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Going Off Grid: Modeling an Automated Record Search to Process Electronically Reported Reactive Nontreponemal Syphilis Tests

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Abstract

Background: Before searching prior records, sexually transmitted disease programs use syphilis reactor grids to exclude some reactive nontreponemal test results (RNTs) based on patient age, gender, and test titer. We propose a new algorithm that starts with comparing RNTs to previous syphilis nontreponemal tests and current treponemal test results.

Methods: Deduplicated RNTs from Florida's surveillance system (2006–2015) were extracted and stratified on morbidity. An algorithm was developed to triage RNTs. Sensitivity and specificity of the algorithm and the current reactor grid were estimated using reported syphilis cases. A random sample of cases missed by the proposed algorithm, stratified by stage of disease, was reviewed to verify case classification.

Results: Reported RNTs increased 58% from 2006 (n = 34,808) to 2015 (n = 55,001) (total = 372,902). The current reactor grid removed 91,518 (24.5%) RNTs and missed 1149 potential cases. Strictly following the reactor grid would result in a sensitivity of 97.4% and a specificity of 27.5%. The proposed algorithm would remove 242,078 (64.9%) RNTs and miss 2768 potential cases. This results in a slightly lower sensitivity of 93.8%, but nearly triples the specificity, 72.9%. A review of a random sample of the 2768 cases estimated that 72.7% would not have met the syphilis surveillance case definition, resulting in an adjusted sensitivity of 98.4%.

Conclusions: In Florida, an algorithm that starts by searching previous syphilis test results vastly improved specificity and slightly improved sensitivity compared with the current reactor grid. Implementing an automated algorithm could increase case ascertainment efficiency and further prioritize likely cases for investigation.

Surveillance for syphilitic infections in the United States has been ongoing since 1941.[–] In the following decades, reported primary and secondary syphilis cases have generally decreased to the lowest number of cases in 2001 as a result of widely available treatment,

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public health programs, and changes in sexual behavior. However, since the turn of the century, syphilis rates have steadily increased in Florida and in other US states.

Over this same timeframe, technology and methods have evolved to assist in improving surveillance quality and efficiency[–] Syphilis case reporting began with providers reporting cases to health departments using paper records. Regular reporting of reactive syphilis serologies was added to health department syphilis reactor programs in 1962 to improve identification of syphilis cases. As paper-based syphilis serology reporting became more prevalent, sexually transmitted disease (STD) programs including Florida needed to efficiently triage these results before conducting time-consuming record searches. Syphilis reactor grids prioritized high-titer and younger individuals for syphilis investigations and others were closed without further investigation. While these grids reduce disease intervention specialist (DIS) investigations, they vary from program to program, should be regularly evaluated and depending on their implementation could result in an underreporting (3% to 66%) of the true syphilis burden within a jurisdiction.[–] Moreover, many STD programs now have electronic databases that contain all of a patient's past positive serologic test results from their jurisdictions. Having the ability to electronically query a patient's reported syphilis record could replace syphilis reactor grids with a more efficient process consistent with the syphilis case definition. In San Francisco, a similar approach was estimated to reduce syphilis investigations by 44%.

Expansion of electronic laboratory reporting (ELR) in Florida and other jurisdictions have increased reporting of reactive tests and in turn, increased the number of reactive tests that do not result in a case. For example, after the expansion of ELR in Indiana from 2010 to 2011, reporting rates nearly doubled (35.37 notifiable syphilis results per 100,000 persons per year) compared to the surveillance reported rates, and other sites found only 4% to 12% of ELR syphilis tests lead to a reported syphilis infection.[,]

Despite the increasing syphilis rates, changes in syphilis screening and syphilis laboratory result ascertainment, and shifting DIS roles and priorities; funding for syphilis and other bacterial STDs has mostly stagnated or been reduced.[,–] Many of these issues are not new to STD programs but have been compounding for years. As such, STD programs have had to decrease disease interventions and improve efficiencies.[–,–,]

