Case-finding effectiveness of partner notification and cluster investigation for STD/HIV, unabridged technical report

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Abstract

Objective: To assess the case-finding effectiveness of partner notification (PN) and cluster investigation for STD/HIV

Study Design: 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 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, including patient-delivered therapy and PN provided by staff not employed by a health department, also show promise. 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 empirical foundation of PN and related strategies, including the impact they have on disease transmission.

Key words: partner notification, cluster investigation, yield

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Introduction

Partner notification (PN), or contact tracing, has long been a cornerstone of efforts to control the spread of sexually transmitted diseases (STD) and 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 three 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. Other topics, such as the case-finding

effectiveness of PN relative to other means of finding cases (e.g., screening), cost effectiveness, other potential impacts of PN (e.g., on relationships or sexual behavior), patient/partner attitudes toward and preferences regarding PN, and theoretical examinations—through mathematical modeling—of PN's effect on disease transmission, are beyond the scope of this review. Various aspects of the literature on the effectiveness of PN have been reviewed many times over the past twenty 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.

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 2001 and informal means; an updated search of MEDLINE (via PubMed on May 18, 2003) for relevant articles published in 2001-3 with four pairs of keyword combinations (contact tracing/partner notification x STD/HIV); systematic, selective 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 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 (e.g., a county or set of counties) embedded in a larger area (e.g., 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 non-contiguous time periods as separate observations.

Measures of yield

I used two 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 (i.e., "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" in the jargon of disease intervention workers). Duplicate namings of the same person by different index cases are counted separately in the denominator of this measure. This measure indicates the proportion (or percentage if multiplied by 100) of elicited partners who are newly diagnosed cases ("brought to treatment").

I computed these measures of yield just for those reports that clearly distinguished between new diagnoses and previously diagnosed infections in cases identified through PN. 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 non-independence of results) and the somewhat problematic interpretation of the yield measures (outlined in the next two paragraphs). In addition, I computed annual measures of yield when such data were available for a given area. To study trends in yield over time, I inspected scatterplots of annual case-finding yield and year and calculated Pearson correlations between these variables.

These indices of yield are process measures of the productivity of PN activities, and thus do not necessarily reflect the effectiveness of PN in curbing disease transmission. These measures have a few well-recognized shortcomings. Neither of these measures takes into account the value of epidemiologic, or preventive, treatment usually given to partners who are examined medically or the potential preventive impact of counseling uninfected partners. It is possible that PN could display a low case-finding yield but avert a considerable amount of transmission through preventive treatment, especially when PN takes place quickly after diagnosis. Both measures also tend to produce underestimates of case-finding, as typically there is no information available with which to verify the outcome or disposition for a substantial proportion of elicited partners. However, it is also important to consider that even in settings that lack formal PN services, there may be some new cases found through cases referring partners for examination.

These measures can be influenced by many factors apart from those directly controlled by the local health departments (staffing, staff training, staff motivation, databases for record searches, clinic hours/policies/accessibility, reputation of department in community, proportion of cases interviewed for PN, etc.). These other factors include epidemic phase [20, 21], disease prevalence, sexual/injection network structure [22, 23], prevalence of “anonymous” partnerships among interviewed cases, sensitivity of diagnostic tests used, regularity and prevalence of STD screening/HIV testing in the community, disease characteristics (e.g., frequency and severity of symptoms, duration of infectious periods), community characteristics (e.g., size, mobility, economy, attitude

toward PN, etc.), duration of PN activity on which the reported yield is based, how cases were initially detected (through PN, screening, and/or symptomatic persons spontaneously presenting for care), correspondence between interview period (period for which partners are elicited) and time since case acquired infection, patient cooperation with PN, and number of partners elicited, among other variables. In one sense, reports of case-finding yield can be considered epidemiologic "case studies" that should be compared cautiously.

