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**RISK BEHAVIOUR AND
PREVENTION OF BLOOD
BORNE INFECTIONS AMONG
INJECTING DRUG USERS**

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Institutet**

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To my family

ABSTRACT

In Stockholm County the two major injecting drugs are amphetamine and heroin, injected by about 9 000 persons almost every day. There is no access to needle and syringe program and about 1000 patients are in substitution programs, mostly Methadone and Buprenorphine programs.

This work has focused on markers of blood borne infections, as antibodies for HIV, HBV and HCV, on risk behaviour, gender, age, mortality, perception of risks with HCV infection and preventive measures. 407 unique participants were interviewed about risk behaviour and blood tested when visiting treatment settings and a custody in Stockholm County from the year of 2001-2006. Participants were >15 years of age and had injected drugs.

The main way of transmission for acquiring blood borne infections in this work was sharing injecting equipment (syringes, needles, filter, cooker and drug mixture) but the participants have reported various degrees of risk behaviour. Some HIV negative participants shared needles with known HIV infected and other differentiated between HIV, HBV and HCV. HIV diagnosed participants had a higher mortality rate than non HIV infected participants in a 1.5-5 years follow up after study participation.

The prevalence of HCV positive status and of active HCV infection was high and many acquired their HCV infection short after starting to inject drugs. Gender/sex played a role in transmission of HCV. Young women were at higher risk of acquiring HCV infection than men. But women recovered spontaneously more often from HCV infection and had better response to HBV vaccination compared to men. Sero markers for HBV vaccination were in general low. Men and women had similar patterns of HCV genotypes. Sharing injecting equipment was common regardless of reporting HCV positive or HCV unknown status. Further, assessment of health consequences with HCV infection was not enough for changing risky injecting behaviour as sharing injecting equipment.

In this thesis, preventive measures of blood borne infections in IDUs are suggested to focus; on young injectors, especially females. On persons with injecting risk behaviour infected as well as non infected with HIV and HCV. The measures are also suggested to be individualized and differentiated for HIV, HBV and HCV. To change risk behaviour for not acquiring blood borne infections; risk perception is suggested to be analysed and communicated by professionals in a dialogue, structured in the method of Motivational Interviewing. Focus should be on IDUs' risk assessment, with emphasis on how to identify, quantify and characterize risks.

LIST OF PUBLICATIONS

- I. Lidman C, **Norden L**, Kåberg M, Käll K, Franck J, Aleman S, Birk M Hepatitis C infection among injecting drug users in Stockholm Sweden: Prevalence and gender.
Scandinavian Journal of Infectious Diseases, 2009; 41:679-684
- II. **Nordén L** and Lidman C Needle sharing with known and diagnosed Human Immunodeficiency Virus infected injecting drug users.
Scandinavian Journal of Infectious Diseases, 2003; 35:127-128
- III. **Nordén L** and Lidman C Differentiated risk behaviour for HIV and hepatitis among injecting drug users.
Scandinavian Journal of Infectious Diseases, 2005; 37:493-496
- IV. **Norden L**, Saxon L, Kåberg M, Käll K, Franck J, Lidman C Knowledge of status and assessment of personal health consequences with hepatitis C are not enough to change risk behaviour among injecting drug users in Stockholm County, Sweden.
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LIST OF ABBREVIATIONS

Anti-HBc	Antibody Hepatitis B core antigen
Anti-HBs	Antibody Hepatitis B surface antigen
aRR	Adjusted Relative Risk
ASI	Addiction Severity Index
BBI	Blood Borne Infections
DRID	Drug Related Infectious Diseases
DSM	Diagnostic and Statistical Manual of Mental Disorders
CAN	Swedish Council for Information on Alcohol and Other Drugs
CDA	Swedish Communicable Diseases Act
CDC	Communicable Disease Control
CPR	Central Population Register
CI	Confidence Interval
CMIA	Chemo luminescent Micro particle Immune Assay
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
EU	European Union
e.g.	exempli gratia "for example"
Et al.	et alii "and others"
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HCV-RNA	Hepatitis C Virus Ribonucleic Acid
HIV	Human Immunodeficiency Virus
HIV Ag/Ab	Human Immunodeficiency Virus, Antigens/Antibodies
GT	Genotypes
IDUs	Injecting Drug Users
NSP	Needle and Syringe Program
OR	Odds Ratio
PCR	Polymerase Chain Reaction
RR	Relative Risk
SmE	County Medical Officer
SMI	Swedish Institute for Infectious Diseases
SNIPH	Swedish National Institute of Public Health
STI	Sexual Transmitted Infections
UNAIDS	United Nations Program on HIV/AIDS
UNODC	United Nations Office on Drugs and Crimes
WHO	World Health Organization
Q19	Questionnaire with 19 Items
Q23	Questionnaire with 23 Items

1 INTRODUCTION

1.1 BLOOD BORNE INFECTIONS

“HCV infection is a side effect you have to deal with when injecting drugs in Stockholm County” (Participant in Paper IV)

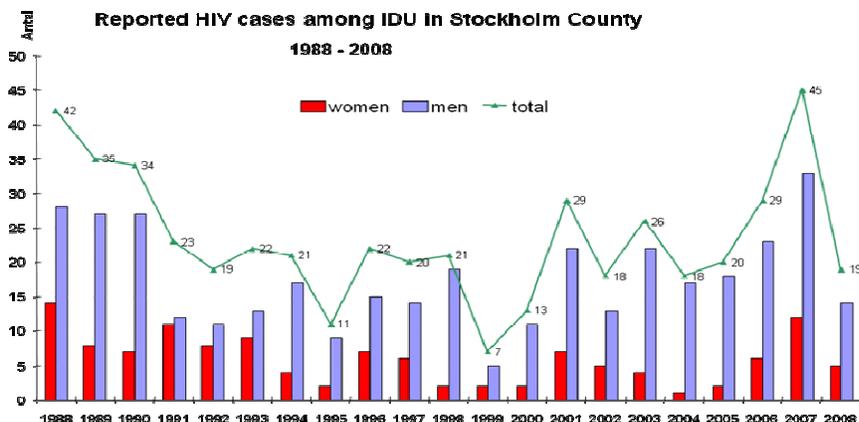
Injecting drugs in a contaminated way can lead to infectious diseases and health consequences. Because of their risk behaviour and life situation injecting drug users (IDUs) are vulnerable to diseases as HIV (Human Immunodeficiency Virus), HBV (Hepatitis B Virus) and HCV (Hepatitis C Virus) infection. Those infections can lead to higher morbidity and mortality compared to the same age groups in the general population (Drug Related Infectious Diseases EMCDDA 2009).

HIV, HBV and HCV are blood borne infections and sharing injecting equipment can lead to virus transmission. HIV and HBV can also be sexually transmitted. Further HCV can be sexually transmissible but it is far less than HIV and HBV (Clarke and Kulasegaram 2006).

1.1.1 Human Immunodeficiency Virus Infection

The number of HIV diagnosed cases among IDUs in Stockholm County was low and stable until the year of 2001, and an increased number of cases were also reported in the year of 2007. The figure below shows reported cases from the last ten years (Zedenius 2008).

Figure 1



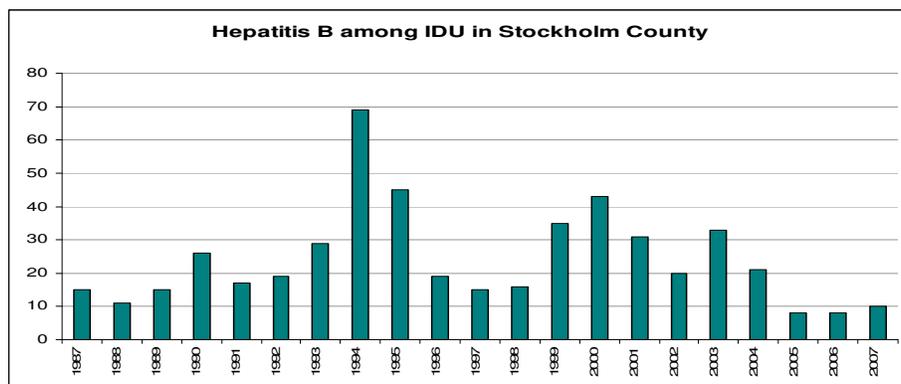
In Stockholm HIV testing among IDUs started in the year of 1982 and the first reported HIV case was a prisoner. There have been about 820 HIV reported cases among IDUs until June 30, 2008 in Stockholm County (Zedenius 2008). In Sweden the prevalence of HIV among IDUs is <5 % compared to other European countries, for example, Portugal, Italy and Spain

which have >10 % HIV cases in the IDU population (Table INF 1 2007 EMCDDA). The HIV epidemic among IDUs in Europe is still growing (Wiessing et al. 2008).

1.1.2 Hepatitis B Virus Infection

Hepatitis B infection is spontaneously healed in about 95 % of virus transmitted cases, if acquired in adulthood. An effective vaccine exists, it is free of charge for the risk groups and it has been so for about twenty years in Stockholm County. About 40-50 acute HBV infection cases were reported yearly in Stockholm County, but since the year of 2005 about ten cases have been reported yearly, Figure 2 (Janzon 2008).

