# The epidemiology of hepatitis C virus infection in Sweden

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In Sweden, infection with hepatitis C virus (HCV) has been a notifiable disease since 1990, when diagnostic methods became available. Blood donor screening indicated that about 0.5% of the Swedish population (9 millions) had been HCV infected. Here we present the Swedish hepatitis C epidemic based on data from all the HCV notifications 1990-2006. During this time about 42,000 individuals (70% men) were diagnosed and reported as HCV infected. The majority (80%) were born in 1950 or later, with a high percentage (60%) born in the 1950s and 1960s. Younger people, 15-24 years old at notification, were reported on the same level each year. The main reported routes of HCV transmission were intravenous drug use in 65%, blood transfusions/products in 6%, and sexual in 2%, though unknown or not stated in 26%. Approximately 6,000 of all notified individuals have died during the study period. To conclude, the Swedish HCV epidemic is highly related to the increase of intravenous drug use in the late 1960s and 1970s, with a high proportion of people now chronically infected for more than 25 years, resulting in an increase of severe liver complications in form of cirrhosis and hepatocellular carcinoma. Furthermore the unchanged number of notifications of newly infected younger people indicates an ongoing HCV epidemic.

## Introduction

Hepatitis C virus (HCV) infection is a global problem affecting about 140 million individuals, corresponding to an estimated global prevalence of 2.2% [1]. However, there are large geographic variations in the distribution. In southern Europe, the overall prevalence ranges between 2.5% and 3.5%, but in Northern Europe the prevalence is below 1% [2]. In Sweden (which has a population of 9 million), the prevalence of HCV infection was estimated in the beginning of the 1990s, when blood donor screening (introduced in 1991) revealed that 0.2-0.5% of Swedish blood donors had antibodies to HCV infection (anti-HCV) [3,4], and a study of a middle-aged urban population in southern Sweden showed that 0.4% were anti-HCV positive [5]. The chronicity rate in HCV infection is high, about 75% [6], with an increased risk of progression to liver cirrhosis and hepatocellular carcinoma (HCC) [1,7,8].

It has been suggested that the initial spread of HCV infection in southern Europe was iatrogenic and started over 50 years ago, leading to high infection prevalence in older people [2]. In recent decades, the European hepatitis C epidemic has mainly been transmitted through intravenous drug use (IDU) among younger people [2]. In Sweden, non-A non-B (NANB) hepatitis (the majority being hepatitis C) existed but was rare in the 1950s – injecting drug users (IDUs) being also very rare in Sweden at that time. NANB hepatitis became more prevalent in the 1970s as a result of the increase of IDUs during the 1960s and 1970s [9]. In a Swedish study, analyses of stored frozen serum samples from patients with acute hepatitis in 1969-1972 revealed that 52% of the intravenous drug users in the study were anti-HCV positive at that time [10]. In the 1990s, it was found that over 90% of Swedish IDUs were anti-HCV positive by the age of 26 to 30 years [11], and even occasional IDU was associated with a high risk of HCV infection [12,13].

In Sweden, HCV infection is by law a notifiable disease since 1990, when diagnostic methods became available. In this study we present the data on HCV infection, based on the national database of communicable diseases with all diagnosed and notified HCV-infected individuals in Sweden. The aim was to study the dynamics and changes over time with respect to age and route of transmission, and to discuss the impact on the Swedish HCV epidemic.

## Patients and methods

In Sweden, both the clinician and the laboratory having diagnosed the HCV infection are obliged to report to the Swedish Institute for Infectious Disease Control (SMI) [14]. The laboratories report all results indicating a present infection, as positive HCV antibodies and/or HCV-RNA analyses. These laboratory results are sent to the clinician who also has to report to the SMI. This clinical notification contains information of epidemiological interest, such as suspected route of transmission, but no information on HCV genotype. The registration does not distinguish acute from chronic HCV infection and in most reports, especially in the beginning of the 1990s, the diagnosis is based on a positive anti-HCV test and therefore some patients with a resolved infection could be in the register. Every Swedish resident has a unique 10-digit personal identification number that is used on these notifications and at all contacts with the healthcare system. The universal use of this personal identification number excludes the risk of double reporting of the same patient.

For this descriptive work, we used the register with all the clinical HCV notifications from year 1990 until the end of December 2006. This closely represents the whole, diagnosed, HCV infected population in Sweden.