In addition to summarizing case-finding yield, I also provide a brief review of research on the relative case-finding effectiveness of different PN referral strategies, factors associated with successful PN at the level of individual cases and partnerships, innovative strategies for PN, coverage of PN, and impact of PN on disease transmission.

Results

Case-finding effectiveness of partner notification

Summary of case-finding yield. The Appendix shows the critical information for each of the reports included in this summary. Clearly, 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).

[Insert Table 1 about here]

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 [24] 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 1935-37 in Buffalo, New York [25]. 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 .18 to .41 [26]. In 1948, this index ranged from .10 to .84 across these areas. Also, in Norfolk, Virginia, in 1944, 15% of elicited partners of syphilis cases were newly diagnosed with syphilis [27]. 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 interviews in the US (from 4 in 1960 to 2 in 1983, as cited by Cates and colleagues [28]).

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 .28 for six states (AL, KY, MI, OH, TN, VA) in 1970-1971 [29]. In 1944, 10% of elicited partners of gonorrhea cases in Norfolk, Virginia, were newly diagnosed with gonorrhea [27].

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[30] 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 to 1.03).

The available data indicate that within communities, case-finding yield can increase, remain stable, or decrease over time. In Louisiana, the brought-to-treatment index for syphilis PN was virtually the same (0.13-0.14) during a period of high incidence (50 per 100,000 [primary and secondary syphilis] in 1993-94) as it was during a subsequent period of lower incidence (19 per 100,000 in 1995-96) [17]. Between 1983 and 1999 in Colorado Springs [31], the brought-to-treatment index for gonorrhea PN decreased from approximately 0.35 in the early part of the period to about 0.20 in the latter part of the

period (r = -.33, p > .1). This period showed a dramatic, steady drop in the number of reported gonorrhea cases, from a peak of 1,530 in 1985 to a nadir of 319 in 1997. Interestingly, case-finding yield more closely corresponded with the annual number of reported gonorrhea cases (r = .42, p < .1), suggesting that case-finding was easier when there were more cases to find. Moreover, the brought-to-treatment index for HIV PN in King County (Seattle), Washington (Washington State Department of Health, unpublished data), declined markedly and linearly between 1993 and 2002, from approximately 0.04 in the early part of the period to essentially 0.00 in the latter part of the period (r = -.83 between annual yield and year, p < .01). In contrast, the region of Washington state with the second highest burden of HIV (including Tacoma and environs) showed an opposite trend of linearly increasing yield over the same period (r = .56, p < .1), from approximately 0.03 in the early part of the series to approximately 0.13 in the latter part of the series (Washington State Department of Health, unpublished data).

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[32]. For instance, Perry and colleagues found that 30% of their sample of 129 HIV+ persons had not notified any of their past sexual partners by more than two years after diagnosis, despite receiving intensive and repeated counseling to do so [33].

In some studies, bacterial STD cases have notified a substantial proportion of their partners on their own. In Colorado Springs in 1975, 76% of untreated female contacts to heterosexual male gonorrhea cases were brought to examination through patient referral after a brief PN interview with the case and one reminder telephone call [34]. In Seattle in 1998-9, only 35% of gonorrhea and chlamydia cases diagnosed by private providers had not notified any partner 7 days after being treated [35]. Other studies show 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].

However, other data paint a different picture. Only 12-41% of untreated female and male contacts to gonorrhea from Colorado Springs from 1976-1981 were examined as a result of patient referral – the rest were examined by public health staff after patients had not succeeded in notifying them [36-39]. Even for male partners of women with gonorrhea who said they had notified all their male partners, only 32-44% were

confirmed to have been examined [37]. Of 86 notified partners of chlamydia cases in Boston in 2002, 48% were notified by patient referral, 36% were notified by provider referral, and 15% were notified through both approaches [40]. In 1981 in Colorado Springs, approximately half of new gonorrhea cases brought to treatment (51% of new male cases, 47% of new female cases) through PN were referred through provider referral [39]. During two different periods between 1988 and 1997 in Colorado Springs, 43-66% of new chlamydia cases brought to treatment through PN were referred through provider referral [41, 42]. Among the 6 AIDS regions of Washington state from 1993-2002 (Washington State Department of Health, unpublished data), between 21% and 71% (median = 42%) of newly diagnosed HIV cases found through PN were referred through provider referral. Hence, the evidence overall indicates that provider referral accounts for a large share of the PN that actually occurs.