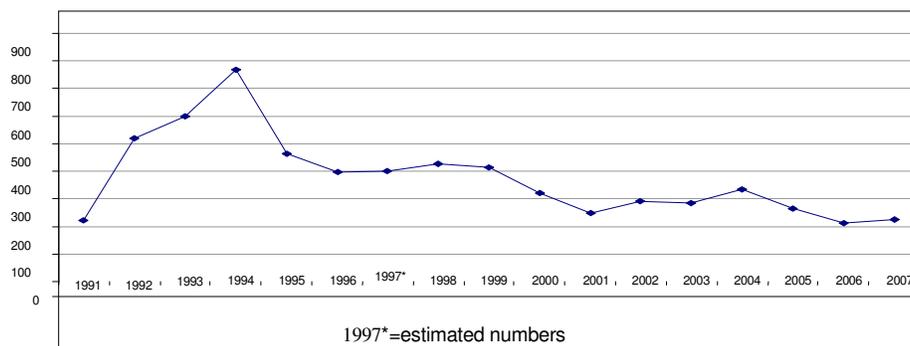
Figure 2 Acute HBV among IDUs in Stockholm County, 1987-2007



1.1.3 Hepatitis C Virus Infection

In the year of 2004 HCV infection was alarmingly high among IDUs in Stockholm County; more than 300 new cases were reported. Thereafter the reported number decreased to about 200 every year, Figure 3 (Janzon 2008). But the almost unchanged number of reported cases indicates an ongoing HCV epidemic among younger people in Sweden (Duberg et al. 2008).

Figure 3 Reported cases of hepatitis C among IDUs in Stockholm County 1991-2007



The HCV antibody test was introduced in the year of 1990 in Stockholm County but HCV Ribonucleic acid (RNA) analysis, marker for active infection, are still not regularly done. Interferon therapy has been available for more than ten years for IDUs, who had been abstinent from drugs for many years. When comparing prevalence with other European countries Sweden is a high prevalence country together with Estonia and Latvia, >80 % of the IDU population have been exposed to HCV (Table INF 2007 EMCDDA).

1.1.4 Sexually Transmitted Infections

There is evidence supporting an association between drug use and having sexually transmitted infections (STI) other than HIV and HBV infection (Shapatava et al. 2006). Besides HIV infection, gonorrhoea and genital chlamydia infections are seen among IDUs in many European countries (DRID testing guidelines 2009 EMCDDA). But STI among IDUs in Stockholm County is not a known problem.

1.2 THE SWEDISH COMMUNICABLE DISEASES ACT

The Swedish Communicable Diseases Act (CDA) is a law that describes how the medical service, the society as a whole and the individual shall behave to reduce the risk of proliferation of communicable diseases. HIV, HBV and HCV infections are such diseases. The aim of the CDA is to protect the population against communicable diseases and to guarantee the infected individuals' protection and support from the society. Premises Communicable disease control (CDC) must be placed primarily on voluntary preventive measures; information on modes of transmission, information on how to protect oneself and medical treatment of the infected person.

The law gives obligations and rights to the infected patient. Obligations when dealing with diseases dangerous to public health are: individuals have to undergo examination, submit information on contacts, follow practical instructions, inform others at risk and protect others. Infected patients are obliged to follow the directions given by their doctor but the rights give them free examination and medical care, psychosocial support needed to prevent transmission and treatment (only voluntary). Measures that are taken against the individuals will be legal only if no other measure is possible. The legislation point out that there has to be a balance between the interests of the patient and the Community (Gröön 2008).

1.3 DRUG USE

It is important to differentiate initial drug use with more regular and compulsive use of drugs when preventing blood borne infections because HCV transmission usually occurs soon after the individuals have started injecting drugs (Maher et al. 2006).

Substance dependence is defined as a chronic relapsing disease, substance use as taking drugs for non medical purpose and substance abuse as continued drug use. Use and misuse of drugs are definitions from more of a social point of view. The definition of drug dependence is based on the criteria of American Psychiatric Association (1994), and the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM IV). Substance dependence has seven criteria, manifested as three or more symptoms under the same twelfth month's period:

1. Tolerance
2. Withdrawal
3. Difficulty controlling use
4. Negative consequences
5. Putting off or neglecting activities
6. Spending significant time or emotional energy
7. Desire to cut down

Drug dependence is characterized by strong, drug seeking behaviour in which the user persistently craves and seeks out drugs, despite the knowledge of harmful consequences. Drug dependence is considered as a pathological state, a disorder that progresses from impulsivity to compulsivity, characterized by craving and preoccupation with obtaining the drug; using more of the drug to experience the effects; and experiencing tolerance and withdrawal symptoms (DSM IV).

Impulsive control disorders are characterized by an increasing sense of tension before the commission of an impulsive act. In contrast compulsive disorders are characterized by anxiety and stress before a compulsive repetitive behaviour. This status can lead to less time and motivation for normal life activities (Kenny 2007, Koob and LeMoal 1997).

In Stockholm County the two major injection drugs are amphetamine and heroin, injected by about 9 000 persons almost every day (CAN 1998). There is no access to Needle and Syringe Programs (NSPs) and about 1000 IDUs are in substitution programs, mostly Methadone and Buprenorphine programs.

1.4 RISK FACTORS AND RISK BEHAVIOUR

“An acceptable risk is associated with the best of the available alternative we can think of” (The British Medical Association Guide 1987)

Sharing needles and unprotected sexual intercourse are the most important risk factors for contracting HIV and HBV infection among IDUs (Battagay et al. 2004, Breen et al. (2005), Strathdee et al. 2003). From Stockholm Käll and Nilsson (1995) reported that markers of high risk behaviour for HIV, both sexually and with needles, were male injecting amphetamine. Dynamics of

relationships with sexual partner may also be an important determinant risk for blood borne infections, especially for HIV and HBV (Miller et al. 2002).

The primary route of transmission for HCV is sharing needles (and syringes) and drug injecting equipment (filter, rinse water, cooker, spoon and drug mixture) (Alter and Moyer 1998, Bruandet et al. 2006, Lucidarme et al. 2004, Maher et al. 2007, Smyth et al. 2005, Thorpe et al. 2002). Other risk factors for acquiring HCV infection can be having multiple sexual partners (unprotected) and/ or sexually transmitted diseases (Yen et al. 2003), being tattooed, using a non sterile technique (Gyarmathy et al. 2002, Mathei et al. 2005) and not being aware of one's HCV status (Kwiatkowski et al. 2002).

Injecting initiates appear to be at increased risk of HCV infection (Maher et al. 2006, Maher et al. 2007, Sutton et al. 2006, Vidal-Trécan et al. 2000). It is further known that duration of injecting drugs is associated with risk of acquiring HCV infection. A study showed that the average time to sero conversion for HCV infection was 4.4 years (Maher et al. 2006). Altogether, rapid transmission of HCV usually occurs soon after the individuals have started injecting drugs.

Risk taking and risk behaviour in the IDU population are complex issues, with a wide variety of components, exempli gratia (e.g.) drug effects per se and drug culture on site, definitions and psycho social factors (Harvey et al. 1998, Rhodes et al. 1999, Stimson et al. 1998). Risk behaviour is often functional and rational within IDUs' context and they do not have factual choices to reduce risks associated with their drug use (Neaigus et al. 2008, Miller 2005).

IDUs that are unaware of their HCV status have been reported to engage in more risk behaviour than those who were aware of their status (Kwiatkowski et al. 2002, Palmater et al. 2008). Other studies report that contributing risk factors may be that IDUs do not understand the meaning and implication of their HCV status and consequences of HCV infection (Rhodes et al. 2004). Strauss (et al. 2007) found in their study that IDUs had many gaps in their knowledge about HCV infection. Similarly, another study reported confusion about HCV diagnosis, and what it means to be HCV infected (Rhodes et al. 2004). Another critical factor for HCV transmission in the environment can be homelessness (March et al. 2007, Rhodes and Treloar 2008, Wright et al. 2005).

1.5 RISK PERCEPTION

“Risk is seen as a concept that human beings have invented to help them understand and cope with the dangers and uncertainties of life” (Slovic and Weber 2002)

Risk perception in IDUs was shown to be impacted by three main factors:

1. “The potential threat or negative consequences associated with the risks”
2. “The extent to which the risks are known or unknown”
3. “The extent to which the risks are immediate or delayed”
(Marsch et al. 2007)

The affective reaction to the hazard seems to play a part in risk perception. The “risk as feelings hypothesis” highlights the role of affect experienced at the moment of decision making and that intuitive feelings play an important role in choosing and decision making (Loewenstein et al. 2001). People evaluate risk cognitively and react to it emotionally (Slovic and Weber 2002). When cognitive assessment and emotions differ, feelings play the most important role; acts are following the emotions (Loewenstein et al. 2001).

