HERPES SIMPLEX VIRUS ADDENDUM
to the
SEXUALLY TRANSMITTED INFECTIONS NATIONAL STRATEGIC PLAN
VISION for the STI National Strategic Plan for the United States, 2021–2025

The United States will be a place where sexually transmitted infections are prevented and where every person has high-quality STI prevention, care, and treatment while living free from stigma and discrimination.

This vision includes all people, regardless of age, sex, gender identity, sexual orientation, sex characteristics, race, ethnicity, religion, disability, geographic location, or socioeconomic circumstance.
Acknowledgments: The Herpes Simplex Virus (HSV) Addendum to the Sexually Transmitted Infections National Strategic Plan (STI Plan) was developed through a robust process that included gathering feedback from partners across health care and related fields. Partners throughout the federal government, as well as nonfederal partners including state, tribal, territorial, and local governments, researchers, health plans and providers, community groups, and national and local organizations that work in STI and related fields, have helped shape the goals, objectives, and strategies in this plan. The Office of the Assistant Secretary for Health (OASH) and its Office of Infectious Disease and HIV/AIDS Policy (OIDP) of the U.S. Department of Health and Human Services (HHS) sincerely thank all those who contributed to making this HSV Addendum a reality, especially staff from the Centers for Disease Control and Prevention (CDC) Division of STD Prevention and the National Institute of Allergy and Infectious Diseases (NIAID) who provided technical support.

Language used in the STI Plan: The HSV Addendum places value on the lived experiences and choices of all people, regardless of age, sex, gender identity, sexual orientation, sex characteristics, race, ethnicity, religion, disability, geographic location, or socioeconomic circumstance. To reflect this vision, a concerted effort was made to use inclusive and person-first language using CDC Preferred Terms throughout the addendum. Evidence-based, contemporary terminology is also used to convey respect and empowerment and to reduce stigma faced by communities and populations disproportionately impacted by these infections. Despite these efforts, specific terminology or language may be unintentionally offensive or stigmatizing to some individuals or populations. Language is subjective, and the meaning and use of language changes over time, and language from local communities can be used in implementation. This approach is intended to help the HSV Addendum’s users to identify these societal shifts in preferred terminology and to communicate in a manner that reflects its vision for a collective, inclusive, and respectful national response.

Additional information regarding the STI Plan and associated activities may be accessed at www.hhs.gov/STI.

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EXECUTIVE SUMMARY

In 2020, the Office of Infectious Disease and HIV/AIDS Policy (OIDP) in the Office of the Assistant Secretary for Health (OASH), U.S. Department of Health and Human Services (HHS) published the inaugural *Sexually Transmitted Infections National Strategic Plan for the United States: 2021–2025* (STI Plan). The STI Plan sets forth a vision for the nation with goals, objectives, and strategies to meaningfully prevent and control sexually transmitted infections (STIs) in the United States, with a focus on chlamydia, gonorrhea, syphilis, and human papilloma virus. Herpes simplex virus (HSV) was not initially included, because the STI Plan focused on nationally notifiable STIs in the United States for which there are federally funded control programs. In fiscal year 2022, Congress directed HHS to amend the STI Plan to address the prevention and treatment of HSV. In collaboration with subject matter experts from across the federal government and with input from a wide range of community partners, including the public, OIDP identified policy, program, and research gaps and priorities to craft a unified national response to HSV, which are described in this *Herpes Simplex Virus Addendum to the Sexually Transmitted Infections National Strategic Plan for the United States: 2021–2025* (HSV Addendum).

HSV is a lifelong condition that spreads primarily from skin-to-skin contact and can cause recurring outbreaks of painful sores on the mouth or genital areas. In addition to physical discomfort, the stigma associated with HSV can significantly impact quality of life. HSV-2 presents nearly exclusively as genital lesions, while HSV-1 can present as lesions on the mouth and lips or the genitals. Although rare, pregnant people can transmit HSV-1 or HSV-2 to their infants during birth, which can lead to severe infant morbidity and mortality. HSV is one of the most common STIs in the United States, and most people with HSV are asymptomatic and undiagnosed. In 2018, an estimated 18,574,000 cases of HSV-2 were reported in the United States, and the exact number of genital herpes infections attributed to HSV-1 is unknown. Prevention and control of HSV are extremely challenging because reliable diagnostics for asymptomatic individuals are limited and no prophylactic or therapeutic vaccine to prevent transmission or cure HSV exists.

The HSV Addendum integrates HSV in the STI Plan’s vision, goals, objectives, and strategies to improve HSV diagnostics, prevention, care, and treatment. It also identifies and prioritizes federal action steps that agencies are encouraged to incorporate into broader STI action steps in future iterations of the STI Plan and *Sexually Transmitted Infections Progress Reports.*
INTRODUCTION

The Need for an HSV Addendum to the STI National Strategic Plan

In 2020, the inaugural Sexually Transmitted Infections National Strategic Plan for the United States: 2021–2025 (STI Plan) was developed by subject matter experts across 20 federal government agencies, with input from a variety of community partners, under the direction of the Office of Infectious Disease and HIV/AIDS Policy (OIDP) in the Office of the Assistant Secretary for Health (OASH), U.S. Department of Health and Human Services (HHS). The STI Plan sets forth a vision for the nation with goals, objectives, and strategies to meaningfully prevent and control STIs in the United States.

The STI Plan is designed to achieve five goals:

- Goal 1: Prevent New STIs
- Goal 2: Improve the Health of People by Reducing Adverse Outcomes of STIs
- Goal 3: Accelerate Progress in STI Research, Technology, and Innovation
- Goal 4: Reduce STI-Related Health Disparities and Health Inequities
- Goal 5: Achieve Integrated, Coordinated Efforts That Address the STI Epidemic

Although there are more than 30 types of STIs, the STI Plan focuses on four of the STIs with the highest morbidity rates, the most persistent and pervasive inequalities of STI burden according to national data, and the greatest impact on the health of the nation: chlamydia, gonorrhea, syphilis, and human papilloma virus (HPV).

Herpes simplex virus (HSV) is a lifelong infection that spreads from skin-to-skin contact and can cause recurring “outbreaks” of sores on the mouth or genital areas, however, most people with HSV are asymptomatic and undiagnosed.* HSV was not specifically included as one of the STIs of focus within the plan. As noted in the STI Plan:

[The] scope of this plan focuses on nationally notifiable STDs in the United States for which there are federally funded control programs. Chlamydia, gonorrhea, and syphilis are “notifiable” diseases, but other STIs such as genital herpes are not. A disease is “notifiable” if health care providers and/or laboratories in all 50 states are required by state law or statute to report the diagnosis or the positive lab test, respectively, to their state or local health departments. The Council of State and Territorial Epidemiologists works with CDC to determine whether a particular disease should be nationally notifiable, based on several criteria. Other common but not nationally notifiable STIs such as genital herpes and trichomoniasis are neither specifically addressed in the plan, nor are emerging sexually transmitted pathogens such as Mycoplasma

*For the purposes of the HSV Addendum to the STI Plan, HSV is primarily considered in the context of sexual transmission. However, HSV is not exclusively transmitted through sexual contact. HSV can also be transmitted through other exposures, including non-sexual contact with saliva, and, in some cases, autoinoculation to different areas of the body. Pregnant people can also transmit HSV to their child before birth, but it is more commonly transmitted during delivery. The term “asymptomatic” refers to individuals with no known past or current history of HSV.
Although HSV is not a nationally notifiable disease, it is one of the most prevalent STIs in the United States. Known limitations of some available diagnostic methods challenge surveillance efforts, and current HSV antiviral treatments are not optimal. There is no existing prophylactic vaccine to prevent transmission and no therapeutic vaccine to provide long-term viral suppression for individuals who have HSV. The physical discomfort from recurrent outbreaks and stigma associated with HSV can significantly impact quality of life. The absence of a coordinated national response or strategic plan for HSV may perpetuate stigma associated with HSV and contribute to the lack of advancement and innovation of HSV diagnostics, treatment, and cure. HSV advocates play a critical role in raising awareness and education about the virus—providing support to individuals with HSV and working toward improving health care policies and research to address HSV. As a result of advocacy efforts, Congress directed OASH to develop the first-ever national strategic plan for the treatment and prevention of genital herpes.

**Scope, Approach, and Development of the HSV Addendum**

The STI Plan is intended to serve as a roadmap for federal and other partners to reverse the upward trends in STI rates in the United States. Its vision, goals, objectives, and strategies are not infection specific and can be used to guide efforts to address HSV. The STI Federal Implementation Plan documents the specific actions that federal partners are taking to achieve the STI Plan’s goals and objectives with annual monitoring and reporting of progress toward meeting the STI Plan’s goals. However, acknowledging the need to develop a strategic approach to treat and prevent HSV, detail specific to this infection is provided in this addendum (see Box 1). The Overview of HSV section describes the available epidemiological data for HSV, consequences of HSV infection, and challenges and opportunities for HSV surveillance, prevention, diagnostics, treatment, and cure.

