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RHODE ISLAND
MEDICAL JOURNAL

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Sexually Transmitted Infections (STIs)

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GUEST EDITORS

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Addressing Sexually Transmitted Infections in Rhode Island

PHILIP A. CHAN, MD, MS
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Sexually transmitted infections (STIs) include a diverse set of bacterial, viral, protozoa and other types of infections that are primarily transmitted through sex. Rates of human immunodeficiency virus (HIV) are decreasing in the United States due to effective public health approaches such as routine testing, antiretroviral therapy, and pre-exposure prophylaxis (PrEP).[1] However, bacterial STIs such as syphilis, gonorrhea, and chlamydia have increased dramatically during the last decade. In 2022, there were over 2.5 million cases of syphilis, gonorrhea, and chlamydia reported to the Centers for Disease Control and Prevention (CDC).[2] Other STIs such as genital herpes and human papillomavirus (HPV) are not reported to the CDC given high prevalence in the general population. Importantly, cases of STIs disproportionately impact specific populations including younger individuals, cisgender women, men who have sex with men (MSM), and non-binary and gender-diverse groups, as well as African American/Black and Hispanic/Latino communities. Improved efforts are needed to address STIs across the country, including Rhode Island.

STIs can lead to significant complications and morbidity.[3] Cisgender females experience significant sequelae of STIs. Untreated gonorrhea and chlamydia can lead to pelvic inflammatory disease (PID), infertility, ectopic pregnancy, and chronic pain. Those with an STI are also at significantly increased risk of HIV, which continues to disproportionately affect MSM and transgender women (TGW).[4] Untreated or inappropriately treated syphilis can cause significant sequalae, including cardiovascular and neurological complications. Importantly, congenital syphilis is increasing in Rhode Island and across the United States, which can lead to serious fetal complication, including death. In addition to potential physical consequences of these STIs, there are also social and psychological ramifications of testing positive for an STI.

Both the CDC and United States Preventative Service Task Force (USPSTF) provide recommendations for STI screening.[5] These recommendations vary for different populations and include: 1) **Cisgender women:** Gonorrhea and chlamydia screening for all sexually active women under 25 years of age, and for women 25 years of age and older at increased risk (i.e., new partner, more than one partner, not in a monogamous relationship, history of incarceration, etc.), syphilis if at increased risk; 2) **Cisgender heterosexual men:** Although there is insufficient evidence for gonorrhea, chlamydia and syphilis screening in cisgender heterosexual men, this group should be screened in higher prevalence clinical settings (i.e., if STIs are being found in the corresponding cisgender heterosexual female population); 3) **MSM:** Chlamydia, gonorrhea, and syphilis screening at least annually and every three to six months if multiple sex partners; 4) **Transgender, gender-diverse:** STI screening in transgender and gender-diverse individuals should be adapted based on anatomy and types of sexual activity; 5) **Pregnant persons:** All pregnant persons should be screened for syphilis, HIV, and hepatitis B virus. Screening for gonorrhea and chlamydia is recommended in pregnant persons under 25 years of age or 25 years or older and at increased risk; 6) **All individuals:** Routine screening for genital herpes and trichomonas is generally not recommended. All individuals aged 13–64 years should be screened once in their lifetime for HIV, and more frequently if at risk (i.e., MSM). STIs should be treated in a timely manner according to current clinical CDC STI Treatment Guidelines.[5]

In Rhode Island, multiple options exist for specialty sexual healthcare and STI expertise. This includes infectious disease physicians at local academic centers and hospital systems, as well as community-based clinics, which commonly provide care for primary care and sexual health in general. The Miriam Hospital has a specific STI clinic dedicated to the care and management of STIs (www.lifespan.org/centers-services/infectious-diseases/sexually-transmitted-infections-clinic). Open Door Health is the state's only community-based LGBTQ+ clinic and provides timely STI testing and treatment, as well as expert consultation as needed (odhpvd.org). Planned Parenthood and Federally-Qualified Health Centers (FQHCs) such as Providence Community Health Center (PCHC) and Thundermist also provide robust and comprehensive STI services to their patients. Congenital syphilis should be managed in consultation with the Reproductive Infectious Diseases Service at Women & Infants Hospital (www.womenandinfants.org/services/infectious-disease).

In addition, the Rhode Island Department of Health (RIDOH) provides extensive resources related to STI prevention and public health, including free condoms, Testing 1-2-3 (an online program where asymptomatic individuals can be screened without visiting a clinic, www.testing123ri.

com), and the Right Time app (which provides education and resources for the community, www.righttimeapp.com). RIDOH staff routinely conduct partner-notification services with all newly diagnosed cases of HIV and cases of primary syphilis in order to ensure engagement in care and that partners are notified in a timely manner of potential exposure. RIDOH provides case management for pregnant people living with HIV or diagnosed with syphilis to ensure the health of their newborns. RIDOH has an active surveillance system to monitor trends (see the latest HIV, Sexually Transmitted Infections, Viral Hepatitis, and Tuberculosis Surveillance Report at health.ri.gov) and conduct individual and community-level interventions. With the increase in STIs both nationally and within the state, it is imperative that primary care providers and other healthcare professionals be aware and engaged in strategies for STI care and prevention.

There are multiple approaches for addressing and preventing STI transmission: 1) routine STI screening, especially given that many STIs are asymptomatic and people may not know they are infectious; 2) timely treatment; 3) notification of sex partners about exposure; 4) vaccination for STIs, if available (i.e., HPV, Hepatitis A virus, Hepatitis B virus, Mpox); 5) condoms; 6) reductions in the number of sex partners; 7) talking to partners about STIs and asking sex partners to be tested; and 8) chemoprophylaxis (i.e., HIV PrEP). Different approaches may work best for different people. STIs and sexual health can be sensitive topics, and it is important that discussions with patients are presented in a non-judgmental and respectful manner.

In addition, a new and exciting approach to STI prevention includes doxycycline as post-exposure prophylaxis (DoxyPEP). DoxyPEP is an effective method in preventing bacterial STIs in MSM and TGW,[6] and may be effective in other groups, although data is limited. DoxyPEP involves taking a single 200mg dose of doxycycline, ideally within 24 hours and up to 72 hours after condomless sex. The landmark study published in 2023 was conducted in Seattle and San Francisco and demonstrated the efficacy of this intervention in preventing syphilis, gonorrhea and chlamydia in both MSM and TGW with HIV and those taking HIV PrEP.[6] Generally, MSM and TGW who have been diagnosed with an STI in the past should consider DoxyPEP depending on current behaviors. At the very least, sexually active MSM and TGW should be made aware of DoxyPEP and the indications for use. Doxycycline is generally well tolerated.[7] Similar to HIV PrEP, DoxyPEP will likely become an important component of STI prevention.

The United States Department of Health and Human Services released their first Federal STI Implementation Plan for the country in 2023 in response to the increasing national burden.[8] The plan highlights five major goals: 1) Prevent New STIs by increasing awareness, expanding access to care, and with HPV vaccination; 2) Improve the Health of People by Reducing Adverse Outcomes of STIs by expanding affordable STI services including prevention, testing, and treatment; 3) Accelerate Progress in STI Research, Technology, and Innovation; 4) Reduce STI-Related Health Disparities and Health Inequities, including reducing stigma and addressing STI-related social determinants of health; 5) Achieve Integrated, Coordinated Efforts That Address the STI Epidemic (including the "syndemic" of STIs, HIV, viral hepatitis, substance-use disorders, and mental health disease).

In summary, STIs have been significantly increasing in Rhode Island and across the United States. Healthcare professionals should be aware of current testing and treatment guidelines, including newer prevention approaches such as DoxyPEP. Together, we can address the burden of STIs in the state and improve the overall health of people in Rhode Island.

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HIV and Other Sexually Transmitted Infections in Rhode Island: Trends, Disparities, and Health Equity

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ABSTRACT

Over the past 10 years, sexually transmitted infections (STIs) have seen a significant resurgence in the United States despite the availability of effective treatments and reliable prevention methods. Rhode Island has experienced a similar uptick in the incidence of syphilis, chlamydia and gonorrhea, with many cases occurring among gay, bisexual, men who have sex with men (GBMSM), which coincides with a recent concerning rise in congenital syphilis cases. We reviewed the most recent STI trends for the state of Rhode Island in 2022. During this year, 6,883 cases of STIs were reported to the Department of Health (N=5,199 chlamydia, 1,444 gonorrhea, and 240 infectious syphilis cases). Compared to 2012, this represented a 21%, 185%, and 253% increase in chlamydia, gonorrhea, and syphilis infections, respectively. Since 2020, eight cases of congenital syphilis have been reported. Prior to 2020, no cases of congenital syphilis were reported since 2009. This resurgence is mainly attributed to shifting social and behavioral trends, particularly among younger individuals and shared sexual networks across diverse groups.[1] Further efforts and resources are needed to effectively address these concerning trends in STIs.

BACKGROUND

Sexually transmitted infections (STIs) are on the rise in the United States (US), including in Rhode Island. According to preliminary data from the Centers for Disease Control and Prevention (CDC), there were more than 2.5 million new cases of syphilis, chlamydia, and gonorrhea reported in the US in 2022.[2] Syphilis infections saw a substantial 26% increase, reaching levels not observed since the 1950s. Increases among males and females, all age groups, and most racial/ethnic groups have been observed. Syphilis may be diagnosed at an infectious (primary, secondary, or early non-primary, non-secondary) stage, or at a latent/unknown stage of infection. In 2000 and 2001, total syphilis incidence (all stages) reached historic lows nationally,[2] but since then, rates have increased every year, with the greatest increases observed in the non-Hispanic American Indian or Alaska Native population.

Gay, bisexual, and other men who have sex with men (GBMSM) are disproportionately impacted by syphilis. In 2021, nearly half of all infectious male cases in the US were reported in this population. Women are generally impacted less by syphilis. However, between 2017–2021, there was a 217.4% increase in reported female cases, highlighting a growing epidemic in heterosexual populations. Congenital syphilis (CS) is a growing concern nationally. The national congenital syphilis rate of 102.5 cases per 100,000 live births in 2022 represents a 30.6% increase compared to 2021 and is the highest reported rate since 1991. In 2022, nearly all US states reported at least one case of CS.[2]

Chlamydia is the most common STI in the US. Rates of reported chlamydia continue to increase annually among both males and females, most age groups, and all racial/ethnic groups, with the highest rates occurring among adolescents and young adults aged 15–24 years. Gonorrhea is the second most common STI in the US. Similar to chlamydia, rates of gonorrhea continue to increase annually among both males and females, most age groups, and most racial and ethnic groups. In 2009, gonorrhea reached a historic low, but as of 2021, national rates have increased by 118%. Case increases among men and the higher frequency of extragenital testing in recent years likely reflect cases being identified both among GBMSM and heterosexual males.

ANALYSIS OF RHODE ISLAND SURVEILLANCE DATA ON STIS

Following national trends, syphilis increases have been observed annually in Rhode Island since 1998, with a record high occurring in 2021 with 565 total cases reported (all stages). Rates of infectious syphilis in Rhode Island have been highest in males, non-Hispanic Black/African American and Hispanic populations, and among those aged 25–34 years. Syphilis disproportionately impacts GBMSM. However, the incidence is also increasing in women of reproductive age. Untreated syphilis in pregnant individuals can lead to stillbirth and/or adverse outcomes, including death. This highlights the need to focus on timely treatment for congenital syphilis prevention. From 2020–2022, the Rhode Island Department of Health received eight reports of congenital syphilis, with most cases meeting the CDC's maternal criteria of diagnosis (i.e., inadequate treatment prior to delivery).

Before 2020, the most recent report of congenital syphilis was in 2009.

Gonorrhea is the second most common STI in Rhode Island. In 2021 a record high of 1,681 (159.4 cases per 100,000) gonococcal infections were reported, with the highest rates observed in males, those aged 20–34 years, and non-Hispanic Black/African American populations. Although a slight decrease in total incidence was observed in 2022, preliminary 2023 data suggests a continuing overall upward trend in gonorrhea infection in Rhode Island. Efforts at the RIDOH State Health Laboratory and other testing facilities have focused on the ability to detect antimicrobial resistance among cases suspected of meeting resistance criteria. Fortunately, to date, Rhode Island has not confirmed any cases of ceftriaxone-resistant gonorrhea.

Chlamydia is the most common STI in Rhode Island, with over 5,000 cases reported annually since 2017. Rates are highest among females, individuals aged 20-34 years, and in non-Hispanic Black/African American and Hispanic populations. In the last 10 years (2013–2022), rates of chlamydia have increased 68.3% in those aged 15–24 years old. Complications of both chlamydia and gonorrhea can include pelvic inflammatory disease, ectopic pregnancy, infertility, and chronic pain.

The number of newly diagnosed cases of HIV in Rhode Island has decreased overall in the last 10 years, from 79 cases in 2013 to 65 cases in 2022. However, this decline has not been consistent across all demographic groups, with certain populations experiencing a greater impact. When compared to non-Hispanic Whites, in 2022, the rate of HIV was four times higher among non-Hispanic Black/African Americans and Hispanic populations. Similarly, there were almost three times as many cases of HIV among GBMSM when compared to females, male heterosexuals, and people who inject drugs, combined. Rates among individuals ages 20–24 and 25–34 have remained consistently high compared to other groups. For a detailed description of trends, please see the Rhode Island 2021 HIV, STI, Viral Hepatitis, and Tuberculosis Surveillance Report.[3]

DISPARITIES IN STI OUTCOMES: A GLIMPSE INTO SPECIAL POPULATION GROUPS

Various social determinants of health impact outcomes and disparities related to STIs. These determinants encompass conditions at individual and structural levels that influence the prevention, diagnosis, and treatment of STIs. Although STI rates have increased across all populations in the US, marginalized groups – youth and young adults, women, GBMSM, and Black/African American and Hispanic/Latino people – continue to experience a disproportionate share of STI cases. Disparities in disease trends within each population group are particularly evident for some diseases (**Figures 1–3**). In addition, estimates of sexual behaviors that impact

Figure 1. Rates of Gonorrhea, by Racial and Ethnic Group, Rhode Island, 2018–2022

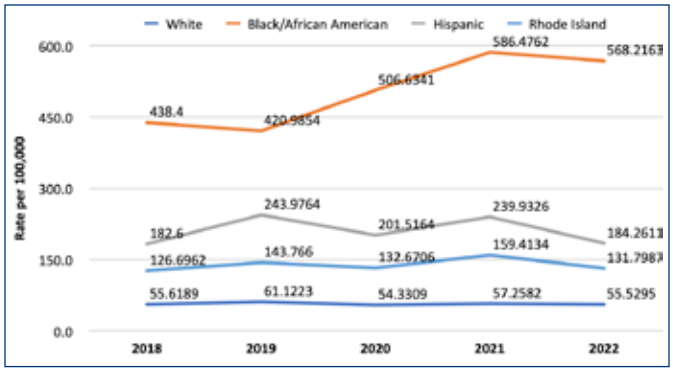


Figure 2. Number of Chlamydia Cases, by Sex, Rhode Island, 2013–2022

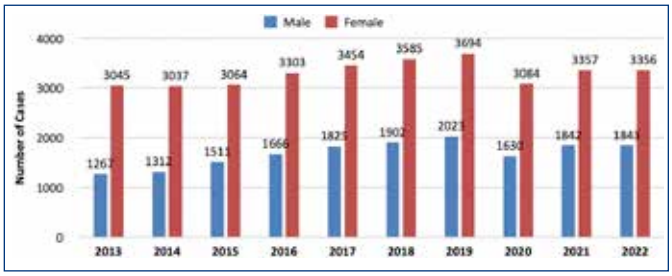
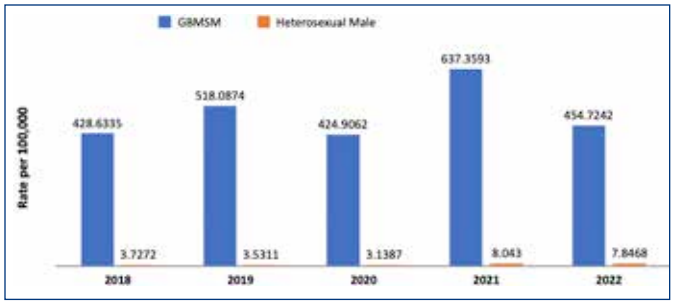


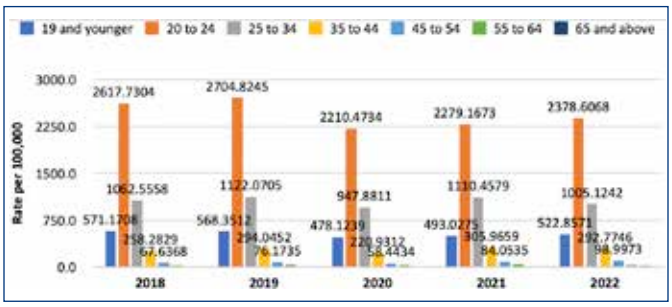
Figure 3. Rates of Infectious Syphilis in Males, by Sexual Orientation, Rhode Island, 2013–2022



STI trends are also reported as part of the Rhode Island Youth Behavioral Risk Survey (YRBS) and the Rhode Island Behavioral Risk Factor Surveillance System (BRFSS). The YRBS is an anonymous and voluntary survey of Rhode Island high school students. In 2021, 21% of students reported being currently sexually active, and among these students, 57% used a condom at their last sexual encounter. The BRFFS is a random digit telephone survey among Rhode Island adults aged 18–65. In 2022, 9% of adults reported having two or more sexual partners in the past year, and among them, 53% used a condom at their last sexual encounter.

In terms of gonorrhea, diagnoses have increased in the last 10 years and disproportionately affect minority populations (**Figure 1**). In 2022, gonorrhea rates among the Black/African American population were more than 10 times higher than

Figure 4. Rates of Chlamydia Cases, by Age, Rhode Island, 2018–2022



among the non-Hispanic White population and three times higher than among the Hispanic/Latino population. Most chlamydia cases in the last 10 years have been diagnosed in females. In 2022, nearly twice as many cases were diagnosed in females compared to males (**Figure 2**). This difference is likely due to two factors. First, women generally access routine healthcare and subsequent screening more than men. Second, men who have chlamydia often do not have symptoms and do not seek health care for screening and treatment. Between 2018–2022, the highest rates of chlamydia were observed in the 20–24-year-old age group, followed by those in the 25–34 years-old age group (**Figure 4**).

In the last five years, the rates of infectious syphilis cases among GBMSM have been substantially higher compared to heterosexual men (**Figure 3**). In the GBMSM population, the rate of infectious syphilis cases in 2022 was 58 times higher compared to the rate of infectious syphilis cases among heterosexual men. According to the CDC, transgender and gender diverse people often experience high rates of stigma and socioeconomic and structural barriers to care that negatively affect healthcare usage and increase susceptibility to HIV and STIs (**Table 1**). As defined by the CDC, persons who are transgender have a gender identity that differs from the sex that they were assigned at birth.[4]

Pregnant people who are diagnosed with HIV, syphilis, and hepatitis C can pass these infections to their newborns. While the number of babies born with these infections remains low in Rhode Island, the health consequences of these infections can be severe. HIV and syphilis screening are now incorporated into routine prenatal care. People who are diagnosed with HIV or syphilis during pregnancy receive medical case management from RIDOH nursing staff to promote healthy outcomes for their newborns. In 2022, among the 10,709 births in Rhode Island, there were five infants diagnosed with congenital syphilis and one with HIV. Before 2020 no cases of congenital syphilis or perinatal HIV were reported in more than 10 years.

Table 1. Reported Cases of Selected Diseases Among Transgender People, Rhode Island, 2021–2022

HIV	<5
Infectious Syphilis	9
Latent or Unknown Duration Syphilis	5
Gonorrhea	10
Chlamydia	19

PROGRAMS AND INITIATIVES BY THE RHODE ISLAND DEPARTMENT OF HEALTH

In recent years, the Rhode Island Department of Health (RIDOH) has implemented many innovative and evidence-based strategies to prevent and control STIs and HIV. A full description of clinical and community services offered by RIDOH can be found in the resource guide and are briefly outlined below.[5]

CASE INVESTIGATION AND CONTACT TRACING

As part of surveillance activities, all new HIV diagnoses and high-priority syphilis cases are interviewed by RIDOH staff to conduct contact tracing and ensure testing of close contacts. High-priority syphilis cases in order of workup priority include:

- Cases with signs or symptoms of syphilis as reported by patient or provider indicative of syphilis infection;
- All pregnant women and women of childbearing age (<45 years);
- Any child under 18 years of age;
- Any case with test results indicative of a new infection (four-fold increase in titer or a negative titer in the last 12 months);
- Cases with late or unknown duration infection (no symptoms and no negative titer in prior 12 months to suggest recent infection).

NEEDLE EXCHANGE AND HARM REDUCTION SERVICES

Needle exchange programs, often called "syringe services programs (SSPs)," provide a full spectrum of services to individuals who use drugs, including safe injection kits, sharps disposal containers, naloxone, fentanyl test strips, condoms, rapid HIV and hepatitis C testing, and referrals to mental health and social services as appropriate. AIDS Care Ocean State (ACOS), Project Weber/RENEW, and Parent Support Network operate SSPs throughout Rhode Island through a multi-faceted approach, including three fixed sites, mobile/street-based outreach in core cities, home-delivered services, and most recently, harm reduction vending machines which are co-located in places that serve high-risk individuals. Further, sterile syringes can be purchased without a prescription at retail pharmacies in Rhode Island.

CONDOM ACCESS

In the beginning of the COVID-19 pandemic, many individuals experienced increased barriers to accessing condoms, as many of the community distribution locations were closed or limited to the public. Starting in August 2020, individuals can request RIDOH to mail a small package with approximately 15 condoms to their home. Since program inception, RIDOH has provided condoms to over 3,200 individuals representing all 39 cities and towns. RIDOH plans to continue the Condoms by Mail program as there is a consistent demand, reaching a population with an otherwise unmet need.

RAPID HIV AND HEPATITIS C TESTING IN COMMUNITY SETTINGS

RIDOH-funded community-based organizations, including AIDS Care Ocean State (ACOS), Project Weber/RENEW, and AIDS Project Rhode Island (APRI), conduct community-based rapid HIV screening tests. APRI also offers home test kits where individuals can fill out an online form and receive a rapid HIV test kit in the mail. In 2022, there were 1,457 community-based rapid HIV tests conducted. Approximately 85% of all community-based rapid HIV tests conducted were among individuals who are at high risk of contracting HIV, demonstrating that we are reaching those most in need of testing.

TESTING 1-2-3 PROGRAM

Testing 1-2-3 is a program created by RIDOH to help asymptomatic Rhode Islanders get easily tested for HIV and other STIs. Individuals who want to be tested complete a registration form online at www.testing123ri.com, go to the lab of their choice to provide samples, and then receive their results and follow-up for positive cases. Using this service, individuals can be tested for HIV, chlamydia, gonorrhea, and syphilis. In 2022, 110 individuals received STI testing through this program.

EDUCATION AND AWARENESS FOR YOUTH AND ADOLESCENTS

RIDOH, in collaboration with Planned Parenthood of Southern New England (PPSNE), conducts sexual and reproductive health education to schools via assemblies/workshops, which are centered around STIs, contraception, gender identity and sexual orientation, etc. In the next phase of this collaboration, professional development will be offered to teachers, nurses, and other relevant school staff, which will focus on teaching teens about STIs, HIV prevention, testing and treatment, stigma, and addressing barriers to accessing care. Lastly, this partnership includes a parent-child communication program called LiFT, that increases parent-child communication and youth self-efficacy.

SEXUAL AND REPRODUCTIVE ONLINE WEBSITES AND APPS

RIDOH released the RIght Time app in 2019 to include information about sexual health and well-being in Rhode Island.[6] RIDOH is also developing the RIght to Know website and app to provide resources and information specific to adolescents. RIDOH is committed to promoting prevention, testing, and engagement in care for STIs and HIV with a focus on health equity. Fully addressing STIs and HIV in Rhode Island requires collaboration and commitment across public health, clinical, academic, and community-based organizations and institutions.

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Considerations for Sexual History-Taking and Screening for Sexually Transmitted Infections Among Persons Identifying as Part of the LGBTQIA+ Community

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In the United States, rates of sexually transmitted infections (STIs) are increasing. In 2022, there were over 2.5 million cases of syphilis, gonorrhea and chlamydia reported to the Centers for Disease Control and Prevention (CDC).[1] STIs are often asymptomatic and when untreated, may lead to significant morbidity and associated healthcare costs. Lesbian, gay, bisexual, transgender, queer/questioning, intersex, and asexual/agender/aromantic (LGBTQIA+) individuals experience significant disparities related to healthcare access and outcomes, including sexual health and STIs. Gay, bisexual, and other men who have sex with men (MSM) are disproportionately at risk for HIV infection. They also have higher rates of STIs, including gonorrhea, and syphilis when compared with the general population.[2] In addition, transfeminine persons have a 49-times greater odds of HIV infection when compared to all adults.[3] Queer individuals may be at increased risk for developing gynecologic cancers and are less likely to undergo cervical cancer screening compared to their heterosexual counterparts.[4] CDCs recent annual report underscores that the prevention and treatment of STIs must be a public health priority. Enhanced STI screening and improved access to safe and affirming sexual health care is needed, especially among the LGBTQIA+ community.