There is no safe, but there are varying degrees of safety and varying degrees of risks and we are usually trying to minimize unwanted consequences. Further, the risks are reduced to negligible levels to make it safe enough and the risk may be reduced to an acceptable level. We can perceive risks higher or less significant than they really are which may lead us to poor decisions (The British Medical Association Guide 1987).

Risk can be defined by different meanings but the most common are:

- Risk as hazard. Which risks should we rank?
- Risk as probability. What is the probability of getting HIV from an infected needle?
- Risk as consequence. What is the consequence of living with HIV infection?
- Risk as potential adversity or threat. How great is the threat of injecting drugs?
(BMAG 1987, Slovic and Weber 2002).

Drug use provides immediate reinforcement by producing strong positive short term consequences but may lead to negative long term consequences. Possible HCV related consequences of risk behaviour, such as sharing needles and other injecting equipment, are delayed for perhaps twenty years. In the process of risk perception a person must understand aspects of danger and the personal consequences that can result (Slovic and Weber 2002).

Table I Factors influencing some aspects of risk perception

Aspect	Meaning	References
Knowing status	It is not enough to know one's status to avoid risk situations. Knowing one's status motivates you to avoid risk situations.	Crisp and Barber 1995 Kwiatkowsky et al. 2002
Unknown risk	If you do not know about the risk or consequences, it is difficult to avoid them.	Mullet 1993
Voluntary risk	If you do it voluntarily you usually underestimate the degree of risk.	Mullet 1993
Familiar risk	If you get used to the risk it is easier being involved in risk situations.	BMAG 1987
Situation/context	Having implemented tactics and practices for protection.	Mateu-Gelabert et al. 2007
Delayed risk	If the consequences come later on, it is easier to neglect the risk.	Marsch et al. 2007
Controllable risk	If you think you can control the risk you are more involved in risks.	Sjöberg 2004
Potential threat	It can be from negligible to fatal.	Marsch et al. 2007
Lack of alternative	Injecting drugs and no access to NSPs.	Miller 2005
Not easily reduced	It is not easy to change behaviour.	Sjöberg 2004
Emotional acting	Feelings play a role in choosing and decision making.	Slovic and Weber 2002
Trust	Trust can be an expression of intimacy and higher risk taking.	Rhodes and Treloar 2008
Exposure/ frequency/duration	"Every day", "once a year" and "for a long time" are of importance.	MBAG 1987

1.6 PREVENTION

"Risks to health are of two kinds; to the length of life and to the quality of life" (The British Medical Association Guide 1987)

It is necessary for the society to give IDUs improved access to prevention communication, information; testing and diagnosis of chronic infections which need specialist care (Metzger D and Navaline H 2003, Wright et al. 2005). Professionals have to be well educated in communication skills and how to present information (Hampel 2006). Some factors have been suggested by Peters (et al. 1997) to be important for people's perceptions of trust and credibility. These factors are; "perceptions of knowledge, expertise, openness, honesty, concern and care".

Health measures can be divided into primary, secondary and tertiary prevention.

1.6.1 Primary Prevention

It is activities including: available screening and testing of blood, risk reduction counselling and services; and implementation and maintenance of infection control practices.

1.6.2 Secondary Prevention

The activities are aimed at early disease detection, thereby increasing opportunities for interventions to prevent disease progression and symptoms emergence. To reduce the spread and consequences of infectious diseases among drug users, the European Union (EU) member states employ a combination of those measures: drug treatment, including substitution treatment, health information and counselling, distribution of sterile injection materials, and education towards safer sex and safer use (Prevention of infectious diseases 2009 EMCDDA). Risk analyse, peer education and changing peer norms are other preventive measures (Garfein et al. 2007, Golub et al. 2007, Slovic and Weber 2002, Sylvestre and Zweben 2007).

1.6.3 Tertiary Prevention

The purpose is to reduce the negative impact of an already established disease by restoring function and reducing disease related complications, to give antiviral therapy for HIV and HCV infection (Birkhead et al. 2007). It can also be specialised prevention, which means that special risk behaviour may be in focus for risk reduction.

1.7 HARM REDUCTION

“It is almost impossible to avoid HCV infection when injecting drugs in Stockholm County” (Participant in Paper IV)

Needle and syringe programs and opiate substitution treatment are available in all EU Member States, although with considerable diversity in both delivery settings and targeted population (Prevention of infectious diseases 2009 EMCDDA). WHO (2009) have developed a clear position on a comprehensive approach of harm reduction for IDUs. The comprehensive package includes: “Targeted information and education, needle and syringe programs, opiate substitution therapy and other drug dependence treatment. It also includes voluntary testing and counselling, HIV care, (including anti retroviral therapy), sexually transmitted infections control and treatment, condom programming, primary care, (including wound care and prevention), vaccination and treatment of other blood borne infections”.

1.8 DEATHS RELATED INDIRECTLY TO DRUG USE

“To minimize the risk of early death or illness and maximizing the happiness of life, is one of the mankind’s most fundamental imperatives” (The British Medical Association Guide 1987)

AIDS deaths attributed to injecting drug use is important cause of death. But overdose mortality is considerably higher than AIDS related mortality among drug users (Infectious diseases and deaths 2008 EMCDDA). Consequences of other infectious diseases, violence, accidents and other cases are difficult to assess. The highest risk of death was found among persons over 35 years old, male and using opiates in Stockholm County (Adamsson Wahren 1997). In the year of 2007 drug related deaths were about 350 persons in the whole of Sweden (SNIPH 2007).

1.9 CLINICAL EXPERIENCE

In Sweden, research in the field of treatment of drug use has a history of about fifty years and a lot of important scientific works have been done by prominent researchers. Also injecting behaviour has been focus for valuable research. This has been a good starting point for the dual perspective (behavioural and epidemiological) of this dissertation.

Being a member of a professional team at the Addiction Centre Stockholm at Huddinge University Hospital since the year of nineteen seventies grounded my assessment of the importance of having a scientific approach, when working with patients using illegal drugs. Today I am a member of an addiction team, and my clinical work is in a unit for infectious diseases specialised in patents using drugs. This is making me aware of the harm problems of injecting drugs. Being a member of “Modelling network in drug related infectious diseases”, European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) in Lisbon is giving me a European perspective on drug related infectious diseases. Also being a member of the “Stockholm County Council for HIV/STI prevention” is giving me knowledge about transmissible diseases in the county. The “Network of HIV, HBV and HCV infection” is another source of knowledge about injecting drug users.

My research in IDUs started with investigations why they injected drugs in a contaminated way. Further I wondered what the risk behaviour looked like. Other questions were: How did the injecting habits look like? How to prevent the transmission of blood borne infections among injecting drug users?

2 AIMS

I. To investigate the prevalence of previous exposure and active HCV infection, and to study HCV genotypes, needle sharing in relation to gender, to inform the planning of future intervention and prevention measures, and to compare sero markers for HIV and HBV infection to HCV data.

II. To study risk behaviour among newly diagnosed HIV infected IDUs compared to HIV negative IDUs, for prevention measures.

III. To explore and find factors for future intervention purposes, associated with risk behaviour for blood borne infections, e.g. needle sharing among IDUs, with an emphasis on socio financial factors, physical and mental health.

IV. To investigate if risk behaviour changes with awareness of one's HCV status and/or if risk behaviour differs with assessed personal health consequences with HCV infection.

2.1 RESEARCH QUESTIONS

I. What is the prevalence of HBV and HCV infection among IDUs and is there a gender difference?

II. What kind of risk behaviour is associated with HIV among IDUs?
What kinds of markers for HIV prevention are detectable among the HIV negative IDUs?

III. What kind of factors other than needle sharing; and especially socio financial, physical and mental health factors, associate with risk behaviour for blood borne infections?

IV. Does risk behaviour differs with awareness of one's HCV status and assessed personal health consequences of HCV infection among injecting drug users?

3 MATERIALS AND METHODS

3.1 OVERVIEW OF PARTICIPANTS

Table II Participants in different papers

	Participants	Unique Participants
Paper I	310	310
Paper II	44 [*]	43
Paper III	42 ^{**}	41
Paper IV	213 ^{***}	13
Total	609	407

* one individual is also included in paper I

** one individual is also included in paper I

*** 200 individuals are also included in paper I

3.2 PAPER I

3.2.1 Design

This was a cross sectional study, describing and exploring the prevalence of HBV and HCV infection, in relation to gender among HIV negative IDUs.

3.2.2 Participants

The participants in this multi centre study were selected from six drug users care units in Stockholm County, from March 22, 2004 until June 6, 2006. Three hundred and eighty-five persons were asked for participation when visiting one of the units. Forty-seven declined and 28 accepted but had incomplete data, 310 retained for final analysis. The inclusion criteria were age 18 years or older, and history of injecting drugs. Exclusion criteria were known HIV infection, and earlier participation in this study. Informed consent was obtained from all participants.

