

# **Master Thesis**

**The incidence of urogenital chlamydia, gonorrhea, syphilis and  
HIV at the University Hospital of St. Poelten  
– an explorative retrospective study**

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## **Statutory Declaration**

I declare that I have developed and written the enclosed Master Thesis completely by myself and did not use sources or means without declaration in the text.

Any thoughts from others or literal quotations are clearly marked.

The Master Thesis was not used in the same or in a similar version to achieve an academic grading or is being published elsewhere.

Vienna, May 2022

Pracherstorfer Carina, BSc

## **Abstract English**

### **Background**

Sexually transmitted diseases are still an important topic. In this thesis, the incidence of urogenital chlamydia, gonorrhea, syphilis and HIV at the University Hospital of St. Poelten is observed. It is an explorative retrospective study that includes data from 2012 to 2019.

### **Methods**

Data used in this study were provided by the Department of Hygiene and Microbiology of the University Hospital of St. Poelten. For each patient positively tested for any of the above sexually transmitted infections, the following additional parameters were retrieved from the available electronic patient records accessible at the Department of Dermatology and Venereology at the University Hospital of St. Poelten: age, gender, postal code, the initial year of diagnosis, reinfection and coinfection (including hepatitis B or hepatitis C).

### **Results**

From January 1<sup>st</sup>, 2012 to December 31<sup>st</sup>, 2019 a total of 299 patients are included in this study: 123 are female and 176 are male. Of those, the fewest are patients infected with HIV. Twelve patients were newly diagnosed with HIV. Fifty-six patients with gonorrhea, 111 patients with syphilis, and 120 patients with chlamydia are included in this study. The year with the highest number of patients diagnosed was 2015. Ninety-five patients were younger than 25 years old, 159 patients were between 25 and 50 years old, 39 patients were between 51 and 75 years old and 6 patients were older than 75.

Study data: Incidences of HIV, gonorrhea, syphilis and chlamydia of all included individuals living in Lower Austria from 2012 to 2019<sup>1,2</sup>

<b>Year</b>	<b>Incidence HIV</b>	<b>Incidence gonorrhea</b>	<b>Incidence syphilis</b>	<b>Incidence chlamydia</b>
<b>2012</b>	0.06	0.06	0.43	0.5
<b>2013</b>	0	0.43	0.56	1.54
<b>2014</b>	0.12	0.49	1.11	1.85
<b>2015</b>	0.24	0.37	1.16	2.63
<b>2016</b>	0.06	0.42	0.3	0.36
<b>2017</b>	0	0.54	0.9	0
<b>2018</b>	0.12	0.24	0.84	0.06
<b>2019</b>	0.06	0.54	1.01	0.06

Study data: Incidences of HIV, gonorrhea, syphilis and chlamydia of all included individuals living in St. Poelten City and County from 2012 to 2019<sup>1,2</sup>

<b>Year</b>	<b>Incidence HIV</b>	<b>Incidence gonorrhea</b>	<b>Incidence syphilis</b>	<b>Incidence chlamydia</b>
<b>2012</b>	0.56	0.56	0.56	3.38
<b>2013</b>	0	1.69	1.69	8.43
<b>2014</b>	0.56	2.24	1.68	10.62
<b>2015</b>	1.11	0.55	2.77	17.2
<b>2016</b>	0	2.74	2.19	1.1
<b>2017</b>	0	2.71	3.26	0
<b>2018</b>	0.54	1.08	3.78	0.54
<b>2019</b>	0	1.61	4.84	0.54

## Conclusion

This study concludes that a total of 299 patients were newly diagnosed with HIV or infected with gonorrhea, syphilis, or chlamydia between 2012 and 2019. With 59% the number of male patients was higher compared to the number of female patients. Most patients included were between 25 and 50 years old. Despite sexual education and advertising the number of people infected with sexually transmitted diseases is still increasing.

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## List of abbreviations

AIDS	Acquired Immune Deficiency Syndrome
CDC	Centers for Disease Control and Prevention
CLIA	Chemiluminescent-Immunoassay
CMV	Cytomegaly Virus
DIG	Disseminated Gonococcal Infection
ECDC	European Centre for Disease Prevention and Control
ELISA	Enzyme-Linked Immunosorbent Assay
HIV	Human Immunodeficiency Virus
INSTI	Integrase Strand Inhibitors
LGV	Lymphogranuloma Venereum
MSM	Men who have Sex with Men
NAAT	Nucleic Acid Amplification Test
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitors
NRTI	Nucleoside Reverse Transcriptase Inhibitors
PCR	Polymerase Chain Reaction
PI	Protease Inhibitors
PID	Pelvic Inflammatory Disease
RPR	Rapid Plasma Reagin Test
RT-PCR	Reverse Transcriptase-Polymerase Chain Reaction
STI	Sexually Transmitted Infection
TPPA	Treponema pallidum Particle Agglutination
WHO	World Health Organization



# 1 Introduction

## 1.1 Current situation

According to the World Health Organization (WHO), about one million new sexually transmitted infections (STIs) occur worldwide every day.<sup>3</sup> Over the last years increasing numbers of STIs have been observed.<sup>4</sup> According to the Centers for Disease Control and Prevention (CDC) combined cases of gonorrhea, chlamydia and syphilis in the United States were more than 2.4 million in 2018 compared with 1.8 million in 2013.<sup>5</sup> Epidemiologic data from the European Centre for Disease Prevention and Control (ECDC) show that 'chlamydia is the most frequently reported STI in Europe.'<sup>6</sup> (p1)

O'Connell's statement 'Chlamydia trachomatis is the leading cause of bacterial sexually transmitted infection in the world.'<sup>7</sup> (p391) and the statement above from the ECDC support each other. The most affected groups include young women 15 to 24 years and heterosexuals. This leads to the conclusion that the rates of infections are higher in women compared to men. In the past years, there was a stable trend of overall urogenital chlamydia infections. About 400.000 cases were reported in 2018. It has to be noted that Austria was among those countries that did not report any cases from 2014 to 2018.<sup>8</sup>

The incidence rate of gonorrhea has increased since 2008 from 8.2 cases per 100,000 to 23 cases per 100,000 in 2017. The increase was most evident in men who have sex with men (MSM) but was also seen for women and heterosexual men.<sup>9</sup> The incidence of syphilis has also increased since 2011, especially in MSM, whereas the rates in heterosexual men seem to stay stable. Among heterosexual women a small increase has been observed since 2016.<sup>10</sup> During the past ten years, there has been a slight decrease in the number of people newly diagnosed with HIV in the European Union/European Economic Area overall, although with a high variation at the national level.<sup>11</sup>

Multiple aspects are promoting the rising numbers of STIs. The rate of change in sexual partners has accelerated owing to increasing global travel and online social networking amongst others.<sup>12</sup> As HIV has become a chronic disease with a low risk

of transmission when adequately treated, the use of barrier precautions in vulnerable groups seems to have decreased.<sup>13</sup> In 2019 '1.7 million people were newly infected with HIV.'<sup>14</sup> (p1) It is currently a matter of debate whether or not the introduction of pre-exposure prophylaxis with Tenofovir-Emtricitabine against HIV and therefore decreased safer sex is also a factor for the increasing numbers of other STIs.<sup>15</sup> Since there are high rates of asymptomatic STIs, there is a great risk of unrecognized further transmission.

## **1.2 Human Immunodeficiency Virus (HIV)**

### **1.2.1 Pathogen**

HIV is caused by a retrovirus, the Human Immunodeficiency Virus, which belongs to the lentiviruses.<sup>16</sup> Two types of the virus exist: HIV-1 and HIV-2. It has to be noted that the pathogenic potential of HIV-2 is not as high as the pathogenic potential of HIV-1.<sup>17</sup> HIV-1 can further be divided: M, N, O and P. Worldwide most infected patients have HIV-1 group M. HIV-2 has twice as many subgroups compared to HIV-1.<sup>16</sup>

### **1.2.2 Transmission**

HIV can be transmitted via infectious fluids that include blood or genital fluids. The transmission of these fluids can occur during sexual contact, during blood-to-blood contact, or from mother to child. The viral load in these fluids correlates with the infectiousness. Blood-to-blood contacts are associated with needle-stick-injuries, blood splatters, or needle-sharing. The risk of being infected with HIV through blood that was contaminated with HIV is >90%.<sup>16</sup>

### **1.2.3 Clinical presentation**

HIV infections are categorized into several clinical stages: A, B and C. Stage A including 'asymptomatic HIV-infection, persistent generalized lymphadenopathy and acute (primary) HIV-infection.'<sup>16</sup> (p1130) Patients with HIV-infections in the acute stage have general, gastrointestinal, dermatological and neurological symptoms. Fever, pharyngitis, lymphadenopathy, diarrhea, exanthema, oral thrush or mucocutaneous erosions can be symptoms shown in the acute stage. None of the symptoms seen in acute infection are specific. Especially other acute viral diseases have to be taken

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into consideration. Herpes, Epstein-Barr-Virus or Cytomegaly-Virus are differential diagnoses.

Stage B includes:

- 'Bacillary angiomatosis
- Oropharyngeal candida infection
- Vulvovaginal candida infection: chronic (>1 month) or difficult to treat
- Cervical dysplasia or carcinoma in situ
- Constitutional symptoms such as fever  $>38.5^{\circ}$  (>1x/month) or diarrhea (>1x/month)
- Oral hairy leukoplakia
- Herpes zoster
- Idiopathic thrombocytopenic purpura
- Listeriosis
- Inflammations of the small pelvis, especially with complications (tube- or ovarian abscess)
- Peripheral neuropathy and visceral leishmanosis'<sup>16</sup> (p1130)

All the symptoms and diseases from stage B listed above are not AIDS-defining diseases. Stage C is commonly called AIDS (Acquired Immune Deficiency Syndrome).

Following diseases are AIDS-defining diseases (Stage C):

- 'Candidiasis of the trachea, the bronchia or the lungs
- Candidiasis of the esophagus
- Invasive cervical carcinoma
- Disseminated coccidioidomycosis (on different locations or additionally to lymph nodes in the lung, hilus or cervical lymph nodes)
- Extrapulmonary cryptococcosis
- Chronic intestinal cryptosporidiosis (>1 month persistent)
- Cytomegaly virus infection in patients >1 month
- Cytomegaly virus retinitis with loss of vision
- HIV-encephalopathy or 'subacute HIV-encephalitis'
- Herpes simplex virus (ulcer persistent >1 month) or pneumonia/esophagitis of undefined duration in patients older than one month

- Disseminated histoplasmosis (different localization or additionally to lymph nodes in the lung, cervical or hilus lymph nodes)
- Chronic intestinal isosporiasis, persistent >1 month
- Kaposi-Sarcoma
- Lymphoma: Burkitt- or non-Burkitt-type
- Lymphoma: immunoblastic type
- Lymphoma of the central nervous system
- Every disseminated mycobacterial disease caused by mycobacteria other than mycobacteria tuberculosis, extrapulmonary tuberculosis: in at least one location except the lungs, without consideration of the concurrent pulmonary contribution
- Pulmonary tuberculosis
- Pneumocystis jirovecii pneumonia
- Recurring pneumonia
- Progressive multifocal leukoencephalopathy
- Recurrent septicemia (nontyphoid) caused by salmonella
- Toxoplasmosis of the central nervous system
- HIV-wasting-syndrome (HIV-cachexia) in children <13 years
- Lymphoid interstitial pneumonia and/or pulmonary lymphoid hyperplasia (LIP/PLH-complex)
- Severe multiple or recurrent bacterial infections, every combination of at least two infections within two years: septicemia, pneumonia, meningitis, bone- or joint infections or abscess of an inner organ or a visceral cavity (excluding otitis media, superficial skin- and mucous membrane infections and catheter-associated infection)<sup>16</sup> (p1130)

#### Clinical manifestations of HIV infections:

- Infections of the lung including pneumocystis jirovecii pneumonia, tuberculosis and bacterial pneumonia
- Infections of the gastrointestinal tract including candida stomatitis, oesophagitis with the formation of ulcers and diarrhea
- Infections of the central nervous system including cerebral toxoplasmosis, cryptococcal meningitis and encephalopathy
- Infections due to cytomegalovirus (CMV) including CMV-retinitis

- Malignant tumors including Kaposi-Sarcoma, lymphoma and anogenital squamous cell carcinoma
- Dermatological manifestations including folliculitis, herpes zoster or simplex, Mollusca contagiosa (common in advanced stages) and seborrheic eczema
- Neurological diseases including HIV associated neurocognitive disorders, myelopathies and peripheral neuropathies
- Wasting-Syndrome
- HIV-associated nephropathy<sup>16</sup>

#### **1.2.4 Prevention**

##### **1.2.4.1 Non-medical prevention**

Non-medical prevention includes testing blood donations or blood transfusions for HIV, handling needles (needle-stick-injury) and scalpels with caution, giving away clean needles or syringes to addicts to prevent infections via needle-sharing, usage of condoms and counseling.<sup>16</sup>

##### **1.2.4.2 Medical prevention**

In 2012 pre-exposure prophylaxis (PrEP) with Tenofovir-Emtricitabine was approved by the U.S. Food and Drug Administration (FDA) for people with substantial risk for infection. In 2016 PrEP was also approved by the European Medicines Agency (EMA). Post-exposure prophylaxis, short-term treatment with antiretroviral drugs after a potential HIV exposure to decrease the risk of seroconversion, has already been established for a long time.<sup>18,19</sup>

#### **1.2.5 Diagnosis**

For the detection of HIV, HIV-antigen-antibody-combination (ELISA) and western blot for HIV-1-RNA can be used.<sup>16</sup> 'Every positive HIV ELISA result has to be confirmed by a second venipuncture and the performance of at least two test methods, of which one has to be western blot analysis.'<sup>20 (p56)</sup> More detailed information about the diagnostic methods can be seen in Table 1 on the next page.

