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.

> *genitalium*; however, this should not deter community partners from using available data to identify where their resources will have the most impact. The scope of future iterations of the STI Plan may be broadened to include other common STIs. (p. 11)

Although HSV is not a nationally notifiable disease, it is one of the most prevalent STIs in the United States.[1] 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.[2] 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;

[†] Consolidated Appropriations Act, 2022, 117th Cong., Pub L No. 117-103.https://www.congress.gov/117/plaws/publ103/PLAW-117publ103.pdf.

- 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>
<tr><th colspan="2">BOX 2
HSV Snapshot</th></tr>
<tr><td colspan="2">• Treatable but not currently curable
• Most people with HSV types 1 or 2 have no or mild symptoms; however, stigma and psychosocial burden can be significant
• Routine screening is not recommended for asymptomatic individuals or pregnant people</td></tr>
<tr><td>Epidemiological Facts
• 18,574,000 HSV-2 cases (2018, ages 18–49), with an overall 0.8% decrease in HSV-2 cases from 2014 to 2018
• 48.1% of people have HSV-1 (2016, ages 14–49); the proportion of genital herpes caused by HSV-1 is unknown
• 10 per 100,000 live births present with neonatal HSV, with an infant mortality rate of 7.9% from 2003 to 2014</td><td>Potential Consequences of Infection
• Transmission from pregnant person to fetus or newborn, which can lead to infant morbidity and mortality
• Discomfort from recurrent outbreaks
• Psychological stress due to stigma
• Increased risk of HIV acquisition</td></tr>
<tr><td>Populations Disproportionately Impacted
• Pregnant people
• Newborns and infants
• People who are immunosuppressed</td><td>Current Challenges
• Current testing methodology does not distinguish between primary and recurrent infections, making routine notifiable disease surveillance extremely challenging
• Most people with HSV are asymptomatic and undiagnosed
• Diagnostics for asymptomatic HSV can produce false-positive results
• Few prevention strategies exist to limit the spread of HSV
• Available treatments may reduce and shorten duration of symptoms, and there is currently no cure</td></tr>
</table>

HSV-1 and HSV-2 are among the most common STIs in the United States.[1] 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.[‡] 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

[‡]See Food and Drug Administration. *HSV-2 Tests for Genital Herpes Can Produce False Reactive Results - Letter to Clinical Laboratory Staff and Health Care Providers*. https://www.fda.gov/medical-devices/letters-health-care-providers/hsv-2-tests-genital-herpes-can-produce-false-reactive-results-letter-clinical-laboratory-staff-and.

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.

BOX 5
HSV Surveillance and Fact Sheets

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.[10] Oral HSV-1 infections tend to occur during childhood,[10] 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.[11] Symptoms usually occur at the site where the virus first entered the body[12] 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.[13,14]

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.[1]

CDC estimates that 48.1% of people aged 14–49 in 2015–2016 had HSV-1, a decrease from 59.4% in 1999–2000.[15] 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.[16]

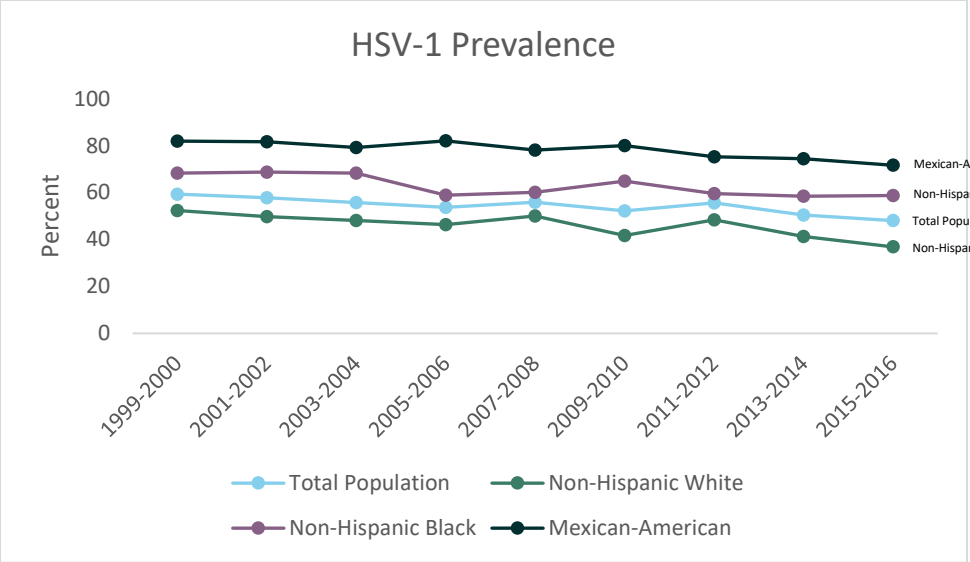


Figure 1. Percent cases of HSV-1 in persons aged 14–49 by race and Hispanic origin, United States, 1999–2016.[15] For a description of data source and methods, refer to McQuillan et al. (2018).

