

Who's at risk of catching Chlamydia trachomatis?

Identifying factors associated with increased risk of
infection to enable individualized care and
intervention

Helena Carré
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**Department of Clinical Medicine and Public Health,
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*To my family
with love*

*“Life is a
sexually transmitted disease”*

André Brink

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Abstract

Who's at risk of catching *Chlamydia trachomatis*? Identifying factors associated with increased risk of infection to enable individualized care and intervention

Chlamydia trachomatis (CT) can cause infertility and is the most common sexually transmitted infection (STI) of bacterial origin in Europe. Surveys in seven countries estimated a population prevalence of 1.4-3.0 % in people 18 to 44 years.

Approximately 87% of those diagnosed in Sweden are 15-29 years. Since 1997, with the exception of 2009-2010, despite all efforts, CT has increased steadily in many European countries including Sweden. That made us investigate risk factors associated with catching STIs, especially CT.

In Sweden partner notification is mandatory by law when a patient is diagnosed with CT. Centralised partner notification, performed by a few experienced counsellors, and evaluation of the sexual history for at least 12 months back in time, shows superior results compared to other studies. Phone-interviews are a good option in remote areas. "The Västerbotten model" for partner notification fulfils these criteria and our evaluation has functioned as a model for changing recommendations of partner notification in Sweden. Preventing CT by primary prevention such as information and counselling is, however, still of great importance.

We investigated whether it was necessary to test for CT in the throat. We found that patients testing positive for pharyngeal CT neither had more symptoms or signs nor a sexual history that differed from others. We therefore believe that we will find most or all of these patients by conventional testing of urine and cervical/vaginal samples.

We wanted to further identify *risk factors* among patients attending a clinic for sexually transmitted infections to enable individualized care depending on risk. None or inconsistent use of condoms with new/temporary partners in combination with having at least one new/temporary partner within the past 6 months could identify persons with risk behaviour and at increased risk of CT (re)infection. Additional information about whether the condom was used during the whole intercourse did not add any risk of infection. A drop-in reception is a good contribution to an opportunistic screening approach. The rate of CT infected is high and the clinic attracts men and individuals ≥ 25 years old at risk of infection, groups which usually have a reduced test rate. The mean age was 28 years and 58% of the patients were men. The figure of correct condom usage is very low indicating the need for risk reducing counselling also in this grown-population.

Among adult STI patients anxiety was common and depression uncommon. Neither was linked to high risk sexual behaviour nor ongoing CT infection. Hazardous alcohol consumption, however, was common and linked to anxiety and high risk sex. We conclude that preventive work can not only focus on STI prevention, but must consider the high frequency of hazardous alcohol consumption, which probably is contributing to sexual risk behaviour.

Key words: *Chlamydia trachomatis*; contact tracing; partner notification; sexual behaviour; screening; condom use; individualized care; risk; anxiety; binge drinking

Populärvetenskaplig sammanfattning på svenska

Vem riskerar att smittas av klamydia?

Chlamydia trachomatis, eller klamydia som man oftast säger, är den vanligaste sexuellt överförbara bakterien i Europa. Upp till 10 % av den sexuellt aktiva befolkningen är smittad. Infektionen är ofta symtomlös, men kan orsaka allvarliga komplikationer t.ex. salpingit (äggledarinflammation) med efterföljande ärrbildning och sammanväxning i äggledarna på kvinnan. Detta kan i sin tur leda till infertilitet, utomkvedshavandeskap och kroniska bäckensmärtor. Klamydia har också associerats med nedsatt fertilitet hos män. Kronisk inflammation orsakad av långvarig klamydia- infektion är en möjlig cancerorsak. Obehandlad klamydia gör att man har två till fem gånger ökad mottaglighet för HIV. Det finns alltså all anledning att försöka minska spridningen av klamydia. På 1980-talet gjorde man intensiva insatser för att förhindra den pågående klamydiaepidemin. Man hade informationskampanjer och ungdomsmottagningarna öppnade, vilket gjorde provtagning enklare. Klamydia blev också en anmälningspliktig sjukdom under Smittskyddslagen. Detta innebär bland annat att alla fall av klamydia måste rapporteras till Smittskyddsinstitutet (SMI) och den lokala Smittskyddsläkaren, all provtagning och medicinering är gratis och smittspårning måste utföras om man finner en klamydiasmittad, för att försöka ta reda på vem som kan ha smittat patienten och vem patienten eventuellt har fört smittan vidare till. Efter att dessa insatser hade införts sjönk klamydia incidensen, och även komplikationerna. Sedan mitten av 1990-talet har dock klamydiaförekomsten ökat stadigt, trots intensivt förebyggande arbete. Det blev uppenbart att de aktuella insatserna inte räckte.

Västerbotten har sedan länge haft bland de lägsta klamydiaförekomsterna i Sverige, trots att befolkningen är yngre än rikets genomsnitt. Här har man haft en centraliserad kontaktspårning sedan år 2000, dvs. ett fåtal erfarna personer utför majoriteten av all smittspårning. Smittspårarna har letat potentiellt smittade partners minst 12 månader tillbaka i tiden och intervjuerna har utförts över telefon om detta har varit nödvändigt. Denna så kallade "Västerbottensmodell" för smittspårning utvärderade vi under 2002. Vi kom fram till att den visade bättre resultat än andra publicerade metoder. Sedan år 2007 rekommenderar Socialstyrelsen smittspårning enligt vår modell.

Munsex (oralsex/fellatio) är vanligt bland svenska ungdomar och kondom används sällan. För svalgklamydia är smittsamheten, komplikationsrisken och bästa diagnostiseringsmetod är inte helt känd. Under 2002 och 2005 tog vi prover för svalgklamydia, samtidigt med prov för könsklamydia, på alla som hade haft oskyddat oralsex de senaste sex månaderna. Av 172 patienter hade 22 klamydia i könsorganen och fyra svalgklamydia. Alla med svalgklamydia hade samtidig infektion i könsorganen. Bara en person med svalgklamydia hade ont i halsen. Ont i halsen kan alltså inte användas för att ta reda på vem som ska provtas för svalgklamydia. Vi rekommenderar att man tar prov för svalgklamydia om patienten bara har haft oralsex, och inte har haft "vanligt" samlag.

På grund av den fortsatt stigande klamydiaförekomsten i Sverige har Socialstyrelsen tagit fram en nationell handlingsplan. Där slår man bland annat fast att unga människor med riskbeteende ska kunna identifieras och erbjudas speciell riskreducerande rådgivning. Under 2008-2010 har vi genomfört enkätstudier vid drop-in mottagningen, STD-mottagningen, STDHud-kliniken, Norrlands Universitetssjukhus, Umeå, där vi undersökt sexuellt riskbeteende, alkoholvanor och psykisk ohälsa i kombination med aktuell klamydiasmitta. Personer som inte alltid använde kondom vid ny/tillfällig partner och hade haft en ny/tillfällig partner de senaste sex månaderna utgjorde 61 % av patienterna, men stod för 81 % av samlade klamydiasmittan. En tilläggsfråga om kondom användes under hela samlaget adderade inte någon risk för infektion i detta screeningsammanhang. Generellt var kondomanvändningen låg och bara 5 % av patienterna hade använt kondom under hela samlaget med sin senaste nya/tillfälliga kontakt. Klamydiaincidensen bland patienterna på drop-in mottagningen var generellt hög (11 %) och mottagningen verkade attrahera män (58 % av besökarna var män) och individer 25 år eller äldre (51 % av patienterna), personer som vanligen har en lägre testningsfrekvens. Trettio procent av besökarna hade tecken till ångestsyndrom utifrån det screeningformulär som användes (Hospital Anxiety and Depression Scale, HADS) och 7 % tecken till depression. Varken ångest eller depression var kopplat till ökat sexuellt risktagande eller aktuell klamydia smitta. Femtiotre procent av kvinnorna och 54 % av männen nådde gränsen för riskabel alkoholkonsumtion (en konsumtion som är potentiellt skadlig) i screeningformuläret AUDIT (Alcohol Use Disorder Identification Test). Riskabel alkoholkonsumtion var kopplat till ökat antal partners och lägre kondomanvändning men inte till aktuell klamydiainfektion. Det var också kopplat till tecken på ångestsyndrom. Vi drar slutsatsen att i det förbyggande arbetet mot klamydia och andra sexuellt överförbara infektioner är det mycket viktigt att arbeta med alkoholvanor hos ungdomar och hur det sexuella riskbeteendet förändras under inflytande av alkohol. Sannolikt är

berusningsdrickande (konsumtion av stora mängder alkohol på kort tid) ännu mer korrelerat till sexuellt risktagande än riskkonsumtion av alkohol i största allmänhet.



Figure 1. *En klamydiainficerad cell/ A Chlamydia trachomatis infected cell.*

Original papers

This thesis is based on the following papers, which are referred to by their Roman numerals.

- I. **Carré H**, Boman J, Österlund A, Gärdén B, Nylander E. Improved contact tracing for Chlamydia trachomatis with experienced tracers, tracing for one year back in time and interviewing by phone in remote areas. *Sexually Transmitted Infections* 84(3):239-42, 2008. Epub 2008 Jan 23.
- II. **Carré H**, Edman A-C, Boman J, Nylander E. Chlamydia Trachomatis in the throat — is testing necessary? *Acta Dermato Venereologica*, 88(2):187-188, 2008.
- III. **Carré H**, Lindström R, Boman J, Janlert U, Lundqvist L, Nylander E. Asking about condom use, a key to individualized care when screening for Chlamydia. *Submitted*.
- IV. **Carré H**, Lindström R, Nordström A, Boman J, Janlert U, Nylander E. High prevalence of anxiety and hazardous alcohol consumption among patients attending an STI-clinic in northern Sweden. *Submitted*.

