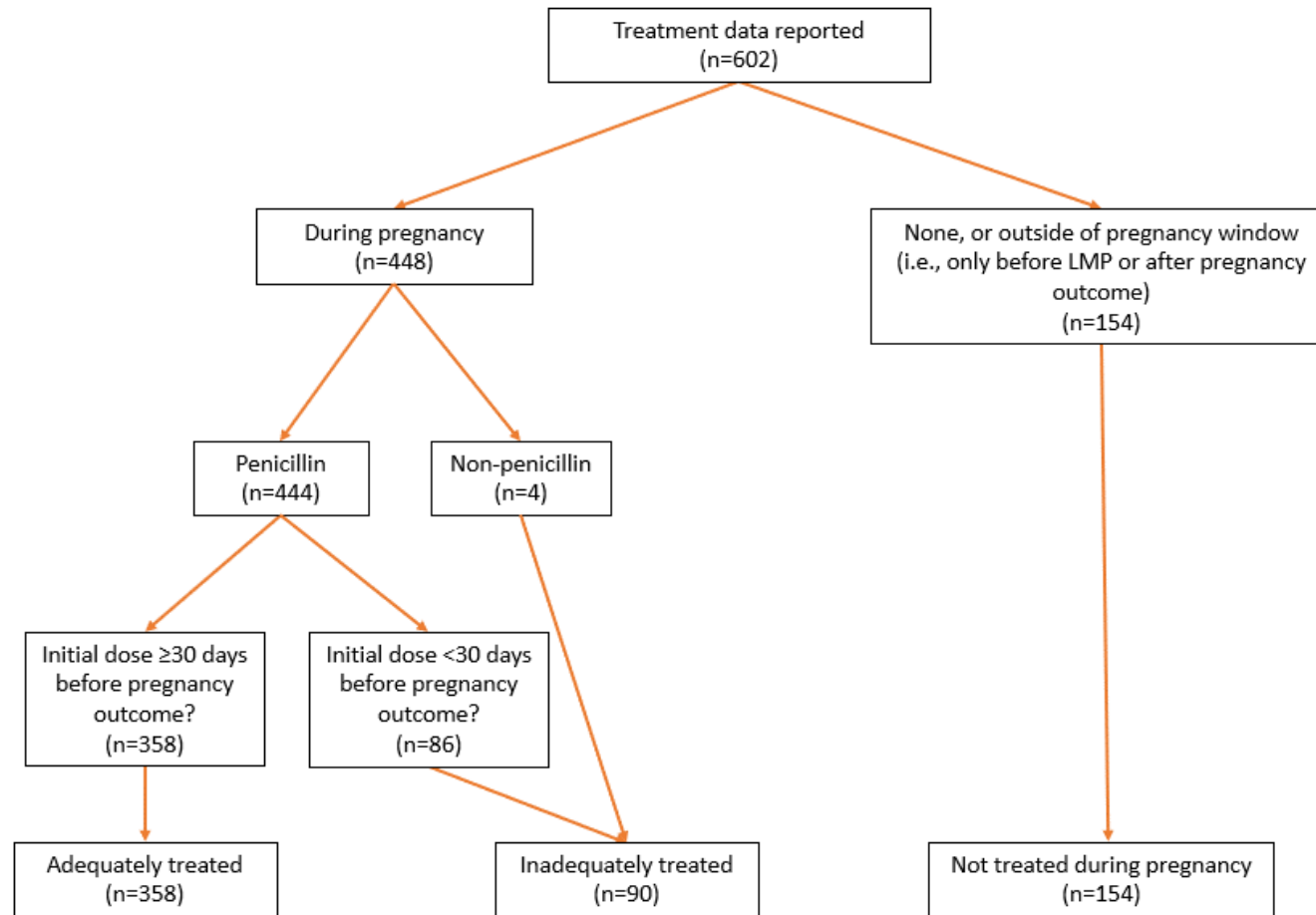


**Appendix 1. Flowchart for categorization of treatment status for those diagnosed with primary, secondary, or early latent syphilis, Surveillance for Emerging Threats to Pregnant People and Infants Network (SET-NET), Six States, 2018–2021.**