3.2.3 Measurements

Behavioural measures

The participants were interviewed about demographic data and risk factors for acquiring HCV infection by one to two professionals at the different study units. The interview guide, Questionnaire 19 (Q19), comprised nineteen items regarding age, sex, drug of choice and injecting debut, duration of injecting, HCV status and assessment of personal health consequences with HCV infection and injecting equipment sharing during the previous six months. The questionnaire, Q 19, was produced by Lillebil Nordén (LN).

In this paper we defined “needles” as needles and syringes; “other injecting equipment” as filter, rinse water, cooker, spoon and drug mixture and “injecting equipment” as needle, syringe, filter, rinse water, cooker, spoon and drug mixture.

To assess the reliability of the interview guide (Q 19) was performed a test-retest, with eight participants. The participants were interviewed twice within 24-30 hours with Q19 by the same interviewer (LN and a co worker). These resulted in a total of 152 answers out of which seven were changed.

Biological measures

Serum/plasma was analysed for HIV, HBV, and HCV antibodies. The following analyses were applied: HIV: HIV Ag/Ab combo, HBV: Anti-HBc, HBs-Ag, Anti-HBs; HCV: Anti HCV, HCV-RNA and among participants with measurable HCV antibodies, was performed a qualitative HCV-RNA test. PCR based genotyping (subtypes 1a, 1b, 2a, 2b, 3a, 3b, 4, 5a and 6a) was also performed.

3.2.4 Statistical Analysis

JMP® software version 6.03 (SAS Institute, Cary, North Carolina, USA) was used for statistical analysis. Student’s t-test was used for parametric variables, and Chi-Square or Fischer’s exact test were used for categorical dependant variables. In the adjusted models of gender differences duration of injecting drug use was chosen as a marker for duration of exposure to blood borne infections. A p -value <0.05 was considered statistically significant.

3.2.5 Ethical Approval

This study was approved by the Regional Ethics Review Board Stockholm.

3.2.6 Grants

The study was supported financially by the Swedish National Drug Policy Coordinator.

3.3 PAPER II

3.3.1 Design

This was a case control study comparing risk behaviour among newly HIV diagnosed IDUs and HIV negative IDUs.

3.3.2 Participants

Twenty-four IDUs diagnosed with HIV infection in Stockholm County, between January 1, 2001 and December 31, 2001, were included in this study.

Two persons were lost to follow up and one person died, 21 retained for analysis. The control group comprised 30 IDUs who had injected drugs the last year, who had tested HIV negative within the past 31 days and admitted as inpatients from January 8, 2002 until March 28, 2002 to the Department of Infectious Diseases, Huddinge University Hospital. Seven patients (four were confused and three needed terminal care) were excluded from further analysis resulting in 23 participants. Patients were excluded if they had participated in this study previously.

3.3.3 Measurements

Behavioural measures

Selected data on patients and risk behaviour for acquiring HIV were collected from routine notification for HIV, performed by counsellors. Patients in the control group were interviewed by LN about injecting behaviour, as sharing needles and syringes, for acquiring HIV infection.

3.3.4 Statistic Analysis

JMP software (SAS Institute, Cary, North Carolina, USA) was used for statistical analysis. Student's t-test was used for parametric variables, Wilcoxon's rank sum test for non parametric variables and Fisher's exact test for categorical data. A *p*-value <0.05 was considered as significant.

3.3.5 Ethical Approval

This study was approved by the Local Ethics Committee at Huddinge University Hospital.

3.4 PAPER III

3.4.1 Design

The study was cross sectional, describing and investigating if social, physical and financial factors were risk factors for acquiring blood borne infections as HIV, HBV and HCV.

3.4.2 Participants

Fifty-one IDUs, admitted as inpatients to the Division of Infectious Diseases, Karolinska University Hospital, Huddinge from September 1, 2002 until May 31, 2003 fulfilled the inclusion criteria and 42 were included in the study. Nine patients were excluded because they were unable to follow the study protocol. The inclusion criteria were: injecting drugs at least once during the past year, negative HIV test and more than 48 hours as an inpatient. Patients were excluded if they had participated in this study previously. Informed consent was obtained from all participants.

3.4.3 Measurements

Behavioural measures

The participants were interviewed using the validated Addiction Severity Index (ASI) (Andréasson et al. 1996, McLellan et al. 1992) and a questionnaire with 23 items, Q 23, produced by LN. The participants were mostly interviewed by LN and the interviews were conducted at least 48 hours after admission to the unit. The questionnaire focused on risk behaviour for acquiring blood borne infections during the previous 6 months. Emphasis was on sharing needles (needles were defined as needles and syringes), drug mixture and filter, sharing with HIV/hepatitis infected acquaintances and strangers.

Biological measures

Participants were tested for HIV antibodies as well as for HBV and HCV antibodies.

3.4.4 Statistical Analysis

JMP® software (SAS® Institute, Cary, North Carolina, USA) was used for statistical analysis. Student's t-test was used for parametric variables, Wilcoxon's rank sum test for non parametric variables and Fischer's exact test for categorical data. In addition, for the screening of ASI variables we used logistic regression analysis for categorical dependent variables. A p -value <0.05 was considered as significant.

3.4.5 Ethical Approval

This study was approved by the Local Ethics Committee at Karolinska University Hospital, Huddinge.

3.4.6 Grants

The Swedish National Institute of Public Health supported this study financially.

3.5 PAPER IV

3.5.1 Design

A cross sectional study, describing and exploring risk behaviour and risk assessment associated to HCV infection among IDUs in Stockholm County.

3.5.2 Participants

From March 22, 2004 until November 28, 2006, 406 persons visiting any of the seven study units were asked to participate in the study, 47 individuals declined and 349 accepted participation, but 28 had incomplete data and 331 were retained. From these 331 participants, 213 fulfilled the criteria; injecting drugs in the previous six months and age between 15 and 40 years. The inclusion criteria for

six of the seven study units were age 18 years and from one unit age 15 years. Exclusion criteria were HIV diagnosis and previous participation in this study. Informed consent was obtained from all participants.

3.5.3 Measurements

Behavioural measures

The participants were interviewed about demographic data and risk factors for acquiring HCV infection by one to two professionals at the different study units. The interview guide, Questionnaire 19 (Q19), comprised nineteen items regarding age, sex, drug of choice and injecting debut, duration of injecting, HCV status and assessment of personal health consequences with HCV infection and injecting equipment sharing during the previous six months. The questionnaire, Q 19, was produced by LN. In this paper we defined “needles” as needles and syringes; “other injecting equipment” as filter, rinse water, cooker, spoon and drug mixture and “injecting equipment” as needles, syringes, filter, rinse water, cooker, spoon and drug mixture.

Biological measures

The participants were blood tested for HCV antibodies.

3.5.4 Statistical Analysis

JMP® software version 6.03 (SAS Institute, Cary, North Carolina, USA) was used for statistical analysis. Chi-square or Fischer’s exact test was used for categorical variables. Variables were: self reported and verified HCV infection, assessment of personal health consequences of HCV infection, sharing injecting equipment and age. Risk factors for verified HCV infection and sharing needles were analysed, using uni and multivariate logistic regression models, expressed as Risk Ratio (RR) and adjusted Risk Ratio (aRR), with 95 % confidence intervals (95 % CI). A *p*-value <0.05 was considered as statistically significant.

3.5.5 Ethical Approval

This study was approved by the Regional Ethics Review Board Stockholm.

3.5.6 Grants

The study was supported financially by the Swedish National Drug Policy Coordinator.

3.6 OTHER MEASURES

All participants (407) (in paper I, II, III, IV) were followed up, from medical records and from Central Population Register (CPR), for HIV diagnosis and mortality December 7, 2007.

4 RESULTS AND DISCUSSION

4.1 Hepatitis C Infection among Injecting Drug Users in Stockholm Sweden: Prevalence and Gender (Paper I)

Three hundred and ten participants were retained for final analysis, of whom 268 (86.5 %) had injected drugs during the last year.

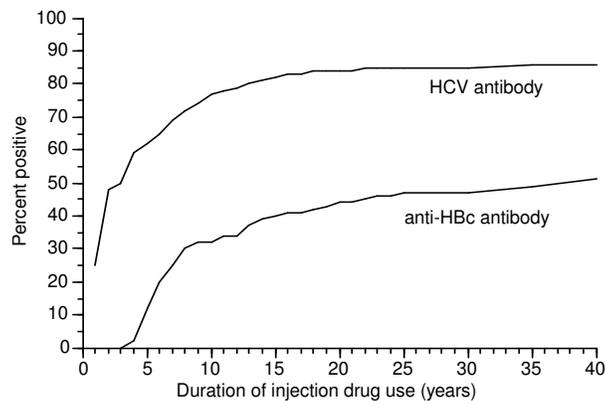
Table III Demographic data

	All n = 310 n (%)	Women n (%)	Men n (%)	<i>p</i> Women vs. Men
Age ¹	35.6 (18-67)	32.9 (20-52)	36.6 (18-67)	0.006
Age at first injection of drugs ¹	21.5 (10-52)	21.5 (12-40)	21.5 (10-52)	0.99
Duration of injecting drug use ¹	12.1 (0-41)	10.4	13.4	0.02
Sharing needles	184 (59.4)	47 (61.0)	37 (58.8)	0.72
Sharing other injecting equipment	177 (57.0)	50 (64.9)	127 (54.5)	0.11
Drug at last injection				
Amphetamine	151 (48.7)	44 (57.1)	107 (45.9)	
Heroin	120 (38.7)	25 (32.5)	95 (40.7)	0.23
Mixed	39 (12.6)	8 (10.4)	31 (13.3)	

¹mean years (range)

Age and duration of injecting drug use correlated ($R^2 = 0.43$, $p < 0.001$) and both variables were associated with HCV ($p < 0.001$) and HBV status ($p < 0.001$) (Figure 5).