LGBTQIA+ individuals face multiple challenges to obtaining sexual health care and STI services. Health disparities can be attributed to discrimination, stigma, lack of knowledge among providers and financial and insurance barriers.[5] LGBTQIA+ persons have endorsed avoiding or delaying care because of negative experiences with healthcare providers or within the healthcare setting.[6] Trans-identifying individuals are at higher risk for physical and sexual violence, highlighting the need for a gender-inclusive and trauma informed approach.[7] It is important for all providers to make LGBTQIA+ persons feel comfortable and respected in the clinical space to achieve optimal health outcomes.

One important step in addressing sexual health care for LGBTQIA+ persons involves taking a comprehensive sexual health history that is inclusive for all people. The five "Ps," a framework created by CDC, can guide the dialogue with patients and highlights the major aspects of a sexual health history (**Table 1**).[2] Providers should inform patients that these questions are asked of everyone, and the responses are an important part of their care plan. Providers should ask questions in a manner that does assume monogamy, gender, or anatomy of partners. One consideration is to tailor questions by asking about preferred language regarding body parts, internal organs, or genitals. The gender identity of patients can exist independently of sexual orientation, and both may exist across a spectrum. Gender identity refers to a person's current gender which may be the same (cisgender) or different (transgender) from the sex assigned at birth. Sexual orientation refers to attraction including to the opposite gender (i.e., heterosexual) or same gender. It is important to understand the anatomy a person has and to base sexual health discussions and STI screening on sexual behaviors. Providers should also be informed about the types of tissue used to construct a neovagina or neopenis, as this may also impact STI screening recommendations.[2] Patients are not

Table 1. Suggested Dialogue for Taking a Comprehensive Sexual Health History

Aspect of Sexual Health History	Suggested Dialogue
Partners	• Are you currently having sex of any kind? • When was the last time you were sexually active? • Do your partners tend to be people with penises, vaginas, or both?
Practices	• To take the best care of you, I need to ask some specific questions about the types of sex that you have. There are different types of tests that we use for screening, depending on the type of sex you have, or the body parts you use to have sex. • In relation to oral/anal/vaginal sex, do you give, receive, or both?
Protection from STIs	• Do you use any sexual prevention tools? • How do you decide when to use condoms?
Past history of STIs	• Have you ever been diagnosed with an STI in the past?
Pregnancy Intention	• Are you interested in being a parent in the future? • Do you have any intentions of becoming pregnant in the future?
Sexual function and satisfaction	• Are you engaging in consensual sex? • Are you comfortable with who you are having sex with and how often? • Do you have pain with sex?

*Adapted from the Centers for Disease Control and Prevention (CDC)

Table 2. Screening Recommendations and Considerations Based on Population

Population	Screening Recommendation by Infection
Women	**Chlamydia/Gonorrhea:** Sexually active <25 years old; sexually active women ≥25 years old at increased risk **Syphilis:** Screen asymptomatic adults at increased risk for syphilis infection **HIV:** All women age 13–64 years (opt out); all women who seek evaluation and treatment for STIs **Trichomonas:** Consider screening in high-prevalence settings and for asymptomatic women at increased risk for infection
Men who have sex with women	**Chlamydia/Gonorrhea:** Consider screening in high prevalence settings **Syphilis:** Screen asymptomatic adults at increased risk for syphilis infection **HIV:** All men aged 13–64 years (opt out); all men who seek evaluation and treatment for STIs
Men who have sex with men	**Chlamydia:** At least annually for sexually active MSM at sites of contact (urethra, rectum); every 3–6 months if at increased risk (multiple partners, on HIV PrEP) **Gonorrhea:** At least annually for sexually active MSM at sites of contact (urethra, rectum, pharynx); every 3–6 months if at increased risk (multiple partners, on HIV PrEP) **Syphilis:** At least annual for sexually active MSM; every 3-6 months if at increased risk **HIV:** At least annually for sexually active MSM; consider more frequent screening (every 3–6 months) for MSM at increased risk of acquiring HIV infection
Transgender and gender-diverse persons	**Chlamydia:** Screening recommendations should be adapted based on anatomy; consider screening at the rectal site based on reported sexual behaviors and exposure **Gonorrhea:** Screening recommendations should be adapted based on anatomy; consider screening at the pharyngeal and rectal sites based on reported sexual behaviors and exposure **Syphilis:** Consider screening at least annually based on reported sexual behaviors and exposure **HIV:** HIV screening should be discussed and offered; frequency of repeat screening should be based on risk level

*Adapted from the Centers for Disease Control and Prevention (CDC)

always forthcoming or honest about their sexual risk. This should be taken into consideration when screening for HIV and other STIs. One approach is to offer the different types of screening available and the indication for each type of screening, allowing patients to opt in or out of the testing and make decisions without disclosing sexual activity.

Given that many LGBTQIA+ persons may be at risk for STIs, the CDC has developed specific screening recommendations and considerations for this group (**Table 2**).[2] Engaging patients in routine STI screening is not complex and does not require elaborate resources. Routine screening for STIs is imperative to diagnosis and treatment and reducing morbidity and associated health costs. It is important to highlight the need for extragenital screening for chlamydia and gonorrhea for patients at risk. Data reviewed from the STD Surveillance Network demonstrates that extragenital chlamydia and gonorrhea are common among MSM. Offering only urogenital screening to MSM patients may result in a missed opportunity to diagnosis and treat over 70% of extragenital chlamydia and gonorrhea infections.[8] Extragenital screening is straightforward and acceptable to patients and can be performed via the use of self-collected swabs.

In addition to screening, healthcare providers should be aware of other prevention tools. Pre-exposure prophylaxis (PrEP) for HIV is a safe and effective tool to reduce HIV acquisition. PrEP is available in both an oral and injectable formulation and is approved for persons who are at risk of acquiring HIV via sexual activity or injection drug use. Importantly, emtricitabine tenofovir disoproxil fumarate (FTC-TDF) is the only oral formulation approved in vagina-owning persons. Gender affirming hormones have not been shown to impact daily PrEP efficacy, and thus are safe to use among transfeminine or transmasculine patients taking gender affirming therapy. Oral medications can be used daily or on-demand dosing. FTC-TDF is the only oral medication studied for on-demand dosing and is currently recommended only for MSM at risk for sexual acquisition of HIV. On-demand dosing has not been studied in transfeminine patients and there are potential concerns about decreased efficacy in patients on gender affirming therapy with estrogen.[9] It also is important to be aware and educate patients that the use of testosterone can lead to vaginal atrophy, which may lead to vaginal discomfort or bleeding and potentially an increased risk for STIs including HIV.[2] PrEP can easily be prescribed in primary care settings and generally can be available with limited or no out-of-pocket expenses. Injectable cabotegravir is a newer formulation of PrEP that is available and an option for those who may struggle with adherence or taking pills.

Another approach to addressing the STI epidemic is the use of antimicrobials after an STI exposure or potential STI exposure. DoxyPEP is the use of a single dose of doxycycline (200mg) taken orally within 24–72 hours after condomless sex. Studies demonstrated that DoxyPEP prevented syphilis, gonorrhea, and chlamydia among MSM and transgender women with HIV and those taking HIV PrEP.[10] Research of DoxyPEP in other populations is ongoing. This medication is safe and commonly used for other indications in the primary care setting. Healthcare professional should be aware of DoxyPEP and offer to appropriate patients which had the potential of improving rates of STIs in the United States.

There are several other methods of STI prevention. Condoms should be encouraged and provided if possible.

Disclosure and communication (i.e., asking partners about recent screening) are examples of behaviors that can help mitigate STIs. Vaccines are also readily available for many infections that can be sexually transmitted including human papilloma virus (HPV), hepatitis A and B virus, meningococcal disease, and monkeypox virus (Mpox). Optimizing sexual health in LGBTQIA+ persons involves taking a comprehensive sexual health history and providing options and shared decision making to determine optimal health approaches.

In conclusion, STI rates are rising steadily, resulting in a substantial financial and social burden for all, but especially among the LGBTQIA+ community. There are significant and inherent barriers for LGTBQIA+ persons to receiving adequate healthcare including sexual health. Providers should be aware of approaches and current clinical recommendations on STI screening, care, and prevention. Making simple clinical changes such as taking a comprehensive sexual health history, utilizing gender inclusive dialogue, offering routine STI screening and promoting the use of HIV PrEP and DoxyPEP, has the potential to improve STI care and overall health.

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Syphilis in Pregnancy and Congenital Syphilis

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ABSTRACT

Syphilis, once in decline, is seeing a rapid re-emergence throughout the United States. A sexually transmitted infection caused by the spirochete *Treponema pallidum*, syphilis infection in pregnancy can result in serious complications and have a profound impact on maternal and neonatal health. As rates of syphilis have increased among people of reproductive age, so too have cases of congenital syphilis. In 2021, congenital syphilis rates in the United States reached a 30-year high.[1] This article provides a review of syphilis in pregnancy and congenital syphilis to help clinicians respond to this emerging public health concern.

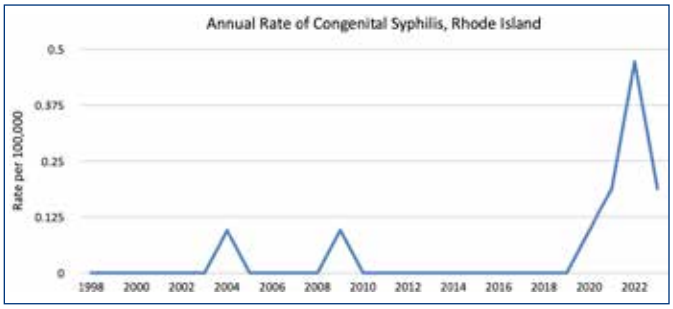
KEYWORDS: Syphilis, congenital syphilis, sexually transmitted infections

EPIDEMIOLOGY

The incidence of syphilis infections in the United States (US) has increased among men and women of all age groups. In 2022, the national rate of primary and secondary syphilis infections was 17.7 per 100,000, a 9.3% increase from 2021.[2] Rhode Island currently ranks 31st in the nation with 133 cases reported in 2022 (12.2 per 100,000 population).[2] The incidence among women is surging, with dramatic increases among women of reproductive age. Between 2012 and 2021, there was a 676% increase in primary and secondary syphilis in women aged 15–44 years.[3] In Rhode Island in 2022, there were 93 cases of syphilis reported in women of this age group, resulting in a rate of 43.1 per 100,000 population.[3]

The increase in syphilis in women has been mirrored by a spike in congenital syphilis cases. Between 2012 and 2021, there was a 755% increase in congenital syphilis cases reported in the US and the numbers continue to climb.[3] Between 2021 and 2022 alone, there was a 30.6% increase in reported cases resulting in a national congenital syphilis rate of 102.5 per 100,000 live births.[3] Rhode Island ranked 27th amongst US states in 2022 with five cases reported during this time period, resulting in a rate of 47.8 per 100,000 live births (**Figure 1**).[3] This was after a decade of zero congenital syphilis cases in Rhode Island. Given these significant increases, healthcare professionals should be aware of screening recommendations and clinical presentations of syphilis including congenital syphilis.

Figure 1. Congenital Syphilis Rates, Rhode Island, 1998–2023



Data Sources: RI-NEDSS Base System (NBS); 2000 US Census Population Estimate; 2010 US Census Population Estimate; 2016 US Census Population Estimate; 2021 5-Year ACS

NOTE: All rates are expressed per 100,000 population.

Source: RI Department of Health, Division of Emergency Preparedness and Infectious Disease

MATERNAL FACTORS ASSOCIATED WITH CONGENITAL SYPHILIS

While vertical transmission (transmission from a pregnant person to fetus during pregnancy) can occur at any gestational age or stage of syphilis, the highest risk of transmission is for infants born to pregnant persons with primary or secondary stages of infection, when spirochetemia is highest.[1,4,5] The risk of vertical transmission also increases when maternal acquisition of infection occurs at later gestational ages.[1,4,5] The rate of transmission ranges from 60 to 100% in pregnancies affected by primary or secondary infection. Those rates drop to approximately 40% in early latent infection and to <8% with late latent infection.[6]

Sociodemographic factors associated with adverse syphilis-related pregnancy outcomes include concurrent infection with another sexually transmitted infection (STI), low educational attainment, Medicaid insurance, non-Hispanic Black race/ethnicity, and delayed or inadequate prenatal care.[5,7] These factors reflect socioeconomic inequities which limit access to appropriate prenatal care, rather than biological predisposition to infection or transmission.

SCREENING IN PREGNANCY

Current Centers for Diseases Control and Prevention (CDC) guidelines recommend that serologic screening for syphilis

be performed at the initial prenatal visit.[8] Repeat screening is recommended at 28 weeks gestation for women categorized as being at high risk for syphilis acquisition during pregnancy.[8] Pregnant people are categorized as high risk if they live in an area of high prevalence, and/or have the following risk factors: sex with multiple partners, sex in conjunction with drug use or transactional sex, late entry to prenatal care or no prenatal care, methamphetamine or heroin use, incarceration of the woman or her partner, and unstable housing or homelessness.[8] Most states (including Rhode Island) mandate syphilis screening at least in the first trimester of pregnancy, and some states mandate screening later in pregnancy and at delivery.[9] Due to the increasing rates of syphilis and congenital syphilis nationally and in Rhode Island, Rhode Island recently outlined new testing guidance.[10] All pregnant people should continue to be tested for syphilis at the first prenatal encounter. Pregnant people at high risk of infection should have repeat testing at 28–32 weeks and at delivery.[10] This includes pregnant people with individual risks of infection outlined above, as well as those individuals living in Providence, Kent or Newport counties, which have exceeded the rate of primary and secondary syphilis of 4.6 per 100,000, which is considered a threshold for consideration as a high prevalence community.[10] If the partner tests positive for syphilis at any time, the pregnant person should be tested again as soon as possible.[10] Pregnant people who have not been tested in pregnancy or who experience a stillbirth after 20 weeks of gestation should be tested at delivery. Fetal and placental tissue should be tested as well.[10] Cases of syphilis in pregnancy should be reported to Rhode Island Department of Health (RIDOH) and care coordination can be initiated by calling 401-222-2577.[10]

Pregnant persons may continue to have exposures that place them at risk for syphilis acquisition throughout pregnancy. Negative first trimester screening does not, therefore, eliminate the possibility of congenital infection and clinicians should remain vigilant. Furthermore, data suggest that a substantial proportion of women with pregnancies affected by congenital syphilis do not report any high-risk behaviors.[1,5,11,12] The approach of selectively screening based on presumed risk factors in the third trimester may therefore result in missed infections.

SYPHILIS DISEASE PRESENTATION IN PREGNANCY

During pregnancy, the clinical presentation of syphilis does not differ from the presentation outside of pregnancy. Syphilis is classified into stages, and management is based on the stage of disease at presentation.[8] Primary syphilis is characterized by one or more painless chancres (i.e., similar to an ulcer) at the site of inoculation. These typically appear within three weeks of exposure and will resolve even without treatment. Subsequently, the secondary stage manifests as a systemic illness with clinical findings that may include fever, fatigue, generalized lymphadenopathy, pharyngitis, rash, mucocutaneous lesions, condyloma lata, or alopecia. Symptoms typically present one to two months following the primary chancre.[8] Many may not notice a painless chancre. A common presentation of secondary syphilis is a rash, and syphilis should be on the differential diagnosis of any patient with a compatible rash in pregnancy, and testing for syphilis should be performed. The rash can have a varied appearance, it can be maculopapular, and can involve the palms of the hands and soles of the feet but may not involve those areas. A low threshold for syphilis testing in any pregnant patient with a rash is a reasonable approach. Without treatment, secondary syphilis symptoms will also resolve, which may decrease the chance that a patient will seek care for the symptoms, or further evaluation by a provider. The next stage of syphilis is the latent stage (where the patient is asymptomatic but serologic testing will remain positive). Latent infection of less than a year is considered early latent disease. Beyond one year, asymptomatic infection is described as late latent. Patients may have recurrent secondary syphilis if untreated and 30% of untreated patients go on to develop tertiary disease, and often decades after initial infection. Clinical findings may include gumma formation (granulomatous growths which destroy tissue in skin, bones, other organs) and cardiovascular manifestations (most commonly aortitis). Neurosyphilis, caused by the invasion of T. pallidum into the central nervous system (CNS), can occur at any stage of the disease. Clinical findings of neurosyphilis are varied and may include ocular and otic anomalies and should be screened for in all patients diagnosed with syphilis since the treatment may be different.[8] According to the CDC STI guidelines, manifestations of neurologic involvement include cognitive dysfunction, motor or sensory deficits, cranial nerve palsies, or symptoms or signs of meningitis or stroke.[8]

DIAGNOSIS AND TREATMENT IN PREGNANCY

The approach to testing in pregnancy is the same as for non-pregnant patients. Testing modalities are categorized as treponemal tests (i.e., treponemal antibodies, FTA-ABS, TPPA, EIA, CIA) and non-treponemal tests (i.e., RPR, VDRL). The traditional testing algorithm starts with a non-treponemal test followed by a treponemal test if positive. The reverse testing algorithm starts with a treponemal test and reflexes to a non-treponemal test, with an additional treponemal test for discordant results between the initial treponemal and non-treponemal tests. Treponemal tests are qualitative and often remain reactive regardless of treatment. For anyone, including pregnant persons, with a known history of syphilis, testing should be conducted with a non-treponemal test (such as RPR) which is quantitative and correlates with disease activity.[8] When following disease activity, it is

important to always use the same test (RPR or VDRL) and ideally within the same laboratory.

Treatment in pregnancy is exclusively with penicillin G, given its established efficacy and safety.[8] Early infection (primary, secondary, or early latent disease) typically requires a single dose of benzathine penicillin G, while three weekly doses are recommended for patients with late latent infection or infection of unknown duration.[8] One nuance in syphilis treatment in pregnancy is that the optimal duration between doses of penicillin G when treating late latent syphilis in pregnant patients is seven days. If more than nine days elapse between doses in a pregnant patient, the whole course should be repeated. In a non-pregnant patient, up to 14 days between doses is acceptable (although not optimal).[8] Patients with a history of penicillin allergy should undergo skin testing or oral challenge and, if appropriate, desensitization as there are no treatment alternatives. Infectious disease specialist consultation is recommended in the setting of a penicillin allergy in pregnancy.[8] In non-pregnant patients, doxycycline can be used but should not be used to treat syphilis in pregnancy since penicillin G is the only known antimicrobial to be effective in treating fetal infection and preventing congenital syphilis.[8]

Adequate response to treatment can be evaluated with repeat RPR testing with an adequate treatment response being a four-fold (2 dilution, such as 1:32 to 1:8) decrease in titer 12 months after treatment (though this does not exclude neonatal infection).[8] For people diagnosed before 24 weeks gestation, titers should be repeated after at least eight weeks and again at delivery.[8] For those diagnosed after 24 weeks gestation, titers should be repeated at delivery.[8] Those diagnosed later in pregnancy will likely not achieve a four-fold decrease before the end of pregnancy; however, a sustained four-fold increase in titer could be concerning for reinfection or treatment failure and warrants evaluation.[5,8]

POTENTIAL OBSTETRIC COMPLICATIONS AND MANAGEMENT

Vertical transmission of syphilis can result in varied and severe pregnancy complications. These include spontaneous abortion, pre-term labor, intrauterine growth restriction, placentomegaly, polyhydramnios, fetal anemia, fetal hepatomegaly, nonimmune hydrops, and ascites.[1,4] Fetal abnormalities typically present after 18 to 20 weeks gestational age when the fetus can mount an immunologic response which can lead to the characteristic abnormalities.[1,13] All pregnancies affected by maternal syphilis infection require a detailed fetal anatomy ultrasound (i.e., level II ultrasound) to evaluate sequelae of intrauterine infection. A normal ultrasound, however, does not exclude congenital infection.[13,14] Infants with abnormal ultrasound results should be closely followed. Anemia and hydrops fetalis typically resolve within 30 days of maternal treatment. Resolution of placentomegaly and hepatomegaly may take up to 90 to 120 days.[13] Early screening, diagnosis, and treatment are essential to mitigate fetal morbidity and mortality.

NEONATAL EVALUATION AND MANAGEMENT

Diagnosis of congenital syphilis is challenging as maternal treponemal and non-treponemal antibodies may be passively transferred to the fetus and are not necessarily indicative of fetal infection. Diagnostic and treatment decisions are made after assessing adequacy and timing of maternal treatment, comparison of maternal and neonatal RPR, clinical features, and if indicated laboratory and radiographic results.[6] A blood sample for RPR testing should be taken directly from the baby after delivery. Cord blood samples should not be used due to maternal blood contamination at delivery, and because false negative results can occur from Wharton's jelly contamination.

Diagnosis is further complicated because infants with congenital syphilis are often asymptomatic. Symptomatic newborns may have varied symptoms including syphilitic rhinitis, rash, anemia, thrombocytopenia, hepatobiliary dysfunction, osteochondritis, periostitis, neurologic deficits, and pneumonia, that may be complicated by pulmonary hypertension.[4] Infants meeting criteria for congenital syphilis or with presumed infection should be evaluated for neurosyphilis and receive treatment with aqueous crystalline penicillin G. A pediatric infectious disease consultation is recommended to help interpret test results and determine appropriate treatment. All infants with a reactive RPR at birth should have repeat testing every two to three months until non-reactive.[1,4] For children not identified in infancy, late manifestations include ocular abnormalities, sensorineural hearing loss, Hutchinson's teeth, and bony abnormalities in the midline face or lower extremities.[1,4]

MISSED OPPORTUNITIES FOR INTERVENTION

In conclusion, syphilis has re-emerged as a significant public health concern over the last couple of decades. Children born to pregnant people with undiagnosed and untreated syphilis may experience disease progression, resulting in potentially severe and irreversible complications. Lack of prenatal care is the primary missed opportunity identified in infants with congenital syphilis, followed by inadequate treatment despite diagnosis.[15] Prevention of congenital syphilis is dependent on appropriate and timely screening and treatment of pregnant people. Accessible, timely and comprehensive prenatal care is essential to prevent congenital syphilis. Interventions to address these missed opportunities are necessary to reverse the rising incidence of congenital syphilis.

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Demographics and Clinical Characteristics of Patients with Neurosyphilis in Rhode Island

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ABSTRACT

The incidence of syphilis has been steadily rising throughout the United States over the past decade, including Rhode Island. Neurosyphilis is a manifestation of syphilis involving the central nervous system and can present with a multitude of symptoms. We evaluated all cases of syphilis at a single healthcare system in Rhode Island over a 10.5-year period and identified 33 cases of neurosyphilis (24 confirmed and 9 diagnosed clinically). Neurosyphilis was more common in females, older patients, White/Caucasian patients, and non-Latino patients. Patients with neurosyphilis confirmed by cerebral spinal fluid analysis were more likely to have a higher RPR than patients who did not have neurosyphilis. Six patients with HIV were diagnosed with neurosyphilis and were similar to those with HIV and syphilis except for lower rates of drug use. Given increasing trends, clinicians should be familiar with the diagnosis and management of neurosyphilis.

KEYWORDS: Neurosyphilis, Otosyphilis, Ocular Syphilis, HIV, Rhode Island

BACKGROUND

Syphilis is caused by the bacterial spirochete *Treponema pallidum* and is transmitted both sexually and vertically. Since 2000, there has been an increase in the incidence of primary and secondary syphilis within the United States, in addition to rising rates of congenital syphilis.[1,2] In Rhode Island (RI), there was a 382% increase in the number of infectious syphilis cases from 2012 to 2021.[3] Syphilis has a variable clinical course that is often defined by multiple stages, including primary, secondary, latent, and tertiary. Complications of syphilis include neurosyphilis, syphilis aortitis, hepatic syphilis and other atypical presentations.[4,5,6,7] Neurosyphilis is a manifestation of spirochetal invasion of the central nervous system. This can occur at any stage of infection, but often occurs within days of the initial primary infection. Approximately 1.8% of cases with early syphilis in the United States have neurosyphilis.[8] Early neurosyphilis may be asymptomatic or present with a broad range of symptoms including headache, meningismus, cranial-nerve palsies, and changes in vision or hearing. Late neurosyphilis typically presents decades after primary infection with general paresis, dementia paralytica, and tabes dorsalis; these cases may also present with neuroimaging abnormalities including cerebral gummas and medial temporal lobe enhancements.[1,8,9]

Lack of sensitivity and specificity of both serologic and cerebral spinal fluid (CSF) testing contribute to the difficulty of diagnosing syphilis and neurosyphilis, which necessitates high clinical suspicion for the disease. Sampling of the CSF via a lumbar puncture (LP) is recommended to confirm neurosyphilis.[10] Neurosyphilis is associated with elevated CSF protein (>50mg/dL2) or leukocyte count (>5 white blood cells/mm3).[11] However, neurosyphilis may be diagnosed empirically in clinical practice in some situations where a lumbar puncture may carry excessive risks.

Although late complications of untreated neurosyphilis are likely irreversible, penicillin can help to prevent further progression of neurological complications.[8,12] The treatment for latent syphilis is typically benzathine penicillin G as this has an adequate half-life required to achieve appropriate treponemocidal concentrations over the spirochete's slow dividing cycle. However, benzathine penicillin G does not sufficiently achieve treponemocidal concentrations in the CSF.[13] To treat early and late neurosyphilis, the CDC recommends aqueous crystalline penicillin G 3-4 million units IV every four hours or 18–24 million units every 24 hours as a continuous infusion for 10–14 days.[8] However, there is limited data on neurosyphilis outcomes in the United States.