**BOX 1**

**The STI National Strategic Plan and the HSV Addendum**

The STI Plan and the HSV Addendum are complementary. Although the inaugural STI Plan focused on four STIs—chlamydia, gonorrhea, syphilis, and HPV—the STI Plan vision, goals, objectives, and strategies are not infection specific. Therefore, the STI Plan can be used to guide efforts to address HSV in the United States.

Development of the HSV Addendum followed a core list of guiding principles that sought to

- integrate the latest science in HSV diagnostics, prevention, care, and treatment;
- identify and prioritize federal actions;

• leverage existing infrastructure, capacity, and resources; and
• recognize the need for coordinated action between national, state, territorial, tribal, and local community partners.

The HSV Addendum lays a foundation for a broad range of community partners to build upon by bringing additional capacity and resources to bear and providing role models and ideas that can inform other potential partners’ actions to further national and local progress. Future iterations of the STI Plan will incorporate HSV within its purview.

The Federal Action Steps section of this addendum highlight federal agency action steps that are specific to HSV and aligned with the STI Plan’s goals, objectives, and strategies. Federal agencies will be encouraged to report progress toward HSV action steps in future STI Progress Reports.

Unlike the STI Plan, the HSV Addendum does not identify indicators with quantitative targets to measure progress. Current limitations with HSV diagnostics and therefore data and surveillance render development of HSV-specific indicators both difficult and unreliable (see Overview of HSV section). However, the federal action steps included herein, along with nonfederal activities, can be understood, collectively, to serve as process measures toward advancing HSV priorities. As new diagnostics are developed and data and surveillance methods improve, it may become possible to include HSV-specific indicators in future iterations of the STI Plan.

The HSV Addendum was developed through a process that engaged federal leadership, experts, and a variety of nonfederal partners who compiled subject matter evidence and recommendations on HSV (see Appendixes A and B). A list of acronyms used throughout the document can be found in Appendix C, and references can be found in Appendix D.
OVERVIEW OF HSV

This section provides an overview of HSV and is informed by current CDC guidelines, scientific literature, and reported surveillance data, as well as public input.

<table>
<thead>
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<th>BOX 2</th>
<th>HSV Snapshot</th>
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<tr>
<td></td>
<td>Treatable but not currently curable</td>
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<tr>
<td></td>
<td>Most people with HSV types 1 or 2 have no or mild symptoms; however, stigma and psychosocial burden can be significant</td>
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<td></td>
<td>Routine screening is not recommended for asymptomatic individuals or pregnant people</td>
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<table>
<thead>
<tr>
<th>Epidemiological Facts</th>
<th>Potential Consequences of Infection</th>
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<tbody>
<tr>
<td>18,574,000 HSV-2 cases (2018, ages 18–49), with an overall 0.8% decrease in HSV-2 cases from 2014 to 2018</td>
<td>Transmission from pregnant person to fetus or newborn, which can lead to infant morbidity and mortality</td>
</tr>
<tr>
<td>48.1% of people have HSV-1 (2016, ages 14–49); the proportion of genital herpes caused by HSV-1 is unknown</td>
<td>Discomfort from recurrent outbreaks</td>
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<tr>
<td>10 per 100,000 live births present with neonatal HSV, with an infant mortality rate of 7.9% from 2003 to 2014</td>
<td>Psychological stress due to stigma</td>
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<tr>
<th>Populations Disproportionately Impacted</th>
<th>Current Challenges</th>
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<tr>
<td>Pregnant people</td>
<td>Current testing methodology does not distinguish between primary and recurrent infections, making routine notifiable disease surveillance extremely challenging</td>
</tr>
<tr>
<td>Newborns and infants</td>
<td>Most people with HSV are asymptomatic and undiagnosed</td>
</tr>
<tr>
<td>People who are immunosuppressed</td>
<td>Diagnostics for asymptomatic HSV can produce false-positive results</td>
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HSV-1 and HSV-2 are among the most common STIs in the United States. HSV can spread from one individual to another during active herpes outbreaks through direct contact with lesions, saliva or skin in the oral area, or genital secretions or skin in the genital area. HSV can also spread through direct contact with a person who is infected but does not have symptoms if they are shedding the virus from the skin or mucous membrane. Symptoms and consequences of HSV-1 and HSV-2 can range from lesions or sores on the mouth, lips, or genitals, to eye infections, to more severe symptoms including brain and spinal cord complications or death (see Box 3). However, many individuals with HSV have no or mild symptoms. HSV-2 presents nearly exclusively as genital lesions, while HSV-1 can present as lesions on the mouth and lips or the genitals. HSV is a lifelong infection and can result in additional outbreaks at or near the
initial site of HSV transmission. These recurrences can be spontaneous or triggered by various factors such as stress, fever, suppression of the immune system, and menstruation.³ Individuals who are immunosuppressed are more likely to experience more frequent and severe outbreaks and are less likely to respond to antiviral treatments.

**BOX 3**

**Potential Consequences of HSV Infection**

Because HSV is a lifelong infection, people with HSV can experience long-term consequences beyond symptom recurrence. HIV incidence is nearly tripled in the HSV-2 patient population, with the highest infection risk following initial HSV-2 infection.⁴ This elevated risk may be due to the fact that the frequency and severity of genital lesions are highest when HSV-2 is first acquired, which could provide more opportunities for HIV to enter the body.⁴ However, because most HIV co-infections occur in individuals with HSV-2 who are asymptomatic, researchers should explore how the two viruses interact to facilitate infection.

Although HSV-1 may be more common and is often less disruptive than HSV-2, its long-term effects can be just as profound. Following infection, HSV-1 resides in sensory neurons where it causes sores and blisters on or around the mouth or genitals when reactivated.⁵ HSV-1 can also move into the central nervous system and cause severe inflammation leading to herpetic encephalitis.⁵

Some researchers have proposed a possible association between detection of herpesvirus genetic material in brain specimens and Alzheimer’s disease (AD), especially in the setting of the genetic AD risk factor (APOE-ε4 allele of apolipoprotein E).⁵,⁶ Some observational studies have proposed a possible association between history of antiviral treatment and reduced occurrence of AD, although such studies have had variable results and potential for confounding and bias.⁷ A few small clinical trials have reportedly been initiated to explore the hypothesis of a potential effect.⁵

HSV can be detected directly from swab samples taken from active lesions for a nucleic acid amplification test (NAAT) or viral culture. In the absence of lesions, a blood test can detect antibodies indicative of a history of HSV infection. However, Food and Drug Administration (FDA)-cleared HSV-2 blood tests can have low positive predictive value under certain circumstances, and can lead to false-positive results.⁴ In addition, HSV-1 blood test results alone cannot distinguish between oral or genital infections and should not be used to diagnose active genital HSV-1 infection. The accuracy of these tests depends on the stage of infection, quality of the sample, and performance of the test itself.⁸ The Western blot is the most

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accurate blood test for diagnosing HSV; however, this test is not widely available for commercial use.9 (See Box 4.)

**BOX 4 GENITAL HERPES TESTING GUIDANCE**

Routine testing for herpes is not recommended.

If a patient has herpes-related symptoms, lesions should be swabbed for subsequent testing:
- Nucleic acid amplification testing (NAAT) is preferred.
- Viral culture is less sensitive than NAAT but may be the only option available.
- Cytologic testing (i.e., Tzanck smear) without additional testing is not recommended.

If a patient does not have herpes-related symptoms but is at increased risk for genital herpes,* serologic screening can be considered after an initial assessment.
- Type-common serologic tests cannot distinguish between HSV-1 and HSV-2. Therefore, type-specific serologic testing should be requested.
- Commercial type-specific serologic tests can sometimes provide false positive results and should be confirmed with a CDC-recommended test, e.g., Western blot.
- HSV-1-positive serology results alone cannot distinguish genital herpes from oral herpes.
  - These results can be confirmed later via NAAT or viral culture if genital lesions form.
- HSV-2-positive serology results imply genital infection and should be confirmed with a CDC-recommended test, e.g., Western blot.
- When a confirmatory test is unavailable, patients and providers need to be aware of testing limitations and the risks of false-positive results.

* Risk factors include sexual intercourse with someone who is positive for genital herpes, presenting for an STI evaluation, especially for persons with ≥10 lifetime sex partners, pregnant persons with no history of genital herpes whose sex partner has HSV infection, and persons with HIV infection.

More robust information on HSV epidemiology, surveillance, and screening and treatment guidelines may be found on the CDC website through the links in Box 5.
CDC’s Sexually Transmitted Disease Surveillance 2018 report presents statistics and trends for HSV in the United States through 2018.