In Florida, the current syphilis reactor grid has been automatically applied to all reactive nontreponemal test result (RNTs) based on titer and age since 1999 (Table 1). Reactive nontreponemal test results that are not administratively closed by the reactor grid are manually processed by a surveillance clerk or DIS who creates a syphilis field record for investigation. Each field record is assigned to a DIS for further investigation and at least 1 supervisor for quality assurance review and reporting. A common limitation of reactor grids is the inability to account for a patient's previous syphilis tests, which are needed to distinguish past from current syphilis infections.[,]

In this study, we aim to describe the change in RNT volume within Florida from 2006 through 2015, evaluate the current syphilis reactor grid, and explore a potential new algorithm that compares reported RNTs to previous nontreponemal results and current

treponemal test result. We also describe the new algorithm's sensitivity and specificity, its effect on syphilis field record creation, and potential impact of the model on syphilis surveillance.

MATERIALS AND METHODS

Reactive nontreponemal test results from January 1, 2006, through December 31, 2015, reported to Florida's Patient Reporting Investigation Surveillance Manager were deduplicated and extracted. Laboratory results were deduplicated if they had the same patient name, specimen collection date, test type, and test result. Surveillance data were added to each record including patient's age, gender, associated reported syphilis morbidity; chronological order of the test result on the field record; current test titer and date; and most recent prior nontreponemal test result, titer, and date. Within Florida's syphilis database, tests are added to field records related to an event, and those records may contain other RNTs due to repeat or follow-up syphilis testing. We considered an RNT to be linked to an incident syphilis case if it was the first RNT attached to a unique field record that ultimately became a case.

To describe the current volume of RNTs, we stratified the number of reactive tests and cases by year and patient's gender. Furthermore, we examined the number of RNTs that would be automatically processed (or administratively closed) by the current reactor grid. We determined the grid's impact on reducing field records by dividing RNTs removed by the grid by the total number of deduplicated RNTs. We calculated the sensitivity of the reactor grid and the algorithm by taking the number of reported cases for which a field record would be created and dividing by the total number of reported cases, determined by STD program staff based on the national syphilis case definitions (the standard for case classification and syphilis surveillance). The specificity was calculated using the number of noncases administratively closed by each method divided by all RNTs classified as noncases. These calculations were based on case investigations that used a reactor grid; therefore, RNTs closed by the grid were usually not investigated to determine if they might really be a case using the national syphilis case definition, so we may have overestimated the true sensitivity.

For the proposed algorithm, we took the original deduplicated RNTs and ran them through the algorithm. The algorithm begins by determining if the laboratory result could be matched to a person within the database based on a previous history of STDs in Florida. If a past nontreponemal test was identified, we compared the new titer with the most recent prior nontreponemal test to see if there was at least a 4-fold increase indicative of a new infection or seroconversion from a prior nonreactive nontreponemal test. Potential new cases generated a new syphilis field record for investigation. If not, then the laboratory result was administratively closed.

For RNTs associated with no match in the database or where there was no prior syphilis nontreponemal test titer, the algorithm searched the database for a recent nonreactive treponemal test ≤14 days prior to the RNT. If there was a nonreactive treponemal test during this timeframe, then the investigation would be closed. Otherwise, a new syphilis field record would be created.

We determined how many laboratory results and cases would follow each step in the algorithm. We then determined the impact on the number of field records and the sensitivity and specificity of the algorithm.