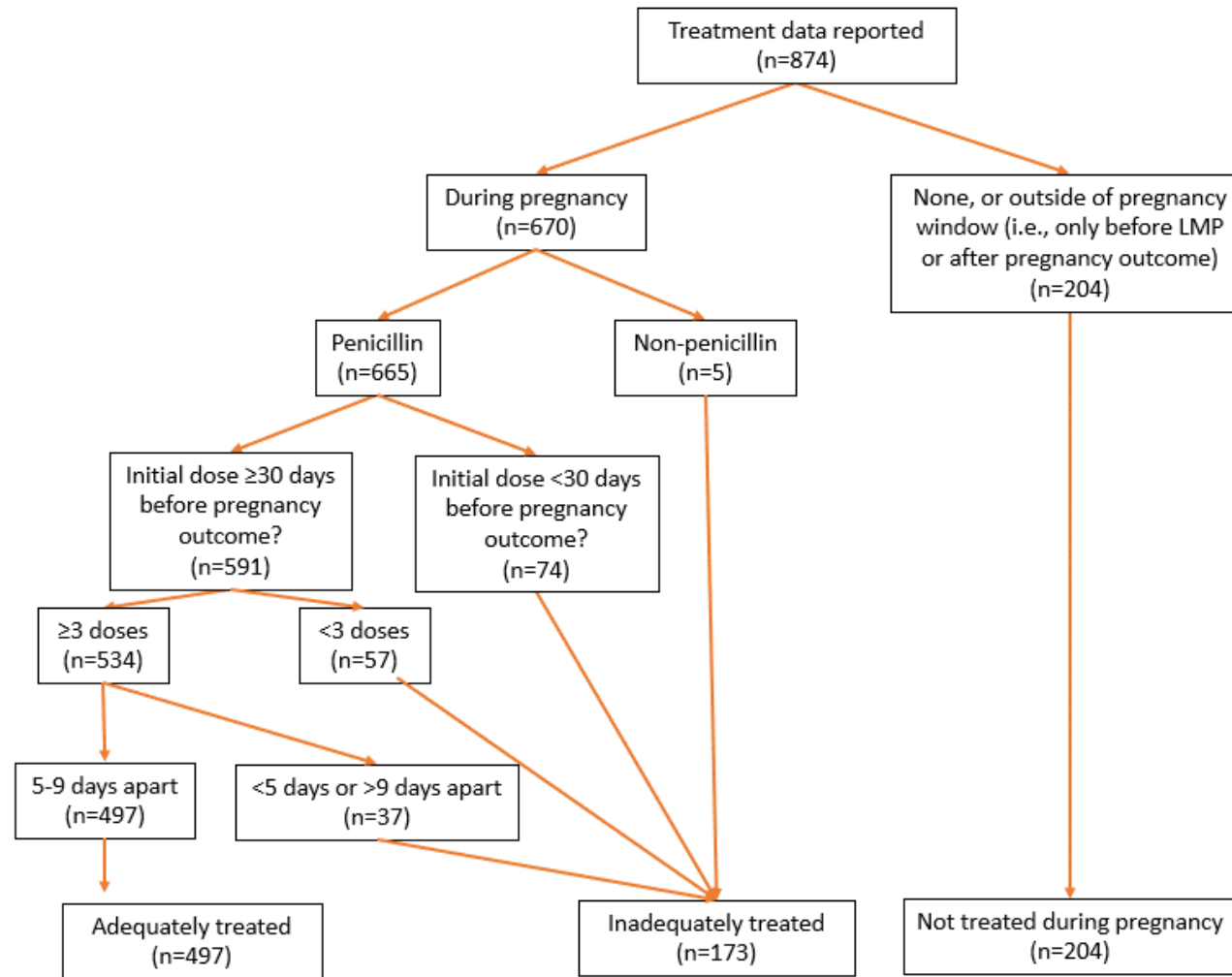


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Appendix 2. Flowchart for categorization of treatment status for those diagnosed with late latent syphilis or syphilis of unknown duration, Surveillance for Emerging Threats to Pregnant People and Infants Network (SET-NET), Six States, 2018–2021.



