



Neurosyphilis, Ocular and Otic Syphilis Cases — Chicago, Illinois, January–August 2023

Amy Nham, PharmD, MPH, BCPS

Epidemic Intelligence Service Officer

Chicago Department of Public Health (CDPH)

Syndemic Provider Conference

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Disclosure:

Presenter has no financial interest to disclose. This continuing education activity is managed by The St. Louis STI/HIV Prevention Training Center and accredited by Missouri State Medical Association (MSMA) in cooperation with the Chicago Department of Public Health.



Patient D.L.

- 41-year-old male
- No past medical history



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3/18: Clinic

- **Corneal abrasion**
- **Prescribed eye ointment**



Patient D.L.

- 41-year-old male
- No past medical history



3/18: Clinic

- Corneal abrasion
- Prescribed eye ointment



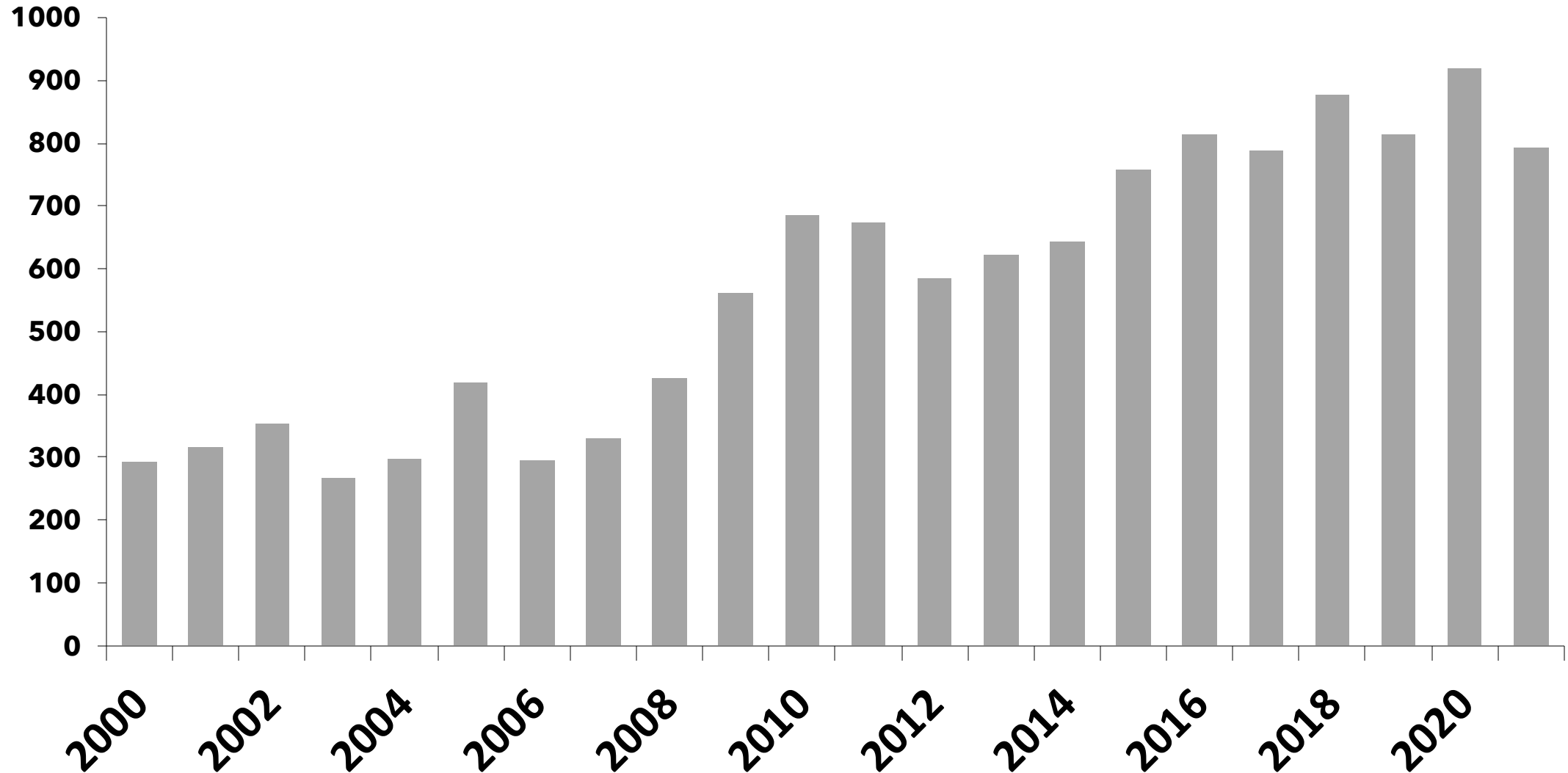
3/21: Emergency Department

- Symptoms worsened
- Ophthalmologist diagnosed uveitis
- Prescribed eyedrops
- Labs obtained before discharge

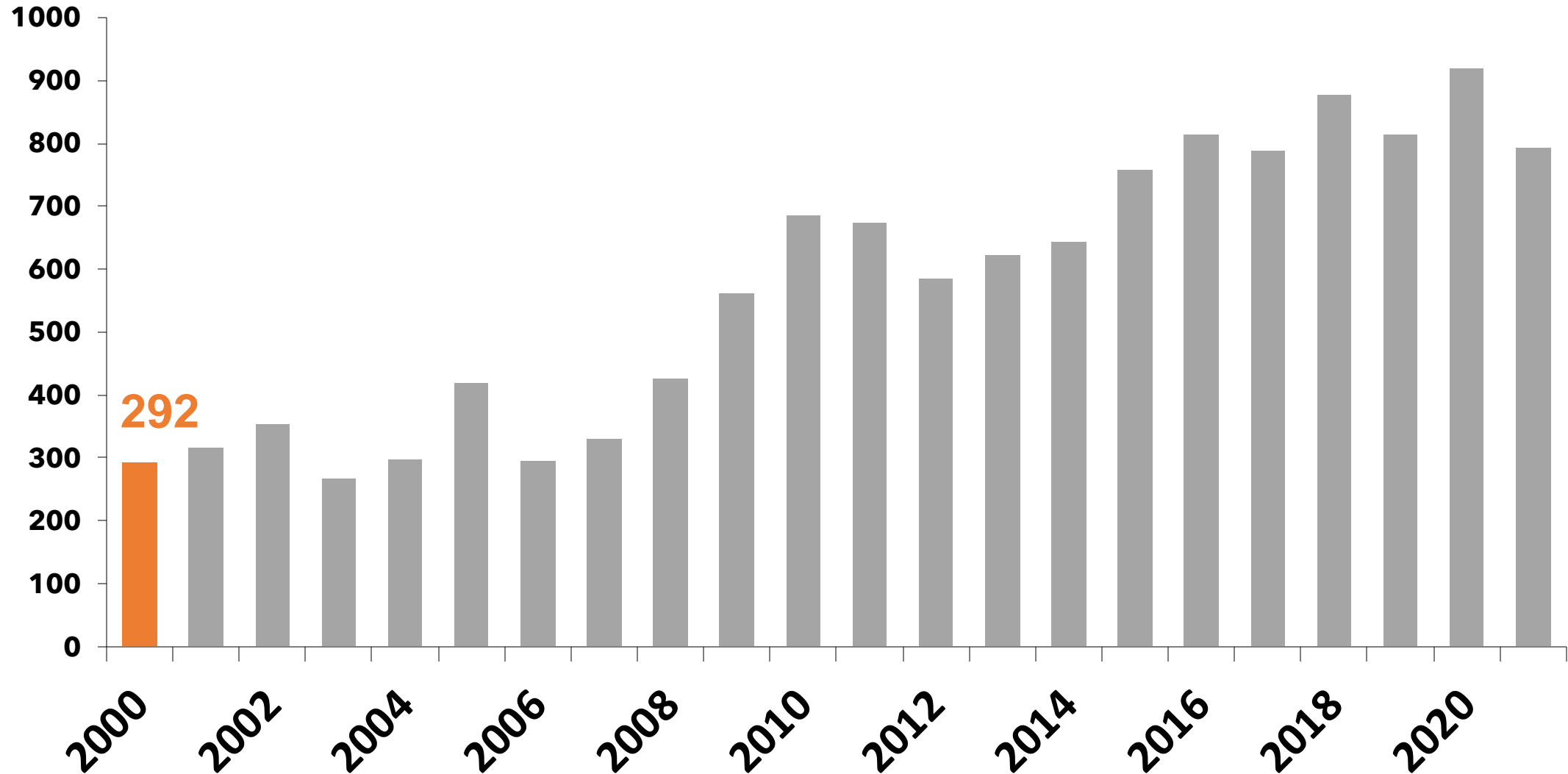


Syphilis is caused by
Treponema pallidum.

