University of Alberta

Hepatitis C Infection in Renal Dialysis Patients:
An investigation within the Northern Alberta Renal Program

by

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Abstract

Hepatitis C virus (HCV) is an emerging global public health issue with particular relevance in multiply transfused renal dialysis patients. This investigation determined the prevalence and risk factors for HCV infection in the Northern Alberta Renal Program (NARP). Ninety-two percent of eligible patients (n=336) provided informed consent to participate. Participants were interviewed to gather risk factor information, and using multiple logistic regression analysis, a predictive model for HCV infection in the NARP was illustrated. Ill-defined modes for propagating blood-borne pathogens have been described and evidence against nosocomial transmission of HCV is provided. Self-reported patient transfusion histories were also validated against documented records. It emphasized the need to communicate clearly medical interventions in chronically ill patients and the responsibility to utilize all available information sources for exposure histories. Communicating about risk of infectious diseases must be reasoned and based on the best available epidemiological evidence.

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Chapter 1

Introduction

Hepatitis Viruses

Viral hepatitis has been recognised since ancient times, but it was only in the early 1940s, through transmission studies in volunteers, that direct evidence for the viral etiology of hepatitis was obtained for the first time (Farci *et al*, 1993). Subsequently, more than two decades elapsed before the first etiological agent of human hepatitis was identified (Kuhns, 1995a). Today, we know there are many varieties of viral hepatitis.

The hepatitis viruses are a diverse group of hepatotropic pathogens that cause liver inflammation and liver cell death. These viruses can be considered as two distinct groups, based on several clinically and epidemiologically important characteristics.

Hepatitis A (HAV) and Hepatitis E (HEV) viruses, which lack a lipid envelope, typically spread by a fecal-oral mode of transmission, and they can cause extensive common source outbreaks of disease. However, neither of these viruses causes persistent infection, and neither has been identified as a cause of chronic viral hepatitis (Lemon *et al*, 1997).

Hepatitis B (HBV), hepatitis C (HCV), and hepatitis D (HDV) viruses in comparison all possess lipid envelopes. These three viruses are not shed in feces in biologically significant amounts. Their transmission occurs by several other routes, most often involving virus shed from a mucosal surface or by direct percutaneous exposures. In addition each may cause persistent infection and have been shown to be important etiological agents of chronic viral hepatitis and cirrhosis (Marcus *et al*, 1997). Infection

with HBV or HCV may lead ultimately to the development of primary hepatocellular carcinoma, often after years of persistent infection and chronic hepatitis (Gane *et al.* 1996).

Recently, a further member has been added to this group of pathogens - hepatitis G (HGV) (Bowden *et al.* 1996: Kimber *et al.* 1996). There will be undoubtedly be other members of the hepatitis alphabet as our knowledge increases. This underlines the need to avoid complacency in further strengthening the blood supply through proactive surveillance for new or emerging blood-borne pathogens (Tobler *et al.* 1997).

Hepatitis C

The pathway leading to the identification of the causative agent of non-A, non-B (NANB) hepatitis has been long and tortuous. In retrospect, the length of this process can be explained by the low levels of infectivity and by the weak and delayed humoral immune response of the host (Houghton *et al. 1993*). It was through an unconventional approach, taking advantage of the increasingly refined techniques of molecular biology, that success was eventually achieved. The availability of the chimpanzee model was critical for the discovery of HCV, as it represented the only suitable source for the biological amplification of the putative agent. It was from a chronically infected chimpanzee that large amounts of pooled plasma with an unusually high titre of infectivity were obtained for the molecular cloning of the viral genome (Choo *et al.* 1989).

HCV is a single-stranded positive-sense RNA virus with a genome of ~9500 bases coding for ~3000 amino acids. This small RNA lipid-envelope virus has been classified in the family Flaviviridae. The cloning and sequence of the HCV genome and the development of serological assays for antibodies to HCV (Kuo *et al.*, 1989) have transformed the diagnosis of NANB hepatitis from one merely based on exclusion into that of a specific disease, hepatitis C. The application of this assay to clinical practice has finally provided the best evidence that HCV is the major etiological agent of post-transfusion NANB hepatitis (Alter *et al.*, 1989; Esteban *et al.*, 1990; Aach *et al.*, 1991) as well as of community-acquired NANB hepatitis (Alter *et al.*, 1992).

The Red Cross in Canada implemented donor screening for HCV immediately after licensure of the first-generation anti-HCV enzyme immunoassay in 1990. Even though this assay facilitated the screening of blood donors for anti-HCV antibodies, it did not detect all infectious blood donations and had a lengthened window of infectivity ranging from 12 weeks to greater than 30 weeks post-infection. Nevertheless it has been estimated at least in the US to have minimized the risk of transfusion acquired hepatitis C (Donahue *et al.*, 1992).

The introduction of a second generation anti-HCV enzyme immunoassay in 1992 further shortened the seroconversion window period to approximately 10-25 weeks. This had significantly improved sensitivity in detecting acute and chronic HCV infections (Alter, 1995).

In 1996 the licensing of a third-generation screening test - that detected antibodies to an even broader spectrum of HCV antigens - further narrowed the seroconversion window to about 8 - 23 weeks (Urdea *et al.* 1997).

Since the availability of diagnostic tests for anti-HCV, serological surveys found that HCV was responsible for approximately 90 per cent of all transfusion-related cases of non-A, non-B (NANB) hepatitis (Dodd, 1992). Although acute hepatitis C is very frequently asymptomatic, and fulminant HCV infection is rare (Farci *et al.* 1993), HCV causes chronic hepatitis in a high proportion of those infected. This may ultimately result in the development of chronic liver disease, cirrhosis and hepatocellular carcinoma (HCC) (Di Bisceglie *et al.* 1994). HCV is now the most common indication for liver transplantation in a number of transplant units around the world (Gane *et al.* 1996).

The genomic and immunologic characteristics of hepatitis C virus have been seemingly more apparent in light of the large amount of conflicting data that has been published regarding the epidemiological patterns of viral transmission of hepatitis C. The transmission of HCV may conveniently be considered in relation to the specific route of infection and the particular groups of individuals at risk of infection. Although the mechanism of transmission of HCV is likely to be similar to that of HBV, it is clear that there are some significant differences.

The main route of HCV transmission is parenteral, and many HCV-infected individuals are recipients of blood and blood products that in the past had not been screened for anti-HCV (Donahue *et al.* 1992). HCV infection is also frequently associated with illicit use of intravenous drugs (Crofts *et al.* 1993). The predominance of anti-HCV in groups of people exposed to sexually transmitted diseases suggests that sexual transmission may also be involved in the spread of HCV infection, though inefficiently (Fairley *et al.* 1990; Melbye *et al.* 1990; Tedder *et al.* 1991). Smaller numbers of HCV infections are related to sexual or vertical transmission (Esteban, 1993), organ transplantation (Candinas *et al.* 1993), tattoos and piercing (Davis, 1995). Blood exchanged in ritual ceremonies have also been reported as a possible route for infection with HCV (Atrah *et al.* 1994). For many patients infected with HCV, however, no source of infection can be established (Curran, 1995). The availability of tests for antibodies to HCV and the use of the polymerase chain reaction (PCR) to detect HCV-RNA has enabled a more definitive characterization of the epidemiology and routes of transmission (Kuhns, 1995b).

Certainly the discovery of HCV and the development of serological screening assays for HCV antibody in blood donors has provided a valuable method for the prevention of post-transfusion non-A, non-B hepatitis (Kiyosawa *et al.* 1990). However, some HCV-infected blood donors may not be detected because of the delay between primary infection and seroconversion to positivity for antibody to HCV (Czaja, 1992; Irshad *et al.* 1995). Alternatively, infection with HCV isolates with sequences divergent from

those of the prototype virus may elicit antibodies that do not cross react with antigens used in certain screening assays (McOmish *et al. 1993*).

Several points need to be borne in mind when analyzing the reported data concerning HCV infection. Firstly, many of the currently quoted prevalence rates for HCV infection are based on first- and second- generation assays, and are often an underestimation. The third generation assays now available are far superior to the original tests with increased sensitivity. Secondly, the lack of subsequent confirmation of the screening results, leads to considerable overestimation of prevalence rates. Thirdly, HCV infection can lead to a chronic carrier state in a proportion of infected individuals that is marked by the presence of HCV-RNA, but not always, in the presence of anti-HCV (Cuthbert, 1994).

Public Health

The apparent ease of transmission (Alter, 1991), the long period between exposure and development of symptoms (Rapicetta *et al.*, 1992; Soni *et al.*, 1995), and the lack of a definitive treatment protocol (Kanai *et al.*, 1995; Terrault *et al.*, 1995a), ensure that HCV is an issue of public health concern.

Hepatitis C virus (HCV) poses a serious global public health dilemma. An estimated 170 million individuals worldwide are chronically infected with HCV (Lavanchy, 1997), and new cases of HCV infection occurs at rates of greater than 175,000 per year in the US and Western Europe and greater than 350,000 per year in Japan (Urdea *et al.*

1997). Canadian surveillance data as reported by the Laboratory Center for Disease Control reported 14. 070 newly diagnosed cases in 1995 (Gully *et al.* 1997). Over 80% of those exposed to HCV become chronically infected. and 20% of these develop cirrhosis. possibly leading to hepatocellular carcinoma or liver decompensation (Murthy *et al.* 1997).

Prevalence studies reporting blood transfusion as a risk factor among patients undergoing surgical or other invasive procedures are sparse. Available data indicate that current risk of transfusion-associated HCV infection is minute compared to estimated risk in the mid 1980s. Risk of hepatitis C infection was estimated to be 12.6 per 1.000 units transfused by Blajchman *et al* (1995) and Preiksaitis *et al* (1995). based on data from the Canadian Red Cross. The risk is now estimated to be on the order of 1 in 100.000 (Tobler *et al.* 1997) that a unit of blood will transmit HCV to a patient. This reduction in risk is due to donor selection. screening. and very sensitive tests for anti-HCV (Tong *et al.* 1995; Holland. 1996; Alter *et al.* 1997).

Determining the presence and risk factors for anti-HCV antibodies in dialysis patients is important for several reasons. Firstly. dialysis patients are often candidates for kidney transplantation which may be associated with a worsening of liver lesions as a result of the immunosuppression required to prevent allograft rejection (Kirk *et al.* 1996). However. the natural history of this infection in immunosuppressed patients remains unclear (Terrault *et al.* 1995b; Roth *et al.* 1996; Bouthot *et al.* 1997). Secondly. at least 50% of these patients may have normal serum transaminases activity

despite biopsy-proven chronic hepatitis (Pol *et al.* 1993). Thirdly, viremic patients could be the source of nosocomial transmission of HCV in hemodialysis units (Santos *et al.* 1996). Finally, interferon treatment may be of value before kidney transplantation (Al Meshari *et al.* 1995; Roth 1995). Prevention of HCV infection in patients with end-stage renal failure maybe important in precluding the progression of liver disease in kidney transplant recipients as well as the risk of potential transmission of HCV in dialysis centers (Allander *et al.* 1994).

The clinical manifestations of the viral hepatitides are similar, so that clinical diagnosis of viral hepatitis frequently relies on an epidemiological history and serological confirmation. Many persons with chronic hepatitis C have silent, asymptomatic disease, and the diagnosis requires the clinician to measure serum aminotransferases and antibody to HCV (Soni *et al.* 1995).

Antibodies to HCV in serum may appear within several weeks after exposure, and most definitely after nine months (Gerberding, 1995). As patients with chronic renal failure have impaired immune response and therefore seroconversions can be delayed or absent, the use of PCR to detect HCV infection is of greater diagnostic value. HCV-RNA is positive much earlier than ELISA tests (Alter, 1995). Further study is required to clarify the still ambiguous situation of HCV-RNA positivity coupled with HCV antibody negativity seen in certain studies (Cuthbert, 1994).

Study Objectives

The objectives of this study were:

- To determine the prevalence of HCV infection among dialysis patients on the Northern Alberta Renal Program (NARP).
- To determine the risk factors associated with anti-HCV positivity.
- To determine the accuracy of self-reported transfusion histories in dialysis patients

Purpose

The study provided a baseline prevalence of hepatitis C infection in the Northern Alberta dialysis population, and a risk factor profile. Future prospective seroconversion studies can be conducted now that a baseline infection has been determined. Better information on risk factors is required to guide control activities for this disease. Once risk factors for HCV infection in this population are identified, practitioners can provide information specific to the individual needs of their patients. Within this framework of description and analysis, current knowledge on hepatitis C in this population can be consolidated and the incidence and impact of hepatitis C in the dialysis environment can be reduced. For example, policies with regard to patient isolation and dedicated dialysis machines for those with HCV infection can be considered and implemented, if required.

Appendices

Several appendices have been included. Specifically:

1. A flow-chart describing the NARP and the study population

2. The risk factor profile questionnaire used
3. A comparison of the interview methods used
4. Bivariate analyses for HCV infection
5. Exact logistic modeling for predictors of HCV infection
6. Assessment of self-reported transfusion history

These have been added to the thesis for completeness and will not be included in the manuscripts that will be submitted for publication. References to the appendices in the following two papers are for the benefit of the reviewer.

References

Aach RD. Stevens CE. Hollinger FB. Mosley JW. et al. (1991): Hepatitis C virus infection in post-transfusion hepatitis - an analysis with first and second generation assays. **New England Journal of Medicine** 325:1325-9.

Allander T. Medin C. Jacobson SH. et al. (1994): Hepatitis C transmission in a hemodialysis unit: Molecular evidence for spread of virus among patients not sharing equipment. **Journal of Medical Virology** 43:415–419.

Al Meshari K. Al Ahdal M. Alfurayh O. Ali A. et al. (1995): New insights into HCV infection of hemodialysis patients: the implications. **American Journal of Kidney Diseases** 25:572-78.

Alter HJ (1995): To C or Not To C: These are the Questions. **Blood** 85:1681-1695.

Alter HJ. Conry-Cantilena C. Melpolder J. Tan D. et al. (1997): Hepatitis C in Asymptomatic Blood Donors. **Hepatology** 26:29S-33S.

Alter MJ. Coleman PJ. Alexander WJ. Kramer E. et al. (1989): Importance of heterosexual activity in the transmission of hepatitis B and non-A. non-B hepatitis. **Journal of the American Medical Association** 262:1201-1205.

Alter MJ. (1991): Inapparent transmission of Hepatitis C: footprints in the sand. **Hepatology** 14:389-91.

Alter MJ. Margolis HS. Krawczynski K. Judson FN. et al. (1992): The natural history of community-acquired hepatitis C in the United States. **New England Journal of Medicine** 327:1899-1905.

Atrah HI. Ala FA. Gough D. (1994): Blood exchanged in ritual ceremonies as a possible route for infection with hepatitis C virus. **Journal of Clinical Pathology** 47:87.

Blajchman MA. Bull SB. Feinman SV. (1995): Post-transfusion hepatitis: impact of non-A. non-B hepatitis surrogate tests. **Lancet** 345:21-25.

Bouthot BA. Murthy BVR. Schmid CH. Levey AS. et al. (1997): Long-term follow-up of hepatitis C virus infection among organ transplant recipients. **Transplantation** 63:849-853.

Bowden DS. Moaven LD. Locarnini SA. (1996): New hepatitis viruses: are there enough letters in the alphabet? **Medical Journal of Australia** 164:87-89.

Candinas D. Joller-Jemelka HI. Largiader F (1993): Hepatitis C virus and organ transplantation. **New England Journal of Medicine** 328:511-513.

Choo QL. Kuo G. Weiner AJ. Overby LR. et al. (1989): Isolation of a cDNA clone derived from a blood-borne non-A. non-B hepatitis genome. **Science** 244:359-62.

Crofts N. Hopper JL. Bowden DS. et al. (1993): Hepatitis C virus infection among a cohort of Victorian injecting drug users. **Medical Journal Of Australia** 159:237-241.

Curran M. (1995): Acute Hepatitis C notifications and associated risk factors in Australia - 1995 first quarter report. **Communicable Disease Intelligence** 19:615-17.

Cuthbert JA. (1994): Hepatitis C: Progress and Problems. **Clinical Microbiology Reviews** 7:505-532.

Czaja AJ. (1992): Chronic Hepatitis C virus infection - a disease in waiting? **New England Journal of Medicine** 327:1949-50.

Davis AR. (1995): Tattoo parlours and hepatitis C virus infection (letter). **The Medical Journal of Australia** 163:556.

Di Bisceglie AM. Interferon therapy for chronic viral heaptitis. **New England Journal of Medicine** 330:137-8.

Dodd RY. (1992): The risk of transfusion transmitted infection. **New England Journal of Medicine** 327:419-21.

Donahue JG. Munoz A. Ness PM. Brown Jnr DE. et al. (1992): The declining risk of post-transfusion hepatitis C virus infection. **New England Journal of Medicine** 327:369-73.

Esteban JI. Gonzalez A. Hernandez JM. Viladomiu L. et al. (1990): Evaluation of antibodies to hepatitis C virus in a study of transfusion-associated hepatitis. **New England Journal of Medicine** 323:1107-1112.

Esteban R (1993): Epidemiology of hepatitis C virus infection. **Journal of Hepatology** 17:S67-S71.