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]

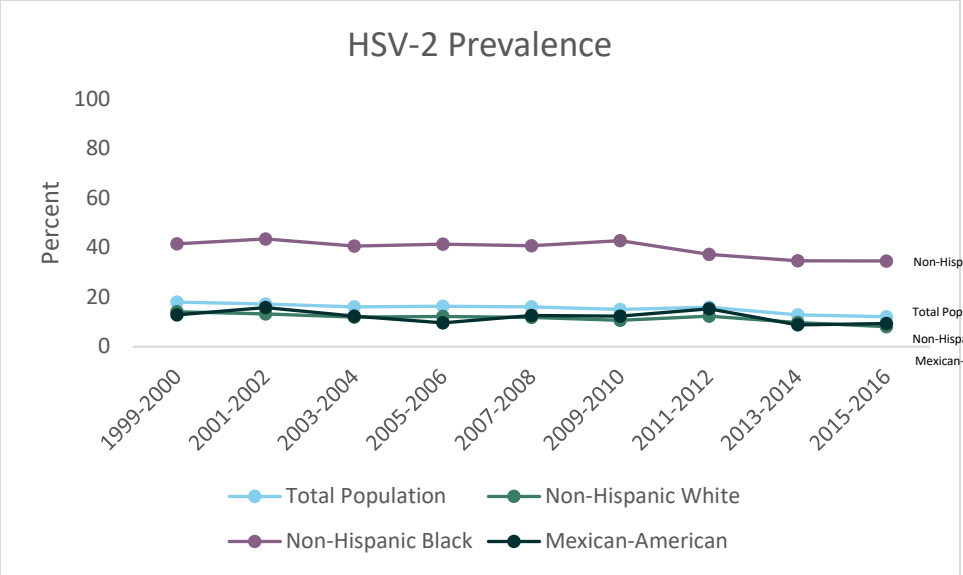


Figure 2. Prevalence of HSV-2 in persons aged 14–49 by race and Hispanic origin, United States, 1999–2016.[15] For a description of data source and methods, refer to McQuillan et al. (2018).

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.[20,21] 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.[22]

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.[23,24] 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.[21] 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.[25]

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.[26] Neonatal HSV may occur more frequently in non-Hispanic Black infants compared to non-Hispanic White infants.[27]

Challenges with Prevention and Control of HSV Infections

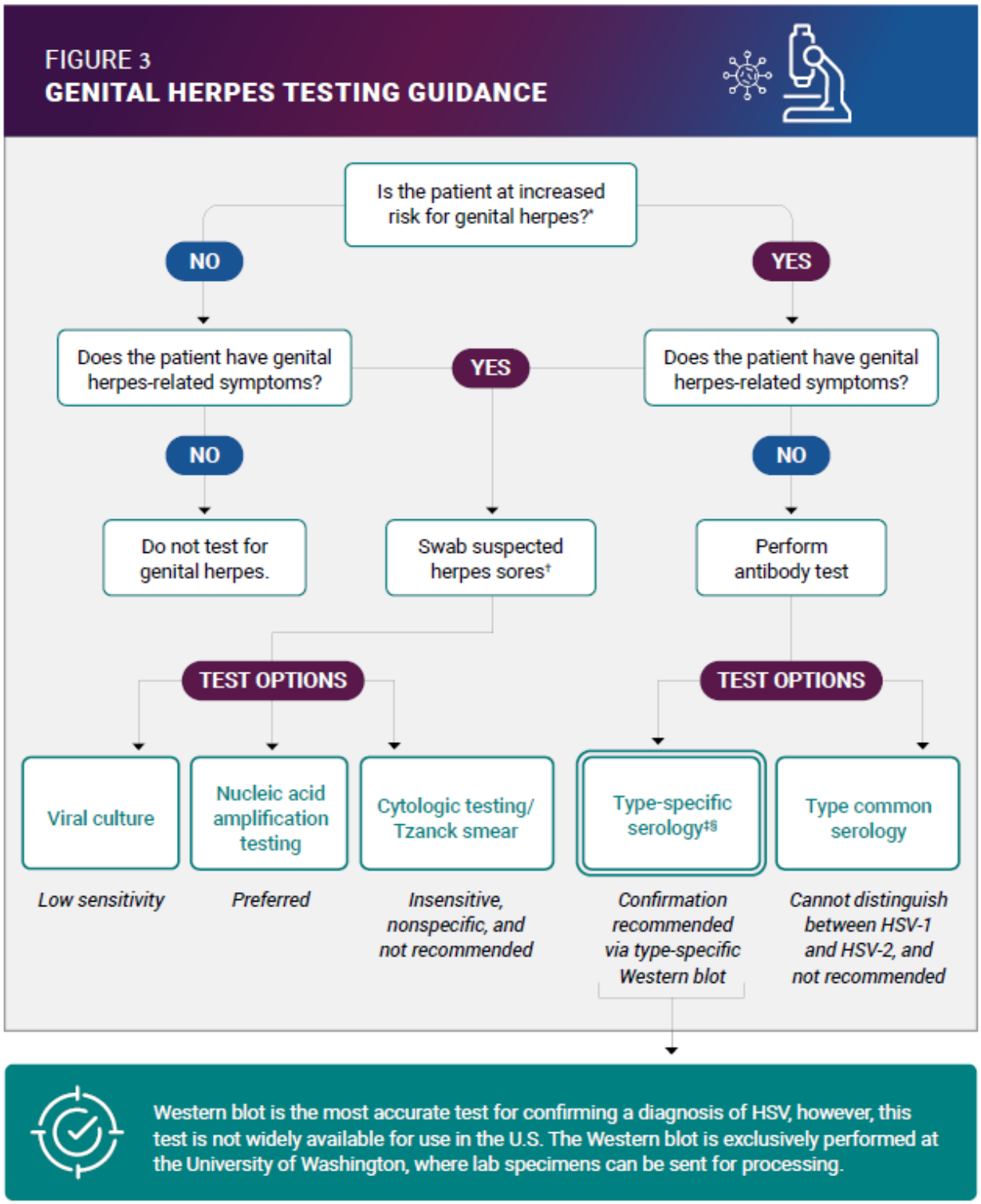
Prevention and control of HSV infections are extremely challenging. Detection of the virus or viral DNA in a lesion can aid in the diagnosis of HSV in people experiencing lesions consistent with HSV, but the low specificity of blood tests for HSV antibodies can lead to false positives; therefore, it 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.