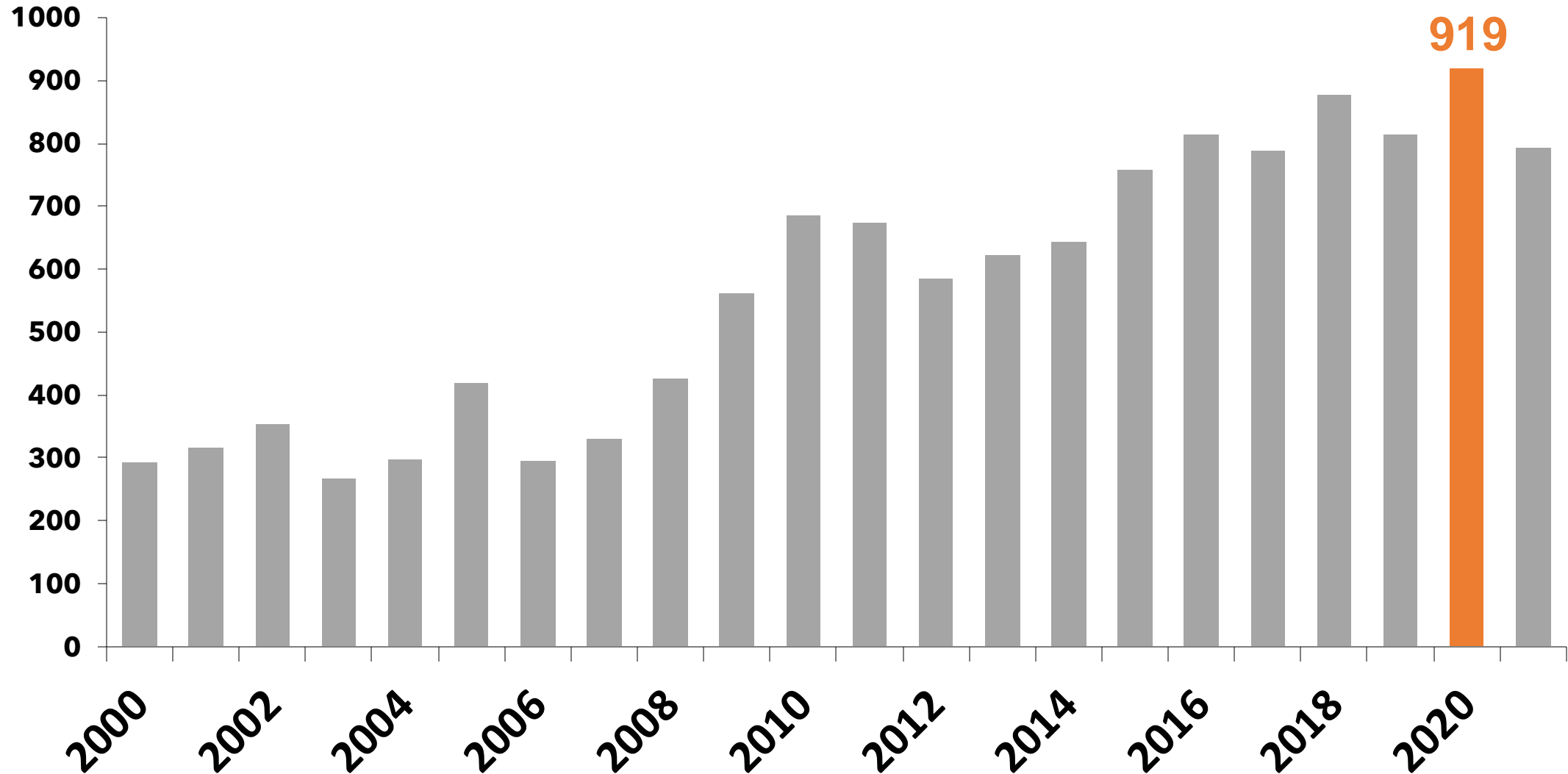
Primary and secondary syphilis cases in Chicago have **tripled** since 2000.

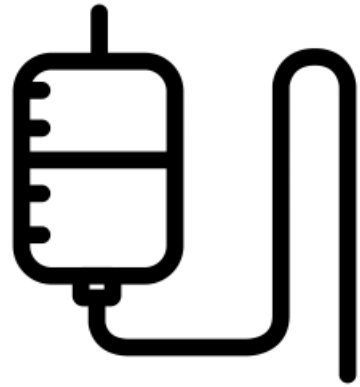


Primary and secondary syphilis cases in Chicago have **tripled** since 2000.



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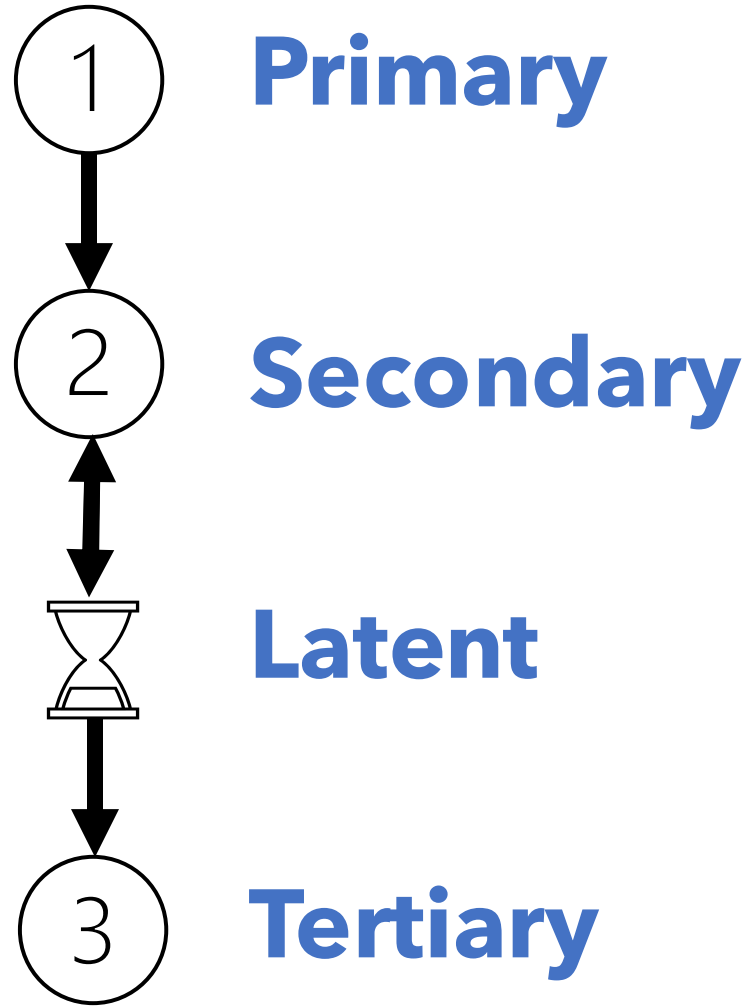




Syphilis is **treatable**
with **penicillin**.

**There are
4 stages of
syphilis.**

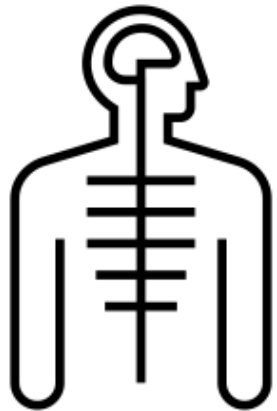
**There are
4 stages of
syphilis.**



AT ANY STAGE of syphilis, *T. pallidum* can cause...

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Neurosyphilis



AT ANY STAGE of syphilis, *T. pallidum* can cause...

Neurosyphilis



Ocular Syphilis



AT ANY STAGE of syphilis, *T. pallidum* can cause...

Neurosyphilis



Ocular Syphilis



Otic Syphilis



AT ANY STAGE of syphilis, *T. pallidum* can cause...

Neurosyphilis



Ocular Syphilis

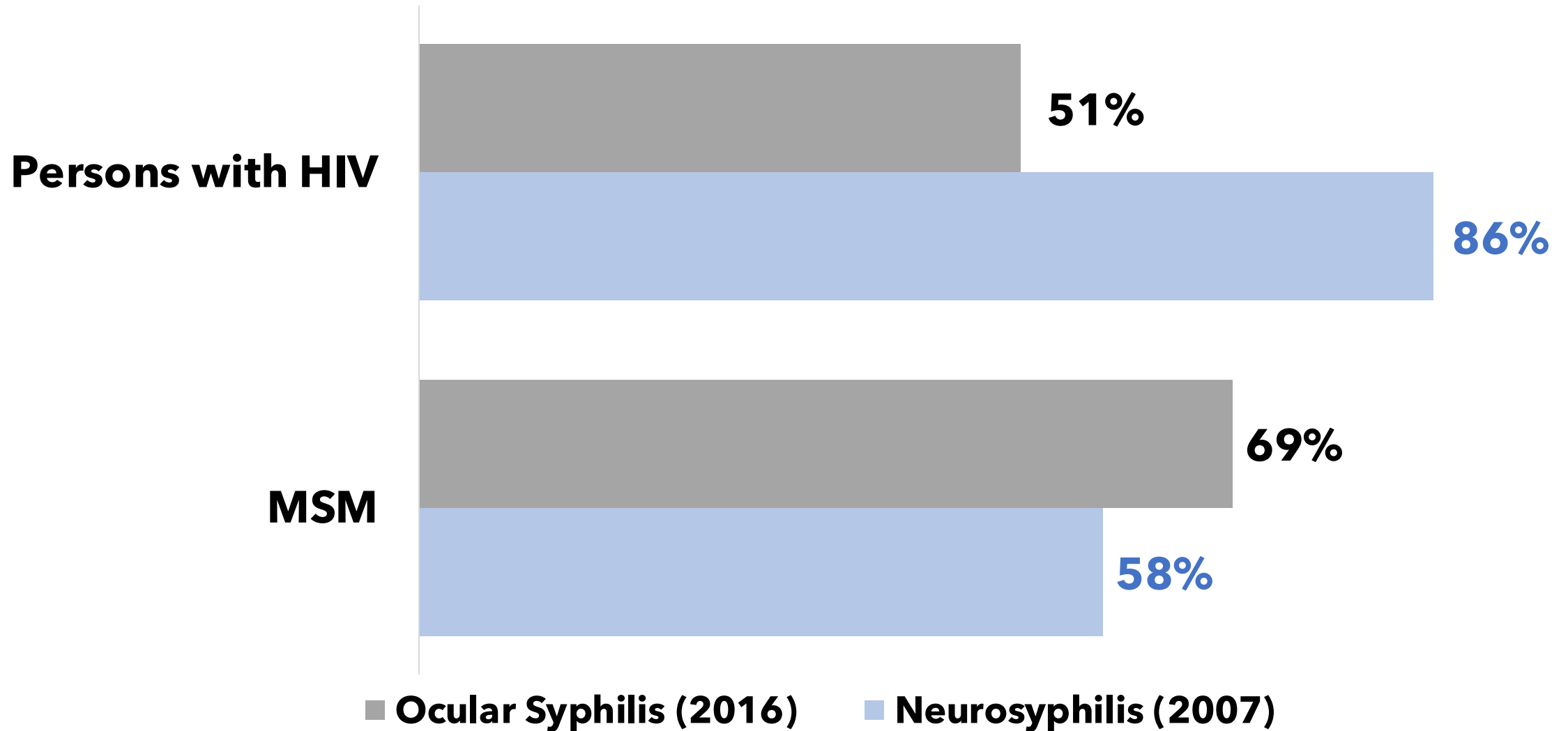


Otic Syphilis



Per previous studies, persons with HIV and MSM are more likely to have NOO syphilis.