Figure 5 Cumulative percent of HCV and anti-HBc antibodies and the association with duration of injecting drug use



Twenty-five percent of participants had detectable HCV antibodies at the end of the first year of injecting drugs. This number increased during the following years, and the cumulative percent at the end of the second year was 47.6 %; the end of the third year, 50.0 %; and the end of the fourth year, 59.1 % (Figure 5). Anti-HBc antibodies were found in 162 (52.1 %) participants of whom 8 (4.9 %) were HBs Ag positive (Table IV).

Table IV Serum markers of HCV, HBV and HIV infection

	All n = 310 n (%)	Women 77 (24.8) n (%)	Men 233 (75.2) n (%)	<i>p</i> Women vs. Men
HCV+ ¹	268 (86.5)	68(88.3)	200 (85.4)	0.55
HCV-RNA+	207 (77.2)	45 (58.4)	162 (69.5)	0.07
Anti-HBc+ ²	162(52.1)	34 (45.5)	127 (54.5)	0.17
HBs Ag+	8 (2.3)	1 (1.0)	7 (3.0)	0.20
Anti-HBc- /anti-HBs+ (vaccinated)	28 (9.0)	13 (16.9)	15 (6.4)	0.02
HIV+	3 (1)	0	3 (1.3)	0.99

¹ of 268 HCV+, 207 (77.2%) were HCV-RNA+

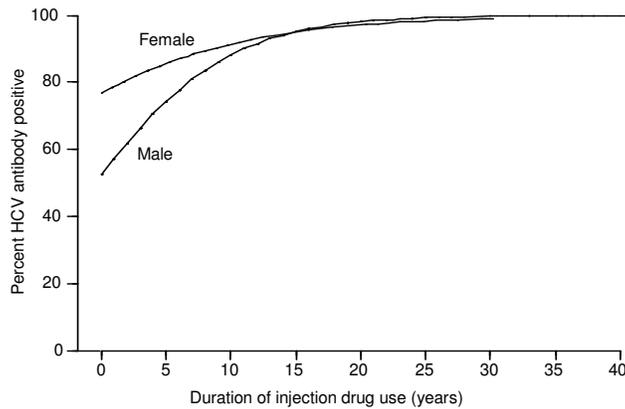
² of 162 Anti-HBc+, 8 (4.9%) were HBs Ag+

Genotypes 1 and 3 dominated, with approximately one third each. Men and women had similar patterns of genotypes. Mixed infection with two different genotypes was detected in eleven patients.

4.1.1 Gender and Hepatitis

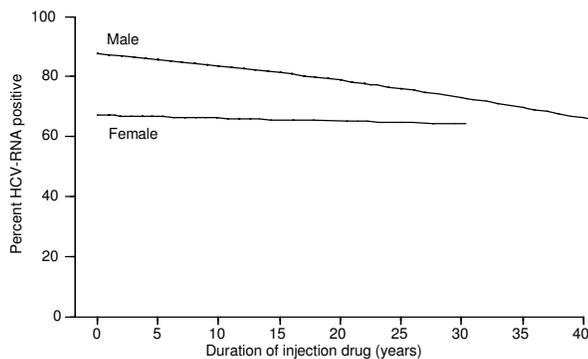
Adjusted for duration of injecting drugs, men and women showed a difference in HCV sero prevalence rate (Figure 6). However, this difference was not significant. The slopes in Figure 6 indicate a difference in HCV sero prevalence between men and women with a history of injecting drugs for fewer than 12 years. Thereafter, the slopes level off, and the gender differences diminish. In sub analysis of these 185 patients with a history of injecting drugs for <12 years, women were significantly more often HCV antibody positive than men ($p=0.03$, RR 2.97, 95 % CI: 1.11-7.93), supporting the visual impression given by Figure 6.

Figure 6 Percent of positive HCV antibodies in women and men, and duration of injecting drugs



Among the 268 (86.5 %) participants with positive HCV serology, women recovered spontaneously from their HCV infections, to the point of undetectable HCV-RNA, more often than men (38.8 % vs. 19.0 %, $p=0.006$, RR 2.49, 95% CI: 1.28-4.53). Figure 7 shows the percent of HCV infected men and women with detectable HCV-RNA in their blood. However, among men there was a tendency ($p=0.07$) to lower prevalence of detectable HCV-RNA with increasing duration of injecting drugs.

Figure 7 Percent of positive HCV-RNA in women and men, and duration of injecting drugs



Women had sero markers of HBV vaccination more often than men ($p=0.02$, RR 2.42, 95 % CI: 1.13-5.20). The HCV-RNA status (positive or negative) had no significant impact on the HBV vaccination status.

In this study of 310 participants, women differed from men in some important aspects of HCV and HBV infection. Women acquired HCV early in their injecting career, and had a higher spontaneously recovery from HCV. Furthermore, more women than men had markers indicating vaccination against HBV.

Compared to men, during the first 12 years of injecting drugs, significantly more HCV antibodies were detected in women who indicate higher transmission rates

among women (Figure 7). This is in line with previous reports on young female IDUs (des Jarlais et al. 2003, Maher et al. 2006, Maher et al. 2007, Miller et al. 2002, Sutton et al. 2006). Assuming that men and women are exposed to HCV to a similar extent, the data might imply a predisposing biological basis. The hypothesis that gender may matter in HCV transmission is also supported by differences in mother to child transmission rates of 4 % in female and 2 % in male newborns (EPHCV 2005).

Even if men and women have different exposures to transmissible HCV, a biological basis for this difference may still exist. The proportion of men with active HCV infection (detectable HCV-RNA) in this study was significantly higher than the proportion of women. This suggests that, with comparable behaviour (e.g. sharing needles), the risk of transmission from men to women is higher than the risk in the opposite direction.

Behavioural differences between men and women may also be responsible for differences in exposure to HCV. A study of 15-23 year old IDUs by Montgomery (et al. 2002) showed that young women were more likely to engage in needle borrowing, auxiliary equipment sharing, and being injected by someone else. In summary, women are more frequently at risk of acquiring HCV infection, particularly young women. Prevention of hepatitis among IDUs is a multiple task issue, which needs special attention to subgroups, especially from the perspective of gender.

4.2 Needle Sharing with Known and Diagnosed Human Immunodeficiency Virus Infected Injecting Drug Users (Paper II)

Twenty-four IDUs with HIV infection were diagnosed in Stockholm during 2001 and 21 were included in the study. The comparison group consisted of 23 HIV negative IDUs. Some demographic data are presented in Table V.

Table V Selected social, drug use and risk behavioural data

	HIV positive n= 21 (%)	HIV negative n=23 (%)	<i>p</i> value
Median age (range)	41 (27-51)	42 (19-63)	NS*
Female gender	5 (23.8)	4 (17.4)	NS
Homeless	17 (81)	15 (65)	NS
Contact with social welfare	17 (81)	15 (65)	NS
Main narcotic drug			
Amphetamine	14 (67)	15 (65)	
Heroin	7 (33)	6 (26)	NS
Amphetamine/heroin	0	2 (9)	
Alcohol abuse	6 (29)	3 (13)	NS
Needle sharing ¹	20 (95)	15 (65)	0.04
Needle sharing with HIV infected ²	12 (57)	0	0.001
Unprotected sexual intercourse	9 ³ (43)	12 (52)	NS
Anti HBc	21 (100)	19 (83)	
Anti HCV	21 (100)	19 (83)	

¹Sharing needles or drug mixture with IDU ²Sharing needles or drug mixtures with HIV infected

³Data on 6 of 21 patients are missing, still NS if 15/21 instead of 9/21 * NS = Not Significant

HIV status was not associated with age, sex, homelessness, contact with social welfare, type of narcotic drug, alcohol abuse or unprotected sex, but with needle sharing and needle sharing with known HIV positive individual.

The major differences between these two groups, HIV positive and HIV negative, were that the HIV positive participants, before HIV diagnosis, shared needles more frequently and more than 50 % of them shared needles with persons they knew were HIV infected. The present data also show that some IDUs who know about their HIV infection deliberately expose uninfected IDUs to HIV. Although the two groups in the current study were selected differently, and therefore must be compared with caution, they shared several important features.