FIGURE 3

GENITAL HERPES TESTING GUIDANCE



* 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).

Table 1. Potential HSV Surveillance Methods

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

[**]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.[34] The initial HSV diagnosis is often accompanied by depression, anxiety, and low self-esteem.[35] 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.[34]

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.[34] 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.[35]

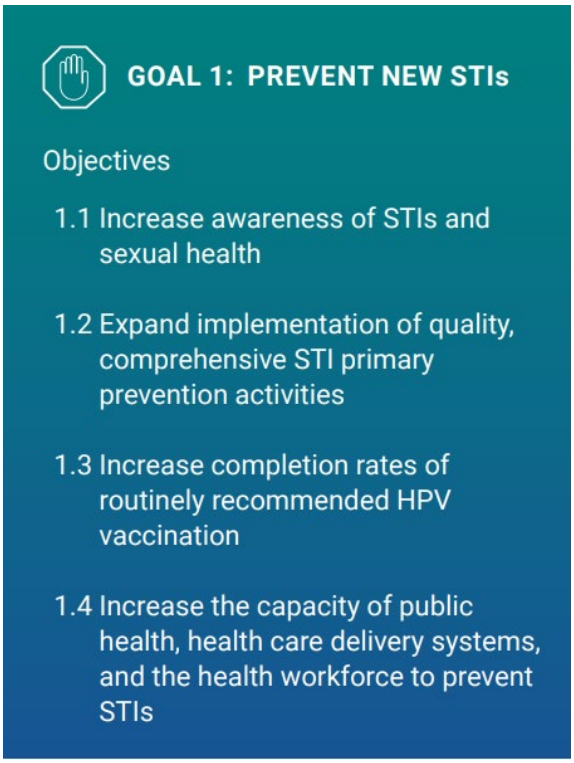
STI PLAN GOALS AND FEDERAL ACTION STEPS FOR HSV

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

STI Plan	Federal Implementation Plan
Goals: Broad aspirations that enable a plan's vision to be realized **Objectives:** Changes, outcomes, and impact a plan is trying to achieve **Strategies:** Choices about how to best accomplish objectives	**Action Steps:** Specific activities that will be performed to implement the strategies and achieve the goals of the plan **Progress Reports:** Reports on progress, successes, and challenges

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.[8] (See Box 7.) 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.[36,37] Shame and fear of rejection are the primary reasons individuals choose to not disclose their HSV status.[37,38] 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.[32] 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

[††]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.[39] 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,[35] and to be extremely concerned about transmission of the virus to sexual partners.[39] Although a small percentage of people with HSV report physical discomfort or pain resulting from genital lesions,[35] diminishment of interest or pleasure in sexual behaviors primarily results from the psychological (rather than physical) impact of the diagnosis.[34]

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.[35] 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.[39] 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.[39]

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.[40] However, no evidence indicates that people without HSV can prevent HSV acquisition by taking antiviral medication prophylactically.[41] 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.[41]

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.[42] For example, many individuals underestimate the actual prevalence rates of

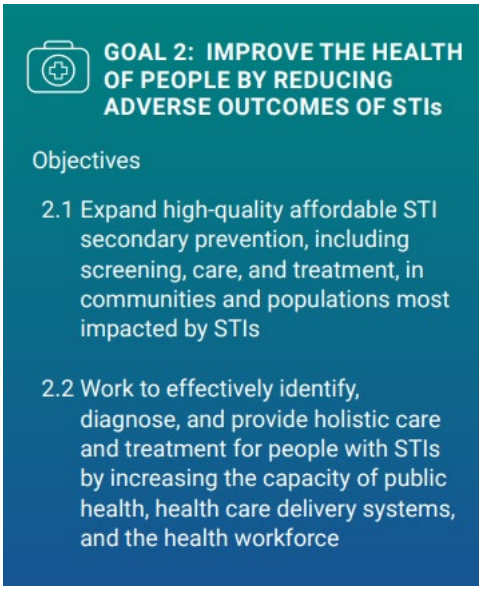
HSV, particularly given the high rate of individuals who are asymptomatic and undiagnosed, and therefore hold inaccurate risk perceptions.[32] Surveyed college students reported that they believe STI prevention strategies offer more protection against HSV than is evident in the literature,[43] and only slightly more than one-half of Americans are aware that herpes is not curable.[44] An increasing amount of genital herpes infections is attributed to HSV-1,[8] suggesting that many individuals might be unaware of the risks of transmission through oral sex.[45] Indeed, many adults and adolescents perceive oral sex to be a risk-free behavior.[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,[16] and adolescents and young adults account for the largest population of new HSV-1 cases.[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.[2] 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.[8,35] 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.[8] 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.[8] 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."[48] 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.[35] 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.[32,35] Inadequate counseling may also occur when patients' and health care providers' perceptions about HSV do not align.[35] 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.[39]

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.[49] 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.[27] 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.[27] 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.[50] Throughout the pandemic, rates of reportable STIs, such as gonorrhea, syphilis, and congenital syphilis, reached record highs.[51] 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.[52,53] 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 commnities.[54] 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.

