Development and Maintenance of a Community-Based Hepatitis C Registry

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Objective: To develop a model for community-population- or health system-based registries of all patients with diagnosed hepatitis C, to facilitate clinical care and epidemiologic studies.

Study Design: Geographically defined, population-based cohort study.

Methods: Registry subjects were identified using January 1, 1990, to December 31, 1999, data from the Rochester Epidemiology Project (REP), which lists all diagnoses for Olmsted County residents recorded by clinicians during visits to Olmsted County medical providers. We supplemented diagnostic data with information from laboratory databases that record all hepatitis C testing in Olmsted County. All diagnoses based on the REP and laboratory databases were confirmed by medical record review. Proposed data elements to be included in a hepatitis C registry were identified and defined, and data collection methodology was tested.

Results: A total of 355 subjects (62% male) were identified in the total community population of 130,000. Both the diagnostic summary database (n = 309, 87%) and the laboratory database (n = 46, 13%) were important in the identification of subjects for the registry. Nine additional subjects with diagnostic or laboratory evidence of hepatitis C refused the legislatively mandated (Minnesota statute) medical records research authorization and could not be included in the registry. Most desired data elements were available in the medical records.

Conclusions: Both medical visit diagnostic summaries (administrative or billing data) and laboratory databases are required to identify subjects with physician-based diagnoses of hepatitis C. Few patients refused the authorization required for inclusion in a research registry.

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Hepatitis C, like many other chronic diseases, is associated with major expenditures for healthcare services and results in significant morbidity and mortality in the United States.[1-4] Yet, for many of these chronic diseases, including hepatitis C, we have limited or conflicting information about the epidemiology, natural history of the disease, and the clinical care provided at the community or entire health systems level.[2,5-12] Most longitudinal data are from national surveys and do not include data on clinical care. Disease- or condition-specific registries are an accepted tool to identify population-based groups of subjects whose clinical, personal, and healthcare utilization data can be collected in a uniform manner. Information from the disease registry may then be used to study the course, treatment, and outcomes of those diseases and conditions, as well as to develop practice tools to improve care.[13-20] Such registries could supplement the existing data for hepatitis C. This would be particularly helpful in the United States, where hepatitis C data are often collected from specialized subgroups (transplant populations or those in hepatology clinics) or in cross-sectional studies of nationally representative populations, in contrast to the longitudinal community-based data available from some other countries.[2,5,6,9,10,21-24]

A national register of persons with hepatitis C virus infection with a known date of acquisition is being developed in the United Kingdom.[25] (This is an extension of the UK transfusion look-back study.[24,26]) The registry will have the advantage of including dates of exposure to the hepatitis C virus, as well as identifying and defining a common set of information to be collected. However, the registry will not be designed to include people who acquired hepatitis C by exposures other than transfusion, and will depend

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on the volunteer efforts of physicians to submit yearly data.[25] Although this will be a valuable resource, transfusion-acquired hepatitis C will represent a declining segment of the incident UK population either infected or diagnosed with hepatitis C.

A population- or health system-based cohort identified by physician diagnosis, rather than through mass screening, provides additional information about the physicians' care of these subjects. Data will be available concerning issues such as whom physicians test for hepatitis C, who they treat, and how they follow or monitor the disease, and whether they attend to secondary prevention measures. Such a population- or health system-based registry could provide information on patients outside clinical trials and could serve as the basis for practice-improvement programs and evaluation of disease course.

This paper describes the design, implementation, and data collection for such a hepatitis C registry. Attention is given to the definition of the data elements, data sources, and confidentiality concerns of persons whose data are included in this registry. It is hoped that this work will facilitate discussion of data elements essential for larger regional or national registries.

··· METHODS ···

This study describes the development and implementation of a hepatitis C research registry in a geographically defined, population-based cohort. The registry population includes all persons living in Olmsted County, Minnesota, who have received a physician or laboratory diagnosis of hepatitis C from January 1, 1990, through December 31, 1999.

Setting

Olmsted County, Minnesota, is a metropolitan statistical area that includes the city of Rochester, Minnesota. The county is medically isolated, being surrounded by rural agricultural land, and is 90 miles south of the metropolitan areas of Minneapolis and St. Paul, Minnesota. Olmsted County is primarily served by 2 medical facilities, the Olmsted Medical Center and the Mayo Clinic, which provide primary through tertiary care locally. Olmsted County has 1 primary care and 2 large tertiary care hospitals.