We examined 3 groups of RNTs that were closed by the algorithm, but were reported as cases in the surveillance system: (1) those with no documented prior syphilis history and a corresponding nonreactive treponemal test; (2) those with a syphilis history, 4-fold or less titer change, and only 1 RNT attached to the field record; and (3) those with a syphilis history, 4-fold or less titer change, and more than 1 RNT attached to the field record. For each of these groups, we randomly selected 20 cases per stage of syphilis disease (primary, secondary, early-latent, and late or unknown duration) for a total of 240 missed cases. Each of these 240 missed cases was further reviewed to determine if that RNT still met the case definition, failed to meet the case definition, or contained insufficient information to reclassify the case. Then each of these reviews were proportionally weighted to provide an estimate of the total missed cases by disease stage and group. We used Wilson's interval to determine 95% confidence interval for the proportional weighting of each of these categories using OpenEpi (www.OpenEpi.Com, updated 4/6/2013, Atlanta, GA). Finally, we reassessed the algorithm following the removal of cases that did not meet the case definition. All data submitted to Patient Reporting Investigation Surveillance Manager are part of routine STD surveillance activities. Centers for Disease Control and Protection determined this project was research that does not involve identifiable human subjects.

RESULTS

From 2006 to 2015, there were 372,902 deduplicated RNTs reported. Annual RNT volume increased 58% from 2006 (n = 34,808) to 2015 (n = 55,001), but 101% from the nadir in 2009 (n = 27,424) (Table 2). Much of the increase was among men as they increased in volume from 19,591 RNTs in 2006 to 37,756 in 2015 (93%). Moreover, the male proportion of RNTs increased from 56% in 2006 to 69% in 2015. Female RNTs increased by 12% during the same timeframe (n = 15,165 in 2006 to 17,050 in 2015). From 2006 to 2015, 44,688 syphilis cases with an RNT were reported, across all stages of syphilis, (34,712 in men, 9,611 in women, and 365 with unknown gender). Therefore, there were 8.3 RNTs per reported syphilis case (6.8 for men and 14.1 for women).

The syphilis reactor grid administratively closed 91,518 RNTs (24.5%) (Table 3). Despite the automated reactor grid, 1149 cases were still reported from cells on the grid that should have been closed (shaded cells), possibly due to provider reporting, linkage to other case investigations, or misclassification. If strictly followed, the reactor grid sensitivity would be 97.4% (43,539/44,688). Moreover, the specificity was low, 27.5% (90,369/328,214), not surprising, as the grid was based on titer and age, not the case definition.

When all 372,902 RNTs and 44,688 cases went through the algorithm (Fig. 1), most RNTs (n = 240,742, 65%) were from individuals with prior nontreponemal tests in the database. Of those with prior results, 22,696 demonstrated a 4-fold or greater titer increase or seroconversion. Of the 132,160 RNTs that were unmatched in the database or among those without a prior nontreponemal test or test titer, 18% (n = 24,032) were closed because they

had a nonreactive treponemal test. The remaining 82% (n = 108,128) would have field records created for investigation. Thus, the algorithm removed 242,078 RNTs (64.9%) from syphilis field record investigation. The sensitivity of the algorithm was 93.8% (41,920/44,688). The specificity for the algorithm was 72.9% (239,310/328,214), nearly triple that of the reactor grid. Based on the algorithm, nearly 65% of the reported RNT could be closed administratively, with only 6.2% (2768 = 155 + 2613) of the cases being missed.

A randomly selected subsets, 240 of 2768 cases, were reviewed after excluding 11 that were congenital (n=7) or neurosyphilis cases (n = 4). Many (an estimated 2013 cases) did not meet the national syphilis case definition (Table 4). This misclassification was primarily among cases that were called latent but had no evidence of an increase in titer compared with previous syphilis test titers. An estimated 687 others (1.5% of all reported cases) fell into 4 groups as follows: (1) treponemal test seroconversion following reactive low-titer RNT (estimated 272 cases); (2) symptom-only cases, missing serological evidence of reinfection (estimated 230 cases); (3) investigation identified nontreponemal titer increase (estimated 116 cases); and (4) discordant treponemal test results (estimated 69 cases). Lastly, an estimated 58 cases were unable to be reclassified most often due to conversion errors from a prior surveillance system. Thus, following case review, the algorithm's adjusted sensitivity was 98.4% (44,001/44,688), slightly higher than the reactor grid. The adjusted specificity of 73.5% (241,391/ 328,214) increased over the unadjusted specificity.