Figure 4. The 2023-2028 NIH Strategic Plan for HERPES Simplex Virus Research.[55]

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.

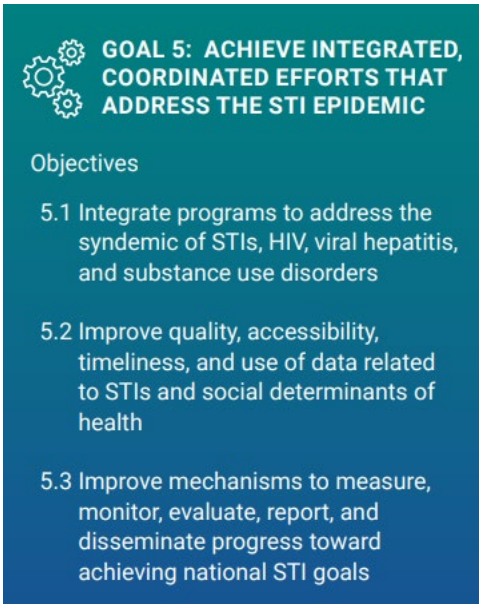
STI Plan Goal 4: Reduce STI-related health disparities and health inequities

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,[15] and an estimated 22% of pregnant women are positive for HSV-2.[66] 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.[15,23] 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.[15] 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.[1,67] HSV seroprevalence is also higher among people with lower incomes and with lower educational attainment.[68] 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[17] and potentially helped to contribute to disparities in HIV rates.[69] 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.[70] 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.[71] It has also been shown to increase the frequency and severity of HSV symptoms;[72] therefore, improved testing and treatment for HSV could help improve outcomes of people with HIV.[4] 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.[73,74]

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.[75–78] This recognition

[‡‡] See National Institute of Allergy and Infectious Disease. *2023-2028 Strategic Plan for Herpes Simples Virus Research*. https://www.niaid.nih.gov/sites/default/files/nih-herpes-simplex-strategic-plan-2023.pdf.

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

Action Step	Timeframe	Federal Agency Partner
Goal 1: Prevent New STIs		
Strategy 1.1.2 Support a non-stigmatizing, comprehensive approach to sexual health education and sexual well-being, especially in adolescents and young adults, that promotes healthy sexual development and relationships and includes both risk-avoidance and risk-reduction messaging at the community level in schools, faith-based organizations, and other community-based organizations.		
Ensure that STI prevention education delivered through the Teen Pregnancy Prevention program include education about HSV.	2023–2025	OPA
Strategy 1.2.1 Ensure that prevention programs are accessible, comprehensive, and culturally, linguistically, and age appropriate.		
Educate adolescents on adulthood preparation subjects through the Adolescent Pregnancy Prevention Program's Personal Responsibility Education Program on age-appropriate and medically accurate information on both abstinence and contraception for the prevention of pregnancy and STIs, including HIV/AIDS, HSV, and syphilis.	2023–2025	ACF
Strategy 1.2.2 Implement STI prevention activities in a broad range of health care delivery, education, and community-based settings through innovative, evidence-based approaches.		
Identify additional technical assistance/support opportunities for health centers on STI (to include HSV) as part of comprehensive STI treatment and prevention program development. Proposed activities include engaging community partners, social service organizations, and state/local health departments to coordinate care, prevention, and treatment services.	Ongoing	**HRSA/BPHC,** BHW; CDC; IHS
Strategy 1.4.1 Provide resources, incentives, training, and technical assistance to expand health workforce and systems capacity. and community centers.		
Provide trainings on genital HSV diagnosis/evaluation, management, and prevention through the CDC-funded National Network of STD Clinical Prevention Training Centers.	Ongoing	CDC
Goal 2: Improve the health of people by reducing adverse outcomes of STIs		
Strategy 2.1.1 Integrate STI screening, diagnosis, care, and treatment as a routine part of a wide variety of programs and settings including those that screen, diagnose, and treat people for other whole health and public health issues such as primary care, urgent care, emergency departments, pediatrics, family planning, HIV, viral hepatitis, substance use disorders, correctional facilities, and school-based health centers		
Deliver patient education, testing, and treatment for STIs, including HSV, to clients in Title X settings in accordance with CDC Guidelines.	Ongoing	OPA

Action Step	Timeframe	Federal Agency Partner
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		
Update FAQ on HSV Screening to remove outdated information and reflect plain language best practices/principles.	2022	CDC
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.	2023	FDA
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.	2024	HRSA/HAB
Conduct health care provider training on HSV diagnostic testing and treatment guidelines and the physical and emotional aspects of an HSV diagnosis.	2024	VA
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.		
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.	2024	IHS
Goal 3: Accelerate progress in STI research, technology, and innovation		
Strategy 3.1.1 Increase research to improve understanding of STI pathogenesis, immunity, and correlates of protection.		
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.	2023–2025	NIH
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.	2023–2025	NIH
Leverage HSV pathogenesis and immunology research to develop new diagnostics for HSV infection.	2023-2025	NIH
Strategy 3.1.2 Develop and leverage academic, public, and private partnerships for vaccine development, approval, and manufacture.		
Identify lead prophylactic and therapeutic vaccine candidates for HSV.	2023–2025	NIH
Evaluate a vaccine candidate that targets HSV.	2023–2025	NIH