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Abbreviations

AUDIT	Alcohol use disorder identification test
C	<i>Chlamydia</i>
Chi ²	Chi squared test
CI 95%	Confidence Interval of 95%
CMO	County Medical Officer
CT	Chlamydia trachomatis
<i>C trachomatis</i>	Chlamydia trachomatis
Dept	Department
DNA	Deoxyribonucleic acid
EB	Elementary body
ECDC	European Centre for Disease prevention and Control
FCU	First catch-urine
FHI	Swedish national institute of public health (Folkhälsoinstitutet)
HADS	Hospital anxiety and depression scale
HIV	Human immunodeficiency virus
HPV	Human papillomavirus
HSP	Heat shock protein
Ig	Immunoglobulin
IVF	In-vitro fertilization
IUD	Intrauterine device
LGV	Lymfograduloma venereum
MI	Motivational interviewing
MSM	Men who have sex with men
NAAT	Nucleic acid amplification test
OR	Odds ratio
PB	Persistent body
PCR	Polymerase chain reaction
PID	Pelvic inflammatory disease
RB	Reticulate body
RNA	Ribonucleic acid
TFI	Tubal factor infertility
SD	Standard deviation
SMI	Swedish institute for infectious disease control (Smittskyddsinstitutet)
STD	Sexually transmitted diseases
STI	Sexually transmitted infections
WHO	World Health Organization
WSW	Women who have sex with women

Introduction

Chlamydia trachomatis (Chlamydia) is the most common sexually transmitted bacterial infection in Europe¹ with case rates up to 10% among sexually active.^{2,3} The infection is often asymptomatic but may be complicated by salpingitis and pelvic inflammatory disease (PID) with subsequent scarring resulting in chronic abdominal pain, ectopic pregnancy and infertility in women.⁴ Chlamydia has also been associated to reduced fertility in men.⁵ Persistent infection and chronic inflammation are discussed as possible cancer initiators/promoters in gynaecological tumors⁶ and co morbid Chlamydia facilitates the transmission of HIV by two to fivefold.⁷ The costs to treat sub fertility due to Chlamydia are high because in-vitro fertilization is often necessary. Being common; often asymptomatic but with serious sequels, good diagnostic tools available and easy to treat with antibiotics, Chlamydia is the perfect target for screening. As an attempt to stop the epidemic of Chlamydia it was incorporated into the *Swedish Communicable Diseases Act* in 1988. The incidence decreased 54 percent between 1989-1994⁸ with a corresponding decrease of complications.^{9,10} Between 1997-2008, despite all efforts with information, screening and partner notification the case rate increased 200%.⁸ This could only partly be explained by increased testing frequency and superior diagnostic methods⁸ but also e.g. by a more liberal attitude to occasional sex.¹¹

In the present work the possibility of identifying risk factors for catching Chlamydia has been studied in order to identify persons with increased risk of infection. The aim of the classification is to individualize the care of patients with counselling and risk reducing intervention for patients with higher risk. Infrequent condom use in combination with at least one new/temporary partner within the past 6 months can identify a group with sexual risk behaviour and increased risk of Chlamydia infection. Contact tracing is an important tool in identifying persons infected with Chlamydia and we found that a centralized contact tracing including one year is the optimal method. It is now recommended by the National Board of Health and Welfare in Sweden.¹²

Chlamydia trachomatis

Chlamydia trachomatis – the bacterium

Chlamydia trachomatis is a gram negative, obligate intracellular bacterium which was first regarded as a virus. Chlamydia requires an eukaryotic host cell to fuel its own growth and replication. The bacterium belongs to the family *Chlamydiaceae*, consisting of two genera; *Chlamydia* and *Chlamydiaophila*. They in their turn are divided into numerous of species, of

which three are responsible for human disease; *C pneumoniae*, *C psittaci* and *C trachomatis*.

The life-cycle of Chlamydia is unique with an intracellular growth or replicate form, the reticulate body (RB), and an extracellular metabolically inert, ineffective form, the elementary body (EB), **figure 2**. In addition to this replicate cycle associated with acute infection, Chlamydia can also cause persistent infections.^{13,14}

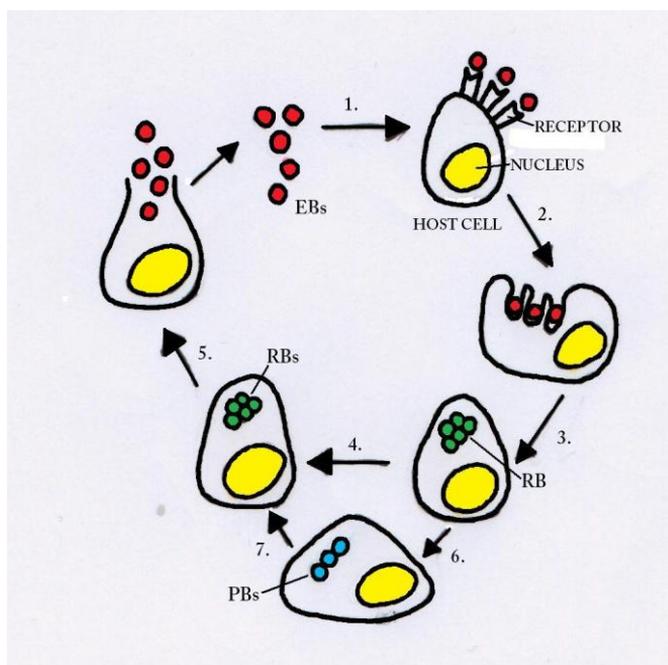


Figure 2. Life-cycle of Chlamydia. 1.

Elementary bodies (EBs) attach to specific host cell receptors. 2. EBs are ingested into the host cell. 3. EBs reorganize into a reticulate body (RB). 4. Multiplication of RBs. 5. RBs are transformed to EBs. 6. RBs cease to divide, not differentiating into EBs, forming persisting bodies (PBs), persistent infection and chronic disease. 7. Stimulus causes PBs to enter the active cycle, leading to

active disease.

The different species of CT have different host cell preferences.

C pneumoniae (TWAR) causes mild to severe respiratory tract infection. It has also been isolated in atherosclerotic lesions, but its role in atherosclerosis development is not clear.

C psittaci causes psittacosis, parrot fever (*psittacos* is Greek for parrot).

Respiratory tract symptoms are most common.

C trachomatis (CT) is subdivided into three biovars, of which *trachoma* and *lymfogranuloma venereum* (LGV) causes human disease. They are further subdivided into serovars (on the basis of antigenic character). Serovars A-C cause the eye disease trachoma. Serovars D-K cause urogenital tract disease (“Chlamydia”) and L1-L3 cause LGV. The EBs of CT are

restricted to non-ciliated epithelial cells of the urethra, endocervix, endometrium, fallopian tubes, anorectum, respiratory tract and conjunctiva. Infection does not confer long-lasting immunity. Rather, reinfection induces a vigorous inflammatory response with subsequent tissue damage. This response can cause vision loss in patients with chronic ocular infections and scarring with subsequent reduced fertility in persons with genital tract infections. CT causes *trachoma*, a chronic inflammatory disease of the eye eventually leading to blindness. The WHO estimates that 6 million people are blind due to trachoma, making it the leading cause of preventable blindness in the world. CT can also cause *adult inclusion conjunctivitis*, often preceded by genital tract infection, and *newborn conjunctivitis* or *pneumonia*. The baby is infected while passing the birth-canal. LGV causes a painless ulcer at the site of infection, which heals spontaneously but is followed by inflammation and swelling of the lymph nodes draining the area, and then progressing into systemic symptoms. The *urogenital tract infection* is often asymptomatic and described further on.

Not many in vivo studies regarding the natural history of genital tract CT-infection has been performed, mainly due to ethical considerations (the sequels are well known and severe and the infection can easily be treated with antibiotics). In a retrospective study 54% of the investigated women healed spontaneously after one year of follow-up and 94% after 4 years.¹⁵ Transmission takes place by direct mucosal contact between individuals, often at sexual contact. In experiments with guinea pigs 63% of the female guinea pigs were infected after intercourse (one or repeated during one day). The mean incubation time was 8.3 days.¹⁶

Epidemiology in Sweden with focus on the county of Västerbotten

During the 1980s the incidence of genital Chlamydia reached epidemic proportions in Sweden. In an attempt to prevent additional increase, Chlamydia was incorporated into *The Swedish Communicable Diseases Act* in 1988. There were also educational campaigns and young people's clinics were established to make testing easily available. Between 1989 and 1994 the number of Chlamydia cases decreased with 54% and the number of complications fell.^{9,10} The fall in rates of Chlamydia coincided with the national campaign to prevent HIV.¹⁷ Between 1997 and 2008 the case rate increased by approximately 200% and today Chlamydia trachomatis is by far the most common bacterial STI in Sweden, **figure 3**.⁸ In 2006 a new variant of Chlamydia was discovered in Sweden.¹⁸ This mutated form of Chlamydia contains a specific deletion in the cryptic plasmid. Three of the, until then, most commonly used NAAT diagnostic tests, the *Cobas Amplicor*, *Cobas TaqMan48* and *Abbott m2000* used this part of the plasmid as a target.^{18,19} This mutated form resulted in several thousand false negative test results,²⁰ causing a slight decrease of reported Chlamydia cases in 2005-

2006. In 2007, when the test methods had been changed to detect the

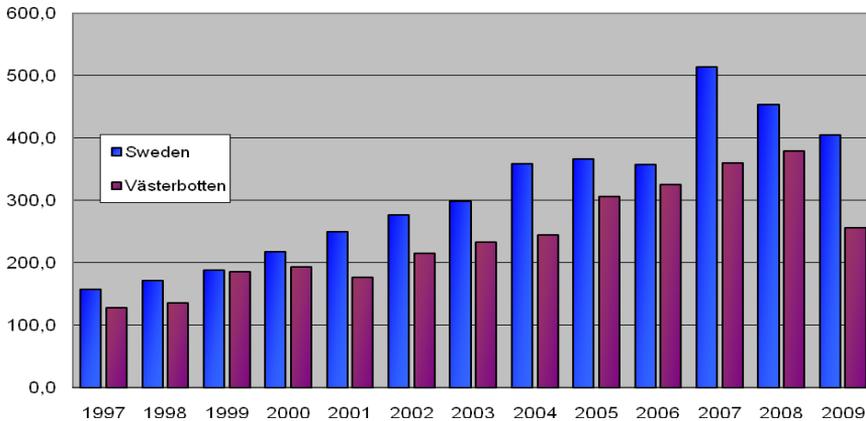


Figure 3. Incidence of Chlamydia 1997-2009 (cases/100 000 inhabitants). Note that 2005-2006 the incidence the whole of Sweden, but not in the county of Västerbotten, was affected because of false low diagnosis due to the mutated form of CT that could not be detected with some test methods. Source: The Swedish Institute for Infectious Disease Control.⁸

the mutated form of Chlamydia as well, a “catch-up” was observed. One must be observant of the fact that if an epidemic phase is defined by secular trend data only, there are often significant artefacts.²¹ Introduction of superior tests for Chlamydia (NAAT) in the mid 1990th, an increased number of analysed tests and change of sexual behaviours and attitudes are also part of the changes in Chlamydia case rates, heterosexuals well as mutation of the bacteria.

Most of Chlamydia infected heterosexuals are women (57% in 2008) and they are in average younger than infected men (21 and 24 years respectively). The average age of infected men who have sex with men (MSM) was 33 years in 2008. The frequency of positive tests is higher among men than women, indicating that men might be “under tested”. Ninety-four percent of all Chlamydia infections are heterosexually transmitted and 86% are infected within Sweden. The majority of infections caught abroad are from Spain, Thailand, Norway and Australia.⁸

The county of Västerbotten comprises approximately 1/8th of the area of Sweden, but only 3% (259 000) of the population lives here. The average age of the inhabitants is lower than in the total of Sweden (approx.10% between 18-24 years, compared to 8%) and 70 % of the inhabitants are living in the two largest cities Umeå and Skellefteå. With the exception of a slight decrease in 2001 the Chlamydia case rate in Västerbotten has increased steadily since 1997 until 2008. Nevertheless it was the second lowest in the country in 2005 and the lowest 2009. Västerbotten has, since the

introduction of NAAT tests in 1999, used diagnostic methods that can detect the new variant of Chlamydia and the number of tests has not decreased. The laboratories in the nearby counties of Norrbotten and Jämtland use the same diagnostic method as Västerbotten and the case rate in those counties increases most in Sweden. This supports the fact that there is no mutant causing the low prevalence in Västerbotten. Since 2000 the partner notification in Västerbotten is centralised and since 2007 people performing partner notification must be certified. It is possible to order a Chlamydia test from the internet (www.klamydia.se), and during 2008 25% of all tests were internet-tests. Since 2008 the accessibility of Chlamydia-testing has increased further by drop-in receptions at the Dept for Dermatology and Venereology, University Hospital, Umeå; the Students' health clinic, Umeå University, Umeå and at youth clinics and a project offering testing to women attending midwife-receptions. Preventive condom-projects at youth recreation centres and pubs have started and risk-reducing counselling with Motivational Interviewing (MI) and condom-information are being introduced. The effectiveness of MI in preventing re-infections are documented,²² and at present being further evaluated by us. The reduced case rate in 2009 could possibly be explained, at least partly, by these measures.