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 [43], majority ethnicity [20, 43-45], having only one partner [44, 45], and older age at sexual debut [45]. Cases detected through screening or spontaneous presentation for care with symptoms produce a higher case-finding yield than those detected through PN [46, 47]. 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 has 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 five of seven 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 [46, 48-53]. 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 vast majority of diagnosed cases are in MSM[30] (also see Appendix). 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 [54-57].

For HIV PN, two to three times more partners are notified when index cases tested confidentially rather than anonymously [58, 59], 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[52, 53], minority ethnicity (not controlled for exposure category)[52, 53], and diagnosis at a public clinic[53].

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 [20, 25, 43-45, 60, 61]. This might indicate cases are more prone

to notify partners to whom they feel a significant emotional commitment or whom 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 [41].

Innovative strategies for PN. Most PN in the US is conducted by local or state health department disease control staff. One report from Chicago, however, described a research project in which outreach workers--former injection drug users (IDUs) who were not employed by the health department--performed PN with newly diagnosed HIV-positive IDUs [62]. Most cases offered provider-referral accepted this service for one or more partners. The brought-to-treatment index value for this sample was .28, higher than most of those reported in the Appendix for HIV PN.

In two 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) [63, 64]. 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 were 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.

This variant of PN also has proved feasible and successful in general practices in Amsterdam [65].

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 [66, 67]. Recent randomized trials in the US comparing PDT and patient referral PN demonstrated that PDT reduced index cases' reinfection with chlamydia by 18-20% and reinfection with gonorrhea by 68% [68, 69]. From a case-finding perspective, there are two potential drawbacks of PDT. First, infected partners receiving the patient-delivered medication are not diagnosed as cases, and thus 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 [70] surveyed 78 local health jurisdictions in the US 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 1973-1979 (31-37%) [1]. In addition, for HIV, gonnorhea, and chlamydia, the proportion of cases interviewed was negatively correlated with the number of cases in a jurisdiction (r's ranged 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. Few attempts have been made to evaluate the impact of PN on disease transmission. Potterat and colleagues have assessed the effects of augmenting and redirecting PN on gonorrhea and chlamydia transmission in Colorado Springs. Beginning in 1971, after a period of rising gonorrhea incidence, they implemented a gonorrhea control program including screening, PN, education, and expansion of public clinics [71]. In 1975 and 1976, Potterat and colleagues shifted priority of PN to interviewing women (to find and treat the reservoir of asymptomatic men thought to sustain endemicity) and began systematic STD surveillance in street prostitutes. The number of cases reported annually remained stable from 1972 to 1974 (during the first three years of the gonorrhea control program), increased in 1975-7 (during the shift of PN efforts and surveillance in prostitute women), and then, by 1979, fell back to the 1972 level. During this period, the population of Colorado Springs grew by 41%, which means that the gonorrhea incidence rate dropped by 29% over the 1972-79 period. The rest of Colorado and the US as a whole showed a plateau in the number

of reported cases by 1975-76, but did not experience any decline from that point through 1979.

