[DRAFT]

Syphilis Outbreak Detection Guidance

STD Subcommittee

Council of State and Territorial Epidemiologists
This document has been created by a workgroup of the CSTE STD Subcommittee and is presented in draft form for discussion at the 2015 CSTE Annual Conference. Questions, comments, or suggestions can be directed to Lynn Sosa (lynn.sosa@ct.gov) and Monica Lachey (mlachey@cste.org).
Introduction

Since 2000, when the lowest rate of primary and secondary syphilis cases ever reported occurred (1.5/100,000), syphilis incidence has steeply increased with a rate of 5.5/100,000 reported in 2013 (2013 CDC STD Surveillance Report, 2015). The national epidemiology of early syphilis is well-recognized with cases occurring primarily among men who have sex with men with a high incidence of HIV coinfection practicing high risk behaviors. State and local Sexually Transmitted Diseases (STD) Programs are responsible for recognizing and understanding their local epidemiology to determine how best to target interventions to decrease the number of cases that are occurring in their jurisdiction. While partner notification activities, usually accomplished through the work of Disease Intervention Specialists, are often one of the primary methods used by STD Programs to prevent spread of syphilis and other STDs in their jurisdiction, sometimes these routine activities alone are not sufficient. It is important for STD Programs to be able to identify those situations where additional resources might be needed (for example, during an outbreak) to curb transmission in a given community.

This document was developed to give STD Programs a framework for understanding their epidemiology and how they can determine if and when an outbreak might be occurring and when additional resources and activities could be needed to prevent further transmission of disease. While many of the tools and strategies described here could be applied to any STD, the focus of this document is syphilis given the scientific complexities of the disease, the high impact on morbidity (e.g. congenital syphilis), and the special attention syphilis receives through partner notification efforts and through grant funding from CDC. The tools and strategies described here are put forth as best practices in syphilis outbreak detection that can be adapted to any jurisdiction’s incidence and burden of disease.

Know the Data

Section Summary:

1. Establish normal baseline data
2. Determine the appropriate frequency of data reports
3. Assess your data by subpopulations of interest
4. Identify reporting providers/laboratories
5. Meet with field/clinic staff regularly

A routine review of case data for your jurisdiction and sub-areas within it will ensure that an outbreak can be easily identified as soon as case data is received by your disease surveillance system. The frequency of review should be at least monthly, but will likely depend on staffing and data analysis...
capacity. Automation of data reports in SAS or other software such as Epi Info is helpful, and requires minimal resources to maintain once processes are established.

Good data review practices could start with a weekly assessment of raw counts (by week) of reported/diagnosed cases at the locality level. This type of review could include a year to date comparison with data from previous years in order to identify possible increases not attributable to seasonal variation. A monthly report displaying case counts for the previous 24 months could also be useful, and would show increases that might not be noticeable on a review of weekly case counts. Quarterly reports should include both case counts and population rates (for the previous years), as well as year to date case counts as of the end of the most recent quarter.

At least quarterly, data should also be assessed by a series of basic demographics and other available variables, in order to better characterize the population affected. Variables to stratify by include age, race, ethnicity, gender, gender of sex partners, provider type, HIV coinfection, stage of disease, geography (county/locality of residence), as well as other meaningful data variables. Through this process, you will identify subpopulations of interest in your jurisdiction in order to be able to identify shifting patterns in disease trends over time. Subpopulations at risk can be defined not only based on demographics, but also on location:

- Men who have sex with men (MSM)
- Persons with multiple sexual partners within the interview period
- Demographic groups with historically high rates of disease
- Geographic areas with high rates/numbers of cases

Since data in any disease surveillance system depends entirely on case reporting from providers and laboratories, it is important to identify which facilities are usually submitting case reports in your jurisdiction. In case of an abnormal change (whether increase or decrease) in the number of cases reported, it is a good idea to investigate whether there are new facilities reporting, or whether any traditional facilities have stopped reporting. Changes in state reporting regulations as well as changes in your program reporting guidelines could affect the number of cases reported. In general, be aware of normal baseline data, both overall and for sub-areas/populations, such that any changes in trends for your jurisdiction can be easily identified. Past outbreaks should be excluded when establishing baselines. For example, if your area experiences an increase in cases among women and heterosexual men, while the baseline data indicates that historically a majority of cases have occurred among MSM, this indicates a shift in disease transmission into the heterosexual population, including the possibility of congenital syphilis cases. This information is important even if the overall case number does not increase.