DISCUSSION

We developed a new algorithm for processing reactive nontreponemal tests as an alternative option to syphilis reactor grids that would, if automated, reduce field staff workloads, and still capture nearly all the reported syphilis cases over a 10-year period. This algorithm prioritizes new syphilis infections, and those with 4-fold or greater serological test result increases rather than prioritizing based on titer and age.[7–9] Most of the benefit from this model comes from identifying persons with previous titers whose new titers are consistent with their past infections.

The improved sensitivity and specificity coupled with the reduced workload due to automating the record search may reduce the need for the syphilis reactor grid. However, applying a reactor grid or other prioritization scheme after the algorithm may still be needed to focus disease investigations on target populations or if programs cannot investigate all cases.[10] Because the algorithm vastly improves the specificity of RNT processing and focuses more of the DIS's workload on likely cases, overall syphilis surveillance quality could improve. Moreover, case ascertainment may increase, and misclassification of syphilis cases based on serology could decrease.

The new algorithm has great potential for time savings from automating the record search, as at least 2 (and often more) staff are currently responsible for processing reactive syphilis serology, creating field records, assigning morbidity, and quality assurance.[7] This does not include investigative work such as contacting providers, interviewing patients, and home visits for individuals who do not meet the case definition. Automation of the algorithm could

remove these steps from the processing of nearly three quarters of reactive syphilis serologies in Florida.

One potential limitation of the model is that it assumes that the surveillance software could match syphilis serologies, as well as surveillance staff. However, even if a fraction of RNTs remain unmatched by the algorithm and require review by surveillance staff, the algorithm could still reduce misclassification and workload. Other issues with automating the algorithm arise from processing treponemal results and the chronological order of processing these 2 types of tests, especially when the reverse algorithm for syphilis testing is used more frequently. Finally, we may not have accounted for all potential scenarios or issues in this theoretical person-based syphilis assessment algorithm that could be actualized in implementing this model within surveillance systems and therefore the final product should be evaluated before and after implementation.[9]

Potentially missing cases in the algorithm is also a concern.[7,8] Further programming or expansion of the algorithm could address the issues with treponemal seroconversions and discordant treponemal results. Moreover, these missed cases should not have been followed currently based on the serological results, suggesting that many of these symptom-only syphilis cases were due to provider case reports. Provider-reported symptomatic cases could be investigated regardless of laboratory test results.

Another limitation of this analysis is that all RNTs were extracted from a system that used a reactor grid throughout the study period. Thus, it is unclear how many cases among older, low-titer individuals were missed because they were closed by the grid.[9] Implementing the algorithm could increase case ascertainment and sensitivity in these populations.

Although this study focused on data from Florida and not yet operationalized within Florida's STD surveillance system, we believe that operationalizing this or similar algorithms could also benefit other STD programs, especially those that have or are developing integrated electronic surveillance platforms; however, replication of this study in other jurisdictions is warranted. The complexity of the algorithms will require coordination between syphilis surveillance staff and system development staff to automate and operationalize within an electronic surveillance system. Initially, implementing these algorithms likely will require more resources than traditional syphilis reactor grids, but they could have greater long-term cost-savings and program efficiencies especially as programs expand their ELR capabilities, syphilis testing increases, and syphilis rates rise.[10,11] Ultimately, the algorithm for processing RNTs leverages technology to meet this burgeoning demand in fiscally challenging environments more efficiently than current reactor grids and should be considered by all programs that have electronic surveillance systems.[11]