This study evaluates patients diagnosed with neurosyphilis over a 10.5-year period within our health system to identify characteristics that may be associated with neurosyphilis. We compare cases of neurosyphilis diagnosed empirically or confirmed by CSF analysis and compare patients with confirmed neurosyphilis with those who were found to not have neurosyphilis upon evaluation of CSF studies.

METHODS

This is a retrospective, cross-sectional, observational study of patients who were diagnosed with syphilis with or without neurosyphilis and being managed within the Lifespan Healthcare system. Study participants were identified as patients who tested positive for syphilis (RPR, *Treponema*

antibody, and/or *Treponema pallidium* particle agglutination (TPPA)) between 1/1/2010 and 6/30/2021, were 18 years or older at the time of laboratory tests, and were receiving care in any of the Lifespan facilities in Providence, Rhode Island. Using this criteria, 692 patients were identified with a positive syphilis test during the study period.

All 692 patients were classified into five groups as: Group 1 (all patients diagnosed with syphilis in study timeframe but not neurosyphilis); Group 2 (all patients with neurosyphilis with lumbar puncture (LP) confirmation); Group 3 (all patients who were clinically diagnosed with neurosyphilis based on history alone without confirmatory CSF analysis); Group 4 (all patients with syphilis but required neurosyphilis to be ruled out via CSF analysis), and Group 0 (all patients excluded from the study). Study exclusion criteria included syphilis infection occurring outside of the study time frame (RPR reflecting treated rather than active infection), age of less than 18 at time of syphilis diagnosis, or no available information in the chart to identify if the RPR reflected an active or prior infection.

The EMR search function was used for all 692 patients for the following phrases: "syphilis", "neurosyphilis", "otosyphilis", and "ocular syphilis." Patients who had no record of these in the chart were excluded. The charts of patients with "neurosyphilis", "otosyphilis", and "ocular syphilis" were reviewed in detail for manual data collection. Detailed chart review (beyond demographic information) of the rest of the patients (those who were diagnosed with syphilis in the study timeframe but not diagnosed with neurosyphilis) was not performed.

Patients' age was calculated as of the first positive syphilis lab result date. Demographic variables including gender, race, and ethnicity were collected from the EMR. Some data items related to HIV diseases were taken from The Miriam Hospital Immunology Center Database (ICDB). Manual data collection included binary information (Yes/No) on: prior history of positive RPR, substance use, diagnoses of HIV, pre-exposure prophylaxis for HIV (PrEP) at time of diagnosis, and current or prior history of STIs (gonorrhea, chlamydia, and HCV). "Current" diagnosis of another STI was defined as a positive diagnosis within a 30-day window from the time of syphilis diagnosis. A comprehensive list of neurosyphilis-related symptoms was also collected manually. This included: fever, headache, nausea/vomiting, weight loss, fatigue, arthralgias, vision change, seizures, strokes/TIA, gait abnormalities, dementia, hearing changes, cranial nerve palsy, rash, myalgias, tremors, hair loss, and altered mental status. Laboratory results were also evaluated at the time of diagnosis to assess if hepatic transaminitis was also present (ALT >3 times the upper limit of normal). Treatment administered, and treatment outcomes were also manually collected.

Primary outcomes included incidence and prevalence of neurosyphilis, but the study also evaluated any trends amongst predisposing factors that could be associated with the development of neurosyphilis. For sub-analyses, these groups were further classified as: Group A (all patients who were diagnosed with syphilis but not neurosyphilis) and Group B (all patient diagnosed with neurosyphilis with or without LP confirmation). For second sub-analyses, all patients with neurosyphilis with LP confirmation were compared with patients diagnosed clinically with neurosyphilis without LP confirmation (Group 2 compared with Group 3). Another sub-analysis compared the patients who had neurosyphilis confirmed with an LP with those who required an LP to rule out neurosyphilis (Group 2 compared with Group 4). An additional sub-analysis compared all cases of persons with HIV (PWH) diagnosed with neurosyphilis and PWH diagnosed with other forms of syphilis.

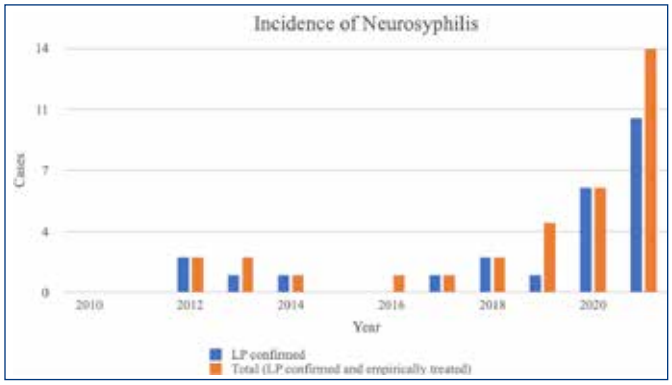
STUDY ANALYSIS

All data was summarized by using descriptive statistics. Bivariate analyses including chi-square, Fisher exact tests, or t-tests were used to assess the marginal effect of demographic and clinical variables on different outcome variables**.** Statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Software for chart reviews and manual data entry was created using MS-Access, and all graphs were created using MS Excel software. For all analyses, a P value <.05 was considered significant. The Institutional Review Board of The Miriam Hospital approved the study.

RESULTS

Out of the 692 patients with positive syphilis testing, 94 were excluded either due to lack of information in the chart, no clear diagnosis of syphilis during the study timeframe, or there was a confirmed old/treated syphilis infection as the etiology for the positive RPR. Three patients were excluded as they were younger than 18 at the time of their diagnosis. Of the remaining 598 patients with a diagnosis of syphilis during the study time frame, 8.7% (52) had

Figure 1. Incidence of neurosyphilis throughout the study time frame.



LP: lumbar puncture

symptoms concerning for neurosyphilis. Of these 52, nine patients were treated empirically for neurosyphilis without CSF analysis for confirmation (either the risks of a lumbar puncture to rule out neurosyphilis were felt to be too high or the clinical suspicion for neurosyphilis was high enough that the patient was empirically treated). Of the 43 patients who underwent a lumbar puncture, neurosyphilis was diagnosed/confirmed in 24 patients and ruled out in 19 patients. In total, 33 patients were treated for neurosyphilis and 568 were treated for non-neurosyphilis syphilis. The incidence of neurosyphilis was low until 2019, with a precipitous rise after that (**Figure 1**). The majority of these neurosyphilis cases (42.42%) occurred during the last six months of the study in early 2021.

The characteristics of patients diagnosed with either syphilis or neurosyphilis are detailed in **Table 1**. The average age of patients with syphilis was 38 years (median 33 years, range 18-100 years) compared to 53 years (median 47 years, range 18-89 years) for patients with neurosyphilis (p=0.0118). Women were more commonly diagnosed with neurosyphilis than men (OR 2.84, 95% CI 1.27–6.36), although syphilis was much more common in men overall (87.46%). Those with neurosyphilis were more likely to be White/Caucasian and less likely to be Black/African American compared to the syphilis group (p=0.0101). Neurosyphilis was more common in Non-Hispanic/Latino patients in comparison to the syphilis group (p=0.0166).

A total of 43 patients underwent a lumbar puncture to diagnose neurosyphilis (**Table 2a**, **2b**). Neurosyphilis was confirmed in 24 patients and ruled out in 19 patients. The majority of these lumbar punctures occurred during or after 2019 (31/43 (72.09%); 14/19 cases in which neurosyphilis was ruled out and 17/24 cases in which neurosyphilis was confirmed). There were no significant differences between these two groups in regard to age, gender, race, ethnicity, recent/remote STI diagnosis, HIV status, use of PrEP, drug use, or MSM status. A prior history of syphilis was more common among patients in which neurosyphilis was ruled out by CSF analysis than those for whom it was confirmed (63.16% compared to 29.17%, p=0.0258). RPR values for those with neurosyphilis were higher. Those diagnosed with neurosyphilis were more likely to have a positive CSF FTA (p=<0.0001) and VDRL (p=0.0023). CSF protein was higher in patients diagnosed with neurosyphilis (62.00 compared to 39.42, p=0.0089), but CSF glucose and WBC were not significantly different. The spectrum of presenting symptoms for the two groups are outlined in **Table 2b**. The most common symptom in Group 4 was headaches (47.36%). The most common symptoms for Group 2 were headaches and vision changes (seen in 37.50% of patients). Symptoms were more likely to fully resolve for the syphilis group compared to neurosyphilis (p=0.0045).

Among the patients diagnosed with neurosyphilis (33), nine (27.27%) were diagnosed clinically without CSF analysis (**Table 3a, 3b**). There were no significant differences between these groups except that symptom resolution after treatment was less common in the confirmed neurosyphilis group (p=0.0088). Most (29/33, 87.88%) of the patients with neurosyphilis were treated with a continuous infusion of penicillin G; the duration was usually 14 days (27/29, 93.10%) with only two patients receiving 10 days of IV penicillin G. One of the patients treated empirically received doxycycline 100mg twice daily for 30 days. One of the patients with confirmed neurosyphilis was treated with ceftriaxone 1g IV daily for 14 days; another was treated with doxycycline 200mg twice daily for 28 days; another was treated with intramuscular penicillin G weekly for three weeks followed by a 60-day course of doxycycline 100mg twice daily. The most common symptoms for those with confirmed neurosyphilis were headaches and vision changes, while the most common symptom for those treated empirically was vision changes followed by altered mental status.

A total of 177 persons with HIV (PWH) were found to be diagnosed with syphilis during the study time frame. Six

Table 1. Characteristics of patients with syphilis compared to those with neurosyphilis

Characteristics	Total	Syphilis (Group A)	Neurosyphilis (Group B)	P-Values
Total Patients	598 (100.00)	565 (94.48)	33 (5.52)	
Age (in years) at Syphilis Diagnoses				0.0118**
Mean Age [Min, Max, STD]	39 [18–100, 15]	38 [18–100, 14]	53 [18–89, 19]	
Median Age [IQR]	34 [20]	33 [19]	47 [29]	
Gender				0.0086
Male	523 (87.46)	499 (95.41)	24 (4.59)	
Female	75 (12.54)	66 (88.00)	9 (12.00)	
Race				0.0101*
Black or African American	113 (18.90)	110 (97.35)	3 (2.65)	
White or Caucasian	326 (54.52)	305 (93.56)	21 (6.44)	
All Others	159 (26.59)	150 (94.34)	9 (5.66)	
Ethnicity				0.0166*
Hispanics or Latino	157 (26.25)	151 (96.18)	6 (3.82)	
Not Hispanic or Latino	414 (69.23)	387 (93.48)	27 (6.52)	
Unknown-Others	27 (4.52)	27 (100.00)	0 (0.00)	

Race: All Others include, American Indian or Alaska (5), Asian (10), Native Hawaiian or Other (1), Other (123), Patient Refused (7), Unknown (13)
Ethnicity: Unknown-Others include, Patient Refused (11), Unknown (16)

Table 2a. Characteristics of patients who required lumbar punctures for further assessment to diagnose or rule out neurosyphilis

Characteristics	Total	Non-Neurosyphilis (Group 4)	Neurosyphilis (Group 2)	P-Values
Total Patients	43 (100.00)	19 (44.19)	24 (55.81)	
Age at Syphilis Diagnosis				0.7117
Mean [Min, Max, STD]	52 [18–89, 20]	52 [24–85, 21]	52 [18–89, 19]	
Median [IQR]	47 [34)	54 [40]	47 [25]	
Gender				0.2721*
Male	32 (74.42)	14 (43.75)	18 (56.25)	
Female	11 (25.58)	5 (45.45)	6 (54.55)	
Race				0.0882*
Black or African American	6 (13.95)	3 (50.00)	3 (50.00)	
White or Caucasian	25 (58.14)	11 (44.00)	14 (56.00)	
All Others	12 (27.91)	5 (41.67)	7 (58.33)	
Ethnicity				0.0878*
Hispanics or Latino	13 (30.23)	8 (61.54)	5 (38.46)	
Not Hispanic or Latino	30 (69.77)	11 (36.67)	19 (63.33)	
Prior Syphilis				0.0258
Yes	19 (44.19)	12 (63.16)	7 (36.84)	
No	24 (55.81)	7 (29.17)	17 (70.83)	
STI Any History				0.3195*
Yes	7 (16.28)	3 (42.86)	4 (57.14)	
No	36 (83.72)	16 (44.44)	20 (55.56)	
Any Drug Use History (Drug use + IVDU)				0.2840*
Yes	8 (18.60)	4 (50.00)	4 (50.00)	
No	35 (81.40)	15 (42.86)	20 (57.14)	
HIV				0.2578
Yes	10 (23.26)	5 (50.00)	5 (50.00)	
No	33 (76.74)	14 (42.42)	19 (57.58)	
Use of PrEP if HIV Negative				0.5581*
Yes	1 (2.33)	0 (0.00)	1 (100.00)	
No	42 (97.67)	19 (51.35)	18 (48.65)	
MSM				0.2240
Yes	17 (53.13)	6 (35.29)	11 (64.71)	
No	15 (46.88)	8 (53.33)	7 (46.67)	
Serum RPR (Median, 25th Percentile-75th Percentile)	1:16 (1:2–1:256)	1:4 (1:2–1:16)	1:128 (1:8–1:512)	<.0.0017

*Fisher's Exact Test

Table 2b. Symptoms of patients who required lumbar punctures for further assessment to diagnose or rule out neurosyphilis

	Total	Non-Neurosyphilis (Group 4)	Neurosyphilis (Group 2)	P-Values
Symptom				
Fever	3 (6.98)	1 (33.33)	2 (66.67)	
Headache	18 (41.86)	9 (50.00)	9 (50.00)	
Nausea/ Vomiting	4 (9.30)	2 (50.00)	2 (50.00)	
Weight Loss	1 (2.33)	0 (0.00)	1 (100.00)	
Fatigue	4 (9.30)	3 (75.00)	1 (25.00)	
Arthralgia	4 (9.30)	2 (50.00)	2 (50.00)	
Vision Changes	11 (25.58)	2 (18.18)	9 (81.81)	
Seizure	3 (6.98)	2 (66.67)	1 (33.33)	
Strokes/TIA	4 (9.30)	2 (50.00)	2 (50.00)	
Gait Abnormalities	8 (18.60)	3 (37.50)	5 (62.50)	
Dementia	11 (25.58)	4 (36.36)	7 (63.63)	
Hearing Changes	4 (9.30)	1 (25.00)	3 (75.00)	
Facial Nerve Palsy	1 (2.33)	0 (0.00)	1 (100.00)	
Rash	8 (18.60)	1 (12.50)	7 (87.50)	
Transaminitis	10 (23.26)	1 (10.00)	9 (90.00)	
Myalgias	5 (11.63)	3 (60.00)	2 (40.00)	
Tremors	2 (4.65)	0 (0.00)	2 (100.00)	
Hair Loss	2 (4.65)	0 (0.00)	2 (100.00)	
Altered Mental Status	9 (20.93)	4 (44.44)	5 (55.56)	
Symptom resolution after treatment				0.0045*
Resolved	15 (34.88)	8 (53.33)	7 (46.67)	
Partially Resolved	5 (11.63)	0 (0.00)	5 (100.00)	
Unresolved	20 (46.51)	10 (50.00)	10 (50.00)	
Unknown	3 (6.98)	1 (33.33)	2 (66.67)	

*Fisher's Exact Test

were diagnosed with neurosyphilis (five confirmed with CSF analysis and one diagnosed clinically). PWH were not more likely to be diagnosed with neurosyphilis compared to syphilis (OR 0.5035 (95% CI: 0.2042–1.2416); p-value 0.1294). There were no significant differences between the groups except for drug use history, with PWH with neurosyphilis being less likely to have any substance use history.

Table 3a. Characteristics of patients treated empirically for neurosyphilis compared to those with confirmed neurosyphilis

Characteristics	Total	Suspected Neurosyphilis Group 3	Confirmed Neurosyphilis Group 2	P-Values
Total Patients	33 (100.00)	9 (27.27)	24 (72.73)	
Age (in years) at Syphilis Diagnoses				0.6334*
Mean Age [Min, Max, STD]	53 [18,89,19]	55 [32,84,21]	52 [18,89,19]	
Median Age [IQR]	47 [29]	59 [33]	47 [25]	
Gender				0.2932*
Male	24 (72.73)	6 (25.00)	18 (75.00)	
Female	9 (27.27)	3 (33.33)	6 (66.67)	
Race				0.1085*
Black or African American	3 (9.09)	0 (0.00)	3 (100.00)	
White or Caucasian	21 (63.64)	7 (33.33)	14 (66.67)	
All Others	9 (27.27)	2 (22.22)	7 (77.78)	
Ethnicity				0.3454*
Hispanics or Latino	6 (18.18)	1 (16.67)	5 (83.33)	
Not Hispanic or Latino	27 (81.82)	8 (29.63)	19 (70.37)	
Prior Syphilis				0.3141*
Yes	10 (30.30)	3 (30.00)	7 (70.00)	
No	23 (69.70)	6 (26.09)	17 (73.91)	
STI Any History				0.4029*
Yes	5 (15.15)	1 (20.00)	4 (80.00)	
No	28 (84.85)	8 (28.57)	20 (71.43)	
Any Drug Use History (Drug use + IVDU)				0.3454*
Yes	6 (18.18)	2 (33.33)	4 (66.67)	
No	27 (81.82)	7 (25.93)	20 (74.07)	
HIV				0.3454*
Yes	6 (18.18)	1 (16.67)	5 (83.33)	
No	27 (81.82)	8 (29.63)	19 (70.37)	
Use of PrEP if HIV Negative				0.4091*
Yes	2 (6.06)	1 (50.00)	1 (50.00)	
No	31 (93.94)	8 (25.81)	23 (74.19)	
MSM				0.3651*
Yes	15 (62.50)	4 (26.67)	11 (73.33)	
No	9 (37.50)	2 (22.22)	7 (77.78)	
Serum RPR (Median, 25th Percentile-75th Percentile)	1:64 (1:8–1:512)	1:64 (1:16–1:512)	1:128 (1:8–1:512)	0.7544

*Fisher's Exact Test

Table 3b. Symptoms of patients treated empirically for neurosyphilis compared to those with lumbar puncture confirmed neurosyphilis

	Total	Suspected Neurosyphilis Group 3	Confirmed Neurosyphilis Group 2	P-Values
Symptom				
Fever	3 (9.09)	1 (33.33)	2 (66.67)	
Headache	11 (33.33)	2 (18.18)	9 (81.81)	
Nausea/ Vomiting	2 (6.06)	0 (0.00)	2 (100.00)	
Weight Loss	1 (3.03)	0 (0.00)	1 (100.00)	
Fatigue	2 (6.06)	1 (50.00)	1 (50.00)	
Arthralgia	3 (9.09)	1 (33.33)	2 (66.67)	
Vision Changes	15 (45.45)	6 (40.00)	9 (60.00)	
Seizure	1 (3.03)	0 (0.00)	1 (100.00)	
Strokes/TIA	2 (6.06)	0 (0.00)	2 (100.00)	
Gait Abnormalities	5 (15.15)	0 (0.00)	5 (100.00)	
Dementia	8 (24.24)	1 (12.50)	7 (87.50)	
Hearing Changes	4 (12.12)	1 (25.00)	3 (75.00)	
Facial Nerve Palsy	1 (3.03)	0 (0.00)	1 (100.00)	
Rash	9 (27.27)	2 (22.22)	7 (77.78)	
Transaminitis	10 (30.30)	1 (10.00)	9 (90.00)	
Myalgias	3 (9.09)	1 (33.33)	2 (66.67)	
Tremors	2 (6.06)	0 (0.00)	2 (100.00)	
Hair Loss	2 (6.06)	0 (0.00)	2 (100.00)	
Altered Mental Status	8 (24.24)	3 (27.50)	5 (62.50)	
Symptom resolution after treatment				0.0088*
Resolved	13 (39.39)	6 (46.15)	7 (53.85)	
Partially Resolved	6 (18.18)	1 (16.67)	5 (83.33)	
Unresolved	11 (33.33)	1 (9.09)	10 (90.90)	
Unknown	3 (9.09)	1 (33.33)	2 (66.67)	

*Fisher's Exact Test

DISCUSSION

This is among the most comprehensive studies of neurosyphilis in the state of Rhode Island. Our retrospective chart review study over a 10.5-year period identified 598 patients with a diagnosis of syphilis and 5.5% (33) with a diagnosis of neurosyphilis. The majority of these neurosyphilis cases (42.42%) occurred at the very end of the observation period, between 1/1/2021 and 6/30/2021. This is consistent with data from the RI Department of Health (RIDOH) reporting a 382% increase in the diagnosis of syphilis since 2012 to

2021, with a particularly sharp increase in 2021 with 328 cases.[3] RIDOH had noted a decrease in syphilis diagnoses in 2020 (186), although this was presumably due to less testing in the setting of the COVID-19 pandemic.

We found that most patients diagnosed with any type of syphilis were predominantly male (87.46%). This is consistent with other studies and data reported by the state health department, with almost 90% of cases of syphilis in 2017 occurring in men, especially MSM.[3,14] However, our study notably found that neurosyphilis was more common among female patients compared to men (OR 2.835). The reason for this is not clear but highlights the need for higher clinical suspicion for neurosyphilis in female patients if they are positive for syphilis. HIV is a known risk factor for development of neurosyphilis, especially in those with low CD4 counts and not on antiretroviral therapy.[15] Our study interestingly found that patients with HIV were not more likely to be diagnosed with neurosyphilis. However, we had a rather low sample size of six patients (18.12% of 33 patients with neurosyphilis). HIV viral loads and CD4 counts were not recorded, but it is possible that the cohort of PWH diagnosed with syphilis were mostly well controlled on antiretroviral therapy, reducing the risk of progression to neurosyphilis. Further analysis of this data should be pursued.

Neurosyphilis can present with a variety of symptoms and can be misdiagnosed as a different neurologic disorder in the absence of high clinical suspicion.[16] In the setting of marked increases in the incidence of syphilis and neurosyphilis over the past few years, further attention is required to identify which patients may be at an increased risk for progression of syphilis to neurosyphilis especially as it can even in the early phases. Otosyphilis was rare with hearing changes only noted in two patients (one treated empirically and another diagnosed by lumbar puncture). Ocular syphilis was more frequent with vision changes reported in 45.45% (15/33), with much higher frequency among the group treated empirically for neurosyphilis (6/9). It should be noted though that CSF examination to diagnose neurosyphilis is not typically recommended if the presenting symptoms are ocular or otic in nature, as approximately 30% of persons with ocular syphilis and at least 30% of persons with otic syphilis will have normal CSF findings.[17,18]

The goal of treatment is to prevent progression of neurologic damage and hopefully reverse symptoms. However, some symptoms of neurosyphilis may remain permanently, especially dementia, tabes dorsalis, and ocular and otic symptoms.[12,19,20] We noted that 39.39% of patients diagnosed with neurosyphilis had full resolution of symptoms, but that 18.18% had only partial improvements and 33.33% had no improvements. Notably, patients who had neurosyphilis confirmed by CSF studies seemed to have poorer outcomes than those diagnosed empirically. This difference could be due to possible overdiagnoses of neurosyphilis among the group diagnosed empirically. Roughly 44% of patients who underwent lumbar puncture to evaluate neurosyphilis were ultimately found to not have neurosyphilis and treated instead for latent syphilis.

After treatment, it is recommended to monitor serum RPR titer to ensure that it decreases four-fold or becomes nonreactive within 12 months as adequate treatment.[8,13] Of note, the response to treatment by serial RPR of syphilis without presumed neurosyphilis can sometimes lead to more diagnostics and diagnosis of neurosyphilis (if RPR does not adequately decrease). This was the case for the PWH who was treated empirically for neurosyphilis in our study; their RPR did not adequately improve after treatment for latent syphilis so they were treated empirically for neurosyphilis after declining a lumbar puncture due to anxiety. This study did not evaluate whether serial RPR titers improved after treatment for neurosyphilis, so it is not possible to assess whether a persistence of symptoms had any association with persistently elevated RPR values. However, none of the patients treated for neurosyphilis were later diagnosed with treatment failure.

Our study has several limitations. We did not perform detailed chart reviews of all patients with syphilis as this was outside the scope of our study. We subsequently were not able to compare certain characteristics of these patients (like drug use, sexual partners, use of PrEP) to those with more detailed chart review. While we were able to identify that the patients were diagnosed with syphilis during the study time frame, we relied on the first date of the syphilis serologic testing to determine the age of diagnosis and were unable to identify cases of re-infection. This likely underestimates the incidence of syphilis in Group 1. Notably though, there were no cases of neurosyphilis re-infections in Groups 2 or 3. Despite these limitations, this remains one of the most comprehensive reviews of neurosyphilis in Rhode Island to date.