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**Appendix 3. Distribution of Demographic and Clinical Characteristics by Syphilis Surveillance Stage and Treatment Status (Adequate, Inadequate, and No Treatment), Surveillance for Emerging Threats to Pregnant People and Infants Network (SET-NET), 6 States, 2018–2021**

	Total (N=1476)	Not treated (N=358)			Inadequately treated (N=263)			Adequately treated (N=855)			Unadjusted risk ratio (uRR)						
		P/S/E (n=154)	LL/U (n=204)	Total (n=358)	P/S/E <sup>A</sup> (n=90)	LL/U <sup>B</sup> (n=173)	Total (n=263)	P/S/E <sup>C</sup> (n=358)	LL/U <sup>D</sup> (n=498)	Total (n=855)	Not treated vs adequate		Inadequately treated vs adequate		Not treated and inadequately treated vs adequate		
		n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		uRR (95% CI) <sup>E</sup>	p-value <sup>F</sup>	uRR (95% CI) <sup>E</sup>	p-value <sup>G</sup>	uRR (95% CI) <sup>E</sup>	p-value <sup>H</sup>
<b>Urbanicity<sup>I</sup></b>													0.002		0.375		0.008
Medium-large metropolitan (≥250,000)	1297 (87.9)	145 (95.4)	184 (90.2)	329 (92.4)	77 (85.6)	155 (89.6)	232 (88.2)	323 (90.2)	413 (83.1)	736 (86.1)	1.00 (ref)			1.00 (ref)		1.00 (ref)	
Rural-small metropolitan (≤249,999)	177 (12.0)	7 (4.6)	20 (9.8)	27 (7.6)	13 (14.4)	18 (10.4)	31 (11.8)	35 (9.8)	84 (16.9)	119 (13.9)	0.60 (0.42 - 0.85)			0.86 (0.62 - 1.20)		0.76 (0.61 - 0.94)	
<i>Missing</i>	2 (0.1)	2 (1.3)	0 (0.0)	2 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)							
<b>Age at first diagnosis (years)</b>																	<.001
Median (IQR)	27 (23-31)	27 (23-31)	28 (24-33)	28 (23-32)	27 (22-31)	28 (23-33)	27 (23-32)	26 (22-30)	26 (23-31)	26 (23-31)		<.001			0.010		
≤24	574 (39.4)	55 (37.2)	56 (27.9)	111 (31.8)	35 (38.9)	58 (34.1)	93 (35.8)	156 (43.8)	214 (43.5)	370 (43.6)	1.00 (ref)			1.00 (ref)		1.00 (ref)	
25-29	434 (29.8)	47 (31.8)	65 (32.3)	112 (32.1)	27 (30.0)	46 (27.1)	73 (28.1)	107 (30.1)	142 (28.9)	249 (29.4)	1.34 (1.07 - 1.68)			1.13 (0.86 - 1.48)		1.20 (1.03 - 1.40)	
30-34	289 (19.8)	27 (18.2)	46 (22.9)	73 (20.9)	18 (20.0)	39 (22.9)	57 (21.9)	65 (18.3)	94 (19.1)	159 (18.8)	1.36 (1.06 - 1.75)			1.31 (0.99 - 1.75)		1.27 (1.07 - 1.50)	
≥35	160 (11.0)	19 (12.8)	34 (16.9)	53 (15.2)	10 (11.1)	27 (15.9)	37 (14.2)	28 (7.9)	42 (8.5)	70 (8.3)	1.87 (1.44 - 2.42)			1.72 (1.25 - 2.37)		1.58 (1.33 - 1.89)	
<i>Missing</i>	19 (1.3)	6 (3.9)	3 (1.5)	9 (2.5)	0 (0.0)	3 (1.7)	3 (1.1)	2 (0.6)	5 (1.0)	7 (0.8)							
<b>Race and ethnicity<sup>I</sup></b>													<.001		0.546		0.004
American Indian, American Native, Native Hawaiian, Pacific Islander	78 (5.4)	11 (7.3)	13 (6.5)	24 (6.8)	3 (3.3)	9 (5.2)	12 (4.6)	18 (5.2)	24 (5.0)	42 (5.1)	0.95 (0.66 - 1.36)			0.79 (0.46 - 1.36)		0.92 (0.70 - 1.20)	