Woodhouse, Potterat, and colleagues intensified gonorrhea PN in Colorado Springs between 1980 and 1982 by instituting systematic PN interviewing and case-finding with the community's largest gonorrhea reporting source (an Army base hospital) [39]. During this period of intensified PN, relative to the 1977-79 period preceding the expansion of PN, there was a higher number and proportion of cases found through PN, a decline in male to female ratio of gonorrhea cases, and a corresponding decrease in gonorrhea incidence locally (particularly among women spontaneously presenting for care with symptoms) but much milder decreases at the state and national levels. Potterat and colleagues initiated a similar expansion of chlamydia PN in Colorado Springs in 1996, adding coverage of cases diagnosed by private providers to cases diagnosed by public and military providers who had received PN services since 1988 [22]. Although chlamydia incidence climbed during the period of enhanced PN, the increase was also associated with the introduction of more sensitive DNA amplification diagnostic tests. Importantly, the percentage of female patients visiting the family planning and STD clinics in Colorado Springs who complained of lower abdominal pain declined from 16.3% in 1994 (before the expansion of PN) to 13% (4 years after the enhanced PN began).

Other observational evidence of the impact of PN comes from New York state[72]. 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 twenty years document the case-finding results from traditional cluster investigation for syphilis [17, 24, 73, 74]. These reports indicate that the yield is substantially less than that for PN (with the brought-to-treatment index ranging from 0.002 to 0.11 and the percentage of suspects/associates who are new diagnoses ranging from 0.3 to 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 1945-1946, 12% of elicited cluster suspects were new cases brought to treatment (for comparison, 14% of elicited sexual partners were new cases brought to treatment) [75]. 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) [76].

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 applied all aspects of this approach in a project designed to curb syphilis transmission in a zip code in Atlanta with hyperendemic early sypyhilis [77]. 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 pencilin-resistant gonorrhea in Colorado Springs [78, 79] and of syphilis in suburban Atlanta [80] and on an Arizona Indian reservation [81]. 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 1987-89 [82].

In contrast, in 1996-97 Rosenberg and colleagues [83] (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 two 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, Alabama, in 1991, during a period of high syphilis incidence (348 per 100,000) [73].

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 [84], 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 also show promise. One study showed that outreach staff not employed by a health department provided HIV PN services effectively to injection drug users and found new cases of disease. PDT is more effective than patient referral in terms of index case reinfection. 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. 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.

Consistent with CDC guidance [85], it is important for disease control programs to collect and report more complete and specific information about cases, partners, and PN outcomes. It is unclear how to interpret published reports of contact index results, as disease control staff often record only those partners, suspects, and associates that are

initiated (and thus likely to be located) [86]. Although this serves an administrative purpose, it leaves little clue as to whether the network structure, levels of partner anonymity, and/or staff recording/investigative behavior underlie differences in this index over time and between programs. Therefore, the recording of all elicited partners, suspects, and associates, regardless of their locatability, as well as information about such persons (demographic, behavioral, and partnership characteristics), should become standard PN procedures. Finally, authors reporting outcomes for PN activities should routinely include results on the key measures of case-finding yield. Many more reports could have been included in this review had such information been reported in the original articles.

Even with the apparent advantage of PDT over patient referral for gonorrhea and chlamydia PN, it is likely that provider referral will still be necessary for some cases and partners (perhaps the most epidemiologically critical ones). Control programs should consider developing triage systems that focus disease control staff's efforts on these persons (Matthew R. Golden, personal communication).

Analyses of PN data and simulations could suggest the impact of PDT on disease transmission and case-finding relative to standard PN. Because patient-delivered therapy does not typically result in diagnosis of infected partners and tracing chains of infection beyond index cases, it is possible that the sexual networks supporting transmission are not penetrated sufficiently to have a long-term effect on incidence. Infected partners of cases identified through screening or symptomatic persons

spontaneously presenting for care are not always terminal nodes in such chains of transmission, as the case-finding yield is still appreciable when such persons participate in PN. Similarly, network analyses of PN data should be performed to examine whether cases discovered through PN, screening, and spontaneous presentation for care differ in their network positions, and thus transmission potential. The results from such analyses could inform next-generation simulations that model the impact of PN on disease transmission.

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 US 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 patient-delivered therapy 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 [87].