Per previous studies, **persons with HIV and MSM** are more likely to have **NOO syphilis**.



**Increased NOO
syphilis in non-
MSM and persons
without HIV**



Is the
epidemiology of
NOO syphilis
changing?



Chicago Health Information Management System for Syphilis



CSF-
VDRL
Lab



IV
Penicillin
Treatment



Signs/
Symptoms



Electronic Medical Records



Enhanced HIV/AIDS Reporting System

Chicago Health Information Management System for Syphilis



**CSF-
VDRL
Lab**



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**Signs/
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Electronic Medical Records



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**Signs/
Symptoms**

↓ **36 cases reported**



Electronic Medical Records



Enhanced HIV/AIDS Reporting System

Chicago Health Information Management System for Syphilis



CSF-
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Signs/
Symptoms



36 cases reported



Electronic Medical Records



Enhanced HIV/AIDS Reporting System

Chicago Health Information Management System for Syphilis



CSF-
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IV
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Treatment



Signs/
Symptoms



36 cases reported



Electronic Medical Records



**28 cases met case
definition**



Enhanced HIV/AIDS Reporting System

Chicago Health Information Management System for Syphilis



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Signs/
Symptoms



36 cases reported



Electronic Medical Records

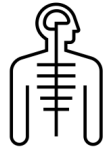


28 cases met case
definition



Enhanced **HIV/AIDS** Reporting System

Of 28 included cases, over a third had **more than 1 type** of NOO manifestation.