Fairley CK. Leslie DE. Nicholson S. Gust ID. (1990): Epidemiology and hepatitis C virus in Victoria. **Medical Journal of Australia** 153:271-273.

Farci P. Purcell RH. (1993): Hepatitis C virus - Natural History and Experimental Models. in Zuckerman AJ. Thomas HC (Eds). **Viral Hepatitis - Scientific basis and clinical management.** 229-240. Churchill Livingstone. Melbourne.

Gane EJ. Portmann BC. Naoumov NV. Smith HM. et al. (1996): Long-term outcome of hepatitis C infection after liver transplantation. **New England Journal of Medicine** 334:815-20.

Gerberding JL. (1995): Management of occupational exposures to blood-borne viruses. **New England Journal of Medicine** 332:444-51.

Gully PR. Tepper ML (1997): Hepatitis C. **Canadian Medical Association Journal** 156:1427-28.

Holland P. Risk of Viral Hepatitis from blood: status report. **IX Triennial International Symposium on Viral Hepatitis and Liver Disease** (abstract volume). April 21-25 1996. Rome. Italy.

Houghton M. Han J. Kuo G. Choo Q. Weiner A. (1993): Hepatitis C virus - Structure and Molecular Virology. in Zuckerman AJ. Thomas HC (Eds). **Viral Hepatitis - Scientific basis and clinical management.** 229-240. Churchill Livingstone. Melbourne.

Irshad M. Acharya SK. Joshi YK (1995): Prevalence of HCV antibodies in the general population and in selected group of patients in Delhi. **Indian Journal of Medical Research** 102:162-64.

Kanai K. Kako M. Aikawa T. Kumada T. et al. (1995): Clearance of serum HCV-RNA after IFN therapy in relation to virus genotype. **Liver** 15:185-88.

Kimber RJ (1996): The recently discovered hepatitis G virus (letter). **Medical Journal of Australia** 164:124.

Kirk AD. Heisey DM. D'Alessandro AM. Knechthle SJ. et al. (1996): Clinical hepatitis after transplantation of hepatitis C virus-positive kidneys. **Transplantation** 62:1758-1762.

Kiyosawa K. Sodeyama T. Tanaka E. et al. (1990): Interrelationship of blood transfusion. NANB hepatitis and hepatocellular carcinoma: analysis by detection of antibody to hepatitis C virus. **Hepatology** 12:671-75.

Kuhns MC. (1995a): Viral Hepatitis - Part 1: The Discovery. Diagnostic Tests. and New Viruses. **Laboratory Medicine** 26:650-59.

Kuhns MC. (1995b): Viral Hepatitis - Part 2: Treatment. Prevention. and Special Precautions. **Laboratory Medicine** 26:786-93.

Kuo G. Choo Q-L. Alter HJ. Purcell RH. Gitnick GL. et al. (1989): An assay for circulating antibodies to a major etiologic virus of non-A. non-B hepatitis. **Science** 244:362-364.

Lavanchy D (1997): The threat to public health of hepatitis C. **Research in Virology** 148:143-145.

Lemon SM. Thomas DL. (1997): Vaccines to Prevent Viral Hepatitis. **New England Journal of Medicine** 336:196-204.

Marcus E. Tur-Kaspa R. (1997): Viral hepatitis in older adults. **Journal of the American Geriatric Society** 45:755-763.

McOmish F. Chan SW. Dow BC. et al. (1993): Detection of three types of hepatitis C virus in blood donors: Investigation of type-specific differences in serologic reactivity and rate of alanine aminotransferase abnormalities. **Transfusion** 33:7-13.

Melbye M. Biggar RJ. Wantzin P. et al. (1990): Sexual transmission of hepatitis C virus: cohort study (1981-9) among European homosexual men. **British Medical Journal** 30:210-12.

Murthy BVR. Pereira BJG (1997): A 1990s perspective of HCV. HIV. and TB infections in dialysis patients. **Seminars in Nephrology** 17:346-363.

Pol S. Romeo R. Zins B. Driss F. et al. (1993): Hepatitis C virus RNA in anti-HCV positive hemodialyzed patients: significance and therapeutic implications. **Kidney International** 44:1097-1100

Preiksaitis JK. Rivet C. (1995): A history of the evolution of hepatitis C testing of blood donors: implications for the Canadian blood supply system. **Transfusion** 35:348-352.

Rapicetta M. Attili AF. Mele A. De Santis A. et al. (1992): Prevalence of Hepatitis C virus antibodies and HCV-RNA in an urban population. **Journal of Medical Virology** 37:87-92.

Roth D (1995): Hepatitis C Virus: The Nephrologist's View. **American Journal of Kidney Diseases** 25:3-16.

Roth D. Zucker K. Cirocco R. Burke G. et al. (1996): A prospective study of hepatitis C virus infection in renal allograft recipients. **Transplantation** 61:886-889.

Santos JP. Loureiro A. Neto MC. Pereira BJG (1996): Impact of dialysis room and reuse strategies on the incidence of HCV infection in hemodialysis units. **Nephrology Dialysis Transplantation** 11:2017-22.

Soni P. Dusheiko GM. Harrison TJ. Dhillon AP. (1995): Genetic diversity of hepatitis C virus: implications for pathogenesis. treatment and prevention. **Lancet** 345:562-566.

Tedder RS. Gilson RJC. Briggs M. Loveday C. et al. (1991): Hepatitis C virus: evidence for sexual transmission. **British Medical Journal** 302:1299-1302.

Terrault N. Wright T. (1995a): Interferon and Hepatitis C. **New England Journal of Medicine** 332:1509-11.

Terrault N. Wright T. (1995b): Hepatitis C Virus in the setting of transplantation. **Seminars in Liver Disease** 15:92-100.

Tobler LH. Busch MP. (1997): History of posttransfusion hepatitis. **Clinical Chemistry** 43:1487-93.

Tong MJ. El-Farra NS. Reikes AR. Co RL. (1995): Clinical outcomes after transfusion-associated hepatitis C. **New England Journal of Medicine** 332:1463-6.

Urdea MS. Wuestehube LJ. Laurenson PM. Wilber JC. (1997): Hepatitis C – diagnosis and monitoring. **Clinical Chemistry** 43: 8B:1507-1511.

Chapter 2

Hepatitis C: Prevalence and Risk Factors in the Northern Alberta Dialysis Population

Introduction

Hepatitis C Virus (HCV) infection is the most common cause of acute and chronic hepatitis in dialysis patients (Pereira *et al.* 1997). The prevalence of HCV antibodies in hemodialysis units has been reported to range from 5% to 54% (Dussol *et al.* 1995: Zeuzem *et al.* 1996). in contrast to a prevalence of 0.3 - 1.5% in the general population (Nordenfelt. 1996: Tandon *et al.* 1996: Vranckx *et al.* 1996). Before the introduction of recombinant erythropoietin. blood transfusions were a common therapeutic approach to treat anemia in hemodialysis patients (Ifudu *et al.* 1995). Beside the risk of HCV transmission via transfusion of blood and blood products. previous renal transplantation and/or insufficient infection control procedures in the hemodialysis facility itself might account for the high prevalence of HCV infection in these patients.

The recovery rate from HCV infection is low. and about 85% of those infected become chronic carriers (Tong *et al.* 1995: Ricci *et al.* 1996: Soni *et al.* 1996). Despite the reduced life expectancy in patients with chronic renal failure. early detection and treatment of chronic hepatitis can be considered (Jenkins *et al.* 1996: Izopet *et al.* 1997) to prevent progression to liver cirrhosis and hepatocellular carcinoma. and associated morbidity and mortality.

Descriptive epidemiologic studies have been used to define high risk groups. and have identified specific risk factors within these groups. Among dialysis patients. the main risk factors for transmission are previous blood transfusions and possibly nosocomial infections within the dialysis environment (Jadoul. 1996: Chauveau. 1996). Fluctuating

hepatitis C viremia with periods of undetectable HCV-RNA among hemodialysis patients has been documented (Umlauft *et al.* 1997). While HCV transmission dynamics are not completely understood and a vaccine is not available. peritoneal dialysis patients generally have a lower prevalence than hemodialysis patients (Golan *et al.* 1996).

Determining the presence and risk factors for anti-HCV antibodies in dialysis patients is important for several reasons. Firstly. dialysis patients are often candidates for kidney transplantation which may be associated with a worsening of liver lesions as a result of the immunosuppression required to prevent allograft rejection (Kirk *et al.* 1996). However. the natural history of this infection in immunosuppressed patients remains unclear (Terrault *et al.* 1995a; Roth *et al.* 1996; Bouthot *et al.* 1997). Secondly. at least 50% of these patients may have normal serum transaminases activity despite biopsy-proven chronic hepatitis (Pol *et al.* 1993). Thirdly. viremic patients could be the source of nosocomial transmission of HCV in hemodialysis units (Santos *et al.* 1996). Finally. interferon treatment may be of value before kidney transplantation (Al Meshari *et al.* 1995; Roth 1995). Prevention of HCV infection in patients with end-stage renal failure maybe important in precluding the progression of liver disease in kidney transplant recipients as well as the risk of potential transmission of HCV in dialysis centers (Allander *et al.* 1994).

This paper reports the results of a cross-sectional study that examined the prevalence and risk factors of HCV infection in the dialysis population of the Northern Alberta Renal Program (NARP).

Methods

Study Population

On 1 July 1997 there were 416 patients in the NARP. Prior to interview five of them were transplanted and 25 had died. A further 20 were unable to provide informed consent, leaving 366 eligible patients. All were approached and asked to participate in the study. NARP is a comprehensive program that includes all renal dialysis patients in Northern Alberta. Three hundred and thirty-six patients, representing ninety-two percent of eligible patients aged 18 years and older provided informed consent. The study protocol was approved by the Medical Ethics Review Board of the Faculty of Medicine at the University of Alberta. Participants and non-participants were comparable for age and gender (appendix 1). After obtaining the informed consent of patients, participants were interviewed and data abstracted from their medical records. The interviewer/data abstractor was blinded to participants' HCV status to the extent possible.

Participants were interviewed by the same interviewer using a questionnaire (appendix 2) comprising demographic, dialysis-specific, medical history and lifestyle variables. The demographic variables included age, gender, country of birth and ethnic background. Medical variables included a history of blood transfusions, surgery,

medical treatment in a developing nation. jaundice and abnormal liver function. Lifestyle factors. including injection drug use and sexual activity were also requested. A combination of in-person and telephone interviews was employed. No systematic differences were seen between the two interview methods (appendix 3) and interviewees were comparable for age and gender irrespective of interview method (appendix 1). Conforming with ethics requirements. patients were not required to answer every question on the questionnaire. Consequently. there are some missing responses. especially for *"sensitive"* lifestyle questions. although this represented no more than 7.7 % for any variables.

Because there was concern regarding self-reported transfusion history. blood bank records and all accessible patient medical records were thoroughly reviewed to provide accurate patient transfusion histories based on best available information. However. ten of the participants (six females. four males) who were enrolled in the NARP reported a history of blood transfusion prior to their enrollment that could not be documented in the blood bank or their medical records. In all cases the transfusion occurred outside of the northern Alberta region. When the respondent was able to recall the year and place of transfusion prior to dialysis. the validity of the self-report was accepted. Included among these ten participants were five who received transfusions during surgery. one who received a transfusion following a motor vehicle collision. three who were transfused after a Caesarian section. and one who received a transfusion as a result of cancer chemotherapy.

Laboratory Methodology

Confirmation of HCV infection was initially done using UBI®HCV EIA 4.0. A second screen with Abbott IMx® microparticle enzyme immunoassay was used to detect antibodies to four recombinant HCV proteins. The RIBA 3.0 immunoblot assay was used as a supplemental assay to discriminate between true and false positive EIA-reactive patients. Serum from all patients was also examined for HCV-RNA by polymerase chain reaction (PCR). The HCV-RNA assay directly detects circulating virus in an infected patient, and HCV infection in cases with ambiguous serology.

Statistical Analysis

All statistical analyses were performed with standard statistical software (SPSS, EpiInfo). Associations between HCV status and categorical variables were assessed with the chi-square statistic. Chi-square for linear trend was used for associations between continuous or ordinal variables and HCV status. When the expected number in any cell was less than five, a two-tailed Fisher's exact test was used. Two-sample t-test, Satterthwaite's method for independent samples with unequal variances, was used to compare means.

In an effort to reduce the number of covariates, preliminary bivariate analyses were conducted between each covariate with HCV status (appendix 4). The following independent variables were entered into a multiple logistic regression model, with HCV infection as the outcome variable: age group (18-55 years versus 56 years and over), education (post-secondary versus grade 12 and lower), length of time on dialysis

(less than 5 years versus 5 years and greater), number of hours on hemodialysis (less than 1300 hours versus 1300 hours and greater), serum ALT in last six months (elevated versus normal), blood transfusion, number of units transfused prior to 1990 (4 units or less versus 5 units or more), organ transplant before 1990, acupuncture, marijuana use, household contact with a known hepatitis case, multiple sexual partners, a history of high-risk lifestyle behaviour (yes/no), and two or more high risk lifestyle behaviours. Cut-points were chosen to optimize the number of participants per cell while providing logical dichotomies. Using $p > 0.15$ as a removal criterion, a parsimonious model was chosen by backward elimination (appendix 5). Logistic-regression modeling with exact inference (Mehta *et al.* 1995) was used to determine the independent contributions of risk factors in predicting anti-HCV positivity, adjusting for all other significant covariates. Adjusted odds ratios and 95% confidence intervals were derived.

Results

The mean age of the dialysis population (Table 2-1) was 57.4 years. Sixty percent were males and the mean length of dialysis was less than three and half years. Almost sixty-percent of participants were undergoing hemodialysis.

The prevalence of anti-HCV antibody in this population was determined to be 6.5% (22/336). There was no case of anti-HCV negativity and HCV-RNA positivity. Seventy-seven percent (17/22) of anti-HCV positive patients also had detectable HCV-RNA. The prevalence of HBsAg was only 1.2% (4/336) and independent of HCV

infection. The mean age of anti-HCV positive patients was significantly lower than that for anti-HCV negative patients (45.8yrs vs. 58.2. t=2.40. p=0.023). Conversely. the mean length of time on dialysis was shorter for anti-HCV negative patients (7.3yrs vs. 3.1yrs. t=1.77. p=0.091).

Table 2-1. Description of the Study Population

Characteristic	**N = 336**
Age in Years (mean. SD)	57.4. ± 15.5
Gender (n. %)	
Females	132 (39.3)
Males	204 (60.7)
Years of Dialysis* (mean. SD)	3.3. ± 3.8
Current Dialysis Mode (n. %)	
Peritoneal Dialysis	135 (40.2)
Hemodialysis	201 (59.8)

* Excluding time on transplant

The prevalence of HCV infection was comparable for the 3 main hemodialysis centres in the NARP (9.5% vs. 9.6% vs. 9.3%).

Gender and birth country did not vary significantly with anti-HCV positivity (Table 2-2). Age was shown to be significantly associated to HCV status in this population. The risk being the greatest for those aged 40 – 59 years of age.

Table 2-2. Demographic characteristics in relation to anti-HCV Positivity

Variable	Total No. of Patients	Anti-HCV Positive n (%)	Odds Ratio	95% C.I.
Gender				
Male	204	15 (7.4)	1.4	0.53, 4.2
Female	132	7 (5.3)	1.0	(referent)
Age				
18 – 39 yrs	51	4 (7.8)	13.8	1.3, 694.3
40 –59 yrs	119	17 (14.3)	27.3	4.2, 1159.7
60+ yrs	166	1 (0.6)	1.0	(referent)
Birth				
In Canada	234	18 (7.7)	2.0	0.65, 8.5
Abroad	102	4 (3.9)	1.0	(referent)

Among dialysis history determinants of HCV status (Table 2-3), an increasing length of time on dialysis, greater than 2800 hours of hemodialysis, elevated serum ALT over six months, previous transplantation, and transplant before 1990 were found to be significant.

A history of previous transfusion in itself was not significantly associated with anti-HCV status (Table 2-4). Although a transfusion history prior to 1990 (the year that donor testing for anti-HCV was made available) carried an unadjusted risk of 6.2 (95% CI: 2.3, 17.3). This risk was further demonstrated by a dose-response relationship when the number of units transfused prior to 1990 was examined by HCV status.

Table 2-3. Dialysis History characteristics in relation to anti -HCV Positivity

Variable	Total No. Of Patients	Anti-HCV Positive n (%)	Odds Ratio	95% C.I.
Years of Dialysis[#]				
< 2 years	166	4 (2.4)	1.0	(referent)
2 – 4 years	109	6 (5.5)	2.4	0.54, 11.6
≥ 5 years	61	12 (19.7)	9.8	2.8, 43.5
Dialysis History				
PD only	61	2 (3.3)	1.0	(referent)
HD only	168	12 (7.1)	2.3	0.48, 21.5
HD & PD	107	8 (7.5)	2.4	0.45, 23.7
Current Dialysis Mode				
PD	135	6 (4.4)	1.0	(referent)
HD	201	16 (8.0)	1.9	0.67, 6.0
HD Hours*				
None	61	2 (3.3)	1.0	(referent)
< 600	120	5 (4.2)	1.3	0.20, 13.8
600 – 1300	52	1 (1.9)	0.6	0.01, 11.4
1300 – 2800	51	3 (5.9)	1.8	0.20, 22.8
≥ 2800	52	11 (21.2)	7.8	1.6, 75.8
ALT in last 6 months				
Normal	298	15 (5.0)	1.0	(referent)
Elevated[∞]	38	7 (18.4)	4.2	1.4, 12.1
Transplant				
Yes	69	11 (15.9)	4.6	1.7, 12.3
No	267	11 (4.1)	1.0	(referent)
Transplant before 1990				
Yes	41	8 (19.5)	4.8	1.6, 13.5
No	295	14 (4.8)	1.0	(referent)

[#] Excluding time on transplant HD = Hemodialysis PD = Peritoneal Dialysis

* Includes PD patients who initially received HD ALT = serum alanine aminotransferase

[∞]Greater than 60 IU/L in any month

Other parenteral exposures (Table 2-5) associated with being anti-HCV positive included acupuncture (OR = 3.6, 95% CI: 1.21 – 9.91) and tattoo (OR = 3.8, 95% CI: 1.00 – 12.13).

