 2 potential drawbacks of PDT. First, infected partners receiving the patient-delivered medication are not diagnosed as cases, and thus the partners of such undetected cases are not sought for PN. In addition, female partners with PID may go undiagnosed as they are not clinically evaluated in the PDT model.

*Coverage of PN.* The percentage of diagnosed cases of disease who participate in PN is as or more critical to disease control as the level of case-finding yield from PN. Even if PN were very effective in finding new cases, it is likely to have little to modest overall impact on incidence if rarely employed. Golden and colleagues[60] surveyed 78 local health jurisdictions in the United States with the highest rates of STD and HIV in 1998. They found that in the aggregate for the 60 responding jurisdictions, 89% of syphilis cases were interviewed for PN, 52% of HIV cases were interviewed, 17% of gonorrhea cases were interviewed, and only 12% of chlamydia cases were interviewed. This survey's estimate of PN coverage for gonorrhea is somewhat lower than that observed nationally in 1973 to 1979 (31%–37%).[1] In addition, for HIV, gonorrhea, and chlamydia, the proportion of cases interviewed was negatively correlated with the number of cases in a jurisdiction (Pearson correlations ranging from −.55 to −.15). That is, jurisdictions with relatively many cases of disease had lower proportions of cases interviewed than jurisdictions with relatively few cases.

*Impact of PN on Disease Transmission.* Relatively few attempts have been made to evaluate the impact of PN on disease transmission. Woodhouse et al.[34] and Potterat and colleagues[61,62] have assessed the effects of augmenting and redirecting PN on

gonorrhea and chlamydia transmission in Colorado Springs in 3 separate reports covering different time periods between 1971 and 1998. During the periods of intensified PN, disease incidence or complications from disease declined relative to the period preceding the intensified PN. Other observational evidence of the impact of PN comes from New York state (Du et al., unpublished data). Multivariate analyses of county-level data on gonorrhea from 1992 to 2002 showed that the extent of PN coverage and success of PN (percentages of partners identified, located, and preventively treated) at one point in time were independently associated with future incidence rates.

### *Case-Finding Effectiveness of Cluster Investigation and Similar Strategies*

Cluster investigation has almost as long a history in STD control as PN. Traditionally, cluster investigations for STD (typically syphilis) occur parallel to PN and involve interviewing cases and their partners to elicit persons who have symptoms of STD, are partners of STD cases, and/or may otherwise benefit from screening. In disease control jargon, such persons named by cases are called "suspects," and those named by uninfected partners are called "associates." A few reports from the last 20 years document the case-finding results from traditional cluster investigation for syphilis.[17,20,63,64] These reports indicate that the yield is substantially less than that for PN (with the brought-to-treatment index ranging from 0.002–0.11 and the percentage of suspects/associates who are new diagnoses ranging from 0.3–9). These yields appear to be less than those found in earlier years of syphilis control, when syphilis prevalence was many times higher than in recent decades. For instance, in North Carolina in 1945 to 1946, 12% of elicited cluster suspects were new cases brought to treatment (for comparison, 14% of elicited sexual partners were new cases brought to treatment).[65] For 62 CDC program areas between 1968 and 1974, the percentages of syphilis suspects and associates who were newly diagnosed ranged from 4% (suspect/associates who might benefit from screening) to 21% (associates with lesions).[66]

In the last 15 years, some investigators have modified and extended the traditional approach to cluster investigation for bacterial STD. This newer approach involves tracing the sexual and/or social contacts of cases, and often, uninfected persons as well. In some applications of this strategy, such tracing can continue for several generations (or steps) beyond the initial persons interviewed, and may also involve ethnographic fieldwork to identify other promising persons to interview and social settings to investigate for disease control purposes. In 1998, Rothenberg and colleagues[67] applied all aspects of this approach in a project designed to curb syphilis transmission in a zip code in Atlanta with hyperendemic early syphilis. They noted that apportioning credit for newly diagnosed cases to PN or network-based cluster investigation is arguable, given that uninfected sexual and social contacts can eventually lead to case detection. Nonetheless, conservative calculations of the yield from interviewing persons for social contacts produce a brought-to-treatment index value of 0.13 and an estimate that 3% of elicited social contacts were new diagnoses. Had the network investigation not been done in this study, as few as 38% of the new cases ultimately detected would have been found. Thus, the value of this approach can be much greater than the sum of its parts.