In trials of PN and related strategies, the primary outcomes should include disease incidence (measured by reported cases for STD, reported STD cases presenting spontaneously with symptoms, STD reinfection rates, and the STARHS algorithm for detecting recent HIV infections [88] among cases not discovered through PN), bacterial STD prevalence (as assessed by probability sample surveys of the community [89]) and incidence of complications of infection [22, 39, 90, 91]. Effective PN will likely produce an overall increase in case-finding initially [22, 39, 71], thus outcome measures other than overall incidence are crucial to include.

As Rothenberg and Potterat have observed, "the valuation of partner notification 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 [92-98]. 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.

Appendix

Summary of reports of STD/HIV yield from partner notification and cluster investigation from 1975-2003 in developed countries

Partner notification

Author	Location	Year(s)	Disease	Number of cases interviewed[a]	Brought-to-treatment index	% of elicited who are new cases[b]
Brewer et al. (unpublished data)	King County, WA	1998-2003	Early syphilis	271 (88% MSM)	0.09	---
Chen et al. (2002)	Los Angles County, CA	1999-2000	Early syphilis	87 MSM	0.07	7
Engelgau et al. [73, 74]	Montgomery County, AL	1991	Early syphilis	373 (4% MSM)	0.30	11
Gunn & Harper [24]	San Diego County, CA	1994-95	Early latent syphilis	156	0.05	1
Jayaraman et al. [49]	Calgary, Canada	2000-02	Early syphilis	14 MSM	0.29	11
Jayaraman et al. [49]	Calgary, Canada	2000-02	Early syphilis	17 heterosexual cases	0.12	3
Kohl et al. [17c]	Louisiana	1993-96	Early syphilis	5,732 males	0.32	12
Kohl et al. [17c]	Louisiana	1993-96	Early syphilis	7,182 females	0.30	8
Kohl et al. [17c]	Louisiana	1993-96	Early syphilis	1,782 primary cases	0.33	7
Kohl et al. [17c]	Louisiana	1993-96	Early syphilis	3,765 secondary cases	0.39	8
Kohl et al. [17c]	Louisiana	1993-96	Early syphilis	7,360 early latent cases	0.26	12
Merino & Richards [50]	Los Angeles County, CA	1976	Primary and secondary syphilis	811	0.20	8
Oxman & Doyle [99]	Portland, OR	1989-92	Early syphilis	300	0.15	---

Partner notification (continued)

Author	Location	Year(s)	Disease	Number of cases interviewed[a]	Brought-to-treatment index	% of elicited who are new cases[b]
Peterman et al. [100]	Broward County, FL	1990-93	Early syphilis	1,191 (14% MSM across sites)	0.18	3
Peterman et al. [100]	Tampa, FL	1990-93	Early syphilis	569 (14% MSM across sites)	0.22	3
Peterman et al. [100]	Paterson, NJ	1990-93	Early syphilis	206 (14% MSM across sites)	0.22	3
Poulton et al. [101]	Brighton, UK	1999-2001	Early syphilis	30 (93% MSM)	0.17	2
Romanowski et al. [102]	Alberta, Canada	1981-87	Early syphilis	1,089 (17% MSM)	0.23	23
Rothenberg et al. [77]	Atlanta, GA	1998	Early syphilis	48	0.38	14
Schulte et al. [103]	4 rural Texas towns	1992	Early syphilis	118	0.46	16
Cleveland[104]	Dade County, FL	N/A	Gonorrhea	1,266 (patient referall, no partner elicit.)	.25	8
Cleveland[104]	Dade County, FL	N/A	Gonorrhea	632 (contract referral with partner elicit.)	.37	13
Curran et al. [105]	Columbus, OH	1978-79	Gonorrhea	333 females	0.40	34
David et al. [46]	Coventry, United Kingdom	1991-94	Gonorrhea	201 heterosexual males	0.43	---
David et al. [46]	Coventry, United Kingdom	1991-94	Gonorrhea	167 females	0.14	---
David et al. [46]	Coventry, United Kingdom	1991-94	Gonorrhea	36 MSM	0.17	---