Registry Subject Identification Criteria

The purposes of this registry are 2-fold: (1) To study the disease course of known hepatitis C, and (2) to study the interaction of people with known hepatitis C and the healthcare system. Therefore, we chose to use medical records as the confirmatory resource for subject identification. Using medical contact as the entry criteria allows inclusion of people who interact with the healthcare system and have been diagnosed in the context of their medical care. Registries for other purposes may need to select different subject inclusion or identification criteria.

Residence

To assure that the registry is community-population-based and subjects receive care in Olmsted County, only residents of Olmsted County for at least 1 year prior to the diagnosis of hepatitis C are included. In addition to a liver transplant service at the Mayo Clinic, Olmsted County has several inpatient and outpatient chemical-dependency treatment programs and "halfway houses" that may bring patients with hepatitis C to the community to live for short periods of time. Inclusion of these people would skew the community-based focus of the registry and the subsequent population-based epidemiologic data. Prisoners incarcerated in local facilities were also excluded. Our inclusion criteria are similar to requiring at least 1 year of enrollment in a health system.

Data Sources

In Olmsted County, all visits to physicians' offices, emergency departments (EDs), and hospitals are recorded in the database of the Rochester Epidemiology Project (REP).[27,28] The information contained in the REP database includes the person's name, county of residence, birth date, site-specific medical record numbers, and for each encounter, the date, site of visit, and up to 4 diagnoses. The visits to individual clinics are linked by subject name and birth date and address, if necessary. Linking is done by fussy matches for names that are confirmed by birth dates. More than 88% of matches are done electronically, with the rest completed manually. Further matching to avoid duplicate registry entries for the same person is possible when the medical records are reviewed. This diagnostic database is available from 1920 through the current year. All medical offices in the community, with the exceptions of 1 small psychiatry and psychology group and the regional mental health center, participate in the REP, allowing complete capture of medical (if not psychological) data on more than 98% of the residents of Olmsted County.[28]

To assure the broadest possible ascertainment of physician-diagnosed hepatitis C, all persons with diagnoses of hepatitis C and non-A/non-B hepatitis [*International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9 CM) codes 070.51, 070.41, V20.62, 070.54, 070.44, 070.9, 155.00, 573.1, 571.00, and 571.49][29] coded from January 1, 1990, through December 31, 1999, were included for review. These codes were selected after a pilot study using 1992 and 1993 data demonstrated that all of the selected codes added at least 5 cases in either year, without identifying more than 1 false positive for each case identified.

To increase ascertainment, the database of the Mayo Medical Laboratories was searched to identify any Olmsted County residents who had any positive tests for hepatitis C. All hepatitis screening and diagnostic tests for patients of both the Mayo Clinic and the Olmsted Medical Center are processed in this Mayo Clinic laboratory. Any subject who had a laboratory record of positive polymerase chain reaction (PCR) or positive or indeterminate recombinant immunoblot assay (RIBA) tests, but whose name did not appear in the list obtained from the diagnostic database (REP), was added to the group whose medical records were reviewed.

Second Source. Final determination of who was included in the registry was based on the review of the medical records as a second data source. Specifically, the medical records were used to confirm that the diagnostic criteria were met, and to assure that the person was an Olmsted County resident for at least 1 year prior to the first hepatitis C diagnosis. If the initial diagnosis was made within less than 1 year of moving into Olmsted County or prior to moving to Olmsted County, the person was included in the registry only if they were not living in a halfway house, incarcerated, or on the liver transplant waiting list. State and national death tapes were used to affirm subjects' vital statistics if no visits were recorded in the medical record after December 31, 1999, or if the patient was not otherwise known to be dead.

Definition of Hepatitis C Infection

The criteria used to determine who was actually included in the registry were intended to have the greatest sensitivity possible, while maintaining adequate specificity. The following criteria were used to define people to be included:

- A positive PCR test, or
- No PCR test but a positive RIBA test, or
- An indeterminate RIBA test plus 1 or more risk factors.

People with only a positive anti-hepatitis C serology and negative results for all other hepatitis C tests were considered false-positive subjects and were not included in the registry. This allowed inclusion of people with both acute and chronic hepatitis C.

Data Form

In addition to demographic data, the data collected were used to describe the initial diagnostic process, the liver disease-related conditions of the person at diagnosis, and the follow-up care and liver disease progression in the years after the initial diagnosis.