Table 1 Diagnostic of HIV-infection (Fritsch, 2018)<sup>16</sup> (p1145)

	<b>Combination test HIV-1/HIV-2-antibodies and p24-antigen</b>	<b>Western blot (a confirmation test)</b>	<b>HIV-1 RNA</b>
<b>Material</b>	Serum	Serum	Fresh EDTA-plasm
<b>Function</b>	Antibodies against HIV-1 and HIV-2, confirmation of viral protein p24	Antibodies against HIV and its separation (confirmation of single protein bands)	Amplification of viral RNA
<b>Methods</b>	ELISA (EIA)	Western blot; result positive if at least two of bands p24, gp160, gp120 are positive	RT-PCR
<b>Indication</b>	Search test	Confirmation, differentiation HIV-1/-2	Search test of fresh infections, confirmation, progression parameter, therapy control
<b>Acute HIV infection (early confirmation)</b>	Day 18	Day 25	Day 11 (sensitivity 100%, specificity 98-100% - depending on the chosen cut-off)

'Indications for an HIV-test:

- AIDS-defining diseases
- Indicator-disease (hepatitis B or C, fever of unknown origin...)
- Diseases in which the non-identification of HIV could have considerable disadvantages for the treatment of this person (transplantation...)
- Pregnancy<sup>16</sup> (p1144)

### 1.2.6 Treatment

The treatment of HIV infections is mostly an adjunction of three medications. Stopping the further replication of the virus in the infected patients is the goal of the antiretroviral therapy, which has to be taken lifelong. Current medications act as fusion inhibitors, receptor blockers or interfere with enzymes called reverse transcriptase, integrase and HIV-specific protease. Nucleoside reverse transcriptase inhibitors (NRTI) and non-nucleoside reverse transcriptase inhibitors (NNRTI) inhibit the enzyme reverse transcriptase. Integrase strand inhibitors (INSTI) inhibit the enzyme integrase and HIV protease inhibitors (PI) inhibit the enzyme protease. NRTIs include Abacavir, Emtricitabin, Lamivudin, Tenofovir and alternatively Zidovudine. NNRTIs include Rilprivirin and alternatively Efavirenz, Nevirapine and Etravirine. INSTIs include Raltegravir, Dolutegravir and Elvitegravir. For PI only alternative medications exist, namely Darunavir, Atazanavir and Lopinavir. In diseased adults the therapy of choice is a combination of INSTI and two NRTI or NNRTI and two NRTI. Without treatment HIV further progresses to AIDS. This takes about ten years.<sup>16</sup>

### 1.2.7 Reporting obligation

There is no reporting obligation for HIV in Austria. It has to be noted that having AIDS or dying from it underlies the reporting obligation.<sup>21</sup>

## 1.3 *Neisseria gonorrhoeae* (gonorrhea)

### 1.3.1 Pathogen

Gonorrhea is caused by gram-negative diplococci called *Neisseria gonorrhoeae*.<sup>16,22</sup> Regarding treatment resistances and diagnostics it is important to know that these bacteria can develop mutations.<sup>4</sup>

### 1.3.2 Transmission

The only way to transmit *Neisseria gonorrhoeae* is through mucosal contact. Mucosal contact occurs during sexual intercourse or birth.<sup>4</sup> Transmission can also occur via oral sex, oral-anal sex, sex toys and more.<sup>23</sup>

### 1.3.3 Clinical presentation

The clinical presentation of these sexually transmitted infections shows local mucosal manifestations. They are located at the site of infection. An important fact is that infections with *Neisseria gonorrhoeae* can also remain asymptomatic in about 50% of cases. When being symptomatic a distinction between women and men must be noticed because their symptoms differ. Systemic complications of gonorrhea include disseminated gonococcal infection, gonococcal arthritis, exanthema and gonococcal endocarditis and meningitis.<sup>16</sup>

#### 1.3.3.1 Women

In comparison, about 50% of infected women remain asymptomatic. Others develop symptoms related to the cervix and the cervical canal which lead to vaginal discharge and dysuria.<sup>4,16</sup> If women remain untreated pelvic inflammatory disease (PID) can develop, which further leads to infertility or chronic pelvic pain. Not only *Neisseria gonorrhoeae* can cause PID but also *Chlamydia trachomatis*. Another further disease that can occur is salpingitis. Very rarely (in about 0.5-3%) disseminated gonococcal infection (DIG) develops. The classic triad of this infection includes 'undulating fever, acute painful polyarthritis and acral vasculitic skin lesions.'<sup>4</sup> (p299) Gonorrhea can also lead to premature birth or abortion in pregnant women. The baby can also be infected which could lead to neonatal conjunctivitis or oropharyngeal infection.<sup>4</sup>

#### 1.3.3.2 Men

The first symptom of gonorrhea in men is in most cases urethritis anterior, which includes dysuria, reddening and burning of the urethra followed by purulent discharge. Urethritis posterior can develop if the infection further ascends due to lack of treatment. If the infection remains untreated for weeks or months the above-mentioned symptoms disappear, and the patient is asymptomatic. Spontaneous healing or the development of mild chronic urethritis can occur. Exacerbations of urethritis can occur and complications can develop.<sup>16</sup> It has to be noted that 'the rectum is frequently the primary site of infection (proctitis)'<sup>4</sup> (p299) in men who have sex with men.<sup>4</sup>





Figure 1 'Bonjour-drop on the ostium urethrae externum with surrounding reddening in gonorrhea' <sup>24</sup> (p68) (Image from Prof. Dr. med. Gernot Rassner, Tübingen)

#### 1.3.4 Prevention

To prevent the transmission of gonorrhea condoms can be used. Testing can also be used for early detection in people with frequently changing sexual partners.<sup>23</sup>

#### 1.3.5 Diagnosis

Until the establishment of the highly sensitive NAAT (Nucleic Acid Amplification Test), culture was the gold-standard method for the diagnosis of urogenital gonorrhea. Currently, the confirmation of suspected infection by direct pathogen detection via NAAT should be performed. Due to the increasing number of antimicrobial resistances, culture is additionally recommended.<sup>25</sup> It has to be noted that NAAT can use PCR (Polymerase Chain Reaction) or isothermal amplification. At the University Hospital of St. Poelten PCR is used.<sup>26</sup>

#### 1.3.6 Treatment

The gold-standard therapy for 'uncomplicated genitoanal infection in adults' is a combination therapy of Ceftriaxone 500mg intramuscular or intravenous as a single dose and Azithromycin 1.5g oral as a single dose.<sup>20</sup> (p18) This is also the recommended therapy for pregnant women or women during lactation.<sup>20</sup>

In general, sexual abstinence is recommended until one week after successful treatment. Patients should inform their sexual partners and should themselves be informed about complications. Complications in diseased men include balanoposthitis, periurethritis, periurethral abscess or prostatitis. Complications in diseased women include vulvitis, cystitis or PID. Screening patients for chlamydia and syphilis is suggested. A reinspection is recommended after about two weeks following treatment.<sup>16</sup>

### **1.3.7 Reporting obligation**

In Austria there is no reporting obligation, unless 'a further spread of the disease is feared or the patient withdraws from medical treatment or observation.'<sup>21</sup> (p4)

## **1.4 Treponema pallidum (syphilis)**

### **1.4.1 Pathogen**

Syphilis, which is also called Lues venerea, is caused by gram-negative bacteria called *Treponema pallidum*. These bacteria belong to the Spirochaetaceae.<sup>16</sup>

### **1.4.2 Transmission**

The most important way of transmission is contact with a highly contagious syphilitic chancre, mostly during sexual intercourse. Another way of transmission is from mother to child during pregnancy.<sup>16</sup>

### **1.4.3 Clinical presentation**

The clinical presentation of syphilis depends on the stage of the infection.<sup>16</sup> There are several stages of syphilis. They are commonly called primary, secondary and tertiary syphilis or syphilis I-III. Syphilis I and II together with early latent syphilis are summarized under the term early syphilis. Late latent syphilis and syphilis III constitute late syphilis. The WHO and the CDC chose different periods from when it is called late syphilis. The WHO chose the end of the 1<sup>st</sup> year of infection and the CDC chose the end of the 2<sup>nd</sup> year of infection.

Syphilis I develops 10 to 90 days after contact. Ulcus durum is also called a syphilitic chancre. The color is mostly reddish-brown and it is not painful. Ulcus durum is representative of the early stages of syphilis and can be seen at the site of the bacterial entrance. Entry points are in the genital or anal region or the 'oral cavity (lips, palate, tongue, tonsils).'<sup>16</sup> (p1058) Commonly affected are 'the frenulum praeputii, the inner leaf of the prepuce and the sulcus coronarius'<sup>16</sup> (p1058) in men and 'the rear commissure, the small labia and the portio uteri'<sup>16</sup> (p1058) in women. Figure 2 shows a syphilitic chancre.<sup>16</sup>



Figure 2 Syphilitic chancre (Ghanem et al., 2020)<sup>27</sup> (p846)

Syphilis II arises 'six to nine weeks after the infection.'<sup>16</sup> (p1059)

Symptoms of secondary syphilis include:

- 'Systemic signs: fever, malaise, weight loss
- Lymphadenopathy
- Exanthema
- Condyloma lata (mostly in intertriginous areas)
- Hepatitis (generally subclinical)
- Neurologic: headache, meningism, meningitis, disturbance of cranial nerves (Neuritis Nervi optici, defective hearing), stroke
- Periostitis (subclinical)
- Uveitis, Iritis
- Glomerulonephritis
- Arthritis
- Alopecia'<sup>16</sup> (p1059)

The first occurring exanthema is called roseola syphilitica.<sup>16</sup> An example of roseola syphilitica, as well as an example of condyloma lata can be seen in Figures 3 and 4.



Figure 3 'Secondary syphilis. Roseola syphilitica' (H. Schöfer, FFM)<sup>4</sup> (p291)



Figure 4 'Condyloma lata' (H. Schöfer, FFM)<sup>4</sup> (p292)

Syphilis II is represented by generalized swelling of the lymph nodes and exanthema. Stages between I and II are asymptomatic latent stages. The combinations and changes of these stages are characteristic of this chronic bacterial infection. Benign syphilis, neurosyphilis and cardiovascular syphilis are the clinical distinctions of tertiary syphilis. It is possible to suffer from more than one of them. Benign syphilis characteristically shows 'gummas'. Gummas are granulomas that can be proliferative or destructive. Nowadays neurosyphilis mostly presents as specific meningitis, endarteritis, or parenchymal degeneration. Symptoms can include deficiencies of

the cranial nerves or tabes dorsalis. Aortic insufficiency or aneurysms are examples of manifestations of cardiovascular syphilis.<sup>16</sup> The course of untreated syphilis infection and important symptoms can be seen as an overview in Figure 5 below.

Conatal syphilis is transmitted from mother to fetus and can lead to consequences.

Following outcomes are generally possible for the child:

- Abort (late abort, mostly after 18 weeks of gestation)
- Stillbirth at the due date
- Syphilis connata (prematurity or at the due date)
- Absence of infection<sup>16</sup> (p1072)

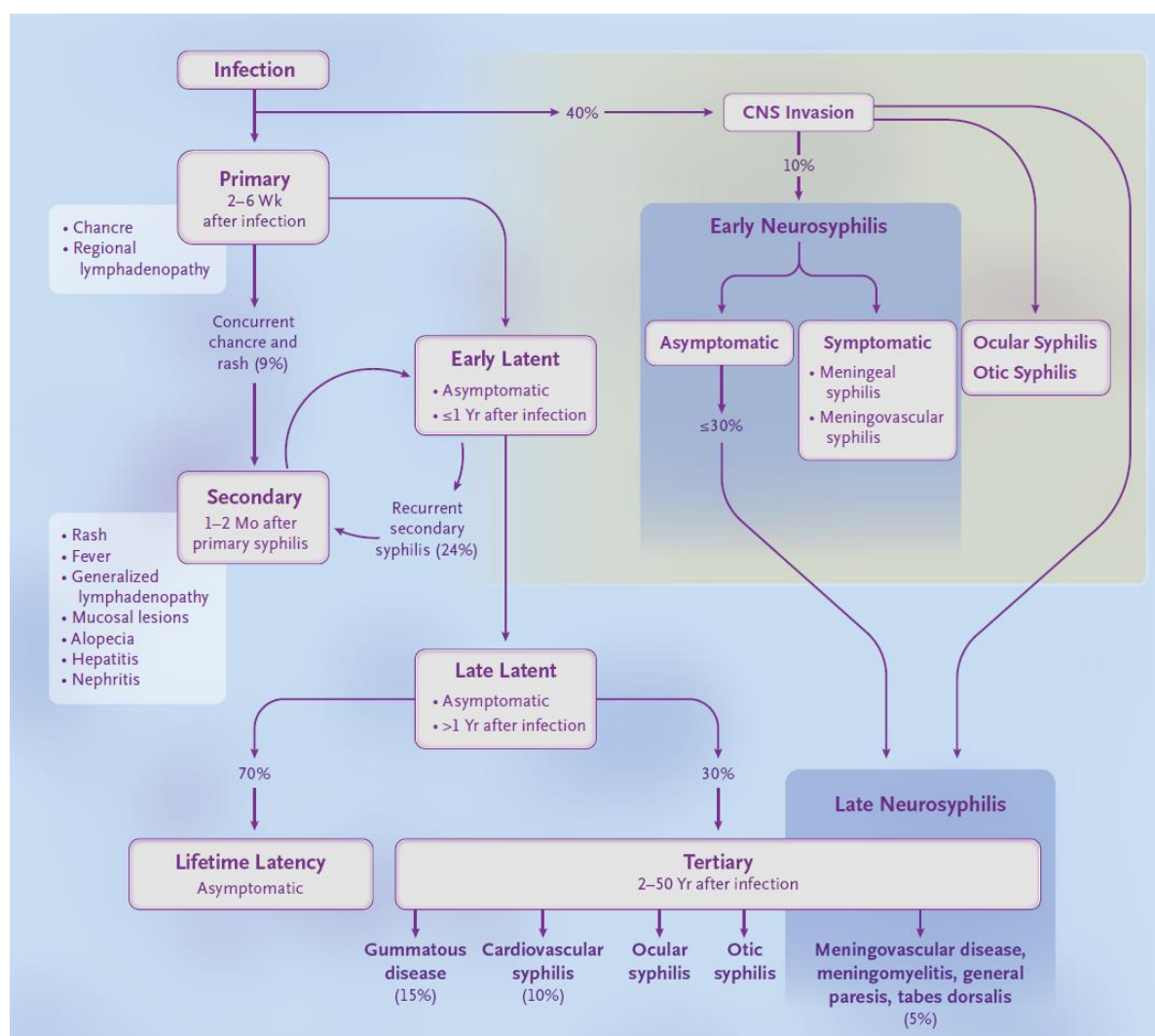


Figure 5 'Natural History of Untreated Syphilis' (Ghanem et al., 2020)<sup>27</sup> (p847)

#### 1.4.4 Prevention

To decrease the risk of infection condoms should be used. Testing can also be useful for early detection of the infection in people with frequently changing sexual partners.<sup>28</sup>

#### 1.4.5 Diagnosis

Although there are different possibilities for direct detection of *Treponema pallidum*, serological tests are the gold-standard in the diagnosis of syphilis. Two different types of serological tests are performed to confirm the diagnosis. Treponemal tests such as TPPA (*Treponema Pallidum* Particle Agglutination Assay) are highly specific and sensitive and can be used as screening tests, they stay positive even after effective treatment. Non-treponemal tests include the VDRL (*Veneral Disease Research Laboratory*), the RPR (*Rapid Plasma Reagin*) test and the toluidine red unheated serum test. These tests detect antibodies, which are present in florid syphilis but are non-specific. Non-treponemal tests are used to monitor the treatment success and a possible reinfection.<sup>29,30,31</sup> At the University Hospital of St. Poelten *treponema pallidum* screen antibody test, TPPA and RPR tests are used. In some cases, IgM and IgG are also used.