Additional data about HSV are available in the following HSV-specific documents prepared by CDC:

- Herpes Detailed Factsheet
- 2021 STI Treatment Guidelines – Genital HSV Infections
- Genital Herpes Screening-FAQ

Epidemiology

HSV-1

Although HSV-1 is commonly associated with oral herpes (commonly referred to as cold sores), it is increasingly becoming the cause of genital herpes lesions. Oral HSV-1 infections tend to occur during childhood, but exposure can occur at any point throughout the lifespan. Symptoms may begin 2–12 days after initial infection, although as many as 70% of people with HSV-1 never have symptoms and are unaware of their infection. Symptoms usually occur at the site where the virus first entered the body and present as painful sores on or around the mouth and sore throat for oral herpes and genital lesions if transmitted on the genitalia. In more serious cases, HSV-1 can cause eye infections and inflammation of the brain or liver. Genital lesions caused by HSV-1 may be less severe and less likely to recur than those caused by HSV-2.

Globally, the World Health Organization estimates that 3.8 billion people under age 50 have HSV-1. Of these people, an estimated 3.6 billion have oral HSV-1, and 192 million people aged 15–49 have genital herpes caused by HSV-1. This global prevalence differs by age, sex, and geographic region.

CDC estimates that 48.1% of people aged 14–49 in 2015–2016 had HSV-1, a decrease from 59.4% in 1999–2000. Prevalence of HSV-1 increases with age, is more common among women compared to men, and is lowest in the non-Hispanic White population compared to non-Hispanic Black and Mexican American populations (see Figure 1). The proportion of genital herpes cases caused by HSV-1 is unknown.
Figure 1. Percent cases of HSV-1 in persons aged 14–49 by race and Hispanic origin, United States, 1999–2016.15 For a description of data source and methods, refer to McQuillan et al. (2018).

HSV-2

HSV-2 nearly exclusively causes genital herpes and is almost always sexually transmitted. Therefore, the prevalence of HSV-2 infections increases from the start of sexual activity throughout adulthood.17 However, less than 25% of people with HSV-2 antibodies are aware they have genital herpes, so the spread of genital herpes often occurs through people who are unaware of their status.18,19 HSV-2 symptom severity can vary and depends on immune status.

Prevalence estimates are calculated using nationally representative survey data. Over the past several decades, HSV-2 infection rates in the United States have declined, but certain populations remain disproportionately affected. Approximately 12.1% of people aged 14–49 had HSV-2 in 2015–2016, compared to 18.0% in 1999–2000 (see Figure 2).15 Another study estimated that in 2018 18.6 million people in the United States had HSV-2, with women accounting for 66% of these cases. Each year, an additional 572,000 new cases of genital HSV-2 infections among people aged 18–49 occur.8
Neonatal HSV

Pregnant people can transmit HSV-1 or HSV-2 to their infants during birth. People who acquire HSV during pregnancy, especially those who are infected late during pregnancy, are at the highest risk of transmitting HSV during birth. Consequences of neonatal HSV range from mild to fatal, including localized disease on the skin, eyes, or mouth; brain and spinal cord disease; and disseminated disease, although these categories can overlap. HSV-1 is more associated with localized disease, while HSV-2 is associated more with severe brain, spinal cord, and disseminated disease types. After birth, recommendations have been made for infants with HSV to receive intravenous antiviral treatment for at least 3 weeks, followed by oral antiviral therapy for months.

Greater than 85% of neonatal HSV cases are caused by exposure during delivery; 5% are believed to occur during pregnancy but before birth; and 10% are believed to occur from exposure to caregiver saliva containing HSV-1. Improved recognition and treatment of the disease has resulted in improvements in mortality; however, mortality of infants with neonatal herpes is still reported to be about 41%, and 45% of infants with brain and spinal cord disease had notable neurological deficits even at 24 months. Unfortunately, many mothers of infants with neonatal HSV do not have obvious genital lesions, a history of HSV, or risk factors at the time of delivery.

The number of infants who acquire HSV each year in the United States remains unknown, but one report estimated an increase in neonatal HSV from 7.9 per 100,000 live births in 2003 to 10 per 100,000 live births in 2014; approximately 7.9% of these cases result in death. Neonatal HSV may occur more frequently in non-Hispanic Black infants compared to non-Hispanic White infants.
Challenges with Prevention and Control of HSV Infections

Prevention and control of HSV infections are extremely challenging. Detection of the virus or viral DNA in a lesion can aid in the diagnosis of HSV in people experiencing lesions consistent with HSV, but the low specificity of blood tests for HSV antibodies can lead to false positives; therefore, it is difficult to diagnose or screen for HSV when lesions are not present. The lack of robust diagnostics for people without lesions makes it difficult to obtain accurate HSV tracking across populations. Although cases of genital herpes due to HSV-2 infection have declined over time, HSV-1 is an increasing cause of the first episode of genital herpes lesions. However, with current testing technologies, it is impossible to determine the total number of genital herpes cases due to HSV-1.8

The U.S. Preventive Services Task Force (USPSTF)§ recommends against routine blood testing for HSV in people without symptoms, including pregnant people, because the harms associated with false-positive results and unnecessary treatments, outweigh the benefits for population-based screening for genital HSV infection.9,28 CDC recommends blood testing for (1) people with recurrent or atypical genital symptoms or lesions whose lesions originally tested negative for the virus, (2) sexual partners of individuals with genital herpes, and (3) people at increased risk for HSV-2 whose clinical assessment is compatible with genital herpes.8 Further, while tests for other STIs are used to screen pregnant people, no current HSV blood tests would be suitable for this purpose.8,29 (See Figure 3.)

§ USPSTF is an independent, volunteer panel of national experts in disease prevention and evidence-based medicine. The Task Force works to improve the health of people nationwide by making evidence-based recommendations about clinical preventive services.
Flowchart of CDC guidance for genital herpes testing. For patients who have genital herpes-related symptoms, clinicians should swab suspected herpes sores. In these cases, test options include viral culture, NAAT, and cytologic testing/Tzanck smear. For patients at increased risk of genital herpes who do not have genital herpes-related symptoms, clinicians should perform an antibody test. Test options for these cases are type-specific serology testing (with confirmation recommended by Western blot); and (2) type-common serology testing (cannot distinguish between HSV-1 and HSV-2). Western blots are the most accurate test for diagnosing HSV, but this test is not widely available for commercial use in the U.S. Western blot is the most accurate test for confirming a diagnosis of HSV, however, this test is not widely available for use in the U.S. The Western blot is exclusively performed at the University of Washington, where lab specimens can be sent for processing.

Risk factors include sexual intercourse with someone who is positive for genital herpes, presenting for an STI evaluation, especially for persons with ≥ 10 lifetime sex partners, pregnant persons with no history of genital herpes whose sex partner has HSV infection, and persons with HIV infection.

Swab newly-formed lesions for the most accurate assay results.

HSV-1-positive serology results alone cannot distinguish genital herpes from oral herpes. Genital herpes can be confirmed later via NAAT or viral culture if genital lesions form.

HSV-2-positive serology results imply genital infection.
HSV is not a nationally notifiable condition, and, therefore, no existing national surveillance system for HSV or neonatal herpes exists. Because HSV surveillance data are not available on an annual basis, CDC does not currently include HSV in STI surveillance reports. **However, different methods could potentially be used to monitor HSV, including population-based surveys, opportunistic surveillance, case-based reporting, and sentinel surveillance. Until tests that yield very few false results for diagnosing asymptomatic HSV are developed, as well as tests for differentiating a primary or recurrent HSV infection, no surveillance method will fully capture the burden of HSV (see Table 1 and Appendix B for more in-depth descriptions of HSV surveillance methods).**

**In 2018, CDC revised STI surveillance reports to exclude data points that were not available to be published annually. This change included HSV seroprevalence along with other data points not consistently available every year.**

### Table 1. Potential HSV Surveillance Methods

<table>
<thead>
<tr>
<th>Type of Surveillance</th>
<th>What It Does</th>
<th>Strengths</th>
<th>Limitations</th>
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<tbody>
<tr>
<td>Population-based surveys</td>
<td>Randomly samples individuals selected to represent a larger population</td>
<td>Can estimate HSV seroprevalence and evaluate seroprevalence by sociodemographic characteristics, sexual risk behaviors, and co-infections</td>
<td>Data collection is not timely&lt;br&gt;Administration is expensive and resource intensive&lt;br&gt;Accuracy depends on high response rate for a large sample size, and response rates have been declining&lt;br&gt;Blood tests for HSV antibodies can yield false results and therefore cannot reliably estimate prevalence&lt;br&gt;Knowing the timing of infection is not possible</td>
</tr>
<tr>
<td>Case-based reporting</td>
<td>Case reports submitted by 59 U.S. jurisdictions</td>
<td>Can describe the trends in diagnosed and reported cases nationally and by geographic area</td>
<td>Most infections are asymptomatic; only those reliably diagnosed can be reported&lt;br&gt;There is no way to tell true incident from recurrent infection</td>
</tr>
<tr>
<td>Sentinel surveillance</td>
<td>Collects data on individuals diagnosed with HSV from a “sentinel” or subset of a larger population</td>
<td>Can enable collection of more detailed information</td>
<td>Administration is expensive and resource intensive&lt;br&gt;Data represent only the population of interest from</td>
</tr>
</tbody>
</table>