## Results

### Annual reporting

Out of a total of 42,153 HCV notifications during the study period, more complete clinical information was reported for 41,026 individuals. The clinical reporting started with only 459 notifications in 1990, rising to a maximum peak of 4,537 in 1992, over some

**Figure 1**

**Number of notifications of hepatitis C by sex and year of notification, Sweden, 1990-2006**

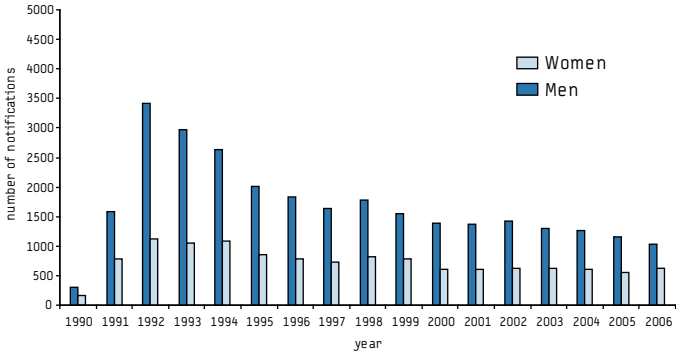



**Figure 2**

**Number of notifications of hepatitis C by sex and year of birth, Sweden, 1990-2006**

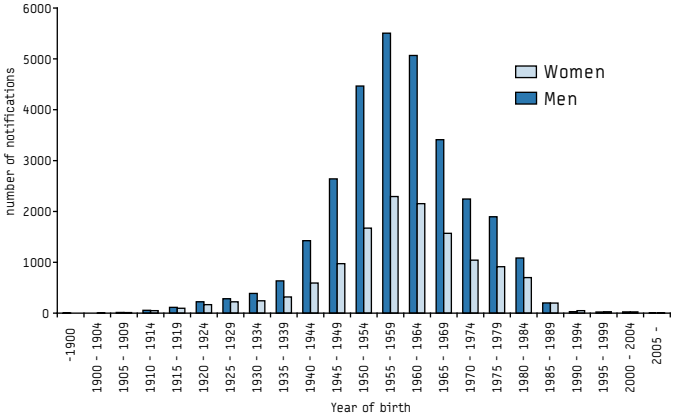



**Figure 3**

**Number of hepatitis C notifications by age at notification and year, Sweden, 1990-2006**

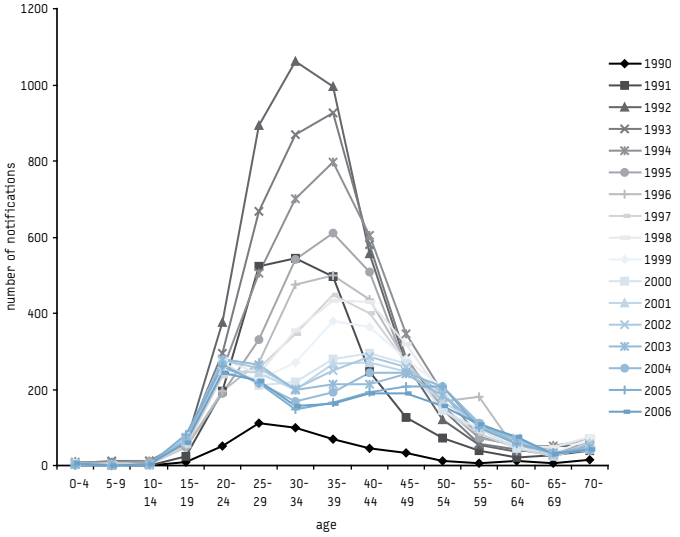
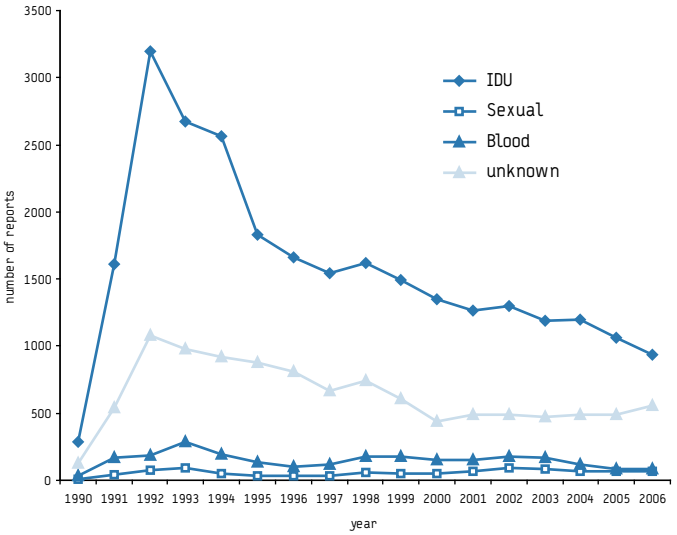