#### 1.4.6 Treatment

The treatment of syphilis depends on the stage of the disease. The therapy of choice in early syphilis (including primary and secondary syphilis) and early latent syphilis is Benzathine-Benzylpenicillin. A single dose of 2.4 million units is applied intramuscularly. If contraindications against Penicillin exist Doxycycline is applied twice daily for two weeks. Follow-ups must be done 3, 6 and 12 months after the end of therapy. Tertiary or latent syphilis is treated with Benzathine-Benzylpenicillin. For three weeks patients receive one dosage per week intramuscularly containing 2.4 million units. Penicillin G is applied in patients with neurosyphilis. For two weeks they receive 24 million units intravenously. Pregnant women and children should receive Penicillin as well, as there is a contraindication for tetracyclines in children and pregnant women.<sup>20</sup>

### **1.4.7 Reporting obligation**

In Austria there is no reporting obligation, unless 'a further spread of the disease is feared or the patient withdraws from medical treatment or observation.'<sup>21</sup> (p4)

## **1.5 Urogenital Chlamydia trachomatis (chlamydia)**

### **1.5.1 Pathogen**

Urogenital chlamydia infection is caused by *Chlamydia trachomatis*, a gram-negative obligate intracellular pathogen. *Chlamydia trachomatis* can be divided into several serovars causing different types of infection: Serovar A-K and L1-L3.<sup>7</sup> Urogenital chlamydia infections are caused by serovar A-K. Serovars L1-L3 cause lymphogranuloma venereum (LGV). This disease is endemic in Asia and Africa. In Europe, LGV is not endemic and is most commonly found in men who have sex with men.<sup>4</sup>

### **1.5.2 Transmission**

*Chlamydia trachomatis* is highly infectious and can be transmitted during sexual intercourse or from mother to child during birth.<sup>16</sup>

### **1.5.3 Clinical presentation**

The clinical presentation of chlamydia infection differs in women and men. It is important to note that about 80% of infected women and 50% of infected men show no symptoms.<sup>4</sup>

Serovars A-C cause an endemic ocular infection called trachoma, which is not classified as STI. It is transmitted via smear infection and leads to conjunctivitis. Serovars D-K cause the classic urogenital chlamydial infection as well as proctitis, pharyngitis and conjunctivitis. Serovars L1-L3 cause a rare infection of the lymphatic system leading to lymphogranuloma venereum.<sup>7,16</sup>

#### **1.5.3.1 Women**

In women, urogenital chlamydia most commonly infects the cervix.<sup>4</sup> 'Changes in vaginal discharge, intermittent, intermenstrual and/or post-coital bleeding'<sup>7</sup> (p391) are common symptoms in women.<sup>7</sup> Infertility which may develop due to fallopian tube



obstruction can be observed if the infection arises. The pelvic inflammatory disease may develop if the urogenital chlamydia infection progresses further.<sup>4</sup> This can lead to infertility. Women with urogenital chlamydia in their past medical history have an increased risk for ectopic pregnancy. These bacteria are also 'associated with spontaneous abortion, stillbirth and preterm delivery.'<sup>7</sup> (p391)

According to the study 'Chlamydia Trachomatis Infection-Associated Risk of Cervical Cancer: A Meta-Analysis' there is a link between Chlamydia trachomatis and cervical cancer. The results of this study showed that this STI is associated with a higher risk of developing cervical cancer.<sup>7</sup>

#### 1.5.3.2 Men

In men, urogenital chlamydia can cause urethritis including dysuria and discharge. Painful epididymitis can develop if urogenital chlamydia infections arises. Proctitis can also be caused by Chlamydia trachomatis in women or MSM. In women, this can be linked to a rectal spread of the sexually transmitted infection. In MSM symptoms can include anorectal pain or discharge.<sup>4</sup>

### 1.5.4 Prevention

To decrease the risk of being infected with chlamydia condoms can be used. Testing is also recommended in people with frequently changing sexual partners.<sup>32</sup>

### 1.5.5 Diagnosis

The gold-standard test for the diagnosis of urogenital chlamydia is direct pathogen detection via a nucleic acid amplification test.<sup>33</sup> For this very sensitive and also very specific test 'urethral, cervical, vulvovaginal, conjunctival, pharyngeal and anal swabs'<sup>4</sup> (p305) or first-void urine are needed.<sup>4</sup>

### 1.5.6 Treatment

The treatment of choice for serovars D-K of Chlamydia trachomatis showing symptoms such as 'urethritis, cervicitis, proctitis, pharyngitis or conjunctivitis'<sup>20</sup> (p24) is either Doxycycline or Azithromycin. Doxycycline in 100mg dosage is taken two times daily for one week. The form of application is oral. Due to its side effects, Doxycycline is contraindicated during pregnancy. Azithromycin in the amount of 1g is given



as a single dose orally. During pregnancy Azithromycin, Amoxicillin or Josamycin is used instead of Doxycycline. For treatment of serovar L1-L3, which cause lymphogranuloma venerum, Doxycycline is used for three weeks. It has to be taken two times a day orally. Erythromycin can be used as an alternative also for three weeks but four times a day orally.<sup>20</sup>

If a patient with urogenital chlamydia remains untreated the possibility of the persistence of the STI exists.<sup>7</sup>

### **1.5.7 Reporting obligation**

There is no reporting obligation in Austria.<sup>21</sup>

## **1.6 Hepatitis B Virus (HBV)**

### **1.6.1 Pathogen**

Hepatitis B is caused by a DNA virus consisting of a surface antigen (HBsAg), a core antigen (HBcAg) and an envelope antigen (HBeAg).<sup>16</sup> For every antigen there is a corresponding antibody.<sup>34</sup>

### **1.6.2 Transmission**

Hepatitis B can be transmitted perinatal, via contaminated food (rare) and via infectious fluids, including 'blood, seminal fluid, vaginal secretion, saliva and lacrimal fluid.'<sup>16</sup> (p1098), <sup>20</sup> There is no fecal-oral transmission.<sup>34</sup> Compared to HIV its infectiousness is considerably higher. According to Fritsch, sexual contacts account for the most transmission of hepatitis B.<sup>16</sup>

### **1.6.3 Clinical presentation**

The course of a hepatitis B infection can be asymptomatic, acute or chronic.<sup>20</sup> Over 50% of patients with a spontaneous healing infection develop life-long immunity after infection.<sup>16</sup> Severe consequences of chronic hepatitis B infection, which can also lead to death are hepatocellular carcinoma or cirrhosis. They occur in about 25% of chronically infected patients.<sup>20</sup>

Acute hepatitis B starts with a prodromal stage followed by organ manifestation. The first symptoms patients show are flu-like symptoms and gastrointestinal symptoms. When infections manifest in the liver patients may develop icterus or enlargement of the liver.<sup>34</sup>

Laboratory values of patients with acute hepatitis B show positive HBsAg, HBcAb IgM and positive HBV-DNA. Coinfections with HIV and/or acute hepatitis D can occur. Due to these laboratory values, HIV and hepatitis D have to be determined. Spontaneous healing occurs in almost all adult patients with acute hepatitis B.<sup>20</sup>

After persisting for six months the infection is chronic. Patients then have an enlarged liver, fatigue, reduced appetite, abdominal pain or reduced output. Hepatitis A and hepatitis B vaccinations are recommended for those patients.<sup>34</sup> Laboratory values of patients with chronic hepatitis B show positive HBsAg and/or positive HBV-DNA.<sup>20</sup>

#### **1.6.4 Prevention**

For pre-exposure prophylaxis there is a vaccination. In Austria, hepatitis B is included in the sixfold vaccination for children in their first year. There is also a combined vaccination for hepatitis A. Besides the vaccination non-medical preventive measures can be taken. This includes the use of condoms, handling needles and scalpels with caution or using clean syringes. There is also the possibility of post-exposure prophylaxis. Depending on the patient's status this includes serology (titer) and anti-HBs further measures must be taken. These can include a vaccination or the administration of immunoglobulins.<sup>35</sup>

#### **1.6.5 Diagnosis**

For the diagnosis of hepatitis B infection anamnesis, clinical presentation, diagnostic imaging and laboratory values are needed.<sup>34</sup>

#### **1.6.6 Treatment**

The treatment of hepatitis B consists of general measures and antiviral therapy. It is important to stop drinking alcohol, stop taking hepatotoxic medication and physically rest. Antiviral therapy depends on whether the infection is acute or chronic. Acute hepatitis B infection does not necessarily require therapy.

Antiviral therapy with nucleoside- or nucleotide analogs is needed in patients with decreased liver function. Interferon is not used for therapy. According to the S3-guidelines,<sup>34</sup> (p528) all patients with chronic HBV-infection are candidates for an antiviral therapy. For treatment of chronic hepatitis B, alpha-interferon or nucleoside- or nucleotide analogs are used.<sup>34</sup>

### **1.6.7 Reporting obligation**

For hepatitis infectiosa, there is a reporting obligation in Austria. The reporting obligation results from suspicion of disease and death due to hepatitis infectiosa.<sup>21</sup>

## **1.7 Hepatitis C Virus (HCV)**

### **1.7.1 Pathogen**

Hepatitis C is caused by an RNA virus.<sup>16</sup>

### **1.7.2 Transmission**

Transmission of hepatitis C occurs parenterally, via transfusion, sexual contact, perinatal or sporadic. There is no fecal-oral transmission.<sup>34</sup>

### **1.7.3 Clinical presentation**

The course of a hepatitis C infection can be acute or chronic. Most patients with acute hepatitis C infections are asymptomatic. These patients often develop a chronic infection, compared to patients with acute infections, which can heal spontaneously. Patients with chronic hepatitis C can have reduced output, abdominal pain, fatigue, loss of appetite, icterus or enlarged liver. After a hepatitis C infection, no immunity develops. Hepatitis C can further lead to liver cirrhosis or carcinoma of the liver.<sup>34</sup>

### **1.7.4 Prevention**

Currently, there is no vaccination against hepatitis C. For the prevention of an infection condoms can be used. Clean syringes and needles should be used as well.

### **1.7.5 Diagnosis**

For the diagnosis of hepatitis C infection anamnesis, clinical presentation, laboratory values and diagnostic imaging are used.

### **1.7.6 Treatment**

General measures for the treatment of hepatitis C infection include: no longer taking hepatotoxic medication, no longer drinking alcohol and smoking. Patients with symptomatic hepatitis C infection can heal spontaneously in 50% of cases. Acute hepatitis C infection further progresses into chronic hepatitis C infection in about 80% of the patients. Chronic hepatitis C infection is treated with an adjunction of antiviral medication. Hepatitis A and hepatitis B vaccinations are recommended for all patients with chronic hepatitis C.<sup>34</sup>

### **1.7.7 Reporting obligation**

For hepatitis infectiosa, there is a reporting obligation in Austria. The reporting obligation results from suspicion of disease and death due to hepatitis infectiosa.<sup>21</sup>

## **1.8 Aim of this study**

After having discussed the current situation and having given a comprehensive overview about STIs in general, the goal of this work is to identify newly diseased individuals of HIV, gonorrhea, syphilis and chlamydia administered to the University Hospital of St. Poelten in the years between 2012 and 2019. From these people we obtain the subsequent incidences for Lower Austria and St. Poelten City and County and compare it to the official data provided by the ECDC, 'Statistik Austria' and 'Stadt Wien'. With this approach we want to get a deeper insight into the geographical distribution of STIs on a national and regional level in Austria.

## 2 Materials and Methods

This is a retrospective investigation of registered data of positive microbiological tests for urogenital gonorrhea and chlamydia and serologic tests for syphilis and HIV at the University Hospital of St. Poelten.

The data of interest were identified at the Department of Hygiene and Microbiology at the University Hospital of St. Poelten. Data of positive serologic tests for *Treponema pallidum* and Human Immunodeficiency Virus and data from direct microbial tests for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are included from January 1<sup>st</sup>, 2012 to December 31<sup>st</sup>, 2019.

For each patient positively tested for any of the above STIs the following parameters were retrieved from the available electronic patient records accessible at the Department of Dermatology and Venereology at the University Hospital of St. Poelten: age, gender, postal code, the initial year of diagnosis, reinfection and coinfection (including hepatitis B or hepatitis C). The reference date for the initial year of diagnosis of chlamydia, gonorrhea and syphilis is the completion date provided by the department of microbiology. The postal code is a parameter of interest because it identifies an increased incidence of infections in a particular area.

The data were transferred to an Excel Spreadsheet. Afterwards, patient data were pseudonymized for further evaluation in SPSS.

### 2.1 Inclusion criteria

All patients who tested positive for at least one of the above-mentioned STIs between January 1<sup>st</sup>, 2012 and December 31<sup>st</sup>, 2019 are included in the study. Only data that were available for involved patients when a positive ethics vote was issued are included.

### 2.2 Exclusion criteria

For HIV alone, only newly diagnosed patients are included in the study. For syphilis alone, patients who received treatment before January 1<sup>st</sup>, 2012 and present only with residual antibodies without evidence of reinfection are excluded.

## 2.3 *Treponema pallidum*

Patients infected with syphilis between 2012 and 2019 who received therapy are included in this study. Patients without clear anamnesis or further information and with reactive TPPA and non-reactive RPR are summarized under the term 'serological scar' ('Serumnarbe'). They are not included in this study. Those without clear anamnesis or further information and with reactive TPPA and reactive RPR probably require treatment and are included in this study. Also, patients that should have received treatment but did not appear for their appointment are included. Those were reported to the local health authorities.

## 2.4 Endpoints

The primary endpoints are the incidences of chlamydia, gonorrhea, syphilis and HIV at the University Hospital of St. Poelten from January 1<sup>st</sup>, 2012 to December 31<sup>st</sup>, 2019. The secondary endpoints include age, gender, postal code, the initial year of diagnosis, reinfection and coinfection (including hepatitis B or hepatitis C).

## 2.5 Statistics

Descriptive statistics were used to analyse all parameters. Type of STI, the initial year of diagnosis, age, gender, postal code and rates of re- and coinfections (including hepatitis B and hepatitis C) were described with the help of SPSS. Gender is described as female or male. Age is split up into age groups: <25 years, 25 to 50 years, 51 to 75 years and >75 years.