In summary, cases of syphilis and neurosyphilis are increasing across the United States, including in Rhode Island. The etiology for this is still unclear. While the most significant increases were seen over the most recent years during the COVID-19 pandemic, data from RIDOH indicates that the rise appeared to begin before the onset of the pandemic. It is possible that there has been increased vigilance for neurosyphilis (as demonstrated by the overall increase in lumbar punctures performed to investigate neurosyphilis from 2019 onward) and that perhaps cases of neurosyphilis were previously being underdiagnosed. Further evaluation is also needed to determine if perhaps there may be a more neurotrophic strain of syphilis circulating within Rhode Island. This study highlights the importance for an ongoing need to maintain high clinical suspicion for neurosyphilis in patients who present with neurologic symptoms with a new diagnosis of syphilis.

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Achieving Top National Mpox Vaccination Coverage for Gay, Bisexual, and Other Men Who Have Sex with Men in Rhode Island: The Critical Role of Community Engagement, Public Health Collaboration, and Health Equity

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ABSTRACT

Since 2022, mpox (formerly known as monkeypox) has emerged as a sexually-associated infection that disproportionately impacts gay, bisexual, and other men who have sex with men (GBMSM). Fortunately, the JYNNEOS vaccine, which was initially developed for smallpox, has demonstrated significant efficacy against mpox and was distributed across the United States. In January 2024, the Centers for Disease Control and Prevention (CDC) reported that Rhode Island ranked first among the 50 states for rates of full vaccination coverage (two doses) against mpox among people at increased risk including GBMSM, and second among the 50 states for rates of partial vaccination (single dose).[1] The Rhode Island Department of Health (RIDOH), in partnership with other state agencies, clinicians, and community-based organizations, succeeded in rapid outbreak response focusing on community engagement and health equity to address the mpox epidemic.

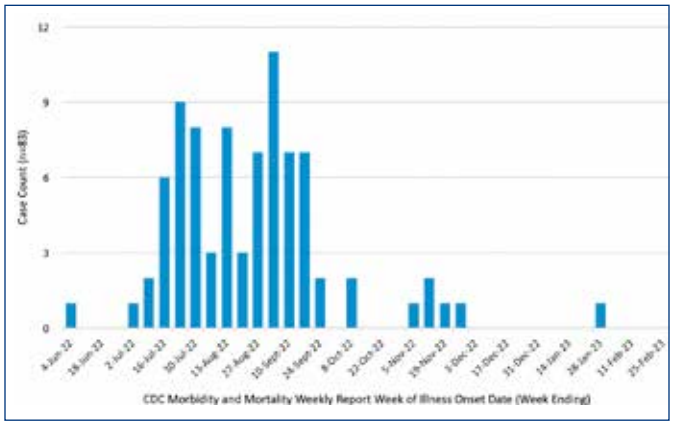
KEYWORDS: Mpox, Health Equity, Vaccination, Community Engagement, Gay, Bisexual, and other Men Who Have Sex with Men

BACKGROUND

In May 2022, a worldwide outbreak of mpox began in Europe, spreading to 113 countries and affecting more than 93,000 people.[2] Mpox is characterized by the emergence of pox lesions. Fever and systemic symptoms may follow with severe cases involving the oropharynx and the central nervous system. Mild cases resolve with supportive care, while more severe cases can be treated with tecovirimat (TPOXX). During this outbreak, mpox was found to be spread largely through sexual/intimate contact, with most cases occurring among gay, bisexual, and other men who have sex with men (GBMSM).

The first mpox cases in Rhode Island were identified in June 2022, peaking July–September 2022 (**Figure 1**). The total number of cases reported to the Rhode Island Department of Health as of February 1, 2024 was 90.[3] Vaccination as post-exposure prophylaxis and for individuals at high risk of exposure has been recommended, utilizing an existing

Figure 1. Epidemic curve of mpox cases by week of illness onset, Rhode Island, June 2022–February 2023



smallpox vaccine, JYNNEOS, administered in a two-dose series over 28 days. The effectiveness of the JYNNEOS vaccine in preventing mpox disease has been demonstrated to be 35% to 75% after one dose and 66% to 85% after two doses.[4,5] Initial efforts to vaccinate individuals at high risk of mpox exposure were hampered by significantly limited supplies and high demand. Once a limited supply of vaccine was announced for those at highest risk, RIDOH started planning for and established a system of public vaccination clinics using existing collaborations with hospitals, health centers, and contracted vendors.

RIDOH's Center for Emergency Preparedness and Response and Center for Preventive Services have significant experience planning, staffing, supplying, and executing public vaccination clinics with little lead time. This infrastructure and support from key healthcare partners quickly launched a successful vaccination campaign. Using technology developed during Rhode Island's COVID-19 response, RIDOH created an mpox Vaccine Interest Notification List, prompting interested individuals to receive text message or email notifications when the vaccine was available. An online clinic and appointment management software (also acquired during the COVID-19 response) was used to coordinate clinics. Vaccination administration data were transmitted to the Rhode Island Child and Adult Immunization Registry and these data informed vaccine distribution decisions.

Figure 2. Example of RIDOH advertisement on GBMSM dating sites.

RIDOH adopted a health equity framework for the mpox campaign development to identify groups for targeted outreach and vaccination access, including GBMSM and gender-diverse individuals, individuals living with HIV, people facing housing instability, people who use drugs, communities of color, and individuals who exchange sex for money. Reaching these groups and the broader vaccine-eligible populations was achieved through partnerships with community organizations, including AIDS Care Ocean State (ACOS), AIDS Project Rhode Island (APRI), and Project Weber/RENEW.

An important early step was to raise targeted awareness of mpox risk and the need for vaccination among GBMSM, given that this group has historically experienced societal stigma and discrimination.[6] A comprehensive community engagement and communications plan was created with guidance from an mpox community advisory group formed by APRI. Special efforts were needed to avoid stigmatizing language and images in campaign materials (see **Figure 2**), encourage low-risk sexual behaviors without appearing "preachy," identify trusted spokespeople, and address privacy and confidentiality concerns.

The Miriam Hospital Infectious Diseases and Immunology Center was the first Rhode Island location to treat mpox cases with TPOXX and offer post-exposure vaccination and routine vaccination protocols for its at-risk patients. Post-exposure prophylaxis (PEP) for mpox can be given with the mpox vaccine, JYNNEOS, to people with known or presumed exposure to the mpox virus. Ideally, when used as mpox PEP, one dose of the mpox vaccine should be given as soon as possible, with protection possible from days 4 through 14 after exposure. The standard regimen for routine vaccination with JYNNEOS for pre-exposure prophylaxis is a two-dose series administered 28 days apart.

Open Door Health (an LGBTQ+ health center), Thundermist Health Center, and Tri-County Community Health Center soon established clinics. RIDOH's contracted vaccination and emergency response force multipliers, including the Rhode Island Medical Reserve Corps and The Wellness Company, conducted 44 public clinics.

RIDOH created a webpage about GBMSM sexual health, highlighting mpox information. During the initial campaign period, this webpage received 35,000 page views. Advertising on GBMSM dating apps was the primary strategy for raising mpox awareness. The most popular advertisement resulted in a 42% click-through rate, compared to an average 1.2% click-through rate for public health campaigns.

Other innovative communications methods included a text-messaging system encouraging people who received one dose of vaccine to complete their series as well as displaying video advertisements in cinemas during the run of *Bros* and *Wakanda Forever*, among other PG-13 and R-rated films. Advertisements encouraged moviegoers to scan a QR code to learn about mpox and schedule a vaccination appointment. Advertising materials were prepared in English and Spanish featuring images of people representing diverse backgrounds.

A key response feature was conducting large- and small-scale mpox public vaccination clinics in various community settings. Locations were selected to reduce stigma, maximize access, and respond to diverse preferences among GBMSM and other eligible individuals. Locations included Rhode Island College, AAA of Southern New England, Beneficent Church, Providence Gay Flag Football League games, Drag Bingo, and high-risk venues. A total of 6,220 doses of JYNNEOS vaccine were administered in Rhode Island as part of the campaign (**Table 1**). As of January 2024, the CDC reports that 62% of Rhode Island's target population received one dose, and 46% received two doses (fully vaccinated) of JYNNEOS.[1]

Table 1. Doses of Mpox Vaccine Administered by Clinic Setting, Rhode Island, June 10, 2022–January 31, 2024

Setting	Mpox Vaccine Doses Total = 6,970	Percent
Community-based	3,420	50%
Open Door Health	1,142	16%
The Miriam Hospital Immunology Center/Rhode Island Hospital ED	1,006	14%
Tri-County Community Health Center	386	5%
Thundermist Health Center	204	4%
Other	62	1%
Out of State	750	10%

In conclusion, many aspects of Rhode Island's nation-leading mpox outbreak response can inform future infectious disease outbreaks: (1) a non-stigmatizing education campaign informed by community engagement; (2) a nimble infrastructure for rapid establishment of public vaccination clinics; (3) existing collaboration with community and advocacy groups, and (4) strong support from local healthcare professionals. With this experience, RIDOH will remain a national leader in responding to emerging public health threats.

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Implementing a Community-Based LGBTQ+ and Sexual Health Program in Providence, Rhode Island

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ABSTRACT

BACKGROUND: Lesbian, gay, bisexual, transgender, and queer (LGBTQ+) communities experience significant health disparities related to sexual health, including sexually transmitted infections (STIs). Improved access to culturally congruent primary care and sexual health services, including HIV/STI prevention and care, are needed. We describe how we developed a new community-based LGBTQ+ primary care clinic and implemented safety-net sexual health and STI screening and care services in Providence, Rhode Island.

METHODS: Open Door Health in Providence, Rhode Island, was started in 2020 to improve access to HIV/STI care and prevention services, primary care, and gender-affirming care for the LGBTQ+ community. We reviewed demographics and behaviors of patients presenting for STI screening services from February 2021 to October 2023 at the clinic. Bivariate and multivariate analyses were used to evaluate demographics and behaviors among patients testing positive for HIV and other STIs.

RESULTS: A total of N=1,633 people presented for STI screening. Of these, 56% were 30 years or younger, 65% identified as male, 24% as female, and 9% as non-binary or gender diverse. Forty-three percent were MSM, 19% were Black/African American (B/AA), and 22% were Hispanic/Latino (H/L). Seventy-one percent reported two or more partners in the last three months. The prevalence of STIs was 22.3% (4.4% syphilis, 7.5% gonorrhea, and 9.7% chlamydia). Those who tested positive for an STI were more likely to be B/AA (23.3% of B/AA individuals versus 15.9% of White, $p<0.05$), H/L (23.1% versus 17.4%, $p<0.05$), and MSM (25% versus 16.9%, $p<0.05$).

CONCLUSION: Open Door Health provides important safety-net STI services for the LGBTQ+ community. Individuals presenting for services had a high prevalence of HIV/STIs. Improved approaches are needed for HIV/STI care and prevention in this group, including among B/AA and H/L communities.

INTRODUCTION

Lesbian, gay, bisexual, transgender, and queer (LGBTQ+) communities experience significant health disparities in the United States.[1] Among these, gay, bisexual, and other men who have sex with men (MSM) and transgender women (TGW) are disproportionately impacted by HIV and other sexually transmitted infections (STIs). Bacterial STIs such as syphilis, gonorrhea, and chlamydia have significantly increased across the United States. In 2022, there were approximately 2.5 million cases reported to the Centers for Disease Control and Prevention (CDC).[2] STIs also disproportionately impact people of color, including African American/Black (AA/B) and Hispanic/Latino (H/L) populations.[2] Novel approaches are required to enhance healthcare access and combat the rising burden of STIs within the LGBTQ+ community in the United States.

The LGBTQ+ community encounters numerous barriers to accessing healthcare services, including lack of healthcare access, stigma, discrimination, homophobia, and a shortage of culturally tailored services.[3] Stigma and discrimination is even more pronounced among AA/B and H/L MSM.[4] This results in suboptimal HIV/STI care and prevention outcomes, including less HIV/STI testing, limited awareness and education about HIV/STIs, and suboptimal access to biomedical prevention interventions such as HIV pre-exposure prophylaxis (PrEP). Improved access to culturally competent primary care and sexual health services, including HIV/STI care and prevention, are needed.

With support from the Executive Office of Health and Human Services (EOHHS) and the Rhode Island Department of Health (RIDOH), and with a groundswell of community support, Open Door Health was opened in March 2020. Open Door Health began offering primary care, gender-affirming care, sexual health services, including walk-in appointments. Despite the initial challenges of the COVID-19 pandemic, the clinic became an immediate success in providing primary and gender-affirming care, as well as HIV/STI care and prevention services to the entire state. The clinic is supported by diverse funding streams, including clinical billing, 340B revenue, grants, and private philanthropy. This ensures that care is provided to every person who walks through the door regardless of one's ability to pay. Staff and medical providers prioritize creating a welcoming and affirming environment for all patients. To date, Open Door Health has

provided care to over 8,000 unique patients. Although many identify as part of the LGBTQ+ community, the clinic provides care to all regardless of background.

We review demographics and behaviors of individuals presenting to Open Door Health for STI screening services.

METHODS

Open Door Health is the only community-based LGBTQ+ clinic in the state of Rhode Island. All individuals presenting for HIV/STI testing complete a clinical intake form which includes demographics, behavioral risk factors, and other conventional HIV/STI surveillance information. We reviewed de-identified patient data for all individuals presenting for HIV/STI testing from February 2021 to October 2023. We assessed the following data: age, sex at birth, gender, race, ethnicity, risk behaviors, state of residence, insurance status, prior HIV and STI testing, injection drug use, and number of sex partners in the last 12 months (oral, vaginal, and/or anal). Other behavioral data included sex with anonymous partner(s), alcohol or drug use during sex, sex with someone of unknown HIV status, sex with someone who exchanges sex for drugs or money, history of exchanging drugs or money for sex, having ever been forced to have sex, and prior history of incarceration. Laboratory testing reviewed included HIV (antibody/antigen testing), syphilis (treponemal and non-treponemal), gonorrhea (nucleic acid amplification testing, NAAT), and chlamydia (NAAT) results. Review of de-identified data was approved by the Brown University Institutional Review Board.

Bivariate analyses including the chi-square test were used to compare demographics and behaviors between groups. Significance was defined as alpha less than 0.05, and all reported p-values are two-sided.

RESULTS

A total of N=1,633 people presented for sexual health care during the time period (**Table 1**). Of these, 56% were 30 years or younger, 65% identified as male, 24% as female, and 9% as non-binary or gender diverse. Forty-three percent were MSM, 19% were Black/African American (B/AA), and 22% were Hispanic/Latino (H/L). Twenty-six percent reported earning $25,000 or less. Seventy-one percent reported 2+ partners in the last three months. Other behaviors associated with STI risk included condomless anal sex (11.2%), sex with an HIV-positive partner (3.3%), exchanging sex for money, drugs or other goods (5.1%), sex with someone who exchanges money, drugs or other goods (6.6%), sex while intoxicated (39.9%), sex with an anonymous partner (33.3%), history of incarceration (5.2%), methamphetamine use (1.8%) and ever injecting drugs (2.2%) (**Table 2**).

The prevalence of STIs was 22.3% (4.4% syphilis, 7.5% gonorrhea, and 9.7% chlamydia). Those who tested positive for an STI were more likely to be B/AA (23.3% of B/AA individuals versus 15.9% of White individuals were STI positive, $p<0.05$), H/L (23.1% H/L versus 17.4% non-H/L, $p<0.05$), and MSM (25% MSM versus 16.9% non-MSM, $p<0.05$).

DISCUSSION

Since opening in 2020, Open Door Health has provided important safety-net services for LGBTQ+ individuals, including sexual health and STI care and prevention. Open Door Health is the first and only clinic dedicated to providing LGBTQ+ services as the core function of its clinical mission. In addition, Open Door Health also focuses on research, education/training, and public health, which distinguishes it from other organizations in the state and region. Open Door Health provides primary care, gender-affirming care, HIV care and prevention including PrEP, Hepatitis C Virus (HCV) management, and STI care and prevention. The clinic also includes an anal health program and offers high-resolution anoscopies. In this analysis, individuals presenting to the clinic for HIV/STI testing had high positivity rates, particularly among MSM and B/AA and H/L communities. These findings highlight the significant disparities that exist among the LGBTQ+ community and communities of color. Improving and ensuring access to primary care, gender-affirming care, and HIV/STI care and prevention is critical for the LGBTQ+ community in Rhode Island and elsewhere.

LGBTQ+ individuals may experience significant challenges successfully engaging with the healthcare system, including stigma, lack of culturally tailored services, and limited access to health care services. LGBTQ+ individuals have highlighted that a lack of culturally competent knowledge and affirming care among providers contributes to perceived stigma within the healthcare landscape.[5] As a result, patients may question whether to disclose their sexual identity to a healthcare provider.[6] A unique challenge for LGBTQ+ patients is accessing comprehensive care for basic health needs. Often, patients must visit multiple providers to fulfill these needs, highlighting the importance of establishing comprehensive, integrated healthcare settings tailored to the needs of LGBTQ+ individuals. Creating a "one-stop-shop" setting for LGBTQ+ health services is ideal to address this challenge.[7] Inconsistent insurance coverage exacerbates these challenges, particularly for sexual and gender minorities.[8] Open Door Health works to achieve cultural competency by providing training and education to providers and staff with the goal of increasing cultural awareness, knowledge and skills; hiring staff who reflect the community the clinic serves; providing interpreter services; patient navigators to help facilitate care; and promoting culture-specific attitudes and values at the organization.

In addition, our results highlight STI disparities across race and ethnic groups. B/AA and H/L communities are more likely to experience social and structural barriers that

Table 1. Demographics of Individuals Presenting for Sexually Transmitted Infection (STI) Testing

			ANY STI					
	Total (All)		Positive[1]		Negative		Missing	P-Value
	%	N	%	N	%	N	N	
Total	100	1,633	22.3%	297	77.7%	1,033	303	
Age								0.161
<25	24.2%	395	27.6%	82	22.0%	227	86	
25–30	31.6%	516	31.7%	94	32.2%	333	89	
31–40	29.2%	477	28.3%	84	31.2%	322	71	
41–50	8.7%	142	8.8%	26	8.3%	86	30	
>50	6.3%	103	3.7%	11	6.3%	65	27	
Sex at Birth								0.000
Male	68.5%	1,118	83.1%	246	66.8%	679	193	
Female	29.3%	478	15.9%	47	32.4%	329	102	
Other or Unknown	0.8%	13	1.0%	3	0.9%	9	1	
Missing	1.5%	24		1		16	7	
Gender								0.000
Man	64.8%	1,058	81.9%	240	63.0%	635	183	
Woman	24.3%	397	15.0%	44	26.1%	263	90	
Non-binary or gender diverse	8.6%	141	3.1%	9	10.9%	110	22	
Other or Unknown	2.3%	37		4		25	8	
Race								0.008
Black/African American	19.4%	317	29.3%	74	22.6%	193	50	
White	51.6%	842	53.0%	134	63.7%	545	163	
Other	12.1%	198	17.8%	45	13.7%	117	36	
Missing	16.9%	276		44		178	54	
Ethnicity								0.023
Non-Hispanic/Latino	69.4%	1,133	70.4%	197	77.0%	723	213	
Hispanic/Latino	22.0%	359	29.6%	83	23.0%	216	60	
Missing	8.6%	141		17		94	30	
Sexual Orientation								0.000
Same-sex	35.3%	577	29.3%	87	36.5%	377	113	
Straight	39.1%	475	42.1%	125	26.3%	272	78	
Other	35.6%	581	28.6%	85	37.2%	384	112	
MSM								0.002
Yes	43.1%	703	71.5%	176	60.4%	410	117	
No	25.4%	415	28.5%	70	39.6%	269	76	
Missing and assigned female at birth	31.5%	515		51		354	110	
Household Income								0.110
More than $100,000	10.3%	168	12.3%	27	14.1%	111	30	
$50,001–$100,000	20.5%	335	25.9%	57	27.9%	219	59	
$25,001–$50,000	19.2%	313	22.3%	49	27.0%	212	52	
$25,000 or less	25.7%	419	39.6%	87	31.0%	243	89	
Missing	24.4%	398		77		248	73	

MSM=Men who have sex with men (Defined as born male sex, sex with at least one reported male sex partner)
[1]Some ppl tested positive for more than one type of STI

Table 2. Behaviors of Individuals Presenting for Sexually Transmitted Infection (STI) Testing

			Any Sti					
	Total (All)		Positive		Negative		Missing	P-Value
	%	N	%	N	%	N	N	
Total	100	1,633	22.3%	297	77.7%	1,033	303	
Total Sex Partners (Last Three Months)								0.000
0	3.3%	53	2.0%	6	3.0%	31	16	
1	25.7%	420	17.9%	53	26.5%	274	93	
2-4	46.4%	758	41.1%	122	48.5%	501	135	
5+	24.6%	402	39.1%	116	22.0%	227	59	
Condomless Anal Sex								0.306
No	55.2%	901	85.2%	201	82.3%	547	153	
Yes	11.2%	183	14.8%	35	17.7%	118	30	
Missing	33.6%	549		61		368	120	
Sex with an HIV+ Partner								0.000
No	87.6%	1,430	92.6%	250	97.6%	918	262	
Yes	3.3%	54	7.4%	20	2.4%	23	11	
Missing	9.1%	149		27		92	30	
Exchanged sex for money/drugs/goods								0.133
No	90.5%	1,477	93.0%	265	95.2%	940	272	
Yes	5.1%	83	7.0%	20	4.8%	47	16	
Missing	4.5%	73		12		46	15	
Sex with someone who exchanges money/drugs/goods								0.179
No	89.0%	1,454	90.9%	259	93.2%	922	273	
Yes	6.6%	108	9.1%	26	6.8%	67	15	
Missing	4.4%	71		12		44	15	
Sex while intoxicated (yes/no)								0.231
No	55.9%	912	60.4%	172	56.4%	558	182	
Yes	39.9%	651	39.7%	113	43.6%	432	106	
Missing	4.3%	70		12		43	15	
Sex with an anonymous partner (yes/no)								0.011
No	62.2%	1,016	58.1%	165	66.3%	656	195	
Yes	33.3%	544	41.9%	119	33.7%	333	92	
Missing	4.5%	73		13		44	16	
History of incarceration (yes/no)								0.057
No	90.5%	1,477	92.2%	261	95.2%	942	274	
Yes	5.2%	85	7.8%	22	4.9%	48	15	
Missing	4.4%	71		14		43	14	
Injected drugs (ever)								0.072
No	93.5%	1,526	96.1%	272	98.0%	971	283	
Yes	2.2%	36	3.9%	11	2.0%	20	5	
Missing	4.4%	71		14		42	15	
Crystal Meth Use (Last 12 months)								0.000
No	98.2%	1,603	94.3%	280	99.3%	1,026	297	
Yes	1.8%	30	5.7%	17	0.7%	7	6	

contribute to higher rates of STIs.[9,10] These disparities persist in B/AA and H/L communities across the spectrum of sexual orientation and gender identity,[11] underscoring the critical need for culturally competent care across all populations. Addressing the disproportionate impact of STIs on these communities will require a multilevel approach that addresses both social and individual determinants of health.

Importantly, Open Door Health provides care to all individuals regardless of ability to pay. Out-of-pocket costs have been shown to be significant barriers to STI care and prevention. In our prior work, we demonstrated that 40% of people presenting for HIV/STI services in Rhode Island may be uninsured.[12] Those patients also reported that out-of-pocket costs were a significant concern.[12] To sustain its operation, Open Door Health leverages multiple revenue sources, including clinical billing of insurance, grant support, philanthropy, and safety-net funding sources such as 340B.[12-14] These diverse revenue sources allow the organization to provide care regardless of any individual's ability to pay. These safety net services have had high uptake among sexual and gender minorities as well as people of color.

Open Door Health's STI service structures have also been leveraged to implement new STI prevention programs. Open Door Health recently began offering STI post-exposure prophylaxis (PEP), which involves taking an antimicrobial after an STI exposure or a potential exposure. PEP can be distinguished from PrEP, which involves taking a medication before exposure. Doxycycline has been evaluated as PEP for STI prevention and is taken as a single 200mg dose ideally within 24 hours and up to 72 hours after condomless sex. In 2022, the DoxyPEP study conducted in Seattle and San Francisco demonstrated that doxycycline as PEP prevented syphilis, gonorrhea, and chlamydia in both MSM and TGW with HIV and those taking HIV PrEP.[15] Other recent studies have confirmed that doxycycline is effective as PEP in preventing bacterial STIs in MSM and TGW.[16] Studies of other populations which also include doxycycline as PrEP for STI prevention are ongoing and holds promise for expanding the toolkit for STI prevention interventions.

In conclusion, improved efforts are needed to address sexual health and the burden of STIs among the LGBTQ+ community, as well as communities of color. Open Door Health provides critical safety-net health care services for LGBTQ+ individuals in Rhode Island, including sexual health and STI care and prevention. Resources and investments in infrastructure including mechanisms to ensure sustainability of STI services for these groups are essential.

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Delayed-Onset Isolated ICI (pembrolizumab)-Associated Gastritis with Concomitant Intussusception

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ABSTRACT

Immune checkpoint inhibitors are increasingly used in the treatment of a number of malignancies and carry a known risk of immune-related adverse events (irAEs). IrAEs cover a broad range of affected organ systems and presenting symptoms. While the gastrointestinal system is a commonly affected system, isolated gastritis is an uncommon diagnosis. We present a patient with isolated ICI-related gastritis presenting with concomitant intussusception caused by the anti-programmed cell death-1 antibody, pembrolizumab.