Neurosyphilis

71%, n = 20



Ocular Syphilis

61%, n = 17

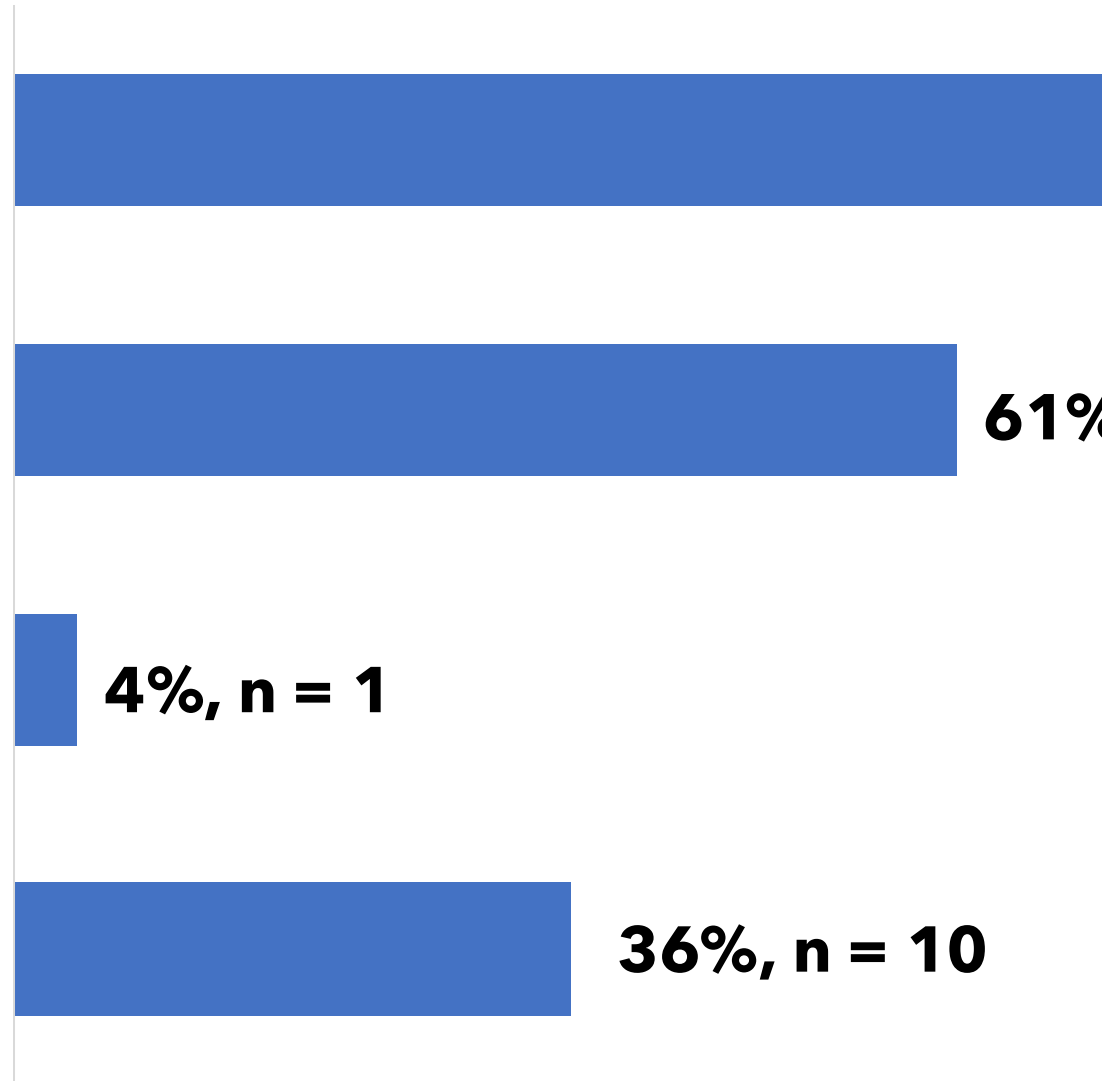


Otic Syphilis

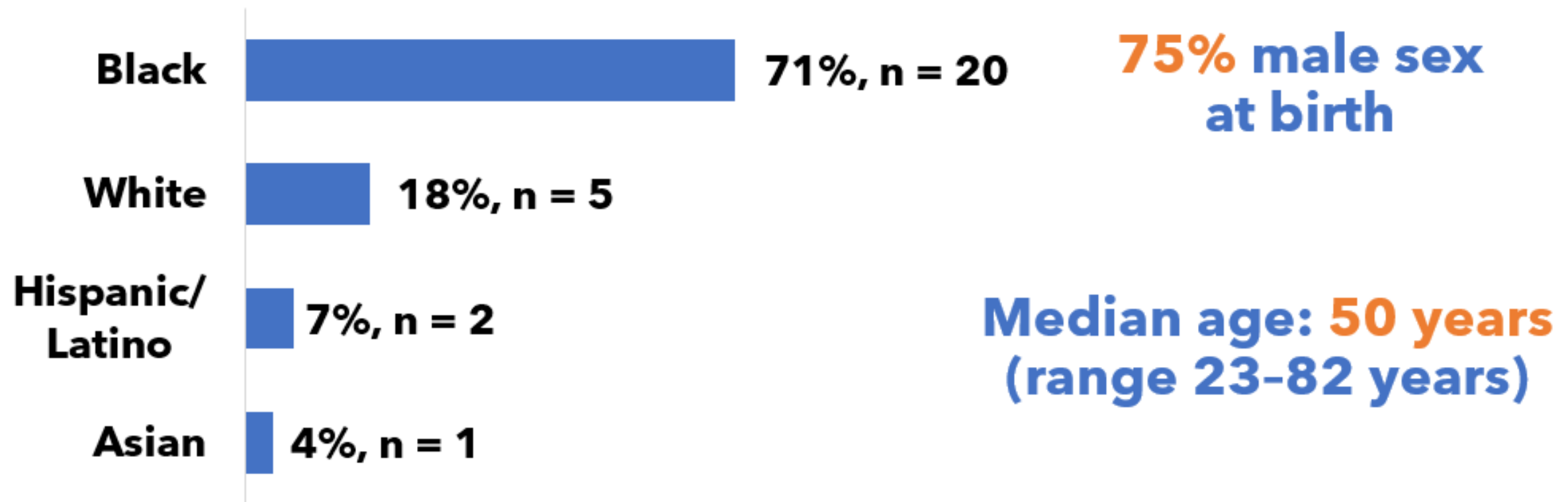
4%, n = 1

>1 type of NOO syphilis

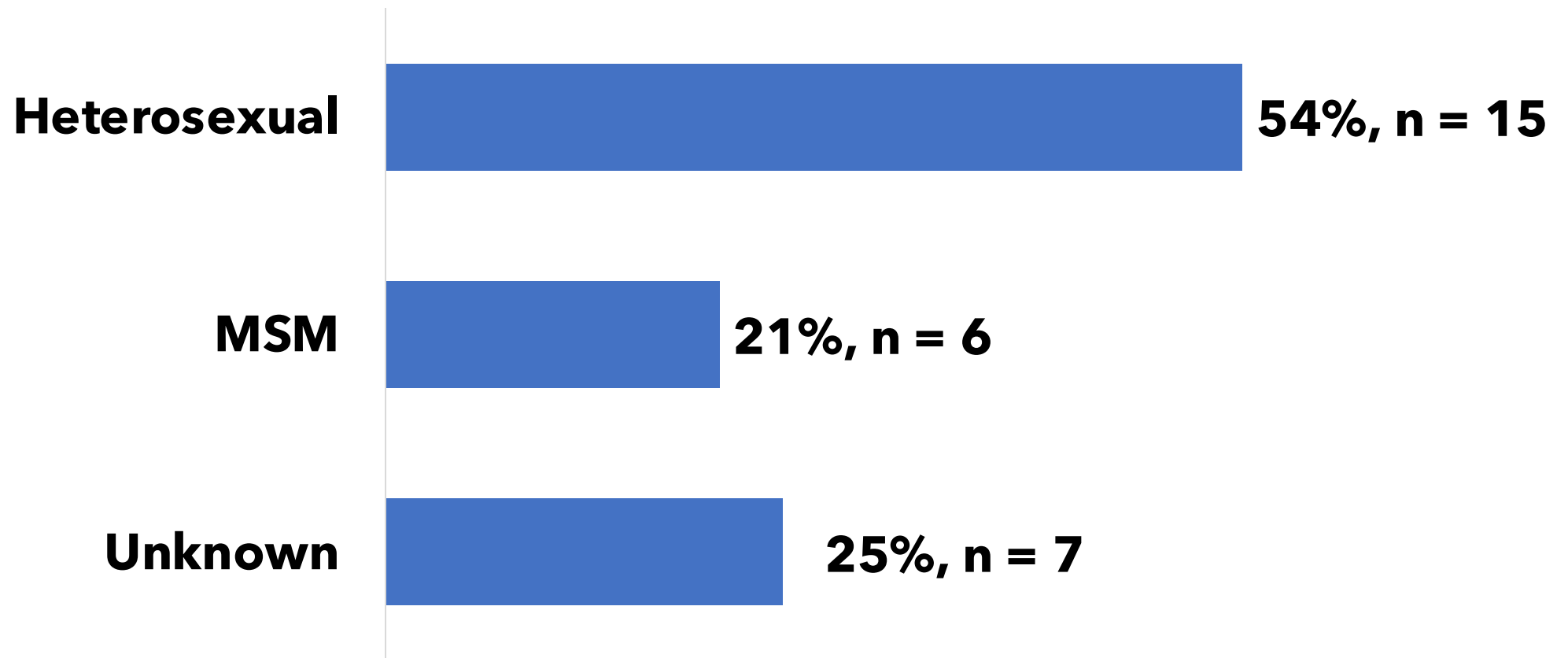
36%, n = 10



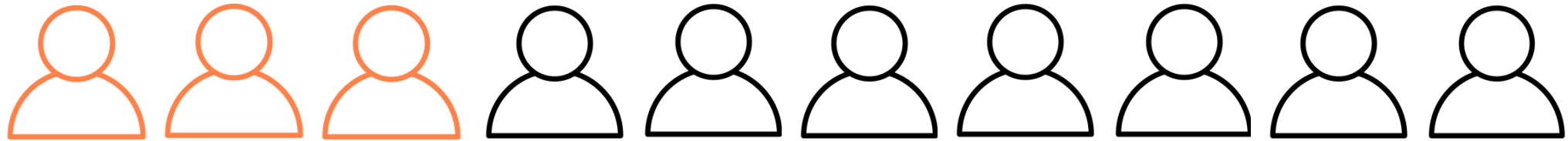
Cases occurred mostly in **Black and male** individuals.



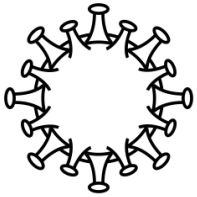
The **majority** of cases were among individuals who identify as **heterosexual**.



Only 32% of cases were in persons with HIV.



Only 32% of cases were in persons with HIV.



56% had an undetectable viral load.

Comparing persons with and without HIV,
there were **no significant differences** in...



Demographics



Prior syphilis history



Sign/symptom presentation



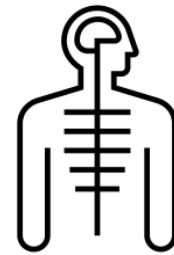
Hospital admission rates

The most common signs/symptoms were...

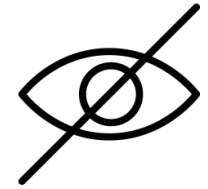
Neurosyphilis



30%



25%



25%

The most common signs/symptoms were...

Neurosypphilis



30%

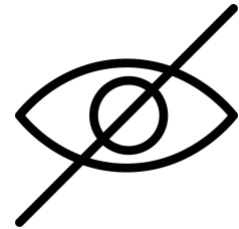


25%



25%

Ocular Syphilis



65%



35%



29%

The most common signs/symptoms were...

Neurosyphilis



30%



25%



25%

Ocular Syphilis



65%

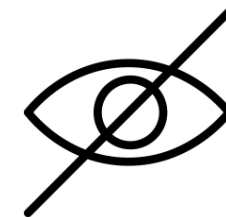


35%

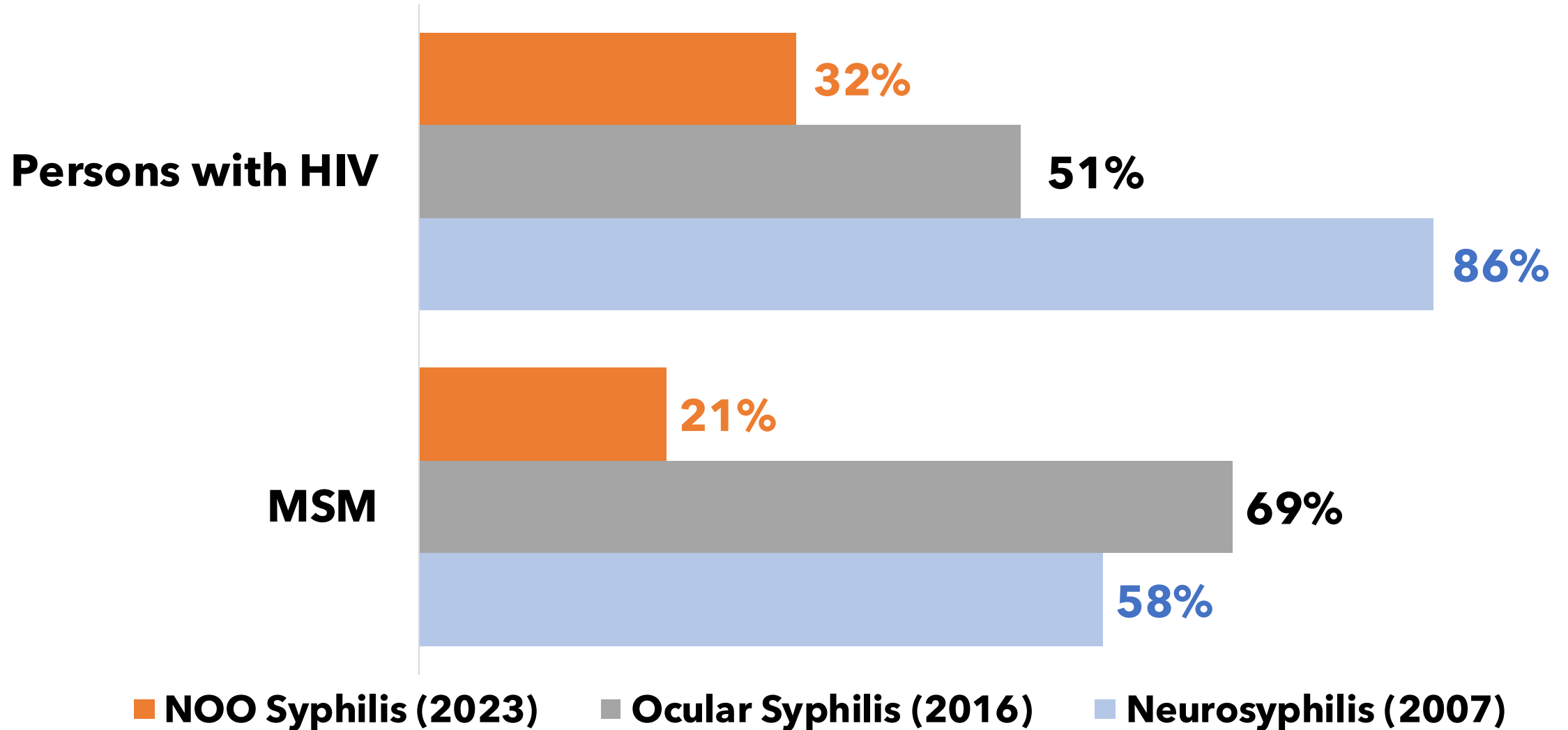


29%

Otic Syphilis



Per this analysis, NOO syphilis cases were mostly in persons without HIV and non-MSM.



Why?

Why?



Increase in untreated cases

Why?



Increase in untreated cases



Increase in syphilis nationwide

Implications

Implications



**Better understanding of local
epidemiology**

Implications



Better understanding of local epidemiology



**Enhanced surveillance and
timely reporting**

Implications



Better understanding of local epidemiology



Enhanced surveillance and timely reporting



More provider and patient education



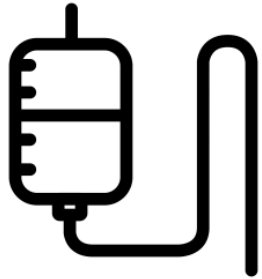
3/22: Returned to Hospital

- **Reactive syphilis labs**
- **Reactive neurosyphilis lab (CSF-VDRL)**
- **Neurosyphilis & ocular syphilis**



3/22: Returned to Hospital

- Reactive syphilis labs
- Reactive neurosyphilis lab (CSF-VDRL)
- Neurosyphilis & ocular syphilis



3/23: Hospital Admission

- Started on treatment



3/22: Returned to Hospital

- Reactive syphilis labs
- Reactive neurosyphilis lab (CSF-VDRL)
- Neurosyphilis & ocular syphilis



3/23: Hospital Admission

- Started on treatment



7/21: Clinic

- Improved overall



[Chicago.gov/Health](https://chicago.gov/Health)



HealthyChicago@cityofchicago.org



[@ChicagoPublicHealth](https://www.facebook.com/ChicagoPublicHealth)



[@ChiPublicHealth](https://twitter.com/ChiPublicHealth)