Similar applications of related techniques helped describe and likely contain rapidly expanding epidemics of penicillin-resistant gonorrhea in Colorado Springs[68,69] and of syphilis in suburban Atlanta[70] and on an Arizona Indian reservation.[71] In addition, tracing of sexual partners of female chlamydia cases' partners (whether infected or not) produced a brought-to-treatment index value of 0.09 in Gothenburg, Sweden, in 1987 to 1989.[72]

In contrast, in 1996 to 1997 Rosenberg and colleagues[73] (and Rosenberg et al., unpublished data) found no new cases from tracing social contacts of 10 syphilis index cases in the environs of Baton Rouge and repeating the tracing process, in snowball fashion, for the contacts' sexual and social contacts. The difference between this project and the Atlanta project in case-finding effectiveness may be due to differences in the incidence of the 2 areas (260 per 100,000 in the Atlanta zip code vs. approximately 30 per 100,000 in the Baton Rouge environs). Similarly, the traditional cluster investigation with the highest reported yield (brought-to-treatment index = 0.11, 3% of elicited suspects/associates newly diagnosed) was in Montgomery County, AL, in 1991 during a period of high syphilis incidence (348 per 100,000).[63]

Two studies have investigated the case-finding yield of asking persons with or at high risk of acquiring HIV to refer for testing others whom they believe to be at risk. One project involved "recruiters" drawn from an HIV clinic in Los Angeles,[74] and another included MSM recruiters drawn from various clinical and community sources in Seattle (Golden et al., unpublished data). The Los Angeles investigators observed a much higher brought-to-treatment index (0.61) than have the Seattle investigators to date (0.06). It seems that to maintain the long-term productivity of this approach, new recruiters who occupy positions in the social network of persons at risk different from other recruiters must be enrolled on a continual basis, thereby preventing significant "saturation" of recruiters' peers.

The primary value of cluster investigation and related strategies may stem from the possibility of detecting new sexual network components (or "lots" in disease control jargon) with infected persons. Only by traversing sexual links of uninfected persons and nonsexual social links of infected or uninfected persons can these new sexual network components (and their constituent cases) be discovered, outside of screening or symptomatic cases spontaneously presenting for care. It also appears that this approach to case-finding may be productive only in settings with high disease incidence, as regions of the social network surrounding infected persons in low incidence settings are less likely to include other cases.

## Discussion

A review of the literature on PN case-finding effectiveness in developed countries since 1975 indicates a similar yield for syphilis, gonorrhea, and chlamydia PN (about 1 new case found for every 4 or 5 cases interviewed, on average). The yield for HIV PN is approximately half as large, although there is substantial variability in yield across reports for each disease. Many reports underline the central role provider referral plays in effective PN and case finding. Successful PN is more likely with index cases who are of majority ethnicity and detected through screening or spontaneous presentation for care with symptoms and with partners whom index cases have had sexual contact that is recent, frequent, and of long duration. The case-finding yield for HIV PN also is much higher when cases are diagnosed through confidential, rather than anonymous, testing.

Innovative approaches to case-finding and STD/HIV control, such as PDT and testing, also show promise. In the US, nearly all syphilis cases are interviewed for PN but the proportion of gonorrhea, chlamydia, and HIV cases interviewed for PN is low. Cluster investigation and related strategies tend to have lower case-finding yields than PN but can play a very useful case-finding role, especially in settings with high disease incidence, that is not reflected in traditional measures of yield.

This review suggests several priorities for research and practice in this area (see online technical report for expanded discussion). For instance, more research is needed to bolster the relatively thin empirical record on some topics, such as case-finding yield in MSM, the proportion of partners referred by different referral approaches, correlates of successful PN, and yield for cluster investigation and related strategies. In addition, analyses of PN data and simulations could suggest the impact of PDT on disease transmission and case-finding relative to standard PN.

Perhaps the most fundamental question about PN is the degree to which it reduces disease transmission. The available observational evidence suggests PN may play an important role in disease control, although rigorous evaluations are lacking. Randomized trials of PN with communities as the units randomized are necessary to address this major gap in knowledge. Such trials could be done ethically in most areas of the United States for gonorrhea, chlamydia, and HIV PN, as the current standard of care for most gonorrhea and chlamydia cases, and half of HIV cases, is no PN. The trials could occur in the context of an overall expansion of PN services, made possible by increased funding; redirection of local, state, and/or federal program resources to PN (especially in the case of HIV); and/or launching more efficient (in terms of staffing) variations of PN, such as PDT and testing. Similarly, trials of social network-based cluster investigation in areas with high syphilis incidence might be feasible in the context of CDC's syphilis elimination initiative.[75]

As Rothenberg and Potterat have observed, "the valuation of PN does not depend solely on its evaluation."[3] Even when the case-finding yield for PN is very low, it should not be abandoned as a routine public health activity because it still produces epidemiologic insight. For example, by gathering information from cases on the characteristics of their partners and where they meet partners and engage in risky behavior can be used to target screening efforts[76–80] (also Koopman et al. and Lo et al., unpublished data). In such low-yield situations, it may be most efficient, from the standpoint of allocating scarce program resources, to continue some form of interviewing and counseling for PN that does not require significant staff involvement (such as through audio computer-assisted self-interviewing) to gather these data. To be useful, however, these data must be analyzed and the results must inform control efforts; otherwise, PN in such circumstances is of little public health value.

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