**Figure 4**

**Number of hepatitis C notifications by year and route of transmission, Sweden, 1990-2006**




years declining to about 2,000 notifications each year, and then the lowest since 1990 with 1,648 notifications in 2006 (Figure 1).

### Demography

Of the 41,026 individuals with a clinically reported HCV infection 12,384 (30%) were women. The majority (80%) were born in 1950 or later, with a high representation of people born in the 1950s (32%) and the 1960s (28%), and the median birth year was 1958 (Figure 2). Until the end of 2006, there were 185 (<0.5%) notifications of people born 1990 or later. Diagnosis and notification were most common at ages from 20 to 50 years (82%) and totally 84% (women 82%, men 87%) were notified before 50 years of age (median age 37 years). Age at notification has changed over the years (Figure 3). In the 1990s, the number of notifications peaked at ages representing the cluster of earlier infected people born in the 1950s and 1960s. However, from 2000 to 2006 there were still high numbers of late diagnosis in people born in those decades. The total number of people notified at age 20-24 was 375 in 1992, but has since then been about the same over the years (ranging from 188 to 294; mean 254 per year), but 20-24 was the most prevalent age at notification in 2006 as the number of notifications of older people had decreased.

According to the reports, 91% of the HCV infected were native Swedes. In patients reported 1990-1996 there were 6% immigrants, and among those reported in 1997-2006 there were 11% immigrants.

### Reported route of transmission

According to the notifications, the most probable route of transmission was former or ongoing IDU in 26,772 (65%), transfusion of blood or blood products in 2,534 (6%), and sexual contact in 971 (2%). There were also a few reports on mother-to-child (n=73) and occupational (n=29) transmission, but in 26% the transmission route was unknown or not stated. Notifications by year and reported route of transmission (Figure 4) revealed that in

**Table**

**Number of notifications of hepatitis C by age group and route of transmission, Sweden 1990-2006 (n=42,153)**

| Age at notification | Reported route of transmission | | | | | | Total | |
|---|---|---|---|---|---|---|---|---|
| years | Blood/blood products | Intravenous drug use | Sexual | Mother to child | Occupa-tional | Unknown/not stated | | % |
| 0-4 | 5 | 0 | 0 | 38 | 0 | 29 | 72 | 0.2 |
| 5-9 | 22 | 0 | 0 | 9 | 0 | 21 | 52 | 0.1 |
| 10-14 | 38 | 2 | 0 | 6 | 0 | 26 | 72 | 0.2 |
| 15-19 | 52 | 629 | 31 | 9 | 0 | 190 | 911 | 2 |
| 20-24 | 73 | 3,322 | 97 | 8 | 1 | 661 | 4,162 | 10 |
| 25-29 | 96 | 4,140 | 121 | 1 | 2 | 1,160 | 5,520 | 13 |
| 30-34 | 145 | 4,675 | 143 | 2 | 2 | 1,527 | 6,494 | 15 |
| 35-39 | 188 | 5,103 | 148 | 0 | 6 | 1,865 | 7,310 | 17 |
| 40-44 | 197 | 4,089 | 167 | 0 | 5 | 1,775 | 6,233 | 15 |
| 45-49 | 262 | 2,677 | 128 | 0 | 1 | 1,401 | 4,469 | 11 |
| 50-54 | 270 | 1,490 | 67 | 0 | 7 | 1,066 | 2,900 | 7 |
| 55-59 | 240 | 580 | 35 | 0 | 2 | 678 | 1,535 | 4 |
| 60-64 | 195 | 229 | 15 | 0 | 2 | 475 | 916 | 2 |
| 65-69 | 197 | 62 | 5 | 0 | 1 | 320 | 585 | 1 |
| 70-74 | 144 | 30 | 1 | 0 | 0 | 236 | 411 | 1 |
| 75-79 | 130 | 2 | 0 | 0 | 0 | 159 | 291 | 0.7 |
| 80-84 | 81 | 0 | 0 | 0 | 0 | 65 | 146 | 0.3 |
| 85- | 32 | 2 | 0 | 0 | 0 | 40 | 74 | 0.2 |
| **Total (%)*** | 2,367 (6) | 27,032 (64) | 958 (2) | 73 | 29 | 11,694 (28) | 42,153 | 100 |

* Some of the % figures are not exactly the same as in the text where we used the 41,026 notifications.