Three groups with risk behaviour were found in this study:

- HIV negative who shared needles
- HIV negative who shared needles with IDUs they knew were HIV positive
- HIV positive who shared needles

Diagnosed HIV positive individuals played an important role in the spread of HIV among IDUs. They had various degrees of risk behaviour for acquiring blood-borne infectious diseases such as HIV. Multiple reasons contribute to the risk behaviour of HIV positive and HIV negative individuals, making the task of reducing HIV transmission complex. Thus, supported by Strathdee (et al. 1998), this study emphasizes that initial efforts and subsequent preventive measures should be concentrated on finding HIV positive and HIV negative individuals with risk behaviour.

4.3 Differentiated Risk Behaviour for HIV and Hepatitis among Injecting Drug Users (Paper III)

Forty-two patients were included in the study. The median duration of injecting drugs was 19.0 (range 0-43) years. The study participants (n=42) were divided into two main groups, those who shared needles (n=26) and those who did not (n=16).

Table VI Selected data from Addiction Severity Index (ASI) interviews

	All participants n=42 (%)	Sharing needles		p-value
		No n=16 (%)	Yes n=26 (%)	
Men	28 (67)	13 (81)	15 (58)	0.74
Age*	42.5 (18-61)	44.5 (18-57)	40.5 (23-61)	0.09
Homeless	15 (36)	5 (31)	10 (38)	0.74
Pension/social security	31 (74)	11 (69)	20 (77)	0.72
Heroin	9 (21)	3 (19)	6 (23)	1.0
Amphetamine	10 (24)	5 (31)	5 (19)	0.46
Poly drug use	23 (55)	8 (50)	15 (58)	0.75
First injection/age ¹	20 (11-44)	20 (16-44)	20.5 (11-40)	0.84
Overdose(s)	27 (64)	10 (62)	17 (65)	0.87
Criminal convictions (lifetime)	35 (83)	14 (86)	21 (81)	0.69
HBV antibody reactive	31 (74)	13 (81)	18 (69)	0.48
HCV antibody reactive	37 (88)	13 (81)	24 (92)	0.35
HIV test past year	31 (75)	12 (75)	19 (73)	1.0
Any time experienced:				
Lack of control of violent behaviour	16 (38) ²	4 (25)	10 (38)	0.51
Hallucinations	7 (17) ²	4 (25)	3 (12)	0.39
Forced to engage in sexual acts	8 (20) ²	3 (21)	5 (19)	1.0
Attempted suicide	15 (36) ²	6 (38)	9 (35)	1.0

¹ median (range) ² two answers are missing

Addiction Severity Index (ASI) data on social and financial situation, drug use, and criminality, physical and mental health were similar in the two groups (Table VI). There was a significant association between participants who shared needles (n=26) and those who shared drug mixture/filter (n=25). Nineteen (73 %) of 26 participants who shared needles also shared drug mixture/filter. Odds ratio for sharing needles when also sharing drug mixture/filter was 4.5 (95 % CI: 1.23-18.26).

Among the 26 participants who shared needles it was found that 18 (69 %) shared needles with a person with a known hepatitis whereas 7 (27 %) participants shared needles with a person with known HIV infection, $p=0.002$. Data were similar for the 25 participants who reported sharing drug mixture/filter (20/25, 80 % vs. 8/25, 32 %, $p=0.0014$) and the 30 who had had sexual intercourse during the previous 6 months (18/30, 60 % vs. 4/30, 13 %, $p=0.0004$). Thus, the risk behaviours (sharing needles/drug mixture/filter or sexual intercourse) were associated with the type of blood borne diseases to which they were exposed.

Most needle sharing and sexual risk was undertaken with sexual partners and acquaintances, while mixture/filter sharing was undertaken with partners, acquaintances and strangers, supporting the idea that IDUs show a differentiated risk behaviour depending on to whom they were exposed. Twelve (29 %) of 42 participants reported no sexual intercourse within the past six months, and of the remainder, four have unprotected sexual intercourse with a known HIV infected person. Condoms were used by 18 of 30 (60 %) participants.

This study shows that participants had multiple social problems and a complicated life situation needing a great deal of help to change their life styles. We were unable to find factors from the ASI data associated with needle sharing and thus indirectly with transmission of blood borne infections.

Knowing about others' and one's own HIV, HBV and HCV status seemed to be an important preventing factor when sharing needles or drug mixture/filter. This idea is supported by Des Jarlais (et al. 2004) and Amundsen (et al. 2003) who reported that testing and counselling are the most important prevention methods for HIV transmission. Kwiatkowski (et al. 2002) found that injecting drug users who were not aware of their hepatitis C status engaged in more risk behaviours than those who were aware of their positive status.

Another explanation for differentiated risk behaviour can be that IDUs had knowledge about the transmission of HIV but were not aware that HBV and HCV is more transmissible than HIV through blood exposure (CDC 2001) and that sharing drug mixture/filter can be an important cause of HBV and HCV transmission (Thorpe et al. 2002).

Furthermore, IDUs may not be fully aware of the possibility of preventing HBV infection by vaccination. Finally, IDUs may not be aware of running the risk of re-infection with HCV or/and infection with a new genotype; the latter having implications for future treatment options (Wejstål et al. 2003).

To reduce transmission of HIV, HBV and HCV infection among IDUs, testing and knowledge about one's own and others' status regarding blood borne infections are fundamental. Our study participants showed differentiated risk behaviours for HIV, HBV and HCV regarding those they were exposed to.

4.4 Knowledge of Status and Assessment of Personal Health Consequences of Hepatitis C are not Enough to Change Risk Behaviour among Injecting Drug Users in Stockholm County, Sweden (Paper IV)

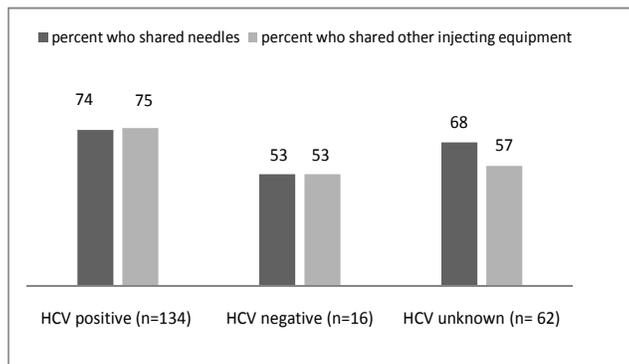
The responses from 213 participants aged 15 to 40 years who had injected drugs the previous six months were analysed.

Table VII Demographic data

n=213	n (%)
Men	149 (70)
Mean age	29.5 (95 % CI: 28.6-30.3)
Mean age at first injection	20.4 (95 % CI:19.7-21.1)
Shared needles	151 (71)
Shared other injecting equipment	145 (68)
Last injection: Amphetamine	89 (47)
Last injection: Heroin	87 (41)
Last injection: Poly drugs	24 (12)
Verified HCV infected	168 (79)
In substitution program	20 (11)
More than ten sexual partners in lifetime	160 (75)
Tattooed	122 (66)

Sharing other injecting equipment seems to be a more important risk factor for HCV infection than sharing needles in the adjusted model (for complete data see Table I in manuscript IV). Heroin use was significant for HCV infection. Participants who shared needles were verified as HCV positive in higher rate than participants who did not share needles. Sharing other injecting equipment was significantly more common than sharing needles among participants with verified HCV positive status. Verified HCV infection increased with age but was most common among participants aged 31-35.

Figure 8 Percent sharing needles and other injecting equipment in relation to self-reported HCV status (Self reported HCV status one answer is missing)



Participants associating very severe personal health consequences with HCV infection and those who did not know of any personal health consequences with HCV infection shared needles at almost the same rate.

Sensitivity of self report compared against the gold standard of detection of HCV is the proportion of anti HCV positive participants interviewed who correctly reported they were HCV positive (131 out of 168) thus 78 %, and for participants reporting they were HCV negative it would be the proportion correctly reporting they were negative (13 out of 45) thus 29 %.

In fact the ability to detect positivity and the ability to detect negativity are really two separate tests, both with a sensitivity value. In this context, the specificity of the two tests was the false positive rates for self reports of participants saying they were positive when in fact they were negative (2 %, 3 out of 134) and for those who say they were negative who truly were negative the false negative rate was 19 % (3 out of 16). Sixty-two of 212 (29 %) of the participants reported they did not know about their HCV status but 33 (53 %) were verified HCV positive (Table VIII).

Table VIII Self reported and verified HCV status, age and years of injecting drugs (One answer is missing in self reported HCV status)

	Self reported HCV status		
	Positive n=134 (95 % CI)	Negative n=16 (95 % CI)	Unknown n=62 (95 % CI)
Age (mean)	31 (30.1-32)	27.5 (24.4-30.6)	27 (25.3-28.7)
Years of injecting (mean)	11.2 (10.2-12.2)	5.1(2.7-7.4)	6.4 (4.7-8.0)
Verified HCV	131	3	33

Both participants 36-40 years old and younger participants 15-20 years old had lack of knowledge about personal health consequences with HCV infection. But the younger participants also were aware of potentially very severe consequences with HCV infection compared to those aged 36-40.