Several lifestyle factors were strongly associated with being hepatitis C positive (Table 2-6). These included the use of street drugs, sexual contact with a street drug user (SDU) or a hepatitis case, household contact with a SDU or a hepatitis case, and having been jailed.

Table 2-4. Transfusion History characteristics in relation to anti -HCV Positivity

Variable	Total No. of Patients	Anti-HCV Positive n (%)	Odds Ratio	95 % C.I.
Blood & Blood Products	256	20 (7.8)	3.3	0.77, 29.7
Yes	80	4 (4.2)	1.0	(referent)
No				
Before 1990				
Yes	72	13 (18.1)	6.20	2.3, 17.3
No	264	9 (3.4)	1.0	(referent)
No. of Transfusions				
Never	80	2 (2.5)	1.0	(referent)
1 – 4	92	2 (4.4)	1.8	0.25, 20.0
5 – 9	43	6 (14.0)	6.2	1.1, 65.8
≥ 10	121	10 (8.3)	3.5	0.71, 9.5
No. of Transfusions Before 1990				
Never	264	9 (3.4)	1.0	(referent)
1 – 4	50	6 (12.0)	3.8	1.1, 12.8
5 – 9	11	6 (54.55)	32.5	6.9, 164.3
≥ 10	11	1 (9.1)	2.82	0.06, 24.3

Table 2-5. Other Parenteral characteristics in relation to anti -HCV Positivity

Variable	Total No. of Patients	Anti-HCV Positive n (%)	Odds Ratio	95 % C.I.
Acupuncture				
Yes	53	8 (15.1)	3.6	1.21, 9.91
No	275	13 (4.7)	1.0	(referent)
Ear Piercing				
Yes	108	9 (9.1)	1.5	0.60, 3.53
No	222	13 (5.9)	1.0	(referent)
Body Piercing				
Yes	2	0 (0)	6.1	0.00, 79.30
No	326	21 (6.4)	1.0	(referent)
Tattoo				
Yes	27	5 (18.5)	3.8	1.00, 12.13
No	303	17 (5.6)	1.0	(referent)

Table 2-6. Lifestyle characteristics in relation to anti -HCV Positivity

Variable	Total No. of Patients	Anti-HCV Positive n (%)	Odds Ratio	95 % C.I.
Currently Smoke				
Yes	77	7 (9.1)	1.7	0.55. 4.7
No	249	14 (5.6)	1.0	(referent)
Ever Used Marijuana				
Yes	61	11 (18.0)	5.1	1.9. 13.8
No	268	11 (4.1)	1.0	(referent)
Ever Used Cocaine				
Yes	18	7 (38.9)	14.2	4.00. 48.6
No	309	13 (4.2)	1.0	(referent)
Ever Injected Drugs				
Yes	11	8 (72.7)	55.3	11.8. 358.6
No	317	14 (4.4)	1.0	(referent)
Household Contact With SDU*				
Yes	41	7 (17.1)	4.0	1.3. 11.5
No	287	14 (4.9)	1.0	(referent)
Sex with SDU*				
Yes	21	7 (33.3)	11.3	3.3. 37.6
No	289	12 (4.2)	1.0	(referent)
Household Contact with Hepatitis Case †				
Yes	41	8 (19.5)	5.1	1.7. 14.4
No	287	13 (4.5)	1.0	(referent)
Sex with Hepatitis Case†				
Yes	8	3 (37.5)	10.6	1.5. 60.1
No	303	16 (5.3)	1.0	(referent)
STD History				
Yes	28	4 (14.3)	3.0	0.67. 10.4
No	284	15 (5.3)	1.0	(referent)
Sexual Partners				
None / One	170	6 (3.5)	1.0	(referent)
Multiple	139	13 (9.4)	2.8	0.96. 9.3
Been Jailed				
Yes	23	5 (21.7)	5.0	1.3. 16.5
No	305	16 (5.2)	1.0	(referent)

*SDU – Street Drug User

†any type of hepatitis infection

As several of the lifestyle factors were not mutually independent, and to facilitate the multivariate analysis, the number of high risk lifestyle behaviours per participant was calculated. A high risk lifestyle behaviour was defined as having engaged in any one of the following activities: body piercing, tattooing, cocaine use, injecting drug use, household contact with a street drug user, sexual contact with a street drug user, sexual contact with a known hepatitis case, a STD history, being jailed and taking part in blood rituals.

Table 2-7. High Risk Lifestyle Behaviour in relation to anti -HCV Positivity

Variable	Total No. of Patients	Anti-HCV Positive n (%)	Odds Ratio	95 % C.I.
HRLB				
Yes	93	16 (17.2)	7.9	2.8, 25.7
No	237	6 (2.5)	1.0	(referent)
No. of HRLBs				
0	237	6 (2.5)	1.0	(referent)
1	55	7 (12.7)	5.6	1.5, 21.0
2+	38	9 (23.7)	11.8	3.5, 43.3

HRLB = High-Risk Lifestyle Behaviour

Having at least one high-risk lifestyle behaviour yielded an OR = 7.9 (95% CI: 2.8 – 25.7) indicating a significant association with anti-HCV positivity. More interestingly, a strong cause and effect relationship is exhibited between the number of high-risk lifestyle behaviours and anti-HCV positivity (χ^2trend = 27.4, $p < 0.00001$).

The multiple logistic regression analysis revealed significant predictors of HCV infection to include age, years on dialysis and high-risk lifestyle behaviour (Table 2-8). Specifically the odds ratio was 4.86 for the 18-55 years of age category compared to those 55 years old and over, 3.7 for those having been on dialysis for more than five

years. and 4.95 for those having engaged in two or more high-risk lifestyle behaviours. The odds ratio for multiple (≥5) transfusions prior to 1990 was 4.02 with a lower 95 percent confidence limit of 0.96. The Hosmer-Lemeshow test statistic (3.644. p > 0.30) indicated that the null hypothesis was not rejected and the model was useful in predicting the outcome accurately.

Table 2-8. Predictors of HCV infection

Predictor Variable	Odds Ratio	95 % CI	p-value
Age (18 – 55 years)	4.86	1.24. 27.90	0.019
≥ 5 years of dialysis	3.70	1.16. 12.04	0.026
≥ 2 HRLBs*	4.95	1.48. 16.72	0.008
Transfusion with more than 5 units prior to 1990	4.02	0.96. 16.30	0.057
Model diagnostics:	*Likelihood Ratio Statistic = 347.68. 5 df* *Deviance = 15.44. 9 df. p > 0.05* *Hosmer-Lemeshow Test Statistic = 3.644. 3 df. p > 0.30*		

*HRLBs = High-risk lifestyle behaviours

Discussion

This study was conducted to provide representative data for Northern Alberta. while supplying data that may be more useful broadly. Because of the inherent differences that may exist in geographically and demographically dissimilar areas. these findings may not necessarily apply to other dialysis populations. and should be generalised only with caution.

A significant age difference between eligible and ineligible participants was detected (mean age 57.2 vs. 63.4. t = 2.21. p < 0.05). The ineligible were older. and given the

lower prevalence of HCV infection documented in the older age group of participants. it is reasonable to expect that the actual prevalence within our dialysis population is lower than the 6.5 % reported here. The burden of HCV infection was often found to be greatest in those 40 – 50 years of age. which was well below the mean age of NARP patients.

The prevalence of anti-HCV antibodies among dialysis patients in Northern Alberta appears low compared to other dialysis centers (Chan *et al.* 1993: Niu *et al.* 1993: Dussol *et al.* 1995). In particular. HCV prevalence was well below that of the 10 – 20% quoted for North American centres (Alter. 1997). As HCV-RNA was not detected in any patient who was anti-HCV negative. the data suggest that renal dialysis patients with HCV infection are able to mount an immune response. Because highly sensitive. third generation tests were used to document the presence of anti-HCV antibodies. the low prevalence is unlikely to result from under ascertainment of infection. but rather reflects stringent infection control practices.

The fact that 68.2 % (15/22) of the HCV-positive patients had normal ALT levels over a six-month period. suggests that ALT cannot be used as a surrogate marker of HCV infection in dialysis patients. With 77 % of positive patients being viremic (HCV-RNA detected) and two-thirds having normal ALT levels. a biopsy may be necessary to determine whether these patients have liver injury.

The finding that 77 % of anti-HCV positive dialysis patients had detectable HCV-RNA. and that serologic positivity correlated with length of time on dialysis raised the question of whether non-infected dialysis patients were at risk of nosocomial infection. and whether specific dialysis machines should be dedicated for use by anti-HCV positive patients. Several factors argue against this interpretation: (1) infection may have been acquired for many of these patients before they began dialysis: (2) similar prevalence of HCV was seen among the three main hemodialysis units: and (3) there was not a statistically significant difference in HCV prevalence between dialysis modalities. This is consistent with other studies that report adherence to the universal infection control guidelines in a dialysis population is sufficient to prevent nosocomial transmission of HCV (Jadoul. 1996: Seme *et al.* 1997). Given that baseline infection has been determined. prospective seroconversion studies can now be conducted to verify the issue of nosocomial transmission.

The published literature on anti-HCV among patients on dialysis have attributed transfusion history. dialysis history. previous organ transplantation and nosocomial transmission as risk factors (Druwe *et al.* 1994: Huraib *et al.* 1995: Terrault *et al.* 1995b: Murthy *et al.* 1997). Others have reported injecting drug use as an additional risk factor in this population (Stempel *et al.* 1993: Jadoul. 1996: Periera *et al.* 1997). Nonetheless. there has been a distinct gap in the literature regarding other potential risk factors in dialysis patients. This study documented previously unreported lifestyle risk factors for HCV infection in patients with renal failure.

In the NARP, all HCV-infected patients had at least one risk factor (either a high-risk lifestyle behaviour or a transfusion history prior to 1990). The majority of HCV infected dialysis patients (> 70%) had evidence of high-risk lifestyle behaviour(s). Bivariate analyses suggested that those high risk lifestyle behaviours were more strongly associated with HCV status than transfusion history, even transfusions prior to 1990. The multiple logistic analysis corroborated this, finding that high risk lifestyle factors remained significantly associated with HCV status while multiple transfusions prior to 1990 only marginally associated with it, suggesting independent effect of transfusion-related infection after controlling for high-risk lifestyle behaviours. It should also be considered that the relationship between high-risk lifestyle behaviours and anti-HCV positivity might have been underestimated as patients could have withheld this sensitive information.

This study documented the low prevalence of HCV infection in dialysis patients in northern Alberta and described the risk factors. Thorough review of all transfusion records and the use of highly sensitive tests for HCV infection permitted a valid assessment of the impact of transfusion prior to 1990 on risk of HCV infection. However, the dialysis population in 1997 probably includes relatively few of those who were in the NARP and received transfusions prior to 1990. Many of those who were transfused prior to 1990 (especially those multiply transfused) would have died. As a result the risk estimates for those transfused prior to 1990 reflects accurately the current situation, but may underestimate the historical impact of transfusion related HCV infection in this population.

The data suggest that blood transfusions are no longer a risk factor for hepatitis C seroconversion and the *control* of blood products for the presence of anti-HCV antibodies is working in practice. It is worthwhile to note that within this poly-transfused population. risk-taking lifestyle behaviour are important predictors of hepatitis C risk.

References

Allander T. Medin C. Jacobson SH. et al. (1994): Hepatitis C transmission in a hemodialysis unit: Molecular evidence for spread of virus among patients not sharing equipment. **Journal of Medical Virology** 43:415-419.

Al Meshari K. Al Ahdal M. Alfurayh O. Ali A. et al. (1995): New insights into HCV infection of hemodialysis patients: the implications. **American Journal of Kidney Diseases** 25:572-78.

Alter MJ (1997): Epidemiology of Hepatitis C. **Hepatology** 26:62S-65S.

Bouthot BA. Murthy BVR. Schmid CH. Levey AS. et al. (1997): Long-term follow-up of hepatitis C virus infection among organ transplant recipients. **Transplantation** 63:849-853.

Chan T. Lok AS. Cheng IK. Chan RT (1993): Prevalence of HCV infection in hemodialysis patients: a longitudinal study comparing the results of RNA and antibody assays. **Hepatology** 17:5-8.

Chauveau P (1996): Epidemiology of hepatitis C virus infection in chronic hemodialysis. **Nephrology Dialysis Transplantation** 11(S4):39-41.

Druwe PM. Michielsen PP. Ramon AM. De Broe ME (1994): Hepatitis C and nephrology. **Nephrology Dialysis Transplantation** 9:230-237.

Dussol B. Berthezene P. Brunet P. Roubicek C. et al. (1995): Hepatitis C Virus infection among chronic dialysis patients in the south of France: A Collaborative Study. **American Journal of Kidney Diseases** 25:399-404.

Golan E. Korzets Z. Cristal-Lilov A. Ben-Tovim T. et al. (1996): Increased prevalence of HCV antibodies in dialyzed Ashkenazi Jews - a possible ethnic predisposition. **Nephrology Dialysis Transplantation** 11:684-686.

Huraib S. Al-Rashed R. Aldrees A. Aljefry M. et al. (1995): High prevalence of and risk factors for hepatitis C in hemodialysis patients in Saudi Arabia: a need for new dialysis strategies. **Nephrology Dialysis Transplantation** 10:470-474.

Ifudu O. Macey LJ. Friedman EA (1995): Resurgence of blood transfusion therapy in erythropoietin treated hemodialysis patients. **ASAIO Journal** 41:426-30.

Izopet J. Rostaing L. Moussion F. Alric L. et al. (1997): High rate of HCV clearance in hemodialysis patients after interferon- therapy. **Journal of Infectious Diseases** 176:1614-1617.

Jadoul M (1996): Transmission routes of HCV infection in dialysis. **Nephrology Dialysis Transplantation** 11(S4):36-38.

Jenkins PJ. Cromie SL. Dudley FJ. Chronic hepatitis C: Factors predictive of hepatic fibrosis and disease progression. **IX Triennial International Symposium on Viral Hepatitis and Liver Disease** (abstract volume) April 21-25 1996. Rome. Italy.

Kirk AD. Heisey DM. D'Alessandro AM. Knechthle SJ. et al. (1996): Clinical hepatitis after transplantation of hepatitis C virus-positive kidneys. **Transplantation** 62:1758-1762.

Mehta C. Patel N (1995): Exact Logistic Regression: Theory and Examples. **Statistics in Medicine** 14:2143-2160.

Murthy BVR. Pereira BJG (1997): A 1990s perspective of HCV. HIV. and TB infections in dialysis patients. **Seminars in Nephrology** 17:346-363.

Niu MT. Coleman PJ. Alter MJ (1993): Multicenter study of hepatitis C virus infection in chronic hemodialysis patients and hemodialysis center staff members. **American Journal of Kidney Diseases** 22:568-573.

Nordenfelt E. Current Epidemiological trends in Northern Europe. **IX Triennial International Symposium on Viral Hepatitis and Liver Disease** (abstract volume) April 21-25 1996. Rome. Italy.

Pereira BJG. Levey AS (1997): Hepatitis C virus infection in dialysis and renal transplantation. **Kidney International** 51:981-90.

Pol S. Romeo R. Zins B. Driss F. et al. (1993): Hepatitis C virus RNA in anti-HCV positive hemodialyzed patients: significance and therapeutic implications. **Kidney International** 44:1097-1100

Ricci A. Scalori A. Simeoni E. Bellati G. et al. Interferon neutralizing antibodies in breakthrough during therapy with natural alpha IFNs for HCV chronic hepatitis. **IX Triennial International Symposium on Viral Hepatitis and Liver Disease** (abstract volume) April 21-25 1996. Rome. Italy.

Roth D (1995): Hepatitis C Virus: The Nephrologist's View. **American Journal of Kidney Diseases** 25:3-16.

Roth D. Zucker K. Cirocco R. Burke G. et al. (1996): A prospective study of hepatitis C virus infection in renal allograft recipients. **Transplantation** 61:886-889.

Santos JP. Loureiro A. Neto MC. Pereira BJG (1996): Impact of dialysis room and reuse strategies on the incidence of HCV infection in hemodialysis units. **Nephrology Dialysis Transplantation** 11:2017-22.

Seme K. Poljak M. Zuzek-Resek S. Debeljak M. et al. (1997): Molecular evidence for nosocomial spread of two different HCV strains in one hemodialysis unit. **Nephron** 77:273-278.