Clinical manifestations

Chlamydia affects the mucosal membranes. In women it causes cervicitis, urethritis and pelvic inflammatory disease (PID). Up to ninety percent of the infected women, however, are asymptomatic.²³ Symptoms of infection can be discharge; bleeding; pain; cervical edema/friability or cervical ulcers.²³⁻²⁵ Thirty to sixty percent of women infected with Chlamydia have Bacterial Vaginosis.^{26,27}

In men the spectrum of disease covers urethritis, prostatitis, orchitis and epididymitis.^{28,29} Up to 50% of men are asymptomatic. Symptoms can be dysuria, discharge and scrotal pain.²³

Chlamydia can also affect other organs resulting in for example conjunctivitis; arthritis; perihepatitis; periappendicitis and proctitis.³⁰ The triad of arthritis, urethritis/cervicitis and conjunctivitis is called *Reiters' syndrome*.

Sequels

In Sweden the term *acute salpingitis* is most often used but it is virtually synonymous with the Anglo-Saxon "*pelvic inflammatory disease (PID)*". *Fitz-Hugh-Curtis syndrome* refers to PID with perihepatitis resulting in pain in the right upper quadrant and hepatic tenderness at palpation.⁷

Ascending CT infections can result in salpingitis and PID and cause scarring with subsequent adhesions and obstructions of the fallopian tube, resulting in tubal factor infertility, chronic abdominal pain and ectopic pregnancy. The risk of ectopic pregnancy or TFI increases six times after one episode of PID and 17 times after two episodes.³¹ Asymptomatic PID may delay diagnosis, which has been shown to increase the risk of subsequent ectopic pregnancy and TFI.³² Worldwide 5-26% of couples in the reproductive age-group are infertile.³³ The inability of having children is a trauma for most of the affected persons and many report severe depressive symptoms.³⁴ TFI accounts for 14-35% of all infertility in the Western World.³⁵ Presence of antibodies against Chlamydia is strongly related to PID/TFI^{36,37} and Chlamydia is the main known geneses of PID and TFI in the developed world.⁴ Recently *Mycoplasma genitalium* was observed as another agent of clinical importance causing PID.³⁸ In the developing world, *Neisseria gonorrhoeae* and genital tuberculosis are also important causative agents. In a WHO-study women with antibodies against Chlamydia and/or *Neisseria gonorrhoeae* had a significantly increased risk of having bilateral tubal occlusion. The majority of the women never had any symptoms of infection/PID.³⁹ Infertile women have a significantly greater risk of having been infected with Chlamydia than fertile.⁴⁰ If untreated approximately 10-20% of infected women will develop PID^{31,41} and 10-20% of women with PID will have ectopic pregnancy or infertility.⁴² On the other hand the difficulties with diagnosing PID are well known. Recent studies and reviews report much lower rates of complications.⁴³⁻⁴⁵ The absolute magnitude of the complication rate and costs associated to Chlamydia complications is thus not known.⁴⁶ That makes the estimation of the costs of Chlamydia associated complications uncertain. In UK the costs of complications have been estimated at a minimum of 110 million Euro annually.⁴⁷ Couples infertile due to TFI can be helped by IVF (in-vitro fertilization). TFI itself is associated with poor IVF outcome, compared to other infertility diagnoses. Presence of Chlamydia HSP60IgG and IgA antibodies in follicular fluid are associated with reduced implantation rate after IVF.^{48,49}

The Chlamydia 10 kDa and 60 kDa heat shock proteins (cHSP10 and cHSP60) show an amazing analogy to human proteins. There could be cross-reactivity between the human HSP60 and the bacterial cHSP60, resulting in antibody formation against the HSP60 in the women infected with Chlamydia. HSP10 and 60 seem to have negative impact on embryonic growth, and increase the probability of negative pregnancy outcomes. HSP60 has also been shown to induce trophoblast apoptosis.⁵⁰ Women positive for Chlamydia and with antibodies against HSP60 have a greater probability of tubal scarring and ectopic pregnancy. HSP10 may cross react with an embryonic protein.⁵¹ This can cause spontaneous abortions.

There is evidence for a correlation between antibodies against Chlamydia and reduced sperm quality.⁵²⁻⁵⁴ Presence of IgA antibodies against Chlamydia in the male part of infertile couple reduced the chances of achieving pregnancy with one-third over a 3-year period. If both IgA and IgG antibodies were present, the reduction was almost two-thirds.⁵ These results are somewhat controversial because there are other studies that have failed to detect decreased sperm parameters.⁵⁵ Chlamydia infection can cause production of anti-sperm-antibodies (ASA). Their affect on fertility is not clarified.

Chlamydia is also discussed as a co-factor in the development of cervical cancer. Cervical cells, which are persistently infected with oncogenic types of HPV, could be transformed into cancer cells because of chronic cervical inflammation due to persistent Chlamydia.⁶ Chlamydia increases the patients' susceptibility to HIV by two to fivefold.⁷

Diagnostic methods

Tissue culture was earlier considered as the "golden standard" for detecting genital tract infection due to Chlamydia. The specificity is 100%, but the sensitivity is often only 60%, meaning that up to 4/10 patients with Chlamydia are false negative at testing.⁵⁶ Nucleic acid amplification test (NAAT) has been shown to be more sensitive⁵⁷ and is now the method of choice. The high sensitivity is due to the fact that viable bacteria are not needed and due to the amplification process. Principally NAATs amplify either a) the target nucleic acid, DNA (polymerase chain reaction, PCR; strand displacement assay, SDA) or ribosomal RNA (rRNA) (transcription mediated amplification, TMA); or b) the probe after it has annealed to the target nucleic acid (ligase chain reaction, LCR). The high sensitivity makes it possible to use non-invasive tests such as first catch urine (FCU) or vaginal swabs instead of cervical or urethral samples. Although sensitivity and specificity do vary slightly between different manufacturers, the latest versions of the NAATs of major brands are all adequate,²³ with sensitivity and specificity ranging from 86-93% and >97% respectively.⁵⁸ Among men NAAT on FCU has become a routine method with a sensitivity and specificity of 84-93% and 97-99% respectively.⁵⁸ In women a sensitivity of about 98% has been found for PCR on urethra-/cervix- and urine-/cervix-samples.⁵⁹ FCU only had a sensitivity of 88-93%.^{58,59} In women though it is recommended to take tests from two different locations to increase the sensitivity, often FCU in combination with a cervix sample or a self collected vaginal swab. A new study confirms a lower sensitivity on FCU (88%) compared to invasive samples and indicates that endocervical or vaginal samples alone has at least as good sensitivity as combined vaginal/FCU specimens.⁶⁰ To be noted though is that the authors refer to two different

diagnostic methods. Self taken vaginal swabs are easier to perform and more accepted by the patients than clinician-collected cervical or vaginal samples and the sensitivity is, at least, just as good.⁵⁷

Sexually transmitted infections FCU tests should, as the name indicates, be from the first catch of urine. Vaginal samples are collected inserting a sampling bud approximately 4 cm into the vagina and firmly rotate it 3-4 times against the vaginal wall. This could be performed by the patient herself. The cervix should be wiped off with a vaginal swab, before taking a cervical sample. The sampling bud is inserted 1-2 cm into the cervical canal. The cervical or vaginal sample can be inserted into the urinary sample and sent to the laboratory for analysis. This procedure seems to increase sensitivity compared to analyzing the samples separately.⁵⁹ It seems like NAAT can detect a Chlamydia infection at earliest one week after the patient was infected. Because of the low resistance level, test of cure is not generally recommended, but could be valuable if a higher risk of reinfection is suspected. If a new Chlamydia test is performed, it should be taken at the earliest three weeks after finishing antibiotics.

Pharyngeal infections with Chlamydia trachomatis

Fellatio (oral sex) has become more common over the years and condom is seldom used.⁶¹ The association between pharyngeal Chlamydia, fellatio and throat symptoms is not fully investigated. At least 9% of homosexual men with urogenital Chlamydia infection had been infected after fellatio.⁶² The prevalence of pharyngeal Chlamydia among heterosexual females in Sweden reporting recent unprotected fellatio was 1.5-7% and 8% of urogenitally infected had pharyngeal infection as well.^{61,63} All persons infected in the pharynx were infected in the urogenital tract as well. Among MSM the prevalence of pharyngeal Chlamydia was 1.4-2%.^{62,64,65} The optimal diagnostic methods are discussed. To date the highest sensitivity data for culture of Chlamydia in pharyngeal samples are 44%.^{66,67} NAATs detect Chlamydia in extra genital sites with superior sensitivity but they have not been adequately evaluated for extra genital infections.⁶⁷ The sensitivity differs between different NAATs; Becton Dickinson's ProbeTec (SDA) has a sensitivity of 67-80%, compared to Gen-Probe's APTIMA Combo 2 (AC2) 100%. The specificity is over 98% for all NAATS.^{64,66} There is no consensus regarding the best way of collecting samples. A small study indicates that the sensitivity increases if the patient gargles water and spits into a test tube instead of using a pharyngeal swab.⁶⁸

Treatment

In Sweden the most common recommendation of treatment of Chlamydia infections are doxycycline 200 mg day one followed by 100 mg day 2-9. Testing and treating for Chlamydia is free of charge according to the law.⁶⁹

Resistance, although infrequently reported, does occur in Chlamydia, and is associated with treatment failure.^{70,71} At the moment it is though considered rare, and a test of cure is not generally recommended of that reason. A single dose of azithromycin is equally as effective as a 9-day course of doxycycline though more expensive.⁷² Intercourse without barrier protection is prohibited until the whole treatment is finished, or until the partner has finished his/her treatment. For azithromycin intercourse without using a condom is prohibited for one week as well. The risk is considered greater that this is forgotten when giving a single dose of azithromycin, with subsequent re-infection risk. Pregnant women are treated with tetracyclines, for example doxycycline in the first trimester and erythromycin 500 mg x 2 later on in pregnancy.

The Swedish Communicable Diseases Act⁶⁹

The Swedish Communicable Diseases Act from 2004 aims to diminish the prevalence and spreading of infectious diseases in Sweden by interventions.