Another key tool for early outbreak identification is knowledge of ongoing field activities. Regular weekly/monthly discussions about trends in observed cases should include DIS and DIS supervisors; they will provide additional insight and possible explanations for observed trends in cases. It is important to assess any anecdotal information, including any unusual clusters/cases observed in populations not normally at risk. Many times this type of information is known by field staff ahead of
the case reports’ entry in the surveillance system. Field staff will also have information on the number of cases not yet reported that are still under investigation, as well as cases observed in areas where they do not normally occur. Furthermore, field staff can also tell you if they have noticed changes in methods of meeting partners, such as usage of new websites/apps, or new hangout spots in their area. Information on local STD prevention efforts, such as large screening events, may result in an increased number of cases identified; other community events involving populations at risk, such as conventions or large parties, may also explain an observed increase in cases.

Any case reporting issues in your jurisdiction will impact the number of cases in your disease surveillance data system. To identify a jurisdiction/area that may not be reporting in a timely manner, look for decreased case counts compared to previous years, especially where surrounding areas continue to show high morbidity. Delays between diagnosis and report dates are also a good indicator of problems in reporting cases. Areas that are short-staffed might experience investigation and reporting delays. Be aware of DIS and DIS supervisor position vacancies, whether any staff are on extended leave, or perhaps instances when an area is fully staffed, but dealing with an increased number of cases resulting in reporting backlogs.

It may also be beneficial to meet with clinic staff regularly. Different clinics have different diagnosis capabilities; for example, they may or may not offer cultures or extragenital screening. Increases in clinic demand for services, changes in the number of clinic visits and/or populations requesting services are all possible indicators of increased morbidity. However, changes in the number of cases detected may also be the result of modifications to clinic hours or schedules, such as the opening of an evening specialty clinic.

Apply the Data

Outbreaks of STDs differ from food-borne or other point source outbreaks. Since STDs by design are transmitted from person to person through sexual contact, outbreaks do not generally appear spontaneously with large numbers of cases, as is common in food or waterborne outbreaks. Instead, outbreaks of STDs tend to grow gradually as the infection moves through sexual networks with increased velocity. Therefore, defining a true STD “outbreak” may be more complex than with other infectious pathogens. Here, we provide guidance in ways to approach applying locally available data to help establish and define an outbreak.

Defining an outbreak

Section Summary:

- An outbreak may be an increase in disease or markers of infection above historic numbers of cases.
- Caution should be taken when defining the geographic boundary where an outbreak occurs.
Outbreaks represent increases in disease above what would be expected. The challenge in defining an outbreak is often determining “what would be expected”. For example, in states where chlamydia is endemic, a large increase in cases may represent an outbreak situation. Alternatively, small numbers of new cases of congenital syphilis in a county with no recent cases reports could also be considered an outbreak. Rather than focusing on one definition, here we present multiple ways to identify possible outbreaks related to STDs in a local or state jurisdiction. It is important to keep in mind that geographic boundaries are generally arbitrary and individuals cross state, county and city boundaries often for work and play. Therefore, caution is needed in defining a geographic boundary too narrowly, which may obscure or minimize possible outbreaks affecting at risk populations.

The most common approach to identification of outbreaks involves the review of case counts. Recent aggregate totals of case counts are compared to historic trends to determine whether recent activity may represent an outbreak (1). Important caveats to this approach include:

- Delays in reporting of cases
- Under-reporting of cases
- Asymptomatic infections that go undiagnosed

Alternatively, markers of possible new infections may also be useful to monitor. For example, analysis of trends in reactive syphilis serologic reports, or high titer syphilis serologic reports to the local or state health jurisdiction may help identify possible increases in local infection (2). Increases in syphilis in women may predict increases in cases of congenital syphilis.

**Approaches to thinking about outbreaks**

**Section Summary:**

- Better transportation and electronic technologies have facilitated meetings across geographic boundaries; thinking about where outbreaks occur has changed.
- Along with geography, one must also consider the population or venue that is associated with the outbreak.