**In 2018, CDC revised STI surveillance reports to exclude data points that were not available to be published annually. This change included HSV seroprevalence along with other data points not consistently available every year.**
Example: Detailed information about patients diagnosed with HSV from STI clinics
Can enable longitudinal tracking of patients and evaluation of annual trends
which the sample was selected
There is no way to tell true incident from recurrent infection

| Opportunistic surveillance | Uses data collected for other purposes (e.g., administrative claims data) for disease surveillance
Example: Evaluation of health care services related to HSV | Can draw from large sample of collected data
Can be less expensive to administer because data collection is outsourced to other entity | User has no input over what or how the data are collected
Some systems may not be timely or include key demographics (e.g., race) |

Source: Kreisel et al. (2022).¹

Even when accurately diagnosed, HSV cannot currently be cured. Antiviral treatment is often used in symptomatic individuals to reduce the duration and severity of HSV outbreaks, prevent recurrence, and reduce the risk of transmission to a sexual partner. Further studies are needed to determine whether antiviral therapy can be used to prevent HSV transmission from asymptomatic individuals.⁸ Because of the lifelong nature of HSV, people with HSV may experience intense stigma and mental health challenges related to their diagnosis, including depression, anxiety, isolation, fear of rejection, loss of relationships, and shame (see Box 6).¹⁵ This stigma may also hinder testing and disclosure of infection status to sexual partners, contributing to further spread of HSV.³⁰

Although a vaccine could help control the spread of HSV, there are no approved vaccines for the treatment or prevention of HSV. However, some vaccine candidates are in early clinical development.³¹ Genital herpes is most contagious when sores are visible, so abstaining from sexual contact during recurrences can reduce the risk of transmission, but HSV can still be spread when a person has no symptoms. Consistent and correct condom use can also reduce this risk, although it does not prevent HSV spread due to contact with areas not covered by the condom.⁸

**BOX 6
Stigma**

Although HSV is one of the most common STIs in the United States, it is also one of the most stigmatized.³² For example, a survey of young women’s beliefs on HSV found that women often carry negative perceptions of an HSV diagnosis, including sexual promiscuity or deviance and moral weakness and that of being unclean or tainted.³⁰ HSV genital lesions are an important factor in this stigma; in a study comparing perceptions of various dermatological conditions, greater than 75% of participants indicated discomfort at the prospect of touching or sharing food with someone with a visible HSV lesion.³³
Stigma can negatively affect the mental health of people with HSV: 47% have reported feeling stigmatized since their diagnosis, and this experience is associated with a lower quality of life. The initial HSV diagnosis is often accompanied by depression, anxiety, and low self-esteem. People with HSV also struggle with a fear of rejection in social and romantic relationships if they disclose their diagnosis, which can lead to social isolation and loneliness.

Although these negative emotions decline with time for many people with HSV, social and emotional support from friends and loved ones is the factor most associated with reducing psychological distress from internalized stigma. Empowering people with HSV to self-manage their treatment and to develop successful coping strategies can also help counter the shame and stigma experienced upon diagnosis.
STI PLAN GOALS AND FEDERAL ACTION STEPS FOR HSV

The STI Plan sets forth objectives for each goal, and strategies for each objective (see Table 2 for definitions). These objectives and strategies are designed to guide federal partners and other community partners in achieving the STI Plan’s vision and goals. The objectives provide direction for the attainment of each goal. The strategies recommend approaches to achieve the objectives. The STI Federal Implementation Plan details federal partners’ plans and action steps to implement the goals, objectives, and strategies set forth in the STI Plan. The HSV Addendum describes how HSV can be integrated into the STI Plan’s five goals.

Table 2. Definitions Included in the STI Plan

<table>
<thead>
<tr>
<th>STI Plan</th>
<th>Federal Implementation Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Goals:</strong> Broad aspirations that enable a plan’s vision to be realized</td>
<td><strong>Action Steps:</strong> Specific activities that will be performed to implement the strategies and achieve the goals of the plan</td>
</tr>
<tr>
<td><strong>Objectives:</strong> Changes, outcomes, and impact a plan is trying to achieve</td>
<td><strong>Progress Reports:</strong> Reports on progress, successes, and challenges</td>
</tr>
<tr>
<td><strong>Strategies:</strong> Choices about how to best accomplish objectives</td>
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</tbody>
</table>
### STI Plan Goal 1: Prevent new STIs

Goal 1 objectives and strategies from the STI Plan exemplify the use of primary prevention to halt the spread of STIs, specifically by preventing them before they occur, including through raising awareness and education. Primary prevention is uniquely challenging for HSV because of its high prevalence rate, asymptomatic transmission, and the lack of reliable diagnostics for asymptomatic HSV, primary prophylactic treatment, and vaccine. In the absence of these preventive interventions, provider education and public awareness of HSV transmission, symptoms, and risk factors are critical for preventing new cases.

Evidence-based prevention strategies cited in CDC’s STI clinical guidelines that are applicable to HSV include behavioral counseling about risk-reduction behaviors, such as consistent and correct condom use and reduction in the number of sex partners. Disclosure of HSV status to sexual partners has also been shown to reduce transmission, although it is less likely to occur among casual sexual partners. Shame and fear of rejection are the primary reasons individuals choose to not disclose their HSV status. Individuals should receive appropriate guidance regarding disclosure during patient counseling that includes accurate information regarding transmission risks and messaging to decrease the anxiety and shame associated with diagnosis.

### BOX 7

**Addressing HSV through the Sexual Health Paradigm**

As with other STIs, education is critical to counter misinformation about HSV in the general population, especially among underserved populations groups. A survey of college-aged women found that 96% believed that HSV infection would result in genital sores and that 68% believed that they would be able to discern whether their partner had HSV. Yet, in fact, the majority of people with HSV are asymptomatic, and transmission can occur because of unprotected sex with a partner without genital lesions. Although most of the survey respondents understood that HSV lasts for a lifetime, about one-third believed that HSV infection could either be eliminated with a pill or could not be treated at all. People with HSV

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*Primary prevention of STIs includes assessment of behavioral risk (i.e., assessing the sexual behaviors that can place persons at risk for infection) and biologic risk (i.e., testing for risk markers for STI acquisition or transmission). Secondary prevention aims to detect illness through forms of screening or testing. Tertiary prevention aims to reduce the adverse outcomes of illness through treatment and other therapeutic interventions.*
can be affected by misinformation; one study found that 38% of people with HSV surveyed believed that the virus could only be passed to a partner during an outbreak, and only 40% were aware of available treatments that could reduce the chance of transmitting the virus. These studies reflect a general lack of knowledge about HSV among the public, which should be addressed.

HSV can have a significant effect on the sexual health and behavior of people with HSV, particularly within the first year after diagnosis. It is common for people who are newly diagnosed with HSV to initially reduce or abstain from sexual contact, particularly during a recurrence, and to be extremely concerned about transmission of the virus to sexual partners. Although a small percentage of people with HSV report physical discomfort or pain resulting from genital lesions, diminishment of interest or pleasure in sexual behaviors primarily results from the psychological (rather than physical) impact of the diagnosis.

The partnership between health care providers and patients plays a key role in the successful management of HSV. Health care providers should be aware of the profound psychological impact of an HSV diagnosis and be prepared to offer resources to support people newly diagnosed with HSV. Health care providers should also acknowledge patients’ concern about transmitting the virus and discuss how condom use and medication can reduce this risk. Indeed, although health care providers said that 74% of their patients were taking prescription medications for their HSV, only 29% of patients reported receiving medication, with most not on treatment believing their outbreaks were not severe or frequent enough. Because suppressive antiviral therapy can reduce asymptomatic shedding and the risk of transmission, health care providers should consider discussing the benefits of treatment with people with HSV regardless of outbreak frequency or severity.

According to CDC, individuals with a history of symptomatic genital HSV can also decrease the risks of transmission to sexual partners by taking daily suppressive antiviral medication to reduce outbreaks and asymptomatic viral shedding, and by abstaining from vaginal, anal, and oral sex during outbreaks, when the risk of transmission is highest. However, no evidence indicates that people without HSV can prevent HSV acquisition by taking antiviral medication prophylactically. Risk of neonatal herpes can also be reduced when pregnant people who have recurrent HSV outbreaks take antivirals beginning at 36 weeks gestational age or have a cesarian delivery if they are experiencing symptoms at the time of labor.

Although many clinical prevention guidelines for STIs also apply to HSV, further education and awareness about prevention is required, because HSV is not exclusively transmitted through sexual contact. HSV can also be transmitted through other exposures, including non-sexual contact with saliva, during childbirth, and, in some cases, autoinoculation to different areas of the body. Although HSV is primarily discussed in the context of sexual transmission in the HSV Addendum, other modes of transmission must be considered in primary prevention activities.