Participants who shared needles also shared other equipment (82 %, n=124) at a significantly ($p \leq 0.001$) higher rate than participants who did not share needles (66 %, n=44). Participants who shared needles also had a tendency ($p=0.1$) to be more HCV positive (82 %, n=124) than participants who did not (71 %, n=44) share.

Table IX Self reported HCV status and assessed health consequences with HCV infection associated with sharing injecting equipment

	Shared needles RR (CI 95 %)	Shared other injecting equipment RR (CI 95 %)
Self reported status ^a		
HCV negative	0.45 (0.16-1.31)	0.44 (0.15-1.26)
HCV positive	1	1
HCV unknown	0.8 (0.41-1.55)	0.47 (0.25-0.89)
Assessed:		
very severe consequences	1	1
severe consequences	0.38 (0.14-1.05)	1.17 (0.45-3.01)
marginal consequences	1.07 (0.37-3.13)	1.62 (0.63-4.15)
negligible consequences	1.10 (0.25-4.88)	8.52 (1.01-72.04)*
do not know consequences	0.63 (0.25-1.60)	1.39 (0.60-3.22)

^aone answer is missing in self reported status, *significant p -value < 0.05

This study has shown that sharing needles and other injecting equipment was common regardless of participants' reported HCV positive or HCV unknown status (Figure 8, Table IX). This finding is supported by Hagan (et al. 2006) suggesting that it is not enough to know one's HCV status in order to change health threatening behaviours. After adjustment for potential confounding variables, (for complete data see Table 1 in manuscript IV), sharing of other injecting equipment was a more important risk factor for acquiring HCV infection than sharing needles, this is supported in a study by Thorpe (et al. 2002).

Participants shared needles and other injecting equipment regardless whether they reported they did not know about consequences or assessed very severe personal health consequences with HCV infection. This suggests that IDUs consider HCV infection as the kind of risk you have to accept when injecting drugs.

The study shows that needle sharing was common regardless of self reported HCV status or assessment of personal health consequences with HCV infection. The findings also suggest that changing IDU's risk behaviour is not merely a health

information issue, an idea supported by Crisp and Barber (1995) who reported that greater awareness did not result in safer injection practice. Moreover, the effect of HCV testing on injecting risk behaviour is small if more comprehensive counselling is not given during the testing process (Craine et al. 2004).

There were influences of the three main study sites on age, drug use and sharing needles, the participants from one unit were younger, used amphetamine and shared needles in higher rate than participants from the other sites.

The findings show that threat of personal health consequences is not sufficient for changing behaviour among participants who reported very severe personal health consequences with HCV infection (Table IX).

Of course access to sterile injecting equipment plays a crucial role in avoiding and stopping further virus transmission. It seems that access to sterile injecting equipment is not enough to reduce HCV transmission; it is also about changing risk perception, risk behaviour and injecting habits to “safer” injecting practice.

Slovic and Weber (2002) suggest to “Identify risk assessment”. This means asking about injecting habits, when, how and with whom? To “Quantify risk assessment”. How safe is safe enough? Is it safe enough to cook the equipment before sharing if sterile injecting equipment is not available? To “Characterize risk assessment”. What feelings are experienced when making decisions?

In a study by Marsch (et al. 2007) risk perception in IDUs was shown to be impacted by three main factors. The first factor was, “The potential threat or negative consequences associated with the risks”. Findings in this paper show that threat of personal health consequences is not enough for changing behaviour because among participants who reported very severe personal health consequences with HCV infection also shared needles. One can question can be, to what extent the participants actually understood the threat/serious meaning of HCV infection for personal health.

The second factor was “The extent to which the risks are known or unknown”. Participants sharing needles and other injecting equipment showed the highest rate of awareness of their positive HCV infection status, so the extent to which the risks were known was high, e.g. low risk for acquiring and high risk for transmission to others. On the other hand, they did not know if they had recovered spontaneously (undetectable HCV-RNA) because this is not regularly tested in Stockholm. Perhaps IDUs would behave more safely to protect themselves with knowledge of their HCV- RNA status due to risk of acquiring re and super infections.

The third factor was “The extent to which the risks are immediate or delayed”. Drug use provides immediate reinforcement by producing strong positive short term consequences but may lead to negative long term consequences. Possible

HCV related consequences of risk behaviour, such as sharing needles and other injecting equipment, are delayed for perhaps twenty years.

It is suggested, these factors to be analysed and communicated by professionals in a dialogue, grounded in Motivational Interviewing, with IDUs about risk assessment, with emphasis on how to identify, quantify and characterize risks and how to cope with decision making and risk perception to avoid transmission of HCV infection.

4.5 Follow Up (Paper I, II, III and IV)

A total of 407 unique study participants from paper I, II, III and IV, were followed up on December 07, 2007 for mortality and HIV diagnosis. Thirty seven participants (9 %) were dead and 17 (5 %) participants had been HIV diagnosed.

In paper II, 21 participants were HIV infected “at study start point”, 8 (38 %) participants were dead when they were followed up and in the control group (23 HIV negative participants “at study start point”) 4 (17 %) participants have died.

Mortality rate was higher than HIV diagnosis among participants when followed-up 1.5-5 years after study participation. Mortality rate was about 50 % higher among “at study start point” already HIV diagnosed participants compared to “at start point” HIV negative participants in paper II.

5 DISCUSSION OF METHODS

In this work, studies used cross sectional and case control design done for a couple of years ago. Selected were patients in contact with addiction and infectious care units, and with custody. This may limit the external validity, the generalisation to the IDU population. But the studies include different units with participants of different age, sex and drug of choice.

We interviewed about sexual behaviour but we did not get useful information because the items were not good enough and we were concentrating on injecting behaviour. It would have been useful for preventive measures to get more information about IDUs sexual habits and behaviour for acquiring blood borne infections.

6 SUMMARY

In this work, 407 unique participants who had injected drugs reported various degrees of risk behaviour for acquiring blood borne infections and the main way of transmission was sharing injecting equipment. This work has focused on markers of blood borne infections, as antibodies for HIV, HBV and HCV, on risk behaviour, gender, age, mortality, perception of risks with HCV infection and preventive measures.

The prevalence of HCV positive status and of active HCV infection was high and many IDUs have acquired HCV infection short after start to inject drugs. They started injecting drugs at mean age of 21.5 years and one third of the participants were females. Gender/sex played a role in transmission of HCV and young women were at higher risk of acquiring HCV infection than men. But women also healed better from HCV and had better response to HBV vaccination, compared to men. Sero markers for HBV vaccination were in general low. Women and men had a similar HCV genotypes distribution. Prevention of hepatitis among IDUs needs special attention to subgroups, especially from the perspective of gender and age.

Many factors contributed to risk behaviour of HIV positive and HIV negative IDUs. The main differences in this work were that HIV positive participants shared needles frequently, before HIV diagnosis, and they shared needles with known HIV infected IDU. HIV negative IDUs also shared needles but they differentiated between HIV and HCV infection. HIV diagnosed participants also had a higher mortality rate than non infected participants when followed up 1.5-5 years after study participation. Initial efforts and subsequent preventive measures should be concentrated on finding HIV positive and HIV negative IDUs with risk behaviour.

In this work, some participants reported unprotected sex, some reported they not have been sexually active the past six months and lot of the participants had more than ten sexual partners in lifetime. Homelessness was not a significant factor for sharing needles and thus indirectly transmission of blood borne infections. But it is shown that many participants had multiple social problems and a complicated life situation, probably needing help to change life style.

To reduce transmission of HIV, HBV and HCV infection among IDUs, testing and knowledge about one's own and others' status regarding blood borne infections seems to be keystones. Study participants showed differentiated risk behaviours for transmission of HIV, HBV and HCV regarding to which they were exposed. This suggests that testing, counselling and vaccination should be individualized and focused on the person's risk behaviour, as well as being adapted separately for HIV, HBV and HCV.

Sharing needles was common regardless of self reported HCV status or of assessment of personal health consequences with HCV infection. Knowledge about HCV status and awareness of personal health consequences with HCV infection seemed not to be enough to change injecting risk behaviour. There is no safe, but there are various degrees of safety and we can minimize unwanted consequences. To change risk behaviour for acquiring blood borne infections risk perception are suggested to be analysed and communicated by professionals in a dialogue that is structured and grounded in the method of Motivational Interviewing. Focus should be on IDUs risk assessment, with emphasis on how to identify, quantify and characterize risks.

This work recommends that the primary, secondary and tertiary preventive measures for blood borne infections in IDUs focus on:

- Injecting initiates, especially on young females
- Individualised measures
- Differentiated measures for HIV and HCV infection
- HIV infected and non infected individuals with risky injecting behaviour
- HCV infected and non infected individuals with risky injecting behaviour
- Completing sets of HBV vaccination programs
- Changing risk perception and risky injecting behaviour

7 GENERAL CONCLUSIONS

"True fear is a gift. It is a survival signal that sounds only in the presence of danger" (de Becker 1997)

This work has focused on markers of blood borne infections, as antibodies for HIV, HBV and HCV, on risk behaviour as sharing injecting equipment, gender, age, mortality, perception of risks with HCV infection and preventive measures among 407 unique participants who were >15 years of age and had injected drugs. Participants were interviewed about risk behaviour and blood tested when visiting treatment settings and custody in Stockholm County from the year of 2001-2006.