Patient DL — Additional Information

- **L eye vision:** 20/250
- **Slit Lamp Exam**
 - R eye: Normal
 - L eye: Diffuse injection, diffuse endothelial haze covering 50% of inferior cornea, 2+ cells, 1+ flare
- **Fundus Exam**
 - R eye: Normal
 - L eye: Disc edema, mildly hyperemic
- **Recommended Labs**
 - Syphilis, ACE, lysozyme, TB quant, CBC, CMP, HLA-B27, ANA, ANCA, ESR, CRP, RF, CCP

Primary & Secondary Syphilis Cases — Chicago, 2022

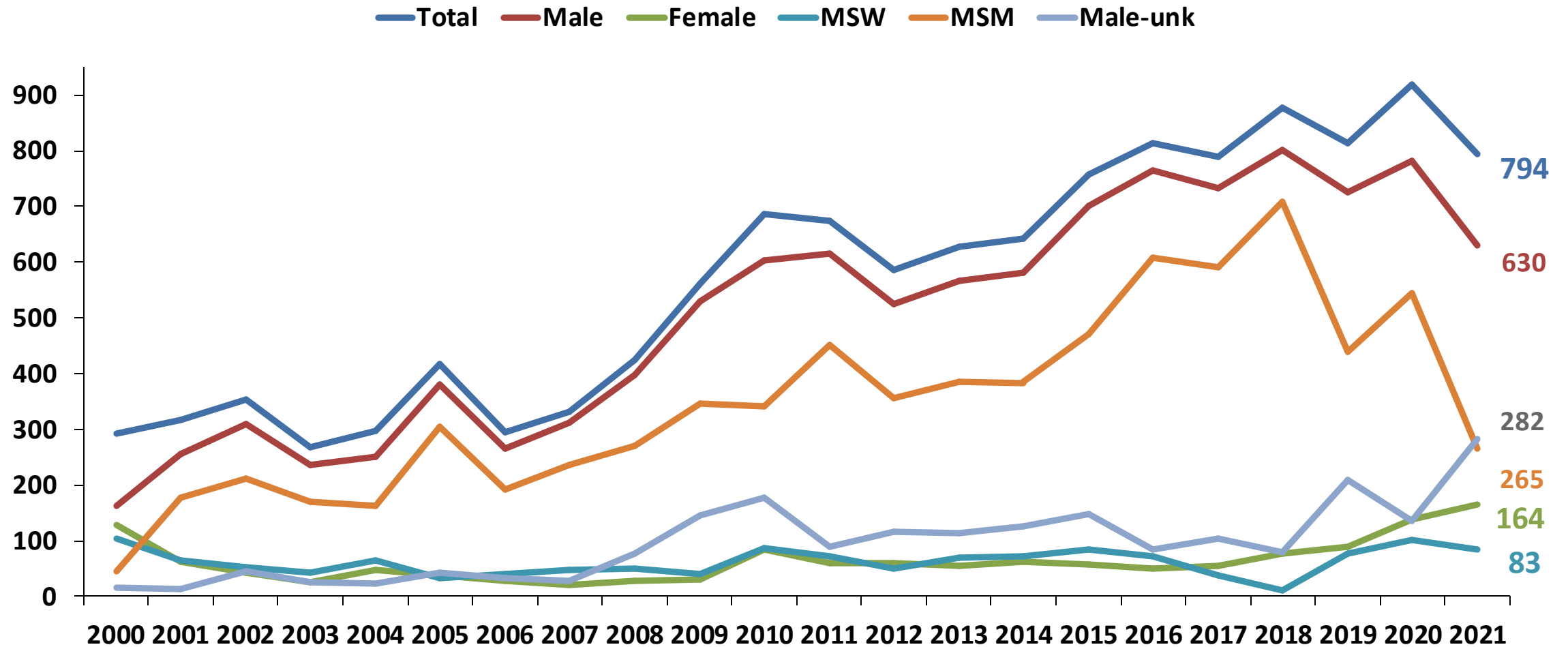
- 82% male sex at birth
- 47% Black, non-Hispanic
- Median age: **33** (range 14–83)

Demographic Characteristics	P&S Syphilis		
	No.	%	Rate
RACE/ETHNICITY[^]			
Black, non-Hispanic	377	46.8%	47.9
White, non-Hispanic	137	17.0%	15.9
Hispanic	138	17.1%	16.8
Asian/PI, non-Hispanic	8	1.0%	4.2
AI/AN, [^] non-Hispanic	<5	<1%	30.1
Other, non-Hispanic	10	1.2%	12.2
Unknown	135	16.7%	
GENDER			
Female	146	18.1%	10.3
Male	660	81.9%	49.5
Unknown	0	0.0%	0.0
TRANSMISSION GROUP[†]			
Male sex w/Male	295	36.6%	
Heterosexual Males	79	9.8%	
Females	146	18.1%	
Male unknown	286	35.5%	
AGE GROUP[†]			
Less than 13	0	0.0%	
13-19	28	3.5%	
20-29	258	32.0%	
20-24	96	11.9%	
25-29	162	20.1%	
30-39	255	31.6%	
40-49	146	18.1%	
50+	119	14.8%	
TOTAL^{**}	806		29.3

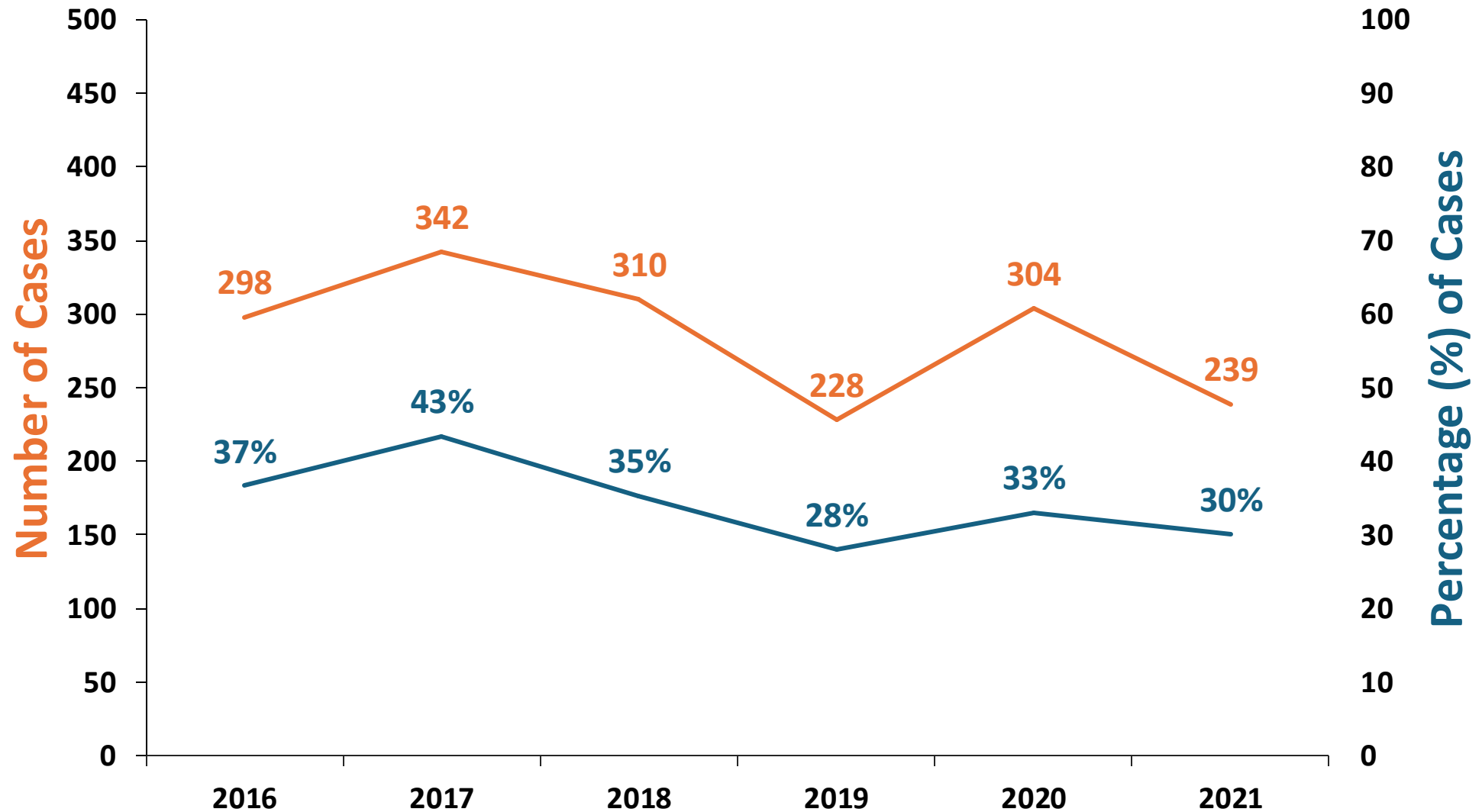
Chicago Demographics Comparison

	Census (2022)	Primary & Secondary Syphilis (2022)	NOO Syphilis in This Analysis (Jan–Aug 2023)
Male	49%	82%	75%
Black	28%	47%	71%
MSM	5%	37%	21%
Median Age	35	33	50

Primary & Secondary Syphilis Cases by Gender and Sexual Orientation — Chicago, 2001–2021



Primary & Secondary Syphilis/HIV Comorbidity — Chicago, 2016–2021



CSTE syphilis surveillance case definitions changed in 2018.