1. *Diseases dangerous to public health (Allmänfarliga sjukdomar)*
Diseases which could be life-threatening or cause protracted illness or severe suffering or other severe consequences. If diagnosing such an infection one must report it to the County Medical Officer (CMO) and to the Swedish Institute of Infectious Disease Control (SMI) and perform contact tracing. Examples: HIV; gonorrhoea; syphilis; Chlamydia trachomatis; hepatitis A-E; tuberculosis; polio; rabies; salmonella.
2. *Diseases dangerous to society (Samhällsfarliga sjukdomar)*
Diseases which, if spread in the society, could cause severe damage to important social services and where extraordinary efforts are demanded to diminish spread of the infections. Examples: Smallpox and SARS (Severe Acute Respiratory Syndrome).

Notification and/or contact tracing is mandatory for some other diseases apart from diseases dangerous to public health. Those are referred to as *Notifiable diseases (Anmälningspliktiga utöver allmänfarliga)* and *Diseases subjects to mandatory contact tracing (Smittspårningspliktiga)*. The National Board of Health and Welfare is responsible for the control of infectious diseases nationally. The Swedish Institute of Infectious Disease Control (SMI) is responsible for analyzing the epidemiology and proposes

necessary measures to prevent spreading of infections. In every county there must be a responsible physician, the County Medical Officer (CMO) for Communicable Disease Control. According to the legislation every Swedish citizen is obliged to prevent spreading of infectious diseases. A physician that diagnoses a disease incorporated into the legislation must inform the patient, report to the CMO and the Swedish Institute of Infectious Disease Control and, if demanded, perform contact tracing. Contact tracing can be referred to other professions within the healthcare system. Patients are demanded to contribute to the contact tracing with necessary information. Once notified, partners or people at risk for being infected must seek medical advice for examination. If he/she does not show up he/she is reported to the CMO who may force testing. Chlamydia trachomatis and other STIs are reported to the CMO and to the Swedish Institute of Infectious Disease Control with a six-digit code. Examination and treatment are free of charge. Prescription of antibiotics without previous testing is not allowed.

Partner notification and “the Västerbotten model”

Partner notification or contact tracing is defined as the work with identifying the source of infection and persons who the patient might have passed the infection on to.⁶⁹ Partner notification in STIs is not a modern phenomenon. Already in 1820 the “Sundhetskollegium” in Sweden (the precursor to The National Board of Health and Welfare) encouraged physicians to try to find out who might have infected their syphilis patient. The duty to perform partner notification was prescribed by law in 1918 (“Lex veneris”). The great decrease in gonorrhoea in the US in the 1970th ⁷³ and the reduction of Chlamydia and its complications in Sweden in the 1990th has partly been explained by effective partner notification.^{9,10}

The basic principle for partner notification is that the tracer proceeds from the infected index patient and should go on until all infected subjects are identified.⁶⁹ The tracer must try hard to create a trustful relation to the patient and to make him or her understand the importance of notifying all partners that might be infected, so they can be tested and, if necessary, treated.¹² The law prescribes that the identity of the index must not be revealed when the medical services contacts partners.⁷⁴ Steady partner should start medication directly after testing, without waiting for test results.¹² Partner notification must not include possible partners living abroad.⁶⁹

In Västerbotten partner notification is centralised since 2000 and since 2007 people performing contact tracing must be certified. Because of the high level of contagiousness the National Board of Health and Welfare points out the importance of partner notification to be carried out as fast as possible to inhibit further spread of disease.¹² The county of Västerbotten is sparsely

populated and to enable centralised tracing within a reasonable time, partner notification is performed by phone in remote areas. The combination of highly centralised contact tracing with experienced counsellors exploring the sexual history for at least 12 months back in time and by phone in remote areas have been referred to as “The Västerbotten model”. Our evaluation of “The Västerbotten model” changed the recommendations and made it a model for contact tracing in Sweden 2007.¹²

Screening and other preventive strategies

If a disease is common, causes severe sequels or is potentially mortal, has a safe and secure diagnostics and with treatment available, the disease is convenient for screening. Chlamydia fulfils all these criteria. The European Centre for Disease Prevention and Control (ECDC) has outlined four levels of Chlamydia control programmes; 1. *Primary prevention*: Measures to prevent infection by information, condom distribution etc. 2. *Case management*: Routine case surveillance, accurate diagnostic services, clinical services, and patient and partner management services. 3. *Opportunistic screening*: Testing routinely offered to one or more specified groups of people with the aim to identify asymptomatic cases. 4. *Screening programmes*: Organized provision of regular Chlamydia testing to cover a substantial proportion of a defined population, with the aim of reducing Chlamydia prevalence in the population.¹ Because of the rising incidence of Chlamydia in the 1980th measures with the aim to stop the epidemic took place. The disease was incorporated into The Swedish Communicable Diseases Act in 1988. Partner notification became obligatory and testing and treatment free of charge. There were also educational campaigns and establishment of youth clinics to make testing easily available and local opportunistic screening programmes were established. The decrease of case rates of Chlamydia and its complications in the 1990th has been attributed to the widespread testing and the opportunistic screening.^{9,10,75} This though coincided with the national HIV-prevention campaigns and change in sexual risk behaviour has also been associated to the reduced incidence.^{17,76} There has been an increasing incidence of Chlamydia since the mid 1990th.⁸ It has been attributed to an increased test rate and more sensitive test methods (NAAT);¹⁰ inadequate partner notification;^{77,78} loss of immunity after widespread early treatment;⁷⁹ and an increase in sexual risk behaviour again.¹¹ An inadequate effectiveness of the opportunistic screening approach might also be an explanation.^{80,81} Two randomized controlled trials (RCT) have shown a reduction of PID at 12 months follow up, after one episode of systematic screening.^{82,83} There is a lack of evidence for sustained reductions of disease after opportunistic screening.⁸⁴

Although screening is widespread in Sweden, Chlamydia control activities, except for partner notification, are founded and implemented by each county separately and not coordinated nationally. Primary prevention programmes are common and sex instruction is obligatory at school. The norm in the group is more important than each person's individual knowledge when decisions are made ⁸⁵ and group tuition at school is the most important arena for changing attitudes to safe sex.⁸⁶ In Västerbotten free condoms are delivered at youth recreation facilities and pubs. Opportunistic screening is often offered different subpopulations i.e. patients seeking abortion, pregnant women, patients attending youth clinics and STI-receptions. Contact tracing and testing of partners to infected patients are obligatory.

The national plan of action against Chlamydia trachomatis 2009-2014

The National Board of Health and Welfare in Sweden has completed a national plan of action against Chlamydia. It states that within the year of 2014;

1. The number of persons always using a condom with a new/temporary partner has increased considerably.
2. The knowledge of consequences of un-safe sex has increased considerably.
3. The number of persons 15-29 years who know when they should get tested for Chlamydia has increased and people with risk behaviour should get tested on regular basis, at least every 6 months.⁸⁷

Some measures of improvement are proposed, for example; • Better Sex instruction at school. • Improving the accessibility of testing and actively looking up youths that do not seek testing themselves. (Today the majority of persons tested are women. It is important to increase number of men tested.) • Identifying groups at increased risk for infection and offering them special risk reducing interventions. • Improving and centralizing the partner notification.

In England an opportunistic national screening programme (The National Chlamydia Screening Programme, NCSP) offers testing of all sexually active 16-25 years old at change of partner or at least once a year.³ The National Board of Health and Welfare in Sweden suggests that, if it turns out to be successful, it could be an alternative in Sweden as well.⁸⁷ Compared to national screening at specified intervals, opportunistic screening in Sweden usually occurs only once or at irregular intervals. There is evidence that those at high risk are tested infrequently or not at all, while regular users of health services at lower risk tend to be tested unnecessarily often.⁸⁸

The ECDC recommends that patients attending STI receptions should be offered Chlamydia tests routinely, regardless of symptoms.¹ Since the mid 1980th this is the case at all STI receptions in Sweden. In other health care settings Chlamydia testing should be offered to all patients where clinically indicated. Chlamydia testing should also be considered prior to any instrumentation of the cervix, such as insertion of IUD or termination of pregnancy.¹

Sex in Sweden

The attitude to sex among the Swedish population 16-44 years old has regularly been investigated. Since 1987 Swedes have become more liberal to occasional and multiple sexual contacts.¹¹ In combination with later family setting this means that more persons expose themselves to risks of catching STIs for a longer period in life. Twenty years ago more than 50% agreed on the statement that sex should only occur in a steady relationship; today only one third agrees. The biggest change in attitudes has occurred among women. Among men, the norm towards occasional sex has been more permitting.

	Women 1989	Women 2007	Men 1989	Men 2007
≥3life-time partners	13% 18-19 years 14% 20-24 years	26% 18-19 years 19% 20-24 years	17% 18-19 years 17% 20-24 years	23% 18-19 years 26% 20-24 years
Sexual debut	51% 16-17 years	66% 16-17 years	40% 16-17 years	52% 16-17 years
Sex at first date	15% 18-19 years 14% 20-24 years	34% 18-19 years 28% 20-24 years	25% 18-19 years 24% 20-24 years	36% 18-19 years 38% 20-24 years

Table 1. Sexual behaviour among 18-24 years old in Sweden between 1989 and 2007.¹¹

People living in cities have more partners than people in remote areas. The use of condoms have been quite steady between 1989 and 2007, except for an increase among 16-17 years old in the last years. 2007 approximately 25% of 16-24 years old have had sex with a new/temporary partner without using a condom. Sex at the first date becomes more and more common. Fellatio (oral sex) is common, 59-70% of youths have some kind of experience.^{11,89} Today the internet is very easily available to youths in Sweden. Sex is the most common word to seek at the internet. How is our behaviour affected by the easily accessed sex and porn? The internet increases the sexual networks and may thus increase the risk of spreading STIs.⁹⁰ It has become more common to travel and different STIs may be caught abroad as well. Harmful alcohol habits become more and more common. Twenty-five percent of pupils at school had had unprotected sex after the intake of alcohol.⁹¹