KEYWORDS: gastritis; pembrolizumab; immune checkpoint inhibitor; immune related adverse events

INTRODUCTION

Immune checkpoint inhibitors (ICIs) are a relatively new immunomodulatory class of drugs that enact their effects by up-regulating key aspects of host immunity to improve the anti-tumor immune response. However, this up-regulation of the immune system can cause immune-related adverse events (irAEs), which can affect many organ systems but most commonly the skin and gastrointestinal tract. ICI enterocolitis is a common irAE, but there is a comparative paucity of data on isolated ICI gastritis. It is not known why ICI gastritis is rare compared to ICI enteritis. Further information on the presentation, diagnosis, and treatment of ICI gastritis will enable more expeditious diagnosis and management for these patients.

CASE REPORT

A 55-year-old woman with adenocarcinoma of the lung and recently on pembrolizumab therapy (anti-PD1, 200 mg every three weeks, from 10/2/2023–5/20/24) presented with subacute month-long nausea, vomiting, inability to tolerate PO, and weight loss. Her initial workup was notable for CT abdomen/pelvis with a small bowel intussusception in the left lower quadrant measuring up to 6.6 cm.

An upper endoscopy was performed and showed universal erosive, ulcerative, and hemorrhagic gastritis with oozing blood and friability in the antrum and fundus. Gastric biopsy results showed diffuse severe active and erosive gastropathy with diffuse severe loss of epithetical elements compatible with ICI-induced effect.[5] The biopsies were negative for dysplasia, malignancy, and Heliobacter pylori. Of note, histology found a completely destructed mucosa in the cardia, fundus, and antrum with entirely absent vital epithelial glands. Furthermore, parietal cells were completely absent in the gastric body.

In conjunction with the gastroenterology consult team and the patient's outpatient oncologist, the patient was diagnosed with ICI gastritis and was started on a trial of IV steroids with prolonged oral taper, similar to previously described treatments of ICI enterocolitis. She was also followed by the general surgery consult team for her intussusception; operative management was deferred. Her symptoms improved on a prolonged steroid treatment course and discontinuation of pembrolizumab.

DISCUSSION

ICI gastritis has been previously described in the literature, but it remains an uncommon diagnosis. In prior studies, gastritis represented only approximately 5% of all GI luminal irAEs.[1] Other studies have reported the overall incidence of ICI-related gastritis to be 0.35–1.46%.[2] Overall, isolated ICI-related gastritis is less common – a retrospective study found that 70% of patients had concurrent ICI enteritis/colitis, and only 30% of patients with isolated gastritis.[1]

There does not appear to be a higher prevalence of ICI gastritis based on sex.[1,5] There is an increased risk of ICI gastritis in patients with pre-existing gastroesophageal and liver disorders, such as gastroesophageal reflux disease.[2] Risk of irAE in general is associated with preexisting autoimmune disease and chronic use of drugs including proton pump inhibitors, diuretics, and anti-inflammatory drugs.[3] It is recommended to obtain a thorough medication history to evaluate for past medications that could have damaged the stomach in patients with ICI-related gastritis.[2] In addition, the median time from ICI initiation to onset of gastritis is variable. One study found the timeline to be 3.4 months,[1] while another study found that the median time to onset was 29.3 weeks (6.7 months).[2]

It is difficult to diagnose ICI-related gastritis based on symptoms alone.[4] Thus, endoscopic findings as well as biopsy and pathologic diagnosis are very important. One

retrospective study found that common patterns of inflammation in ICI gastritis include chronic active gastritis, reactive gastropathy, and focally enhanced gastritis.[5] Another retrospective study similarly found that the two main patterns of injury were a chronic gastritis pattern and a focal-enhancing pattern of injury.[1] Another study found peri-gland gastric inflammation was best correlated for patients with GI-irAE.[6] Common endoscopic findings included erythema, edema, and friability.[5]

Our case is interesting in that the histology was described as "universal erosive, ulcerative and hemorrhagic gastritis." The diffuse histological changes are different from previous reporting that describes focal changes as more characteristic. Of note, our patient failed conservative management, which included discontinuing pembrolizumab as well as symptomatic management including ondansetron, pantoprazole, scopolamine, and sucralfate. During this time, the patient reported an unintentional 15 lb. weight loss. The time to onset of symptoms from starting ICI therapy was nine months for this case, which is longer than the median time reported in the above studies. Thus, suspicion for ICI-related gastritis must remain high for patients on ICI therapy even if they had previously been tolerating treatment well over the course of many months. For improvement of symptoms, there was a need for treatment with steroids. The steroid taper was formulated based on guidelines for ICI enterocolitis,[7] as guidelines do not currently exist for the treatment of isolated ICI-related gastritis. Our patient was also started on high dose proton pump inhibitor therapy, for both symptom management and GI prophylaxis. Of note, while there is a risk of adverse gastrointestinal effects associated with steroids, this adverse effect is generally not associated with steroid use alone but with concurrent steroid and non-steroidal anti-inflammatory drug use.[8]

Interestingly, our patient presented with concurrent intussusception. The relationship between ICI therapy and the intussusception remains unclear and this was managed conservatively in our patient.

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The Embryonal Body: Pathognomonic in Mixed Testicular Germ Cell Tumors

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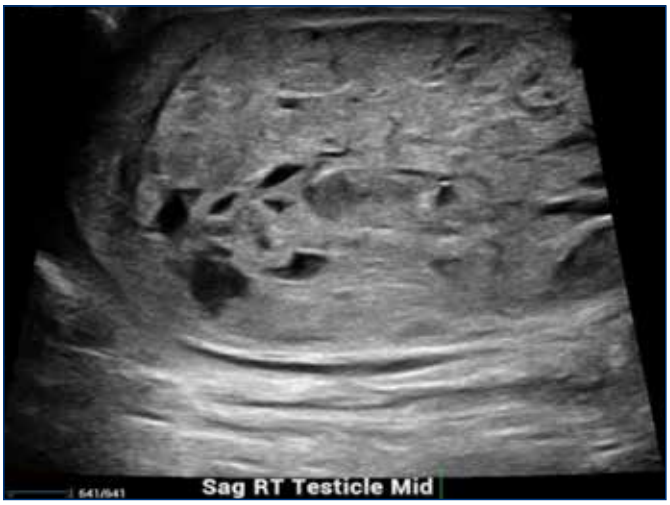
OBJECTIVES

We present the characteristics of pathognomonic images of an "embryonal body" in a patient with testicular germ cell tumor (GCT).

CASE PRESENTATION

A 26-year-old male with no family history of testicular cancer presented with right groin pain and associated firm, enlarged right testicular mass for one month. Scrotal ultrasound showed a 5.6 x 5.4 x 3.6 cm heterogeneous, mixed hypoechoic cystic and solid mass with internal vascularity replacing the entire right testicle (**Figure 1**). Serum tumor markers were elevated, and he underwent right radical orchiectomy. Pathology resulted as mixed GCT: 30% Embryonal Carcinoma (EC), 30% yolk sac tumor (YST), and 40% teratoma. Post-operatively, he was staged at Stage IA (pT1N0M0S0) with no evidence of metastatic disease in the chest, abdomen, or pelvis on imaging and normal tumor markers. He is now on surveillance.

Figure 1. 5.6 x 5.4 x 3.6 cm heterogeneous, hypoechoic cystic and solid mass with internal vascularity nearly replacing the entirety of the right testicle.



DISCUSSION

Testicular cancer is the most common tumor in men aged 20–40.[1] Diagnosis involves physical examination and testicular ultrasound, supplemented by serum tumor marker including B-HCG, AFP, and LDH. Radical inguinal orchiectomy is the gold standard. For cases confined to the testis, adjuvant treatments include single-dose chemotherapy or radiotherapy for seminomas, or several cycles of chemotherapy vs. primary retroperitoneal lymph node dissection (RPLND) for non-seminomatous germ cell tumors (NSGCT). Most patients undergo surveillance following Stage I GCT. The five-year survival rate for stage I GCT reaches 97–99%.[2]

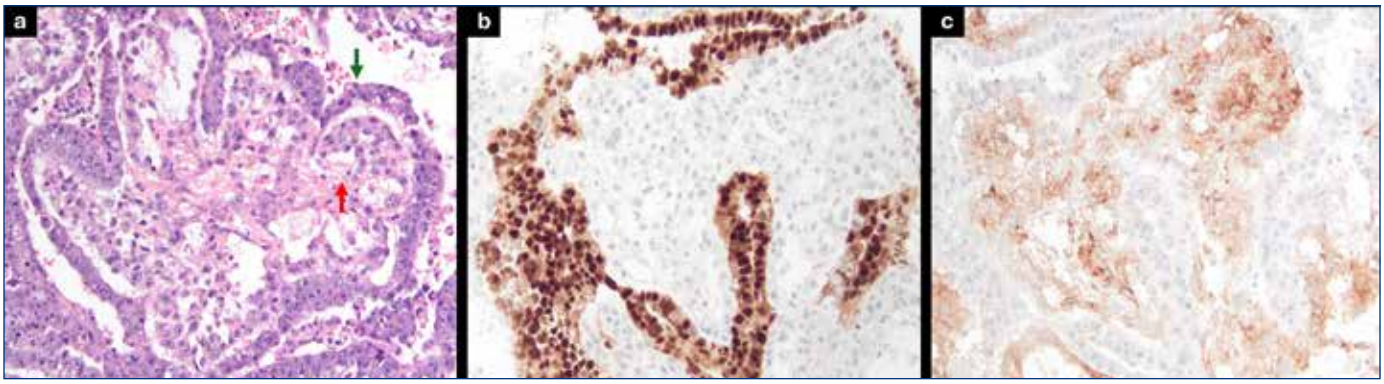
Within the NSGCT subtypes (EC; YST; Teratoma; choriocarcinoma), EC is known to be poorly differentiated and with high rates of metastasis. EC consists of undifferentiated malignant cells resembling primitive epithelial cells with crowded pleomorphic nuclei.[3] (**Figure 2A**). Grossly, EC exhibits areas of hemorrhage and necrosis. The microscopic appearance varies, and may grow in solid sheets or in papillary, glandular-alveolar, or tubular patterns. The presence and proportion of EC is associated with increased risk of occult metastases in clinical stage I NSGCT. Immunohistochemically, EC stains positive for: AE1/AE3, PLAP, and OCT3/4 and negative for c-Kit.[4] (**Figure 2A**)

YST often occurs in pediatric tumors and primary mediastinal cases[5] but is less common in primary adult testicular GCT than other subtypes.[6] Pure YSTs produce AFP but not HCG. Mixed GCTs include elements of YST, consisting of a reticular network of cuboidal cells with cytoplasmic and extracytoplasmic eosinophilic, hyaline-like globules, (**Figures 2A,C**). YSTs grow in glandular, papillary, or micro-cystic patterns, with the classic pathologic "Schiller-Duval bodies" in roughly 50% of cases.[7]

Embryonal bodies (**Figures 2A–C**) present as a minor component of mixed GCTs. Microscopically they appear as a hyperchromatic disc of EC with YST admixed. The EC cells have amphophilic cytoplasm and high-grade nuclei while the surrounding YST cells have variable pattern-dependent cytological atypia.[8]

Teratoma contains elements of two or more of intermixed three germ cell layers: endoderm, mesoderm, and ectoderm, often intermixed. Most tumors have solid and cystic areas. Approximately 50% of adult mixed GCTs contain a component of teratoma.[3]

Figures 2A–C. [**A**] Pathognomonic architecture of the Embryonal Body, highlighting the uniquely organized arrangement of YST (red arrow) and EC (green arrow) in the periphery, forming an embryonal body. [**B**] Octamer binding transcription factor 3/4 (OCT3/4) highlights embryonal cells with strong nuclear and diffuse cytoplasmic reactivity. Positive embryonal cells in the periphery contrast with negative yolk sac cells centrally. [**C**] Yolk sac cells present diffuse cytoplasmic Glypican 3 reactivity, contrasting with peripheral negative embryonal cells. Positive foci within embryonal bodies or EC reflect differentiation into yolk sac tumor.



In conclusion, our case demonstrates a distinctive pathognomonic histologic finding of the "embryonal body" in a testicular mixed germ cell tumor.

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Lead Level ≥5 μg/dL and Neurodevelopmental Outcomes of Preterm Infants at Five Years of Age

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ABSTRACT

INTRODUCTION: Prior studies have not examined blood lead levels (BLL) in the preterm population relative to their developmental and behavioral outcomes.

METHODS: Neonatal demographic and clinical characteristics and results on scales of intelligence, development, and behavior were compared between children born ≤32 weeks gestation (n=354) with detected lead levels in childhood of ≥5 μg/dL (n=37, 10%) and <5 μg/dL (n=317, 90%).

RESULTS: The 10% rate of BLL ≥5 μg/dL for this cohort was higher than rates previously reported for the general population, and was associated with low SES. Preterm infants with a lead level of ≥5 μg/dL were twice as likely to score in the borderline to clinical range for sleep problems on the Childhood Behavioral Checklist.

CONCLUSIONS: Robust screening and follow-up may protect against negative developmental outcomes in the setting of elevated lead levels. The association of higher lead levels with poor sleep supports continued lead screening efforts and appropriate support services for preterm children.

KEYWORDS: lead exposure, preterm infants, development, behavior

INTRODUCTION

Childhood lead exposure has been associated with cognitive, behavioral, and motor deficits throughout the life course.[1-7] Cognitive difficulties associated with lead exposure have included lower IQ, poorer information processing, and impaired attention.[5,6] Studies of the effects of lead exposure on motor development have found that exposure can cause impaired fine motor functioning, and that lead levels were inversely correlated with measures of bilateral coordination, upper limb speed, dexterity, and visuomotor functioning in young children.[5,8] Lead exposure has also been linked to a spectrum of behavioral problems including increased rates of depression, aggression, anti-social behavior and sleep problems, and may even play a mediating role within the relationship between social adversity and externalizing behaviors in children.[6]

In 2012, the Centers for Disease Control and Prevention (CDC) lowered the standard "level of concern" for lead exposure from ≥10 μg/dL to 5 μg/dL and recommended discontinuation of a designated "level of concern," as research has shown that there is no "safe" level of blood lead.[3,9] In May 2021, the CDC again updated the elevated blood lead reference value to 3.5 μg/dL. The CDC currently recommends that children with a blood lead level (BLL) ≥3.5 μg/dL be referred for follow-up, as per CDC guidance.[10] In Rhode Island, universal blood lead screening is required by law for all children by three years of age and it is recommended that all children from nine months to six years of age be screened at least once annually.[11]

Infants born prematurely are at increased risk for delayed cognitive and motor development as well as behavioral problems.[12-17] The period from 20 to 37 weeks gestation is one of rapid brain development; birth during this time alters the trajectory of development and can lead to lasting brain abnormalities.[15] Preterm infants are often delayed in crawling and walking, and experience impairment in fine and gross motor skills.[15,18] Studies of cognitive functioning have found that delays exist in infancy and early childhood[13,17] and can persist through school age.[12,14]

CDC data shows that from 2012–2018, the percent of children ages one-three years living in Rhode Island with BLL ≥5 μg/dL decreased from 6.5% to 2.9%.[10] Data are not available, however, on former preterm infants. Preterm infants with delayed onset of crawling and walking may be exposed to increased and/or a prolonged window of exposure to environmental lead sources. To date, no studies have examined rates of BLL in the preterm population relative to developmental and behavioral outcomes. A decision was made to analyze study groups by the cut-point of 5 μg/dL, consistent with the cut-point recommendation for the time period the samples were collected, and consistent with the majority of previous studies that use a cut-point for elevated blood lead level. Since multiple lead levels were reported for children with increasing age, the highest recorded lead level was used for analysis.

The study objectives therefore were to: 1) identify the rate of BLL ≥5 μg/dL in a defined cohort of children born preterm and 2) examine rates of cognitive delays, motor delays and behavior problems for children with BLL ≥5 μg/dL compared to <5 μg/dL at five years of age. It was hypothesized that

preterm children with a BLL ≥5 μg/dL would have higher rates of cognitive, motor and behavior problems at five years of age compared to children with a BLL <5 μg/dL.

METHODS

The study was approved by the Women & Infants Hospital (WIH) and the Rhode Island Department of Health Institutional Review Boards and informed consent was waived because of the retrospective study design. The cohort consisted of 354 infants <33 weeks gestation born 2005 to 2014 and seen in the follow-up clinic for a five-year visit between 2010 and 2019.

The study was conducted at WIH, which has a level 3–4 Neonatal Intensive Care Unit (NICU) and a Neonatal Follow-up Clinic. Maternal and infant demographic and clinical characteristics and morbidities are collected prospectively in conjunction with longitudinal follow-up data. Preterm infants are considered high risk for developmental challenges and are automatically referred to the Neonatal Follow-up Clinic. Initial study eligibility included birth weight ≤1250 grams and a gestation of 22 to <33 weeks.

The follow-up clinic provides longitudinal multidisciplinary assessments and clinical management of high-risk infants. Certified examiners perform comprehensive medical, neurologic and developmental assessments. Infants in the study cohort were born between 2005 and 2014 and cared for in the NICU and Follow-up Clinic.

ASSESSMENTS

Tests administered included the Wechsler Preschool and Primary Scale of Intelligence (WPPSI III and IV),[19,20] the Child Behavior Checklist (CBCL),[21] the Behavior Rating Inventory of Executive Function Preschool (BRIEF-P),[22] the Developmental Test of Visual Motor Integration (VMI),[23] and the Movement Assessment Battery for Children (ABC-2).[24] Two versions of the Wechsler were used since the test was updated in 2012 from the WPPSI III to the WPPSI IV. The WPPSI was designed to measure cognitive development for children age two-and-a-half to seven years of age. Both versions of the test have a mean and standard deviation of 100±15. The BRIEF-P is a parent self-report questionnaire that examines behavioral problems in preschoolers associated with difficulties with executive function. A score ≥65 is rated as potentially clinically elevated.

The Child Behavior Checklist (CBCL) is a widely-used standardized instrument designed to assess the social competencies and behavioral problems of children aged three to 18 years. Parents complete 100 questions regarding their child's performance in sports, classroom activities, chores, and the quality of relationships with friends and family. The CBCL provides T-scores (≥65 meets criteria for borderline clinical significance; ≥70 meets criteria for clinical significance) for internalizing behavior, externalizing behavior, and total behavior problems. The Visual Motor Integration (VMI) and Movement ABC-2 are assessments of fine motor and gross motor development, respectively.

Sample size: There were 354 preterm children (born to 321 mothers) with comprehensive neonatal and outcome data for whom BLLs were available to be linked from the Rhode Island KIDSNET database.

STATISTICAL ANALYSES

Descriptive analyses were used to compare social environment and clinical characteristics (infant sex, gestational age, neonatal health outcomes, maternal age, maternal insurance coverage, maternal primary language, etc.) and test scores of preterm children with a highest lead level of <5 μg/dL compared to ≥5 μg/dL. Group comparisons based on the BLL categories were made using bivariate analyses, with Fisher's exact test used for categorical variables and t-tests for linear variables. Multivariate regression models were explored to assess independent effects of lead.

RESULTS

Maternal and infant demographics and clinical characteristics compared across preterm group with highest lead level of <5 μg/dL vs. ≥5 μg/dL closest to the time of their 60-month exam are shown in **Table 1**. A total of 37 (10%) premature infants in our sample had a maximum lead level ≥5 μg/dL and 317 (90%) had a maximum lead level <5 μg/dL. Of the 37 infants with elevated BLLs, 65% (n=24) were initially tested with venous samples and 35% (n=13) were initially tested via capillary sample. Of the 13 infants with BLLs ≥5 μg/dL initially tested by capillary sample, n=6 were subsequently tested via venous sample per recommendations from the Rhode Island Department of Health Childhood Lead Poisoning Prevention Program[25]; n=2 were confirmed within three months by venous sample which remained ≥5 μg/dL, n=3 had a follow up venous sample obtained within a month that was <5 μg/dL, n=1 had a follow-up venous sample six months later that was <5 μg/dL, and n=7 did not have their level confirmed by venous sample. The two study groups had similar mean maternal age, maternal marital status, history of prenatal care, non-Hispanic White versus Black, Indigenous, and people of color (BIPOC) racial identity, and education level. However, the group with high lead levels ≥5 μg/dL were significantly more likely to have Medicaid insurance (p=0.01) and have mothers who were non-English speaking (p=0.03).

The two study groups also had similar neonatal demographic and clinical characteristics including gestational age, birthweight, sex, and singleton birth status. Infants

Table 1. Maternal and Infant Characteristics by Highest Lead Level*

	Highest Lead Level by Time of 60-month Exam		
MATERNAL CHARACTERISTICS			
M ± SD or N (%)	**<5 μg/dL (N=288, 89.7%)**	**≥5 μg/dL (N=33, 10.3%)**	**P value****
Maternal Age	30.4 ± 5.9	30.2 ± 6.3	0.82
Maternal Age < 20	8 (2.8)	0 (0.0)	1.00
Not Married	120 (42.4)	19 (57.6)	0.14
Had Prenatal Care	282 (97.9)	32 (97.0)	0.54
Medicaid Insurance	137 (48.1)	22 (68.8)	0.04
Non-Hispanic White	193 (67.3)	23 (69.7)	0.85
Some college	175 (71.1)	13 (52.0)	0.07
Non-English speaking	31 (10.8)	8 (24.2)	0.04
INFANT CHARACTERISTICS			
M ± SD or N (%)	**<5 μg/dL (N=317, 89.6%)**	**≥5 μg/dL (N=37, 10.4%)**	**P value****
Gestational age	27.6 ± 2.5	26.8 ± 2.2	0.07
Birth weight	1005.5 ± 348.7	957.9 ± 211.9	0.24
SGA, weight <10%	71 (22.4)	2 (5.4)	0.02
Male	148 (46.7)	21 (56.8)	0.30
Multiple	80 (25.4)	9 (24.3)	1.00
IVH 3-4 or PVL	21 (6.6)	0 (0.0)	0.15
BPD	87 (27.5)	7 (18.9)	0.33
ROP	134 (42.8)	17 (46.0)	0.73
NEC (proven)	15 (4.7)	3 (8.1)	0.42
Sepsis (early or late)	53 (16.7)	8 (21.6)	0.49
Days of oxygen	37.4 ± 43.6	33.3 ± 33.3	0.58
Days on ventilator	9.3 ± 17.0	7.9 ± 11.5	0.51
Days in NICU	79.0 ± 38.5	80.3 ± 27.3	0.79
Breast Milk at discharge	155 (53.8)	15 (46.9)	0.46
Cerebral Palsy at 2 years	21 (6.7)	1 (2.7)	0.67

*Highest lead level among all lead tests completed by time of 60-month exam.
**P values from Fisher's exact test or two sample t-test.

Table 2. WPPSI-III & WPPSI-IV Scores by Highest Lead Level*

	Highest Lead Level by Time of 60-month Exam		
M ± SD or N (%)	**<5 μg/dL (N=314)**	**≥5 μg/dL (N=37)**	**P value****
WPPSI-III & WPPSI-IV			
Full Scale IQ	89.3 ± 15.5	88.6 ± 19.0	0.79
Full Scale IQ <85	106 (33.9)	13 (35.1)	0.86
Full Scale IQ <70	34 (10.9)	5 (13.5)	0.58

*Highest lead level among all lead tests completed by time of 60-month exam.
**P values from Fisher's exact test or two sample t-test

with highest lead level ≥5 μg/dL were less likely to be born small for gestational age (birthweight <10%; p=0.01). The two groups also had similar rates of neonatal morbidities, rate of receiving breast milk at time of discharge from the NICU, and a diagnosis of cerebral palsy at two years of age (**Table 1**).

WPPSI-II and WPPSI-IV scores were statistically similar for the two groups of children based on highest lead level (**Table 2**). Mean Full Scale IQ (FSIQ) scores were 89.4 and 88.6 for children with lead level <5 μg/dL and ≥5 μg/dL, respectively. There were also no differences between the two groups on the WPPSI score cut-points or subscales (analyses not shown).

CBCL T-scores ≥65 (borderline to clinical range) were higher for preterm children with a lead level ≥5 μg/dL but did not achieve statistical significance with the exception of sleep problems (p=.04) (**Table 3**). With the exception of somatic complaints, all rates of CBCL measures in the clinical range (CBCL T-scores ≥65) were higher for children with a BLL ≥5 μg/dL, although none were statistically significant. In multivariate models adjusting for Medicaid insurance, non-English primary language of caregiver, and SGA status, there was no significant association between blood lead level and CBCL scores.

The percent of children with BRIEF-P T-scores ≥65 did not differ between study groups. The percent with T-scores ≥65 on the BRIEF-P (19) subscales ranged from 11–21% for infants with a highest lead level <5 μg/dL and between 11–23% for infants with a highest lead level ≥5 μg/dL (**Table 4**). Visual Motor Integration (VMI) and Movement ABC-2 scores did not differ between groups. (**Tables 5,6**).

All analyses were repeated using the lead level cutoff of 3.5 μg/dL in accordance with the most recent CDC guidelines for lead level screening. In this secondary analysis, all comparisons demonstrated differences in the same direction as detailed above, but no longer met statistical significance.