Soni PN. Tait DR. Gopaul W. Sathar MA. Simjee AE (1996): Hepatitis C virus infection in chronic liver disease in Natal. **South African Medical Journal** 86:80-3.

Stempel CA. Lake J. Kuo G. Vincenti F (1993): Hepatitis C – Its prevalence in end-stage renal failure patients and clinical course after kidney transplantation. **Transplantation** 55:273-276.

Tandon BN. Tandon A. Acharya SK. Current epidemiological trends of viral hepatitis in Asia. **IX Triennial International Symposium on Viral Hepatitis and Liver Disease** (abstract volume) April 21-25 1996. Rome. Italy.

Terrault N. Wright T. (1995a): Hepatitis C Virus in the setting of transplantation. **Seminars in Liver Disease** 15:92-100.

Terrault N. Wright T. Pereira B. (1995b): Hepatitis C Infection in the transplant recipient. **Infectious Disease Clinics of North America** 9:943-964.

Tong MJ. El-Farra NS. Reikes AR. Co RL (1995): Clinical outcomes after transfusion-associated hepatitis C. **The New England Journal of Medicine** 332:1463-6.

Umlauft F. Gruenwald K. Weiss G. Kessler H. et al. (1997): Patterns of hepatitis C viremia in patients recieving hemodialysis. **American Journal of Gastroenterology** 92:73-8.

Vranckx R. Van Damme P. The epidemiology of HCV in Belgium. **IX Triennial International Symposium on Viral Hepatitis and Liver Disease** (abstract volume) April 21-25 1996. Rome. Italy.

Zeuzem S. Scheuermann EH. Waschk D. Lee J. et al. (1996): Phylogenetic analysis of hepatitis C virus isolates from hemodialysis patients. **Kidney International** 49:896-902.

Chapter 3

Validation of self-reported transfusion histories in renal dialysis patients

Introduction

Blood transfusion was commonly given to patients with end-stage renal disease prior to the introduction of recombinant erythropoietin (Pereira *et al.* 1997). Despite the introduction of a variety of pharmacological agents and greater awareness of existing and emerging blood-borne diseases, blood transfusions persist as an important therapy to combat anemia and other complications arising in dialysis patients (Ifudu *et al.* 1995).

Most investigations of the relationship between transfusion history and hepatitis C status in dialysis populations have relied on self-reported information (Dussol *et al.* 1995; Knudsen *et al.* 1993; Neto *et al.* 1995; Niu *et al.* 1993). Self-reported exposure data are vulnerable to recall bias, which threatens the internal validity of a study. Retrospective interviews rely heavily on respondents' recall, and often there are no existing records available for validation of the self-reported exposures (Clark *et al.* 1997). Factors that may influence accuracy of self-report include: 1) the importance of the exposure(s) to the individual, 2) the way the exposure is defined and its interpretation by the participant, 3) the time frame in which the exposure(s) occurs and 4) the participant's knowledge about the exposure and how precisely it is disclosed to the interviewer (Warnecke *et al.* 1997; Olson *et al.* 1997).

The purpose of this paper is to assess the validity of self-reported transfusion histories in dialysis patients. Using data from a cross-sectional study of a dialysis population being investigated for hepatitis C infection, the correspondence between self-reported

transfusion history and transfusion records was explored. Demographic data and dialysis histories were examined in relation to the accuracy of self-reports. The data may have implications for other studies involving patients with chronic conditions.

Method

Data were taken from a study into risk factors for hepatitis C infection among the Northern Alberta dialysis population. This was a cross-sectional survey of patients actively dialyzing on the Northern Alberta Renal Program (NARP) on July 1, 1997. The NARP serves all renal dialysis patients in northern Alberta. Three hundred and thirty-six patients, representing ninety-two percent of eligible patients aged 18 years and older provided informed consent. The study protocol was approved by the Medical Ethics Review Board of the Faculty of Medicine at the University of Alberta. Participants and non-participants were comparable for age and gender (appendix 1). Participants were interviewed by the same interviewer using a questionnaire (appendix 2) comprising demographic, dialysis-specific, medical history and lifestyle variables. A combination of in-person and telephone interviews was employed. No systematic differences were seen between the two interview methods (appendix 3) and interviewees were comparable for age and gender irrespective of interview method (appendix 1).

Participants were asked whether they had ever had a blood transfusion. Separate questions enquired about transfusions while on dialysis and transfusion prior to dialysis. The number of transfusions and their locations were also requested.

The transfusion records of the University of Alberta Hospital (UAH) Blood Bank have been computerised back to 1988. The UAH Blood Bank records all transfusions of dialysis patients in the NARP. Although complete transfusion histories were sought from the UAH Blood Bank records for all dialysis patients, there was less confidence in the completeness of these records prior to 1988. Therefore, the present analysis was limited to dialysis patients who enrolled in the NARP since 1988 (n=294). The accuracy of the self-reports was assessed by comparison with the UAH Blood Bank records (i.e., "gold standard"). Ten of the participants (6 females, 4 males) who were enrolled in the NARP since 1988 reported a history of blood transfusion prior to their enrollment that could not be documented in the blood bank records. In all cases the transfusion occurred outside of the northern Alberta region. When the respondent was able to recall both the year and place of transfusion prior to dialysis, the validity of the report was accepted (i.e., a "true positive"). Included among these ten participants were five who received transfusions during surgery, one who received a transfusion following a motor vehicle collision, three who were transfused after a Caesarian section, and one who received a transfusion as a result of cancer chemotherapy.

With the exception noted directly above, participants were classified as true positives if the blood bank records and the questionnaires both indicated that a transfusion had been done. True negatives had no record of a transfusion on either the questionnaire or the blood bank records. False positives reported a transfusion that was not documented

by the blood bank, and false negatives had documentation of a transfusion in the blood bank records but denied having had a transfusion in the questionnaire.

Agreement between the two transfusion history measures was summarized by the kappa statistic. Chi-square tests were used to compare the demographic and dialysis history characteristics of participants who were categorized according to the accuracy of measurement. For continuous variables (e.g. age and years on dialysis), the groups were compared using analysis of variance techniques.

Results

The mean age of the dialysis population (Table 3-1) was 58.9 years. Nearly two-thirds were males and the mean length of dialysis was less than two and half years. Almost sixty-percent of participants were undergoing haemodialysis.

Table 3-1. Description of the Study Population

Characteristic	**n = 294**
Age in Years (mean, SD)	58.9, ± 15.2
Gender (n, %)	
Males	174 (62.4)
Females	105 (37.6)
Years of Dialysis (mean, SD)	2.4, ± 2.0
Current Dialysis Mode (n, %)	
Peritoneal Dialysis	115 (41.2)
Haemodialysis	164 (58.8)

Comparison of the two sources of transfusion histories (Table 3-2) showed that 66.0% of the participants were true positives (194/294), 6.5% were false positives (19/294), 4.8% were false negatives (14/294) and 22.8% were true negatives (67/294). Overall, the questionnaire data and the blood bank records agreed for 89 percent of participants. The Kappa statistic was 0.72 ($Z=12.43$, $p < 0.0001$), indicating an acceptable level of agreement that was significantly greater than that expected by chance (Fleiss, 1981).

Table 3-2. Comparison of questionnaire response and blood bank records for a history of a blood transfusion

		Blood Bank Records	
		Yes n (%)	No n (%)
Questionnaire Response	Yes	194 (93.3)	19 (22.1)
	No	14 (6.7)	67 (77.9)
		208 (100)	86 (100)

Of those who had a record of a blood transfusion, 93 percent reported this on their questionnaires (i.e., sensitivity = 0.93) (Table 3-3). Of those who did not have a record of a blood transfusion, 78 percent were correctly classified by the questionnaire. In this population with 71 percent having a documented history of a blood transfusion, 91 percent of those who reported a blood transfusion had a documented history (i.e. positive predictive value = 0.91). Eighty-three percent of those who claimed no history of a transfusion had no documented evidence of a transfusion.

Table 3-3 Validity measures of self-reported transfusion history

Measure	Transfusion since Dialysis
Sensitivity [95% CI]	0.93 [0.89. 0.96]
Specificity [95% CI]	0.78 [0.67. 0.85]
Positive Predictive Value [95% CI]	0.91 [0.86. 0.94]
Negative Predictive Value [95% CI]	0.83 [0.72. 0.90]

The groups were found to differ significantly by age and by years on dialysis (Table 3-4). The average age of the false negatives was the highest and the true negatives the lowest of the four groups. The true negatives had the lowest mean number of years of dialysis.

Table 3-4 Comparison of age and years on dialysis for dialysis patients classified by agreement between blood bank records (reference) and self-report.

	True Positives mean ± SD	False Positives mean ± SD	False Negatives mean ± SD	True Negatives mean ± SD	ANOVA p value
Age (yrs)	59.9 ± 15.7	60.2 ± 9.8	64.9 ± 8.8	54.6 ± 15.1	F=2.91. p=0.006
Years on Dialysis	2.8 ± 2.2	2.3 ± 2.0	2.6 ± 2.1	1.4 ± 1.1	F=8.59. p=0.001

There was a significant association between the validity of the self-report and education (Table 3-5). The overall level of agreement was greatest for those with at least some post-secondary education. None of the participants with post-secondary

education were false negatives (i.e., had a documented history of a transfusion but stated they did not).

Some of the participants (n=26) were unable to complete the questionnaires themselves. Twenty-four of these had been transfused and the proxies were aware of 23 of them.

As expected transfusion was more common among haemodialysis patients compared to those on peritoneal dialysis. Of the haemodialysis patients, 80 percent had a history of transfusion (true positives plus false negatives) compared to 58 percent of the peritoneal dialysis patients. Nearly equal proportions of both groups were misclassified by the questionnaire. Only two of the 124 peritoneal dialysis patients (1.6 %) were unaware of a past transfusion.

Those who had received a transplant in the past were more likely to have received a blood transfusion and were more likely to accurately recall their transfusion history. Of those who had not undergone a transplant, 25 percent had received a transfusion that was not acknowledged on the questionnaire. [Results for other variables are outlined in appendix 6.]

Table 3-5 Comparison of dialysis patients classified by agreement between blood bank records (reference) and self-report.

	True Positives n (%)	False Positives n (%)	False Negatives n (%)	True Negatives n (%)	χ^2, df p value
Education					
≤ Grade 9	74 (71.8)	7 (6.8)	8 (7.8)	14 (13.6)	
Grade 10 - 12	75 (63.0)	6 (5.0)	6 (5.0)	32 (26.9)	12.9. 6 df
Post-Secondary	45 (62.5)	6 (8.3)	0 (0)	21 (29.2)	0.04
Proxy Interview					
Yes	23 (88.5)	0 (0)	1 (3.8)	2 (7.7)	6.9. 3 df
No	171 (63.8)	19 (7.1)	13 (4.9)	65 (24.3)	0.07
Dialysis Centre					
Haemodialysis	124 (72.9)	7 (4.1)	12 (7.1)	27 (15.9)	19.3. 3 df
Peritoneal	70 (56.5)	12 (9.7)	2 (1.6)	40 (32.3)	0.001
Transplant					
Yes	31 (88.6)	1 (2.9)	1 (2.9)	2 (5.7)	9.3. 3 df
No	163 (62.9)	18 (6.9)	13 (5.0)	65 (25.1)	0.03

Discussion

Use of the blood bank records as the *'gold standard'* implies certain assumptions that may not be true in all cases. It is possible. for example. that patients may have been transfused while on dialysis but outside of northern Alberta. This would have affected mainly the rate of false positives but may also have affected the true negatives. Those with transfusion during dialysis but outside of the NARP would have been wrongly included as false positives while those who were transfused outside of the NARP and did not recall their transfusion would have been incorrectly classified as true negatives.

It should be noted that clinical charts were reviewed for all participants. It is likely that transfusions received outside of the catchment area would have been noted on return to the area. Also this analysis included only patients who were continuously enrolled in the NARP since the time that the blood bank records were computerised. The comprehensive nature of the NARP and the blood bank records minimised the possibility of missing transfusion data.

The primary outcome of interest in the main study was the presence of hepatitis C infection. To explore the effect of exposure misclassification on the risk estimates, hepatitis C status was compared to transfusion history classified according to the blood bank records and the questionnaire responses. Using the blood bank records, the odds ratio for hepatitis C infection associated with blood transfusion was 1.87 (95% CI: 0.40 - 8.83). Using the questionnaire response, the odds ratio was 1.40 (95% CI: 0.29, 6.64). This result illustrates the usual effect of nondifferential and independent misclassification on a measure of association (i.e. bias towards the null value) (Kelsey *et al*, 1996).

Of the 26 proxy respondents in this study there was 96% agreement between their recollection of the participant's transfusion history and that documented in the blood bank records. This is reassuring in this population that includes a significant number of older and/or very ill individuals. Misclassification of exposures by proxy respondents has been shown to bias estimates of exposure-disease associations (Nelson *et al*, 1990).

Underreporting of transfusions caused by forgetting may account for the associations between both age and length of time on dialysis and the validity of the questionnaire responses. Whether this is a result of the impaired neuropsychological mechanisms in the abnormal chemical environment imposed by renal failure cannot be excluded (Brickman *et al.* 1996).

Although the relationship between the validity of self-reported transfusion history and education level was not strong, the (generally) better recall among the more highly educated patients underlines the need to communicate clearly information on medical procedures in this population.

A recent inquiry into Canada's blood supply noted "few hospitals considered asking patients to sign a consent form before they were given blood or blood products" (Capen, 1995). Conceivably within a dialysis setting, where patients sign a one-time consent form to all medical treatments for their end-stage renal failure, patients may be unaware of being transfused while haemodialyzing. Given the findings presented here, it appears that epidemiological investigations (in Canada at least) into blood-borne pathogens acquired by transfusion will require strict scrutiny of all available information sources for patient transfusion histories. Communicating transfusion-related risk must be reasoned and based on the *best available* epidemiological evidence.

References

Brickman AL. Yount SE. Blaney NT. Rothberg S. De-Nour AK (1996): Pathogenesis of cognitive complaints in patients on hemodialysis. **General Hospital Psychiatry** 18:36–43.

Capen K (1995): Informed consent and blood transfusions: What does Krever's interim report mean to doctors. **Canadian Medical Association Journal** 152:1663-65.

Clark K. Fu C. Burnett C (1997): Accuracy of birth certificate data regarding the amount and. timing. and adequacy of prenatal care using prenatal clinic medical records as referents. **American Journal of Epidemiology** 145:68-71.

Dussol B. Berthezene P. Brunet P. Roubicek C. et al. (1995): Hepatitis C Virus infection among chronic dialysis patients in the south of France: A Collaborative Study. **American Journal of Kidney Diseases** 25:399–404.

Fleiss JL (1981): **Statistical Methods for Rates and Proportions.** 2nd Ed. New York. John Wiley & Sons.

Ifudu O. Macey LJ. Friedman EA (1995): Resurgence of blood transfusion therapy in erythropoietin treated hemodialysis patients. **ASAIO Journal** 41:426-30.

Kelsey JL. Whittemore AS. Evans AS. Thompson WD (1996): **Methods in Observational Epidemiology.** 2nd Ed.. New York. Oxford University Press.

Knudsen F. Wantzin P. Rasmussen K. Ladefoged SD. et al. (1993): Hepatitis C in dialysis patients: relationship to blood transfusions. dialysis and liver disease. **Kidney International** 43:1353-1356.

Law MG. Hurley SF. Carlin JB. Chondros P. et al. (1996): A comparison of patient interview data with pharmacy and medical records for patients with AIDS or HIV infection. **Journal of Clinical Epidemiology** 49:997-1002.

Nelson LM. Longstreth WT. Koepsell TD. van Belle G (1990): Proxy respondents in epidemiologic research. **Epidemiologic Reviews** 12:71-86.

Neto MC. Rodrigues-Manzano SI. Canziani ME. Silva AEB. et al. (1995): Environmental transmission of hepatitis B and hepatitis C viruses within the hemodialysis unit. **Artificial Organs** 19:251-255.

Niu MT. Coleman PJ. Alter MJ (1993): Multicenter study of hepatitis C virus infection in chronic hemodialysis patients and hemodialysis center staff members. **American Journal of Kidney Diseases** 22:568-573.

Olson JE. Shu XO. Ross JA. Pendergrass T. Robison L (1997): Medical records validation of maternally reported birth characteristics and pregnancy-related events: a report from the children's cancer group. **American Journal of Epidemiology** 145:58-67.

Pereira BJG. Levey AS (1997): Hepatitis C virus infection in dialysis and renal transplantation. **Kidney International** 51:981-90.

Warnecke RB. Sudman S. Johnson TP. O'Rourke D. et al. (1997): Cognitive aspects of recalling and reporting health-related events: Papanicolaou smears. clinical breast examinations. and mammograms. **American Journal of Epidemiology** 146:982-92.

Chapter 4

Discussion and Conclusions

A comparatively low prevalence of hepatitis C virus infection in the northern Alberta dialysis population has been established. The 6.5 percent prevalence of HCV infection in this population is significantly higher than the 0.15 percent prevalence detected in the local blood donor population (Canadian Red Cross Society, 1991). This suggests transmission modes other than transfusion are responsible for this several-fold difference.