Alcohol consumption and mental illness among young people in Sweden

There is a growing body of literature which suggests that public education campaigns continue to have low impact on reducing the rates of sexual risk behaviour due to demographic, psychosocial, and cognitive variables mediating in the decision making process.⁹² Unprotected sex is more common when sex is unplanned/”an action in the heat of the moment” or under the influence of alcohol, but is seldom due to lack of knowledge. Pressure from the man not to use a condom might also be the reason.⁹³ Adolescents affected by depression have higher rates of sexual risk taking behaviour⁹⁴ and are much more likely to have multiple sexual partners.⁹⁵ Mental illness, in terms of depression and anxiety, becomes more and more common in Sweden, especially among young people. In a survey performed by the Swedish National Board of Health and Welfare, 30% of women and 14% of men aged 16-24 years reported feeling anxious or worried within the last 2 weeks. The amount of 20-24 years old that are hospitalized due to depression has duplicated between 1997 and 2007 and tripled among 16-19 years old. The number of suicide-attempts has increased as well although death due to suicide is still uncommon. Mental illness is increasing no matter family situation, ethnicity, employment etc but the amount of increase differs among the groups. The greatest increase is observed among those who neither study nor work and among female students.⁹⁶ Among 25-44 years old the self reported mental health has improved somewhat within the past years.⁹⁶ Sex while intoxicated with alcohol independently predicted condom non-use and multiple partners.⁹⁷ Consuming alcohol at an early age, consumption of larger amounts of alcohol currently consumed on a “heavy night” predicted the need for Chlamydia treatment.⁹⁸ Every fourth pupil at school has had unprotected sex after intake of alcohol. Unprotected sex or sex that one regretted afterwards was twice as common among heavy consumers compared to all others.⁹¹ The alcohol consumption in Sweden has increased since the beginning of the 1990th, but from the middle of the 2000th decade this development has leveled out and even a small decrease is found.⁹⁶ The current alcohol consumption is approximately 10 litres of pure alcohol per person aged 15 years or more, and year, which is somewhat below the European average. Young people in Sweden drink the same amount of alcohol as adolescents in the rest of EU. There is not an international consensus on the definitions and terminology of alcohol consumption.⁹⁹ The World Health Organization promotes the term *hazardous consumption* for substance use that increases the risk for harmful consequences for the user and *harmful consumption* for use that is causing damage to the health.¹⁰⁰ The National Institute of Public Health in Sweden uses the term hazardous consumption (“riskbruk”) for both potentially

harmful consumption and consumption that has already caused harm to the health, but where there is no current addiction.¹⁰¹ Men consuming 2 units of alcohol per day and women consuming 1.5 units are considered having a hazardous consumption.¹⁰¹ The content of alcohol in one unit differs from 8 to 14 grams of alcohol between different countries.⁹⁹ In Sweden one unit contains 12 g alcohol and equals approximately 15 centilitres wine, 33 centilitres strong beer and 4 centilitres liquor.¹⁰¹ Intensive consumption of large amounts of alcohol at one occasion (*binge drinking*) causes intoxication and is associated to acute injuries and accidents¹⁰² and adverse social consequences.¹⁰³ It is also associated to sexual risk behaviour and Chlamydia infection.⁹⁸ The Swedish National Institute of Public Health defines binge drinking (“berusningsdrickande”) as 5 units or more consumed at one occasion for men and 4 units or more for women.¹⁰¹ In Sweden 34% of 16-24 years old men and 25% 16-24 years old women are found to have hazardous alcohol use.⁹⁶ The alcohol consumption decreases with age. Many situations where alcohol is consumed are of positive social nature, for example dinners; celebrations and festivities. Hazardous consumption, however, is also strongly associated to depression and anxiety.¹⁰⁴ In a survey among 1400 visitors at primary healthcare centres in the county of Västerbotten, every third patient was found to suffer from depression, anxiety and/or alcohol problems.¹⁰⁵ Half of those with hazardous alcohol consumption had contemporary symptoms of anxiety or depression.

Aims

The general aim of this study was to identify factors associated with an increased risk of catching Chlamydia trachomatis, to enable individualized care and intervention.

Specific aims

- To evaluate the so called “Västerbotten model” for partner notification, to optimize finding of infected partners of Chlamydia patients to prevent further spread.
- To evaluate whether Chlamydia trachomatis infection in the throat could be identified by symptoms and whether testing for pharyngeal Chlamydia should be a routine.
- To establish whether persons attending a drop-in STI-reception with an increased risk for genital Chlamydia (re)infections, could be identified by some easy screening questions in order to individualize care with counselling and intervention.
- To establish whether depression; anxiety and/or abuse of alcohol is associated to sexual risk behaviour and with catching genital Chlamydia infections.

Materials and methods

Study I included the whole of the county of Västerbotten. Study II-IV took place at the STD clinic, Dept of Dermatology and Venereology, University Hospital, Umeå, Sweden. All Chlamydia samples were examined at the Dept of Laboratory Medicine/Virology, University Hospital, Umeå, Sweden.

Improved partner notification for Chlamydia trachomatis (Paper I)

In the first part of the study, all cases of Chlamydia reported to the County Medical Officer (CMO) during one year (2002) were included. A questionnaire was sent to all persons reporting a Chlamydia case to the CMO. The person performing the partner notification was supposed to complete the questionnaire. No directions regarding the partner notification was given.

Part two included the counsellors at the STD Clinic, Dept of Dermatology and Venereology, University Hospital, Umeå, doing the majority of the partner notifications in the county during one year (November 2005 - December 2006). Patients could chose themselves whether they preferred a partner notification interview by phone or at the reception.

Identifying risk factors associated with Chlamydia trachomatis (Paper II, III, IV)

Patients attending the STD Clinic, Dept of Dermatology and Venereology, University Hospital, Umeå, Sweden confirming fellatio within the past 6 months, were included in the study of Chlamydia in the throat (Paper II).

We established a drop-in reception at the STD Clinic and all patients attending were consecutively included. The only exclusion criteria were; not mastering Swedish good enough to fill in the questionnaires, recent treatment with antibiotics or former participation in the study within the previous six months (Paper III, IV).

When defining “sexual risk behaviour” in Paper IV two variables significantly correlated to Chlamydia infection in Paper III and describing a specific behaviour were selected; inconsistent condom use and new/temporary partners within the past 6 months. For “inconsistent condom use” the variable “Not always using condom with new/temporary partner” was chosen over “Condom at last intercourse with new/temporary partner” because it had a higher answer rate and was significantly associated to Chlamydia in both sexes.

Questionnaires for evaluation of sexual risk behaviour (Supplement 1; Paper III, IV)

The questionnaire used for investigating sexual risk behaviour and factors potentially correlated to present Chlamydia infection is attached (supplement 1). It consisted of questions regarding medication; demographic information; marital status; symptoms; STIs within the past year and sexual behaviour. Patients reporting at least one new/temporary partner within the past year were asked to plot these events on a time-axis. The time-axis was followed by some thorough questions regarding condom use. Information about age; lifetime STIs; sexual preferences; condom at last new/temporary contact and contraceptives was collected from the patients' medical records. Anamnesis at the STI-reception is supposed to be taken using a standard formula where, among others, all these questions are covered. The test results of the Chlamydia tests were collected from the medical records as well.

Hospital Anxiety and Depression Scale (HADS) (Supplement 2; Paper IV)

The HADS questionnaire is compiled for the use in somatic and primary care and contains 14 statements, each with four answer alternatives.¹⁰⁶ Seven statements measure anxiety and seven signs of depression. The answer alternatives are weighted on a scale 0-3. A compiled score of ≥ 8 in the respective areas indicates symptoms of mental disorder. The predictive validity for identification is about 70%.¹⁰⁷ For possible diagnosis of an anxiety or depression disorder, the HADS should be followed by a clinical interview. The cut-off ≥ 8 is unlikely to have overestimated the prevalence of mental disorder since it has been validated against psychiatric interviews in an STI clinic.¹⁰⁸ In validation the threshold of ≥ 8 gave the best balance of sensitivity (depression: 82%; anxiety: 70%) and specificity (depression: 94%; anxiety: 68%). The HADS is short and quick to answer, and we found it appropriate as a first screening tool.

Alcohol Use Disorder Identification Test (AUDIT) (Supplement 3; Paper IV)

AUDIT is aimed at early identification of people with hazardous/harmful alcohol consumption. The questionnaire has been compiled by a group within the WHO and is standardized in several countries.^{109,110} The questionnaire consists of 10 questions with three or five answer alternatives per question. The points are weighted between 0-4 for each question. The maximal score is 40. Depending on whether the aim is to identify as many persons, with potentially harmful alcohol consumption, as possible, or to select persons with a more extreme alcohol addiction, different cut-offs are

recommended. If a high sensitivity is preferred over specificity a cut-off point ≥ 6 for women and ≥ 8 for men is often recommended.¹¹¹ Among men this threshold gives a sensitivity of 97% and a specificity of 69%.¹¹¹ The AUDIT with a cut off 6 and 8 respectively is considered an appropriate screening tool but with the low sensitivity at this threshold a positive finding should be followed by a clinical interview before a possible diagnosis is set.¹¹¹

In our study binge-drinking was defined as 6 or more standard glasses at one occasion at least once a week.

Diagnostic methods (Paper I, II, III, IV)

At the STI-clinic FCU specimens were collected from men. An incubation time of one, preferably two, hours was recommended as microscopy of urethral discharge was done as well. In women FCU was combined with a self collected vaginal swab or a personnel collected endocervical sample. The vaginal/cervical sample was inserted into the urinary sample and sent to the laboratory for analysis.

For analysis of pharyngeal Chlamydia we both took a pharyngeal swab and let the patient gargle 10 ml of water for about 30 seconds and then spit it into a test tube. The swab was placed in the tube with the water that had been gargled. All tests included in the four studies were analyzed with nucleic acid amplification technology (NAAT) at the Dept of Laboratory Medicine/Virology, University Hospital, Umeå, Sweden. During the whole study period the Becton & Dickinson ProbeTec ET was used. This is a Strand Displacement Amplification (SDA) test, which also detects the mutated form of CT.^{58,112}

Statistical analysis (Paper I, II, III, IV)

The statistical analysis was performed in SPSS 17.0 for Windows. Possible associations were evaluated using Chi-squared (χ^2) test for categorical variables and Student's t-test for continuous variables. A significance level of $p < 0.05$ was chosen. A multivariate logistic regression model was constructed to evaluate whether a variable was independently associated to ongoing infection or not (Paper III). Variables showing a significant association to present Chlamydia infection and possible confounders were included into the multivariate logistic regression as independent variables and Chlamydia as dependent. A confidence interval of 95% was considered significant. To avoid co linearity problems the variables' level of correlation were evaluated using bivariate correlation analysis (Pearson's correlation coefficient) before they were included into the multivariate model. Different variables association to anxiety, depression and hazardous alcohol consumption were evaluated using the same principles (Paper IV). Missing cases were not included in the χ^2 and multivariate analysis or the t-test.

Results

Partner notification (Paper I)

The Chlamydia infected patients reported in average 2.5 partners/index and 0.9 Chlamydia infected partners/index were identified after contact tracing, **figure 4**. The number of partners reported and the percentage of infected partners declined with time since last intercourse, **figure 5**. Still 30% of partners with a known test result who had had contact with the index 7-12 months before the index was diagnosed with Chlamydia, were infected themselves. The results of the contact interviews differed between the different professions, as did patient demographics. The counsellors performed almost 80% of all tracings, and in 80% of the cases their contact interview covered a minimum of the previous 12 months. Their index patients also reported the highest number of partners.

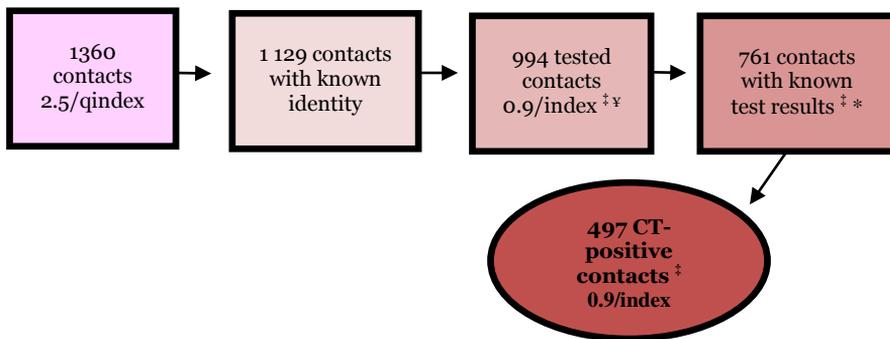


Figure 4. ^{*}Number of partners that the tracer knew were tested/ knew test results for/ knew was infected. [‡]The tracer did not know whether 321 (24%) contacts were tested. ^{*}230 (23%) had a test result unknown to the tracer.