Absolute frequencies are provided for a description of the number of infected patients per STI per year and over the whole period as well as the number of infected patients per STI divided by gender, age group, postal code and coinfection and reinfection per STI.

For the performance of the Mann-Whitney-Tests IBM SPSS Statistics 27 was used.

## **2.6 Confidentiality**

To maintain confidentiality and to protect sensitive personal information all data sets were pseudonymized. After completion of data collection (done at the password secured IT system of the University Hospital of St. Poelten) a unique code was assigned to every individual included in the study to replace personal identifiers (name, date of birth, address). Only pseudonymized data were used for further evaluation. The code is password protected and secured separately from the file with pseudonymized information and is only accessible for me at a password-secured computer at the Department of Dermatology and Venerology at the University Hospital of St. Poelten, allowing data security and protection within the network of the Lower Austria Landeskliniken-Holding. At the end of this study, pseudonymized data will be stored on this password-protected computer at the University Hospital of St. Poelten. Access to pseudonymized data will only be provided to the study personnel who are named on the application form. Data will be inalterable and can only be viewed. If further processing of the data is desired a new ethics votes application will be filed.

## **2.7 Ethical aspects**

Since this is a retrospective study the only relevant ethical aspect concerns the protection of private data. To provide data protection, pseudonymization is used (see 2.6 Confidentiality).

## **2.8 Conflict of interest**

There are no conflicts of interest. No personal or financial profit will be gained from the results of this study.

## **2.9 Financing**

No financing is needed for this study.

### 3 Results

From January 1<sup>st</sup>, 2012 to December 31<sup>st</sup>, 2019 a total of 299 patients are included in this study: 123 are female and 176 are male. Twelve patients were newly diagnosed with HIV. Fifty-six patients with gonorrhea, 111 patients with syphilis and 120 patients with chlamydia.

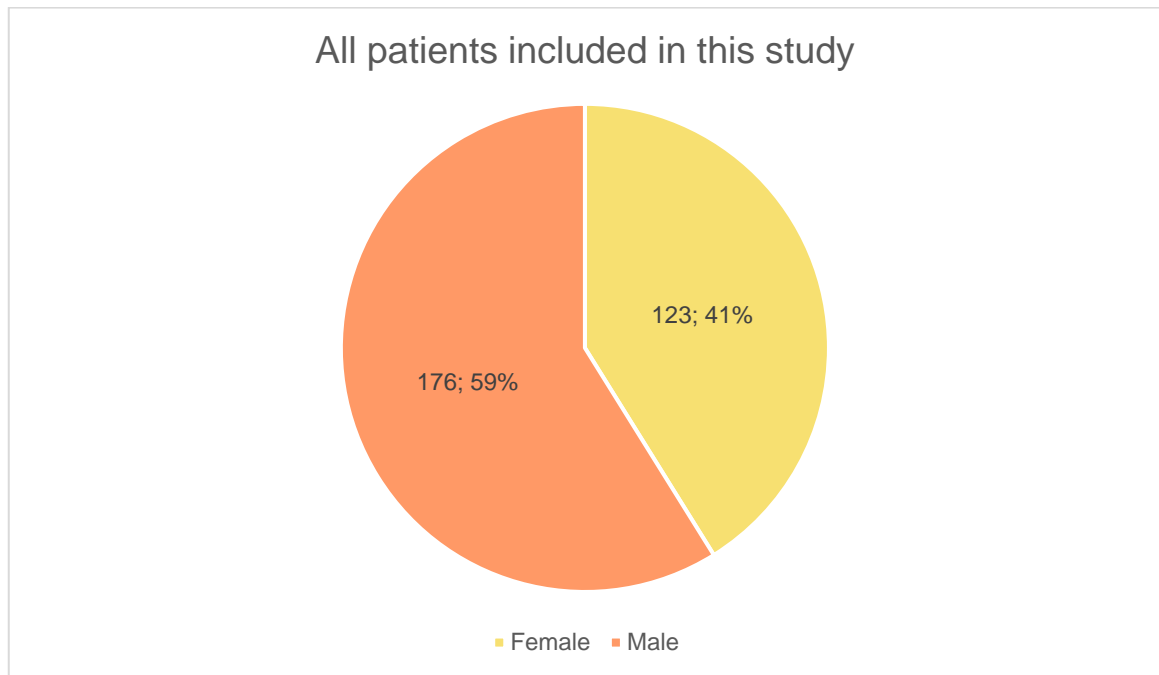


Figure 6 Number of all patients included in this study from 2012 to 2019



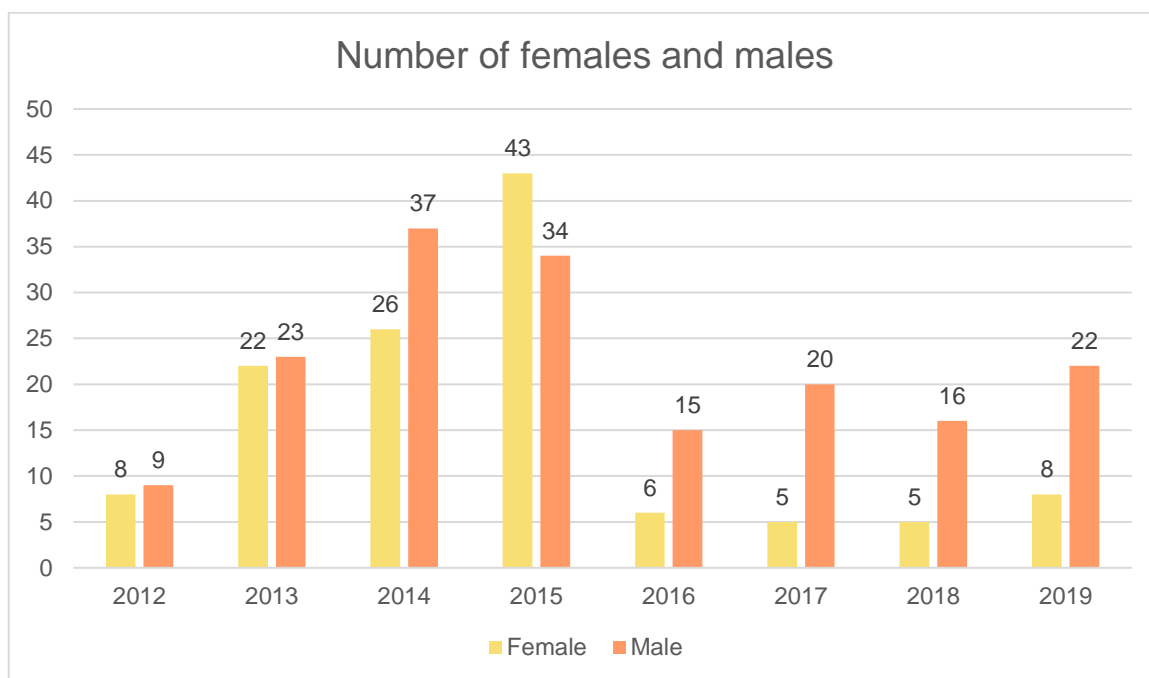


Figure 7 Number of females and males per year included in this study from 2012 to 2019

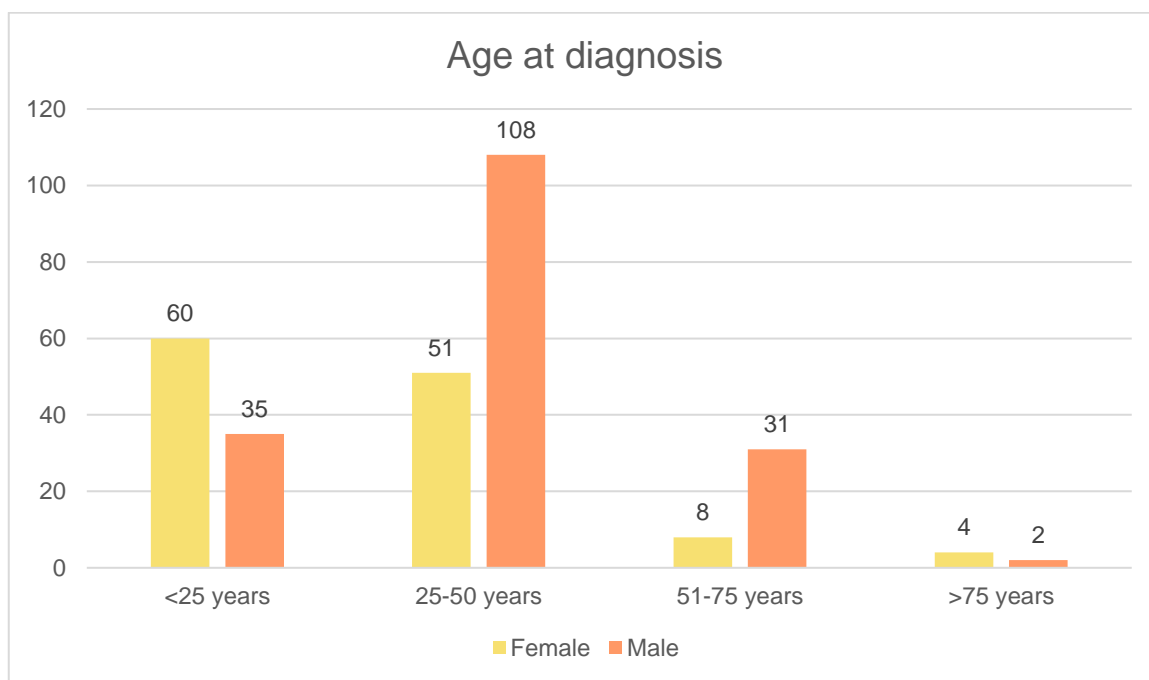


Figure 8 Age at diagnosis females and males included in this study 2012 to 2019

The age distribution of all women and men included in this study differs statistically significant with a p-value of <0.000.

### 3.1 Human Immunodeficiency Virus

A total number of twelve patients are included. One of those is female and eleven are male. One patient had a coinfection with hepatitis C. There was no coinfection with hepatitis B, chlamydia, gonorrhea or syphilis or no further information was provided.

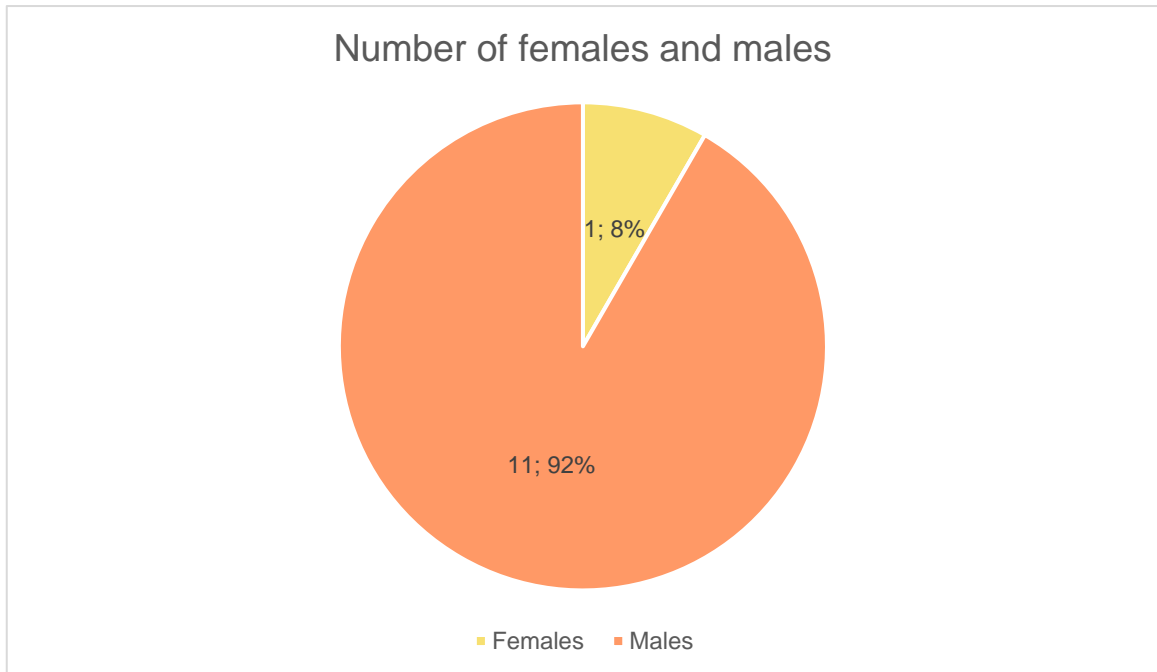


Figure 9 Number of females and males newly diagnosed with HIV from 2012 to 2019

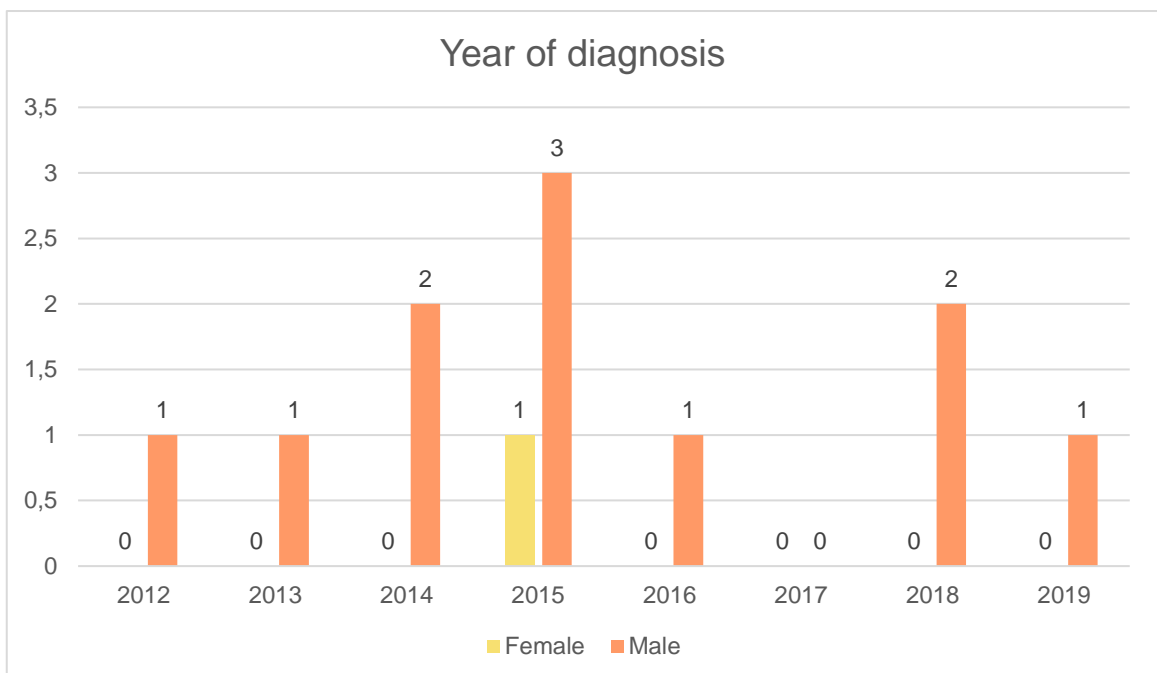


Figure 10 Year of diagnosis of patients newly diagnosed with HIV from 2012 to 2019  
Incidence of sexually transmitted infections

