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# Neurosyphilis Surveillance: Exploring the Use of Multiple Data Sources to Better Understand Morbidity in California

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**Abstract:** Accurate reporting of neurosyphilis diagnoses is important to quantify and monitor severe outcomes associated with infection of *Treponema pallidum*. This analysis compared the demographic distribution of neurosyphilis diagnoses in sexually transmitted disease surveillance data with administrative hospital data in the California Project Area from 2016 to 2018. Although neurosyphilis morbidity was similar, significant differences were noted by sex, age group, race/ethnicity, and region. Both sexually transmitted disease surveillance and administrative hospital data may be imperfect systems to understand the true morbidity of neurosyphilis.

Neurosyphilis, a *Treponema pallidum* infection of the central nervous system that can occur during any stage of syphilis, may be associated with severe sequelae including vision impairment, loss of hearing, difficulty with muscle coordination, meningitis, altered behavior, dementia, and, if untreated, death.<sup>1-3</sup> Although national rates are unknown, 2 studies that included data from multiple jurisdictions in the United States found the prevalence of neurosyphilis to be 1.7% to 1.8% among early syphilis cases.<sup>4,5</sup>

Surveillance of neurosyphilis is important to quantify overall disease burden and improve the field's understanding of the impact of syphilitic infection. Accurate surveillance for neurosyphilis requires documentation of clinical neurologic symptoms on a case report for a staged syphilitic infection.<sup>6</sup> Inconsistent reporting to surveillance may occur if neurologic symptoms are not reported by the patient, not assessed by the provider, or not communicated to the public health department but noted in the patient's electronic health record (EHR).

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The objective of this analysis was to compare the demographic distribution of neurosyphilis diagnoses in the California sexually transmitted disease (STD) surveillance system to those in administrative hospital data, which contains information on diagnoses received during an inpatient or emergency department (ED) visit. As the recommended treatment for neurosyphilis is administered within the hospital setting,<sup>7</sup> administrative hospital data should capture these diagnoses at the time of treatment. Furthermore, the goal of comparing these 2 data sets was to identify ways to improve surveillance data collection. If the demographic distributions were found to be different, it could indicate that neurosyphilis diagnoses are being missed and further investigation is necessary; if similar, it could indicate that administrative hospital data may be able to serve as a sentinel surveillance system for neurosyphilis.

## MATERIALS AND METHODS

Neurosyphilis diagnoses are reported as part of routine STD surveillance activities within the California Project Area (CPA), which includes all of California except Los Angeles and San Francisco counties (due to separate federal funding streams and surveillance systems). Syphilitic infections are required to be reported to the local health authority via California's electronic disease reporting and surveillance system.<sup>8</sup> We extracted data on syphilitic infections (all stages) that met the surveillance case definition with neurologic symptoms noted on the provider case report or via patient self-report from January 1, 2016, to December 31, 2018.

Data from January 1, 2016, to December 31, 2018, were requested from inpatient hospitalization and ED records collected by California's Office of Statewide Health Planning and Development from all licensed facilities in the state, excluding military or federally administered facilities. Records were collected for each inpatient stay and ED outpatient encounter. Records for patients admitted for inpatient services through the ED of the same hospital were only included in the inpatient data set. We combined the ED and inpatient data sets and will refer to them collectively as administrative hospital data. This data set was limited to patients with CPA residence.

Both STD surveillance and administrative hospital data included patient demographic information: sex, date of birth, race/ethnicity, and county of residence. In addition, administrative hospital data included patient social security number (SSN) and admission or service dates, which were used to identify unique neurosyphilis episodes. For records with an SSN, those within 60 days of each other were considered part of a single episode; records with no SSN were assumed to be unique episodes. Administrative hospital data included up to 25 *International Classification of Diseases, Tenth Revision (ICD-10)* codes per inpatient stay or ED encounter.