Action Step	Timeframe	Federal Agency Partner
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.		
Solicit white papers and proposals for the "Development of a Confirmatory Serologic Assay for Herpes Simplex Virus (HSV-1/2) Diagnosis."	2023	CDC
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.	2022	CDC, NIH
Provide advice, guidance, and review related to sponsor proposals and data submissions	2021-2025	FDA
Convene NIH Multi Council Working Group of members from NIAID, NICHD, and NINDS to develop *NIH Strategic Plan for Herpes Simplex Virus Research*.	2022–2023	NIH
Convene federal and community partners to discuss the current landscape of HSV diagnostic testing and surveillance.	2024	OIDP
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

Action Step	Timeframe	Federal Agency Partner
Goal 5: Achieve Integrated, Coordinated Efforts That Address the STI Epidemic		
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.		
Conduct evaluation of neonatal HSV to determine feasibility as a candidate for being made nationally notifiable.	2024–2025	CDC
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.		
Identify methods to regularly estimate the annual prevalence of HSV and incidence of neonatal HSV using laboratory data and/or administrative claims data.	2023–2024	CDC
5.2.6 Ensure timely dissemination of data and analyses related to STI surveillance, public health, and health care data to inform decision-making.		
Conduct an HSV literature review to update the herpes section of the STI Treatment Guidelines.	2023–2024	CDC
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.	2023–2024	CDC
Monitor genital HSV incident cases and trends, gathered by the Armed Forces Health Surveillance Division for publication in the Medical Surveillance Monthly Report.	Ongoing	DOD
Strategy 5.3.3 Develop and implement recommendations promoting policies, programs, and activities that accomplish goals and address areas for improvement.		
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.	2022–2025	OIDP

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

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

APPENDIX D: REFERENCES

1. Kreisel KM, Spicknall IH, Gargano JW, et al. Sexually Transmitted Infections Among US Women and Men: Prevalence and Incidence Estimates, 2018. *Sex Transm Dis*. 2021;48(4):208-214. doi:10.1097/OLQ.0000000000001355

2. You S, Yaesoubi R, Lee K, et al. Lifetime quality-adjusted life years lost due to genital herpes acquired in the United States in 2018: a mathematical modeling study. *Lancet Reg Health - Am*. 2023;19:100427. doi:10.1016/j.lana.2023.100427

3. Doerr H, Gurtler L, Wittek M. Biology of Sexually Transmitted Herpes Viruses. In: Gross G, Stephen K. T, eds. *Sexually Transmitted Infections and Sexually Transmitted Diseases*. Springer; 2011:285-312.

4. Looker KJ, Elmes JAR, Gottlieb SL, et al. Effect of HSV-2 infection on subsequent HIV acquisition: an updated systematic review and meta-analysis. *Lancet Infect Dis*. 2017;17(12):1303-1316. doi:10.1016/S1473-3099(17)30405-X

5. Protto V, Marcocci ME, Miteva MT, et al. Role of HSV-1 in Alzheimer's disease pathogenesis: A challenge for novel preventive/therapeutic strategies. *Curr Opin Pharmacol*. 2022;63:102200. doi:10.1016/j.coph.2022.102200

6. Ge T, Yuan Y. Herpes Simplex Virus Infection Increases Beta-Amyloid Production and Induces the Development of Alzheimer's Disease. *BioMed Res Int*. 2022;2022:8804925. doi:10.1155/2022/8804925

7. Itzhaki RF. Overwhelming Evidence for a Major Role for Herpes Simplex Virus Type 1 (HSV1) in Alzheimer's Disease (AD); Underwhelming Evidence against. *Vaccines*. 2021;9(6):679. doi:10.3390/vaccines9060679

8. Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. *MMWR Recomm Rep Morb Mortal Wkly Rep Recomm Rep*. 2021;70(4):1-187. doi:10.15585/mmwr.rr7004a1

9. US Preventive Services Task Force, Mangione CM, Barry MJ, et al. Serologic Screening for Genital Herpes Infection: US Preventive Services Task Force Reaffirmation Recommendation Statement. *JAMA*. 2023;329(6):502-507. doi:10.1001/jama.2023.0057

10. James C, Harfouche M, Welton NJ, et al. Herpes simplex virus: global infection prevalence and incidence estimates, 2016. *Bull World Health Organ*. 2020;98(5):315-329. doi:10.2471/BLT.19.237149

11. Tuddenham S, Hamill MM, Ghanem KG. Diagnosis and Treatment of Sexually Transmitted Infections: A Review. *JAMA*. 2022;327(2):161-172. doi:10.1001/jama.2021.23487

12. Whitley R, Kimberlin DW, Prober CG. Pathogenesis and disease. In: Arvin A, Campadelli-Fiume G, Mocarski E, et al., eds. *Human Herpesviruses: Biology, Therapy, and Immunoprophylaxis*. Cambridge University Press; 2007. Accessed August 2, 2023. http://www.ncbi.nlm.nih.gov/books/NBK47449/

13. Johnston C, Magaret A, Son H, et al. Viral Shedding 1 Year Following First-Episode Genital HSV-1 Infection. *JAMA*. 2022;328(17):1730-1739. doi:10.1001/jama.2022.19061

14. Benedetti JK, Zeh J, Corey L. Clinical reactivation of genital herpes simplex virus infection decreases in frequency over time. *Ann Intern Med*. 1999;131(1):14-20. doi:10.7326/0003-4819-131-1-199907060-00004

15. McQuillan G, Kruszon-Moran D, Flagg EW, Paulose-Ram R. Prevalence of Herpes Simplex Virus Type 1 and Type 2 in Persons Aged 14-49: United States, 2015-2016. *NCHS Data Brief*. 2018;(304):1-8.