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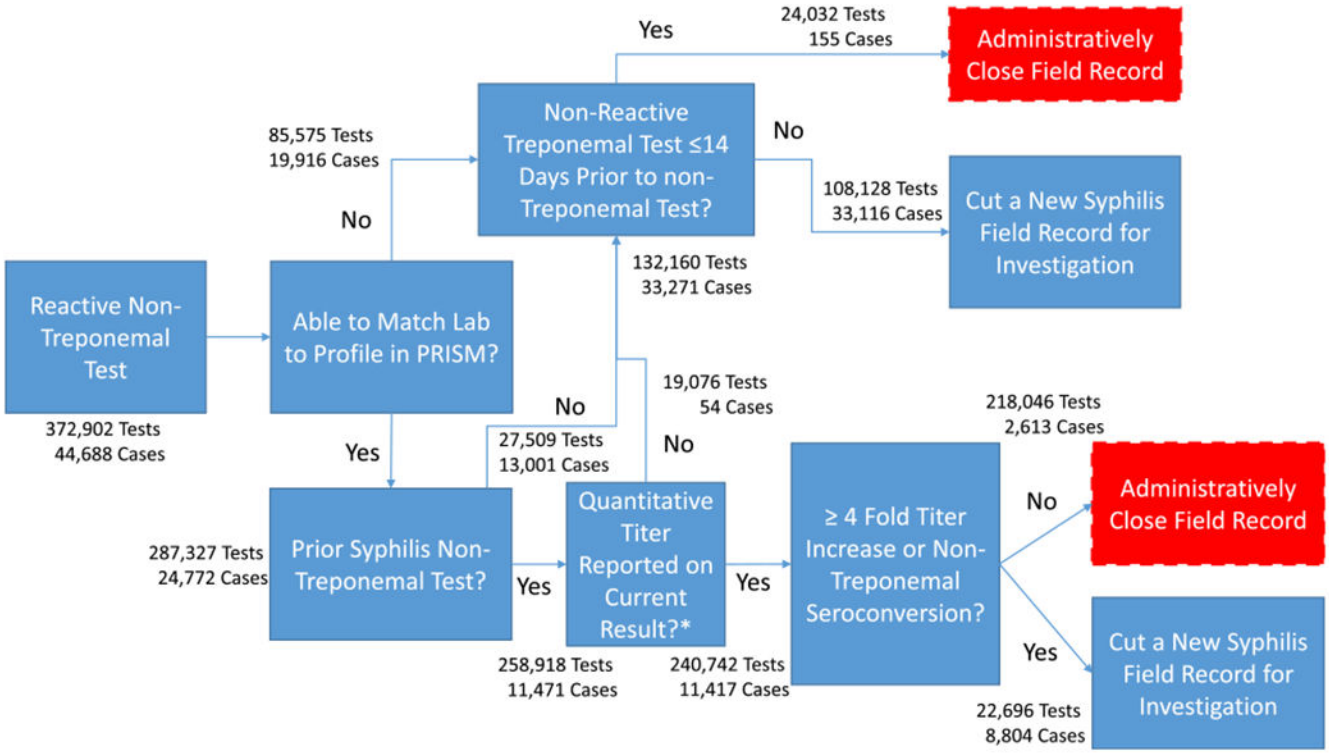

Figure 1.

Model for an assessment algorithm of electronic laboratory reports of reactive nontreponemal tests results and reported syphilis cases in Florida, 2006–2015. * Electronically transmitted nontreponemal results have 2 components a qualitative (ie, reactive or nonreactive) and quantitative (i.e. the titer value).

TABLE 1.

Reactor Grid Currently in Use by the Florida Department of Health for Syphilis Surveillance of Reactive Nontreponemal Test Titers

	Reactive Nontreponemal Test Titer								
Age group, y	WR	R	1:1	1:2	1:4	1:8	1:16	1:32	1:64+
<30	FR	FR	FR	FR	FR	FR	FR	FR	FR
31–40	AC	FR	FR	FR	FR	FR	FR	FR	FR
41–50	AC	FR	AC	FR	FR	FR	FR	FR	FR
51–60	AC	FR	AC	AC	FR	FR	FR	FR	FR
61–69	AC	AC	AC	AC	AC	FR	FR	FR	FR
70+	AC	AC	AC	AC	AC	AC	FR	FR	FR

WR, weakly reactive; R, reactive with no titer; FR, field record created; AC, field record administratively closed.

TABLE 2.