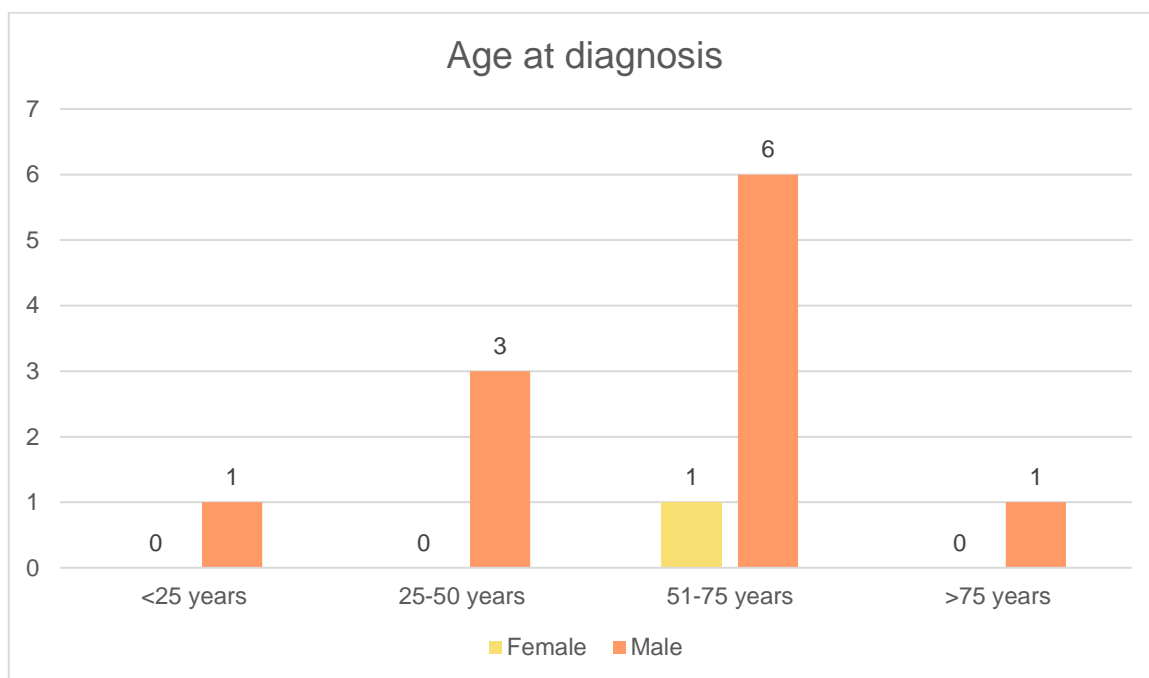


Figure 11 Age at diagnosis of patients newly diagnosed with HIV from 2012 to 2019

With a p-value of 0.625 there is no statistically significant difference in the age distribution of women and men newly diagnosed with HIV.

Table 2 Postal code of patients newly diagnosed with HIV from 2012 to 2019

Postal code	Number of patients	Year of diagnosis
2000 Stockerau	1	2015
3100 St. Poelten	4	2012, 2015, 2015, 2018
3100 Spratzern	1	2014
3153 Eschenau	1	2015
3251 Purgstall	1	2019
3430 Tulln an der Donau	1	2016
3443 Sieghartskirchen	1	2018
3860 Heidenreichstein Kautzen	1	2014
60325 Frankfurt am Main	1	2013

### 3.2 *Neisseria gonorrhoeae*

A total number of 56 patients are included. Eleven patients are female and 45 patients are male. One patient had a coinfection with syphilis. Ten patients had a coinfection with chlamydia. Not one patient had a coinfection with hepatitis B and/or C or no further information was provided. Two patients had a reinfection with gonorrhea.

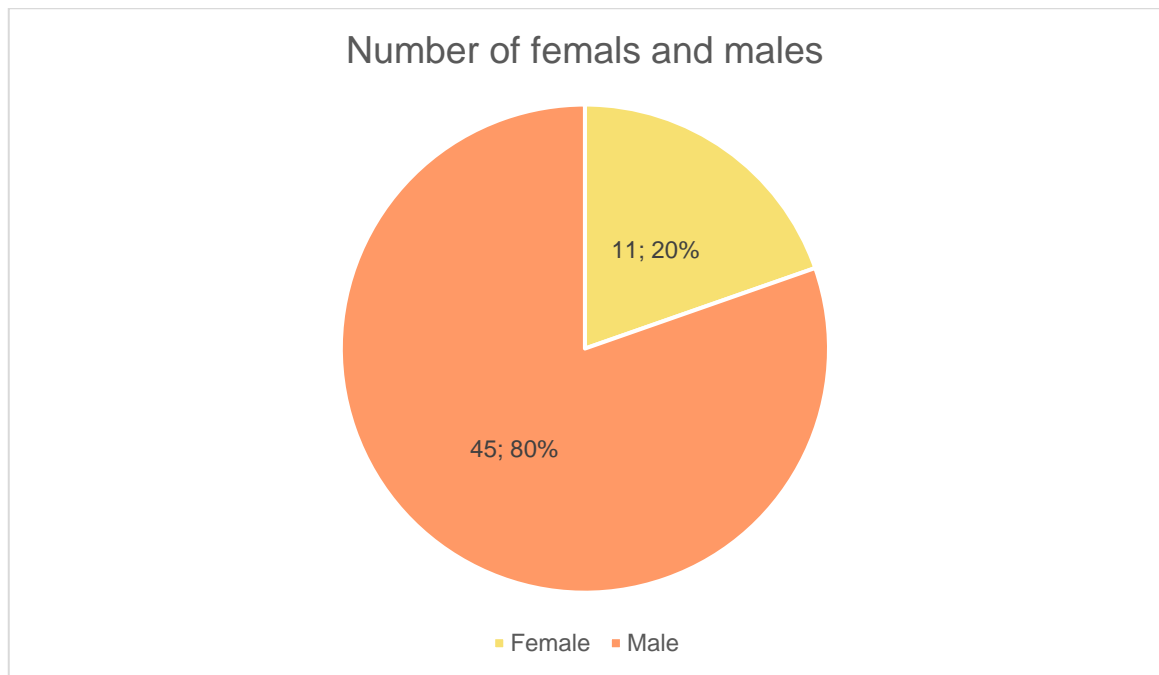


Figure 12 Number of females and males infected with gonorrhea from 2012 to 2019

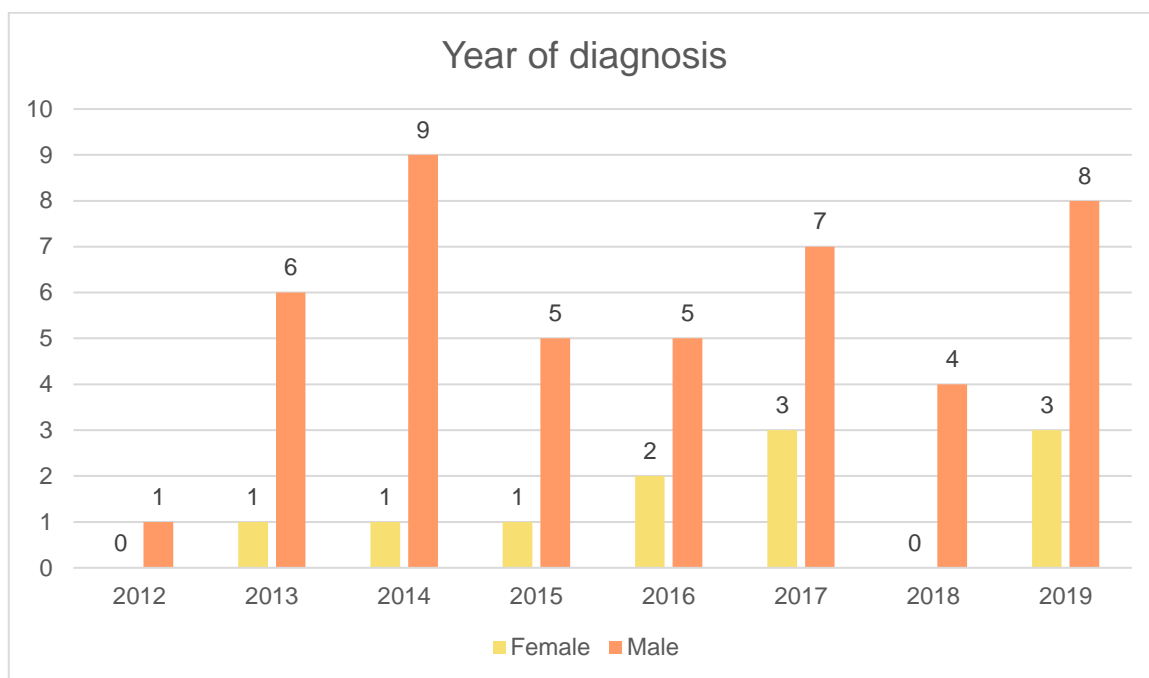


Figure 13 Year of diagnosis of patients infected with gonorrhea from 2012 to 2019

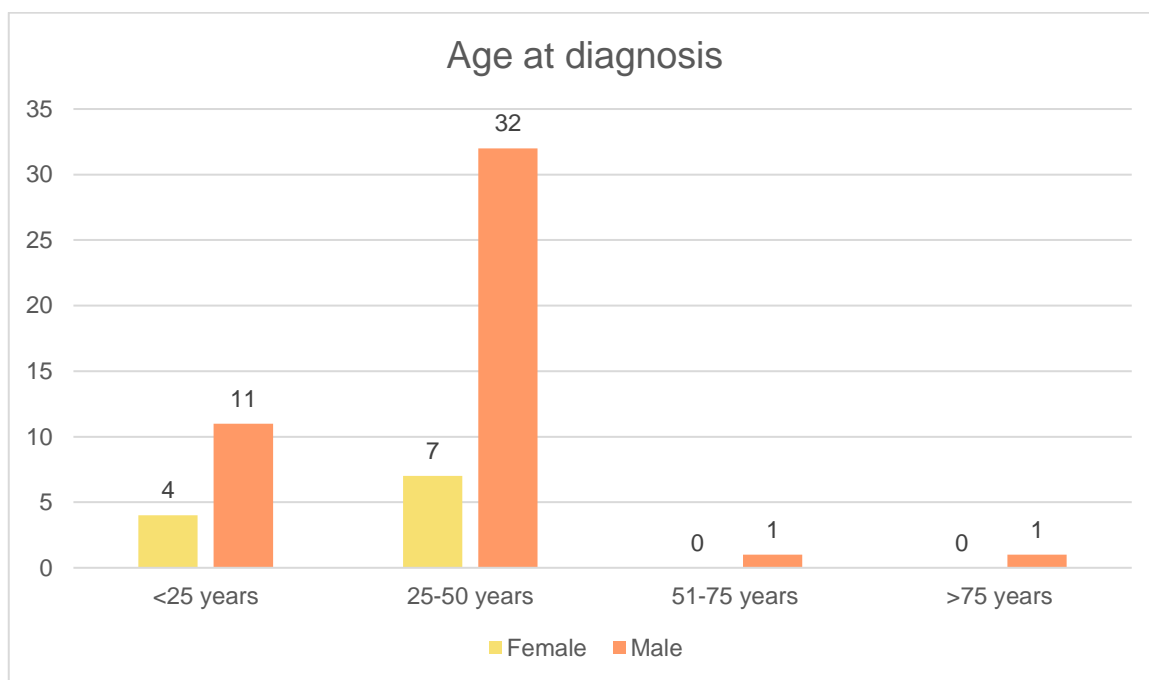


Figure 14 Age at diagnosis of patients infected with gonorrhea from 2012 to 2019

There is no statistically significant difference in the age distribution of women and men infected with gonorrhea with a p-value of 0.348.

Table 3 Postal code of patients infected with gonorrhea from 2012 to 2019

Postal code	Number of patients	Year of diagnosis
1200 Wien Brigittenau	1	2014
1210 Wien Floridsdorf	1	2014
1504 HG Zaanstad	1	2019
2275 Bernhardstal	1	2017
3032 Eichgraben	3	2014, 2017, 2019
3071 Boeheimkirchen	1	2017
3100 St. Poelten	8	2013, 2x 2014, 2015, 3x 2016, 2018
3107 St. Poelten – Traisenpark	1	2018
3130 Herzogenburg	3	2012, 2x 2016
3133 Traismauer	2	2x 2017
3140 Pottenbrunn	1	2017
3150 Wilhelmsburg	1	2013
3160 Traisen	2	2013, 2018,
3170 Hainfeld	1	2015
3171 Kleinzell	1	2013
3205 Weinburg	1	2013
3230 Herzogenburg	1	2014
3233 Kilb	2	2015, 2019
3241 Kirnberg an der Mank	1	2019
3250 Wieselburg	1	2019
3313 Wallsee	1	2013
3325 Ferschnitz	1	2017
3340 Waidhofen an der Ybbs	1	2015
3361 Aschbach	1	2017
3370 Ybbs an der Donau	1	2017
3380 Poehlarn	1	2013
3382 Loosdorf	1	2014

3384 Groß Sierning	1	2019
3435 Zwentendorf/Donau	1	2016
3452 Atzenbrugg	3	2016, 2x 2019
3481 Fels am Wagram	1	2014
3485 Haitzdorf	1	2015
3500 Krems an der Donau	1	2015
3671 Marbach an der Donau	2	2x 2014
3680 Persenbeug	1	2018
3684 St. Oswald	1	2019
3933 Altllengbach	1	2019
7000 Eisenstadt	1	2019
9163 Unterloibl	1	2017

### 3.3 *Treponema pallidum*

A total number of 111 infected patients are included: 29 are female and 82 are male. Three patients had a coinfection with chlamydia trachomatis, one patient had a coinfection with gonorrhea, one had a coinfection with hepatitis B and three had a coinfection with hepatitis C. There were no further coinfections or no further information was provided. Reinfection occurred in three patients. These are included in both years in which they required treatment. In a further five patients, reinfection can be assumed. There were two patients in 2012 and 2013 and one patient in 2018 where according to their diagnostic findings it was unclear whether they needed treatment, or the disease had been cured. Unfortunately, no further information was provided. In 2012 there was one patient in whom lues latens could not be excluded. Those patients from the paragraph above are not included in this study. There was one patient who received treatment in 2016. His laboratory findings in 2019 showed persistent antibodies or insufficient therapy. A reinfection could be excluded by the patient himself. He was included in the study in 2016.