16. Spicknall IH, Flagg EW, Torrone EA. Estimates of the Prevalence and Incidence of Genital Herpes, United States, 2018. *Sex Transm Dis*. 2021;48(4):260-265. doi:10.1097/OLQ.0000000000001375

17. Fleming DT, McQuillan GM, Johnson RE, et al. Herpes simplex virus type 2 in the United States, 1976 to 1994. *N Engl J Med*. 1997;337(16):1105-1111. doi:10.1056/NEJM199710163371601

18. Schillinger JA, McKinney CM, Garg R, et al. Seroprevalence of herpes simplex virus type 2 and characteristics associated with undiagnosed infection: New York City, 2004. *Sex Transm Dis*. 2008;35(6):599-606. doi:10.1097/OLQ.0b013e3181666fb1

19. Bernstein DI, Bellamy AR, Hook EW, et al. Epidemiology, clinical presentation, and antibody response to primary infection with herpes simplex virus type 1 and type 2 in young women. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2013;56(3):344-351. doi:10.1093/cid/cis891

20. Cruz AT, Freedman SB, Kulik DM, et al. Herpes Simplex Virus Infection in Infants Undergoing Meningitis Evaluation. *Pediatrics*. 2018;141(2):e20171688. doi:10.1542/peds.2017-1688

21. Melvin AJ, Mohan KM, Vora SB, Selke S, Sullivan E, Wald A. Neonatal Herpes Simplex Virus Infection: Epidemiology and Outcomes in the Modern Era. *J Pediatr Infect Dis Soc*. 2022;11(3):94-101. doi:10.1093/jpids/piab105

22. Kimberlin DW. *Red Book (2018): Report of the Committee on Infectious Diseases*. American Academy of Pediatrics; 2018. doi:10.1542/9781610021470

23. Corey L, Wald A. Maternal and neonatal herpes simplex virus infections. *N Engl J Med*. 2009;361(14):1376-1385. doi:10.1056/NEJMra0807633

24. Looker KJ, Magaret AS, May MT, et al. First estimates of the global and regional incidence of neonatal herpes infection. *Lancet Glob Health*. 2017;5(3):e300-e309. doi:10.1016/S2214-109X(16)30362-X

25. Caviness AC, Demmler GJ, Selwyn BJ. Clinical and laboratory features of neonatal herpes simplex virus infection: a case-control study. *Pediatr Infect Dis J*. 2008;27(5):425-430. doi:10.1097/INF.0b013e3181646d95

26. Donda K, Sharma M, Amponsah JK, et al. Trends in the incidence, mortality, and cost of neonatal herpes simplex virus hospitalizations in the United States from 2003 to 2014. *J Perinatol Off J Calif Perinat Assoc*. 2019;39(5):697-707. doi:10.1038/s41372-019-0352-7

27. Matthias J, du Bernard S, Schillinger JA, Hong J, Pearson V, Peterman TA. Estimating Neonatal Herpes Simplex Virus Incidence and Mortality Using Capture-recapture, Florida. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2021;73(3):506-512. doi:10.1093/cid/ciaa727

28. Feltner C, Grodensky C, Ebel C, et al. Serologic Screening for Genital Herpes: An Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA*. 2016;316(23):2531-2543. doi:10.1001/jama.2016.17138

29. Tita ATN, Grobman WA, Rouse DJ. Antenatal herpes serologic screening: an appraisal of the evidence. *Obstet Gynecol*. 2006;108(5):1247-1253. doi:10.1097/01.AOG.0000236433.29679.9a

30. Bickford J, Barton SE, Mandalia S. Chronic genital herpes and disclosure.... The influence of stigma. *Int J STD AIDS*. 2007;18(9):589-592. doi:10.1258/095646207781568484

31. Awasthi S, Friedman HM. An mRNA vaccine to prevent genital herpes. *Transl Res*. 2022;242:56-65. doi:10.1016/j.trsl.2021.12.006

32. Royer HR, Falk EC, Heidrich SM. Genital herpes beliefs: implications for sexual health. *J Pediatr Adolesc Gynecol*. 2013;26(2):109-116. doi:10.1016/j.jpag.2012.11.007

33. Jm Donigan J, Pascoe V, Kimball A. Psoriasis and herpes simplex virus are highly stigmatizing compared with other common dermatologic conditions: A survey-based study. *J Am Acad Dermatol*. 2015;73(3). doi:10.1016/j.jaad.2015.06.035

34. Bennett C, Rebafka A, Carrier J, Cook S, Edwards D. Impact of primary and recurrent genital herpes on the quality of life of young people and adults: a mixed methods systematic review. *JBI Evid Synth*. 2022;20(6):1406-1473. doi:10.11124/JBIES-21-00057

35. Alexander L, Naisbett B. Patient and physician partnerships in managing genital herpes. *J Infect Dis*. 2002;186 Suppl 1:S57-65. doi:10.1086/342964

36. Wald A, Krantz E, Selke S, Lairson E, Morrow RA, Zeh J. Knowledge of partners' genital herpes protects against herpes simplex virus type 2 acquisition. *J Infect Dis*. 2006;194(1):42-52. doi:10.1086/504717