Deduplicated Reactive Nontreponemal Test by Year of Specimen Collection Stratified by Gender of Patient from Florida, 2006–2015

	Year of Specimen Collection for Reactive Nontreponemal Test										
Gender	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Total
Male	19,591	21,800	19,627	16,032	18,683	19,676	21,995	26,180	33,117	37,756	23,4457
Female	15,165	15,622	13,798	11,028	11,005	10,887	11,222	13,184	16,179	17,050	135,140
Unknown	52	775	910	364	168	179	217	227	218	195	3305
Total	34,808	38,197	34,335	27,424	29,856	30,742	33,434	39,591	49,514	55,001	372,902

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TABLE 3.

Current Syphilis Reactor Grid With Deduplicated Reactive Nontreponemal Test Titers and Reported Syphilis Cases Stratified by Titer and Age from Florida, 2006–2015

	Reactive Nontreponemal Test Titer																	
	R*		1:1		1.2		1.4		1:8		1:16		1:32		1:64+		Total	
Age group, y	Case	Total	Case	Total	Case	Total	Case	Total	Case	Total	Case	Total	Case	Total	Case	Total	Case	Total
< 30	193	8000	859	20773	991	15,930	1125	12,602	1392	9871	1696	7476	2407	6475	7776	14,657	16,439	95,784
31–40	91	6018	957	17,533	892	14,282	858	10715	982	7917	1091	5722	1315	4445	4566	9688	10,752	76,320
41–50	75	6489	356	20,802	1021	18203	872	13,004	989	9556	1110	7038	1244	4925	4787	10,638	10,454	90,655
51–60	46	4237	161	15223	227	12714	641	8787	634	6149	533	3788	576	2451	2154	4954	4972	58,303
61–69	15	1789	65	6827	68	5907	100	4066	345	2615	193	1455	147	723	465	1164	1398	24546
70+	5	2077	25	6995	36	6955	34	4948	57	3215	236	1689	116	779	164	636	673	27,294
Total	425	28,610	2423	88,153	3235	73991	3630	54,122	4399	39,323	4859	27,168	5805	19,798	19,912	41,737	44,688	372,902

*R, reactive test with no titer and combined with weakly reactive tests. The shaded area (gray) represents reactive nontreponemal tests and reported syphilis cases that by strictly following the current syphilis reactor gird would be administratively closed without investigation. Moreover, this represents a minimum number of reported cases administratively closed as an unknown number of cases in the shaded area were closed by the grid and not investigated.

TABLE 4.

Outcomes of Reviewed Misclassified Syphilis Cases Stratified by Stage of Disease

Disease Stage	Review Outcome	No. Reviewed	Total/Extrapolated Total*	95% Confidence Interval†	
Primary syphilis	Total	60	163	—	—
	Meets case definition	37	102	67	130
	Does not meet case definition	21	55	27	118
	Unclear case	2	6	2	35
Secondary syphilis	Total	60	294	—	—
	Meets case definition	40	187	123	237
	Does not meet case definition	18	99	44	219
	Unclear case	2	8	1	59
Early latent syphilis	Total	60	710	—	—
	Meets case definition	12	104	42	247
	Does not meet case definition	43	566	348	710
	Unclear case	5	40	8	173
Late or unknown duration syphilis	Total	60	1590	—	—
	Meets case definition	15	294	104	634
	Does not meet case definition	43	1292	830	1590
	Unclear case	2	4	1	262
All stages‡	Total	240	2757‡	—	—
	Meets case definition	104	687	335	1248
	Does not meet case definition	125	2013	1249	2758
	Unclear case	11	58	12	529

*Extrapolated totals were examined individually for each of the 3 types of misclassification: (1) Previous infections with only 1 laboratory result on a field record, (2) previous infections with more than 1 laboratory result on a field record, and (3) administratively closed field records with a negative treponemal test result; and combined to create the expected total.

†Wilson interval was used to determine 95% confidence interval for each scenario which extrapolated totals were determined and aggregated to obtain a combined interval.

‡Seven congenital syphilis and 4 neurosyphilis cases were not included in case totals for review.