2014

 **Neurosyphilis**

Classifications

- Probable
- Confirmed



2018

 **Neurosyphilis**
 **Ocular Syphilis**
 **Otic Syphilis**

Classifications

- Possible
- Likely
- Verified

Syphilis Case Definitions from 2014 to 2018

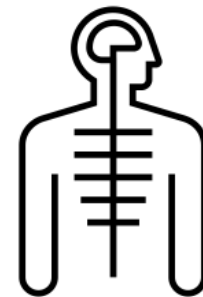
2014

- Primary syphilis
- Secondary syphilis
- Early latent syphilis
- Late latent syphilis
- Late with clinical manifestations (including late benign syphilis and cardiovascular syphilis)
- Syphilitic stillbirth
- Congenital syphilis
- Neurosyphilis



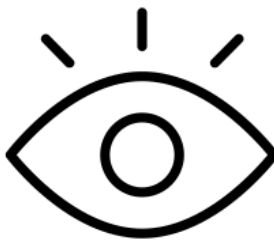
2018

- Primary syphilis
- Secondary syphilis
- Early non-primary non-secondary syphilis
- Unknown duration or late syphilis
- Syphilitic stillbirth
- Congenital syphilis
- Neurosyphilis
- Ocular syphilis
- Otic syphilis



Neurosyphilis Case Definition (as of 2018)

- **Possible:**
 - A person with a **reactive nontreponemal test** (e.g., VDRL, RPR) and a **reactive treponemal test** (e.g., TP-PA, EIA, CIA) AND clinical **symptoms or signs** that are consistent with neurosyphilis without other known causes for these clinical abnormalities.
- **Likely:**
 - Everything listed in the possible criteria AND
 - Elevated cerebrospinal fluid (**CSF**) **protein (>50 mg/dL²)** or leukocyte count (**>5 white blood cells/cubic millimeter CSF**) in the absence of other known causes of these abnormalities.
- **Verified:**
 - Everything listed in the possible criteria AND
 - A **reactive VDRL in CSF** in the absence of grossly bloody contamination of the CSF.



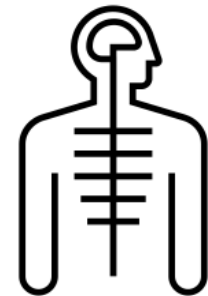
Ocular Syphilis Case Definition (as of 2018)

- **Possible:**
 - A person with a **reactive nontreponemal test** (e.g., VDRL, RPR) and a **reactive treponemal test** (e.g., TP-PA, EIA, CIA) AND clinical **symptoms or signs** consistent with ocular syphilis without other known causes for these clinical abnormalities.
- **Likely:**
 - Everything listed in the possible criteria AND
 - **Findings on exam by an ophthalmologist** that are consistent with ocular syphilis in the absence of other known causes for these abnormalities
- **Verified:**
 - Everything listed in the possible criteria AND
 - Demonstration of **T. pallidum in aqueous or vitreous fluid** by darkfield microscopy, or by polymerase chain reaction (PCR) or equivalent direct molecular methods.



Otic Syphilis Case Definition (as of 2018)

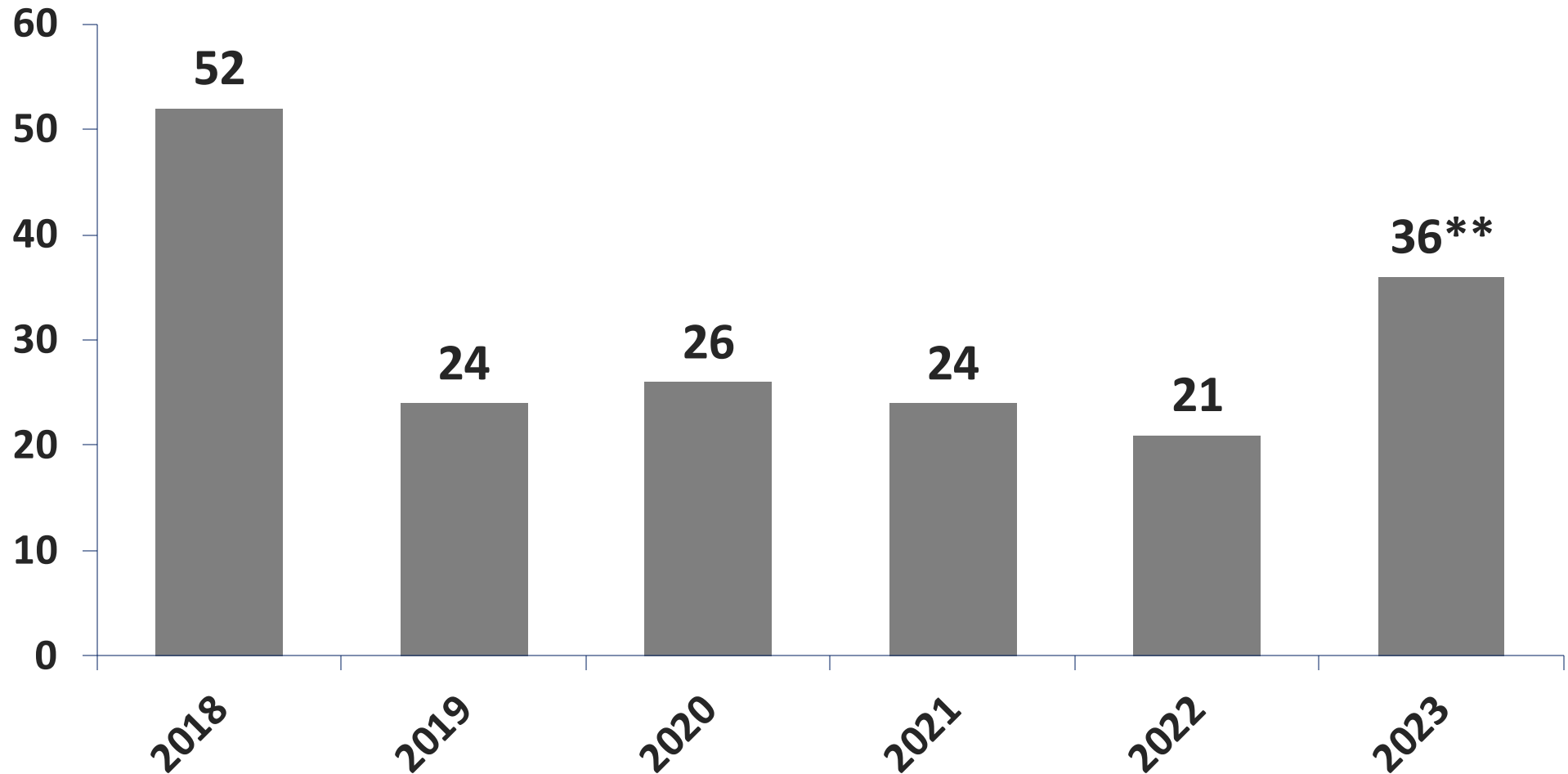
- **Possible:**
 - A person with a **reactive nontreponemal test** (e.g., VDRL, RPR) and a **reactive treponemal test** (e.g., TP-PA, EIA, CIA) AND clinical **symptoms or signs** consistent with otosyphilis without other known causes for these clinical abnormalities.
- **Likely:**
 - Everything listed in the possible criteria AND
 - **Findings on exam by an otolaryngologist** that are consistent with otosyphilis in the absence of other known causes for these abnormalities.
- **Verified:**
 - Everything listed in the possible criteria AND
 - Demonstration of **T. pallidum in inner ear fluid** by darkfield microscopy, or by polymerase chain reaction (PCR) or equivalent direct molecular detection methods.



Prior Neurosyphilis Case Definition (2014)

- **Probable:**
 - Syphilis of any stage with a **negative VDRL** test in CSF specimen AND either
 - **Reactive treponemal** serologic test for syphilis (e.g., FTA-ABS, TP-PA, EIA, CIA) OR
 - **Reactive non-treponemal** serologic test for syphilis (VDRL, RPR),AND both the following:
 - **Elevated CSF protein (>50mg/dl²)** or **leukocyte count (>5 white blood cells/cubic millimeter CSF)** in the absence of other known causes of these abnormalities, AND
 - Clinical **symptoms or signs** consistent with neurosyphilis without other known causes for these clinical abnormalities
- **Confirmed:**
 - A **reactive VDRL** in cerebrospinal fluid (CSF) AND either
 - **Reactive treponemal** serologic test for syphilis (e.g., FTA-ABS, TP-PA, EIA, CIA, or equivalent serologic methods) OR
 - **Reactive nontreponemal** serologic test for syphilis (VDRL, RPR, or equivalent serologic method)