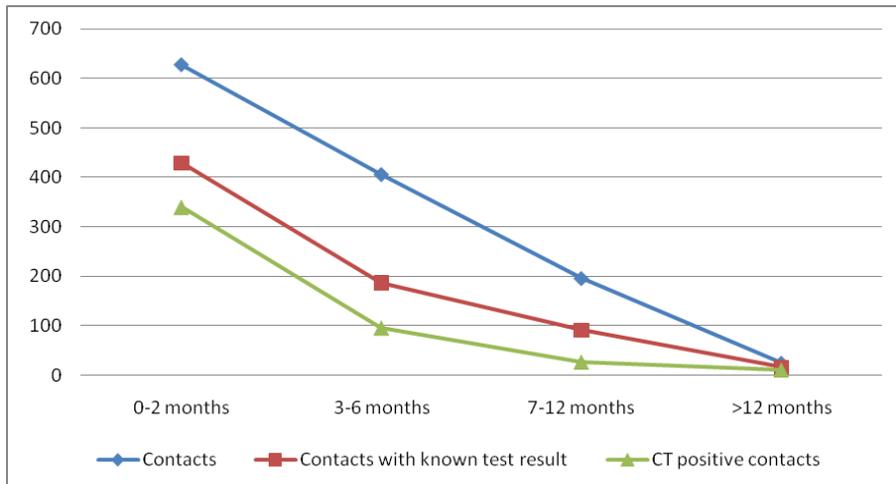


Figure 5. Sexual contacts of Chlamydia infected index patients by time since last sexual contact between the index patient and the contact.

There were no significant differences between contact interviews performed at the clinic or by phone. In phone-interviews the index reported 2.3 patients in average, compared to 3.0 at the clinic-interviews, and 99% of the interviews covered at least the past 12 months compared to 100%. Even if the patients could chose themselves which method they preferred, the groups were similar regarding sex and age

Pharyngeal Chlamydia trachomatis infections (Paper II)

All patients infected with Chlamydia in the throat had an urogenital infection as well. One of the patients with pharyngeal Chlamydia had symptoms of pain in the throat, **figure 6**.

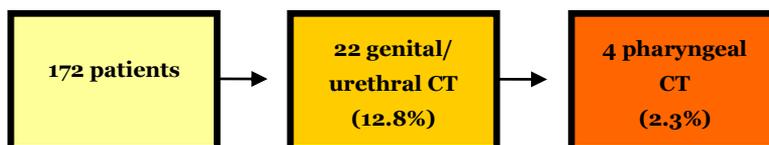


Figure 6. All patients with pharyngeal Chlamydia were also infected in the genital/urethral tract.

Risk factors associated with Chlamydia trachomatis infections (Paper III, IV)

After analysis with Chi-squared test the following factors were significantly associated with Chlamydia

Men:

- New/temporary partner within the past 6 months (p=0.11)
- Inconsistent condom use (p=0.042)
- Partner with current/recent CT (p<0.001)
- Single status (p=0.026)
- Low education (p=0.043)
- Symptoms (dysuria or discharge) (p<0.001)

Women:

- New/temporary partner within the past 6 months (p=0.013)
- Inconsistent condom use (p=0.012)
- Partner with current/recent CT (p<0.001)
- Sick-listed or unemployed (p=0.038)
- Hormonal contraceptives (p=0.007)

Inconsistent condom use was defined as not always using a condom with new/temporary partner. Eighty-seven percent had practiced unprotected sex with a new/temporary partner within the past year. Twenty-four percent of the patients used a condom at last intercourse with their last new/temporary partner, and 23% of them always used it during the whole intercourse. That means that only 5% of patients attending a drop-in STI-reception in fact used a condom correct at last intercourse. Not using condom during the whole intercourse did not increase the frequency of Chlamydia infection, neither among consistent nor among inconsistent condom users.

Table 2. Selection criteria sensitivity for ongoing Chlamydia infection

Selection criteria	Resp.‡	Meeting selection criteria(%)	CT+ resp.‡	Criteria sensitivity[‡]	PPV[‡]
Inconsistent condom use [‡]	1209	979(81%)	135	123(91%)	12.6
≥1 new partners within the past 6 months	1204	890(74%)	133	116(87%)	13.0
≥1 new partners within the past 6 months and inconsistent condom use [‡]	1137	707(62%)	126	102(81%)	14.4
≥2 new partners within the past 6 months	1204	443(37%)	133	65(49%)	14.7
≥2 new partners within the past 6 months and inconsistent condom use [‡]	1137	370(33%)	126	58(46%)	15.7
0 new partners within the past 6 months or consistent condom use [‡]	1209	430(36%)	24	4(17%)	5.6

Table 2. [‡]Responders, [‡]CT infections among those meeting the selection criteria compared to all responders with CT infection, [‡]Positive predictive value, [‡]Inconsistent condom use with new/temporary partner.

Alcohol, depression and anxiety in association with sexual risk behaviour (Paper IV)

Anxiety and depression

Thirty-two percent of the patients showed signs of anxiety and/or depression; 7% had signs of depression but 81% of them had simultaneous signs of anxiety. There was no association between depression and sexual risk behaviour including present Chlamydia infection. Anxiety was common (30% of the patients), significantly more common among women than men. There was a significant association between anxiety and hazardous alcohol consumption.

Is hazardous consumption of alcohol associated with sexual risk behaviour?

Fifty-four percent had hazardous alcohol consumption, women 53% and men 55%. Hazardous alcohol consumption was significantly more common among single persons, students, women aged <25 years and men <30 years old. Hazardous alcohol consumption was independently correlated to inconsistent condom use in both sexes. Number of new partners within the past 6 months increased with increasing AUDIT. Hazardous alcohol consumption was positively associated to ≥ 1 partner within the past 6 months (men OR 1.9 CI 95% 1.1-3.3; women OR 2.3 CI 95% 1.2-4.5) and ≥ 2 new partners within the past 6 months (men OR 2.0 CI 95% 1.2-3.5; women OR 3.0 CI 95% 1.6-5.6). When possible confounders were taken into consideration, a significant association did only remain for ≥ 2 new partners within the past 6 months among women (OR 2.8 CI 95% 1.3-5.7). Hazardous consumption was not significantly associated to Chlamydia infection.

Does binge drinking promote high-risk sex?

Binge-drinking was associated to present Chlamydia infection; at least 2 new partners within the past 6 months; low education; being single. The association to present Chlamydia infection and multiple partners did not remain when corrected for possible confounders. Binge-drinkers were not significantly less tended to use condom compared to non-binge drinkers.

Discussion

“The Västerbotten model” for partner notification

“The Västerbotten model” i.e. a centralized partner notification method with experienced tracers; notification periods of at least 12 months and contact tracing by phone as a complement if necessary, showed superior results compared to other studies published. This strategy revealed in average 2.5 partners/index. Other studies have shown 1.2-2.2 partners/index, with the higher results in investigations of centralized tracing.^{77,113,114} In our study almost 80% of the tracings were performed by four experienced counsellors, mostly with notification periods of at least 12 months. Such long notification periods were rare among persons doing only one contact interview during the study period and their patients also revealed less partners during tracing. The number of partners revealed at tracing decreased with time since the intercourse had occurred. The number of infected partners decreased with time as well. Reasons why more partners were reported close to time of diagnosis could be that a contact from long ago might be somewhat more likely to be forgotten or repressed.¹¹⁵ Individuals with symptoms probably get tested soon after infected, while the incubation time for Chlamydia is approximately 7-14 days. They probably met their infected partner just before diagnosis. Chlamydia may clear spontaneously or persist.^{15,115} The precise proportion of infections cleared is unknown but this could have influenced our results. Infected partners who caught the infection from the index long ago, might have been tested and cured before tested in our study. Nevertheless, in the group of partners having had intercourse with the index within 7-12 months before the index was diagnosed with Chlamydia, 30% tested positive. This could be compared to rates in sexually active populations of 5-10%.^{2,3} Our study confirms the importance of extended notification periods.

Because Chlamydia is highly contagious the National Board of Health and Welfare points out the importance of partner notification to be carried out as fast as possible to inhibit further spread of the infection.¹² The county of Västerbotten is sparsely populated, and to enable centralized partner notification within a reasonable time contact interviews are performed by phone if necessary. Slightly fewer partners were reported if interviewed by phone compared to interview at the clinic. The difference between the two methods were not significant and the results of 2.3 partner reported at phone interview is still better than in other contact tracing studies.^{77,113,114} In this study patients could chose themselves whether they preferred an interview by phone but patients with many partners were encouraged to attend the clinic. That may be one reason why more partners were reported in that group. Patients may feel more anonymous if interviewed by phone and one

may lose dimensions of the conversation used to create trust and convey the importance of the tracing. Our phone interviews were all performed by experienced tracers. It is probably even more important to be experienced in partner notification skills if interviews are performed by phone.

Shortcomings of the partner notifications in Sweden have been pointed out.^{77,78} This was combined with increasing rates of infections. The good evaluations of “The Västerbotten Model” made the National Board of Health and Welfare change their recommendations regarding partner notification in 2007.¹² According to the Swedish Institute for Infectious Disease Control the decreasing rates of Chlamydia can probably partly be explained by improved contact tracing.⁸

Pharyngeal Chlamydia infections

Symptoms of “pain in the throat” can not be used for deciding whether patients who had recent fellatio should be tested for pharyngeal Chlamydia. Our low correlation between symptoms and infection is in correlation with other research.^{62,116} Seventy-five percent or all pharyngeal Chlamydia would have been missed with this selection criterion. “Pain in the throat” is very common in the society and many unnecessary tests would have been taken as well. Since all patients with pharyngeal Chlamydia had a urogenital infection as well, we propose that pharyngeal samples would be taken only from patients who stress having had fellatio exclusively. This is probably rare among heterosexuals. Among MSM pharyngeal or rectal infection, without contemporary urogenital infection is more frequent.^{62,116} Among MSM it is not uncommon to practice fellatio exclusively with new/temporary partners, because this is considered safer from a HIV-point of view.⁶² In the MSM population, one should probably be more liberal with pharyngeal testing. The NAAT used in our investigation (SDA) has a sensitivity of only 67-80%.^{64,66} There are NAATs with a sensitivity of approximately 100% (AC2), but at the time of our investigation it did not detect the mutant form of CT, which the SDA did.¹¹² Though, the diagnostic method used must be considered due to the risk of false negative test results.