1992 IDU was reported in 3,200 (70%), this had decreased to 932 (57%) in 2006. Reports of infection through blood or blood products (before 1992) had an absolute peak with 289 (7%) notifications in 1993, but have then declined to the lowest value since 1990, 87 (5%) individuals in 2006. The reported route of HCV transmission by age at date of notification (Table 1) revealed that already at the age of 15-19 years IDU was important, but in high ages (>65 years) transfusion of blood/blood products or unknown/not stated were the most reported routes of transmission.

## Discussion

The notification of HCV in Sweden started in 1990 when the first generation of diagnostic tests for anti-HCV became available. In 1991, the second-generation anti-HCV assays were introduced, the blood-donor screening was initiated, and anti-HCV testing became common. People with elevated liver enzymes, liver disease of unknown cause, a diagnosis of chronic NANB hepatitis, or a history of former IDU or blood transfusions, were tested. In 1992, more than 4,000 individuals were diagnosed with an HCV infection and reported to the SMI. This peak was due to testing of people, most of them born in the 1950s and 1960s, who had been infected for a long time without the opportunity to get a correct diagnosis. The annual reporting has then slowly declined to less than 2,000 notifications per year as the number of notifications of persons born in the 1950s and 1960s decreased. However, the number of notifications of younger people, 15-24 years old, has remained the same over the years, indicating that the epidemic has been ongoing with about the same intensity during the last decades.

The spread of HCV in Southern Europe probably started more than 50 years ago, leading to high infection prevalence in older people [2]. In Sweden, 80% of the reported HCV infected individuals were born in 1950 or later and 60% in the 1950s and 1960s. This is consistent with the theory that the spread of HCV in Sweden started with the introduction of IDU in the mid 1960s, with an increase in the 1970s when IDU became more common, mostly among young people, i.e. those born in the 1950s [9]. According to the Swedish report to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA, http://www.emcdda.europa.eu), the prevalence of illegal drug use then declined in the 1980s but has increased again in the late 1990s, and so has the number of direct drug related deaths. There is a risk that this increase during the last decade will cause an increase in the spread of HCV, though still not apparent in the surveillance system. The dominance of men in the HCV-infected population is due to the high percentage of IDU that is more common in Swedish men than women according to the EMCDDA.

The percentage of immigrants (9%) in the HCV infected population was somewhat lower than in the general population of which 12.9% (December 2006) were born in another country than Sweden ( http://www.scb.se/templates/tableOrChart____26040.asp ). This is in contrast to reports from other European countries where immigrants from high endemic countries are considered to account for a large proportion of the HCV population [2]. However, also in Sweden a high proportion of immigrants have come from countries with a high HCV prevalence and the low percentage among reported HCV infected individuals could indicate a lower

screening activity among immigrants or a selection of immigrants with a lower HCV prevalence than the general population of their former home countries.

In 26%, no probable route of transmission was given on the notification. This could to some extent be explained by the fact that many notifications were made at the time of diagnosis after only brief contact with the infected individual. A probable route of transmission could have been identified later on, for example sporadic IDU, but the notification will usually not be corrected. However, there is also a possibility of unknown routes of transmission and iatrogenic transmission associated with medical procedures. In Sweden, a few outbreaks of HCV transmission through medical procedures have been reported [15-19] – in some of these, the most likely route of transmission was contamination of saline multidose vials.

The risk of HCV transmission through blood transfusions and blood products is very low as a result of the introduction of blood donor screening in 1991. However, some patients receiving intravenous immunoglobulin were HCV infected until February 1994, when contaminated batches of immunoglobulin were recalled and exposed patients traced [20]. Recently, the National Board of Health and Welfare recommended that all people who during childhood have been treated with blood transfusions during 1965 to 1991, because of heart surgery, neonatal exchange transfusion, prematurity, or cancer, should be identified and tested for HCV infection (http://www.socialstyrelsen.se/Publicerat/2007/9775/2007-130-6.htm).