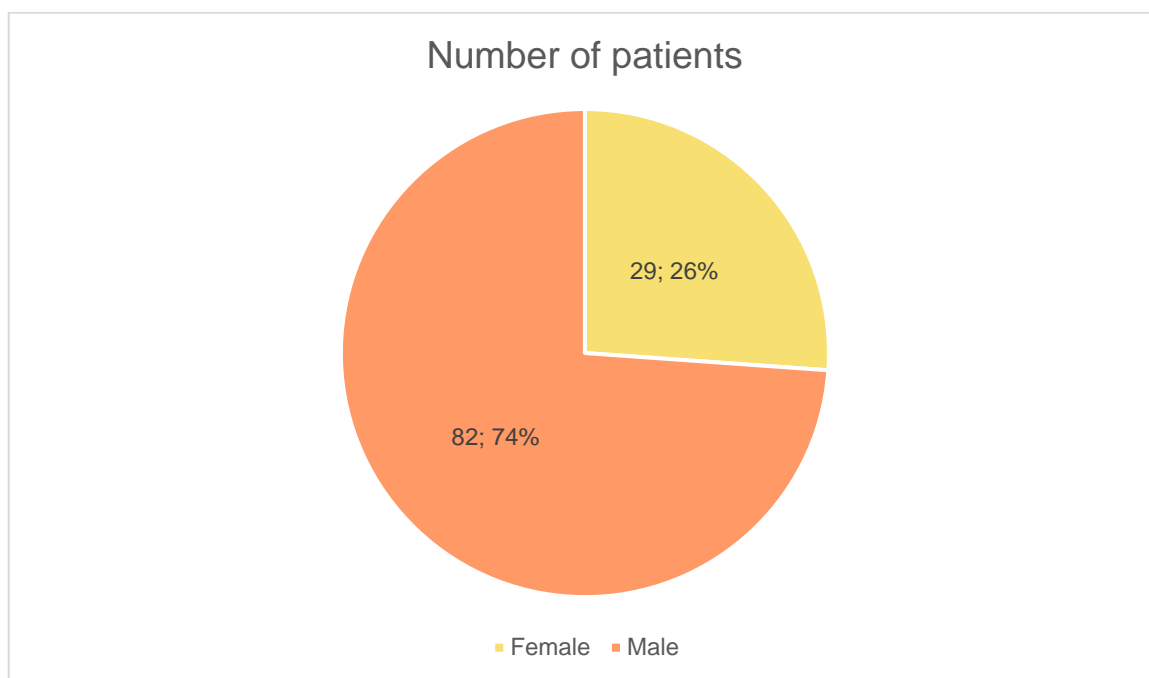


Figure 15 Number of patients infected with syphilis that required treatment from 2012 to 2019

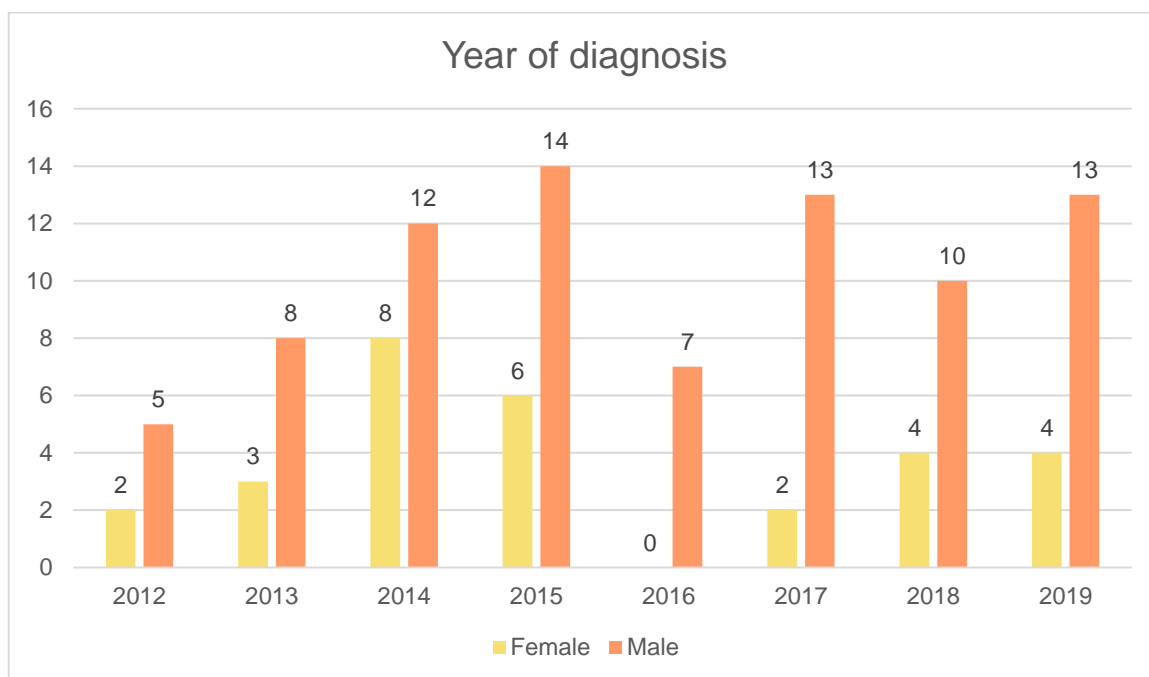


Figure 16 Year of diagnosis of patients infected with syphilis that required treatment from 2012 to 2019



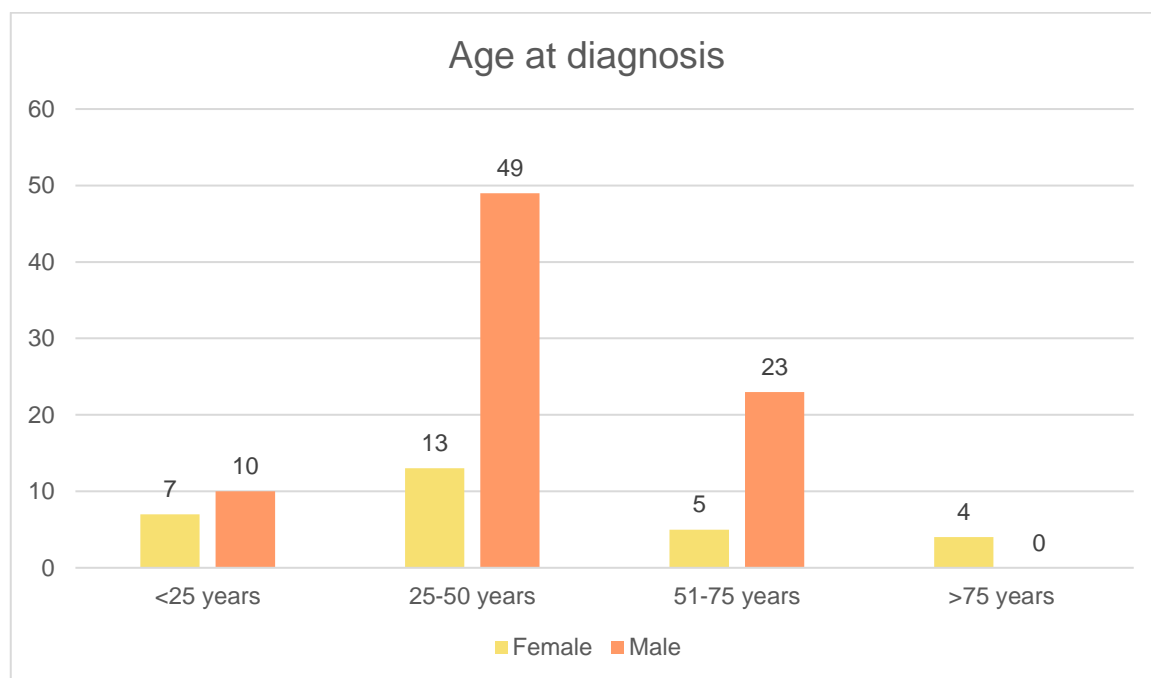


Figure 17 Age at diagnosis of patients infected with syphilis that required treatment from 2012 to 2019

With a p-value of 0.852 there is no statistically significant difference in the age distribution of women and men.

Table 4 Postal code of patients infected with syphilis that required treatment from 2012 to 2019

Postal code	Number of patients	Year of diagnosis
10117 Berlin	1	2013
1040 Wien	1	2014
1140 Wien	1	2015
1230 Wien	1	2013
2011 Sierndorf	1	2013
2052 Pernersdorf-Pfaffendorf	1	2019
2082 Merkersdorf	1	2014
2100 Korneuburg	1	2012
2136 Laa an der Thaya	1	2014
2170 Poysdorf	1	2019

2253 Weikendorf	1	2019
2263 Duernkrut	1	2019
3033 Alt lengbach	2	2018, 2019
3042 Wuermla	1	2015
3100 St. Poelten	20	2x 2013, 2x 2015, 2x 2016, 3x 2017, 6x 2018, 5x 2019
3104 Harland	1	2014
3107 St. Poelten- Traisenpark	1	2018
3125 Statzendorf	1	2019
3130 Herzogenburg	2	2015, 2017
3133 Traismauer	1	2017
3142 Perschling	1	2014
3150 Wilhelmsburg	2	2013, 2019
3153 Eschenau	1	2019
3170 Hainfeld	2	2x 2014
3200 Ober-Grafendorf	2	2012, 2019
3202 Hofstetten	3	2015, 2016, 2017
3205 Weinburg	1	2015
3244 Ruprechtshofen	1	2014
3251 Purgstall	1	2012
3300 Amstetten	1	2015
3313 Wallsee-Sindelburg	1	2012
3331 Kematen	1	2018
3342 Opponitz	1	2015
3361 Aschbach	2	2017, 2019
3370 Ybbs an der Donau	1	2012
3372 Blindenmarkt	1	2017
3380 Poehlarn	1	2015
3382 Loosdorf	1	2019
3383 Huerm	1	2017
3385 Prinzendorf	1	2014
3390 Melk	1	2017

3430 Tulln an der Donau	3	2x 2012, 2017
3462 Absdorf	1	2017
3465 Koenigsbrunn am Wagram	1	2018
3484 Grafenwoerth	1	2013
3485 Haitzendorf	1	2014
3500 Krems an der Donau	3	2x 2014, 2017
3512 Mautern	1	2019
3522 Lichtenau	1	2013
3522 Ebergersch	1	2015
3522 Kuchtenbach	1	2015
3542 Gfoehl	1	2014
3550 Langenlois	1	2017
3552 Lengenfeld	1	2018
3644 Emmersdorf	1	2018
3652 Leiben	1	2018
3822 Karlstein an der Thaya	1	2015
3830 Waidhofen an der Thaya	1	2015
3873 Faistenau	2	2x 2015
3900 Schwarzenau	2	2015, 2018
3910 Zwettl	3	2014, 2015, 2016
3911 Rappottenstein	1	2013
3920 Groß Gerungs	1	2015
3922 Großschoenau	1	2014
3924 Rosenau	1	2017
3931 Siebenlinden	1	2016
3932 Hollenstein	1	2013
3932 Kirchberg am Walde	1	2013
3943 Schrems	3	3x 2014
3945 Hohenreich	1	2015

3970 Weitra	1	2014
4362 Bad Kreuzen	1	2014
8010 Graz	1	2016
Unknown	1	2016

### 3.4 Urogenital Chlamydia trachomatis

In total, 120 patients are included: 82 are female and 38 are male. No patient had an HIV coinfection. Three patients had a coinfection with syphilis and five patients had a coinfection with gonorrhea. Five patients had a reinfection with chlamydia trachomatis. No patient had a coinfection with hepatitis B and/or C or no further information was provided.