Table 3. CBCL-T Scores in Borderline (T score ≥65) and Clinical Range (T score ≥70) by Highest Lead Level*

	Highest Lead Level by Time of 60-month Exam					
CBCL scores	**Borderline Range (T score≥65)**			**Clinical Range (T score ≥70)**		
N (%)	**<5 µg/dL (N=307)**	**≥5 µg/dL (N=34)**	**P value****	**<5 µg/dL (N=307)**	**≥5 µg/dL (N=34)**	**P value****
Total Problem	38 (12.4)	6 (17.7)	0.42	21 (6.8)	4 (11.8)	0.29
External	25 (8.1)	5 (14.7)	0.20	15 (4.9)	3 (8.8)	0.41
Internal	45 (14.7)	5 (14.7)	1.00	24 (7.8)	3 (8.8)	0.74
Emotionally Reactive	50 (16.2)	4 (11.8)	0.63	20 (6.5)	3 (8.8)	0.49
Anxious/Depressed	33 (10.7)	4 (11.8)	0.77	18 (5.8)	3 (8.8)	0.45
Somatic complaints	56 (18.2)	6 (17.7)	1.00	30 (9.7)	3 (8.8)	1.00
Withdrawn	35 (11.4)	6 (17.7)	0.27	26 (8.4)	6 (17.7)	0.11
Sleep problems	32 (10.4)	8 (23.5)	0.04	18 (5.8)	5 (14.7)	0.06
Attention	50 (16.2)	8 (23.5)	0.33	38 (12.3)	6 (17.7)	0.42
Aggressive behavior	21 (6.8)	4 (11.8)	0.29	16 (5.2)	3 (8.8)	0.42

*Highest lead level among all lead tests completed by time of 60-month exam.
**P values from Fisher's exact test or two sample t-test

Table 4. BRIEF-P T-Scores (N (%) for scores ≥ 65) by Highest Lead Level*

	Highest Lead Level by Time of 60-month Exam		
N, (%)	**<5 µg/dL (N=303)**	**≥5 µg/dL (N=35)**	**P value****
Global Executive composite (GEC)	58 (19.1)	7 (20.0)	0.82
Inhibitory Self-Control Index (ISCI)	49 (16.1)	6 (17.1)	0.81
Initiate	42 (13.9)	5 (14.3)	1.00
Emergent Metacognition index (EMI)	65 (21.4)	7 (20.0)	1.00
Inhibition	50 (16.5)	7 (20.0)	0.63
Shift	40 (13.2)	4 (11.4)	1.00
Emotional control (EC)	36 (11.9)	4 (11.4)	1.00
Working memory (WM)	65 (21.4)	8 (22.9)	0.83
Plan/organize (PO)	55 (18.1)	6 (17.1)	1.00

*Highest lead level among all lead tests completed by time of 60-month exam.
**P values from Fisher's exact test or two sample t-test

Table 5. Visual Motor Integration(VMI) Scores by Highest Lead Level*

	Highest Lead Level by Time of 60-month Exam		
M ± SD or N(%)	**<5 µg/dL (N=317)**	**≥5 µg/dL (N=37)**	**P value****
VMI Standard Scores	90.8 ± 12.3	91.6 ± 12.4	0.70
VMI <85	73 (23.3)	9 (24.3)	0.84
VMI <70	8 (2.6)	2 (5.4)	0.28

*Highest lead level among all lead tests completed by time of 60-month exam.
**P values from Fisher's exact test or two sample t-test

DISCUSSION

It is well-established that lead exposure and elevated BLLs in childhood are associated with negative cognitive, motor, and behavioral outcomes. To date, our study is the first to investigate BLLs and associated developmental and behavioral outcomes in children born prematurely. Ninety percent of our sample of premature infants had a maximum detected BLL <5 µg/dL, likely a testament to current strong public health and screening measures given the history of elevated BLLs in Rhode Island.[25] The social environment factors in our sample associated with infants having BLL ≥5 µg/dL (Medicaid insurance and maternal primary language) are consistent with previously reported associations between lower socioeconomic status and lead exposure.[26] While our study did not establish causality, hypothesized mechanisms for how these demographic measures may lead to higher child lead exposure include factors related to poverty, exposure to older homes, and differences in access to childcare and medical care.[26] The 10% rate of BLL ≥5 µg/dL for this preterm cohort was higher than rates previously reported for the general population,[10,27] suggesting that former preterm infants, especially those of low socioeconomic status, are at increased risk for lead exposure.

Contrary to our hypotheses based on existing literature correlating lead exposure with neurodevelopmental risk, there were no significant differences between infant groups detected on most cognitive, behavioral, and motor outcome measures. This lack of significance may be due to limitations in the study methods including limited sample size. Future studies can aid in exploring these questions further.

Our study did identify a significant association between BLL ≥5 µg/dL and the CBCL domain of impaired infants' sleep. Prior studies also report a correlation between elevated blood lead levels in early childhood and sleep problems in adolescence.[7,28] Possible mechanisms for this correlation may be a neurotoxic effect of lead on brain structures involved

Table 6. Movement ABC-2 scores (≤15th %) and ≤5th %by Highest Lead Level at Time of 60-month exam

	MABC-2 scores ≤15th %			MABC-2 scores ≤5th %		
N (%)	<5 μg/dL (N=287)	≥5 μg/dL (N=34)	P value**	<5 μg/dL (N=287)	≥5 μg/dL (N=34)	P value**
Manual Dexterity	214 (74.6)	23 (67.7)	0.41	189 (65.9)	17 (50.0)	0.09
Aim & Catch	81 (28.1)	11 (33.3)	0.55	58 (20.1)	8 (24.2)	0.65
Balance	128 (44.8)	12 (37.5)	0.46	82 (28.7)	9 (28.1)	1.00
Total Score	182 (65.7)	15 (48.4)	0.07	149 (53.8)	11 (35.5)	0.06

*Highest lead level among all lead tests completed by time of 60-month exam.
**P values from Fisher's exact test or two sample t-test

in sleep, other cognitive and behavioral outcomes that impact on sleep, or an interaction of both. Future studies are needed to investigate these possible mechanisms.

Study limitations include a limited sample size of preterm infants with elevated BLLs. We did not perform statistical analyses using a correction factor for multiple comparisons due to the nature of our small sample size and limitation in power. Further study of the effects of lead in preterm infants with a larger sample size is needed to confirm our findings and explore moderating effects on developmental outcomes, such as age of detection of elevated blood lead level, participation in early intervention, and other demographic factors. Strengths include a study sample that was recruited from a well-resourced NICU follow-up clinic in which infants receive regular neuro-logic screening, developmental testing, and referral to Early Intervention, Women, Infants, and Children (WIC), and social work as needed. An additional strength is access to a well-coordinated statewide universal lead screening program for children nine months to five years of age. Access to these resources through the follow-up clinic may mitigate the increased risk that lead exposure has on early developmental outcomes.

CONCLUSIONS

Our findings support the importance of lead screening, regular developmental assessment, and access to childcare resources, especially for vulnerable infants born prematurely. We identified that former preterm infants with Medicaid insurance and mothers who are non-English speaking are at increased risk of elevated blood lead levels, which are associated with a doubling of the rate of sleep problems at age five. Future studies with larger sample sizes are needed to evaluate the associations of lead exposure with long-term academic, behavioral, and health outcomes in children and adolescents with a history of prematurity. These data could potentially facilitate both early identification and initiation of intervention, and establish the importance of protective factors.

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Increase in the Incidence of Type 2 Diabetes in Young Children During the COVID-19 Pandemic

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ABSTRACT

OBJECTIVE: To describe the incidence of new onset type 2 diabetes (T2D) among children younger than 11 years old diagnosed during the COVID-19 pandemic (March 1, 2020–December 31, 2021) compared to those diagnosed during the pre-pandemic period (January 1, 2017–February 29, 2020) and to compare the metabolic parameters of those with T2D diagnosed before age 11 years with those diagnosed after age 11 years.

METHODS: We conducted a retrospective cohort study of youth <21 years with new onset T2D treated at Hasbro Children's Hospital between January 1, 2017 and December 31, 2021. Patients diagnosed at age <11 years were compared to those ≥11 years.

RESULTS: Out of 145 patients with T2D diagnosed 2017–2021, eight (5.5%) were <11 years and all presented during the COVID-19 pandemic (8.9% of those diagnosed during the pandemic). Patients diagnosed <11 years had higher median body mass index percentile compared to patients diagnosed ≥11 years (169% of 95th percentile vs. 137%, p=0.03). Frequency of diastolic hypertension was greater among the younger group compared to older patients (62.5% vs 23.8%, p=0.03).

CONCLUSIONS: An increase in T2D incidence was seen in children <11 years old during the COVID-19 pandemic compared to prior. Multifactorial influences favoring an obesogenic environment may have had a stronger impact on the younger population during the COVID-19 pandemic. Research is needed to help understand these trends and develop mitigation plans to reduce complications of early-onset obesity and insulin resistance.

KEYWORDS: Children, COVID-19, pandemic, type 2 diabetes, body mass index

INTRODUCTION

An alarming increase in youth onset type 2 diabetes (T2D) over the last two decades[1] has been associated with the rise in obesity rates among youth.[2] Obesity is a major health concern, affecting more than 16.67% of children in the United States.[3] The impact of the COVID-19 pandemic and the societal responses that aimed to contain the spread of COVID-19 infection favored an obesogenic environment, owing to increased stress levels, less physical activity, increased consumption of high calorie foods, increased snacking, and screen time.[3-7] There was a rise in the rate of body mass index (BMI) increase among youth ages 2–19 years during the COVID-19 pandemic compared to pre-pandemic period, and the rate of increase in BMI was higher in those with prior moderate or severe obesity.[3] An increase in the incidence of T2D among youth during the COVID-19 pandemic compared to prior period was also observed.[8]

Historically, the average age of onset of T2D in youth averaged 13–14 years of age with a female predominance at younger ages, suggesting the potential role of puberty-induced insulin resistance in the pathogenesis of T2D among youth.[2] The SEARCH for Diabetes in Youth study reported that the prevalence of T2D in children <10 years was less than 2.3%.[9] In the years prior to the COVID-19 pandemic, reports described increasing incidence of younger and pre-pubertal children with T2D.[10,11] T2DM in the pediatric population, compared to that in the adult population, is characterized by a more rapid decline of beta cell function with poor glycemic control and early development of micro- and macrovascular complications.[12]

We previously reported a significant increase in the incidence of T2D during the first two years of the COVID-19 pandemic, including a rise in T2D among children <11 years old.[13] In this study, we aimed to describe the clinical characteristics of children <11 years with new onset T2D and to compare how children <11 years with type 2 diabetes differed from older children diagnosed during the same period.

METHODS

We conducted a retrospective chart review of newly diagnosed T2D cases among youth <21 years treated in Hasbro Children's Hospital between January 1, 2017 to December 31, 2021 to identify children <11 years at the time of diagnosis during the COVID-19 pandemic (March 1, 2020–December 31, 2021) compared to the prior three years (January 1, 2017–February 29, 2020). We also compared the clinical and metabolic parameters of patients aged <11 years diagnosed during the COVID-19 pandemic with those aged ≥11 years during the same period.

Clinical diagnosis of T2D was made per the American Diabetes Association (ADA) guidelines.[14] Youth aged <21 years who were diagnosed with T2D during the study period were included. Subjects with positive diabetes autoantibodies and those with a prior diagnosis of diabetes, new onset type 1 diabetes, medication-induced diabetes or cystic fibrosis-related diabetes were excluded.

The following data were extracted from the electronic medical record (EMR): Date of presentation, age, gender, race, ethnicity, family history of diabetes, COVID-19 positivity at diagnosis, weight, height, BMI and BMI percentile, blood pressure, blood pressure percentile, pubertal staging, hemoglobin A1c (HbA1c), aspartate amino transferase (AST), alanine amino transferase (ALT), and serum creatinine. The presence of ketonemia or ketonuria, diabetic ketoacidosis (DKA) or hyperglycemic hyperosmolar syndrome (HHS) was also recorded. Data extraction from the EMR included options of "other" and "unknown" for race and ethnicity which were self-reported.

DKA was defined as per the International Society for Pediatric and Adolescent Diabetes 2018 guidelines[15] with blood glucose >200mg/dl, pH <7.3 or bicarbonate15 and ketonemia or ketonuria. HHS was defined as serum osmolality ≥320 mOsm/kg and serum glucose >600mg/dL. Hypertension was defined as per the 2017 American Academy of Pediatrics clinical practice guidelines with blood pressure >95th percentile for age, gender and height for those <13 years and for those ≥13 years as blood pressure of 130/80 mm Hg or higher.[16] Obesity was classified as class 1 (95th percentile to <120% of the 95th percentile), severe obesity class 2 (120% to <140% of the 95th percentile or BMI 35.0 to <40. kg/m^2), and severe obesity class 3 (BMI ≥140% of the 95th percentile or BMI ≥40.0 kg/m^2).[17] Estimated glomerular filtration rate (eGFR) was calculated using the Schwartz short formula for those aged ≥18 years[18] and the 2021 CKD-EPI Creatinine equation[19] for those >18 years. Renal injury was defined if eGFR was <60 mL/min/1.73 m^2 [20] or >130 mL/min/1.73 m^2 (hyperfiltration).[21] AST and ALT values were interpreted using the Canadian Laboratory Initiative on Pediatric Reference Intervals (CALIPER) database.[22]

The primary outcome compared the incidence of new onset T2D in children <11 years of age during the COVID-19 pandemic versus the prior three years. The secondary outcomes were the proportion of patients presenting with metabolic decompensation (DKA, HHS, or mixed DKA-HHS) and metabolic complications (obesity, hypertension) among patients <11 years of age compared to patients ≥11 years diagnosed with T2D during the COVID-19 pandemic.

STATISTICAL ANALYSIS

We described univariate distributions of all variables. Continuous variables are reported with medians and interquartile ranges, and categorical variables are presented as frequencies and percentages. Comparisons between patients <11 years and ≥11 years were conducted with Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables. All tests were 2-sided and a p-value <0.05 was considered statistically significant. All analyses were conducted using Stata/SE 16.1 (College Station, TX).

RESULTS

A total of 145 patients <21 years were diagnosed with new onset T2D during the study period; 56 patients prior to the COVID-19 pandemic and 89 during the pandemic. One patient initially had a mildly positive insulin antibody of 7.9 uIU/mL (negative <5 uIU/mL); repeat insulin antibody level was negative, and all other pancreatic antibodies were negative, and the patient was included in the study. Out of 145 patients, eight (5.5%) were ≤11 years at time of T2D diagnosis. All eight were diagnosed during the COVID-19 pandemic (8/89, 8.9%) and seven of them (87.5%) were diagnosed during the first year of the COVID-19 pandemic (March 1, 2020–December 31, 2020). Patient characteristics are shown in **Table 1**. Four patients were <10 years, and six were female. Five patients had symptoms of polyuria and/or polydipsia which led to laboratory evaluation and diabetes diagnosis, while three were diagnosed after routine laboratory screening for complications of obesity. Four of the subjects were hospitalized at diagnosis due to DKA (n=1), HHS (n=1), or the need for insulin initiation (n=2), all during the initial five months of the pandemic. COVID-19 status at diagnosis was available for four patients, and all were negative. All eight patients had a positive family history of T2D and seven had a first-degree relative with T2D. Four patients were participating in remote learning at the time of diagnosis. Six of the children had class 3 obesity and two had class 2 obesity. Four patients were prepubertal, including both male patients. Five patients had both systolic and diastolic hypertension, one with isolated systolic hypertension, and one with isolated diastolic hypertension. HbA1c was >8.5% in four patients and all of them presented in the initial five months of the pandemic. High density lipoprotein (HDL) cholesterol result was available for three patients, and all had HDL below 35 mg/dl.

We compared the children diagnosed at <11 years to those diagnosed at ≥11 years during the COVID-19 pandemic (**Table 2**). Compared to older children, those below <11 years at diagnosis had higher median BMI percentile (169 % of 95th percentile vs. 137 %, p=0.03), and the proportion of children with diastolic hypertension was higher among children <11 years compared to those ≥11 years (62.5% vs 23.8%, p=0.03).

Table 1. Patient characteristics at presentation

Patients	1	2	3	4	5	6	7	8
Age	9y 7mo	10y 4mo	10y 11mo	7y 10mo	10y 4mo	9y 11mo	8y 8mo	10y 2mo
Gender	F	F	F	F	F	M	M	F
Self-identification	Black NH	Black NH	Other Hispanic	Black NH	Cape Verdean, NH	Other, Hispanic	Black NH	Other Hispanic
Pubertal staging	Tanner 3–4 breast	Attained menarche	Tanner 3–4 breast	Tanner 1 breast	Tanner 1 breast	Tanner 1 testes	Tanner 1 testes	Tanner 4 breast
Month and year of diagnosis	June 2020	June 2020	July 2020	July 2020	August 2020	September 2020	December 2020	March 2021
Visit location	IP	IP	IP	IP	OP	OP	OP	OP
DKA/HHS/ Mixed DKA-HHS	HHS	No	DKA	No	No	No	No	No
BMI % of 95th percentile	140	172	128	177	167	171	247	128
SBP percentile	98	99	99	96	99	49	99	60
DBP percentile	96	99	98	66	96	94	99	34
HbA1c (%)	10.1	11	12.1	9.1	7	7.1	7.6	8.2
Elevated transaminases	No	–	–	–	No	Yes	No	No
Creatinine (mg/dl)	1.3	0.71	0.86	0.44	0.53	–	0.61	–
eGFR	52.45	88.65	74.39	128.59	114	–	102.98	–
Cholesterol (mg/dl)	162	–	–	–	62	193	–	117
HDL(mg/dl)	27	–	–	–	28	31	–	–
LDL(mg/dl)	67	–	–	–	14	121	–	63
TG (mg/dl)	525	–	–	–	100	444	–	34

BMI-body mass index, DBP-diastolic blood pressure, DKA-diabetic ketoacidosis, HbA1c- hemoglobin A1c, HHS-hyperglycemic hyperosmolar syndrome, eGFR-estimated glomerular filtration rate, SBP-systolic blood pressure, T2D-type 2 diabetes

DISCUSSION

During the COVID-19 pandemic, we observed an increase in the number of young patients <11 years of age with new onset T2D compared to none during the pre-pandemic period. Compared to patients ≥11 years with new onset T2D, the younger cohort was characterized by higher BMI percentile and higher proportion of patients with diastolic hypertension.

Prior studies on the incidence of T2D among youth before and during the COVID-19 pandemic revealed similar age at presentation during both the pandemic and pre-pandemic periods and did not observe an increase in the incidence of T2D among patients <11 years.[23-26] We previously described our finding of younger mean age at T2D diagnosis (12.9 years vs. 14.8, p <0.001) during the first year of the pandemic compared to prior.[13] Most of the patients <11 years were diagnosed during the first year of the pandemic, including the two who presented with DKA and HHS in our study. Those who presented during the initial five months of the pandemic (March 2020–August 2020) had higher HbA1c compared to those that presented later in the pandemic. Severe stress and multifactorial influences favoring an obesogenic environment might have had a stronger impact on the younger population during the COVID-19 pandemic, especially during the first year.

Our study observed that BMI percentile was higher in those diagnosed <11 years compared to those ≥11 years. A previous multi-center study by Maggie et al reported a rise in the prevalence of T2D along with significantly higher BMI at presentation during the COVID-19 pandemic compared to the prior two years.[8] A Centers for Disease Control (CDC) report observed a significant increase in the rate of BMI change in youth aged 2-19 years during the COVID-19 pandemic, and the rate of BMI increase was higher in those with obesity compared to those without obesity. Compared to different age groups, children of 6-11 years had the greatest increase in their rate of BMI change during the pandemic.[3]

The pathophysiology of T2D begins with reduction of insulin sensitivity in peripheral tissues. When the compensatory insulin secretion from pancreatic beta cells fails to thwart deteriorating insulin sensitivity, hyperglycemia ensues. This leads initially to prediabetes and finally to T2D. Obesity is a major risk factor of insulin resistance.[27]

Table 2. Clinical, and demographic factors during the COVID-19 pandemic: Those <11 years vs. those ≥11years

N = 89	Total Cohort (N=89)	<11 years (n=8)	≥11 years (n=81)	p-value
Sex Female	 51 (57.3)	 6 (75.0)	 45 (55.6)	 0.461
First year of COVID-19 pandemic (3/2020–12/2020) (n (%))	31 (34.8)	7 (87.5)	24 (29.6)	0.0021
Race White Black Other Did not answer	 27 (30.3) 23 (25.8) 32 (35.9) 7 (7.9)	 0 (—) 4 (50.0) 3 (37.5) 1 (12.5)	 27 (33.3) 19 (23.5) 29 (35.8) 6 (7.4)	 0.091
Ethnicity Hispanic Non-Hispanic Did not answer	 41 (46.1) 47 (52.8) 1 (1.1)	 3 (37.5) 5 (62.5) 0 (--)	 38 (46.9) 42 (51.9) 1 (1.2)	 0.741
DKA/HHS/Mixed (n (%))	8 (8.9)	2 (25.0)	6 (7.4)	0.151
BMI (kg/m2) Median (IQR)	(n=88) 36.8 (31.3–41.8)	(n=8) 36.9 (31.2–39.5)	(n=80) 36.8 (31.3–42.3)	 0.722
Ext BMI % of 95th percentile Median (IQR)	(n=87) 138 (118–157)	(n=8) 169 (134–174.5)	(n=79) 137 (115–154)	 0.032
SBP percentile Median (IQR)	(n=83) 93 (77–98)	(n=8) 98.5 (78–99)	(n=75) 92 (77–98)	 0.232
DBP percentile Median (IQR)	(n=83) 91 (77–96)	(n=8) 96 (80–98.5)	(n=75) 89 (77–95)	 0.142
Systolic hypertension (n (%))	(n=88) 41 (46.6)	(n=8) 6 (75.0)	(n=80) 35 (43.8)	0.142
Diastolic hypertension (n (%))	(n=88) 24 (27.3)	(n=8) 5 (62.5)	(n=80) 19 (23.8)	0.032

BMI-body mass index, DBP-diastolic blood pressure, DKA-diabetic ketoacidosis, HHS-hyperglycemic hyperosmolar syndrome, SBP-systolic blood pressure, T2D-type 2 diabetes
*Categorical data are N (%)
[1]Fisher's exact test
[2]Wilcoxon rank-sum

Obesity with insulin resistance might have paved the way for T2D in the younger patients in the current study. Prior to the pandemic, a few studies reported higher BMI percentile in younger children with T2D compared to older patients with T2D.[10,11] A study from Texas Children's Hospital found that prepubertal children (n=35) with T2D had higher BMI z-scores compared with pubertal children with T2D. Among the prepubertal children, 13 were below 10 years of age and all of them had obesity.[10] Another study reported 20 children below 10 years of age with T2D diagnosed between 2000–2015 and all of them had obesity.[12] While the incidence of pre-pubertal onset of T2D was observed in other regions of the United States, no children <11 years had presented with T2D at our hospital until the start of the COVID-19 pandemic. We suspect that factors associated with the COVID-19 pandemic accelerated local youth weight gain, and the rise in BMI was likely a contributing factor to T2D development.

The proportion of children with diastolic hypertension was significantly higher in the younger group compared to those ≥11 years in the present study. Increase in the BMI percentile might contribute to the increase in incidence of hypertension observed in the current study. Each unit increase in BMI may increase the risk of hypertension by up to 6%.[28] Torchinsky et al reported that the elevation in diastolic blood pressure is associated with structural and functional alterations in kidney and increases in diastolic blood pressure, even when in the normal range, may increase the risk for diabetic kidney disease.[29] The observation of elevated blood pressure in younger patients with T2D onset, with our knowledge of increased risk for diabetes complications in youth-onset T2D, is extremely concerning.[12]

Our study observed a female predilection (75%) among patients <11 years. Both males with T2D diagnosed <11 years were prepubertal. Female predilection has been reported by prior studies on younger children with T2D.[10,11]

The retrospective nature of the data collection was the major limitation of our study. Also, data regarding current or prior COVID-19 status was not available for all the patients. Another limitation was that the diagnosis of T2D was made based on clinical phenotype and absence of diabetes autoantibodies and genetic testing for maturity-onset diabetes of young (MODY) was not performed. Hence it is possible that some of the patients had MODY. However, being the only dedicated children's hospital in the state, our catchment area stayed the same during the study period. The trends observed in this study likely mirror the changes in T2D in youth in our state.

Our finding of an increase in the incidence of T2D in patients <11 years during the COVID-19 pandemic is concerning, as earlier onset of T2D place these patients at higher risk for the development of micro- and macrovascular complications. Further research is needed to help understand these trends and develop mitigation plans to prevent or reduce complications of obesity and insulin resistance.

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Cannabis-Related Emergency Department Visits Among Rhode Island Residents Under the Age of 25, 2019–2023

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INTRODUCTION

As of November 1, 2024, cannabis is legal for adult use in 28 U.S. states and territories and legal for medical use in 42 U.S. states and territories. In Rhode Island (RI), the Medical Marijuana Program began in 2006, and in December 2022, sales began for adult use cannabis. While cannabis is legal for purchase over the age of 21, cannabis can have negative health effects if used while the brain is still developing. As brain development can continue until age 25, youth and young adults are at elevated risk of negative health outcomes from cannabis use.[1] Youth who use cannabis frequently are at higher risk for mental health complications such as schizophrenia, psychosis, and suicidal ideation. Given the risks of cannabis use to youth and young adults, this analysis focuses on emergency department (ED) visits among patients under 25-years-old who present for cannabis-related reasons. To date, this is the first time cannabis-related ED visits among individuals under the age of 25 in RI have been described.