Available evidence shows that society holds many misconceptions about HSV, particularly regarding risk reduction strategies, asymptomatic transmission, and suppressive antiviral medications. For example, many individuals underestimate the actual prevalence rates of
HSV, particularly given the high rate of individuals who are asymptomatic and undiagnosed, and therefore hold inaccurate risk perceptions.\textsuperscript{32} Surveyed college students reported that they believe STI prevention strategies offer more protection against HSV than is evident in the literature,\textsuperscript{43} and only slightly more than one-half of Americans are aware that herpes is not curable.\textsuperscript{44} An increasing amount of genital herpes infections is attributed to HSV-1,\textsuperscript{8} suggesting that many individuals might be unaware of the risks of transmission through oral sex.\textsuperscript{45} Indeed, many adults and adolescents perceive oral sex to be a risk-free behavior.\textsuperscript{46} Increasing awareness of individuals’ risk for acquiring HSV may increase prevention measures and in turn decrease the proportion of new HSV cases. A greater understanding about HSV prevalence and transmission will enable individuals to navigate sexual encounters with more awareness of their risks. Patients can then accurately explain those risks to health care providers, who can assess whether HSV testing might be appropriate during behavioral counseling.

HSV incidence is highest among adults aged 18–24,\textsuperscript{16} and adolescents and young adults account for the largest population of new HSV-1 cases.\textsuperscript{47} Increasing opportunities for HSV awareness in adolescence is critical in preventing HSV prior to early adulthood. It is also important to seek opportunities to target this demographic, such as through strengthening primary prevention activities in comprehensive quality sexual health education programs and social media campaigns.

Many HSV misconceptions are perpetuated by the lack of HSV knowledge among health care providers as well. As stated in the STI Plan, there is a clear need and opportunity to expand overall sexual health education and training among all types of health care providers throughout the stages of their career including during training (e.g., medical school, residency) and once in practice (e.g., through continuing education, certification, and maintenance of certification).

HSV is neglected in many existing STI prevention programs and strategies because of the diagnostic and surveillance limitations discussed in the Overview of HSV section. The HSV Addendum aims to look beyond those limitations and incorporate HSV more into existing STI prevention strategies, and to seek ways to leverage current resources and further engage health care providers, schools, families, and communities about HSV transmission. Additional capacity, resources, incentives, training, partnerships, and integration of efforts are all critical elements to integrating HSV into STI objectives and strategies.
STI Plan Goal 2: Improve the health of people by reducing adverse outcomes of STIs

Goal 2 objectives and strategies from the STI Plan exemplify secondary and tertiary prevention approaches to impede the progression from infection to disease and to treat disease when it occurs. Secondary prevention aims to detect illness through forms of screening or testing, and tertiary prevention aims to reduce the adverse outcomes of the list through treatment and other therapeutic interventions. Although HSV infection can present as asymptomatic or benign, many individuals with HSV, particularly those who are immunosuppressed, experience adverse physical outcomes, as well as infants, who are at increased risk for severe morbidity and death. This Addendum acknowledges that quality of life can be greatly impacted for individuals with HSV because of the physical discomfort from primary and recurrent outbreaks, and the psychological distress following diagnosis and while navigating future sexual and romantic relationships. Improved screening, treatment, and counseling for people with HSV is critical to reducing potential adverse physical and psychological health outcomes and improving their overall quality of life.

An accurate HSV diagnosis, which can be informed through detection of the virus in lesions or type-specific blood tests, is important for preventing new infections and initiating treatment. Among data related to patient and provider engagement, 73% of patients reported that their HSV diagnosis was based on clinical suspicion, which can frequently be inaccurate. This finding highlights the opportunities to increase provider knowledge and adherence to HSV testing in accordance with CDC’s STI Treatment Guidelines.

Most genital herpes infections are transmitted by individuals who are asymptomatic and undiagnosed. USPSTF and CDC do not recommend routine HSV screening for asymptomatic individuals, including pregnant people. Unfortunately, some health care providers are unaware of these testing guidelines and do not always explain the limitations of available diagnostics for asymptomatic patients who request HSV screening. Patients may also be unaware that HSV is often not included in traditional routine STI testing panels, and therefore may falsely assume they are HSV-negative after receiving a negative STI screening. During STI screenings, it is important that patients be informed about all the STI tests they are receiving. Patients should also be made aware of what testing options are available for HSV and why they are not included in general STI screenings. CDC’s STI Treatment Guidelines suggests that all individuals with HSV also be tested for HIV, because HSV increases the risk of HIV transmission. As stated in the STI Plan, STI screening is viewed as “an essential and underutilized component of an STD/HIV risk assessment in most clinical settings.” When patients seek treatment or evaluation for a particular STI (or pregnancy prevention or testing), health care providers are
encouraged to screen for other STIs based on prevalence within their specific community and national recommendations and to perform a comprehensive risk assessment.

After receiving an HSV diagnosis, patients should receive comprehensive counseling on transmission and available therapeutic treatments. Patients often report conflicting guidance from health care providers on risks regarding asymptomatic shedding and transmission of HSV to sexual partners. Similarly, patients report not being informed about or prescribed antiviral suppressive treatment to manage primary and recurring outbreaks. Dissatisfactory patient counseling occurs in part because health care providers lack knowledge about HSV, as well as time or resources to dedicate to clinical consultations. Inadequate counseling may also occur when patients’ and health care providers’ perceptions about HSV do not align. When health care providers underestimate the psychological and physical burden of HSV, patients may not effectively manage their diagnosis and disclosure of status to current and future sexual partners.

In addition to medical treatment, individuals with HSV may require mental health counseling to cope with psychological distress associated with receiving an HSV diagnosis and living with HSV. Individuals diagnosed with HSV report higher levels of anxiety and depression compared to individuals with other STIs and exhibit minimal improvement in the months following diagnosis. Efforts should be made to integrate psychotherapy as part of initial and longer-term HSV treatment and management protocols.

Although rare, neonatal herpes can lead to severe long-term morbidity, neurologic impairment, and mortality. Linked birth-death files for infant deaths from 1995 to 2017 from the National Center for Health Statistics show an increase in neonatal herpes deaths that outpaced those caused by HIV and congenital syphilis. It is important to prioritize interventions that enable the public health community and health care providers to prevent mother-to-child HSV transmission and to appropriately recognize neonatal herpes in order to rapidly administer antiviral therapy and prevent infant morbidity and mortality.

As stated in the STI Plan, the COVID-19 pandemic further exposed vulnerabilities in the STI infrastructure and influenced the national response to STIs, as well as other infectious diseases. After the emergence of COVID-19, STI disease intervention specialists and other STI resources were redirected to COVID-19 mitigation efforts, causing disruptions and lags in STI screening and surveillance. Throughout the pandemic, rates of reportable STIs, such as gonorrhea, syphilis, and congenital syphilis, reached record highs. There have also been reports of HSV reactivation in some patients with COVID-19, hypothesized to be attributable to multiple factors such as psychological stress, fever, immunological suppression, and the possibility that COVID-19 might directly affect neurons harboring dormant HSV. The COVID-19 pandemic underscored the importance of investment in public health infrastructure and maintenance of a robust public health workforce that can respond to emerging infectious diseases, while not neglecting current epidemics. As the COVID-19 pandemic wanes, it is uncertain whether long-term investments in the public health workforce, which are also essential to combating current STI epidemics, will continue. Harnessing opportunities to increase resources and implement
innovative approaches, during and after public health emergencies such as COVID-19, is necessary to ensure access to and continuity of STI services.

**STI Plan Goal 3: Accelerate progress in STI research, technology, and innovation**

The STI Plan acknowledged that a robust innovation agenda is needed to move scientific advances in STIs into clinical practice and communities. Despite the high prevalence of HSV in the United States and globally, the field has seen limited scientific advances regarding innovative preventive measures, improved diagnostics for asymptomatic HSV, and more effective therapeutic treatments. CDC and the National Institutes of Health (NIH) sponsored a workshop titled “Joint Workshop on Genital Herpes” in November 2022 to define the U.S. and global burden and epidemiology of HSV, and to identify gaps and research opportunities in vaccines, therapeutics, prevention, and diagnostics development. Building on the opportunities identified during the workshop, NIH developed the Strategic Plan for Herpes Simplex Virus Research (see Figure 4), which was coordinated by the National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), and National Institute of Neurological Disorders and Stroke (NINDS) with the following priorities: (1) improve fundamental knowledge of HSV biology, pathogenesis, and epidemiology; (2) accelerate research to improve diagnosis; (3) improve strategies to treat and cure HSV; and (4) advance research to prevent HSV infection.
As addressed throughout the Addendum, HSV is not a national notifiable disease, partially because of known limitations of technology employed by HSV blood tests that can lead to false-positive results. Detection of the virus through direct methods, such as through molecular testing or culture are the most sensitive methods to aid the diagnostic of HSV, but they can only be conducted when an individual has an active lesion or sore. Current blood tests for HSV antibodies can yield false-positive results for asymptomatic individuals, and the serological Western Blot test is not widely accessible for confirmatory testing for the general population.9 The lack of a reliable diagnostic test for asymptomatic individuals is a barrier to creating a national surveillance system for HSV and neonatal herpes, which is necessary for accurate estimation of HSV prevalence and overall burden of disease and enhancement of primary and secondary prevention activities. New diagnostic technologies should be widely available, easy to conduct, cost-effective, and accurate in identification of HSV infection. Ideally, diagnostic tests should be able to accurately differentiate between HSV-1 and HSV-2 infections. Some investigators have also suggested that differentiating primary and recurring outbreaks can be useful in understanding the relative likelihood of viral shedding and recurrent symptoms. Patients can then be more effectively counseled on how they may have obtained the virus and minimize risks for transmission to partners.13