37. Green J, Ferrier S, Kocsis A, et al. Determinants of disclosure of genital herpes to partners. *Sex Transm Infect*. 2003;79(1):42-44. doi:10.1136/sti.79.1.42

38. Myers JL, Buhi ER, Marhefka S, Daley E, Dedrick R. Associations between individual and relationship characteristics and genital herpes disclosure. *J Health Psychol*. 2016;21(10):2283-2293. doi:10.1177/1359105315575039

39. Romanowski B, Zdanowicz YM, Owens ST. In search of optimal genital herpes management and standard of care (INSIGHTS): doctors' and patients' perceptions of genital herpes. *Sex Transm Infect*. 2008;84(1):51-56. doi:10.1136/sti.2007.027631

40. STD Facts - Genital Herpes. Published June 7, 2022. Accessed October 17, 2023. https://www.cdc.gov/std/herpes/stdfact-herpes.htm

41. Johnston C. Diagnosis and Management of Genital Herpes: Key Questions and Review of the Evidence for the 2021 Centers for Disease Control and Prevention Sexually Transmitted Infections Treatment Guidelines. *Clin Infect Dis*. 2022;74(Supplement_2):S134-S143. doi:10.1093/cid/ciab1056

42. Patel R. Educational interventions and the prevention of herpes simplex virus transmission. *Herpes J IHMF*. 2004;11 Suppl 3:155A-160A.

43. Hirschler C, Hope A, Myers JL. College Students' Perceptions of and Experiences with Human Papillomavirus and Herpes: Implications for College Sexual Health Education. *Am J Sex Educ*. 2015;10(4):298-315. doi:10.1080/15546128.2015.1091760

44. Kirzinger A, Muñana C, Brodie M, et al. Public Knowledge and Attitudes About Sexually Transmitted Infections: KFF Polling and Policy Insights. KFF. Published February 18, 2020. Accessed October 18, 2023. https://www.kff.org/womens-health-policy/issue-brief/public-knowledge-and-attitudes-about-sexually-transmitted-infections/

45. Looker KJ, Magaret AS, Turner KME, Vickerman P, Gottlieb SL, Newman LM. Global Estimates of Prevalent and Incident Herpes Simplex Virus Type 2 Infections in 2012. *PLoS ONE*. 2015;10(1):e114989. doi:10.1371/journal.pone.0114989

46. Strome A, Moore-Petinak N, Waselewski M, Chang T. Youths' Knowledge and Perceptions of Health Risks Associated With Unprotected Oral Sex. *Ann Fam Med*. 2022;20(1):72-76. doi:10.1370/afm.2761

47. Ayoub HH, Chemaitelly H, Abu-Raddad LJ. Characterizing the transitioning epidemiology of herpes simplex virus type 1 in the USA: model-based predictions. *BMC Med*. 2019;17(1):57. doi:10.1186/s12916-019-1285-x

48. Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep Morb Mortal Wkly Rep Recomm Rep*. 2015;64(RR-03):1-137.

49. Singh S, Singh SK. Psychological health and well-being in patients with sexually transmitted infections: A prospective cross-sectional study. *Indian J Sex Transm Dis AIDS*. 2021;42(2):125. doi:10.4103/ijstd.IJSTD_77_19

50. Wright SS, Kreisel KM, Hitt JC, Pagaoa MA, Weinstock HS, Thorpe PG. Impact of the COVID-19 Pandemic on Centers for Disease Control and Prevention–Funded Sexually Transmitted Disease Programs. *Sex Transm Dis*. 2022;49(4):e61. doi:10.1097/OLQ.0000000000001566

51. Sexually Transmitted Disease Surveillance, 2021. Published April 11, 2023. Accessed October 17, 2023. https://www.cdc.gov/std/statistics/2021/default.htm

52. Shanshal M, Ahmed HS. COVID-19 and Herpes Simplex Virus Infection: A Cross-Sectional Study. *Cureus*. 2021;13(9):e18022. doi:10.7759/cureus.18022

53. Giacobbe DR, Di Bella S, Lovecchio A, et al. Herpes Simplex Virus 1 (HSV-1) Reactivation in Critically Ill COVID-19 Patients: A Brief Narrative Review. *Infect Dis Ther*. 2022;11(5):1779-1791. doi:10.1007/s40121-022-00674-0

54. America Leading the World in Science and Technology – The White House. Accessed October 17, 2023. https://trumpwhitehouse.archives.gov/articles/america-leading-world-science-technology/

55. NIH Releases Strategic Plan for Research on Herpes Simplex Virus 1 and 2 | NIH: National Institute of Allergy and Infectious Diseases. Published September 18, 2023. Accessed November 9, 2023. https://www.niaid.nih.gov/news-events/nih-releases-strategic-plan-research-herpes-simplex-virus-1-and-2

56. Birkmann A, Zimmermann H. HSV antivirals – current and future treatment options. *Curr Opin Virol*. 2016;18:9-13. doi:10.1016/j.coviro.2016.01.013

57. Reichman RC, Badger GJ, Mertz GJ, et al. Treatment of recurrent genital herpes simplex infections with oral acyclovir. A controlled trial. *JAMA*. 1984;251(16):2103-2107.