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Asian	30 (2.1)	4 (2.7)	2 (1.0)	6 (1.7)	1 (1.1)	2 (1.2)	3 (1.1)	5 (1.4)	16 (3.4)	21 (2.6)	0.58 (0.28 - 1.20)		0.44 (0.15 - 1.31)		0.60 (0.34 - 1.04)	
Black, NH	486 (33.8)	46 (30.7)	40 (19.9)	86 (24.5)	35 (38.9)	62 (35.8)	97 (36.9)	135 (39.1)	168 (35.2)	303 (36.9)	0.80 (0.65 - 1.00)		0.83 (0.62 - 1.10)		0.85 (0.73 - 0.99)	
Hispanic/Latinx	530 (36.9)	56 (37.3)	79 (39.3)	135 (38.5)	27 (30.0)	65 (37.6)	92 (35.0)	125 (36.2)	178 (37.3)	303 (36.9)	1.61 (1.01 - 2.54)		0.59 (0.10 - 3.59)		1.28 (0.85 - 1.92)	
Multiple or other unspecified	14 (1.0)	3 (2.0)	5 (2.5)	8 (2.3)	0 (0.0)	1 (0.6)	1 (0.4)	2 (0.6)	3 (0.6)	5 (0.6)	0.58 (0.45 - 0.74)		0.86 (0.65 - 1.14)		0.75 (0.64 - 0.88)	
White, NH	298 (20.7)	30 (20.0)	62 (30.8)	92 (26.2)	24 (26.7)	34 (19.7)	58 (22.1)	60 (17.4)	88 (18.4)	148 (18.0)	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Missing	40 (2.7)	4 (2.6)	3 (1.5)	7 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	13 (3.6)	20 (4.0)	33 (3.9)						
<b>Health insurance at delivery</b>												0.010		<.001		<.001
Private	174 (15.0)	15 (14.3)	15 (10.2)	30 (11.9)	10 (14.3)	10 (7.0)	20 (9.4)	45 (15.7)	79 (19.3)	124 (17.8)	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Public	897 (77.1)	80 (76.2)	117 (79.6)	197 (78.2)	53 (75.7)	113 (79.0)	166 (77.9)	227 (79.1)	307 (74.9)	534 (76.6)	1.38 (0.98 - 1.95)		1.71 (1.11 - 2.62)		1.41 (1.10 - 1.80)	
Other/None/Self-pay	91 (7.8)	10 (9.5)	15 (10.2)	25 (9.9)	7 (10.0)	20 (14.0)	27 (12.7)	15 (5.2)	24 (5.9)	39 (5.6)	2.01 (1.29 - 3.12)		2.95 (1.79 - 4.85)		1.99 (1.48 - 2.67)	
Missing	314 (21.3)	49 (31.8)	57 (27.9)	106 (29.6)	20 (22.2)	30 (17.3)	50 (19.0)	71 (19.8)	87 (17.5)	158 (18.5)						
<b>History of incarceration<sup>K</sup></b>												0.001		0.507		0.008
Yes	91 (8.5)	9 (8.7)	23 (18.7)	32 (14.1)	6 (8.6)	10 (7.7)	16 (8.0)	13 (4.9)	30 (7.8)	43 (6.6)	1.75 (1.31 - 2.34)		1.16 (0.75 - 1.80)		1.37 (1.11 - 1.69)	
No	984 (91.4)	95 (91.3)	100 (81.3)	195 (85.9)	64 (91.4)	120 (92.3)	184 (92.0)	250 (95.1)	355 (92.2)	605 (93.4)	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Missing	401 (27.1)	50 (32.5)	81 (39.7)	131 (36.6)	20 (22.2)	43 (24.9)	63 (24.0)	95 (26.5)	112 (22.5)	207 (24.2)						
<b>History of homelessness<sup>K</sup></b>												<.001		<.001		<.001
Yes	126 (11.7)	20 (20.4)	34 (25.8)	54 (23.5)	11 (16.2)	19 (14.6)	30 (15.2)	23 (8.7)	19 (5.0)	42 (6.5)	2.49 (2.00 - 3.10)		1.91 (1.41 - 2.59)		1.83 (1.58 - 2.13)	
No	946 (88.2)	78 (79.6)	98 (74.2)	176 (76.5)	57 (83.8)	111 (85.4)	168 (84.8)	241 (91.3)	361 (95.0)	602 (93.5)	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Missing	404 (27.4)	56 (36.4)	72 (35.3)	128 (35.8)	22 (24.4)	43 (24.9)	65 (24.7)	94 (26.3)	117 (23.5)	211 (24.7)						
<b>Median prenatal care visits (IQR)</b>	8(3-12)	5(1-10)	0(0-3)	1(0-7)	6(3-10)	6(2-11)	6(2-10)	9(6-12)	10(7-12)	10(6-12)						