Risk factors associated with Chlamydia

Consistent condom use reduces the Chlamydia prevalence by 90%.¹¹⁷ Unprotected intercourse is an absolute condition for catching a Chlamydia infection. The association between present Chlamydia infection and inconsistent condom use is well documented.¹¹⁷⁻¹²¹ The researchers have investigated *if* a condom was used, but not commented on whether it was used during *the whole* intercourse. The fact that there is a considerable prevalence of Chlamydia among the consistent condom users indicates that the condom has not always been used correctly. Only 5% of patients

attending our STI-reception used a condom during the whole intercourse with their last new/temporary partner. Only three out of ten stating always using a condom with new/temporary partner consistently used it during the whole intercourse. Inconsistent condom use (defined as not always using a condom with a new/temporary partner) was significantly associated to present Chlamydia infection. Additional information about whether the condom was used during the whole intercourse did not, however, add any risk of infection. Condoms protect against STIs, but in the case of Chlamydia, our study can not show any increased risk of infection if the condom was used only during part of the intercourse. No other studies investigating this association were found. Probably the persons not using condom during the whole intercourse use it at the end of the intercourse, for contraceptive purposes. It is in association with the ejaculation that the major exchange of body-fluid takes place, and the risk of infection is probably highest then.

The aim of this study was never to question whether a Chlamydia test should be performed at all on patients attending the STI-reception. The aim was to, in a quick and easy way, identify persons at increased risk of infection and to individualize care and offer them risk reducing counselling. Sweden has no systematic screening approach. The present model with primary prevention information; local opportunistic screening models and partner notification has been questioned for being expensive and less effective.⁸¹ Partner notification is a good way of identifying infected persons,¹²² but considering the high prevalence of Chlamydia infections, it is clear that the present strategy must be combined with other measures. Population based studies find the highest rates of Chlamydia among people aged <25 years and risk increases with increasing number of sex partners.^{118,123} The ECDC concludes that age <25 years and multiple partners is the only clear risk factors of infection.¹ Results from national based investigations can not uncritically be applied in every population. For example, it is important to consider the prevalence in the setting before applying screening tools used by others.¹²⁴ Opportunistic screening investigations show different prevalence depending on setting tested, but prevalence increases with decreasing age.^{119,125,126} These studies often investigate urban female populations. Chlamydia is more prevalent in urban settings.¹²⁷ Our urban STI-clinic has a high Chlamydia prevalence (in average 11%) compared to a national based screening investigation which has shown a prevalence of 1.4-3.0%.¹ An urban drop-in STI-reception seems to be a good contribution to an opportunistic screening approach. The rate of infected is high. It attracts people aged 25 years or older and men, groups that often have a lower test rate.^{8,123,127,128} Age <25 years would not be a good way of identifying people at higher risk of infection at our STI-reception. Fifty-one percent of all infected would have been missed. Since age at first birth approaches 30 years in Sweden⁹⁶ and

attitudes towards sex becomes more and more liberal,¹¹ people continues to expose themselves to risk of infection also at higher ages.

The Chlamydia prevalence increased with increasing number of new/temporary sex partners within the past 6 months. After adjusting for other significant risk factors and possible confounders, the association was not independent. Condom use decreased with increasing number of new/temporary partners. A combination of having at least one new/temporary partner within the past 6 months and inconsistent condom use identified a group of 61% of the patients with sexual risk behaviour. They accounted for 81% of all infections. The selection criteria could be different depending on recourses available. Unprotected sex is an absolute condition for catching Chlamydia. If resources were unlimited all patients reporting inconsistent condom use would be offered risk reducing counselling. Since these patients accounts for 91% of all patients, it is not a possibility in reality. The knowledge of having had a partner with recent/present Chlamydia had a high predictive value of ongoing infection. This correlation is supported by the fact that at least 60% of sexual partners to Chlamydia infected people are infected themselves.^{29,122,129}

Individuals with symptoms are more likely to appear at drop-in receptions.¹³⁰ Urogenital symptoms are strongly associated to male Chlamydia infections,^{29,131} and this was also the case in our investigation. Among women, Chlamydia infection was associated to the use of hormonal contraceptives. The association remained after adjusting for having at least one new partner within the past 6 months and inconsistent condom use. There are data indicating that the use of oral contraceptives might increase the susceptibility for Chlamydia.¹³² Among women attending an urban STI-reception, use of contraceptives seems to indicate an independently higher risk of infection. The large number of non-responders makes this statement a bit uncertain. Sick-listed or unemployed women were significantly more likely to be Chlamydia infected. These are measures of lower socioeconomic status, which is correlated to many other health risks including smoking and hazardous alcohol consumption.⁹⁶ These women might be more willing to take sexual risks as well. Low self esteem is also more common among sick-listed and unemployed⁹⁶ and might have negative impact on sexual risk taking.

Alcohol, depression and anxiety in association with sexual risk behaviour

Hazardous alcohol consumption is common among youths and young adults in Sweden.⁹⁶ Patients attending an urban STI-reception have an even higher level of consumption. Hazardous consumption was correlated to a specific lifestyle; students; single persons; women aged <25 years and men aged <30.

Persons with harmful consumption practiced more risk-sex. This behaviour may in the long term lead to STI-infection, even if we could not prove such an association in this material. It is common to have unprotected sex and sex that one regrets during the influence of alcohol.⁹¹ Even if one knows the importance of safe sex while sober, this seems easily forgotten under the influence of alcohol.⁹³ STI-prevention needs to consider other risk behaviours than sexual, since they are associated. According to the high level of hazardous alcohol consumption it is my opinion that alcohol prevention should be in focus and the level of consciousness of increased sexual risk taking under the influence of alcohol must be highlighted. Alcohol increases sexual risk taking partly by activating ones individually held beliefs of ones effect of alcohol.¹³³ Thus, if one believes one will take greater risks under the influence of alcohol there is a great possibility that will be the case. It is important to focus on weakening rather than strengthening these preconceived ideas. How shall I act to remember the condom when I am drunk? Do I need to be “pissed” to have fun? The prevention should also act were the action takes place with for example free condoms at discotheques and pubs.

McMunn *et al* found that binge drinking had negative impact on sexual risk behaviour and increased the risk of Chlamydia infection.⁹⁸ We also found such tendencies, though not independently significant. Our definition of binge drinking was chosen as it could be calculated from the AUDIT formula. It was higher than that used by McMunn *et al* and that recommended by the Swedish National Institute of Public Health.¹⁰¹

Thirty percent of young women and 14% of young men reported feeling anxious or worried within the past two weeks. Their mental health does not improve, like it does among other age categories.⁹⁶ People attending an urban STI-reception experience an even higher frequency of anxiety. Our result was calculated according to the HADS formula in contrast to the figures in *The National Health Survey* which was based on self reported worry or anxiety. Thus the true difference between the levels of anxiety among STI-patients compared to the average population is probably higher. A high prevalence of anxiety among STI-patients is in accordance with earlier research.^{108,134} A qualitative study by Arkell *et al* highlighted the fact that many patients diagnosed with Chlamydia felt stigmatized.¹³⁵ The knowledge of having exposed oneself to the risk of infection; unprotected contacts that one might regret; worry of being infected with an STI including HIV and risk of future infertility caused anxiety among the STI-clinic patients, but sex risk behaviour and Chlamydia infection was not more common among patients with signs of anxiety. According to our results, the high frequency of hazardous alcohol consumption is probably one reason for anxiety. The society has to contribute to lowering the stigmatization that still

seems to be associated with STIs. A care that does not judge but still encourages the patient to change from a risk-behaviour is a challenge for the health-care staff that meeting these patients. Decreasing the amount of hazardous alcohol consumption probably increases the mental health as well.

Studies of young, and often female populations, have shown an association between depression and sexual risk behaviour.^{94,136,137} These results could not be repeated in our study. In a retrospective study by Chen *et al* including 21 560 persons, depressive symptoms were associated to lifetime STIs among women and men 15-34 and women, but not men, aged 35+.¹³⁸ In our population there was no association between depression and sexual risk behaviour or present Chlamydia infection. Neither was any association found in a similar study of a similar setting.¹³⁹ Hutton *et al* found an association between depression and sexual risk behaviour (defined as prostitution, sex while intoxicated with drugs or alcohol, numerous sex partners, substance or alcohol abuse).¹⁴⁰ Depression was not associated to present STI or unprotected sex in that study either. We believe that prostitution and substance abuse is quite unusual in our studied population. Our conclusion is that there does not seem to be an association between depression and sexual risk behaviour among STI-clinic patients with a mean age of 28 years.

Conclusions

- “The Västerbotten model” i.e. a centralized partner notification method with experienced tracers; notification periods of at least 12 months and contact tracing by phone as an alternative, showed superior results compared to other studies published.
- Patients with pharyngeal Chlamydia can not be identified by symptoms and are most often also infected with genital/urethral Chlamydia.
- An urban drop-in STI-reception seems to be a good contribution to an opportunistic screening approach. The Chlamydia prevalence is high. It attracts people aged 25 years or older and men, groups that often have a lower test rates.⁸
- Inconsistent condom use (not always using a condom with new/temporary partner) is associated to present Chlamydia infection. Inconsistent condom use in combination with having a new/temporary partner within the past 6 months can narrow down a group with “higher risk” of Chlamydia infection, among patients attending an urban STI reception, initiating individualized care and counselling. Additional information about whether the condom was used during the whole intercourse does not add any risk of infection. To our knowledge this is the first investigation evaluating this association. In screening investigations regarding Chlamydia the important question seems to be *if*, and not *how*, a condom was used.
- In counselling and investigations of safe-sex attitudes one should be aware of the fact that 30% stating always using condom with new/temporary partner do not use it during the whole intercourse.
- Hazardous alcohol consumption is associated to risky sex behaviour. A question about binge drinking might be a useful question to ask in a short screening tool aimed at finding persons at higher risk of STI infection. Further investigations in this area are required.
- Anxiety is more common among STI-clinic patients than the average young Swede, but not associated to sexual risk behaviour or ongoing Chlamydia infection. Probably the high level of anxiety is partly associated to the high level of hazardous alcohol consumption in this group.
- STI-prevention should focus on reducing alcohol consumption among young people and highlight the changes of attitudes to high-risk sex that might be caused of alcohol intoxication.

Suggestions for the future

How should Swedish Chlamydia prevention be designed in the future? The most important question to be answered is the real impact of Chlamydia infection on the reproductive health.

National opportunistic screening programmes seem to be well accepted¹²⁶ but their sustained effect on reducing the case rate of Chlamydia and on improving the reproductive health is not sufficiently investigated.⁸⁴ The increasing case rates of Chlamydia in Sweden was an indicator of the current approach with locally designed opportunistic screening models, without any national coordination, information campaigns and partner notification, not being sufficient enough. The coverage of the screening was too low to decrease the burden of disease. In 2009 the case rate of Chlamydia decreased in almost all of Sweden, and the trend is the same for 2010.¹⁴¹ The county of Västerbotten had the lowest incidence of Chlamydia in the country in 2009,⁸ despite the highest proportions of tests taken in the country.¹⁴² Extensive primary and secondary preventive actions have been established and I believe that these are strong causative factors for the decrease in Chlamydia case rate. The availability of testing has increased (drop-in receptions and internet testing (www.klamydia.se)) and Chlamydia screening is offered all pregnant women, at contraceptive prescription and at cervical cancer screening. The partner notification is centralized, there are free-condom projects at for example the University and pubs and extensive primary prevention campaigns and condom information. Risk reducing counselling (Motivational interviewing, MI) is offered at the STI-reception, the youth clinics and at the Students' health reception.¹⁴² In 2007 The National Board of Health and Welfare changed its recommendations and now promotes centralized partner notification according to the Västerbotten model.¹² Enhanced partner notification is speculated being a cause of the decreased case rate in Sweden.⁸ In the consideration of the decreasing case rate, the Västerbotten model for partner notification in combination with extensive primary and secondary prevention actions might be good enough to control the epidemic of Chlamydia.