Thinking broadly about the context of outbreaks within the context of STD prevention and control is useful. The typical approach to exploring outbreaks explores increases of disease in a specified geographic area over the course of a defined period of time. The wider availability of geographic information software (GIS) allows for the creation of maps at various resolutions (states, counties, cities, neighborhoods, block groups). Furthermore, statistical software packages such as SatScan ([http://www.satscan.org/](http://www.satscan.org/)) are available to conduct statistical analysis of geographic disease clusters and can be useful in describing geographic areas of increased STD morbidity. It is critical to consider how social networks interact with geographic space. STD morbidity data is often assigned to the residential address of the case. However, the location of the residence may not represent the same area where the sexual exposure has taken place. For example, in periurban areas, people may travel to larger cities to meet partners (3). Robust public transportation or car access may also facilitate sexual partnering across neighborhoods within a city. STD outbreaks may also occur in new populations. For example, after the dramatic decline in early syphilis through the 1980s and 1990s,
where disease was focused on urban sex workers and drug using populations, syphilis began to increase significantly among men who have sex with men (4, 5). STD outbreaks have been reported among Native American populations (6), gang members (7), sex workers (8) and suburban adolescents (9). A number of data sources can be used to identify possible outbreaks among new risk populations. These include routine case report data received by state or local health jurisdictions. Additionally, data collected through supplemental epidemiologic activities, such as studies or other research projects, as well as data collected through partner service investigations may be helpful. Health care or social service providers may also identify increases of STDs in their patient populations and alert the local and state health departments. Finally, sentinel surveillance data collected from activities in various settings (e.g., school based screening, jail or prison screening programs) may also help in the identification of new populations with increases in STDs.

STD outbreaks may also occur in new venues or sexual partner recruitment locations. Recently, an outbreak of syphilis was investigated in a state correctional facility (10). Furthermore, modern approaches to dating and meeting sexual partners may also influence STD outbreaks. On-line chat rooms (11), dating and hook-up sites found on the internet (12, 13) and cell-phone based sexual partner recruitment apps (14, 15) have been associated with increased STD risks. These virtual sites of sexual partner recruitment also function alongside more traditional physical locations such as sex clubs, bathhouse, and cruising areas (16).

STD outbreaks may also be defined by changes in the clinical presentation of disease identifiable through surveillance systems. For example, increased case reports of ocular syphilis in Washington and California (17) called into question whether there have been changes in the tissue tropism of a particular strain of *Treponema pallidum* subspecies *pallidum*. While this has not previously been shown to be of concern for *Treponema pallidum* subspecies *pallidum*, the availability of new molecular sequencing techniques may someday reveal subtleties in sequence changes that are linked to changes in rates of neuro, ocular or otic syphilis.

**What parameters or criteria should be included in defining an outbreak?**

**Section Summary:**

- Quantitative approaches to defining the beginning and end to an outbreak should be established before a suspected outbreak occurs.
- The determination to investigate a potential outbreak should not be based solely on statistical testing; qualitative approaches and epidemiologic judgment may be appropriate.

Quantitative approaches to defining the beginning and end to an outbreak should be developed and documented a priori and applied systematically to locally derived data. Prior to evaluating increases in recent STD morbidity, the baseline, or background, rate of disease needs to be established. A number of options are available for defining the baseline period. Recent data can be compared to
the prior quarter, or the same quarter in the prior year if there is concern about seasonal variability. For a more robust approach, a moving average of quarters can be established and the period of interest compared to that. This approach reduces some of the variability of choosing one quarter as the baseline. Additionally, data can be compared to the same time period from the prior year, which would also reduce the variance in these data. Regardless of approach, it is important to consider lags in reporting. Case report data is often delayed in getting to the local and state health department, and even if reported, the disposition of the case may change upon further investigation. Exploration of the most recently reported data may be useful to get more of a “real time” picture of a possible increase in morbidity, but may also present a distorted picture of true increases and decreases. It is recommended that delays in reporting be routinely evaluated as part of general surveillance hygiene and be considered when defining an outbreak. For example, programs can track average length of time from laboratory specimen collection date to date cases are entered into data systems, both to improve data interpretation and to develop targets for quality improvement.

There are a number of approaches to establishing an outbreak, each with advantages and shortcomings. The simplest approach is to examine the absolute number of excess cases over the established baseline or background count. This has the advantage of being computationally simple and easy to explain to a range of stakeholders. However, this method does not account for the magnitude of the background. For example, an increase from 5 to 25 cases and an increase from 2,400 to 2,420 would both represent an increase in 20 absolute cases, but likely represents two very different epidemiologic phenomena. Using a percent increase method can help better contextualize the relative increase in cases. Using the example above, while both scenarios show a 20 case increase the first represents a 400% increase compared to a 0.8% increase in the second. A more statistically robust approach uses standard deviations to define outbreaks (18). This method is more objectively robust, but may be more computationally complicated and may not be easily understandable to the lay population or community stakeholders. Finally, qualitative approaches (and epidemiologic judgment) may be appropriate in assessing STD increases in areas where no or few cases were previously reported. For example, 5 congenital syphilis cases reported in an area without a reported case in the prior 10 years represents a potential outbreak that would require further investigation given the long history of no cases.