Oral antiviral medications, the standard HSV treatment, can be used episodically and suppressively; however, there are limitations to their efficacy. Unless initiated at the start of an outbreak, they have demonstrated to have minimal effect on the duration of an outbreak, more so with immunocompetent individuals.56 Similarly, antiviral medications have been shown to reduce transmission by 50% when used as suppressive treatment,57 although further studies are needed to understand how antiviral medications affect transmission, particularly among persons with a history of asymptomatic HSV-2 infection identified by a positive HSV-2 serologic test. Although several antivirals have been available for decades, subsequent therapeutics development for HSV has been limited and safety questions have arisen with some candidate products.58 More optimal antiviral treatments, particularly for long-term suppressive use,
should be prioritized because they will help improve the overall health and wellbeing of individuals with HSV by reducing the duration and recurrence of outbreaks. New treatments should also seek to maximize “treatment as prevention” by reassuring people with HSV that they will not transmit the virus to partners, which is cited as the primary concern for patients after initial HSV diagnosis. 39

The STI Plan calls for the development and exploration of other innovative preventive products against STIs. Condoms are an effective—and the most common—tool to prevent transmission of genital herpes, but they must cover the anatomic locations of HSV shedding, which can vary for different individuals. 59 More research is also needed on the efficacy and usage of dental dams as a preventative product for oral to genital HSV-1 transmission. 60 Microbicides, which are topical substances that contain drugs designed to reduce the risk of STI and HIV transmission, offer potential as an HSV prevention tool. Intravaginal gels or rings that contain antiviral medications should be further explored as a means for preventing HSV transmission to women. Given the strong syndemic interaction between HSV and HIV (described further in Goal 5), it would be useful to develop an intravaginal ring that delivers both HSV and HIV antiviral medications in combination. 61,62

The STI Plan also calls for innovation in vaccine development and care delivery models, which aligns with Goal 1 of the Vaccines National Strategic Plan: 2021–2025 (Vaccine Plan) to “Foster Innovation in Vaccine Development and Related Technologies.” As mentioned throughout this addendum, no cure for HSV currently exists. Because of its high prevalence, the development of both a prophylactic vaccine to prevent primary HSV infections and a therapeutic vaccine to reduce the duration and recurrence of outbreaks for people with HSV 63 should be prioritized. Ideally, the prophylactic and therapeutic vaccines would be effective for both HSV-1 and HSV-2 subtypes. Mathematical modeling shows that even an imperfect therapeutic vaccine for HSV-2 of 75% efficacy could reduce HSV-2 incidence by 55% over the course of a decade. 64,65

The STI Plan also calls for innovative service delivery models and comprehensive communication strategies that emphasize the importance of sexual health and reducing stigma. These strategies should be informed by behavioral, social, clinical, and epidemiologic science as well as health economics. Such studies should consider the target demographic for rolling out the vaccine, whether it would be most effective as a preventive option when administered in infants, or in adolescents, such as the HPV vaccine. Regulatory support, commercial investment, and academic, public, and private partnerships are all needed to successfully accelerate progress in these areas.

Investment in research, commercialization, and translation into practice will lead to more innovative, evidence-based prevention models, technologies, and products to decrease the prevalence of HSV and work toward achieving the goals of the STI Plan.
STI Plan Goal 4: Reduce STI-related health disparities and health inequities

As is true for other STIs, HSV disproportionately impacts certain communities and populations, who are often underserved. Women account for 66% of HSV-2 infections, and an estimated 22% of pregnant women are positive for HSV-2. Women are at higher risk of infection because HSV is more easily transmitted from men to women than from women to men during penile-vaginal sex. HSV-1 prevalence is highest among Mexican American persons, and non-Hispanic Black persons have the highest prevalence of HSV-2 infections by nearly three-fold when compared to Mexican American and non-Hispanic White persons. Disparities also exist in neonatal herpes with incidence highest among Black births. Although trends in HSV-2 seroprevalence have decreased overall, racial disparities have continued to increase. HSV seroprevalence is also higher among people with lower incomes and with lower educational attainment. These social and structural determinants of health (SDOH) may contribute to further health disparities, because HSV forms a syndemic with other infections, such as HIV and other STIs. Indeed, racial and ethnic disparities in HSV-2 infection predate the HIV/AIDS epidemic in the United States and potentially helped to contribute to disparities in HIV rates. Further research on racial and ethnic disparities in awareness and recognition of HSV symptoms, as well as access to STI preventive and treatment services, should be conducted to inform appropriate and culturally competent interventions for disproportionately affected populations. More demographic research is needed to understand HSV disparities based on sexual orientation and gender identity. As new treatments and vaccines are developed, racial, ethnic, gender, and sexual minorities must be adequately represented in clinical trials as new therapeutics become available.

The STI Plan also states that the negative impacts of stigma and discrimination must be recognized to address the STI epidemic. For example, 11 states have laws that criminalize behavior that potentially exposes others to STIs, some of which explicitly include genital herpes. Criminalization laws are another and tangible negative impact of stigma that often do not reflect the evidence. Federal partners have a role in reducing STI-related health disparities by supporting communities to engage in local solutions and training health care providers to deliver culturally competent, trauma-informed, and compassionate comprehensive sexual health care, free of judgment and discrimination. SDOH and comorbidities must be addressed to reduce STI-related health disparities and inequities.

The STI Plan’s tailored objectives and strategies support the goal of reducing STI-related health disparities and health inequities by, for example, emphasizing patient-centered improvements such as reducing stigma associated with STIs and fostering treatment service environments that are more conscious of the needs of affected populations.
STI Plan Goal 5: Achieve integrated, coordinated efforts that address the STI epidemic

STIs, viral hepatitis, HIV, substance use disorders, and SDOH such as violence have the potential to form syndemics and are priorities for action in the STI Plan as well as the HSV Addendum (see Box 8). Indeed, HSV has been found to be syndemic with HIV. Co-infection of HSV and HIV has been shown to increase HIV viral load, risk of HIV transmission, and disease progression. It has also been shown to increase the frequency and severity of HSV symptoms; therefore, improved testing and treatment for HSV could help improve outcomes of people with HIV. Likewise, people with HIV and HSV with undetectable HIV viral load due to HIV treatment are no more likely to transmit HIV than those without HSV. The 2022 Mpox outbreak was also syndemic with STIs including HIV. Mpox lesions and other symptoms can mirror those of HSV. In addition, research from CDC shows that about 40% of people diagnosed with Mpox in the United States also have HIV. As a result, clinical guidelines recommend testing potential Mpox lesions for other STIs as well, including HIV and HSV.

BOX 8
Syndemic

Syndemics happen when two or more diseases or health conditions cluster and interact within a population, because of social and structural factors and inequities, leading to an excess burden of disease and continuing health disparities.

Not all areas, individuals, or populations are affected by syndemics similarly or at the same time. Different populations or geographic areas may experience different clustering of disease or different social and structural determinants of health. Further, syndemics may change over time.

Ultimately, a syndemic approach aims to achieve greater reductions in disease and related stigmas by addressing syndemic conditions including related SDOH at the same time, rather than if addressed separately.

Syndemic disease clustering and interactions, including HIV, HSV, and mental health and substance, are facilitated by social and structural determinants of health. This recognition

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requires the need to understand and address the root causes of STI transmission and acquisition. Some of these facilitating factors include lack of health care access, limited sexual health education, criminalization of substance use, stigma and discrimination, and disproportionate clustering of STIs within populations.

Responding to HSV and other STIs, including HIV, through a coordinated, syndemic approach centers the focus on the needs of populations served and engages populations in agenda setting; promotes the conditions necessary for thriving and optimal health; encourages integrated, transdisciplinary partnerships to provide holistic service delivery; enables flexibility to respond to continuously evolving conditions; and supports increased efficiency and cost-effectiveness.

The federal government is taking steps to integrate HSV activities across portfolios. To help drive a coordinated response to the syndemic, the HSV Addendum to the STI Plan complements the National HIV/AIDS Strategy for the United States 2022–2025 (NHAS) and the Viral Hepatitis National Strategic Plan for the United States: A Roadmap to Elimination (2021–2025) (Viral Hepatitis Plan). These plans mutually recognize that both the specific health conditions and the syndemic itself present opportunities to conduct relevant research and analyses, develop evidence-based interventions and policy options, and allocate resources to respond efficiently and effectively. As described in Goal 3, in 2023, NIH released the first-ever Strategic Plan for HSV Research. This event highlights an example of an inter-agency effort across multiple NIH Institutes to advance understanding of herpes virology and accelerate development of diagnostics, vaccines, and therapies. Future federal efforts to better address HSV through existing efforts may include reviewing and updating policies with the latest science, developing education opportunities on HSV diagnosis for health care providers (including the need for trauma-informed approaches), and increasing awareness of the syndemic interactions between HSV and other health conditions.