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<b>Receipt of prenatal care</b>												<.001		<.001		<.001
Timely prenatal care (received ≥30 days before pregnancy outcome)	1143 (82.2)	101 (72.7)	68 (37.0)	169 (52.3)	68 (76.4)	130 (77.8)	198 (77.3)	328 (95.3)	448 (95.7)	776 (95.6)	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Non-timely prenatal care (received <30 days before pregnancy outcome)	71 (5.1)	13 (9.4)	14 (7.6)	27 (8.4)	8 (9.0)	22 (13.2)	30 (11.7)	5 (1.5)	9 (1.9)	14 (1.7)	3.68 (2.84 - 4.77)		3.35 (2.65 - 4.25)		2.50 (2.17 - 2.88)	
No prenatal care	177 (12.7)	25 (18.0)	102 (55.4)	127 (39.3)	13 (14.6)	15 (9.0)	28 (10.9)	11 (3.2)	11 (2.4)	22 (2.7)	4.77 (4.09 - 5.55)		2.75 (2.09 - 3.63)		2.73 (2.47 - 3.02)	
<i>Missing</i>	86 (5.8)	15 (9.7)	20 (9.8)	35 (9.8)	1 (1.1)	6 (3.5)	7 (2.7)	14 (3.9)	29 (5.8)	43 (5.0)						
<b>MOUD receipt<sup>L</sup></b>												<.001		0.002		<.001
Yes	79 (5.5)	12 (8.4)	18 (9.7)	30 (9.1)	5 (6.1)	15 (8.9)	20 (8.0)	16 (4.5)	13 (2.6)	29 (3.4)	1.90 (1.45 - 2.48)		1.86 (1.30 - 2.65)		1.61 (1.34 - 1.93)	
No	1345 (94.4)	131 (91.6)	168 (90.3)	299 (90.9)	77 (93.9)	153 (91.1)	230 (92.0)	338 (95.5)	478 (97.4)	816 (96.6)	1.00 (ref)		1.00 (ref)		1.00 (ref)	
<i>Missing</i>	52 (3.5)	11 (7.1)	18 (8.8)	29 (8.1)	8 (8.9)	5 (2.9)	13 (4.9)	4 (1.1)	6 (1.2)	10 (1.2)						
<b>Any substance use<sup>M</sup></b>												<.001		<.001		<.001
Yes	279 (19.6)	35 (24.5)	93 (50.0)	128 (38.9)	20 (24.4)	44 (26.2)	64 (25.6)	42 (11.9)	45 (9.2)	87 (10.3)	2.84 (2.41 - 3.35)		2.15 (1.72 - 2.70)		2.04 (1.82 - 2.28)	
No	1145 (80.4)	108 (75.5)	93 (50.0)	201 (61.1)	62 (75.6)	124 (73.8)	186 (74.4)	312 (88.1)	446 (90.8)	758 (89.7)	1.00 (ref)		1.00 (ref)		1.00 (ref)	
<i>Missing</i>	52 (3.5)	11 (7.1)	18 (8.8)	29 (8.1)	8 (8.9)	5 (2.9)	13 (4.9)	4 (1.1)	6 (1.2)	10 (1.2)						
<b>Year of diagnosis<sup>N</sup></b>												<.001		<.001		<.001
2017-2019	702 (51.1)	43 (33.3)	60 (31.3)	103 (32.1)	32 (37.6)	86 (51.5)	118 (46.8)	184 (55.6)	297 (63.3)	481 (60.1)	1.00 (ref)		1.00 (ref)		1.00 (ref)	
2020-2021	671 (48.9)	86 (66.7)	132 (68.8)	218 (67.9)	53 (62.4)	81 (48.5)	134 (53.2)	147 (44.4)	172 (36.7)	319 (39.9)	2.30 (1.88 - 2.82)		1.50 (1.21 - 1.86)		1.67 (1.46 - 1.90)	
<i>Missing</i>	103 (7.0)	25 (16.2)	12 (5.9)	37 (10.3)	5 (5.6)	6 (3.5)	11 (4.2)	27 (7.5)	28 (5.6)	55 (6.4)						
<b>Median test-to-treat in days<sup>O</sup> (IQR)</b>	9 (4-18)	NA	NA	NA	6 (2-16)	9 (4-18)	8 (3-18)	8 (5-17)	11 (7-20)	10 (6-20)						
<b>Gestational age at pregnancy outcome</b>												<.001		<.001		<.001
<35 weeks	222 (15.0)	39 (25.3)	79 (38.7)	118 (33.0)	14 (15.6)	35 (20.2)	49 (18.6)	32 (8.9)	23 (4.6)	55 (6.4)	2.96 (2.54 - 3.44)		2.23 (1.76 - 2.83)		2.08 (1.87 - 2.31)	
≥35 weeks	1254 (84.9)	115 (74.7)	125 (61.3)	240 (67.0)	76 (84.4)	138 (79.8)	214 (81.4)	326 (91.1)	474 (95.4)	800 (93.6)	1.00 (ref)		1.00 (ref)		1.00 (ref)	