While application of statistical testing may help alleviate spurious inferences regarding increases, caution is warranted. Statistical significance is driven in part by sample sizes. Therefore, statistically significant differences may be seen with large sample sizes that are not important from a public health perspective. Conversely, important increases may be missed when the background rate and sample size is small. The determination to investigate a potential outbreak should not be solely based on statistical significance testing. It may be prudent to locally develop an escalating scale related to potential outbreaks. One approach is to use visual cues, such as Green/Yellow/Red, to delineate no increases, potential increases, and likely outbreaks, respectively. This may help flag situations for further investigation without having to label the situation an “outbreak”.

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APPENDIX A

Resources

Analytical Software

Epi Info: http://wwwn.cdc.gov/epiinfo/

Free to use analytical software from CDC. Epi Info contains various statistical tools that can assist in outbreak detection. Software contains tools for regression analysis, survival analysis, means, frequencies and graphical construction. Epi Info also contains form creation software and data entry capabilities as well as a GIS mapping function. Epi Info also allows for editing of data and data management. Menu driven user interface allows for users to select menu options as opposed to writing code to perform analysis. Free software from CDC.

R: http://www.r-project.org/

Free to use program for statistical computing and graphics. As with Epi Info, R offers a wide variety of statistical and analytical tools, and offers the ability to download other statistical packages from other users. R does use its own command language so there is a certain barrier to entry although there are multiple online resources, including manuals on R’s webpage. R can also create plots and other graphics.

Statistician: http://www.statisticianaddin.com/

An Excel based add-in statistical tool that has 2 versions, one free (lite) and a paid version. Statistician allows users create a store an actual data set as opposed to having to reselect data each time they use the spreadsheet. Videos are available on YouTube. Statistician includes data management tools along with statistical tools such as ANOVA, regression and binary modeling. Free version includes descriptive statistics, covariance/correlation, means test, ANOVA and multiple regression analysis.

Purchasable Statistical Software

SPSS: http://www-01.ibm.com/software/analytics/spss/
MiniTab: http://www.minitab.com/en-us/
Stata: http://www.stata.com/

Geographic Information System (GIS) Software

SaTScan: http://www.satscan.org/
GIS program that can be used to analyze spatial, temporal and space-time data. Commonly used to detect disease clusters using geographic boundaries via Poisson or Bernoulli based models. The program is also commonly used to perform geographical surveillance of disease, detect statistical significance of disease clusters, and perform repeated time period surveillance for early detection of outbreaks. Free software.

**Epi Info:** [http://wwwn.cdc.gov/epiinfo/](http://wwwn.cdc.gov/epiinfo/)

Has a GIS component which is built around the Environmental Systems Research Institute (ESRI), which is the same company that produces ArcGIS, MapObjects Software. Able to use shapefiles to construct geospatial boundaries, has case cluster tools, choropleth mapping (thematic map in which areas are shaded or patterned in proportion to statistical variable being displayed on the map), and dot density features. Free software from CDC.

**ArcGIS:** [http://www.esri.com/software/arcgis/arcgis-for-desktop](http://www.esri.com/software/arcgis/arcgis-for-desktop)

GIS program with an interactive map component used to show disease distributions across geospatial boundaries. Commonly used as the foundation for GIS analysis due to the ability to create maps in conjunction with programs like SaTScan to map the disease clusters. Has a wide range of tools and options including geospatial analysis, cluster detection, geocoding capabilities, advanced imageries. Pricing available online, free trail also available.

**Networking Software**

**NetDraw:** [https://sites.google.com/site/netdrawsoftware/home](https://sites.google.com/site/netdrawsoftware/home)

Free to use program that is used for drawing social networks. Features include multiple relations to a single node, node attributes, analytical ability to identify isolates, ability to save network maps as images, and print options. Guides and FAQs are available on NetDraw’s website. NetDraw is a network visualization tool which allows for the graphical representation of networks and includes some (limited) analytical capabilities that overlap with UCINET.

**UCINET:** [https://sites.google.com/site/ucinetsoftware/home](https://sites.google.com/site/ucinetsoftware/home)

Purchasable network analytical software. UCINET is social network analytical software which allows for the analysis of social network aspects as well as hypothesis testing. UCINET includes NetDraw network visualization software.