The use of dedicated dialysis machines by HCV-positive patients has been suggested periodically from studies where high prevalences has been noted (Neto *et al.* 1995). There was no strong evidence for nosocomial acquisition of HCV infection in this population. Rather it appears that strict adherence to universal infection control guidelines is sufficient (Jadoul, 1996; Seme *et al.* 1997). Given that baseline infection has been determined, prospective seroconversion studies can now be conducted to verify the absence of nosocomial transmission.

The risk factor study suggested several routes of transmission that have not been reported previously in dialysis patients. These included well-defined activities such as injecting drug use and intranasal use of cocaine. Other factors that are less easily defined were also identified, including household contact with a street drug user, household contact with a hepatitis case, sexual contact with a street drug user and having been in jail. The lack of comparable HCV data from the general population of Northern Alberta precludes a determination of whether the dialysis population is at especially high risk of HCV infection. Few studies of HCV infection have been

conducted in general population samples (as opposed to blood donors). Those that have been done outside of known areas of high endemicity have shown prevalence estimates between 0.3 and 1.5 percent (Nordenfelt, 1996; Tandon *et al.*, 1996; Vranckx *et al.*, 1996). It is likely, therefore, that the prevalence of HCV infection in Northern Alberta is significantly lower than that found in the dialysis population. The reasons for this high prevalence in the light of the importance of high-risk lifestyle behaviours (vis-a-vis transfusions) warrants further research.

In most immunocompetent persons, HCV infection is detected by enzyme immunoassay. Amplification of RNA from serum may be necessary to detect infection in immunocompromised patients (Cuthbert, 1994). In the 336 patients investigated within the NARP, there was no case of anti-HCV negativity coupled with HCV-RNA detection, suggesting that renal dialysis patients with HCV infection are able to mount an immune response culminating in anti-HCV production. This latter finding, although beyond the scope of this thesis, will be published to assist in the development of standardized HCV diagnostic criteria.

With respects to the third objective of this work, the validity of self-reported transfusion history, it has been verified that there is an acceptable level of agreement (kappa = 0.72) between questionnaire responses and documented histories. A permissible level of prediction was also demonstrated (PPV=0.91, NPV =0.83). Given these findings the internal validity of the main prevalence and risk factor study is not in question. An important epidemiological methodological consideration, that of exposure

misclassification, was confirmed herein to bias the measure of association to the null hypothesis. The concern regarding self-reported transfusion history was verified by this observation. Consequently, the extra expense and time in ascertaining accurate patient transfusion histories based on best available information was well justified.

Exploring the discrepancies between self-reports and documented transfusion histories, reiterates the need to communicate clearly medical interventions in chronically ill patients. Additionally, it advocates that future studies into transfusion acquired blood-borne pathogens need to utilize all available information sources on exposure histories.

The low prevalence of HBV (1.2%) in this population can be attributed to the rigorous HBV vaccination protocols. Prevention of HCV infection by vaccine development is proceeding. The main antigenic differences in hepatitis C, particularly in the envelope region due to ongoing viral mutation, means that a polyvalent vaccine will be required (Dusheiko *et al*, 1996).

The long-term morbidity and mortality from HCV infection in this population has yet to be documented. Natural history studies are complicated by the largely asymptomatic onset of infection and the inability to recognize acute HCV infection. Patients with chronic HCV infection usually have a slowly evolving disease over years and decades with few spontaneous recoveries (Kiyosawa *et al. 1990;* Mattsson *et al. 1993*). Current treatment options for chronically infected dialysis patients offers little hope, and the long-term consequences of any treatment choice on the course of the liver disease,

transplant rejection rates and patient survival need to be evaluated (Pereira *et al.* 1997). The value of a detailed explanation of the possible complications from interferon treatment is often neglected, as there is so little to gain from (current) therapy. The explosion of new and often incomplete information about the diagnosis and treatment of chronic hepatitis C poses this dilemma in a large part (Izopet *et al.* 1997).

The wide media coverage of infectious diseases over the past decade has highlighted the importance of effective risk communication. Communicating about risk of infectious diseases is essential to avoid or minimize unwarranted fear, and to engage health providers and the public in decisions about risk-behaviour modification (Glanz *et al.* 1996). There is little doubt that the Krever Inquiry into the blood system has improved the Canadian population's understanding of hepatitis C (Spurgeon, 1997; Hoey, 1997). Unfortunately the same cannot be said for allaying the fears and distrust with the nation's blood supply. Despite several decades in which all healthy adults have been encouraged to donate blood regularly, the most recent decade has made it obvious that donations are no longer welcomed from the entire community. The involuntary risk of infection through blood transfusions is in the public consciousness and has irrevocably changed the landscape of public health policy in this country.

It is crucial to realize that perceived risk will differ from the objectively quantified risk. The intention of this work was to put specific risks in perspective, and to allow for informed decision making in medical care and public health.

HCV as a public health issue requires informed leadership and resources – research into the risks and mechanisms of infection transmission, and a commitment to education and clinical research in all aspects of this difficult area.

References

Canadian Red Cross Society (1991): **Statistical Report – Blood Services 1990/91.**

Cuthbert JA. (1994): Hepatitis C: Progress and Problems. **Clinical Microbiology Reviews** 7:505-532.

Dusheiko GM. Khakoo S. Soni P. Grellier L. (1996): A rational approach to the management of hepatitis C infection. **British Medical Journal** 312:357-64.

Glanz K. Yang H (1996): Communicating about risk of infectious diseases. **Journal of The American Medical Association** 275:253-256.

Hoey J. (1997): Human Rights. ethics and the Krever inquiry. **Canadian Medical Association Journal** 157:1231.

Izopet J. Rostaing L. Moussion F. Alric L. et al. (1997): High rate of HCV clearance in hemodialysis patients after interferon- therapy. **Journal of Infectious Diseases** 176:1614-1617.

Jadoul M (1996): Transmission routes of HCV infection in dialysis. **Nephrology Dialysis Transplantation** 11(S4):36-38.

Kiyosawa K. Sodeyama T. Tanaka E. et al. (1990): Interrelationship of blood transfusion. NANB hepatitis and hepatocellular carcinoma: analysis by detection of antibody to hepatitis C virus. **Hepatology** 12:671-75.

Mattsson L. Sonnerborg A. Weiland O. (1993): Outcome of acute symptomatic NANB hepatitis: a 13-year follow-up study of hepatitis C virus markers. **Liver** 13:274-78.

Neto MC. Rodrigues-Manzano SI. Canziani ME. Silva AEB. et al. (1995): Environmental transmission of hepatitis B and hepatitis C viruses within the hemodialysis unit. **Artificial Organs** 19:251-255.

Nordenfelt E. Current Epidemiological trends in Northern Europe. **IX Triennial International Symposium on Viral Hepatitis and Liver Disease** (abstract volume) April 21-25 1996. Rome. Italy.

Pereira BJG. Levey AS (1997): Hepatitis C virus infection in dialysis and renal transplantation. **Kidney International** 51:981-90.

Seme K. Poljak M. Zuzek-Resek S. Debeljak M. et al. (1997): Molecular evidence for nosocomial spread of two different HCV strains in one hemodialysis unit. **Nephron** 77:273-278.

Spurgeon D. (1997): Canadians sue over hepatitis C infection. **British Medical Journal** 315:330.

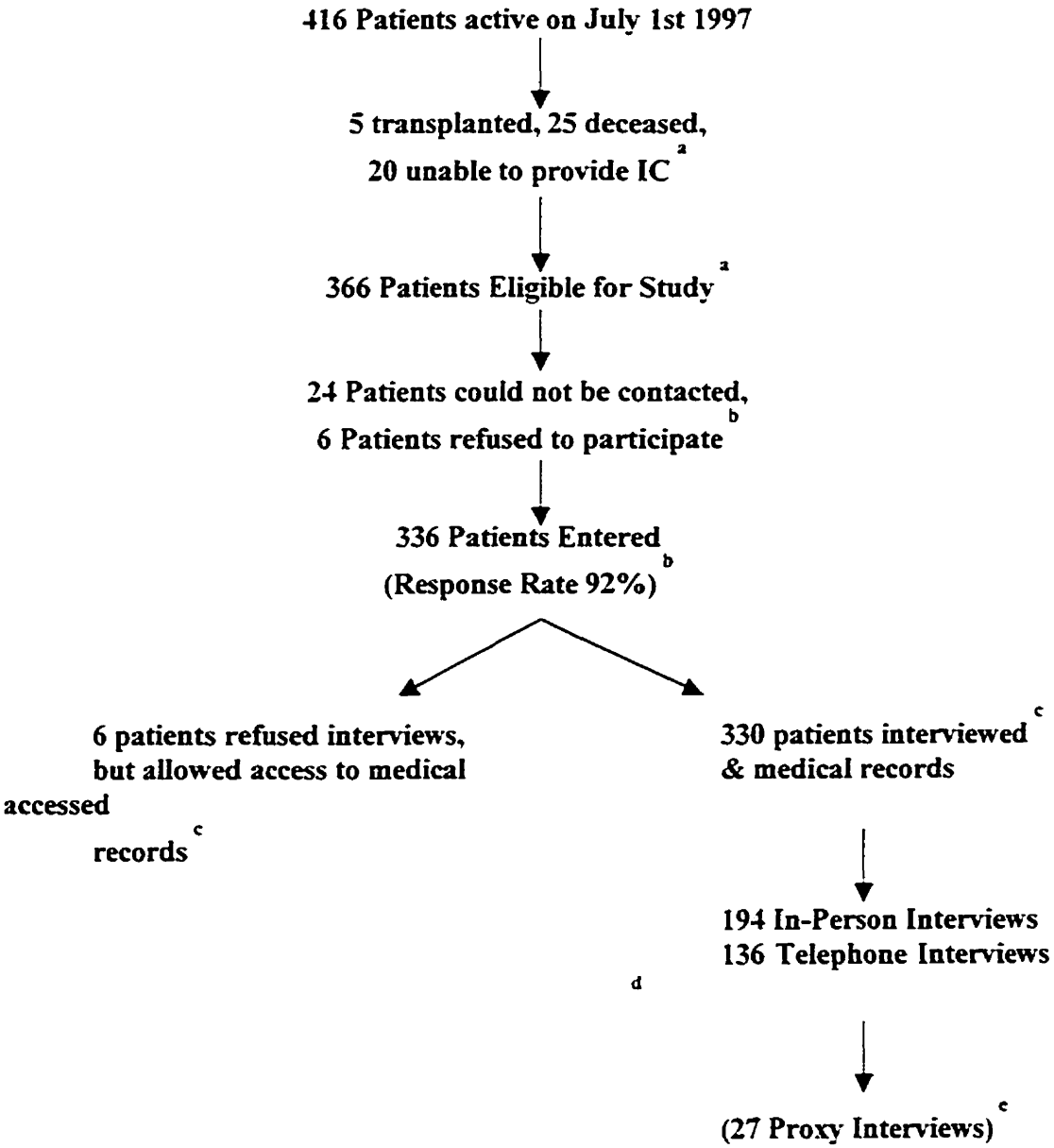
Tandon BN. Tandon A. Acharya SK. Current epidemiological trends of viral hepatitis in Asia. **IX Triennial International Symposium on Viral Hepatitis and Liver Disease** (abstract volume) April 21-25 1996. Rome. Italy.

Vranckx R. Van Damme P. The epidemiology of HCV in Belgium. **IX Triennial International Symposium on Viral Hepatitis and Liver Disease** (abstract volume) April 21-25 1996. Rome. Italy.

Appendix 1

Study Population

Study Population



Comparison Group	Gender (p-value)	Mean Age in Years (p-value)
[a] Eligible vs. Ineligible	Females: 39% vs. 41% (p = 0.81)	63.4 vs. 57.2 (p = 0.03)
[b] Responders vs. Non-Responders	Females: 39% vs. 37% (p = 0.82)	57.4 vs. 54.2 (p = 0.30)
[c] Interviewed vs. Not-Interviewed	Females: 40% vs. 20% (p = 0.47)	57.5 vs. 54.0 (p = 0.58)
[d] Telephone Interviews vs. In-Person Interviews	Females: 42% vs. 38% (p = 0.49)	56.4 vs. 58.3 (p = 0.27)
[e] Proxy Interviews vs. Non-Proxy Interviews	Females: 44% vs. 39% (p = 0.60)	66.8 vs. 56.7 (p = 0.001)

Appendix 2

Patient Questionnaire

HCV DIALYSIS STUDY - PATIENT INTERVIEW QUESTIONNAIRE

Thank you for agreeing to participate in this study and thereby help us to understand about Hepatitis C. First, I'll ask you some personal details about your background and dialysis history. All your responses will be held strictly confidential and no one other than myself will have access to the information you provide. Would you like to start now?

BACKGROUND INFORMATION

Patient's Name : _____
last name other names

Date of Birth : _____ Gender : ☐ Male ☐ Female

Country of Birth: _____

Ethnic Background: ☐ Asian ☐ Aboriginal ☐ Caucasian
☐ Other: _____

Highest Level of Education: ☐ Elementary ☐ Junior High ☐ Senior High ☐ Post-Secondary

Occupation (longest duration): _____

Dialysis Centre : _____

DIALYSIS HISTORY

- Have you ever been on dialysis in another country ? ☐ Yes ☐ No

  ↓
  Where: _____

- For how many years have you been on dialysis ? _____ years
- How many times per week do you spend on dialysis ? _____
- Since you started dialysis, have you ever had a blood transfusion ? ☐ Yes ☐ No

  ↓
  Number: _____

  Were any of these blood transfusions outside of Canada ? ☐ Yes ☐ No
  (whilst on dialysis)

  Were any of these blood transfusions before 1990 ? ☐ Yes ☐ No

  ↓

Number:_____

MEDICAL HISTORY

- Have you ever received donor organs/tissues ? ☐ Yes ☐No

  If yes, please specify organ(s)/tissue(s) & year(s):_____

  _____

  _____

- Have you ever had surgery under general anaesthetic ? ☐ Yes ☐No

  If yes, please specify surgery & date(s): _____

  _____

  _____

- Have you ever had endoscopic investigations ? ☐Yes ☐No
  (examination of lung, bladder, stomach, bowel, joints etc.)

- Have you ever had dental surgery ? ☐ Yes ☐No

  If yes, please specify type & year: _____

- Prior to starting dialysis, were you ever told by a doctor that you have :

  Hepatitis Infection ☐ Yes ☐No

  ↓

  Type:_____

  Jaundice ☐ Yes ☐No

  Abnormal Liver Function ☐Yes ☐No

- Have you ever received hepatitis vaccination ? ☐ Yes ☐No

  ↓

  Type:_____

- Prior to dialysis did you ever receive a blood transfusion ? ☐Yes ☐No

  ↓

  Number:_____

If yes, please specify city/country : _____

If yes, was the blood transfusion(s) before 1990 ? ☐ Yes ☐ No

Number: _____

- Have you ever had acupuncture treatment ? ☐ Yes ☐ No

When : _____

OTHER PARENTERAL RISK FACTORS

- Have you ever been paid to make a blood donation ? ☐ Yes ☐ No

If yes, please specify city/country/year : _____

_____

_____

- Have you ever had any injection of any kind for medical or immunisation purposes in a developing country ? ☐ Yes ☐ No

If yes, please specify city/country/year : _____

- Have you ever had a tattoo ? ☐ Yes ☐ No
- Have you ever had any ear piercing ? ☐ Yes ☐ No
- Have you ever had any body piercing ? ☐ Yes ☐ No

OTHER RISK FACTORS

- Do you have any family members with a history of hepatitis ? ☐ Yes ☐ No

Type : _____

Relationship : _____

- Have you ever had any household contact with a known hepatitis case ? *(other than family)*

☐ Yes ☐ No

Type : _____

Relationship : _____

- Have you ever worked in a healthcare facility or nursing home ? ☐ Yes ☐No

  If yes, did you ever have any needlestick injuries ? ☐Yes ☐No

SENSITIVE QUESTIONS

The next few questions are of a sensitive nature, and you are free **to not** answer them if you wish. If you decline to answer them your continuing medical care **will not** be affected in any way. Your answers will be identifiable to the researchers, but to no one else, because of our commitment to confidentiality. Would you like to continue?

☐ Yes ☐No ⟶ *Thank you for participating.*

- Have you ever smoked cigarettes ? ☐ Yes ☐No
- Do you currently smoke cigarettes ? ☐ Yes ☐No
- Have you ever used marijuana (hashish, pot, grass) ? ☐ Yes ☐No
- Have you ever injected street drugs ? ☐ Yes ☐No

  ↓

  Did you share needles ?

  ☐ Yes ☐No
- Have you ever used cocaine ? ☐ Yes ☐No

  ↓

  Did you share straws ?

  ☐ Yes ☐No
- Have you ever had any household contact with someone with a history of street drug use ?

  ☐ Yes ☐No
- Have you ever had any sexual relationships ? ☐ Yes ☐No
- Are you currently sexually active ? ☐ Yes ☐No
- Have you ever had sexual contact with someone who had hepatitis?