METHODS

We obtained data from the RI Hospital Discharge Dataset (HDD) which collects hospital reports from 10 acute care and two psychiatric care hospitals in RI. We identified cannabis-related ED visits among RI residents under the age of 25 that occurred between January 1, 2019 and December 31, 2023. We defined a "cannabis-related ED visit" as any ED visit that had at least one of the following 10th Clinical Modification of the International Classification of Diseases (ICD-10) codes as a primary or subsequent diagnosis: F12.1-F12.9 (Cannabis abuse, dependence, or use) or T40.7 (Cannabis poisoning).[2] While HDD requires a primary diagnosis, subsequent diagnoses codes are optional and up to 11 additional diagnoses can be entered. Demographic information collected included sex, age, race/ethnicity, and insurance type. Race/ethnicity was defined as: Non-Hispanic White, Non-Hispanic Black, Hispanic, Non-Hispanic Other (Asian, American Indian/Alaska Native, Native Hawaiian/Other Pacific Islander, and Other), and Unknown. Insurance type was categorized into Private, Public (Medicaid or Medicare), and Other (Self-Pay, Workers Compensation, Other). Clinical characteristics collected include cannabis-related ICD-10 codes, hospital of admission, and discharge status.

All analyses were performed in SAS [Version 9.4].

RESULTS

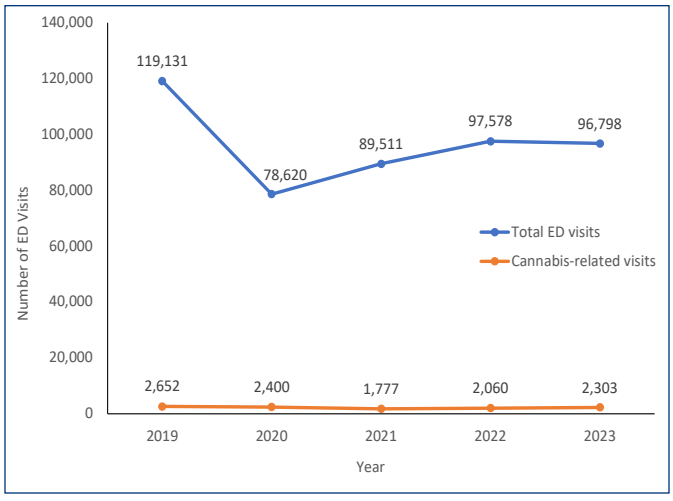
From January 1, 2019 to December 31, 2023, there was a total of 481,638 ED visits to RI hospitals among RI residents under the age of 25 (**Figure 1**), of which, 11,192 (2.3%) ED visits included any cannabis-related ICD-10 code. The total number of ED visits and ICD-10 coded cannabis-related ED visits by under-25-year-old patients both increased from 2021 to 2023 but remained below 2019 counts.

For all ICD-10 coded cannabis-related ED visits, the mean age was 20 years, and most patients were 18–24 years (75.7%), followed by 15–17 years (19.1%; **Table 1**). Overall, 50.1% of cannabis-related ED visits occurred among males. Most patients identified as Non-Hispanic White (55.1%), followed by Hispanic (23.7%), and non-Hispanic Black (14.8%). Public health insurance was most common (61.1%), followed by private (30.0%). Rhode Island Hospital (36.1%) and Landmark Medical Center (20.8%) saw the most ED visits by under 25-year-old patients for cannabis-related reasons (**Table 2**).

For trends within demographic groups, visits by 10- to 14-year-olds increased by 26% from 2019 to 2023. The proportion of visits by female patients increased from 2019 to 2023 (47.1% to 53.8%), and ED visits by Hispanic individuals increased by 15% over the study period.

Only 1,218 (10.9%) of cannabis-related ED visits had a cannabis-related primary ICD-10 code, with the most common

Figure 1. Emergency Department visits for Rhode Island residents under 25-years-old, Rhode Island, 2019–2023



primary diagnosis being F12.9: Cannabis use, unspecified (62.0%; **Table 3**). Most of the ICD-10 codes referred to cannabis use, abuse, and dependence (F12.1–12.9), while fewer visits included ICD-10 codes for cannabis poisoning (T40.7). The most frequent subsequent diagnosis code was F12.9: Cannabis use, unspecified (71.7%). For clinical outcomes among people with a primary cannabis-related ICD-10 code, 96.6% of patients were routinely discharged home from the ED. This outcome was the same across all age and race/ethnicity groups.

Table 1. Demographics of under 25-year-old Rhode Island residents with cannabis-related visits presenting to Emergency Department, Rhode Island, 2019–2023.

Demographic Characteristics	Overall n(%)	2019 n(%)	2020 n(%)	2021 n(%)	2022 n(%)	2023 n(%)
Total	11,192	2,652	2,400	1,777	2,060	2,303
Sex						
Male	5,603 (50.1%)	1,401 (52.8%)	1,255 (52.3%)	865 (48.7%)	1,024 (49.7%)	1,058 (45.9%)
Female	5,562 (49.7%)	1,249 (47.1%)	1,137 (47.4%)	905 (50.9%)	1,031 (50.1%)	1,240 (53.8%)
Other/Unknown/Missing	27 (0.2%)	<5*	8 (0.3%)	7 (0.4%)	5 (0.2%)	5 (0.2%)
Age						
0–4	47 (0.4%)	<5*	9 (0.4%)	10 (0.6%)	11 (0.5%)	14 (0.6%)
5–9	26 (0.2%)	5 (0.2%)	5 (0.2%)	<5*	6 (0.3%)	6 (0.3%)
10–14	514 (4.6%)	120 (4.5%)	73 (3.0%)	78 (4.4%)	92 (4.5%)	151 (6.5%)
15–17	2,133 (19.1%)	573 (21.6%)	448 (18.7%)	302 (16.9%)	376 (18.3%)	434 (18.8%)
18–24	8,472 (75.7%)	1,951 (73.6%)	1,865 (77.7%)	1,383 (77.8%)	1,575 (76.5%)	1,698 (73.7%)
Race/Ethnicity						
Non-Hispanic White	6,168 (55.1%)	1,565 (59.0%)	1,351 (56.3%)	974 (54.8%)	1,088 (52.8%)	1,190 (51.7%)
Non-Hispanic Black	1,651 (14.8%)	382 (14.4%)	370 (15.4%)	241 (13.6%)	319 (15.5%)	339 (14.7%)
Non-Hispanic Other	526 (4.7%)	126 (4.8%)	104 (4.3%)	79 (4.5%)	93 (4.5%)	124 (5.4%)
Hispanic	2,657 (23.7%)	527 (19.9%)	530 (22.1%)	467 (26.6%)	527 (25.6%)	606 (26.3%)
Unknown	190 (1.7%)	52 (2.0%)	45 (1.9%)	16 (0.9%)	33 (1.6%)	44 (1.9%)
Insurance Type						
Private	3,352 (30.0%)	854 (32.2%)	678 (28.3%)	575 (32.4%)	595 (28.9%)	650 (28.2%)
Public (Medicaid, Medicare)	6,835 (61.1%)	1,437 (54.2%)	1,443 (60.1%)	1,085 (61.1%)	1,341 (65.1%)	1,529 (66.4%)
Other (Self-Pay, Workers Comp, other)	1,005 (9.0%)	361 (13.6%)	279 (11.6%)	117 (6.6%)	124 (6.0%)	124 (5.4%)

*Counts less than five are suppressed. Please use caution when interpreting rates. Note: Percentages may add to more than 100% due to rounding.

Table 2. Hospital of admission for under 25-year-old Rhode Island residents with cannabis-related visits presenting to Emergency Department, Rhode Island, 2019–2023.

Hospital	Overall n(%)	2019 n(%)	2020 n(%)	2021 n(%)	2022 n(%)	2023 n(%)
Newport Hospital	647 (5.8%)	168 (6.3%)	132 (5.5%)	73 (4.1%)	128 (6.2%)	146 (6.3%)
Our Lady of Fatima Hospital	445 (4.0%)	102 (3.9%)	76 (3.2%)	77 (4.3%)	92 (4.5%)	98 (4.3%)
The Miriam Hospital	1,306 (11.7%)	477 (18.0%)	190 (7.9%)	176 (9.9%)	222 (10.8%)	241 (10.5%)
Rhode Island Hospital	4,040 (36.1%)	853 (32.2%)	769 (32.0%)	671 (37.8%)	803 (39.0%)	944 (41.0%)
Roger Williams Medical Center	551 (4.9%)	74 (2.8%)	117 (4.9%)	142 (8.0%)	112 (5.4%)	106 (4.6%)
South County Health	298 (2.7%)	42 (1.6%)	54 (2.3%)	75 (4.2%)	63 (3.1%)	64 (2.8%)
Kent Hospital	1,109 (9.9%)	539 (20.3%)	144 (6.0%)	150 (8.4%)	143 (6.9%)	133 (5.8%)
Westerly Hospital	171 (1.5%)	57 (2.2%)	29 (1.2%)	26 (1.5%)	34 (1.7%)	25 (1.1%)
Landmark Medical Center	2,330 (20.8%)	268 (10.1%)	848 (35.3%)	351 (19.8%)	411 (20.0%)	452 (19.6%)
Women & Infants Hospital	182 (1.6%)	69 (2.6%)	35 (1.5%)	29 (1.6%)	23 (1.1%)	26 (1.1%)
Butler Hospital	113 (1.0%)	<5*	6 (0.3%)	7 (0.4%)	29 (1.4%)	68 (3.0%)

*Counts less than five are suppressed. Please use caution when interpreting rates. Note: Percentages may add to more than 100% due to rounding.

Table 3. Cannabis-related ICD-10 Codes for primary diagnosis in under-25-year-old patients presenting to Emergency Department, Rhode Island, 2019–2023.

	Primary Cannabis-Related ICD-10 Code	Subsequent Non-Primary Cannabis-Related ICD-10 Code*
F12.1: Cannabis abuse (F12.10, F12.12, F12.120, F12.121, F12.122, F12.129, F12.15, F12.151, F12.159, F12.18, F12.180, F12.188, F12.19)	246 (20.2%)	1,442 (12.9%)
F12.2: Cannabis dependence (F12.2, F12.20, F12.22, F12.220, F12.221, F12.222, F12.229, F12.25, F12.250, F12.251, F12.259, F12.28, F12.280, F12.288)	40 (3.3%)	709 (6.3%)
F12.9: Cannabis use, unspecified (F12.9, F12.90, F12.92, F12.920, F12.921, F12.922, F12.929, F12.95, 12.950, F12.951, F12.959, F12.98, F12.980, F12.988, F12.99)	755 (62.0%)	8,022 (71.7%)
T40.7: Cannabis poisoning (T40.7 × 1, T40.7X1A, T40.7X1D, T40.7X1S, T40.7 × 2, T40.7X2A, T40.7X2D, T40.7X2S, T40.7 × 3, T40.7X3A, T40.7X3D, T40.7X3S, T40.7 × 4, T40.7X4A, T40.7X4D, T40.7X4S, T40.7 × 5, T40.7X5A, T40.7X5D, T40.7X5S)	177 (14.5%)	107 (1.0%)

*Records can have up to 10 subsequent ICD-10 code so counts will not add up to total. Note: Percentages may add to more than 100% due to rounding.

DISCUSSION

From January 1, 2019, to December 31, 2023, a cannabis-related ICD-10 code was included in 2.3% of all ED visits by RI residents under the age of 25, and among these visits, was listed as the primary diagnosis for only 10.9% of visits. Although this is a small percent of all visits for this population, it is important to note that one in four cannabis-related ED visits occurs in this population in RI and nationally.[3] While RI has seen an increase in cannabis-related ED visits in patients under the age of 25 since 2021, there has been an 18.6% decrease from 2019 to 2023. Reasons for these trends are unknown. The neighboring state of Massachusetts saw increases in ED visits after sales for recreational cannabis began in 2018.[8] While legalizing adult use cannabis in December 2022 does not seem to have had an immediate impact on the number of cannabis-related ED visits in RI, the Rhode Island Department of Health (RIDOH) will continue to monitor these trends.

Within demographic groups, RI saw increases in the proportion of cannabis-related ED visits in females and Hispanic patients. RI survey data also show an increase in self-reported cannabis use among female high school students, and nationally rates of ED visits for females under 25 have increased more than males.[3,4] While self-reported current cannabis use among RI Hispanic high school students increased from 2021 to 2023, it was similar to increases observed among all other race/ethnicity groups during this time period.[5] Exact reasons for these trends are unknown and may include using cannabis to self-medicate, increased access from legalization, and decreased perception of risk.[6,7] RIDOH will continue to monitor cannabis-related ED visits to create tailored and culturally sensitive messaging about the risks of cannabis use to demographic groups experiencing increases or disproportionate burdens in ED visits, such as female and Hispanic youth.

Although patients younger than 10 made up less than 1% of cannabis-related ED visits in RI, children should still be an important focus of outreach and education efforts, as national data have shown a significant increase in pediatric exposures to edible cannabis products.[9] These products often look like products that appeal to children, such as candy or snacks.[10,11] To prevent accidental exposures, caretakers of children should use safe storage practices, including using lock bags to securely store all drugs, medications, and cannabis products to ensure children cannot access them.[12] Caretakers should also have their local poison control center number readily available (for RI: 1-800-222-1222) and be prepared to call if a child in their care has ingested cannabis.[11] RIDOH is working with the RI Cannabis Control Commission to create packaging requirements to ensure cannabis products do not appeal to children.

From 2019 to 2023, in the under-25-year age group, around 25% of ICD-10 coded cannabis-related ED visits were among middle- or high school-aged children (10–17 years old). RI saw a slight increase in 10- to 14-year-old patients from 2021 to 2023, which was similar to national trends in the 11- to 14-year-old population.[3] While ED data do not provide information on intentionality of cannabis use, the RI Youth Risk Behavior Survey (YRBS) asks middle and high school students about cannabis use. In 2023, the first year of the survey since RI legalized adult use cannabis, 5% of middle school students had ever tried cannabis and 20% of high school students reported current cannabis use, both of which increased from 2021.[4] Middle school students also saw a significant increase in current cannabis use in the 2024 RI Student Survey.[13] Since RI is two years post-legalization, it is important to monitor cannabis-related ED visits and self-reported cannabis use trends in this age group to determine if legalization impacted intentional use among youth. Both in RI and nationally, trends have shown decreases in self-reported cannabis use by youth yet increases in cannabis-related ED visits for this

population.[3,4,14,15] RIDOH should partner with prevention coalitions and other state agencies to educate youth on the risks of using cannabis and increase protective factors that can mitigate the use of harmful coping mechanisms.

Our analysis showed the highest percent of ED visits (75.7%) were in those ages 18–24, with 47.4% among ages 21–24. While cannabis is legal to purchase by those 21 and older at RI dispensaries, research recommends waiting until age 25 or later to use cannabis due to the critical period of brain development.[1] Further analyses into this age demographic will be conducted and used to inform educational campaigns on lower-risk use guidelines for those legally able to purchase cannabis.[16]

Analysis of primary diagnosis ICD-10 codes showed inconsistent use and almost 90% of cannabis-related ED visits did not report a cannabis-related ICD-10 code as the primary diagnosis. Future work will evaluate how accurately ICD-10 codes capture cannabis-related ED visits and examine the co-occurrence of cannabis-related ICD-10 codes with other co-morbidities to further define the role of cannabis in ED visits.

Like other states where cannabis was legalized, RIDOH recently developed a public health surveillance program for cannabis use. Findings from this analysis provide direction for our future surveillance, education, and outreach efforts and highlight limitations in relying on ICD-10 codes for surveillance. We will continue to monitor the population utilizing ED care for cannabis for negative health outcomes, especially for the high-risk population under 25 as cannabis becomes more widely available in RI.

LIMITATIONS

Cannabis legalization may have changed willingness to report cannabis involvement in ED visits. Additionally, we cannot determine if the patient is a medical marijuana patient, reason for use of the cannabis product, if the cannabis product was purchased through a regulated source, or if the exposure was intentional or accidental.

The lack of standardization of ICD-10 codes within hospitals and between clinicians may underestimate the burden of cannabis exposure in this population. We cannot infer the effect cannabis exposure had on the patient's clinical presentation or medical severity. We also cannot determine any long-term medical conditions, such as cannabinoid hyperemesis syndrome or cannabis use disorder, that may result from frequent chronic cannabis use and are more accurately diagnosed in other healthcare settings.

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Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

VITAL EVENTS	REPORTING PERIOD		
	APRIL 2024	12 MONTHS ENDING WITH APRIL 2024	
	Number	Number	Rates
Live Births	877	10,911	10.3*
Deaths	839	10,727	10.1*
Infant Deaths	7	48	4.4#
Neonatal Deaths	3	31	2.8#
Marriages	428	6,505	6.1*
Divorces	216	2,511	2.4*

* Rates per 1,000 estimated population
# Rates per 1,000 live births

Underlying Cause of Death Category	REPORTING PERIOD			
	OCTOBER 2023	12 MONTHS ENDING WITH OCTOBER 2023		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	258	2,426	221.1	3,127.0
Malignant Neoplasms	209	2,243	204.4	4,674.0
Cerebrovascular Disease	30	485	44.2	545.0
Injuries (Accident/Suicide/Homicide)	82	1,028	93.7	13,785.0
COPD	36	463	42.2	445.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 estimated population of 1,097,379 for 2020 (www.census.gov)
(c) Years of Potential Life Lost (YPLL).

NOTE: Totals represent vital events, which occurred in Rhode Island for the reporting periods listed above.
Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

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Thanks to RIMJ's Guest Editors of 2024

This issue marks the completion of 107 years of the *Rhode Island Medical Journal* (RIMJ), which transitioned to an online-only journal in 2013, available at rimedj.org.

Although the platform of the Journal has changed to a digital one, its mission remains the same as it has for more than a century – to be the medical journal of record for the state and now regionally, offering diversity of content with a wide variety of article types which have implications for current clinical practice.

Going digital and a LinkOut icon to free articles indexed on PubMed.gov has enhanced its scope exponentially; this year the Journal has reached approximately 64,000 unique viewers worldwide .

As RIMJ is about to enter its 108th year, RIMJ's editors thank the guest editors and contributors of this year and over the decades. Without them and the support of its publisher, the Rhode Island Medical Society (RIMS), and the RIMJ Editorial Advisory Board, the ongoing success of the Journal for more than a century would not be possible. ❖

AUGUST 2024

INJURY PREVENTION AND CONTROL

MICHAEL J. MELLO, MD, MPH

GUEST EDITOR

Introduction: Injury Prevention and Control: Mitigating Risk, Adopting Protective Strategies
MICHAEL J. MELLO, MD, MPH

The Modified 5-Item Frailty Index, Mortality, and Hospital Length of Stay in Geriatric Traumatic Fall Injuries
DANIEL ANTONSON, MD, MSc
JULIE BROMBERG, MPH
STEPHANIE LUECKEL, MD
MICHAEL J. MELLO, MD, MPH

Structure and Function Are Not the Same: The Case for Restoring Mechanoreceptor Continuity Following Anterior Cruciate Ligament Injury
JILLIAN E. BEVERIDGE, PhD
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ATA M. KIAPOUR, PhD
BRADEN C. FLEMING, PhD

Preventing Sleep-Related Deaths in Infants
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MARY KATHRYN CANCILLIERE, PhD
KATE M. GUTHRIE, PhD
KATHLEEN DONISE, MD
TIMMY LIN, MPH
LINDSAY ORCHOWSKI, PhD
ANTHONY SPIRITO, PhD

Characteristics of Interpersonal Violence and Intimate Partner Violence Among Injured Adults Seeking Emergency Care in Nairobi, Kenya
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NICHOLAS MOMANYI
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NOVEMBER 2024

FUNCTIONAL NEUROLOGICAL DISORDER (FND)

HEATHER A. CHAPMAN, MD; REBECCA LAPTOOK, PhD
GUEST EDITOR

Introduction: Functional Neurological Disorder in Children and Adolescents: A Medical Chameleon
HEATHER A. CHAPMAN, MD
REBECCA LAPTOOK, PhD

Functional Neurological Disorder in Pediatrics: Diagnostic Considerations
HALEY MOULTON, MD
DIANE DERMARDEROSIAN, MD
HEATHER A. CHAPMAN, MD

The Importance of Language and Messaging in Psychological Treatment for Functional Neurological Disorder in Children and Adolescents
REBECCA LAPTOOK, PhD

The Rehabilitation Therapist's Role in the Treatment of Functional Neurological Disorder in Children and Adolescents
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KAYLA PETITPAS, MS, OTR/L, CLC
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Supporting Children and Adolescents with Functional Neurological Disorder in the School Setting
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Functional Neurological Disorder in Adults
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JESSICA SCOTT, DPT, ATC, CSCS
HEATHER A. CHAPMAN, MD


DECEMBER 2024

SEXUALLY TRANSMITTED INFECTIONS (STIs)

PHILIP A. CHAN, MD, MS; MICHAELA MAYNARD, NP
GUEST EDITOR

Addressing Sexually Transmitted Infections in Rhode Island
PHILIP A. CHAN, MD, MS
MICHAELA MAYNARD, NP

HIV and Other Sexually Transmitted Infections in Rhode Island: Trends, Disparities, and Health Equity
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CAROLINE GUMMO, MHS
THOMAS BERTRAND, MPH, MA
EMMA CREEGAN, MPH
LAUREN TOSI, MPH
ERIN BROWN, MPH
MEGHAN MACASKILL, MS, MPH
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SUZANNE BORNSCHEIN, MD

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Achieving Top National Mpox Vaccination Coverage for Gay, Bisexual, and Other Men Who Have Sex with Men in Rhode Island: The Critical Role of Community Engagement, Public Health Collaboration, and Health Equity
THOMAS BERTRAND, MPH
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Implementing a Community-Based LGBTQ+ and Sexual Health Program in Providence, Rhode Island
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Reed delivers $1.5M for expansion of Bryant School of Health & Behavioral Sciences

SMITHFIELD — In an effort to help bridge health care education and train more mental health clinicians, U.S. Senator **JACK REED** recently joined students, educators, and Bryant University leadership to deliver a $1.5 million federal earmark to strengthen health and behavioral sciences instruction and prepare more mental health care and health professionals to enter the local workforce.

The $1.5 million federal earmark secured by Senator Reed is for Bryant University's School of Health and Behavioral Sciences (SHBS) and its new doctoral program in clinical psychology (PsyD), which will launch next fall and be the first program of its kind in Rhode Island.

The funding secured by Senator Reed will support renovation and expansion of SHBS to more than double its current footprint and house state-of-the-art teaching and research labs that will support Bryant's curricular efforts to foster the development of a modern health care workforce.

Senator Reed joined Bryant University President **DR. ROSS GITTELL**, Provost and Chief Academic Officer **DR. RUPENDRA PALIWAL**, Director of SHBS **DR. KIRSTEN HOKENESS**, and Associate Director of SHBS and President of the RI Psychological Association **DR. JOSEPH TRUNZO** to tour the SHBS, discuss plans for the two-phase expansion project, and to meet with students currently enrolled in the program.

Phase 1 of the expansion of campus science facilities will directly support the growth of Bryant's PsyD program. The first phase will include:

- Behavioral Health/Psychology suite including seven observation and counseling labs, cognitive and psychophysiology labs, and a child development center.

Phase 2 of the expansion will include:

- Six teaching labs and a healthcare informatics lab;
- Six research labs supporting faculty and student research programs and a shared health care informatics lab which can serve as a core facility for the state; and
- Laboratory prep areas, chemical storage, and waste rooms.

Bryant University launched its new School of Health and Behavioral Sciences in 2022 as part of Bryant's Vision 2030 Strategic Plan, building on successful programs like the university's Master of Physician Assistant (PA) program. ❖

VA Providence celebrates THRIVE kick-off and Center of Innovation's five-year research renewal

PROVIDENCE — The VA Providence Healthcare System hosted its THRIVE (Transformative Health Systems Research to Improve Veteran Equity) kick-off event recently, celebrating the Center of Innovation's renewal for another five years of research.

The event brought together Veterans, staff, and community supporters to mark the occasion and reflect on the Center's contributions to innovative research and Veteran care. The renewal ensures that the Center of Innovation will continue its mission of advancing healthcare solutions that promote resilience and improve outcomes for the Veteran community.

"Receiving a 5-year renewal for our Center of Innovation is a testament to the hard work and dedication of our research team," said **LAWRENCE CONNELL**, Director of VA Providence and retired Army Colonel. "This renewal allows us to further our commitment to leading research that makes a tangible difference in the lives of Veterans." ❖

Rhode Island Hospital first in nation to install QIAcuityDx

PROVIDENCE — Rhode Island Hospital announced that it is the first hospital in North America to install the innovative QIAcuityDx machine. This cutting-edge, revolutionary technology will leverage RNA sequencing to transform clinical testing, offering highly precise quantitation of pathogen RNA targets. While marketed by Qiagen, the QIAcuityDx is set to enhance monitoring of cancer progression and streamline less invasive liquid biopsies; however, this machine will be used initially to better diagnose pathogens causing sepsis.