To classify neurosyphilis diagnoses, unique criteria were used for each data source. For the STD surveillance data, we relied on neurosyphilis specifically reported by a diagnosing provider (nearly two-thirds of neurosyphilis diagnoses), as well as a list of diagnoses or patient-reported symptoms (e.g., headache, dizziness, blurry vision, decreased hearing, meningitis, tabes dorsalis, and general paresis), laboratory results (e.g., cerebrospinal fluid Venereal Disease Research Laboratory), or treatments (e.g., aqueous crystalline penicillin G) that are compatible with neurosyphilis. Most symptoms were obtained from mining a free-text field in the surveillance record. Although the national neurosyphilis surveillance case definition changed in 2018, these changes were not implemented in the CPA until 2019, so the same methodology was used across all 3 years. In the administrative hospital data, we used *ICD-10* codes found anywhere in the diagnosis field related to symptomatic neurosyphilis (excluding A52.16 for Charcot's arthropathy-tabetic), asymptomatic neurosyphilis, unspecified neurosyphilis, secondary syphilitic oculopathy, or late syphilitic oculopathy (Supplemental Table A, <http://links.lww.com/OLQ/A668>). No *ICD-10* codes specific to otic syphilis were identified.

We did not have sufficient identifying information to directly match the STD surveillance data to the administrative hospital data. Therefore, we compared the number and demographic distribution (by sex, age group, race/ethnicity, and region) of neurosyphilis diagnoses within these 2 unique data sources using Pearson  $\chi^2$  tests. SAS version 9.4 (SAS Institute, Inc., Cary, NC) was used for all data management and analyses. This study was submitted to the California Health and Human Services Agency's Committee for the Protection of Human Subjects and considered exempt from review.

**RESULTS**

From 2016 to 2018, there were 1018 neurosyphilis diagnoses in the STD surveillance data and 1372 in the administrative hospital data (Table 1). Although the overall magnitude of diagnoses across the 2 data sources was relatively similar, the number of diagnoses were higher in the administrative hospital data for all 3 years and the difference between the 2 data sources increased over time.

When comparing STD surveillance versus administrative hospital data, significant differences in the distribution of neurosyphilis diagnoses by demographic variables were noted (Table 1). Compared with STD surveillance data, neurosyphilis diagnoses within administrative hospital data had higher proportions of females (28% vs. 18%,  $P < 0.0001$ ), persons aged 65 to 74 years (12% vs. 7%,  $P < 0.0001$ ), persons 75 years or older (13% vs. 2%,  $P < 0.0001$ ), persons identified as Black (16% vs. 9%,  $P < 0.0001$ ), and persons in the Bay Area region excluding San Francisco (27% vs. 20%,  $P = 0.0001$ ). Sexually transmitted disease surveillance data had a higher proportion of males (82% vs. 72%,  $P < 0.0001$ ), persons aged 25 to 34 years (23% vs. 14%,  $P < 0.0001$ ), persons aged 35 to 44 years (23% vs. 18%), persons identified as White (51% vs. 43%,  $P < 0.0001$ ), and persons in the Southern region excluding Los Angeles (42% vs. 36%,  $P = 0.0001$ ). There was a 7-year difference in mean age between the administrative hospital data and STD surveillance data (52 and 45 years, respectively, data not shown).

**DISCUSSION**

The total number of neurosyphilis diagnoses was similar across STD surveillance and administrative hospital data, although

**TABLE 1.** Number and Percent of Neurosyphilis Diagnoses in STD Surveillance and Administrative Hospital Data, by Selected Demographic Factors, 2016 to 2018

	STD Surveillance (n = 1018)		Administrative Hospital (n = 1372)		P
	n	%	n	%	
Diagnosis year					0.2143
2016	339	33	413	30	
2017	321	32	440	32	
2018	358	35	519	38	
Sex					<0.0001
Female	186	18	390	28	
Male	832	82	982	72	
Age group, y					<0.0001
<25	58	6	53	4	
25–34	230	23	193	14	
35–44	230	23	247	18	
45–54	258	25	304	22	
55–64	153	15	230	17	
65–74	68	7	160	12	
75+	21	2	185	13	
Race/Ethnicity					<0.0001*
White	467	51	577	43	
Black	80	9	214	16	
Hispanic	292	32	426	31	
Asian/Pacific Islander	47	5	84	6	
Other	37	4	54	4	
Unknown/Missing	95	—	17	—	
Region					0.0001*
Northern/Sacramento	117	12	106	9	
Bay Area	206	20	326	27	
Central	267	26	324	27	
Southern	428	42	431	36	
Unknown/Missing	0	—	185	—	

\*Unknown/missing values excluded from  $\chi^2$  calculation.

the difference increased from 2016 to 2018. There were several significant differences noted between the 2 data sources by sex, age group, race/ethnicity, and region. Possible explanations for the differences vary from the perspective of STD surveillance or clinical patient management.