  ☐ Yes ☐No

  ↓

  Type : _____

- Have you ever had any sexual contact with someone who used street drugs ?
  ☐ Yes ☐No
- How many lifetime different sexual partners have you had ? Number = _____
- Have you ever had a sexually transmitted disease ? ☐ Yes ☐No
- Have you ever been required to spend time in jail ? ☐ Yes ☐No
- Have you ever participated in any rituals involving the exchange of blood ?
  ☐ Yes ☐No

Thank You for Participating in the Study

Appendix 3

Comparison of Interviewing Methods

Demographics

		Telephone interview n (%)	In-Person interview n (%)	χ^2, df p-value
Gender	Female	57 (41.9)	74 (38.1)	0.47, 1 df 0.49
Age	18 – 39	25 (18.4)	25 (12.9)	
	40 – 59	42 (30.9)	74 (38.1)	3.2, 2 df
	60 +	69 (50.7)	95 (49.0)	0.24
Ethnicity	Asian	16 (11.8)	36 (18.6)	
	Native	4 (2.9)	17 (8.8)	**9.1, 3 df**
	Caucasian	111 (81.6)	131 (67.5)	**p < 0.05***
	Others	5 (3.7)	10 (5.2)	
Birth	In Canada	105 (77.2)	127 (65.5)	**5.3, 1 df p < 0.05***
Education	≤ Grade 9	43 (31.6)	64 (33.0)	
	Grade 10 - 12	53 (39.0)	84 (43.3)	1.4, 2 df
	Post-Secondary	40 (29.4)	46 (23.7)	0.5

*Reflects the ethnic diversity of the Edmonton city population where the majority of patients that were interviewed in-person resided.

Dialysis History

		Telephone interview n (%)	In-Person interview n (%)	χ^2, df p-value
Time On Dialysis	Under 2 years	65 (47.8)	100 (51.5)	
	2 – 5 years	47 (34.6)	60 (30.9)	0.55, 2 df
	4 + years	24 (17.6)	34 (17.5)	0.76
History of Dialysis Modality	Peritoneal	38 (27.9)	126 (64.5)	
	Hemodialysis	46 (33.8)	15 (7.7)	**54.5, 2 df**
	Both	52 (38.2)	53 (27.3)	**p < 0.0001***
Modality at interview	Hemodialysis	46 (33.8)	149 (76.8)	**61.1, 1 df**
	Peritoneal	90 (66.2)	45 (23.2)	**p < 0.0001***
Total Hours of Hemodialysis	< 600 hours	9 (19.6)	37 (24.8)	
	600 –1300	12 (26.1)	39 (26.2)	47.5, 4 df
	1300 – 2800	10 (21.7)	39 (26.2)	0.57
	≥ 2800	15 (32.6)	34 (22.8)	
ALT in last six months	Elevated	19 (14.0)	16 (8.2)	2.8, 1 df 0.10
Hepatitis C	Positive	4 (2.9)	17 (8.8)	**4.5, 1 df p < 0.05**

* In-person interviews are predominantly with in-patients on hemodialysis three times a week. PD patients are out-patients who have clinical appointments every 6 weeks and hence less accessible, and thus predominate the telephone interview group. The HCV status reflects the difference in prevalence with respects to dialysis modality.

Transfusion History

		Telephone interview n (%)	In-Person interview n (%)	χ^2, df p-value
Blood & Blood Products	Questionnaire	103 (75.7)	157 (80.9)	1.29, 1 df 0.26
Before 1990	Questionnaire	36 (26.5)	62 (32.0)	1.2, 1 df 0.28
Blood & Blood Products	Blood Bank Records	89 (65.4)	148 (76.3)	**4.6, 1 df $p < 0.05$***
Before 1990	Blood Bank Records	9 (6.6)	18 (9.3)	0.75, 1 df 0.39
Total Units Transfused (Blood Bank Records)	Never 1 – 4 5 – 9 ≥ 10	47 (34.6) 36 (26.5) 14 (10.3) 39 (28.7)	46 (23.7) 43 (22.2) 27 (13.9) 78 (40.2)	**7.8, 3 df $p < 0.1$***
Units Transfused Before 1990 (Blood Bank Records)	Never 1 – 4 5 – 9 ≥ 10	127 (93.4) 5 (3.7) 1 (0.7) 3 (2.2)	176 (90.7) 7 (3.6) 3 (1.5) 8 (4.1)	1.38, 3 df 0.71

*Reflects the significantly higher transfusion requirements among patients on HD.

Medical History

		Telephone interview n (%)	In-Person interview n (%)	χ^2, df p-value
Transplants	Yes	28 (20.6)	36 (18.6)	0.21, 1 df 0.65
Jaundice	Yes	8 (5.9)	31 (16.3)	**8.2, 1 df $p < 0.005^{\infty}$**
Abnormal LFTs	Yes	4 (2.9)	14 (7.4)	3.1, 1 df $p < 0.1$
Hepatitis*	Yes	3 (2.2)	12 (6.3)	3.1, 1 df $p < 0.1$
Endoscopies	Yes	71 (52.6)	111 (57.8)	0.88, 1 df 0.35
Dental Surgery	Yes	103 (75.7)	100 (51.8)	**19.3, 1 df $p < 0.001^{\varphi}$**

* Previous Hepatitis Infection of any type

$^{\infty}$ Possibly related to the transfusion history and added morbidity of HD patients

$^{\varphi}$ Reflecting ethnicity differences to oral/dental health

Other Parenteral Risk Factors

		Telephone interview n (%)	In-Person interview n (%)	χ^2, df p-value
Acupuncture	Yes	21 (15.4)	32 (16.8)	0.1, 1 df 0.77
Medical treatment in a developing nation	Yes	13 (9.6)	33 (17.4)	4.0, 1 df $p < 0.1$
Ear Piercing	Yes	48 (35.3)	60 (31.3)	0.6, 1 df 0.44
Body Piercing	Yes	1 (0.7)	1 (0.5)	Fishers Exact 0.65
Tattoo	Yes	9 (6.6)	18 (9.4)	0.8, 1 df 0.37
Paid Blood Donation	Yes	2 (14.9)	0 (0)	Fishers Exact 0.17
Healthcare Work	Yes	25 (18.4)	36 (18.8)	0.01, 1 df 0.93

Lifestyle Risk Factors

		Telephone interview n (%)	In-Person interview n (%)	χ^2, df p-value
Ever Smoked	Yes	103 (75.7)	122 (63.5)	**5.5, 1 df p < 0.05**
Currently Smoke	Yes	36 (26.9)	40 (20.9)	1.5, 1 df 0.21
Marijuana Use	Yes	24 (17.6)	36 (18.8)	0.07, 1 df 0.80
Cocaine Use	Yes	4 (2.9)	14 (7.3)	2.9, 1 df p < 0.1
Injecting Drug Use	Yes	3 (2.2)	7 (3.7)	0.57, 1 df 0.53
Household contact with SDU†	Yes	13 (9.6)	28 (14.6)	1.8, 1 df 0.18
Sexual contact with SDU†	Yes	6 (4.7)	15 (8.2)	1.4, 1 df 0.23
Household contact with a known hepatitis case*	Yes	10 (7.4)	31 (16.1)	**5.63, 1 df p < 0.05**
Sexual contact with a known hepatitis case*	Yes	2 (1.6)	6 (3.3)	Fishers Exact 0.48
STD History	Yes	9 (7.5)	19 (10.4)	1.1, 1 df 0.30
Sexual Partners	None One Multiple	1 (0.8) 60 (48.4) 63 (50.8)	6 (3.3) 102 (55.4) 76 (41.3)	4.1, 2 df 0.13
Jail	Yes	4 (2.9)	19 (11.0)	**5.9, 1df p < 0.05**
Blood Rituals	Yes	0 (0)	3 (1.6)	Fishers Exact 0.27
High Risk Lifestyle Behaviour⁂	Yes	30 (22.1)	62 (32.3)	4.1, 1 df 0.04
Number of High Risk Lifestyle Behaviours⁂	0 1 2 +	106 (77.9) 19 (14.0) 11 (8.1)	130 (67.7) 35 (18.2) 27 (14.1)	4.5, 2 df 0.10

* Hepatitis Case of any type

† Street Drug User

⁂ Excluding Marijuana Use

Appendix 4

Bivariate Analysis of HCV Status

Demographics

		Hepatitis C positive n (%)	Hepatitis C negative n (%)	χ^2, df p-value
Gender	Female	7 (31.8)	125 (39.8)	0.55, 1 df 0.47
Age	18 – 39 40 – 59 60 +	4 (18.2) 17 (77.3) 1 (4.5)	47 (15.0) 102 (32.5) 165 (52.5)	**χ^2 trend = 10.2 p < 0.005**
Ethnicity	Asian Native Caucasian Others	2 (9.1) 1 (4.5) 18 (81.8) 1 (4.5)	51 (16.2) 21 (6.7) 227 (72.3) 15 (4.8)	1.1, 3 df 0.78
Birth	In Canada	18 (81.8)	216 (68.8)	1.7, 1 df 0.20
Education	≤ Grade 9 Grade 10 - 12 Post-Secondary	3 (13.6) 12 (54.5) 7 (31.8)	104 (33.5) 126 (40.6) 80 (25.8)	χ^2 trend p = 0.12

Dialysis History

		Hepatitis C positive n (%)	Hepatitis C negative n (%)	χ^2, df p-value
Time On Dialysis	Under 2 years 2 – 5 years 4 + years	4 (18.2) 6 (27.3) 12 (54.5)	162 (51.6) 103 (32.8) 49 (15.6)	**χ^2 trend=18.6 p < 0.0001**
History of Dialysis Modality	Peritoneal Haemodialysis Both	2 (9.1) 12 (54.5) 8 (36.4)	59 (18.8) 156 (49.7) 99 (31.5)	1.3, 2 df 0.52
Modality at interview	Haemodialysis Peritoneal	16 (72.7) 6 (27.3)	185 (58.9) 129 (41.1)	1.6, 1 df 0.20
Total Hours of Haemodialysis	none < 600 hours 600 –1300 1300 – 2800 ≥ 2800	2 (9.1) 5 (22.7) 1(4.5) 3 (13.6) 11 (50.0)	59 (18.8) 115 (36.6) 51 (16.2) 48 (15.3) 41 (13.1)	**χ^2 trend=12.8 p < 0.001**
Elevated ALT in last six months	Yes	7 (31.8)	31 (9.9)	**9.9, 1 df p < 0.01**

Transfusion History

		Hepatitis C positive n (%)	Hepatitis C negative n (%)	χ^2, df p-value
Blood & Blood Products	Questionnaire	19 (90.5)	241 (77.9)	1.8, 1 df 0.18
Before 1990	Questionnaire	13 (61.9)	85 (27.5)	**11.1, 1 df p < 0.001**
Blood & Blood Products	Blood Bank Records	18 (81.8)	222 (70.7)	1.2, 1 df 0.26
Before 1990	Blood Bank Records	5 (22.7)	22 (7.0)	**6.9, 1 df p < 0.05**
Total Units Transfused (Blood Bank Records)	Never 1 – 4 5 – 9 ≥ 10	4 (18.2) 2 (9.1) 6 (27.3) 10 (45.5)	92 (29.3) 78 (24.8) 35 (11.2) 109 (34.7)	χ^2 trend=3.2 p < 0.1
Units Transfused Before 1990 (Blood Bank Records)	Never 1 – 4 5 – 9 ≥ 10	17 (77.3) 3 (13.6) 1 (4.6) 4 (4.6)	292 (93.0) 9 (2.9) 3 (1.0) 10 (3.18)	**χ^2 trend=15.8 p < 0.0001**
Blood & Blood Products	Blood Bank / Transplant	20 (90.9)	236 (75.2)	2.8, 1 df 0.094
Before 1990	Blood Bank / Transplant	13 (59.1)	59 (18.8)	**19.8, 1 df p < 0.0001**
Total Units Transfused (Blood Bank / Transplant)	Never 1 – 4 5 – 9 ≥ 10	2 (9.1) 4 (18.2) 6 (27.3) 10 (45.5)	78 (24.8) 88 (28.0) 37 (11.8) 111 (35.4)	χ^2 trend=3.8 p < 0.052
Units Transfused Before 1990 (Blood Bank / Transplant)	Never 1 – 4 5 – 9 ≥ 10	9 (40.9) 6 (27.3) 6 (27.3) 1 (4.6)	255 (81.2) 44 (14.0) 5 (1.6) 10 (3.2)	**χ^2 trend=20.3 p < 0.0001**

Medical History

		Hepatitis C positive n (%)	Hepatitis C negative n (%)	χ^2, df p-value
Transplants	Yes	11 (50.0)	56 (17.8)	**13.3, 1df p < 0.005**
Jaundice	Yes	4 (19.0)	35 (11.4)	Fishers Exact 0.49
Abnormal LFTs	Yes	1 (4.8)	17 (5.6)	Fishers Exact 0.74
Hepatitis*	Yes	2 (9.5)	13 (4.2)	Fishers Exact 0.25
Endoscopies	Yes	13 (65.0)	171 (55.3)	0.71, 1 df 0.40
Dental Surgery	Yes	15 (71.4)	173 (60.3)	0.89, 1 df 0.34

* Previous Hepatitis Infection of any type
LFTs = Liver Function Tests

Other Parenteral Risk Factors

		Hepatitis C Positive n (%)	Hepatitis C Negative n (%)	χ^2, df p-value
Acupuncture	Yes	8 (38.1)	45 (14.7)	**7.9, 1 df p < 0.05**
Medical treatment in a developing nation	Yes	2 (9.5)	44 (14.4)	Fishers Exact 0.76
Ear Piercing	Yes	9 (40.9)	99 (32.1)	0.72, 1 df 0.40
Body Piercing	Yes	0 (0)	2 (0.7)	Fishers Exact 0.88
Tattoo	Yes	5 (22.7)	22 (7.1)	**6.6, 1 df p < 0.05**
Paid Blood Donation	Yes	0 (0)	2 (0.7)	Fishers Exact 0.88
Healthcare Work	Yes	3 (14.3)	58 (18.9)	Fishers Exact 0.81

Lifestyle Risk Factors

		Hepatitis C positive n (%)	Hepatitis C negative n (%)	χ^2, df p-value
Ever Smoked	Yes	15 (68.2)	212 (68.8)	0.004, 1 df 0.95
Currently Smoke	Yes	7 (33.3)	70 (23.0)	1.2, 1 df 0.41
Marijuana Use	Yes	11 (50.0)	50 (16.3)	**15.4, 1 df p < 0.001**
Cocaine Use	Yes	7 (35.0)	10 (3.6)	**Fishers Exact p < 0.0001**
Injecting Drug Use	Yes	8 (36.4)	3 (1.0)	**Fishers Exact p < 0.0001**
Household contact with SDU†	Yes	7 (33.3)	34 (11.1)	**Fishers Exact p < 0.01**
Sexual contact with SDU†	Yes	7 (36.8)	14 (4.8)	**Fishers Exact p < 0.0001**
Household contact with a known hepatitis case*	Yes	8 (38.1)	33 (10.8)	**Fishers Exact p < 0.001**
Sexual contact with a known hepatitis case*	Yes	3 (15.8)	5 (1.7)	**Fishers Exact p < 0.001**
STD History	Yes	4 (21.1)	24 (8.2)	Fishers Exact 0.14
Sexual Partners	None One Multiple	1 (5.3) 5 (26.3) 13 (68.4)	6 (2.1) 158 (54.5) 126 (43.4)	**χ^2 trend=2.9 p < 0.1**
Jail	Yes	5 (23.8)	18 (5.9)	**Fishers Exact p < 0.001**
Blood Rituals	Yes	1 (4.8)	2 (0.7)	Fishers Exact 0.18
High Risk Lifestyle Behaviour✣	Yes	16 (72.7)	100 (32.5)	**14.6, 1 df p < 0.0005**
Number of High Risk Lifestyle Behaviours✣	0 1 2+	6 (27.3) 3 (13.6) 13 (59.1)	207 (67.2) 62 (20.1) 39 (12.7)	**χ^2 trend=27.0 p < 0.0001**
High Risk Lifestyle Behaviour✳	Yes	16 (72.7)	77 (25.0)	**23.1, 1 df p < 0.0001**
Number of High Risk Lifestyle Behaviours✳	0 1 2+	6 (27.3) 7 (31.8) 9 (40.9)	231 (75.0) 48 (15.6) 29 (9.4)	**χ^2 trend=27.4 p < 0.0001**

* Hepatitis Case of any type †Street Drug User ✣Including Marijuana Use ✳Excluding Marijuana Use

Appendix 5

Model Building – Backward Elimination for LogXact

The model building process outlined below was conducted using LogXact for Windows 2.0, CYTEL Software Corporation ©1992-96. This package uses exact methods in the analysis of highly unbalanced datasets (few number of outcomes) that do not meet the asymptotic assumptions of logistic regression. The computationally complexity with exact inference exceeds the memory limits of most computers and hence its use is limited to the final stages of model-building (fewer covariates).