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Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)						
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Missing data were excluded from the denominators for calculating percentages.

Abbreviations: *P/S/E*, Primary, secondary early latent syphilis; *LL/U*, late latent, unknown syphilis; *uRR*, Unadjusted risk ratio; *IQR*, interquartile range; *NH*, Non-Hispanic; *MOUD*, medications for opioid use disorder; *NA*, not applicable

<sup>A</sup>Treatment other than penicillin or initial dose is given <30 days before pregnancy outcome.

<sup>B</sup>Treatment other than penicillin, the initial dose is given <30 days before pregnancy outcome, <3 doses were given, or doses were given outside of the recommended window (>9 days apart or <5 days apart).

<sup>C</sup>Adequately treated with ≥1 dose of penicillin during pregnancy, with the dose administered ≥30 days before pregnancy outcome.

<sup>D</sup>Adequately treated with ≥3 doses of penicillin, spaced 5–9 days apart, with the first dose administered ≥30 days before pregnancy outcome and the final dose occurring during pregnancy.

<sup>E</sup>Combined across syphilis stages, excluding missing cases.

<sup>F</sup>P-values from chi-squared tests of association and the null hypotheses that the distribution of demographic and clinical characteristics is not associated with no treatment versus adequate treatment.

<sup>G</sup>P-values from chi-squared tests of association and the null hypotheses that the distribution of demographic and clinical characteristics is not associated with inadequate treatment versus adequate treatment.

<sup>H</sup>P-values from chi-squared tests of association and the null hypotheses that the distribution of demographic and clinical characteristics is not associated with inadequate treatment versus no treatment.

<sup>I</sup>The National Center for Health Statistics Urban-Rural Classification Scheme for Counties was used to categorize urbanicity as follows: medium to large metropolitan (population ≥250,000) and rural to small metropolitan (population ≤249,000) (24)

<sup>J</sup>Race and ethnicity is top-coded in the following hierarchy: 1) Native Hawaiian/Pacific Islander, 2) American Indian/Alaska Native, 3) Asian, , 4) Hispanic ethnicity, 5) multiple non-Hispanic races. “Other” race category was a response option in SET-NET for people whose race was not Native Hawaiian, Pacific Islander, American Indian, Alaska Native, Asian, Black or African American, or White.

<sup>K</sup>Within the 12 months preceding case report or positive test results or during pregnancy.

<sup>L</sup>The pregnant person received medication for opioid use disorder during this pregnancy.

<sup>M</sup>Defined as illicit use of opioids (e.g., prescription opioids not taken as prescribed, fentanyl, or heroin), and other illicit, nonprescription substances (e.g., cocaine, methamphetamines, inhalants, ecstasy, or hallucinogens, such as LSD or PCP).

<sup>N</sup>Year of the first positive treponemal or nontreponemal test reported (whichever comes first). Note: no single test or combination of tests can definitively diagnose and stage syphilis in the absence of a comprehensive history and physical examination.

<sup>O</sup>Number of days between first positive treponemal or non-treponemal test during pregnancy and first treatment date during pregnancy.