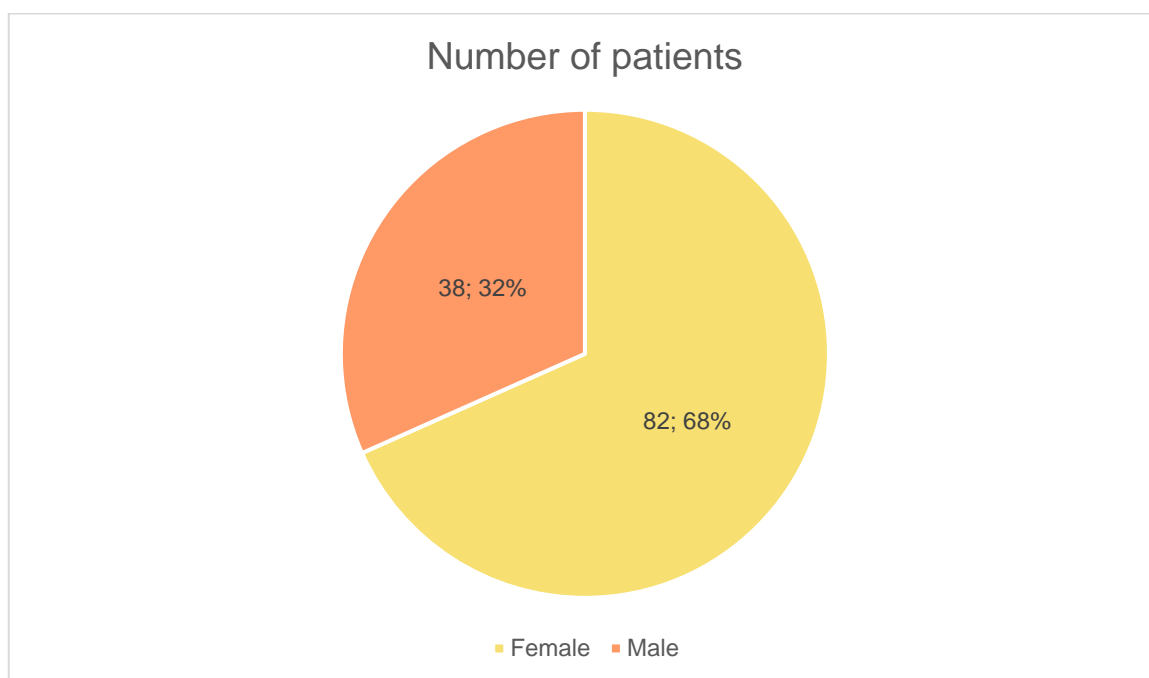


Figure 18 Number of patients infected with chlamydia from 2012 to 2019

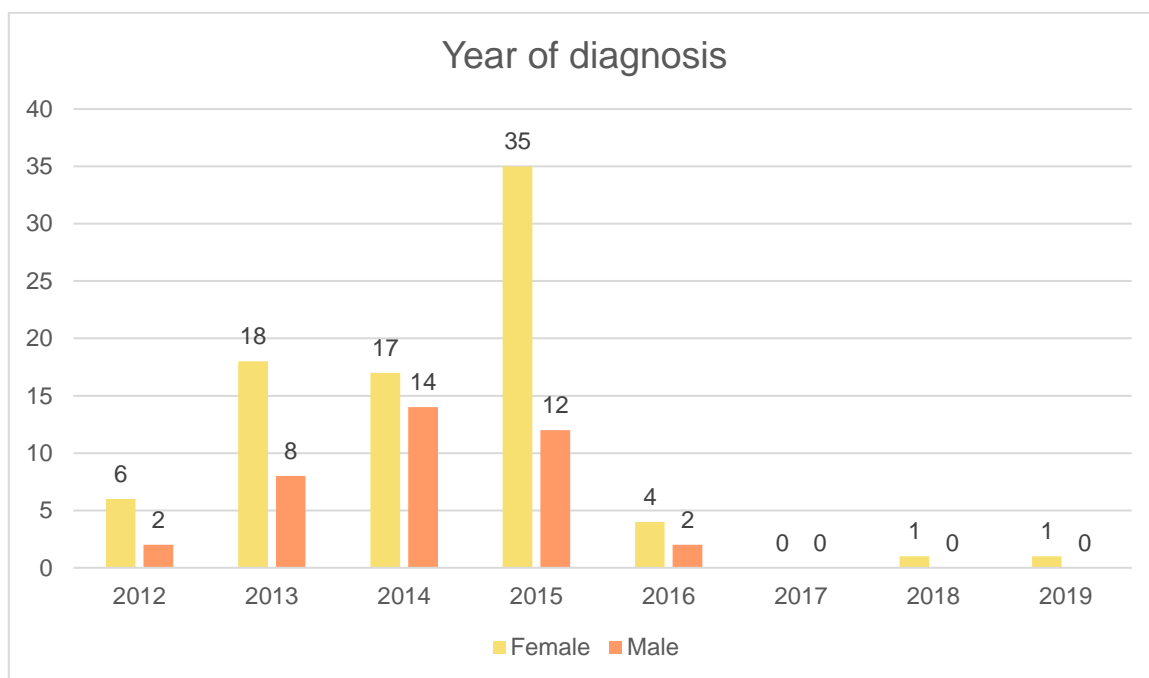


Figure 19 Year of diagnosis of patients infected with chlamydia from 2012 to 2019

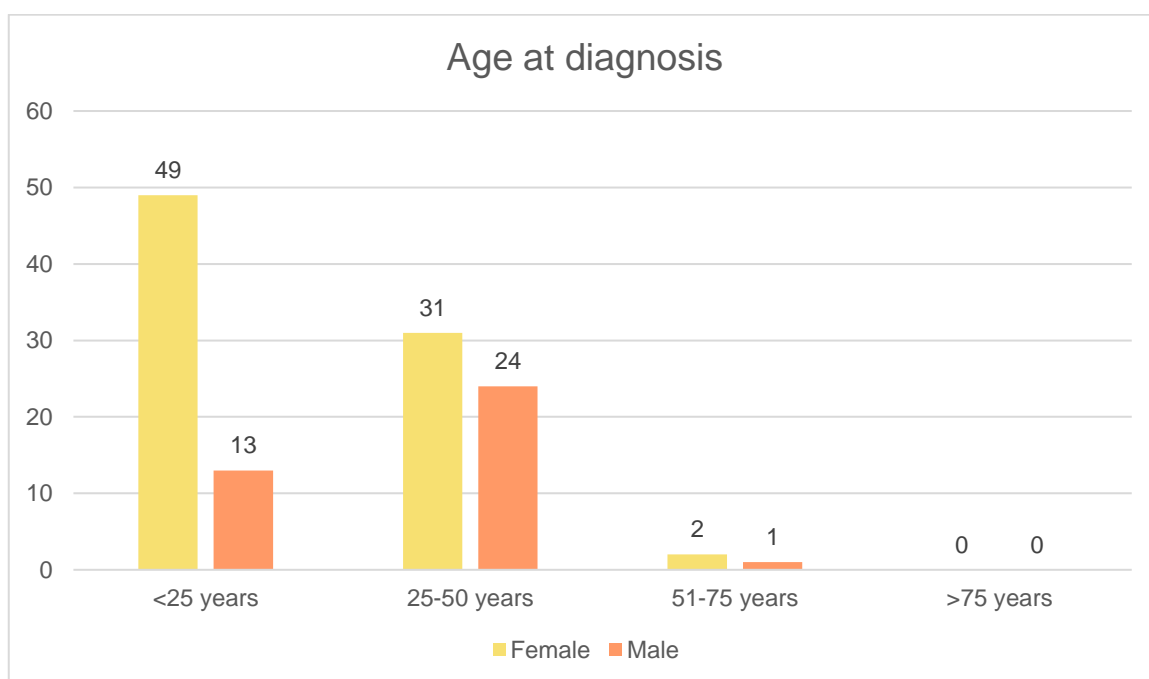


Figure 20 Age at diagnosis of patients infected with chlamydia from 2012 to 2019

There is a statistically significant difference in the age distribution of women and men with a p-value of 0.012.

Table 5 Postal code of patients infected with chlamydia from 2012 to 2019

Postal code	Number of patients	Year of diagnosis
1020 Wien Leopoldstadt	1	2014
1150 Wien Rudolfsheim-Fuenfhaus	1	2015
1210 Wien Floridsdorf	1	2013
1220 Wien Donaustadt	2	2x 2015
2291 Schoenfeld	1	2014
2534 Alland	1	2014
2700 Wiener Neustadt	1	2014
3032 Eichgraben	1	2015
3040 Neulengbach	3	2013, 2x 2014
3042 Wuermila	1	2013
3051 St. Christophen	1	2014
3052 Innermanzing	1	2015
3053 Laaben	1	2013
3061 Ollersbach	1	2013
3062 Kirchstetten	2	2x 2015
3071 Boeheimkirchen	4	2012, 2x 2013, 2015
3072 Kasten bei Boeheimkirchen	1	2015
3073 Stoessing	1	2013
3100 Harland	1	2015
3100 Neidling	1	2015
3100 Oberwagram	1	2015
3100 St. Poelten	31	4x 2012, 4x 2013, 8x 2014, 13x 2015, 2016, 2019
3105 St. Poelten-Radlberg	1	2013
3107 St. Poelten-Traisenpark	2	2013, 2015,
3107 Viehofen	1	2015

3125 Stratzendorf	1	2015
3130 Herzogenburg	2	2x 2015
3133 Traismauer	2	2013, 2014
3134 Nußdorf	1	2015
3140 Pottenbrunn	1	2014
3141 Kapelln	1	2015
3142 Perschling	1	2014
3143 Phyra	1	2014
3150 Wilhelmsburg	2	2016, 2018
3151 St. Georgen am Steinfelde	2	2013, 2014
3160 Traisen	2	2013, 2015
3161 St. Veit an der Goelsen	1	2012
3162 Rainfeld	2	2015, 2016
3170 Hainfeld	5	2x 2013, 3x 2015,
3172 Ramsau	1	2015
3180 Lilienfeld	1	2015
3192 Hohenberg an der Leitha	1	2016
3200 Ober-Grafendorf	4	2012, 2014, 2015, 2016
3205 Weinburg	2	2013
3232 Bischofstetten	1	2014
3233 Kilb	1	2015
3244 Ruprechtshofen	1	2013
3380 Poechlarn	1	2015
3382 Loosdorf	1	2014
3385 Prinzersdorf	1	2014
3393 Matzleinsdorf	1	2014
3400 Klosterneuburg	1	2015
3443 Sieghartskirchen	1	2014
3452 Mitterndorf	1	2014
3485 Haitzendorf	1	2014

3500 Krems an der Donau	1	2015
3521 Peygarten-Ottensstein	2	2x 2013
3652 Leiben	1	2012
3661 Artstetten	1	2015
3671 Marbach an der Donau	1	2014
3701 Großweikersdorf	1	2013
3910 Zwettl-Niederoesterreich	3	2013, 2014, 2016
3922 Groeßschoenau	1	2014
3970 Weitra	1	2015
Unbekannt	1	2015

### 3.5 Incidences of St. Poelten City and County and Lower Austria based on the study data

The collected data obtained by the University Hospital of St. Poelten shows cases not only from Lower Austria but also from Germany, the Netherlands and other federal states like Vienna, Upper Austria, Styria, Carinthia and Burgenland. For further analysis and comparison to the official data from the ECDC and 'Statistik Austria' only people living in Lower Austria (Table 6) are considered. Since residents of Lower Austria are not bound to issue their medical needs to the University Hospital of St. Poelten, we also determined a subgroup of people strictly living in St. Poelten City and County (Table 7). From those two sets of people incidences according to the official population counts were calculated and compared to the official data.



Table 6 Study data: Incidences of HIV, gonorrhea, syphilis and chlamydia of all included individuals living in Lower Austria from 2012 to 2019<sup>1,2</sup>

<b>Year</b>	<b>Incidence HIV</b>	<b>Incidence gonorrhea</b>	<b>Incidence syphilis</b>	<b>Incidence chlamydia</b>
<b>2012</b>	0.06	0.06	0.43	0.5
<b>2013</b>	0	0.43	0.56	1.54
<b>2014</b>	0.12	0.49	1.11	1.85
<b>2015</b>	0.24	0.37	1.16	2.63
<b>2016</b>	0.06	0.42	0.3	0.36
<b>2017</b>	0	0.54	0.9	0
<b>2018</b>	0.12	0.24	0.84	0.06
<b>2019</b>	0.06	0.54	1.01	0.06

Table 7 Study data: Incidences of HIV, gonorrhea, syphilis and chlamydia of all included individuals living in St. Poelten City and County from 2012 to 2019<sup>1,2</sup>

<b>Year</b>	<b>Incidence HIV</b>	<b>Incidence gonorrhea</b>	<b>Incidence syphilis</b>	<b>Incidence chlamydia</b>
<b>2012</b>	0.56	0.56	0.56	3.38
<b>2013</b>	0	1.69	1.69	8.43
<b>2014</b>	0.56	2.24	1.68	10.62
<b>2015</b>	1.11	0.55	2.77	17.2
<b>2016</b>	0	2.74	2.19	1.1
<b>2017</b>	0	2.71	3.26	0
<b>2018</b>	0.54	1.08	3.78	0.54
<b>2019</b>	0	1.61	4.84	0.54

Looking at study individuals coming from Lower Austria we can see a clear hierarchy with highest incidences asserted to chlamydia, followed by syphilis and gonorrhea. On the bottom end HIV with only a fraction of an individual per 100.000 inhabitants. For St. Poelten City and County we could detect the same hierarchy order of incidences, but upscaled by a magnitude between 2- and 6-fold. According to this data there is a real urban-rural gap when it comes to STI distribution in Lower Austria.

## 4 Discussion

The aim of this explorative retrospective study was to compare the cases of STIs of HIV, gonorrhea, syphilis and chlamydia administered to the University Hospital of St. Poelten in the years between 2012 and 2019. It was hypothesised that official incidences seen in Austria and especially Lower Austria are mapped to the incidences assembled at the University Hospital of St. Poelten. In contrast to the status of St. Poelten as regional capital and University Hospital it also could have been expected that cases might have shown a relative over-representation in comparison to the official STI data of Lower Austria.

In total, 299 patients are included in this study from January 1<sup>st</sup>, 2012 to December 31<sup>st</sup>, 2019. There was one patient who could not be included in this study due to technical reasons. The total number of dropouts was not determined.

More male patients are included: 176 males and 123 females. Most patients required treatment for chlamydia, followed by syphilis and gonorrhea. The highest number of patients diagnosed was in 2015 and the lowest number was in 2012. Altogether most patients were between 25 and 50 years old.

Although 'Statistik Austria' and the ECDC provide data for Austria as a whole and the nine federal districts subsequently, a comparison to data in our study is hard to draw and conclude. On the one hand newly developed cases in Lower Austria are not automatically introduced to the University Hospital of St. Poelten, as there is a second department of dermatology in Lower Austria located in Wiener Neustadt and as there are also registered doctors besides the hospitals. On the other hand, there is a geographical proximity to Vienna and high volume of traffic and commuters between Lower Austria and Vienna. Due to this people from Lower Austria seeking medical advice in Vienna can not be excluded or extrapolated.

To provide a more precise model only residents that are directly living in St. Poelten and St. Poelten County are compared. Those people are most likely to seek medical advice and treatment regarding STIs at the University Hospital of St. Poelten.

Following incidences of all above mentioned STIs provided from the ECDC and 'Statistik Austria' for Austria and Lower Austria are put into perspective with the incidence of St. Poelten City and County.

Table 8 The incidence of patients with new HIV diagnosis in St. Poelten City and County compared to Austria from 2012 to 2019

<b>Year</b>	<b>Incidence St. Poelten City and County<sup>1,2</sup> (study data)</b>	<b>Incidence Austria<sup>1,2,36</sup> (official data, ECDC)</b>
<b>2012</b>	0.56	4.41
<b>2013</b>	0	3.68
<b>2014</b>	0.56	3.55
<b>2015</b>	1.11	3.83
<b>2016</b>	0	3.41
<b>2017</b>	0	3.48
<b>2018</b>	0.54	2.35
<b>2019</b>	0	2.63

The incidences documented for St. Poelten do not depict the seen incidences in Austria. A reasonable explanation could be that the University Hospital of St. Poelten does not provide a clinic specifically focussing on HIV, its treatment, and its further handling. In comparison the General Hospital in Vienna has a special clinic for STIs and a special clinic only for HIV.

On years where HIV-positive patients were detected at the University Hospital of St. Poelten the incidences remained stable with roughly half a person per 100.000 inhabitants. The ECDC states that in reference to the WHO European region from 2011 to 2019 'the rate of newly diagnosed HIV infections increased.'<sup>36</sup> (p17) Apparently this does not account for Austria alone, where a steady decline from 2012 to 2019 can be seen according to the ECDC.<sup>36</sup> Whether this decline is driven by the metropolitan areas of Austria, where sensibility and governmental programs might be more prominent than in rural areas have to be investigated in the future. Detecting and targeting areas with a stable or increasing incidence might help to dampen the seen progress even more.