In public health programs, there are often limited resources to conduct thorough investigations into neurologic symptoms for all syphilis diagnoses. Unless a provider specifically reports a diagnosis, individuals with neurosyphilis may not be identified within the surveillance system. Investigative priority is given to females of childbearing age to prevent congenital syphilis, infectious syphilis cases to maximally interrupt disease transmission, and persons coinfecting with HIV to prevent transmission and provide linkage to care. Therefore, older females would be less likely to receive public health follow-up for reactive laboratory results, leading to a potential underestimate of neurosyphilis diagnoses within this population in STD surveillance. Although racial/ethnic differences in STD surveillance and administrative hospital data are recognized, the contributing factors to these differences are not well understood. Missing race/ethnicity within surveillance data may play a role: although 10% of STD surveillance data were missing race/ethnicity, only 1% of the administrative hospital data were missing this information likely because of EHR requirements. Future electronic case reporting for surveillance may ensure higher-quality race/ethnicity data because information could be pulled directly from EHRs. However, missing data cannot fully account for the racial difference and may signify that people diagnosed with neurosyphilis identified as Black may be underrepresented in STD surveillance. County of residence, which may not be a required EHR element, was missing for 13% of the neurosyphilis diagnoses in the administrative hospital data, making it difficult to interpret significant differences by region.

Within the administrative hospital data, one contributing factor to a larger number of neurosyphilis diagnoses among older persons may be related to dementia evaluations.<sup>9</sup> In these cases, patients may have a negative nontreponemal test with 2 positive treponemal test results in the setting of a reverse syphilis screening algorithm. Although these patients might undergo lumbar puncture and neurosyphilis diagnosis, the clinical diagnosis may not meet surveillance criteria, which requires both positive treponemal and positive nontreponemal test results to meet the case definition. This suggests a potential gap in neurosyphilis surveillance, and an evaluation of these criteria may be warranted.

The inability to link STD surveillance data directly to administrative hospital data was a major limitation. Linking these 2 data sources would have allowed for a better assessment of the level of misclassification, strengths, and gaps within both data sources. Another limitation in this analysis is the potential for misclassification of a neurosyphilis diagnosis within both data sources. Administrative hospital data are based on *ICD-10* coding rather than a medical record review for neurologic symptoms. Previous studies have found that the reliability of *ICD-10* codes to identify STD infections is unclear.<sup>10</sup> Furthermore, there may be overdiagnoses of neurosyphilis in administrative hospital data because of presumptive diagnoses, with the provider later ruling out

neurosyphilis. We plan to incorporate current procedural terminology codes into future analyses to increase the specificity in neurosyphilis diagnoses within the administrative hospital data. Finally, although public health departments directly receive laboratory results indicative of neurosyphilis (cerebrospinal fluid Venereal Disease Research Laboratory), much of the surveillance data relies on patient and provider reporting of neurologic symptoms to public health, which likely leads to neurosyphilis being underreported. Although STD surveillance data are often lacking information that could inform neurosyphilis diagnoses, case reports to public health can include other valuable data elements missing from administrative hospital data, such as gender of sex partners and HIV status.

When assessed in isolation, both STD surveillance and administrative hospital data may be imperfect systems to understand the true morbidity of neurosyphilis within the CPA, given the significant differences in distributions for all demographic variables. As we look toward improving future surveillance data collection efforts, it may be warranted for public health departments to look toward integrating sentinel surveillance systems, such as administrative hospital data, to augment, but not replace, aspects of STD surveillance reporting or determine more comprehensive methods to capture neurosyphilis within existing surveillance structures. The eventual shift to electronic case reporting may also provide the opportunity to seamlessly integrate more complete information on key data elements, such as symptoms and race/ethnicity, into surveillance systems.

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