Partner notification (continued)

Author	Location	Year(s)	Disease	Number of cases interviewed[a]	Brought-to-treatment index	% of elicited who are new cases[b]
Du et al.[72]	New York state	1992-2002	Gonorrhea	37,382	0.20	21
EPCDHE [31]	Colorado Springs, CO	1983-99	Gonorrhea	12,284	0.28	27
Judson & Wolf [106]	Denver, CO	1975	Gonorrhea	3,451 males	0.23	---
Judson & Wolf [106]	Denver, CO	1975	Gonorrhea	1,704 females	0.12	---
Katz et al. [107]	Indianapolis, IN	1983-89	Gonorrhea and chlamydia	16,560 heterosexual cases (55% gonorrhea)	0.25	---
Potterat & Rothenberg [34]	Colorado Springs, CO	1975	Gonorrhea	187 hetero-sexual males	0.58	28
Potterat et al. [36]	Colorado Springs, CO	1976-78	Gonococcal PID	110 females	0.38	11
Potterat et al. [36]	Colorado Springs, CO	1976-78	Uncomp. gonorrhea	165 females	0.52	18
Potterat et al. [38]	Colorado Springs, CO	1980-81	Gonorrhea	255 female cases detected through PN	0.24	8
Ruden et al. [47]	Stockholm, Sweden	1987-89	Gonorrhea	671 (2% MSM)	0.27	22
Starcher et al. [108]	Des Moines, IA	1978	Gonorrhea	983 heterosexual cases	0.24	11
van de Laar et al. [20]	Amsterdam, The Netherlands	1986-88	Gonorrhea	98 heterosexual males	0.20	15

Partner notification (continued)

Author	Location	Year(s)	Disease	Number of cases interviewed[a]	Brought-to-treatment index	% of elicited who are new cases[b]
van de Laar et al. [20]	Amsterdam, The Netherlands	1986-88	Gonorrhea	24 heterosexual females	0.42	27
van Duynhoven et al. [43]	Rotterdam, The Netherlands	1994	Gonorrhea	41 males (16% male Gc/Ct cases = MSM)	0.17	---
van Duynhoven et al. [43]	Rotterdam, The Netherlands	1994	Gonorrhea	14 females	0.09	---
Andersen et al. [63]	Aarhus County, Denmark	N/A	Chlamydia	45 females (home urine sampling for partners)	0.27	18
Andersen et al. [63]	Aarhus County, Denmark	N/A	Chlamydia	51 females (standard patient referral)	0.14	10
EPCDHE [31]	Colorado Springs, CO	1988-99	Chlamydia	6,863	0.34	21
Ostergaard et al.[64]	4 counties in Denmark	1999-200	Chlamydia	249 females (office testing of SPs)	0.18	16
Ostergaard et al.[64]	4 counties in Denmark	1999-200	Chlamydia	283 females (home testing of SPs)	0.26	22
Ostergaard et al.[64]	4 counties in Denmark	1999-200	Chlamydia	98 males (office testing of SPs)	0.05	11

Partner notification (continued)

Author	Location	Year(s)	Disease	Number of cases interviewed[a]	Brought-to-treatment index	% of elicited who are new cases[b]
Ostergaard et al.[64]	4 counties in Denmark	1999-200	Chlamydia	111 males (home testing of SPs)	0.15	30
Ramstedt et al. [82]	Gothenburg, Sweden	1987-88	Chlamydia	425 asymptomatic females	0.22	18
Ramstedt et al. [82]	Gothenburg, Sweden	1988-89	Chlamydia	100 female STD clinic cases	0.53	30
van de Laar et al. [20]	Amsterdam, The Netherlands	1986-88	Chlamydia	128 heterosexual males	0.44	23
van de Laar et al. [20]	Amsterdam, The Netherlands	1986-88	Chlamydia	101 heterosexual females	0.23	14
van Duynhoven et al. [43]	Rotterdam, The Netherlands	1994	Chlamydia	97 males (16% male Gc/Ct cases = MSM)	0.19	---
van Duynhoven et al. [43]	Rotterdam, The Netherlands	1994	Chlamydia	85 females	0.20	---
van Duynhoven et al. [43]	Rotterdam, The Netherlands	1994	Chlamydia & gonorrhea	250 (182 Ct, 55 Gc)	---	7