Federal Action Steps for HSV

Table 3 lists HSV-specific action steps for the federal agencies corresponding to the goals and relevant strategies from the STI Plan, which were developed by each agency. These HSV-focused action steps will be incorporated into the STI Federal Implementation Plan and future STI Progress Reports. The years indicate the fiscal year in which the action begins and ends within the context of the STI Plan (2021–2025). Ongoing action steps that extend beyond fiscal years 2021–2025 only list the years within this timeframe. The actions are described as succinctly as possible; it should be noted that the action steps are supported by a level of detail for their conceptualization and implementation not captured in a summary document such as this. When more than one agency will collaborate on an action, the lead agency is listed first in boldface, followed by the partner agencies in alphabetical order.

These action steps are intended to inform and inspire the policy development and program planning process for federal and nonfederal partners. This is not a budget document and does not imply approval for any specific action under Executive Order 12866 or the Paperwork
Reduction Act. All activities included in this document are subject to budgetary constraints and other approvals, including the weighing of priorities and available resources by the Administration in formulating its annual budget and by Congress in legislating authorizations and appropriations.
### Table 3. Federal Action Steps for HSV

<table>
<thead>
<tr>
<th>Action Step</th>
<th>Timeframe</th>
<th>Federal Agency Partner</th>
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</thead>
<tbody>
<tr>
<td><strong>Goal 1: Prevent New STIs</strong></td>
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<tr>
<td>**Strategy 1.1.2 Support a non-stigmatizing, comprehensive approach to</td>
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<tr>
<td>sexual health education and sexual well-being, especially in adolescents</td>
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<tr>
<td>and young adults, that promotes healthy sexual development and relationships</td>
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<td>and includes both risk-avoidance and risk-reduction messaging at the</td>
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<td>community level in schools, faith-based organizations, and other</td>
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<tr>
<td>community-based organizations.</td>
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<tr>
<td>Ensure that STI prevention education delivered through the Teen Pregnancy</td>
<td>2023–2025</td>
<td>OPA</td>
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<tr>
<td>Prevention program include education about HSV.</td>
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<tr>
<td>**Strategy 1.2.1 Ensure that prevention programs are accessible,</td>
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<td>comprehensive, and culturally, linguistically, and age appropriate.</td>
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<tr>
<td>Educate adolescents on adulthood preparation subjects through the</td>
<td>2023–2025</td>
<td>ACF</td>
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<tr>
<td>Adolescent Pregnancy Prevention Program’s Personal Responsibility Education</td>
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<tr>
<td>Program on age-appropriate and medically accurate information on both</td>
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<tr>
<td>abstinence and contraception for the prevention of pregnancy and STIs,</td>
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<tr>
<td>including HIV/AIDS, HSV, and syphilis.</td>
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<tr>
<td>**Strategy 1.2.2 Implement STI prevention activities in a broad range of</td>
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<tr>
<td>health care delivery, education, and community-based settings through</td>
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<td>innovative, evidence-based approaches.</td>
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<tr>
<td>Identify additional technical assistance/support opportunities for Health</td>
<td>Ongoing</td>
<td>HRSA/BPHC, BHW; CDC;</td>
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<tr>
<td>centers on STI (to include HSV) as part of comprehensive STI treatment</td>
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<td>IHS</td>
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<tr>
<td>and prevention program development. Proposed activities include engaging</td>
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<tr>
<td>community partners, social service organizations, and state/local health</td>
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<tr>
<td>departments to coordinate care, prevention, and treatment services.</td>
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<tr>
<td>**Strategy 1.4.1 Provide resources, incentives, training, and technical</td>
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<td>assistance to expand health workforce and systems capacity, and</td>
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<tr>
<td>community centers.</td>
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<tr>
<td>Provide trainings on genital HSV diagnosis/evaluation, management, and</td>
<td>Ongoing</td>
<td>CDC</td>
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<tr>
<td>prevention through the CDC-funded National Network of STD Clinical</td>
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<tr>
<td>Prevention Training Centers.</td>
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<tr>
<td>**Goal 2: Improve the health of people by reducing adverse outcomes of</td>
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<tr>
<td>STIs**</td>
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<tr>
<td>**Strategy 2.1.1 Integrate STI screening, diagnosis, care, and treatment</td>
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<tr>
<td>as a routine part of a wide variety of programs and settings including</td>
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<td>those that screen, diagnose, and treat people for other whole health and</td>
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<tr>
<td>public health issues such as primary care, urgent care, emergency</td>
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<tr>
<td>departments, pediatrics, family planning, HIV, viral hepatitis, substance</td>
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<tr>
<td>use disorders, correctional facilities, and school-based health centers.</td>
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<tr>
<td>Deliver patient education, testing, and treatment for STIs, including</td>
<td>Ongoing</td>
<td>OPA</td>
</tr>
<tr>
<td>HSV, to clients in Title X settings in accordance with CDC Guidelines.</td>
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<tr>
<td>Action Step</td>
<td>Timeframe</td>
<td>Federal Agency/Partner</td>
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<tr>
<td><strong>Strategy 2.2.1 Expand workforce knowledge and experience in STI prevention, screening, diagnosis, and treatment through education and training, maintenance of certification, and continuing education programs for health professionals and paraprofessionals</strong>&lt;br&gt;Update FAQ on HSV Screening to remove outdated information and reflect plain language best practices/principles.</td>
<td>2022</td>
<td>CDC</td>
</tr>
<tr>
<td>Issue letter to clinical laboratory staff and health care providers about the potential for false-positive results in HSV-2 blood tests, including recommendations for conducting HSV-2 blood tests and guidance for reporting false-positive results to FDA.</td>
<td>2023</td>
<td>FDA</td>
</tr>
<tr>
<td>Conduct training through the Ryan White HIV/AIDS Program Part F AIDS Education and Training Centers on individuals co-infected with HSV and HIV that includes HSV testing during the National Ryan White Clinical Conference.</td>
<td>2024</td>
<td>HRSA/HAB</td>
</tr>
<tr>
<td>Conduct health care provider training on HSV diagnostic testing and treatment guidelines and the physical and emotional aspects of an HSV diagnosis.</td>
<td>2024</td>
<td>VA</td>
</tr>
<tr>
<td><strong>Strategy 2.2.2 Expand the capacity of the health workforce to provide STI screening, testing, and care through innovative, evidence-based models such as Project ECHO, mentoring programs, telehealth, express visits, and other models.</strong>&lt;br&gt;Work with the Northwest Portland Area Indian Health Board’s Indian Country ECHO to train IHS, tribal, and urban Indian health care providers on HSV diagnostic testing and treatment guidelines and the physical and emotional aspects of an HSV diagnosis.</td>
<td>2024</td>
<td>IHS</td>
</tr>
</tbody>
</table>

**Goal 3: Accelerate progress in STI research, technology, and innovation**

<table>
<thead>
<tr>
<th>Action Step</th>
<th>Timeframe</th>
<th>Federal Agency/Partner</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strategy 3.1.1 Increase research to improve understanding of STI pathogenesis, immunity, and correlates of protection.</strong>&lt;br&gt;Support work to identify the molecular basis of HSV pathogen-induced pathology and evasion of host immunity to develop mechanisms to induce immunological protection from infection.</td>
<td>2023–2025</td>
<td>NIH</td>
</tr>
<tr>
<td>Support work to utilize in vivo and in vitro models to understand the basis of pathogenicity, discover virulence factors, and identify targets for therapy and prevention of HSV.</td>
<td>2023–2025</td>
<td>NIH</td>
</tr>
<tr>
<td>Leverage HSV pathogenesis and immunology research to develop new diagnostics for HSV infection.</td>
<td>2023-2025</td>
<td>NIH</td>
</tr>
<tr>
<td><strong>Strategy 3.1.2 Develop and leverage academic, public, and private partnerships for vaccine development, approval, and manufacture.</strong>&lt;br&gt;Identify lead prophylactic and therapeutic vaccine candidates for HSV.</td>
<td>2023–2025</td>
<td>NIH</td>
</tr>
<tr>
<td>Evaluate a vaccine candidate that targets HSV.</td>
<td>2023–2025</td>
<td>NIH</td>
</tr>
<tr>
<td>Action Step</td>
<td>Timeframe</td>
<td>Federal Agency Partner</td>
</tr>
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</tr>
<tr>
<td><em>Strategy 3.3.4 Develop and leverage academic, public, and private partnerships for the development, approval, and manufacture of new, as well as short supplied and/or high cost existing, STI diagnostic technologies, therapeutic agents, and other interventions.</em></td>
<td></td>
<td></td>
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<tr>
<td>Solicit white papers and proposals for the “Development of a Confirmatory Serologic Assay for Herpes Simplex Virus (HSV-1/2) Diagnosis.”</td>
<td>2023</td>
<td>CDC</td>
</tr>
<tr>
<td>Convene a joint workshop on genital herpes to define the U.S. and global burden and epidemiology of HSV, and identify gaps and research opportunities in vaccines, therapeutics, prevention, and diagnostics development.</td>
<td>2022</td>
<td>CDC, NIH</td>
</tr>
<tr>
<td>Provide advice, guidance, and review related to sponsor proposals and data submissions</td>
<td>2021-2025</td>
<td>FDA</td>
</tr>
<tr>
<td>Convene NIH Multi Council Working Group of members from NIAID, NICHD, and NINDS to develop <em>NIH Strategic Plan for Herpes Simplex Virus Research</em>.</td>
<td>2022–2023</td>
<td>NIH</td>
</tr>
<tr>
<td>Convene federal and community partners to discuss the current landscape of HSV diagnostic testing and surveillance.</td>
<td>2024</td>
<td>OIDP</td>
</tr>
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</table>