Table 9 The incidence of patients infected with gonorrhea in St. Poelten City and County compared to Lower Austria and Vienna from 2012 to 2019

<b>Year</b>	<b>Incidence St. Poelten City and County<sup>1,2</sup></b> (study data)	<b>Incidence Lower Austria</b> <sup>1,2,37,38,39,40,41,42,43,44</sup> (official data, 'Statistik Austria')	<b>Incidence Vienna<sup>1,2,45</sup></b> (official data, 'Stadt Wien')
<b>2012</b>	0.56	0.56	69.01
<b>2013</b>	1.69	0.43	54.27
<b>2014</b>	2.24	0.68	54.34
<b>2015</b>	0.55	0.31	55.42
<b>2016</b>	2.74	-	58.69
<b>2017</b>	2.71	-	62.86
<b>2018</b>	1.08	-	58.61
<b>2019</b>	1.61	-	79

According to the ECDC, 1,148 people were tested positive for gonorrhea in 2013 in Austria, compared to 7 who were diagnosed at the University Hospital of St. Poelten in 2013.<sup>9</sup> For gonorrhea there were no further data provided by the ECDC from 2014 to 2019.<sup>46</sup> We therefore used data provided from 'Statistik Austria' and 'Stadt Wien' and compared it to our sample from St. Poelten City and County.

Comparing the incidences of St. Poelten City and County, Lower Austria and Vienna no clear pattern can be seen. In contrast to the study results Williamson et al. propose that there is a clear pattern which shows increasing rates of this sexually transmitted disease.<sup>12</sup> What comes to the eye is the incidence of people diseased with gonorrhea in 2014 and 2015, which is higher in St. Poelten City and County compared to Lower Austria in general. It is possible that the disease is overrepresented in larger metropolitan areas like St. Poelten because people have the possibility of low-threshold access to a large hospital in striking distance. The fact that more people living in a highly dense areas of urban areas compared to rural areas can lead to easier availability of sex partners is also an imaginable reason. According to Stry, the movement of populations and the reduced performance of safer sex are reasons for the revival of STIs.<sup>47</sup>

Table 10 The incidence of patients infected with syphilis that required treatment in St. Poelten City and County compared to Lower Austria and Vienna from 2012 to 2019

<b>Year</b>	<b>Incidence St. Poelten City and County<sup>1,2</sup> (study data)</b>	<b>Incidence Lower Austria<sup>1,2,37,38,39,40,41,42,43,44</sup> (official data, 'Statistik Austria')</b>	<b>Incidence Vienna<sup>1,2,45</sup> (official data, 'Stadt Wien')</b>
<b>2012</b>	0.56	0.56	21.43
<b>2013</b>	1.69	0.56	21.65
<b>2014</b>	1.68	0.62	20.15
<b>2015</b>	2.77	0.67	18.42
<b>2016</b>	2.19	-	16.68
<b>2017</b>	3.26	-	21.58
<b>2018</b>	3.78	-	26.9
<b>2019</b>	4.84	-	22.61

In Austria, 538 people had a confirmed syphilis diagnosis in 2013 whereas eleven patients were included in this study from the University Hospital of St. Poelten.<sup>10</sup> Likewise, we used data provided from 'Statistik Austria' and 'Stadt Wien' and compared it to our sample from St. Poelten City and County.

A clear trend with increasing incidences can be seen for St. Poelten City and County. The incidence almost quintupled from 2012 to 2015. Compared to that the incidences of Lower Austria are pretty much stable during this time. In Vienna an overall increase of incidences can be seen. Unfortunately, the current direction of increasing numbers of diseased people gets supported by the ECDC and Williamson et al.<sup>10,12</sup> According to the CDC the number of diseased people is also growing in the United States.<sup>48</sup> Potential factors leading to an increase of STIs include social networks that facilitate human interconnectedness or improved possibilities for travel.<sup>12</sup>

Table 11 The incidence of patients infected with chlamydia in St. Poelten City and County compared to Lower Austria and Vienna from 2012 to 2019<sup>1,2</sup>

Year	Incidence St. Poelten City and County (study data)
2012	3.38
2013	8.43
2014	10.62
2015	17.2
2016	1.1
2017	0
2018	0.54
2019	0.54

There were no data provided for chlamydia infections from 2013 to 2018 from the ECDC in their annual report from 2018.<sup>8,49</sup> Unfortunately neither 'Statistik Austria', nor 'Stadt Wien' provides data regarding chlamydia trachomatis infections, therefore a comparison with our data was not possible. Furthermore, the data gathered throughout St. Poelten City and County did not show any stringent pattern, which is why a rigid conclusion can not be drawn. Nevertheless, the data is shown.

According to O'Connell chlamydia is the most frequently reported bacterial STI worldwide.<sup>7</sup> This statement partly supports the results of this study. From 2012 to 2015 the highest incidences of all STIs included in this study accounted for chlamydia infections. Whereas no clear pattern regarding the incidences related to the entire period of time can be seen in the study results, it is proposed that there are increasing rates of chlamydia infections.<sup>12</sup>

## 4.1 Limitations

Before conducting the study, it was not expected that in some years no or only a few patients could be included. The absence of patients could be due to no patients seeking medical treatment at the University Hospital of St. Poelten or due to errors in the handling of data I received for further processing.

There is a risk of bias regarding reinfections. It is possible that patients developed reinfections but did not seek medical treatment at the University Hospital of St. Poelten again and therefore could not be included. Regarding syphilis, there may be a risk of bias, because in some patients no information was provided as to whether they received treatment or not. In unclear cases, laboratory values were examined and classified by OÄ Dr. Christin Kronschläger and Prim. Univ.-Prof. Dr. Franz Trautinger.

## 5 Conclusion

Human interconnectedness plays a major role in the increase of STI incidences nowadays.<sup>12</sup> Despite sexual education and advertising the number of people infected with STIs is still increasing. It may be ignorance or naivety that leads people to think the practice of safer sex is not necessary anymore. Furthermore, long-term consequences like infertility, miscarriage and cancer are often not considered in the daily conversations about STIs.

This study shows that STIs are not only present in big cities, but also in smaller cities and rural areas. Further, the study states a significant urban-rural gap towards urban regions by a 2- to 6-fold magnitude when it comes to STI distribution in Lower Austria. Sexual education and advertising have to be further intensified to sharpen the sensibility of easily preventable diseases with serious and concerning long-term effects.

The pandemic of Covid-19 leads to worldwide changes in the social behaviour. Social distancing and personal isolation are measures that are taken to dampen the spread of the virus. Future studies may show the effect of these measures and the pandemic in general on the spreading of STIs in Europe and worldwide.



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## Appendix

All incidences were calculated with the help of an online incidence-calculator.<sup>2</sup> 100.000 inhabitants were used as reference value for calculation.

Table 12 The incidence of patients newly diagnosed with HIV from 2012 to 2019

<b>Year</b>	<b>Population of St. Poelten City and County together<sup>1,2</sup></b>	<b>Incidence</b> (reference value of 100.000) <sup>2</sup>
<b>2012</b>	177.469	0.56
<b>2013</b>	177.987	0
<b>2014</b>	178.832	0.56
<b>2015</b>	180.241	1.11
<b>2016</b>	182.477	0
<b>2017</b>	184.314	0
<b>2018</b>	185.256	0.54
<b>2019</b>	186.088	0

Table 13 The incidence of patients infected with gonorrhea from 2012 to 2019

<b>Year</b>	<b>Population of St. Poelten City and County together<sup>1</sup></b>	<b>Incidence</b> (reference value of 100.000) <sup>2</sup>
<b>2012</b>	177.469	0.56
<b>2013</b>	177.987	1.69
<b>2014</b>	178.832	2.24
<b>2015</b>	180.241	0.55
<b>2016</b>	182.477	2.74
<b>2017</b>	184.314	2.71
<b>2018</b>	185.256	1.08
<b>2019</b>	186.088	1.61

Table 14 The incidence of patients infected with syphilis that required treatment from 2012 to 2019

<b>Year</b>	<b>Population of St. Poelten City and County together<sup>1</sup></b>	<b>Incidence (reference value of 100.000)<sup>2</sup></b>
<b>2012</b>	177.469	0.56
<b>2013</b>	177.987	1.69
<b>2014</b>	178.832	1.68
<b>2015</b>	180.241	2.77
<b>2016</b>	182.477	2.19
<b>2017</b>	184.314	3.26
<b>2018</b>	185.256	3.78
<b>2019</b>	186.088	4.84

Table 15 The incidence of patients infected with chlamydia from 2012 to 2019

<b>Year</b>	<b>Population of St. Poelten City and County together<sup>1</sup></b>	<b>Incidence (reference value of 100.000)<sup>2</sup></b>
<b>2012</b>	177.469	3.38
<b>2013</b>	177.987	8.43
<b>2014</b>	178.832	10.62
<b>2015</b>	180.241	17.2
<b>2016</b>	182.477	1.1
<b>2017</b>	184.314	0
<b>2018</b>	185.256	0.54
<b>2019</b>	186.088	0.54

Table 16 The incidence of patients with new HIV diagnoses from 2012 to 2019 in Austria

<b>Year</b>	<b>Population of Austria<sup>1</sup></b>	<b>ECDC<sup>36</sup></b>	<b>Incidence Austria (reference value of 100.000)<sup>2</sup></b>
<b>2012</b>	8.408.121	371	4.41
<b>2013</b>	8.451.860	311	3.68
<b>2014</b>	8.507.786	302	3.55
<b>2015</b>	8.584.926	329	3.83
<b>2016</b>	8.700.471	297	3.41
<b>2017</b>	8.772.865	305	3.48
<b>2018</b>	8.822.267	207	2.35
<b>2019</b>	8.858.775	233	2.63

Table 17 The incidence of patients with gonorrhea in Vienna from 2012 to 2019

<b>Year</b>	<b>Population of Vienna<sup>1</sup></b>	<b>‘Stadt Wien’<sup>45</sup></b>	<b>Incidence Vienna (reference value of 100.000)<sup>2</sup></b>
<b>2012</b>	1.717.084	1.185	69.01
<b>2013</b>	1.741.246	945	54.27
<b>2014</b>	1.766.746	960	54.34
<b>2015</b>	1.797.337	996	55.42
<b>2016</b>	1.840.226	1.080	58.69
<b>2017</b>	1.867.582	1.174	62.86
<b>2018</b>	1.888.776	1.107	58.61
<b>2019</b>	1.897.491	1.499	79

Table 18 The incidence of patients with gonorrhea in Vienna from 2012 to 2019

<b>Year</b>	<b>Population of Vienna<sup>1</sup></b>	<b>'Stadt Wien'<sup>45</sup></b>	<b>Incidence Vienna (reference value of 100.000)<sup>2</sup></b>
<b>2012</b>	1.717.084	1.185	69.01
<b>2013</b>	1.741.246	945	54.27
<b>2014</b>	1.766.746	960	54.34
<b>2015</b>	1.797.337	996	55.42
<b>2016</b>	1.840.226	1.080	58.69
<b>2017</b>	1.867.582	1.174	62.86
<b>2018</b>	1.888.776	1.107	58.61
<b>2019</b>	1.897.491	1.499	79

Table 19 The incidence of patients with syphilis in Vienna from 2012 to 2019

<b>Year</b>	<b>Population of Vienna<sup>1</sup></b>	<b>'Stadt Wien'<sup>45</sup></b>	<b>Incidence Vienna (reference value of 100.000)<sup>2</sup></b>
<b>2012</b>	1.717.084	368	21.43
<b>2013</b>	1.741.246	377	21.65
<b>2014</b>	1.766.746	356	20.15
<b>2015</b>	1.797.337	331	18.42
<b>2016</b>	1.840.226	307	16.68
<b>2017</b>	1.867.582	403	21.58
<b>2018</b>	1.888.776	508	26.9
<b>2019</b>	1.897.491	429	22.61

Table 20 Number of patients infected with gonorrhea in Austria and Lower Austria compared to the study results from 2012 to 2019

<b>Year</b>	<b>Study Results</b>	<b>‘Statistik Austria’: Austria</b>	<b>‘Statistik Austria’: Lower Austria</b>
<b>2012<sup>37</sup></b>	1	1.381	9
<b>2013<sup>38</sup></b>	7	1.148	7
<b>2014<sup>39</sup></b>	10	1.152	11
<b>2015<sup>40</sup></b>	6	978	5
<b>2016<sup>41</sup></b>	7	1.211	0
<b>2017<sup>42</sup></b>	10	1.301	0
<b>2018<sup>43</sup></b>	4	1.194	-
<b>2019<sup>44</sup></b>	11	1.601	-

Table 21 The incidence of patients infected with gonorrhea in Lower Austria from 2012 to 2019

<b>Year</b>	<b>Population of Lower Austria<sup>1</sup></b>	<b>‘Statistik Austria’: Lower Aus- tria<sup>37,38,39,40,41,42,43,44</sup></b>	<b>Incidence of Lower Austria (reference value of 100.000)<sup>2</sup></b>
<b>2012</b>	1.614.455	9	0.56
<b>2013</b>	1.618.592	7	0.43
<b>2014</b>	1.625.485	11	0.68
<b>2015</b>	1.636.778	5	0.31
<b>2016</b>	1.653.691	0	-
<b>2017</b>	1.665.753	0	-
<b>2018</b>	1.670.668	-	-
<b>2019</b>	1.677.542	-	-

Table 22 Number of patients infected with syphilis in Austria and Lower Austria compared to the study results from 2012 to 2019

<b>Year</b>	<b>Study Results</b>	<b>‘Statistik Austria’: Austria</b>	<b>‘Statistik Austria’: Lower Austria</b>
<b>2012<sup>37</sup></b>	7	494	9
<b>2013<sup>38</sup></b>	11	538	9
<b>2014<sup>39</sup></b>	20	553	10
<b>2015<sup>40</sup></b>	20	469	11
<b>2016<sup>41</sup></b>	7	431	0
<b>2017<sup>42</sup></b>	15	526	0
<b>2018<sup>43</sup></b>	14	621	-
<b>2019<sup>44</sup></b>	17	580	-

Table 23 The incidence of patients infected with syphilis from 2012 to 2019 in Lower Austria

<b>Year</b>	<b>Population of Lower Austria<sup>1</sup></b>	<b>‘Statistik Austria’: Lower Aus- tria<sup>37,38,39,40,41,42,43,44</sup></b>	<b>Incidence of Lower Austria (reference value of 100.000)<sup>2</sup></b>
<b>2012</b>	1.614.455	9	0.56
<b>2013</b>	1.618.592	9	0.56
<b>2014</b>	1.625.485	10	0.62
<b>2015</b>	1.636.778	11	0.67
<b>2016</b>	1.653.691	0	-
<b>2017</b>	1.665.753	0	-
<b>2018</b>	1.670.668	-	-
<b>2019</b>	1.677.542	-	-