In the Swedish National Plan of Action against Chlamydia primary prevention is on focus. According to the high level of hazardous alcohol consumption among young people and its association to sexual risk behaviour I think it is important for STI-prevention to focus on reducing alcohol consumption and making people aware of the changes of attitudes to high-risk sex that might be caused of alcohol intoxication. An evaluation of binge drinking and its association to sexual risk behaviour and STIs, with a lower threshold for being a case, would be interesting. I believe that the

acute alcohol intoxication caused by intensive consumption on a “heavy night” is more strongly associated with sexual risk taking than the term *hazardous alcohol consumption*.

At STI-receptions, infrequent condom use in combination with new/temporary partner(s) within the past 6 months can identify persons with risk behaviour who have increased risk of infection. Thus care and counselling can be individualized and addressed towards those who need it the most. Effects of MI on changing sexual risk behaviour are now being evaluated by our group.

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Supplement 1 (Paper III and IV)

Coding number: _____

SCREENING QUESTIONNAIRE FOR MEN

Have you been taking any medication for the last few months?

Yes No

Which medicine have you been taking? _____

What was the medication treatment for? _____

What is your life like? married/living with a partner partner, not living together on my own
 something else _____

What do you do for a living? studying working unemployed on the sick list
 something else _____

Which is your highest finished education? secondary school college university
 something else _____
 commentary _____

Do you have:

1) – discharge? Yes No Don't know

2) – burning or pain when voiding? Yes No Don't know

3) – Are you often in urgent need to void? Yes No Don't know

4) - a partner with whom you have sex and who has symptoms/problems from the urinary tract or genital area? Yes No Don't know

Have you had:

5) - sex with a person who has or recently has had Chlamydia? Yes
No Don't know

6a) – intercourse (vaginally or anally) with a new or temporary partner
within the last 12 months?
 Yes No Don't know

6b) Did you use condom during the ENTIRE intercourse? Yes No
Don't know

7) - intercourse during the last 12 months (vaginally/anally)? Yes No
 Don't know

8a) –intercourse during the last 12 months with someone you know/believe
has had intercourse with someone else within the last 12 months before you
had intercourse?
 Yes No Don't know

8b) Have you always used condom during the ENTIRE intercourse? Yes
 No Don't know

9) – any sexually transmitted disease within the last 12 months? Yes
No Don't know

10) – intercourse with someone from outside Scandinavia within the last 12
months?
 Yes No Don't know

Coding number: _____

SCREENING QUESTIONNAIRE FOR WOMEN

Have you been taking any medication for the last few months?

Yes No

Which medicine have you been taking?

What was the medication treatment for?

What is your life like? married/living with a partner partner, not living together on my own

something else _____

What do you do for a living? studying working unemployed on the sick list

something else _____

Which is your highest finished education? secondary school college university

something else _____

commentary _____

Do you have:

1) – more discharge? Yes No Don't know

2) – burning or pain when voiding? Yes No Don't know

3) – Are you often in urgent need to void? Yes No Don't know

4) – bleeding/spotting between periods? Yes No Don't know

5) – bleeding after intercourse? Yes No Don't know

6) – unexplained pain in the lower part of the belly? Yes No Don't know

7) - a partner with whom you have sex and who has symptoms/problems from the urinary tract or genital area? Yes No Don't know

Have you had:

8) - sex with a person who has or recently has had Chlamydia? Yes
No Don't know

9a) – intercourse (vaginally or anally) with a new or temporary partner
within the last 12 months?

Yes No Don't know

9b) Did your partner use condom during the ENTIRE intercourse? Yes
 No Don't know

10) -intercourse during the last 12 months (vaginally/anally)? Yes No
 Don't know

11a) –intercourse during the last 12 months with someone you know/believe
has had intercourse with someone else within the last 12 months before you
had intercourse?

Yes No Don't know

11b) Have you always used condom during the ENTIRE intercourse? Yes
 No Don't know

12) – any sexually transmitted disease within the last 12 months? Yes
No Don't know

13) – intercourse with someone from outside Scandinavia within the last 12
months?

Yes No Don't know

(This part of the questionnaire was the same for both men and women.)

1) Have you had intercourse with a new or temporary partner within the last 12 months?

Yes No

2) If you have had intercourse within the last 12 months.

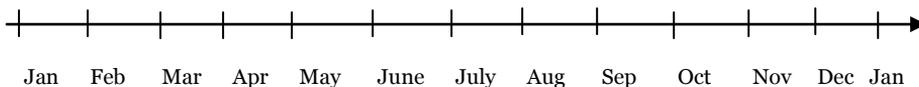
Make an **X** for each sex partner corresponding to the time axis (you don't have to write the name of the partner).

Use 1 line for each partner and mark an **X for each contact with the same partner.**

If a partner has been regular make an X in the beginning and in the end of the relationship and draw a line between. If the relationship is still on let the line continue.

2009

2010



- 1 _____
- 2 _____
- 3 _____
- 4 _____
- 5 _____
- 6 _____
- 7 _____
- 8 _____
- 9 _____
- 10 _____
- 11 _____
- 12 _____
- 13 _____
- 14 _____
- 15 _____
- 16 _____
- 17 _____
- 18 _____
- 19 _____
- 20 _____
- Etc.

3) Do you regularly use a condom at the first vaginal intercourse with a new/temporary partner?

- Always (100% of intercourses)
- Most of the time (approx. 75% of intercourses)
- Sometimes (approx. 50% of intercourses)
- Not very often (approx. 25% of intercourses)
- Never (0% of intercourses)
- I have never had intercourse with a new/temporary partner

4) If you practise vaginal intercourse do you use a condom when having intercourse with a new/temporary partner until you are both tested regarding sexually transmitted diseases?

- Always (100% of intercourses)
- Most of the time (approx. 75% of intercourses)
- Sometimes (approx. 50% of intercourses)
- Not very often (approx. 25% of intercourses)
- Never (0% of intercourses)

5) Do you regularly use a condom at the first anal intercourse with a new/temporary partner?

- Always (100% of intercourses)
- Most of the time (approx. 75% of intercourses)
- Sometimes (approx. 50% of intercourses)
- Not very often (approx. 25% of intercourses)
- Never (0% of intercourses)
- I have never had anal intercourse with a new/temporary partner

6) If you practise anal intercourse do you use a condom when having intercourse with a new/temporary partner until you are both tested regarding sexually transmitted diseases?

- Always (100% of intercourses)
- Most of the time (approx. 75% of intercourses)
- Sometimes (approx. 50% of intercourses)
- Not very often (approx. 25% of intercourses)
- Never (0% of intercourses)

7) If you use a condom, do you use the condom during the entire intercourse?

a) Vaginal intercourse

- A Always (100% of intercourse)
- B Most of the time (approx. 75%)
- C Sometimes (approx. 50%)
- D Not very often (approx. 25%)
- E Never (0%)

b) Anal intercourse

- A Always (100% of intercourse)
- B Most of the time (approx. 75%)
- C Sometimes (approx. 50%)
- D Not very often (approx. 25%)
- E Never (0%)

Supplement 2

Hospital Anxiety and Depression Scale (HADS)

For each statement, choose one alternative from the four given.

1. I feel tense or 'wound up'

Most of the time/ A lot of the time/ From time to time
/ Occasionally/ Not at all

2. I still enjoy the things I used to enjoy

Definitely as much/ Not quite so much/ Only a little/ Hardly at all

3. I get a sort of frightened feeling as if something awful is about to happen

Very definitely and quite badly/ Yes, but not too badly/ A little, but it doesn't worry me/ Not at all

4. I can laugh and see the funny side of things

As much as I always could/ Not quite so much now/ Definitely not so much now/ Not at all

5. Worrying thoughts go through my mind

A great deal of the time/ A lot of the time/ From time to time, but not too often/ Only occasionally

6. I feel cheerful

Not at all/ Not often/ Sometimes/ Most of the time

7. I can sit at ease and feel relaxed

Definitely/ Usually/ Not Often/ Not at all

8. I feel as if I am slowed down

Nearly all the time/ Very often/ Sometimes/ Not at all

9. I get a sort of frightened feeling like 'butterflies' in the stomach

Not at all/ Occasionally/ Quite Often/ Very Often

10. I have lost interest in my appearance

Definitely/ I don't take as much care as I should/ I may not take quite as much care/ I take just as much care as ever

11. I feel restless as I have to be on the move

Very much indeed/ Quite a lot/ Not very much/ Not at all

12. I look forward with enjoyment to things

As much as I ever did/ Rather less than I used to/ Definitely less than I used to/ Hardly at all

13. I get sudden feelings of panic

Very often indeed/ Quite often/ Not very often/ Not at all

14. I can enjoy a good book or radio or TV program

Often/ Sometimes/ Not often/ Very seldom

Supplement 3 (Paper IV)

Alcohol Use Disorder Identification Test (AUDIT)

Chose one of the given answer alternatives for each question.

1. How often do you have a drink containing alcohol?

Never/ Monthly or less/ 2 to 4 times a month/ 2 to 3 times a week/ 4 or more times a week

2. How many “glasses of alcohol” do you have on a typical day when you are drinking?

1 or 2/ 3 or 4/ 5 or 6/ 7 to 9/ 10 or more

3. How often do you have six or more “glasses of alcohol” on one occasion?

Never/ Less than monthly/ Monthly/ Weekly/ Daily or almost daily

4. How often during the last year have you found that you were not able to stop drinking once you had started?

Never/ Less than monthly/ Monthly/ Weekly/ Daily or almost daily

5. How often during the last year have you failed to do what was normally expected of you because of drinking?

Never/ Less than monthly/ Monthly/ Weekly/ Daily or almost daily

6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?

Never/ Less than monthly/ Monthly/ Weekly/ Daily or almost daily

7. How often during the last year have you had a feeling of guilt or remorse after drinking?

Never/ Less than monthly/ Monthly/ Weekly/ Daily or almost daily

8. How often during the last year have you been unable to remember what happened the night before because of your drinking?

Never/ Less than monthly/ Monthly/ Weekly/ Daily or almost daily

9. Have you or someone else been injured because of your drinking?

No/ Yes, but not in the last year/ Yes, during the last year

10. Has a relative, friend, doctor, or other health care worker been concerned about your drinking or suggested you cut down?

No/ Yes, but not in the last year/ Yes, during the last year

11. Do you want to cut down your alcohol consumption?

No/ Yes, and I can manage that myself/ Yes, and I need support