**Single Overriding Communication Objective**
CDC SOCO Worksheet:
http://www.cdc.gov/tb/publications guidestoolkits/forge/docs/13_SampleSingleOverridingCommunicationsObjective_SOCO_worksheet.doc

CDC Syphilis Resources

Syphilis: http://www.cdc.gov/std/syphilis/default.htm


Syphilis Stats: http://www.cdc.gov/std/syphilis/stats.htm
APPENDIX B

Outbreak Response

Summary Action Steps

- Convene outbreak response team and identify coordinator
- Ensure confidentiality throughout response
- Establish a case definition
- Generate hypothesis about causal factors
- Implement case finding and epidemiologic follow up of cases and partners
- Leverage partnerships with community stakeholders
- Utilize communication channels to notify public and stakeholders
- Conduct ongoing epidemiologic analysis
- Evaluate and report on outbreak response findings

- Convene members of Outbreak Response Team
  The ORT represents an investigation team of individuals within each county and regional office who could provide expertise and leadership in an outbreak. Following detection of an outbreak, an initial meeting of the ORT is convened to designate an Outbreak Response Coordinator who will serve as the main point of contact for team members and lead the response. During the initial team meeting, the Outbreak Response Coordinator reviews roles and responsibilities of team members and ensures that personnel are designated to serve in established team member roles. A schedule for communication and routine team meetings is also established. As part of the initial response process, the ORT conducts an assessment of resources and supplies required to implement a response.

- Review Confidentiality Issues
  The ORT is responsible for identifying staff with permissions and a need to know to access data including laboratory, surveillance, and case management information. Data collection is limited to information essential to the investigation and is maintained and transmitted in a secure environment. Data collection, analysis, and reporting adhere to confidentiality and security statutes and protocols.

- Establish a case definition
  In general, federal case definitions for notifiable diseases apply in outbreak investigations of STDs although the case definition may be modified for local use contingent upon increased knowledge of the outbreak. Case definitions are used to confirm the diagnosis. A systematic review of clinical findings, symptom history and laboratory results for the cases should be conducted. In addition, co-infection and risk factors should also be assessed. This information
is used to establish a case line list for review by ORT members. The line list a single, comprehensive summary that is unduplicated, accurate and timely. An ORT member with surveillance or epidemiologic experience should be responsible for generating and updating the line list.

- Generate hypotheses about factors contributing to case increase
  The initial hypothesis is generated by a review of the epidemiology, case interviews, medical records, as well as interviews with LHD, regional and key stakeholders. The hypotheses should address the at-risk population, transmission source, the mode of transmission, as well as the exposure(s) and risk factors that caused the outbreak. The hypothesis will be evaluated and refined based on ongoing systematic review of epidemiologic and surveillance information collected during the course of the outbreak.

- Conduct Case Finding
  Maximize case identification through a review of existing data sources and other potential sources of surveillance data, e.g., active surveillance in high-volume provider offices. Health care provider alerts as well as media and community outreach targeted at high-risk populations and venues support case finding efforts. Case investigation and partner notification by state and local partner services staff also promote case ascertainment.

- Collaborate with Community Partners
  Informing community stakeholders of the outbreak expands opportunities for intervention and outreach to affected populations. The Public Information Officer (PIO) plays a central role in these communication efforts.

- Communication channels
  Utilize existing channels of communication to notify partners and external stakeholders of the outbreak situation. Methods of communication include issuing a Health Care Provider Alert; notifying CDC and border states/jurisdictions; and informing public health officials, health care and laboratory providers. Community based organizations that serve affected populations can promote disease intervention and prevention efforts. Notification of the media is conducted by the state Public Information Officer applying a Single Overriding Communication Objective (SOCO) to ensure uniform messaging about the outbreak.

- Conduct descriptive epidemiology according to established procedures and timeframe
  Describing the epidemiology of the outbreak should begin early and should be updated regularly as additional data is collected. Analyze surveillance and case management data to characterize the outbreak by person, time and place, which may include the development of an epi-curve, geographic and social network maps, and descriptive summaries of demographic and risk characteristics. A review of case management data should include a cluster analysis to identify connections between cases with such analysis performed by network analysis software,
e.g., Netdraw. Contingent upon resources, additional advanced techniques such as molecular susceptibility testing as well as molecular epidemiology may be useful for identifying case-partner relationships.

- Evaluate Outbreak Response
  The evaluation of the outbreak response will occur both during the response and after activities are completed and will primarily focus on the following aspects: 1) effectiveness of the outbreak response, 2) efficient use of resources, including public and private agencies, 3) productivity of epidemiologic interventions, 4) relationships with providers and CBOs, and 5) organization and leadership of the response effort. A summary of the findings includes an oral briefing for state and local health authorities and a written report that serves as an official summary of the outbreak investigation. It serves as a record of performance, a document for potential legal issues, and a reference for the health department for any future outbreaks. The findings may also be presented at conferences and/or published in peer-reviewed journals to contribute to the scientific knowledge base of epidemiology and public health.

  The Outbreak Response Team should convene following the end of the outbreak to review the evaluation findings and discuss strengths and weaknesses of the outbreak response plan. Present report to executive staff.
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