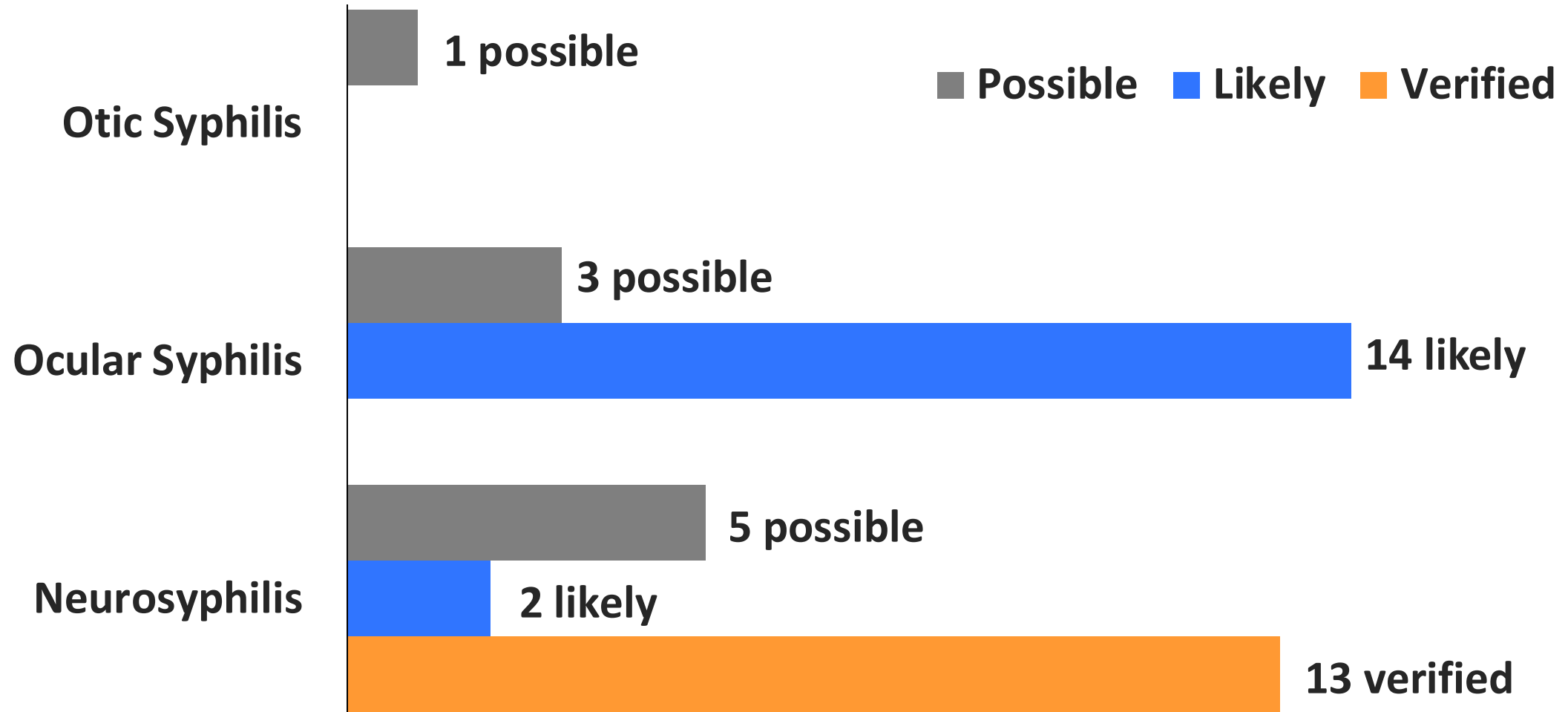
Reported **NOO Syphilis** Cases* — Chicago, 2018–2023



*Not all cases meet surveillance case definitions.

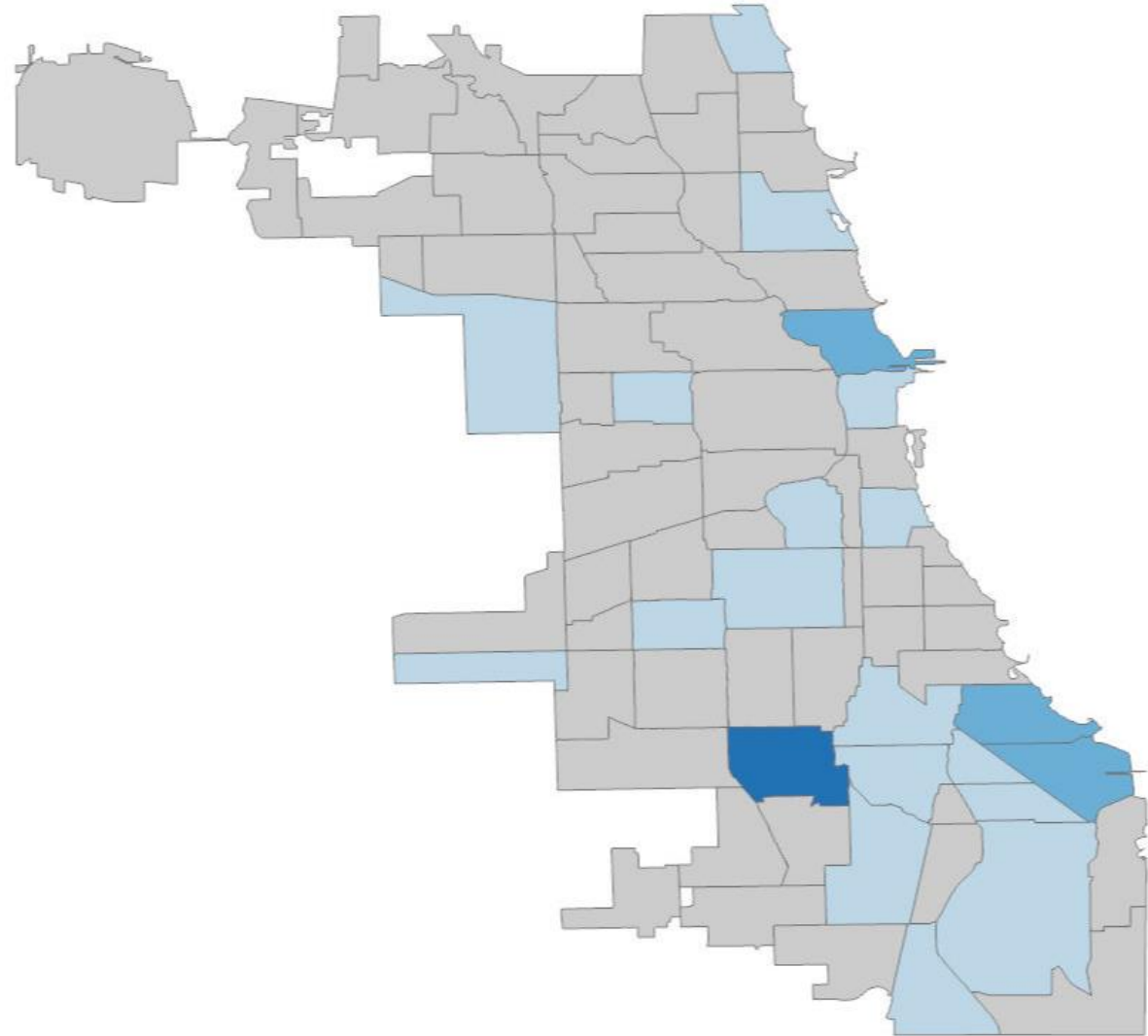
**Only includes data from January–August.

NOO Syphilis Cases by Classification



NOO Syphilis Cases by Chicago Geography

- Cases are dispersed through Chicago, with more cases in the South side.
- Darker color* = more cases



*Key is not provided due to data suppression.

NOO Syphilis Cases by HIV Status — Demographics

TABLE 1: Demographic and clinical presentation characteristics of persons diagnosed with Neuro, Ocular, or Otic syphilis (NOO Syphilis) by HIV status - Chicago, January 1-August 24, 2023 (N = 28)

	NOO Syphilis/HIV + N=9	NOO Syphilis/HIV - N=19	P-value*
Total	Number (%)	Number (%)	
Age group, yrs.			0.6875
20-29	<5 (11.1)	<5 (15.8)	
30-39	<5 (11.1)	<5 (21.1)	
40-49	<5 (33.3)	<5 (10.5)	
50-59	<5 (22.2)	<5 (15.8)	
60+	<5 (22.2)	7 (36.8)	
Median age (Range)	48(29-66)	52(23-82)	0.6908
Sex at Birth			0.0621
Male	9 (100)	12 (61.2)	
Female	0 (0)	7 (36.8)	
Race/Ethnicity			0.6914
Black, non-Hispanic	6 (66.7)	14 (73.7)	
White, non- Hispanic	<5 (11.1)	<5 (15.8)	
Asian or Pacific Islander	<5 (11.1)	0 (0)	
Hispanic	<5 (11.1)	<5 (15.8)	
Sexual Orientation			0.0080
MSM	5 (55.6)	<5 (5.3)	
Heterosexual	<5 (22.2)	13 (68.4)	
Unknown	<5 (22.2)	5 (26.3)	

NOO Syphilis Cases by HIV Status — Clinical Course

NOO Syphilis/HIV co-infection with undetectable HIV viral load in 2023 [†]			
Yes	5 (55.6)	NA	
No	<5 (44.4)	NA	
NOO Syphilis/HIV co-infection CD4 <200 in 2023 [§]			
Yes	<5 (33.3)	NA	
No	6 (66.7)	NA	
NOO Syphilis/HIV co-infection receiving HIV care in last 12 months			
Yes	9(100)	NA	
No	0(0)	NA	
Prior Syphilis diagnosis			0.6591
Yes	<5 (33.3)	<5(15.8)	
No	<5 (44.4)	10 (52.6)	
Unknown	<5(22.2)	6(31.6)	
Treatment received (n=28)			0.2963
Yes	7 (87.5)	19 (100)	
No	<5 (12.5)	0 (0)	
Admitted to hospital			0.7848
Yes	6 (66.7)	9 (47.4)	
No	0 (0)	<5 (5.3)	
Unknown	<5 (33.3)	9 (47.4)	

NOO Syphilis Cases by HIV Status — Signs/Symptoms

NOO Syphilis Signs/Symptoms [†] (n=28)			
Rash	<5 (12.5)	5 (26.3)	0.6334
Ulcer/lesion	<5 (12.5)	<5 (10.5)	1.0000
Fever	<5 (25)	0 (0)	0.0798
Malaise	<5 (12.5)	0 (0)	0.2963
Acute headache	<5(50)	<5 (10.5)	0.0441
Lymphadenopathy	<5 (12.5)	0(0)	0.2963
Meningismus	0(0)	<5(5.3)	1.0000
CNS deficits	<5(25)	3(15.8)	0.6159
Photophobia	<5(12.5)	<5(21.1)	1.0000
Decreased vision	<5(25)	10(52.6)	0.2357
Uveitis	<5(12.5)	<5(21.1)	1.0000
Retinitis	0(0)	<5(5.3)	1.0000
Optic neuritis	<5(12.5)	<5(5.3)	0.5128
Hearing loss	0(0)	<5(5.3)	1.0000
Gait difficulty	<5(25)	<5(5.3)	0.2010
Weakness	<5(37.5)	<5(5.3)	0.0646
Sensory change	<5(12.5)	<5(5.3)	0.5128