Variable Definition

AGE2 = 18-55 yrs vs. 56 yrs and over
DYEARS2 = length of time on dialysis (less than 5yrs vs. 5yrs & more)
BESTBT90 = transfusion before 1990 (Y/N)
B90UTX2 = # of units transfused before 1990 (4 units or less vs. 5+)
MARIUSE = marijuana use (Y/N)
HDHRS2 = hemodialysis hours (less than 1300hrs vs. 1300hrs plus)
NERFS2 = high-risk lifestyle behaviour (0/1 HRLB vs. 2+ HRLB)
HCHEP = household contact with a known hepatitis case (Y/N)
TXPLANT = organ transplant (Y/N)
TXPLNT90 = organ transplant before 1990 (Y/N)
ALT = serum alanine aminotransferase (normal vs. elevated)
BESTUTX2 = # of units transfused (4 units or less vs. 5+)
MSEXPART = multiple sexual partners (Y/N)
EDU3 = education (post-secondary vs. grade 12 & lower)
BESTBT = blood transfusion (Y/N)

Model :
HCV=AGE2+DYEARS2+BESTBT90+B90UTX2+MARIUSE+HDHRS2+NERFS2+HCHEP+TXPLANT+TXPLNT90+ALT+BESTUTX2+MSEXPART+EDU3+BESTBT

Number of Observations : 308
Number of Groups : 187
Likelihood Ratio Statistic : 336.6802 on 17 df

TERM	INFERENCE TYPE	<--- PARAMETER ESTIMATION ---> ODDS RATIO	SE(BETA)	95.0% CONF. INTERVAL		P-VALUE 2*1_SIDED
AGE2	Asymptotic	5.1602	NA	0.8981	29.6494	0.0658
DYEARS2	Asymptotic	2.4858	NA	0.4915	12.5729	0.2709
BESTBT90	**Asymptotic**	**0.9149**	**NA**	**0.1560**	**5.3651**	**0.9215**
B90UTX2	Asymptotic	2.6309	NA	0.4333	15.9730	0.2932
MARIUSE	Asymptotic	1.3938	NA	0.2857	6.7984	0.6813
HDHRS2	Asymptotic	2.3980	NA	0.4961	11.5914	0.2766
NERFS2	Asymptotic	5.9674	NA	1.1673	30.5061	0.0319
HCHEP	Asymptotic	4.4050	NA	1.2008	16.1597	0.0254
TXPLANT	Asymptotic	0.3234	NA	0.0412	2.5368	0.2827
TXPLNT90	Asymptotic	1.6348	NA	0.1661	16.0904	0.6735
ALT	Asymptotic	1.4444	NA	0.3244	6.4314	0.6295
BESTUTX2	Asymptotic	2.2903	NA	0.4813	10.8995	0.2978
MSEXPART	Asymptotic	0.7962	NA	0.1586	3.9968	0.7819
EDU3_2	Asymptotic	1.9147	NA	0.3438	10.6645	0.4585
EDU3_3	Asymptotic	0.6608	NA	0.0989	4.4153	0.6690
BESTBT	Asymptotic	1.4340	NA	0.1181	17.4116	0.7772
CONST	Asymptotic	0.0018	NA	0.0001	0.0268	0.0000

Model :
HCV=AGE2+DYEARS2+B90UTX2+MARIUSE+HDHRS2+NERFS2+HCHEP+TXPLANT+TXPLNT90+ALT+BES TUTX2+MSEXPART+EDU3+BESTBT

Number of Observations : 308
Number of Groups : 176
Likelihood Ratio Statistic : 336.6705 on 16 df

TERM	INFERENCE TYPE	ODDS RATIO	SE(BETA)	95.0% CONF.	INTERVAL	P-VALUE 2*1_SIDED
AGE2	Asymptotic	5.0954	NA	0.9055	28.6728	0.0647
DYEARS2	Asymptotic	2.4425	NA	0.5013	11.9002	0.2690
B90UTX2	Asymptotic	2.5019	NA	0.5594	11.1902	0.2302
MARIUSE	Asymptotic	1.4125	NA	0.2969	6.7205	0.6643
HDHRS2	Asymptotic	2.3960	NA	0.4950	11.5981	0.2775
NERFS2	Asymptotic	5.8719	NA	1.1877	29.0309	0.0299
HCHEP	Asymptotic	4.3434	NA	1.2216	15.4427	0.0233
TXPLANT	Asymptotic	0.3292	NA	0.0432	2.5093	0.2836
TXPLNT90	Asymptotic	1.5765	NA	0.1797	13.8337	0.6812
ALT	Asymptotic	1.4706	NA	0.3446	6.2765	0.6024
BESTUTX2	Asymptotic	2.2738	NA	0.4814	10.7395	0.2997
MSEXPART	**Asymptotic**	**0.7999**	**NA**	**0.1605**	**3.9867**	**0.7853**
EDU3_2	Asymptotic	1.9372	NA	0.3522	10.6544	0.4471
EDU3_3	Asymptotic	0.6646	NA	0.0997	4.4312	0.6730
BESTBT	Asymptotic	1.4122	NA	0.1185	16.8344	0.7849
CONST	Asymptotic	0.0018	NA	0.0001	0.0269	0.0000

Model :
HCV=AGE2+DYEARS2+B90UTX2+MARIUSE+HDHRS2+NERFS2+HCHEP+TXPLANT+TXPLNT90+ALT+BES TUTX2+EDU3+BESTBT

Number of Observations : 328
Number of Groups : 158
Likelihood Ratio Statistic : 351.2754 on 15 df

TERM	INFERENCE TYPE	ODDS RATIO	SE(BETA)	95.0% CONF.	INTERVAL	P-VALUE 2*1_SIDED
AGE2	Asymptotic	5.5004	NA	1.0770	28.0921	0.0405
DYEARS2	Asymptotic	2.2233	NA	0.5156	9.5876	0.2839
B90UTX2	Asymptotic	2.7099	NA	0.6915	10.6204	0.1526
MARIUSE	Asymptotic	0.7893	NA	0.2064	3.0181	0.7295
HDHRS2	Asymptotic	1.2751	NA	0.3078	5.2824	0.7375
NERFS2	Asymptotic	6.4659	NA	1.6648	25.1124	0.0070
HCHEP	Asymptotic	3.0536	NA	0.9020	10.3380	0.0728
TXPLANT	Asymptotic	0.2876	NA	0.0432	1.9150	0.1976
TXPLNT90	Asymptotic	3.1143	NA	0.4108	23.6125	0.2717
ALT	Asymptotic	1.8799	NA	0.5355	6.6003	0.3246
BESTUTX2	Asymptotic	2.5557	NA	0.5880	11.1081	0.2107
EDU3_2	**Asymptotic**	**1.6038**	**NA**	**0.3125**	**8.2318**	**0.5713**
EDU3_3	**Asymptotic**	**0.7621**	**NA**	**0.1267**	**4.5822**	**0.7665**
BESTBT	Asymptotic	1.8233	NA	0.1651	20.1410	0.6241
CONST	Asymptotic	0.0020	NA	0.0002	0.0242	0.0000

Model :
HCV=AGE2+DYEARS2+B90UTX2+MARIUSE+HDHRS2+NERFS2+HCHEP+TXPLANT+TXPLNT90+ALT+BES TUTX2+BESTBT

Number of Observations : 328
Number of Groups : 121
Likelihood Ratio Statistic : 349.9248 on 13 df

	INFERENCE	<---------- PARAMETER ESTIMATION ---------->				P-VALUE

TERM	TYPE	ODDS RATIO	SE(BETA)	95.0% CONF.	INTERVAL	2*1_SIDED
AGE2	Asymptotic	5.1395	NA	1.1294	23.3874	0.0342
DYEARS2	Asymptotic	2.1326	NA	0.5056	8.9944	0.3024
B90UTX2	Asymptotic	2.7943	NA	0.7288	10.7142	0.1340
MARIUSE	**Asymptotic**	**0.9475**	**NA**	**0.2561**	**3.5057**	**0.9356**
HDHRS2	Asymptotic	1.2300	NA	0.3096	4.8860	0.7686
NERFS2	Asymptotic	6.5623	NA	1.6893	25.4919	0.0066
HCHEP	Asymptotic	2.4963	NA	0.7764	8.0266	0.1247
TXPLANT	Asymptotic	0.3037	NA	0.0460	2.0027	0.2156
TXPLNT90	Asymptotic	2.9576	NA	0.3987	21.9414	0.2889
ALT	Asymptotic	1.9597	NA	0.5705	6.7320	0.2853
BESTUTX2	Asymptotic	2.3606	NA	0.5629	9.8992	0.2403
BESTBT	Asymptotic	2.1494	NA	0.2012	22.9634	0.5266
CONST	Asymptotic	0.0022	NA	0.0002	0.0231	0.0000

Model :
HCV=AGE2+DYEARS2+B90UTX2+HDHRS2+NERFS2+HCHEP+TXPLANT+TXPLNT90+ALT+BESTUTX2+BESTBT
Number of Observations : 328
Number of Groups : 105
Likelihood Ratio Statistic : 349.9183 on 12 df

	INFERENCE	<--------- PARAMETER ESTIMATION ---------->				P-VALUE
TERM	TYPE	ODDS RATIO	SE(BETA)	95.0% CONF.	INTERVAL	2*1_SIDED
AGE2	Asymptotic	5.0517	NA	1.1771	21.6799	0.0293
DYEARS2	Asymptotic	2.1604	NA	0.5309	8.7903	0.2820
B90UTX2	Asymptotic	2.7702	NA	0.7343	10.4506	0.1326
HDHRS2	**Asymptotic**	**1.2185**	**NA**	**0.3129**	**4.7445**	**0.7757**
NERFS2	Asymptotic	6.4072	NA	1.8807	21.8286	0.0030
HCHEP	Asymptotic	2.4914	NA	0.7758	8.0002	0.1251
TXPLANT	Asymptotic	0.3047	NA	0.0463	2.0057	0.2164
TXPLNT90	Asymptotic	2.9194	NA	0.4034	21.1269	0.2887
ALT	Asymptotic	1.9757	NA	0.5842	6.6819	0.2734
BESTUTX2	Asymptotic	2.3587	NA	0.5623	9.8944	0.2408
BESTBT	Asymptotic	2.1610	NA	0.2030	23.0088	0.5231
CONST	Asymptotic	0.0022	NA	0.0002	0.0230	0.0000

Model :
HCV=AGE2+DYEARS2+B90UTX2+NERFS2+HCHEP+TXPLANT+TXPLNT90+ALT+BESTUTX2+BESTBT
Number of Observations : 328
Number of Groups : 87
Likelihood Ratio Statistic : 349.8371 on 11 df

	INFERENCE	<--------- PARAMETER ESTIMATION ---------->				P-VALUE
TERM	TYPE	ODDS RATIO	SE(BETA)	95.0% CONF.	INTERVAL	2*1_SIDED
AGE2	Asymptotic	4.9671	NA	1.1670	21.1412	0.0301
DYEARS2	Asymptotic	2.3890	NA	0.7037	8.1107	0.1626
B90UTX2	Asymptotic	2.7711	NA	0.7370	10.4199	0.1315
NERFS2	Asymptotic	6.5035	NA	1.9203	22.0253	0.0026
HCHEP	Asymptotic	2.5739	NA	0.8191	8.0882	0.1056
TXPLANT	Asymptotic	0.3066	NA	0.0465	2.0225	0.2193
TXPLNT90	Asymptotic	2.9698	NA	0.4115	21.4322	0.2804
ALT	Asymptotic	1.9739	NA	0.5850	6.6603	0.2731
BESTUTX2	Asymptotic	2.4320	NA	0.5902	10.0211	0.2187
BESTBT	**Asymptotic**	**2.2142**	**NA**	**0.2097**	**23.3760**	**0.5086**
CONST	Asymptotic	0.0022	NA	0.0002	0.0230	0.0000

Model : HCV=AGE2+DYEARS2+B90UTX2+NERFS2+HCHEP+TXPLANT+TXPLNT90+ALT+BESTUTX2
Number of Observations : 328
Number of Groups : 78
Likelihood Ratio Statistic : 349.3537 on 10 df

	INFERENCE	<---------- PARAMETER ESTIMATION ---------->			P-VALUE
TERM	TYPE	ODDS RATIO	SE(BETA)	95.0% CONF.	INTERVAL 2*1_SIDED
AGE2	Asymptotic	4.7576	NA	1.1236	20.1446 0.0342
DYEARS2	Asymptotic	2.5041	NA	0.7406	8.4670 0.1397
B90UTX2	Asymptotic	2.7705	NA	0.7349	10.4440 0.1323
NERFS2	Asymptotic	6.8654	NA	2.0477	23.0181 0.0018
HCHEP	Asymptotic	2.7202	NA	0.8689	8.5159 0.0857
TXPLANT	Asymptotic	0.3114	NA	0.0462	2.1008 0.2310
TXPLNT90	**Asymptotic**	**2.9623**	**NA**	**0.4053**	**21.6488 0.2846**
ALT	Asymptotic	2.0524	NA	0.6088	6.9189 0.2462
BESTUTX2	Asymptotic	3.0847	NA	0.8447	11.2646 0.0883
CONST	Asymptotic	0.0037	NA	0.0007	0.0184 0.0000

Model : HCV=AGE2+DYEARS2+B90UTX2+NERFS2+HCHEP+TXPLANT+ALT+BESTUTX2
Number of Observations : 328
Number of Groups : 69
Likelihood Ratio Statistic : 348.1073 on 9 df

	INFERENCE	<---------- PARAMETER ESTIMATION ---------->			P-VALUE
TERM	TYPE	ODDS RATIO	SE(BETA)	95.0% CONF.	INTERVAL 2*1_SIDED
AGE2	Asymptotic	4.8968	NA	1.1538	20.7823 0.0312
DYEARS2	Asymptotic	3.0172	NA	0.9431	9.6521 0.0627
B90UTX2	Asymptotic	2.8894	NA	0.7712	10.8259 0.1154
NERFS2	Asymptotic	6.0837	NA	1.8884	19.5993 0.0025
HCHEP	Asymptotic	2.5793	NA	0.8314	8.0022 0.1010
TXPLANT	**Asymptotic**	**0.6447**	**NA**	**0.1861**	**2.2337 0.4887**
ALT	Asymptotic	1.9997	NA	0.6004	6.6606 0.2590
BESTUTX2	Asymptotic	2.7608	NA	0.7762	9.8194 0.1167
CONST	Asymptotic	0.0039	NA	0.0008	0.0189 0.0000

Model : HCV=AGE2+DYEARS2+B90UTX2+NERFS2+HCHEP+ALT+BESTUTX2
Number of Observations : 328
Number of Groups : 50
Likelihood Ratio Statistic : 347.6218 on 8 df

	INFERENCE	<---------- PARAMETER ESTIMATION ---------->			P-VALUE
TERM	TYPE	ODDS RATIO	SE(BETA)	95.0% CONF.	INTERVAL 2*1_SIDED
AGE2	Asymptotic	4.0911	NA	1.0535	15.8877 0.0418
DYEARS2	Asymptotic	2.6994	NA	0.8853	8.2303 0.0808
B90UTX2	Asymptotic	2.8108	NA	0.7491	10.5463 0.1256
NERFS2	Asymptotic	6.0098	NA	1.8649	19.3666 0.0027
HCHEP	Asymptotic	2.5463	NA	0.8206	7.9012 0.1057
ALT	**Asymptotic**	**1.8433**	**NA**	**0.5626**	**6.0392 0.3125**
BESTUTX2	Asymptotic	2.5526	NA	0.7350	8.8646 0.1401
CONST	Asymptotic	0.0043	NA	0.0009	0.0198 0.0000

Model : HCV=AGE2+DYEARS2+B90UTX2+NERFS2+HCHEP+BESTUTX2
Number of Observations : 328
Number of Groups : 35
Likelihood Ratio Statistic : 346.6483 on 7 df

	INFERENCE	<---------- PARAMETER ESTIMATION ---------->	P-VALUE

TERM	TYPE	ODDS RATIO	SE(BETA)	95.0% CONF.	INTERVAL	2*1_SIDED
AGE2	Asymptotic	4.4375	NA	1.1633	16.9265	0.0291
DYEARS2	Asymptotic	2.6896	NA	0.8754	8.2638	0.0841
B90UTX2	Asymptotic	3.1432	NA	0.8450	11.6914	0.0875
NERFS2	Asymptotic	5.7464	NA	1.7873	18.4748	0.0033
HCHEP	Asymptotic	2.5260	NA	0.8148	7.8306	0.1084
BESTUTX2	**Asymptotic**	**2.6184**	**NA**	**0.7567**	**9.0602**	**0.1286**
CONST	Asymptotic	0.0045	NA	0.0010	0.0205	0.0000

Model : HCV=AGE2+DYEARS2+B90UTX2+NERFS2+HCHEP
Number of Observations : 328
Number of Groups : 23
Likelihood Ratio Statistic : 344.2175 on 6 df

	INFERENCE	<---------- PARAMETER ESTIMATION ---------->				P-VALUE
TERM	TYPE	ODDS RATIO	SE(BETA)	95.0% CONF.	INTERVAL	2*1_SIDED
AGE2	Asymptotic	4.4221	NA	1.1639	16.8017	0.0291
	Exact	4.2832	NA	1.0561	25.0340	0.0398
DYEARS2	Asymptotic	3.3259	NA	1.1137	9.9328	0.0313
	Exact	3.1929	NA	0.9332	10.7884	0.0660
B90UTX2	Asymptotic	3.8990	NA	1.0572	14.3799	0.0410
	Exact	3.6752	NA	0.8345	16.1529	0.0916
NERFS2	Asymptotic	4.8157	NA	1.5775	14.7010	0.0058
	Exact	4.5190	NA	1.3076	15.8548	0.0151
HCHEP	**Asymptotic**	**2.6982**	**NA**	**0.8877**	**8.2014**	**0.0801**
	Exact	**2.5867**	**NA**	**0.7264**	**8.5980**	**0.1558**
CONST	Asymptotic	0.0076	NA	0.0021	0.0274	0.0000