The research will employ deep RNA sequencing of whole blood samples from sepsis patients to create targets for use on the QIAcuityDx, enabling the identification of the pathogens responsible for the disease. This knowledge will facilitate better resource allocation, predict patient outcomes, and uncover novel therapeutic targets.

"We are excited to be at the forefront of this important research," said **SEAN MONAGHAN, MD**, trauma surgeon at Rhode Island Hospital. "The QIAcuityDx will allow us to apply cutting-edge technology in the fight against sepsis, improving outcomes for our patients and paving the way for future advancements in precision medicine." ❖

Women & Infants Hospital reaches $35M campaign goal to build state-of-the-art Labor & Delivery Center

PROVIDENCE – Women & Infants Hospital announced *The Campaign to Deliver Our Future* has successfully exceeded its $35 million campaign goal. The campaign, an unprecedented initiative, began in 2021 to build a 20-room labor & delivery center and establish a Women's Health Research Institute.

The Brown University Labor & Delivery Center at Women & Infants Hospital will be completed by the end of December 2024. Patients will begin delivering babies in Spring 2025 and the ceremonial ribbon cutting is scheduled for May 2.

The new building features the latest medical technology, modern design, and improved workspace for clinical staff. The space also enhances interdisciplinary clinical collaboration and education. Patients will benefit from doubled labor room sizes, all with private baths. The unit will also offer no-intervention rooms and accommodate a range of birthing options patients desire, including an alongside unit.

Most importantly, the new unit is designed to improve patient outcomes and provide an equitable birthing environment for all women across the region who rely on this Hospital to deliver their babies.

"With this bold vision for our future, Women & Infants Hospital has undergone one of its most ambitious fundraising campaigns to date," said **SHANNON R. SULLIVAN**, president and COO, Women & Infants Hospital. "We built this labor and delivery space with input from our patients and staff, including designing a mock-up room with whiteboards to collect feedback. It was immensely important to us that we listened to the team to enable us to construct a better-designed birth center."

MICHAEL WAGNER, MD, president and CEO, Care New England, noted, "The Brown University Labor & Delivery Center will be a place of joy and celebration and ensure the highest quality of care for every member of the community. We are so thankful to the many donors and community members who have made this facility possible." ❖

American Lung Association's 'State of Lung Cancer' report reveals stark differences in survival, screening and treatment across states

CHICAGO — Lung cancer is the leading cause of the cancer deaths in the U.S., but the American Lung Association's 2024 "State of Lung Cancer" report reveals positive news. The lung cancer survival rate has improved 26% in the last five years. The report also presents opportunities for states to further improve lung cancer survival by increasing access biomarker testing, and for the federal government to work to increase access to screening.

The organization's seventh annual "State of Lung Cancer" report highlights how the toll of lung cancer varies by state and examines key indicators throughout the U.S. including new cases, survival, early diagnosis, surgical treatment, lack of treatment, screening rates and insurance coverage of comprehensive biomarker testing.

New this year, "State of Lung Cancer" examines insurance coverage of comprehensive biomarker testing across the U.S. Lung cancer biomarker testing, sometimes referred to as tumor, molecular, genomic or genetic testing, looks for changes in the tumor's DNA. The results of the test may show biomarkers that can help determine what treatment options would be best for an individual patient. Insurance coverage of biomarker testing is important for removing a cost barrier to people with lung cancer, but coverage for biomarker testing is only required in some states. The report found that only 15 states require insurance coverage of comprehensive biomarker testing, five states require some plans to cover testing, and 30 states and Washington, D.C. have yet to require any coverage of biomarker testing.

The report also closely tracks lung cancer screening nationally and by state. In 2023, only 16% of those eligible were screened nationally. Rhode Island has the best screening rating at 28.6%, while Wyoming has the worst at 8.6%. Note that this year, the Lung Association used a new data source for lung cancer screening rates, so they cannot be compared to previous "State of Lung Cancer" reports.

Close to 235,000 people in the U.S. will be diagnosed with lung cancer this year. In addition to screening rates and state health coverage of comprehensive biomarker testing, which were discussed above, the 2024 "State of Lung Cancer" report found the following national trends in survival rate, early diagnosis, surgery, lack of treatment and health disparities:

- **Survival Rate:** Lung cancer has one of the lowest five-year survival rates because cases are often diagnosed at later stages, when it is less likely to be curable. The national average of people alive five years after a lung cancer diagnosis is 28.4%. Survival rates were best in Massachusetts (37.9%) and worst in Oklahoma (22.2%).
- **Early Diagnosis:** Nationally, only 27.4% of cases are diagnosed at an early stage when the five-year survival rate is much higher (64%). Unfortunately, 43% of cases are not caught until a late stage when the survival rate is only 9%. Early diagnosis rates were best in Massachusetts (34.7%), and worst in Hawaii (21.1%).
- **Surgery as First Course of Treatment:** Lung cancer can often be treated with surgery if it is diagnosed at an early stage and has not spread. Nationally, 20.7% of cases underwent surgery. Surgical treatment rates decreased by 2% in 2021, likely due to the impact of the COVID-19 pandemic on utilization of medical care.
- **Lack of Treatment:** There are multiple reasons why patients may not receive treatment after diagnosis. Some of these reasons may be unavoidable, but no one should go untreated because of lack of provider or patient knowledge, stigma associated with lung cancer, fatalism after diagnosis or cost of treatment. Nationally, 20.9% of cases receive no treatment. Lack of treatment rates were highest in Nevada (36.7%), and lowest in Massachusetts (13.2%).
- **Health Disparities:** The report also highlights that people of color who are diagnosed with lung cancer face worse outcomes compared to white individuals. According to "State of Lung Cancer," people of color who are diagnosed with lung cancer are less likely to be diagnosed early, less likely to be alive five years after diagnosis, less likely to receive surgical treatment and more likely to receive no treatment. More must be done to eliminate lung cancer health disparities.

The 2024 "State of Lung Cancer" report highlights opportunities for states and the federal government to reduce the burden of lung cancer and encourages everyone to help end lung cancer. This year, the American Lung Association calls for all states to implement policies to require insurance coverage of comprehensive biomarker testing. The Lung Association also calls on Congress to pass the Increasing Access to Lung Cancer Screening Act (H.R. 4286).

Learn more about "State of Lung Cancer" at Lung.org/SOLC. ❖

Attorney General Neronha announces minor amendments to Centurion decision

Rhode Island hospitals to retain the $45M remaining in escrow

PROVIDENCE — Attorney General **PETER F. NERONHA** announced on November 15 a limited series of clarifications and amendments to the Hospital Conversions Act Decision, originally issued on June 20, 2024, to conditionally approve a transaction that would allow a change in ownership of a health care system that includes two local safety net hospitals, Roger Williams Medical Center and Our Lady of Fatima Hospital, from Prospect Medical Holdings to The Centurion Foundation.

The clarifications and amendments set forth, which address four of the 40 Conditions of the Decision, are intended to provide clarity and promote efficiency in the execution of these Conditions.

Importantly, this Amended Decision does not change the core findings or conclusions of this Office's initial review of the Hospital Conversions Act application, nor does it make any changes to the majority of the conditions initially imposed by this Office including:

Condition 13, which requires the creation of a Hospital Fund in the amount of $66.8 million for the benefit of Roger Williams and Fatima. The Fund will include the entirety of the remaining escrow (approximately $45 million plus interest) required to be set aside by Leonard Green and Prospect Medical Holdings for the Hospitals pursuant to this Office's 2021 Hospital Conversions Act Decision.

The following Conditions have been clarified and/or amended:

Condition 5 (Post-Closing Contracts) is amended to clarify that terminations for cause and/or promotions may be executed without prior notice but requires notification to this Office within 14 days following such actions.

Condition 6 (Pre-Closing Obligations) is amended to clarify that the funds required to complete plans of correction may come from the existing pre-closing PACE escrow amount.

Condition 17 (Turnaround Consultant) is amended because the Office learned that the transacting parties had already began their search for a consultant and the submission of a Request for Proposals (RFP), as initially required by Condition 17, would create inefficiencies for the Parties. Therefore, this Office has removed that requirement and replaced it with a requirement that the New CharterCARE System shall share the scope of the role and potential candidates with the Office no later than 14 days prior to final selection. Furthermore, the Office will not require that there be an escrow created prior to closing to fund the Turnaround Consultant.

Condition 35 (Annual Reporting) is amended to allow for an alternative mechanism of annual financial reporting compliance that is sufficient to allow for appropriate oversight of Centurion's financial condition by this Office. Specifically, in the event that Centurion does not produce audited financial statements in a given year, Centurion shall produce unaudited financial statements prepared by an independent third-party certified public accountant.

Lastly, the Rhode Island Department of Health (RIDOH) is in the process of reviewing Change in Effective Control applications from the applicants. This process is in addition to the Hospital Conversion Act review process. When the owners of a hospital (and certain other healthcare facilities) in Rhode Island want to transfer 50% or more of the ownership, assets, membership interest, authority, or control of the hospital, the transacting parties must file a Change in Effective Control application with RIDOH.

Further details about these clarifications and amendments are available on the Attorney General's website. ❖

Adolescent Behavioral Health Unit at Newport Hospital reaches fundraising goal; construction to begin

NEWPORT — Newport Hospital/Brown University Health announced recently it has surpassed its $5 million fundraising goal for a new Adolescent Behavioral Health Unit (ABHU), allowing construction to begin ahead of schedule. It will be housed within the hospital's campus, with construction expected to take 12 to 14 months.

NEWPORT HOSPITAL

The project aims to address the critical need for pediatric mental and behavioral health services in Newport County, where no local acute care options currently exist for struggling youth. Once the unit is complete, care will be provided in partnership with East Providence-based Bradley Hospital, the country's first psychiatric hospital for children. This will allow Newport Hospital to deliver Bradley's worldclass pediatric behavioral and mental health care to more families closer to their homes on and around Aquidneck Island.

The unit will have eight beds and will serve adolescents ages 12 to 18 years old who are in need of short-term stabilization, assessment, and treatment and include bright and modern group therapy rooms and activity rooms. ❖

Appointments

Brandon Lentine, MD, named medical director for Kent's joint program

WARWICK — **BRANDON LENTINE, MD**, has been named medical director for Kent's joint program.

Dr. Lentine specializes in MAKO robotic-assisted knee replacement, anterior hip replacement, total knee replacement, partial knee replacement, and "re-do" procedures when necessary.

In his new role, Dr. Lentine will oversee Kent's specialized joint replacement program, which is fully integrated from start to finish to deliver personalized care. The joint replacement program guides patients through the preparation process before surgery, during surgery, and through the hospital experience, including post-discharge care.

He earned his MD degree from Albert Einstein College of Medicine in New York City, completed orthopedic surgery residency at the University of Vermont Medical Center, and sub-specialized in hip and knee arthritis at Boston Medical Center.

Dr. Thomas Barrett previously held the position. Under Dr. Barrett's leadership, Kent Hospital obtained the prestigious Joint Commission Gold Seal of Approval for Advanced Total Hip & Knee Replacement. ❖

Brown Surgical Associates' Division of Vascular Surgery welcomes Richard Anthony Meena, MD

PROVIDENCE — Brown Surgical Associates announced that **RICHARD ANTHONY MEENA, MD, RPVI**, has joined the practice's Division of Vascular Surgery. Dr. Meena's special interests include aortic disease (both abdominal and thoracic), cerebrovascular disease, end-stage renal disease, peripheral artery disease, mesenteric disease, and venous disease.

Dr. Meena completed his undergraduate studies at the University of Notre Dame in 2014. He then earned his medical degree in 2018 from the Emory University School of Medicine in Atlanta, Georgia. He stayed at Emory for continued training in the Integrated Vascular Surgery Residency Program. His training included a one-year clinical research fellowship, during which he explored the impact of health disparities and access to care on a number of vascular pathologies, including venous thromboembolism, end-stage renal disease, and peripheral artery disease.

"Ever committed to our mission of providing world-class care close to home for the people of Rhode Island and Southeastern Massachusetts, we're extremely excited to welcome a surgeon of Dr. Meena's caliber to Brown Surgical Associates," said **DR. AURORA PRYOR**, President of Brown Surgical Associates. "His addition only strengthens our world-renowned vascular and endovascular surgery team." ❖

Angie Wright, RN, MSN-L, named Chief Nursing Executive at Brown University Health

PROVIDENCE — Brown University Health announced that **ANGIE WRIGHT, RN, MSN-L**, has joined the organization as Chief Nursing Executive (CNE), a newly created role. She will serve as a strategic leader for nursing services across the system and as the Chief Nursing Officer for Rhode Island Hospital and Hasbro Children's. The CNE will play a crucial role in collaborating with senior leaders and nursing staff to implement best practices, drive system-wide initiatives, and maintain compliance with healthcare regulations.

"We see this position as a champion for the voice of nursing, developing talent and ensuring successful recruitment, retention, and succession within our nursing leadership," said **SARAH FROST**, chief of hospital operations and president of Rhode Island Hospital and Hasbro Children's. "I know this new position will be a wonderful resource for nursing across the system. I'm excited to have Angie's focus, expertise, and leadership skills onboard."

She comes from Banner University Medicine in Tucson, Arizona, where she served as Chief Nursing Officer for the past four years at a Magnet-designated medical center. Her experience encompasses oversight of two academic medical centers, a cancer center, and over 30 ambulatory sites. ❖

Appointments

Thundermist Health Center announces Chuck Jones as incoming President and CEO

WARWICK — Thundermist Health Center announced **CHUCK JONES** will be returning to serve as president and CEO. Jones previously worked as president and CEO at Thundermist 2011–2017 before joining Harbor Health Services in Massachusetts. He will start his new tenure beginning December 2.

Chuck Jones pictured here with Interim CEO Maria Montanaro.

MARIA MONTANARO initially stepped in at the Thundermist board of directors' request on September 9 to manage the fiscal crisis the community health center was facing, and subsequently worked with the board in their recruitment of Jones. Montanaro, who also previously served as president and CEO from 1997–2011, has been successful in her effort to stabilize Thundermist and raise the working capital necessary to see the health center through the current crisis. She credits the willingness of stakeholders across Rhode Island to provide cash advances as the key that has allowed Thundermist to enact fiscal recovery plans without any interruption in service at its locations in Woonsocket, West Warwick, and South County.

Jones rejoins Thundermist after an eight-year tenure as CEO of Harbor Health Center, which provides services at various locations in eastern Massachusetts. His strong record of leadership and intimate knowledge of Thundermist and Rhode Island's healthcare environment will ensure Thundermist remains one of the state's premier primary care providers.

"We are thrilled Chuck has agreed to return to Thundermist," says **ERIN COONEY**, Thundermist board chair. "The board has been actively engaged in managing this crisis, including recruiting Maria to provide strong interim leadership. We have implemented a robust approach to board development and training, including adding new members that have a wealth of industry expertise and community experience to strengthen our efforts. We are confident Chuck is the optimal choice to assure Thundermist's success."

Jones is excited to return to Thundermist and lead the organization through its current challenges and beyond. "Thundermist gave me an introduction to community health 15 years ago, and this feels like coming home," he says. "I am committed to working with our team to successfully get through this difficult period. As we do, we will continue to focus on delivering the exceptional care our patients rely on, and our communities have come to expect. I look forward to rejoining my colleagues in Rhode Island as we work to ensure the strength of our primary care system." ❖

Recognition

Westerly Hospital earns "A" Hospital Safety Grade from Leapfrog

WESTERLY — Westerly Hospital earned an "A" Hospital Safety Grade from The Leapfrog Group, an independent national nonprofit watchdog focused on patient safety. "The safety of our patients is our most important priority and the focus of every interaction, every decision and every patient-care plan," said **RICH LISITANO**, president of Westerly Hospital. "I'm extremely proud of our team at Westerly Hospital for their exceptional performance and collaboration in keeping our patients safe in our care."

"This is an outstanding achievement for Westerly Hospital," said **OLIVER MAYORGA, MD**, chief medical officer for Westerly Hospital. "As a high reliability organization we strive to consistently perform safely, efficiently and with high quality."

The Leapfrog Hospital Safety Grade rates the safety of general hospitals in the United States. The grade is based on over 30 measures, including the number of errors, accidents, injuries and infections, as well as the hospital's systems to prevent them. The program is peer-reviewed, fully transparent and free to the public. Grades are updated twice annually, in the fall and spring.

Over the past year, Westerly Hospital has improved its Leapfrog safety grade from a B in the spring and fall of 2023. The hospitals scored an A grade in the fall of 2022. Westerly achieved its latest top rating in several categories, including its nursing and bedside care for patients, effective leadership to prevent errors, hand hygiene, safe medication ordering and administration. ❖

Four Brown hospitals receive high grade for patient safety from Leapfrog Group

PROVIDENCE — Four hospitals within the Brown University Health system received an "A" Hospital Safety Grade from The Leapfrog Group, a national nonprofit upholding the standard of patient safety in hospitals and ambulatory surgery centers. The four hospitals gaining this distinction in patient safety are The Miriam Hospital, Newport Hospital, RI, Saint Anne's Hospital in Fall River, and Morton Hospital in Taunton, MA; in addition, Rhode Island Hospital in Providence, RI earned a "B" for Fall 2024.

"This recognition highlights the dedication of our entire team at Brown University Health. We are steadfast in protecting those we serve, preventing harm, and reducing errors – ensuring that every patient receives the safest, most compassionate care possible," said **SARAH FROST**, chief of hospital operations and president of Rhode Island Hospital and Hasbro Children's.

The Leapfrog Group, an independent national watchdog organization, assigns an "A," "B," "C," "D" or "F" grade to general hospitals across the country based on over 30 national performance measures reflecting errors, accidents, injuries and infections, as well as systems hospitals have in place to prevent harm. ❖

VA Providence achieves 5-Star Patient Survey Rating

PROVIDENCE — VA Providence announced it has achieved a 5-star score on our Patient Survey Rating through Medicare Care Compare. The survey, completed by recently discharged patients, measures key aspects of patient care, including communication with nurses and doctors, staff responsiveness, and the cleanliness and quietness of our environment. These elements are essential to creating a supportive, healing experience for our Veterans, and this 5-star rating shows that we are meeting those expectations.

"We are incredibly proud of this achievement," said **LAWRENCE CONNELL**, Director of VA Providence. "This 5-star rating is a direct reflection of the dedication and compassion our staff bring to their work every day. Our Veterans deserve the best care possible, and this rating reinforces that we are delivering on our commitment to serve those who have served our nation."

The HCAHPS (Hospital Consumer Assessment of Healthcare Providers and Systems) star ratings provide a snapshot of patient experience, one aspect of hospital quality. VA Providence is the only hospital in Rhode Island to receive a 5-star Patient Survey Rating. ❖

South County Health earns "A" Grade for Hospital Safety from Leapfrog Group

WAKEFIELD — South County Health announced that it has once again earned an "A" grade for hospital safety from The Leapfrog Group, a national organization dedicated to promoting transparency and excellence in healthcare. This achievement for the Fall of 2024 marks the eleventh "A" rating South County Health has received since 2018.

"This recognition is an opportunity to reflect on who we are as a healthcare organization and the vital role we fill for the community we are honored to serve," said **KEVIN CHARPENTIER, MD**, VP and Chief Medical Officer at South County Health. "Our 'A' grade represents the collective efforts of every single member of our team, working tirelessly to ensure that South County Health remains a safe and trusted place for care. It's more than a score – it's a promise to our community of prioritizing the highest level of patient care, and our unwavering commitment to ensuring patient safety as Rhode Island's *Most Trusted Health Partner*. Achievements like this reinforce our commitment to being a vital part of this community, not just for today, but for generations to come."

Leapfrog Hospital Safety Grades, formerly known as Hospital Safety Scores, serve as a gold standard measure of patient safety. Utilizing up to 30 national performance measures sourced from the Centers for Medicare & Medicaid Services (CMS), the Leapfrog Hospital Survey, and other supplemental data sources, the Leapfrog Hospital Safety Grade evaluates hospitals' overall performance in safeguarding patients against preventable harm and medical errors. The methodology behind this assessment has undergone rigorous peer review and is published in the esteemed Journal of Patient Safety. ❖

Recognition

Spine Center at Miriam awarded Advanced Certification from The Joint Commission

PROVIDENCE — The Miriam Hospital has earned The Joint Commission's Gold Seal of Approval® for The Spine Center. The Gold Seal is a symbol of quality that reflects a health care organization's commitment to providing safe, quality patient care.

"The Department of Orthopedics is excited that The Spine Center at The Miriam Hospital is now an accredited Spine Center of Excellence after formal review by The Joint Commission. This Center is a joint neurosurgery and orthopedics collaborative center – one that is highly organized, sophisticated, and offers a wide variety medical and surgical services," said **EDWARD AKELMAN, MD**, chief of orthopedics, The Spine Center at The Miriam Hospital.

The Joint Commission's standards are developed in consultation with health care experts and providers, measurement experts and patients. They are informed by scientific literature and expert consensus to help health care organizations measure, assess and improve performance. The Spine Center at The Miriam Hospital underwent rigorous unannounced onsite observations and interviews to achieve advanced accreditation.

"The Spine Center at The Miriam Hospital was conceived from our dedication to providing the best spine care possible to our local patients and those who travel long distances to have their spine surgery here in Rhode Island. Obtaining advanced certification is a testament to that dedication, and the teamwork of many skilled experts at The Miriam Hospital," said **ALAN DANIELS, MD**, chief, division of spine surgery, adult spinal deformity service, The Miriam Hospital. "Our patient outcomes are among the best in the country, even when caring for the most complex cases. We remain dedicated to continuing to improve spine care for all patients who choose The Miriam Hospital for their spinal surgeries." ❖

Philip Rizzuto, MD, receives Hoskins Center IRIS Registry Award

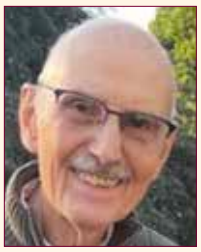
SAN FRANCISCO — The American Academy of Ophthalmology (AAO) announced that **PHILIP RIZZUTO, MD**, Rizzuto Eyelid and Facial Plastic Surgery, is among the 2024 Winners of the Hoskins Center IRIS Registry Research Fund. In 2024, H. Dunbar Hoskins Jr., MD, established and endowed the award, which recognizes outstanding efforts for one private practice ophthalmologist each year who utilized big data from the IRIS Registry to answer important clinical questions that are frequently encountered in a quest to improve eye care for their patients.

Dr. Rizzuto will focus on blepharoptosis and how it affects patients' quality of life and vision, and analyze what factors contribute to its development in a large population-based study. He will investigate using the IRIS Registry data to understand these sociodemographic and clinical factors better, and to describe disparities in access to treatment and outcomes.

The Hoskins Center IRIS Registry Research Fund funds four or more IRIS Registry analytics projects in 2024, with more opportunities expected in the future. Each award is $35,000: $5,000 goes to the investigating member, $30,000 goes to the Academy for expenses related to data access and analysis. Awardees will also be supported for travel to the Academy office in San Francisco. During this visit, awardees will learn about the IRIS Registry database, receive an introduction to big data analytics and work closely with Academy staff on the analysis.

For more information: https://www.aao.org/iris-registry/data-analysis/hoskins-center-research-fund ❖

Obituary



ROBERT D. MERINGOLO, MD, 80, passed away peacefully, surrounded by family, on November 5.

Born in NYC, son of Louis Meringolo and Angela (D'Agastine) Meringolo. Robert is survived by his loving wife Debra, children Claudia and Christopher Meringolo, and stepchildren Courtney and Seth Menard, 5 grandchildren Brittany, Theo, Zion, Zavier and Zakai, his brother Louis and nieces Michelle and Melissa, as well as his dear friends Marvin Cramer, Ed Wittels and Kathy Higginbotham.

He attended prestigious high school Poly Prep in Brooklyn where he played football and lacrosse and was president of his class for all four years. He attended Brown University, attaining a BA in human biology. He was a member of the squash club and was elected president of the chapter of Delta Phi fraternity. He continued his education at Jefferson Medical College earning his MD degree. He then served his medical internship at Metropolitan Hospital in NYC, followed by his residency and fellowship at St. Luke's Hospital. He later joined the Public Health Service, stationed in Washington DC at the HEW (Health, Education & Welfare Dept) as well as a one-year tour in Vietnam as a Lieutenant Commander.

He moved to RI in 1976 where he started in private practice at Providence Cardiology. He later joined Cardiovascular Associates of RI and eventually became affiliated with South Coast Physicians Group. He was also a physician and medical director at The Rhode Island School of Design. He was on staff at Miriam, Veteran's, and Roger Williams Hospitals. He retired in 2017 as an Associate Professor of Medicine and an Emeritus Clinical Associate Professor and was active in teaching students, residents, and fellows. After retirement he was a facilitator in the second year cardiology course at the Warren Alpert Medical School. During his career he was recognized as an outstanding teacher by his students. He also volunteered at the Washington Free Clinic in Georgetown, and at the RI Free Clinic in Providence.

He was appreciative of all that was given to him and tried to reciprocate. He could not have succeeded without the love and support of his wife, family and friends.

Online memorial: jjduffyfuneralhome.com ❖