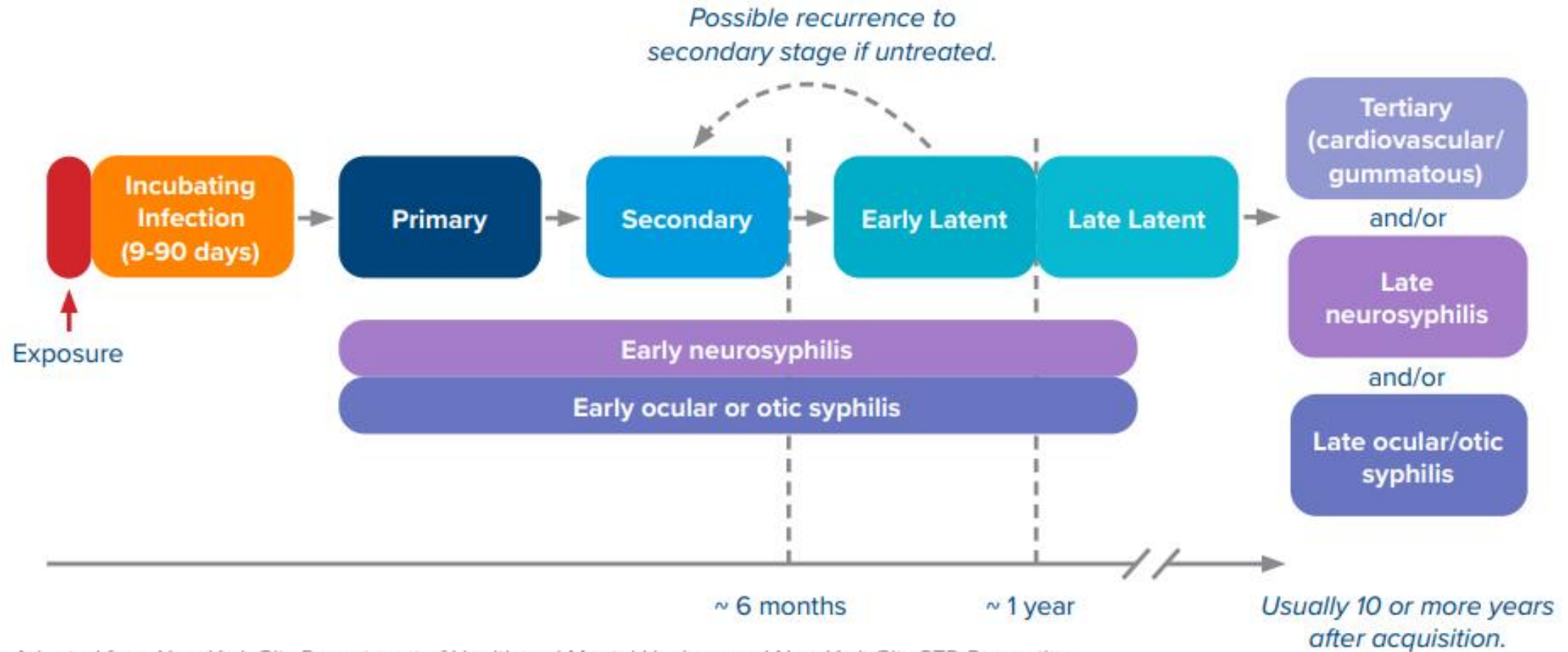
Possible Causes for Increased Syphilis Rates

- Reductions in STI services at the state and local level
- Increases in substance use, which has been linked to less safe sexual practices
- Social and economic conditions that make it more difficult for some groups to stay healthy
- Decreases in condom use among some groups
- STIs continue to be stigmatized

Limitations

- Underdiagnosing/lack of syphilis screening
- Reporting bias/incomplete reporting
- Missing sexual preference information
- Missing information on additional potential risk factors (i.e. drug use, comorbidities)
- Lack of robust historical surveillance data

Stages of Syphilis



Adapted from New York City Department of Health and Mental Hygiene and New York City STD Prevention



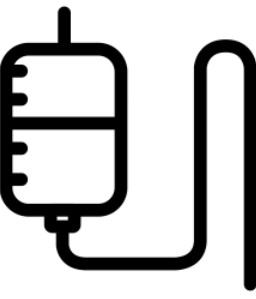
Syphilis Screening Recommendations

- **At least annually**
 - MSM, sexually active
 - Persons with HIV
 - Transgender and gender diverse people
- **Every 3-6 months**
 - MSM with increased risk (i.e. multiple partners, anonymous partners)
 - Persons with HIV with increased risk
- **For each pregnancy** → 1st prenatal visit, at 28 weeks of gestation (and at delivery for increased risk)
- **Not routinely recommended unless risk factors present**
 - Everyone else



Risk Factors for Neurosyphilis

- **HIV** (particularly with **lower CD4+** counts, detectable plasma **HIV RNA**, and/or **no antiretroviral therapy**)
- **Male**
- **MSM**
- **Advanced age** (≥ 45 years)
- **Drug use disorder**
- **Lack of syphilis treatment**
- **Reinfection** after a previous syphilis infection
- **Specific strains** of *T. pallidum* may be more likely to cause neurosyphilis.

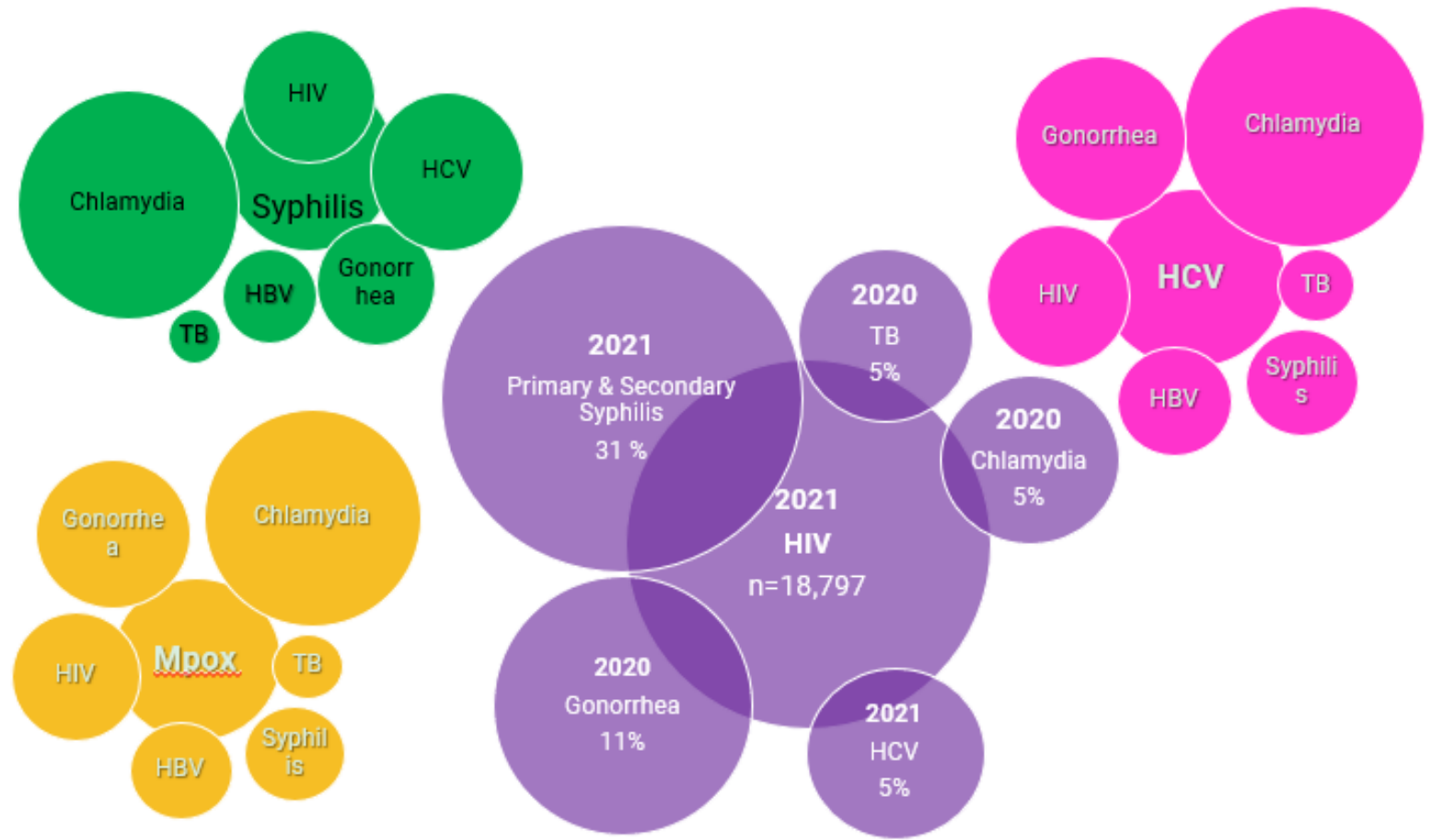


NOO Syphilis Treatment

- **Preferred:**
 - **Aqueous penicillin G** 3 to 4 million units IV Q4H (or 18 to 24 million units continuous IV infusion) for 10-14 days
 - If possible, patients allergic to penicillin should be desensitized and treated with IV penicillin
- **Alternative:**
 - If desensitization is not feasible, **ceftriaxone** 2g IV daily for 10-14 days
- **Last line:**
 - If sensitization is not feasible and patient cannot take a cephalosporin, **doxycycline** 200mg PO BID for 21-28 days

What are **Syndemic** Infectious Diseases?

- Synergistic interaction between multiple health threats, often exacerbated by societal circumstances, which together contribute to an excess burden of disease.
- STIs increase the chance of getting and transmitting HIV.



Source: City of Chicago internal data as of 12/28/2021; Chicago Department of Public Health. *HIV+STI Data Report, 2020*. Chicago, IL: City of Chicago; September 2022.

HIV/HBV co-infection data are not available. Research suggests 5-10% of PLWH are co-infected with HBV. (<https://www.ncbi.nlm.nih.gov/pubmed/20158604>)

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[Sexually Transmitted Infections Surveillance, 2022 \(cdc.gov\)](#)

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