**Goal 4: Reduce STI-Related Health Disparities and Health Inequities**

**Strategy 4.1.2 Work with communities to address misconceptions and reduce stigmas that negatively affect STI prevention, screening, testing, care, and treatment.**

Convene federal and community partners to discuss how health care providers, educators, and researchers can reduce HSV stigma.                                                                                     | 2024           | OIDP                   |

**Strategy 4.2.1 Train providers, including primary care, specialty, and nontraditional providers, to deliver high-quality, culturally and linguistically appropriate, nondiscriminatory, nonjudgmental, compassionate, and comprehensive sexual health services to populations disproportionately impacted by STIs.**

Leverage new and existing strategic partners to increase technical assistance/support on comprehensive STI treatment and prevention (to include HSV) to health centers on recruitment/retention efforts and continued training and education for providers and staff. | Ongoing        | HRSA/BPHC, BHW; CDC   |

Collaborate and disseminate a webinar for health departments and community-based organizations on STI clinical guidelines, including testing for HSV antibodies.                                                   | 2021–2025      | HRSA/BPHC, CDC         |

Conduct literature review on HSV research and survey a sample of health center on HSV knowledge and testing to identify opportunities for technical assistance.                                                     | 2022           | HRSA/BPHC              |

Enhance provider awareness of the latest treatment guidelines for STIs (to include HSV). Incorporate multifaceted approaches including ECHO webinars, grand rounds, resource sharing, and site-specific didactics to expand to nontraditional providers. | 2021-2025      | IHS                    |
<table>
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<tr>
<th>Action Step</th>
<th>Timeframe</th>
<th>Federal Agency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Goal 5: Achieve Integrated, Coordinated Efforts That Address the STI Epidemic</strong></td>
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<tr>
<td><strong>5.2.1 Strengthen and expand existing surveillance infrastructure and methods including the capacity for more real-time data sharing between public health authorities and health care providers.</strong></td>
<td>2024–2025</td>
<td>CDC</td>
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<tr>
<td>Conduct evaluation of neonatal HSV to determine feasibility as a candidate for being made nationally notifiable.</td>
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<tr>
<td><strong>5.2.2 Incorporate novel scientific approaches for monitoring, identifying, and responding to trends in STIs and STI sequelae and social determinants of health related to STIs.</strong></td>
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</tr>
<tr>
<td>Identify methods to regularly estimate the annual prevalence of HSV and incidence of neonatal HSV using laboratory data and/or administrative claims data.</td>
<td>2023–2024</td>
<td>CDC</td>
</tr>
<tr>
<td><strong>5.2.6 Ensure timely dissemination of data and analyses related to STI surveillance, public health, and health care data to inform decision-making.</strong></td>
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</tr>
<tr>
<td>Conduct an HSV literature review to update the herpes section of the STI Treatment Guidelines.</td>
<td>2023–2024</td>
<td>CDC</td>
</tr>
<tr>
<td>Lead a study to evaluate the impact of the neonatal HSV infection in the United States by estimating the incidence, rate, cost, and mortality, using data from the 2019 Healthcare Cost and Utilization Project (HCUP) Kids’ Inpatient Database (KID), a nationally representative sample of all-payer pediatric discharges.</td>
<td>2023–2024</td>
<td>CDC</td>
</tr>
<tr>
<td>Monitor genital HSV incident cases and trends, gathered by the Armed Forces Health Surveillance Division for publication in the Medical Surveillance Monthly Report.</td>
<td>Ongoing</td>
<td>DOD</td>
</tr>
<tr>
<td><strong>Strategy 5.3.3 Develop and implement recommendations promoting policies, programs, and activities that accomplish goals and address areas for improvement.</strong></td>
<td></td>
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</tr>
<tr>
<td>Lead the development through the STI Federal Implementation Working Group of a HSV Addendum to the STI Plan and integration of HSV into future iterations of STI Plan and STI Progress Reports.</td>
<td>2022–2025</td>
<td>OIDP</td>
</tr>
</tbody>
</table>
APPENDIX A: PROCESS/METHODOLOGY FOR DEVELOPING AND ADOPTING THE HSV ADDENDUM

Appendix A will be drafted after receipt and analysis of public comments.
APPENDIX B: STI FEDERAL IMPLEMENTATION WORKING GROUP

Department of Defense

Department of Health and Human Services

Administration for Children and Families (ACF)
Administration for Community Living (ACL)
Centers for Disease Control and Prevention (CDC)
Centers for Medicare & Medicaid Services (CMS)
Food and Drug Administration (FDA)
Health Resources and Services Administration (HRSA)
Indian Health Service (IHS)
National Institutes of Health (NIH)
Office of the Assistant Secretary for Health (OASH)
  Office of Infectious Disease and HIV/AIDS Policy (OIDP)
  Office of Minority Health (OMH)
  Office of Population Affairs (OPA)
  Office of the Surgeon General (OSG)
  Office on Women’s Health (OWH)
Substance Abuse and Mental Health Services Administration (SAMHSA)

Department of Housing and Urban Development (HUD)

Department of Veterans Affairs (VA)
### APPENDIX C: ACRONYMS LIST

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
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<tbody>
<tr>
<td>ACF</td>
<td>Administration for Children and Families</td>
</tr>
<tr>
<td>AD</td>
<td>Alzheimer’s disease</td>
</tr>
<tr>
<td>BHW</td>
<td>Bureau of Health Workforce (HRSA)</td>
</tr>
<tr>
<td>BPHC</td>
<td>Bureau of Primary Health Care (HRSA)</td>
</tr>
<tr>
<td>CDC</td>
<td>U.S. Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>FDA</td>
<td>U.S. Food and Drug Administration</td>
</tr>
<tr>
<td>FY</td>
<td>fiscal year</td>
</tr>
<tr>
<td>HAB</td>
<td>HIV/AIDS Bureau (HRSA)</td>
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<tr>
<td>HHS</td>
<td>U.S. Department of Health and Human Services</td>
</tr>
<tr>
<td>HPV</td>
<td>human papilloma virus</td>
</tr>
<tr>
<td>HRSA</td>
<td>Health Resources and Services Administration</td>
</tr>
<tr>
<td>HSV</td>
<td>herpes simplex virus</td>
</tr>
<tr>
<td>NHAS</td>
<td>National HIV/AIDS Strategy</td>
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<tr>
<td>NIAID</td>
<td>National Institute of Allergy and Infectious Diseases (NIH)</td>
</tr>
<tr>
<td>NICHD</td>
<td><em>Eunice Kennedy Shriver</em> National Institute of Child Health and Human Development (NIH)</td>
</tr>
<tr>
<td>NIH</td>
<td>National Institutes of Health</td>
</tr>
<tr>
<td>NINDS</td>
<td>National Institute of Neurological Disorders and Stroke (NIH)</td>
</tr>
<tr>
<td>OASH</td>
<td>Office of the Assistant Secretary of Health</td>
</tr>
<tr>
<td>OIDP</td>
<td>Office of Infectious Disease and HIV/AIDS Policy (OASH)</td>
</tr>
<tr>
<td>OPA</td>
<td>Office of Population Affairs (OASH)</td>
</tr>
<tr>
<td>SDOH</td>
<td>social and structural determinants of health</td>
</tr>
<tr>
<td>STI</td>
<td>sexually transmitted infection</td>
</tr>
<tr>
<td>USPSTF</td>
<td>U.S. Preventive Services Task Force</td>
</tr>
</tbody>
</table>
APPENDIX D: REFERENCES


71. Freeman EE, Weiss HA, Glynn JR, Cross PL, Whitworth JA, Hayes RJ. Herpes simplex virus 2 infection increases HIV acquisition in men and women: systematic review and meta-analysis


79. NIH. Strategic Plan for Herpes Simplex Virus Research 2023-2028. Published online September 2023:18.