58. Whitley R, Baines J. Clinical management of herpes simplex virus infections: past, present, and future. *F1000Research*. 2018;7:F1000 Faculty Rev-1726. doi:10.12688/f1000research.16157.1

59. Magaret AS, Mujugira A, Hughes JP, et al. Effect of Condom Use on Per-act HSV-2 Transmission Risk in HIV-1, HSV-2-discordant Couples. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2016;62(4):456-461. doi:10.1093/cid/civ908

60. Gutierrez D, Tan A, Strome A, Pomeranz MK. Dental dams in dermatology: An underutilized barrier method of protection. *Int J Womens Dermatol*. 2022;8(1):e008. doi:10.1097/JW9.0000000000000008

61. Mesquita PMM, Rastogi R, Segarra TJ, et al. Intravaginal ring delivery of tenofovir disoproxil fumarate for prevention of HIV and herpes simplex virus infection. *J Antimicrob Chemother*. 2012;67(7):1730-1738. doi:10.1093/jac/dks097

62. Moss JA, Malone AM, Smith TJ, et al. Simultaneous delivery of tenofovir and acyclovir via an intravaginal ring. *Antimicrob Agents Chemother*. 2012;56(2):875-882. doi:10.1128/AAC.05662-11

63. Stanfield BA, Kousoulas KG, Fernandez A, Gershburg E. Rational Design of Live-Attenuated Vaccines against Herpes Simplex Viruses. *Viruses*. 2021;13(8):1637. doi:10.3390/v13081637

64. Ayoub HH, Chemaitelly H, Abu-Raddad LJ. Epidemiological Impact of Novel Preventive and Therapeutic HSV-2 Vaccination in the United States: Mathematical Modeling Analyses. *Vaccines*. 2020;8(3):366. doi:10.3390/vaccines8030366

65. Spicknall IH, Looker KJ, Gottlieb SL, et al. Review of mathematical models of HSV-2 vaccination: Implications for vaccine development. *Vaccine*. 2019;37(50):7396-7407. doi:10.1016/j.vaccine.2018.02.067

66. Xu F, Markowitz LE, Gottlieb SL, Berman SM. Seroprevalence of herpes simplex virus types 1 and 2 in pregnant women in the United States. *Am J Obstet Gynecol*. 2007;196(1):43.e1-6. doi:10.1016/j.ajog.2006.07.051

67. Fanfair RN, Zaidi A, Taylor LD, Xu F, Gottlieb S, Markowitz L. Trends in seroprevalence of herpes simplex virus type 2 among non-Hispanic blacks and non-Hispanic whites aged 14 to 49 years--United States, 1988 to 2010. *Sex Transm Dis*. 2013;40(11):860-864. doi:10.1097/OLQ.0000000000000043

68. Stebbins RC, Noppert GA, Aiello AE, Cordoba E, Ward JB, Feinstein L. Persistent socioeconomic and racial and ethnic disparities in pathogen burden in the United States, 1999-2014. *Epidemiol Infect*. 2019;147:e301. doi:10.1017/S0950268819001894

69. Des Jarlais DC, Arasteh K, McKnight C, Perlman DC, Cooper HLF, Hagan H. HSV-2 Infection as a Cause of Female/Male and Racial/Ethnic Disparities in HIV Infection. *PloS One*. 2013;8(6):e66874. doi:10.1371/journal.pone.0066874

70. HIV and STD Criminalization Laws | Law | Policy and Law | HIV/AIDS | CDC. Published March 29, 2023. Accessed October 18, 2023. https://www.cdc.gov/hiv/policies/law/states/exposure.html

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

of longitudinal studies. *AIDS Lond Engl*. 2006;20(1):73-83. doi:10.1097/01.aids.0000198081.09337.a7

72. Schacker T, Zeh J, Hu HL, Hill E, Corey L. Frequency of symptomatic and asymptomatic herpes simplex virus type 2 reactivations among human immunodeficiency virus-infected men. *J Infect Dis*. 1998;178(6):1616-1622. doi:10.1086/314486

73. Macneil A, Reynolds MG, Braden Z, et al. Transmission of atypical varicella-zoster virus infections involving palm and sole manifestations in an area with monkeypox endemicity. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2009;48(1):e6-8. doi:10.1086/595552

74. Health Alert Network (HAN). Provided by the Centers for Disease Control and Prevention (CDC). Potential Risk for New Mpox Cases. Published May 15, 2023. Accessed October 18, 2023. https://emergency.cdc.gov/han/2023/han00490.asp

75. Hogben M, Leichliter JS. Social determinants and sexually transmitted disease disparities. *Sex Transm Dis*. 2008;35(12 Suppl):S13-18. doi:10.1097/OLQ.0b013e31818d3cad

76. Seiler N, Pearson WS, Organick-Lee P, et al. Medicaid, Sexually Transmitted Infections, and Social Determinants of Health. *Sex Transm Dis*. 2024;51(1):33-37. doi:10.1097/OLQ.0000000000001887

77. Cohn T, Harrison CV. A Systematic Review Exploring Racial Disparities, Social Determinants of Health, and Sexually Transmitted Infections in Black Women. *Nurs Womens Health*. 2022;26(2):128-142. doi:10.1016/j.nwh.2022.01.006

78. Carlson JM, Tannis A, Woodworth KR, et al. Substance Use Among Persons with Syphilis During Pregnancy - Arizona and Georgia, 2018-2021. *MMWR Morb Mortal Wkly Rep*. 2023;72(3):63-67. doi:10.15585/mmwr.mm7203a3

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