Partner notification (continued)

Author	Location	Year(s)	Disease	Number of cases interviewed[a]	Brought-to-treatment index	% of elicited who are new cases[b]
CDC [109]	Idaho	1985-88	HIV	97	0.23	19
CDC [109]	Virginia	1986-87	HIV	387	0.11	---
Cross et al. [110]	New Jersey	1997	HIV	---	---	7 (12% of initiated partners = MSM)
Department of Health (WA) (unpublished data)[d]	AIDSNET region 1 (Spokane)	1993-2002	HIV	164	0.09	2 (elicited) / 6 (initiated)
Department of Health (WA) (unpublished data)[d]	AIDSNET region 2 (Yakima)	1993-2002	HIV	130	0.18	5 (elicited) / 10 (initiated)
Department of Health (WA) (unpublished data)[d]	AIDSNET region 3 (Everett)	1993-2002	HIV	176	0.10	3 (elicited) / 6 (initiated)
Department of Health (WA) (unpublished data)[d]	AIDSNET region 4 (Seattle/King County)	1993-2002	HIV	1,782	0.03	0.2 (elicited)/ 1 (initiated)
Department of Health (WA) (unpublished data)[d]	AIDSNET region 5 (Tacoma)	1993-2002	HIV	305	0.08	2 (elicited) / 6 (initiated)
Department of Health (WA) (unpublished data)[d]	AIDSNET region 6 (Vancouver)	1993-2002	HIV	232	0.08	3 (elicited) / 6 (initiated)
de Souza & Munday[51]	Watford, UK	2000-02	HIV	15 MSM	0.13	12
Souza & Munday[51]	Watford, UK	2000-02	HIV	30 heterosexual females	0.23	11
Souza & Munday[51]	Watford, UK	2000-02	HIV	14 heterosexual males	0.43	17
Elliott et al. [111]	Birmingham, UK	1996-97	HIV	28	0.43	48

Partner notification (continued)

Author	Location	Year(s)	Disease	Number of cases interviewed[a]	Brought-to-treatment index	% of elicited who are new cases[b]
European PN Study Group [16]	Denmark; Scotland, UK; Helsinki, Finland; Athens, Greece; Oslo, Norway	1995-96	HIV	356 "sexually infected" cases (49% MSM)	0.11	13
Fenton et al. [112]	England, UK	1994-95	HIV	70 (54% MSM)	0.11	5
Foust et al.[53]	North Carolina	2001	HIV	385 MSM	0.10	9
Foust et al.[53]	North Carolina	2001	HIV	116 IDU	0.07	7
Foust et al.[53]	North Carolina	2001	HIV	26 MSM/IDU	0.12	10
Foust et al.[53]	North Carolina	2001	HIV	399 heterosexual males	0.08	8
Foust et al.[53]	North Carolina	2001	HIV	401 heterosexual females	0.10	8
Giesecke et al. [48]	Sweden	1989-90	HIV	365 (38% MSM)	0.15	9
Jordan et al. [84]	Los Angeles, CA	1994-95	HIV	68 women	0.13	---
Jordan et al. [84]	Los Angeles, CA	1994-95	HIV	9 men newly diagnosed HIV+ (naming women)	0.67	11
Jordan et al. [84]	Los Angeles, CA	1994-95	HIV	23 men previously tested HIV+ (naming women)	0.35	16

Partner notification (continued)