Sharing injecting equipment was the main way of transmission for blood borne infections among IDUs in this work. Many acquired HCV infection short after starting to inject drugs. They started injecting drugs at mean age of 21.5 years. One third was females and gender/sex played a role in transmission of HCV. In paper II three groups with risk behaviour were found; HIV negative IDUs who shared needles, HIV negative IDUs who shared needles with people that they knew were HIV positive, and HIV positive IDUs who shared needles. HIV diagnosed participants had a higher mortality rate than non infected when followed up 1.5-5 years after study participation.

In paper I, women were more frequently at risk of acquiring HCV infection, particularly young women. They also healed better from HCV infection and had better response to HBV vaccination, compared to men. Sero markers for HBV vaccination were in general low. Women and men had a similar HCV genotypes distribution. In paper III, participants showed differentiated injecting behaviour for HIV, HBV and HCV regarding to whom they were exposed to.

The suggestion is that primary and secondary prevention measures such as testing, counselling, communication and vaccination should be individualised and focused on the individual's risk behaviour, as well as being adapted separately for HIV, HCV and HBV to reduce transmission. But in paper IV, knowing one's HCV status and assessment of personal health consequences of HCV infection seem not enough for changing risk behaviour for acquiring blood borne infections. To stop further transmission tertiary prevention measures are important, which mean taking and giving care to the already transmitted persons.

Having unprotected sex and multiple sexual partners are some other factors for virus transmission for HIV and HBV (Battegay et al. 2004). In this work some participants answered that they had unprotected sex, some that they had not been sexually active the past six months and lot of the participants have more than ten sexual partners in lifetime. So we have to take sexual factors into account for risk factors. Evans et al. (2003 and Frajzyngier et al. (2007) found that overlapping sexual and injecting partnerships were the key factors in explaining increased injection risk, especially in females.

Homelessness is a critical factor in the risk environment (March et al. 2007, Rhodes and Treloar 2008). In the present work homelessness was not a significant factor for sharing needles and thus indirectly transmission of blood borne infections. But this work showed that many participants had multiple social problems and a complicated life situation, probably needing help to change their life style.

WHO (2009) has developed a clear position on a comprehensive approach of harm reduction for IDUs. In Stockholm County we can offer most in this comprehensive approach for IDUs but we are still missing a needle and syringe program and targeted education, e.g. to reduce the high prevalence of HCV infection in Stockholm County.

It is the individual's responsibility not to be infected and not to transfer the infection to others, and it is the society's responsibility to give possibilities to avoid virus transmission. CDA is a Swedish law which obliged infected patients to protect others and it gives rights to medical care and psychosocial support needed to prevent transmission.

A multi disciplinary perspective and co working among different specialities in the field (Addiction Centre, Division of Infectious Diseases, Social Services, Prison and Probation Service, and County Medical Officer) are important factors for stopping further transmission of blood borne infections among IDUs. Also the voluntary organisations play an important role in the fight of reducing blood borne infections.

Dependence makes the IDUs occupied with obtaining the drugs and this may decrease motivation for normal life activities (Koob and Kreek 2007, March et al. 2006). Usually the drug and/or the dependency are of primary importance for IDUs and protections for blood borne infections are of secondary importance. Miller (2005) reported that health consequences alone were not the most important priority in IDUs' life.

Risk, cost and benefits are linked to each other and when changing one factor the others will be affected. Sooner or later it costs too much to reduce risks, but most events also offer benefits (BMAG 1987). Injecting drugs in a non sterile way can be a risk, the cost can be unwanted health consequences as HIV, HBV and HCV infection, and the benefits can be drug effects (reward or free from abstinence) and social group inclusion.

One of several measures to decrease blood borne infections is to start a process for changing risky behaviour e.g. injecting practice, change to "safe enough" injecting practice or ultimately stop injecting drugs. Slovic and Weber (2002) suggest to "Identify risk assessment". This means asking IDUs about injecting habits, when, how and with whom? To "Quantify risk assessment". How safe is safe enough? Is it safe enough to cook the equipment before sharing if sterile injection equipment is not available? To "Characterize risk assessment". What feelings are experienced when making decisions?

Why do people change? Miller and Rollnick (2002) found that it is about “readiness, willingness and ability”, and what is happening at present and values for the future. A half structured dialogue is suggested between the patient and the professional about risk assessment and risk behaviour, structured and grounded in the method of Motivational Interviewing (MI). Prochaska and DiClemente (1986) have developed a key theoretical construct of stages and processes of changing. Usually individuals go through the stages forward and backward before termination. The stages of change show peoples development and the five stages are: “pre contemplation, contemplation, preparation, action and maintenance”.

In this dialogue the goal is; to start a process for changing behaviour, to make independent estimation in a risky situation and to practice “safe enough” behaviour in risk situations when injecting drugs. This communication, after risk analysing, can be as follow; “How important is it for you not to acquire HIV?” (On a scale 1-10) “Why did you choose 4 and not 1?” “What do you need for choosing 6?” “How important is it for you that you not transfer the virus to other people?” (On a scale 1-10) “Is there anything you can do to avoid the virus or to transmit it?” Finally the dialogue has to be summarized.

Altogether, the results of the present thesis show that the main way of transmission of blood borne infections was sharing injecting equipment. It also shows; high prevalence of HCV infection and of active HCV infection among IDUs in Stockholm County. Many of the participants acquired HCV infection soon after they started injecting drugs. Young women were at higher risk of acquiring HCV infection but they recovered spontaneously more often from HCV infection than men. Women also had better response to HBV vaccination but markers for HBV vaccination were uncommon among participants.

Sharing injecting equipment was common and knowing one’s HCV status and assessment of health consequences was not enough for changing injecting risk behaviour. Some IDUs shared needles with known HIV infected and other have different injecting behaviour for HIV, HBV and HCV. To change risk behaviour, risk perception are suggested to be communicated by professionals in a dialogue that is structured and grounded in the method of Motivational Interviewing. The preventive measures need engagement and responsibility from the society and; focus on individual’s risk behaviour and risk perception for minimizing unwanted health consequences of blood borne infections.

8 RISKBETEENDE OCH PREVENTION AV HIV, HEPATIT B OCH C BLAND PERSONER MED INJEKTIONSMISSBRUK

I Stockholms län har 407 olika personer som injicerat droger intervjuats om sina injektionsvanor och blodtestats för hiv, hepatit B (HBV) och hepatit C (HCV). I samband med besök på de åtta olika studieenheter tillfrågades besökarna om deltagande i studien. De var från 15 år och äldre och hade injicerat droger. Studierna pågick mellan åren 2001 och 2006.

Riskbeteendet för att få blodburna infektioner bestod av att dela sprutor, kanyler, blandningskopp, filter, kokare och övrig injektionsutrustning. En stor andel av deltagarna hade varit i kontakt med HCV och många av dem var smittsamma i sin HCV infektion. Många blev smittade av HCV inom två år efter injektionsdebut. Det visade sig att kön hade betydelse vid överföring av HCV och att unga kvinnor smittades i ett tidigare skede än männen men att de unga kvinnornas HCV infektion oftare spontanläkte. Det visade sig även att det inte var tillräckligt att känna till sin HCV status och att uppfatta risker för hälsan med HCV infektion för att ändra sitt beteende när man injicerade. Få av deltagarna hade markörer i blodet för hepatit B vaccination.

En del av deltagarna hade delat spruta med personer som de visste var hivinfekterade. Andra deltagare hade olika beteenden för hiv och hepatit, de delade spruta med hepatitinfekterade men inte med hivinfekterade personer. När deltagarna följdes upp 1.5-5 år efter studiedeltagande visade det sig att deltagare med hivdiagnos var döda i större utsträckning än de som inte hade hivdiagnos.

Utifrån studieresultaten föreslås att preventiva insatser för att förhindra smittöverföring av blodburna infektioner bland personer med injektionsmissbruk fokuserar på:

- personer som börjat injicera droger
- unga kvinnor
- individens riskbeteende
- olika insatser för hiv och HCV
- hiv infekterade personer med riskbeteende
- HCV infekterade personer med riskbeteende
- att HBV vaccinationsprogrammet blir komplett

För att undvika smittöverföring av blodburna infektioner och för att förändra ett riskfyllt injektionsbeteende föreslås samtal om riskuppfattning. Risksamtalet föreslås utgå från metoden Motiverande samtal, och vara en dialog mellan en person som injicerat droger och en för ändamålet utbildad behandlare. Samtalet föreslås utgå från riskuppfattning med betoning på att identifiera, kvantifiera och karaktärisera riskbeteendet.

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