Model : HCV=AGE2+DYEARS2+B90UTX2+NERFS2
Number of Observations : 336
Number of Groups : 14
Likelihood Ratio Statistic : 347.6797 on 5 df

	INFERENCE	<---------- PARAMETER ESTIMATION ---------->				P-VALUE
TERM	TYPE	ODDS RATIO	SE(BETA)	95.0% CONF.	INTERVAL	2*1_SIDED
AGE2	Asymptotic	4.9802	NA	1.3430	18.4675	0.0164
	Exact	**4.8555**	**NA**	**1.2387**	**27.8950**	**0.0186**
DYEARS2	Asymptotic	3.8284	NA	1.3459	10.8900	0.0118
	Exact	**3.7039**	**NA**	**1.1567**	**12.0401**	**0.0257**
B90UTX2	Asymptotic	4.1951	NA	1.2106	14.5371	0.0237
	Exact	**4.0215**	**NA**	**0.9630**	**16.3019**	**0.0571**
NERFS2	Asymptotic	5.1724	NA	1.7549	15.2455	0.0029
	Exact	**4.9535**	**NA**	**1.4789**	**16.7191**	**0.0079**
CONST	Asymptotic	0.0083	NA	0.0024	0.0291	0.0000

HOSMER-LEMESHOW TEST:"
"Statistic=" 3.644 "on" 3 "df" "P-value =" 0.3026

"DEVIANCE:" 15.44 "on" 9 "df" "P-value =" 0.0796

Appendix 6

Assessment of Transfusion History Measurement

Demographics

		True Positives n (%)	False Positives n (%)	False Negatives n (%)	True Negatives n (%)	χ^2, df p-value
Gender	Female	86 (76.1)	8 (7.1)	5 (4.4)	14 (12.4)	**11.7, 3 df**
	Males	108 (59.7)	11 (6.1)	9 (5.0)	53 (29.3)	**p = 0.01**
Age	18 – 45	44 (67.7)	2 (3.1)	0 (0)	19 (29.2)	
	46 – 59	40 (56.3)	5 (7.0)	4 (5.6)	22 (31.0)	**19.8, 9 df**
	60 – 70	53 (63.1)	10 (11.9)	5 (6.0)	16 (19.0)	**p = 0.02**
	70 +	57 (77.0)	2 (2.7)	5 (6.8)	10 (13.5)	
Ethnicity	Asian	31 (70.5)	3 (6.8)	2 (4.5)	8 (18.2)	
	Native	15 (75.0)	1 (5.0)	0 (0)	4 (20.0)	5.7, 9 df
	Caucasian	140 (64.5)	14 (6.5)	10 (4.6)	53 (24.4)	p = 0.77
	Others	8 (61.5)	1 (7.7)	2 (15.4)	2 (15.4)	
Birth	In Canada	129 (62.3)	14 (6.8)	10 (4.8)	54 (26.1)	4.9, 3 df
	Abroad	65 (74.7)	5 (5.7)	4 (4.6)	13 (14.9)	p = 0.18
Education	≤ Grade 9	74 (71.8)	7 (6.8)	8 (7.8)	14 (13.6)	**12.9, 6 df**
	Grade 10 - 12	75 (63.0)	6 (5.0)	6 (5.0)	32 (26.9)	**p = 0.04**
	Post-Secondary	45 (62.5)	6 (8.3)	0 (0)	21 (29.2)	

Interview Method

		True Positives n (%)	False Positives n (%)	False Negatives n (%)	True Negatives n (%)	χ^2, df p-value
Interview	Phone	72 (60.0)	9 (7.5)	6 (5.0)	33 (27.5)	3.4, 3 df
	In-Person	122 (70.1)	10 (5.7)	8 (4.6)	34 (19.5)	p = 0.33
Proxy	Yes	23 (88.5)	0 (0)	1 (3.8)	2 (7.7)	6.9, 3 df
	No	171 (63.8)	19 (7.1)	13 (4.9)	65 (24.3)	p = 0.07

Dialysis History

		True Positives n (%)	False Positives n (%)	False Negatives n (%)	True Negatives n (%)	χ^2, df p-value
Time On Dialysis	Under 2 years	94 (57.3)	10 (6.1)	7 (4.3)	53 (32.3)	**22.8, 6 df**
	2 – 5 years	75 (73.5)	8 (7.8)	5 (4.9)	14 (13.7)	**p = 0.001**
	4 + years	25 (89.3)	1 (3.6)	2 (7.1)	0 (0)	
History of Dialysis Modality	Haemodialysis	102 (69.92)	6 (4.1)	12 (8.2)	26 (17.8)	**39.8, 6 df**
	Peritoneal	23 (39.0)	7 (11.9)	1 (1.7)	28 (47.5)	**p < 0.001**
	Both (HD & PD)	69 (77.5)	6 (6.7)	1 (1.1)	13 (14.6)	
Dialysis Centre	Haemodialysis	124 (72.9)	7 (4.1)	12 (7.1)	27 (15.9)	**19.3, 3 df**
	Peritoneal	70 (56.5)	12 (9.7)	2 (1.6)	40 (32.3)	**p < 0.001**
HD Hours Run	None	23 (39.0)	7 (11.9)	1 (1.7)	28 (47.5)	
	< 600 hours	71 (64.0)	6 (5.4)	4 (3.6)	30 (27.0)	**52.5, 12 df**
	600 –1300	37 (72.5)	4 (7.8)	3 (5.9)	7 (13.7)	**p < 0.001**
	1300 – 2800	40 (87.0)	0 (0)	4 (8.7)	2 (4.3)	
	≥ 2800	23 (85.2)	2 (7.4)	2 (7.4)	0 (0)	
ALT in last six months	Elevated	19 (76.0)	1 (4.0)	1 (4.0)	4 (16.0)	1.26, 3 df
	Normal	175 (65.1)	18 (6.7)	13 (4.8)	63 (23.4)	p = 0.74
Hepatitis C	Positive	8 (72.7)	0 (0)	1 (9.1)	2 (18.2)	1.4, 3 df
	Negative	186 (65.7)	19 (6.7)	13 (4.6)	65 (23.0)	p = 0.71

Medical History

		True Positives n (%)	False Positives n (%)	False Negatives n (%)	True Negatives n (%)	χ^2, df p-value
Transplants	Yes	31 (88.6)	1 (2.9)	1 (2.9)	1 (5.7)	**9.3, 3 df**
	No	163 (62.9)	18 (6.9)	13 (5.0)	65 (25.1)	**p = 0.03**
Jaundice	Yes	26 (68.4)	0 (0)	2 (5.3)	10 (26.3)	3.1, 3 df
	No	164 (65.1)	19 (7.5)	12 (4.8)	57 (22.6)	p = 0.37
Abnormal LFTs†	Yes	10 (62.5)	1 (6.3)	1 (6.3)	3 (25.0)	0.11, 3 df
	No	178 (65.4)	18 (6.6)	13 (4.8)	63 (23.2)	p = 0.99
Hepatitis*	Yes	10 (66.7)	0 (0)	0 (0)	5 (33.3)	2.52, 3 df
	No	180 (65.5)	19 (6.9)	14 (5.1)	62 (22.5)	p = 0.47
Endoscopies	Yes	107 (67.7)	12 (7.6)	4 (2.5)	35 (22.2)	4.6, 3 df
	No	85 (63.4)	7 (5.2)	10 (7.5)	32 (23.9)	p = 0.20
Dental Surgery	Yes	127 (69.0)	10 (5.4)	8 (4.3)	39 (21.2)	2.4, 3 df
	No	66 (60.6)	9 (8.3)	6 (5.5)	28 (25.7)	p = 0.50

* Previous Hepatitis Infection of any type

† LFTs – Liver Function Tests

Other Parenteral Risk Factors

		True Positives n (%)	False Positives n (%)	False Negatives n (%)	True Negatives n (%)	χ^2, df p-value
Acupuncture	Yes	34 (70.8)	3 (6.3)	2 (4.2)	9 (18.8)	0.72, 3 df
	No	158 (64.8)	16 (6.6)	12 (4.9)	58 (23.8)	p = 0.87
Medical treatment in a developing nation	Yes	24 (61.5)	3 (7.7)	1 (2.6)	11 (28.2)	1.1, 3 df
	No	167 (66.5)	16 (6.4)	12 (4.8)	56 (22.3)	p = 0.78
Ear Piercing	Yes	68 (75.6)	4 (4.4)	3 (3.3)	15 (16.7)	5.6, 3 df
	No	124 (61.4)	15 (7.4)	11 (5.4)	52 (25.7)	p = 0.14
Body Piercing	Yes	2 (100)	0 (0)	0 (0)	0 (0)	1.0, 3 df
	No	190 (65.5)	19 (6.6)	14 (4.8)	67 (23.1)	p = 0.79
Tattoo	Yes	14 (56.0)	0 (0)	2 (8.0)	9 (36.0)	4.8, 3 df
	No	178 (66.7)	19 (7.1)	12 (4.5)	58 (21.7)	p = 0.19
Paid Blood Donation	Yes	0 (0)	0 (0)	0 (0)	1 (100)	3.4, 3df
	No	191 (65.9)	19 (6.6)	14 (4.8)	66 (22.8)	p = 0.34
Healthcare Work	Yes	37 (74.0)	3 (6.0)	2 (4.0)	8 (16.0)	2.0, 3 df
	No	155 (64.0)	16 (6.6)	12 (5.0)	59 (24.4)	p = 0.57

Lifestyle Risk Factors

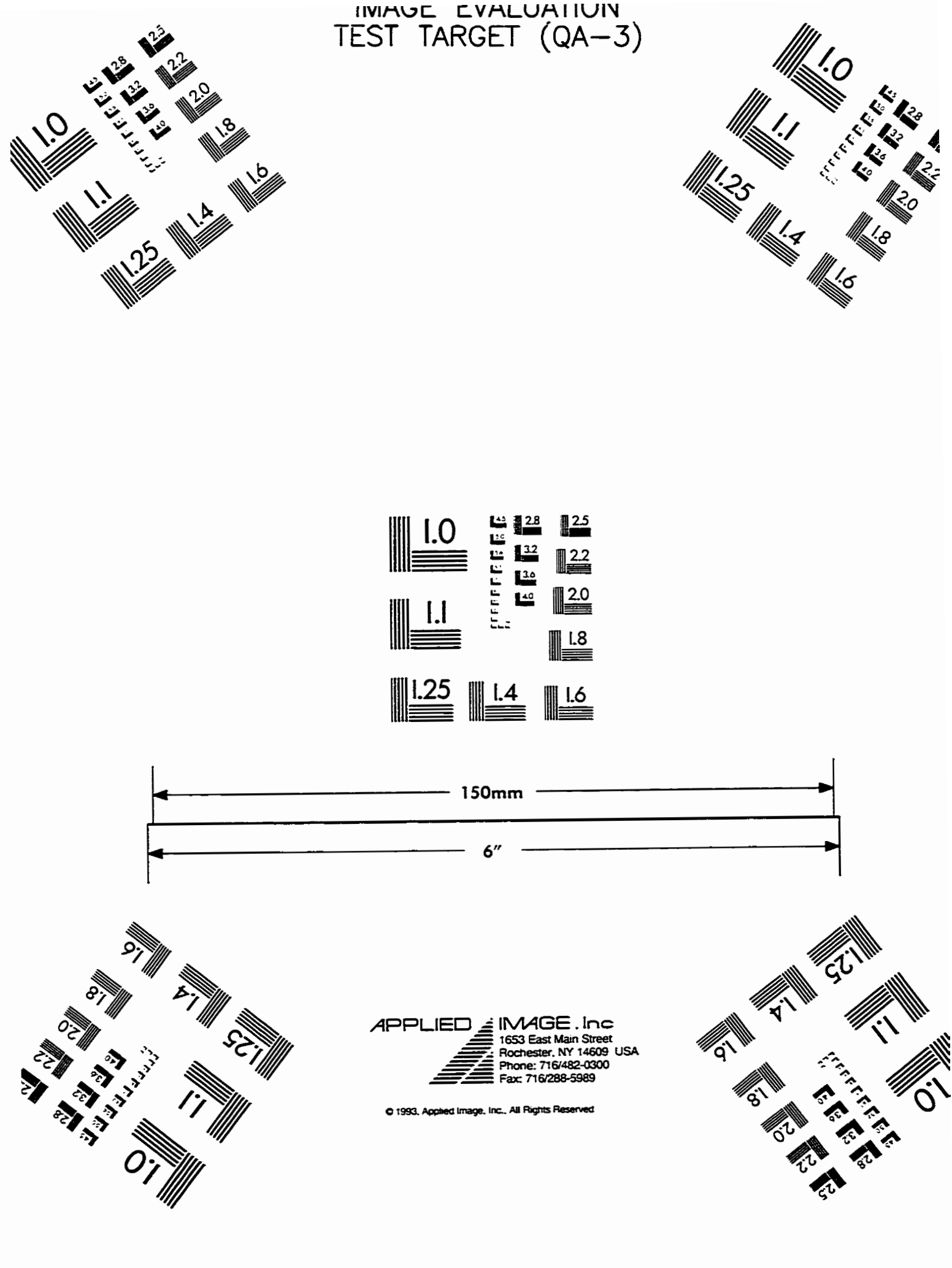
		True Positives n (%)	False Positives n (%)	False Negatives n (%)	True Negatives n (%)	χ^2, df p-value
Ever Smoked	Yes	129 (63.9)	14 (6.9)	12 (5.9)	47 (23.3)	2.4, 3 df
	No	63 (70.0)	5 (5.6)	2 (2.2)	20 (22.2)	p = 0.50
Currently Smoke	Yes	36 (55.4)	4 (6.2)	5 (7.7)	20 (30.8)	5.1, 3 df
	No	154 (68.8)	15 (6.7)	9 (4.0)	46 (20.5)	p = 0.16
Marijuana Use	Yes	28 (57.1)	2 (4.1)	1 (2.0)	18 (36.7)	7.0, 3 df
	No	164 (67.5)	17 (7.0)	13 (5.3)	49 (20.2)	p = 0.07
Cocaine Use	Yes	8 (50.0)	1 (6.3)	1 (6.3)	6 (37.5)	2.3, 3 df
	No	184 (66.7)	18 (6.5)	13 (4.7)	61 (22.1)	p = 0.52
Injecting Drug Use	Yes	6 (66.7)	0 (0)	0 (0)	3 (33.3)	1.5, 3 df
	No	185 (65.6)	19 (6.7)	14 (5.0)	64 (22.7)	p = 0.69
Household contact with SDU†	Yes	25 (69.4)	0 (0)	1 (2.8)	10 (27.8)	3.5, 3 df
	No	167 (65.2)	19 (6.7)	13 (5.1)	57 (22.3)	p = 0.32
Sexual contact with SDU†	Yes	12 (66.7)	1 (5.6)	1 (5.6)	4 (22.2)	0.12, 3 df
	No	171 (66.0)	18 (6.9)	11 (4.2)	59 (22.8)	p = 0.99
Household contact with a known hepatitis case*	Yes	26 (76.5)	3 (8.8)	0 (0)	5 (14.7)	4.0, 3 df
	No	166 (64.3)	16 (6.2)	14 (5.4)	62 (24.0)	p = 0.26
Sexual contact with a	Yes	5 (71.4)	1 (14.3)	0 (0)	1 (14.3)	1.2, 3 df

known hepatitis case*	No	178 (65.7)	18 (6.6)	12 (4.4)	63 (23.2)	p = 0.76
STD History	Yes	14 (58.3)	1 (4.2)	2 (8.3)	7 (29.2)	1.9, 3 df
	No	170 (66.7)	18 (7.1)	10 (3.9)	57 (22.4)	p = 0.59
Sexual Partners	None	4 (80.0)	0 (0)	0 (0)	0 (0)	
	One	100 (67.6)	10 (6.8)	5 (3.4)	33 (22.3)	1.6, 6 df
	Multiple	81 (65.3)	8 (6.5)	7 (5.6)	23 (22.6)	p = 0.96
Jail	Yes	14 (66.7)	0 (0)	2 (9.5)	5 (23.8)	2.5, 3 df
	No	178 (65.7)	19 (7.0)	12 (4.4)	62 (22.9)	p = 0.47
Blood Rituals	Yes	3 (100)	0 (0)	0 (0)	0 (0)	1.6, 3 df
	No	189 (65.4)	19 (6.6)	14 (4.8)	67 (23.2)	p = 0.66
High Risk Lifestyle Behaviour✱	Yes	50 (64.1)	2 (2.6)	4 (5.1)	22 (28.2)	3.9, 3 df
	No	142 (66.4)	17 (7.9)	10 (4.7)	45 (21.0)	p = 0.27
Number of High Risk Lifestyle Behaviours✱	0	142 (66.4)	17 (7.9)	10 (4.7)	45 (21.0)	
	1	29 (65.9)	1 (2.3)	2 (4.5)	12 (27.3)	4.1, 6 df
	2 +	21 (61.8)	1 (2.9)	2 (5.9)	10 (29.4)	p = 0.67

* Hepatitis Case of any type

† Street Drug User

✱ Excluding Marijuana Use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