A recent study on cause of death in HCV-infected individuals in Sweden revealed that approximately 14% of those notified in 1990-2003 were dead by December 2003 [21]. This study demonstrated an increased all-cause mortality about six times higher than the general population, with a 30-40 times excess mortality from liver disease in higher age groups, both in people infected through IDU and blood/blood products, and a great excess mortality from psychiatric (drug-related) and external causes (as injuries, intoxication, suicide) in younger people. This indicates that about 5,800 of the HCV infected in the population presented here may be dead, leaving about 36,000 diagnosed, living, anti-HCV positive individuals in Sweden. However, there are also individuals with an undiagnosed HCV infection; the size of this population is not known but is supposed to be substantial. In the study on cause of death, 16% of all deaths (not included in the statistical analysis) occurred less than six months after HCV diagnosis and the HCV infection was possibly diagnosed because of a lethal disease [21]. In a Swedish study on HCV and liver cancer, a high proportion had the HCV diagnosis close to liver cancer diagnosis [8], indicating that there is a significant population with an undiagnosed HCV infection. Therefore, it seems realistic to estimate the anti-HCV positive population currently alive in Sweden at around 45,000 individuals, i.e. an anti-HCV prevalence of 0.5% as discussed in the early 1990s [4,5], some with a spontaneously resolved infection but the majority with a chronic infection. The treatment for HCV has improved during the last decade, but there are no official statistics on how many have been treated and cured.

The impact of the HCV epidemic is the morbidity and mortality in the long run of this chronic infection. People diagnosed and eligible for treatment are at little risk for spreading the disease, but treatment is important in order to diminish the long-term complications such as liver cirrhosis and hepatocellular carcinoma. The incidence of liver cancer in Swedish HCV patients was recently studied [8]. During the study period, 1990-2004, the primary liver cancers in the HCV cohort represented about 5% of all primary liver cancers in Sweden (approximately 500 per year). In the later years of the study period, as the HCV cohort grew older, about 10% of the liver cancer patients were found in the HCV cohort. The relative risk for liver cancer was about 40 times higher than in the general population in people who had been HCV infected for more than 25 years (age-, sex- and calendar year-specific incidence rates were used). The absolute risk of developing primary liver cancer within 40 years of HCV infection was 7% in the HCV infected population. In the study on cause of death [21], the risk of death from liver cancer was 35 times higher in all HCV infected (20 times among those infected through blood/blood products) than in the general population. HCV related liver cirrhosis is the most common indication for liver transplantation in Europe and the United States. Also in the Nordic countries, according to the Nordic Liver Transplant Registry (www.scandiatransplant.org), the number of transplanted patients with hepatitis C associated cirrhosis has increased markedly over the last 10 years. There have been more than 1,800 liver transplantations performed in Sweden since 1984, of which about 20% were in patients with HCV related cirrhosis, with or without HCC. In 2005, 30% of liver transplantations carried out in Stockholm were in patients with HCV-related liver disease [22]. The number of patients with serious complications to the HCV infection is increasing in spite of new and better treatment opportunities. This could be related to the age distribution in the HCV cohort: the large group infected in the 1970s have now been chronically infected for 25-35 years, which is the reported latency time to develop liver complications [7,8].

## Conclusions

To conclude, the spread of HCV infection in Sweden is highly related to the increase of IDU in the 1970s. The prevalence of anti-HCV in the general population is about 0.5% and a large proportion of the HCV infected in Sweden are born in the 1950s and 60s and have now an increasing risk of morbidity and mortality from liver complications. As a result of a decline in the prevalence of IDU in the 1980s, the epidemic spread probably declined in the 1980s, but is still of the same magnitude as it was in the beginning of the 1990s, and could increase again due to an increase in IDU during the last decade. This will have an overwhelming effect on the healthcare system, a problem that can only partially be met by treating those at risk of developing progressive liver disease. The greatest efforts should be aimed at diminishing the spread, i.e. combating the IDU.

Sweden is a low-prevalence country for HCV infections. The results of this study would likely be relevant also for other low-prevalence European countries. They clearly demonstrate that a full understanding of hepatitis C epidemiology in a country requires a detailed trend analysis of age structures and transmission routes in the notified patients.

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This article was published on 22 May 2008.

Citation style for this article: Duberg A, Janzon R, Bäck E, Ekdahl K, Blaxhult A. The epidemiology of hepatitis C virus infection in Sweden. Euro Surveill. 2008;13(21):pii=18882. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=18882