Author	Location	Year(s)	Disease	Number of cases interviewed[a]	Brought-to-treatment index	% of elicited who are new cases[b]
Kristoffersen & Petersen [18, 113]	Oslo, Norway	1986-89	HIV	225	0.34	29
Lee et al., Wells & Hoff [114, 115]	Kansas City, MO	1989-93	HIV	472 (19990-93: 66% MSM)	0.12	11 (1988-89)
Levy & Fox [15, 62]	Chicago	N/A	HIV	138	0.28	---
Mir et al. [116]	Scotland, UK	1995-96	HIV	114 (49% MSM)	0.10	8
Pattman et al. [117]	Newcastle upon Tyne, UK	1985-92	HIV	114 (82% MSM)	0.22	---
Pavia et al. [118]	Utah	1988-90	HIV	308 (62% MSM)	0.13	4
Rutherford et al. [119]	San Francisco, CA	1985-87	HIV	51 heterosexual/ bisexual cases (63% MSM)	0.14	5
Schwarcz et al. [120]	San Francisco, CA	1998-99	HIV	5	0.20	13
Taylor et al. [121]	San Bernadino County, CA	1985-86	HIV	8 het. cases	0.75	---
Toomey et al. [52]	Tampa Bay & Broward County, FL, Paterson, NJ	1990-93	HIV	396 females	0.14	2
Toomey et al. [52]	Tampa Bay & Broward County, FL, Paterson, NJ	1990-93	HIV	419 heterosexual males	0.09	2
Toomey et al. [52]	Tampa Bay & Broward County, FL, Paterson, NJ	1990-93	HIV	255 MSM	0.13	1
Vernon et al. [122, 123]	Colorado	1986-92	HIV	2,837 (76% MSM in 1988)	0.10	6

Partner notification (continued)

Author	Location	Year(s)	Disease	Number of cases interviewed[a]	Brought-to-treatment index	% of elicited who are new cases[b]
Wykoff et al. [124]	Rural South Carolina	1987-89	HIV	91	0.51	8 (75% of elicited partners = MSM)

[a]Percent of cases who are MSM is indicated if such information was included in the report.

[b]Number of partners initiated is used only when number of partners elicited is unavailable.

[c]The yield from this report is reported in two ways: by sex and stage of disease. The yields by disease stage were used in the summary.

[d]The results from these reports reflect only those PN interviews reported to the state health department, and therefore represent an unknown and likely varying proportion of all HIV PN interviews conducted in these jurisdictions.

Cluster investigation and related strategies

Author	Location	Year(s)	Disease	Number of persons interviewed*	Brought-to-treatment index	% of elicited partners who are new cases
Engelgau et al. [73, 74]	Montgomery Co., AL	1991	Early syphilis	373	0.11	3
Gunn & Harper [24]	San Diego Co., CA	1994-95	Early latent syphilis	156	0.01	0.3
Rosenberg et al. [83] (unpublished data)	Baton Rouge, LA and environs	1996-97	Primary and secondary syphilis	90 heterosexual cases, sexual partners, and social partners (snowballed 2 generations)	0.00	0
Rothenberg et al. [77]	Atlanta, GA	1998	Early syphilis	48	0.13	3
Kohl et al. [17]	Louisiana	1993-96	Early syphilis	12,927	0.03 (suspects)	9 (all clusters)
Kohl et al. [17]	Louisiana	1993-96	Early syphilis	12,927	0.002 (assoc.)	9 (all clusters)
Ramstedt et al. [82]	Gothenburg, Sweden	1987-89	Chlamydia	530 male contacts to chlamydia	0.09	---
Golden et al. (unpublished data)	King County, WA	2002-03	HIV	174 MSM bacterial STD cases & other high-risk MSM	0.06	---
Jordan et al. [84]	Los Angeles, CA	1994-95	HIV	28 HIV clinic patients	0.61	---

*Cluster investigations included tracing of suspects and associates unless otherwise specified.

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Table 1. Summary of measures of PN case-finding yield, 1975-2003

Disease	Number of reports	Median brought-to-treatment index (range)	Median % of 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)