The initial diagnostic data included the date of first hepatitis C diagnosis; information on the tests used to screen and confirm the diagnosis of hepatitis C; tests, signs, and symptoms used to assess liver function at the time of diagnosis; documented hepatitis C risk factors and dates of those risk factors; and specialty of the physician who initially screened for hepatitis C.

Information on risk factors was obtained from the medical records using data documented specifically as "hepatitis C risk factors" at or within 3 months of the time of diagnosis or at the time of evaluation for treatment. The later information was used because it was almost always carefully recorded prior to consideration of treatment. Such risk factors as tattoos, intranasal cocaine use, or occupational exposure (eg, phlebotomist) were recorded in the documented risk factor report only if they were recorded by the physician as a risk factor. Information was collected regarding the national origin of people, with attention to those coming from hepatitis C-endemic areas, such as Africa and Southeast Asia. Risk factor information is important in determining the need for secondary prevention measures, such as hepatitis B immunization and HIV screening and preventive education. Additional data were also collected that recorded other potential risk factors, such as needle stick, which were not documented as risk factors at the time of diagnosis.

Follow-up care and disease progression data included the dates of all visits in which hepatitis C or any liver abnormalities or signs of liver decompensation were mentioned, and the most abnormal liver function test during each 6-month period after the diagnosis. Liver abnormalities included cirrhosis, chronic active hepatitis, and hepatocellular carcinoma. Liver decompensation was defined as the presence of ascites, jaundice, encephalopathy, or

bleeding esophageal varices. Hepatitis C treatment medications and dates of treatment, including participation in all clinical trials, were recorded. Liver transplant and death were also recorded.

In addition, information was collected on important coinfections (hepatitis B and HIV) and potential hepatitis C-accelerating factors, such as continued drug abuse, diabetes mellitus, and heavy alcohol use. These data are important in assessing rates of progression of liver disease, rates of hepatocellular carcinoma, and deaths related to hepatitis C. In addition, they may be useful to studies of clinic treatment and secondary prevention in people with known hepatitis C.

Information from the medical records was supplemented by death certificate data from the Minnesota Department of Health and the National Center for Health Statistics whenever a patient was not known to be deceased and had no visits documented after the end of the data collection period (December 31, 1999).

Data Entry and Monitoring

Data were entered directly onto a laptop computer and into a relational database (Paradox) that is easy to master, allows immediate feedback on data entry errors, and can readily be exported to other programs that might be useful to the clinician (Excel) and the researcher (SAS, S-Plus, and SPSS).

Data are updated every 6 months. A single data abstractor is currently reviewing the medical records and entering both initial and updated information on all subjects. As electronic database systems are refined, plans include collecting laboratory data electronically on a monthly basis and merging that data into the registry files.[20] It is unlikely that it will be possible to electronically collect data from the medical records in the near future because full text search options are not currently available, and relying on only the final diagnostic codes has been shown to be inadequate to reflect the hepatitis C-related care given (unpublished data validation studies for this registry).

Ethical Approval and Patient Confidentiality

Hepatitis C can be acquired from risky behaviors similar to those associated with HIV infections. Therefore, additional care was used in designing the registry confidentiality system and the procedures for user access. Approval was obtained by the Institutional Review Boards (IRBs) of the 2 local medical institutions that have IRBs. Additional patient privacy protection laws in Minnesota require signed authorization for use of medical records in research studies. Only people who have not refused to sign general research authorization forms are included in the registry. From the REP, it is possible to determine how many people with a diagnostic summary or laboratory diagnosis of hepatitis C refused this authorization. Future work on the registry may require information directly from subjects. Prior to any contact with subjects, it will be necessary to obtain IRB permission specifically for patient contact.

Currently, patient confidentiality is assured by the standard methods employed for any research database. Only researchers with IRB-approved studies are allowed access to the registry files, and no patient contact based on the registry data is permissible. Prior to any clinical use of the registry, it will be necessary to obtain the patient's permission for sharing of data across sites. Linking data into a regional or national registry will need to await national data privacy rules. These concerns are less expansive when the registry is maintained within a single healthcare system.

Funding

Due to the initial research-related purpose of this registry, development and early maintenance funding was provided by an unrestricted grant from a pharmaceutical company having an interest in hepatitis C therapy. The funder's interest in the registry was in the identification of the percentage of patients who received hepatitis C therapy and the average length of time from diagnosis to treatment. Continued funding will come from patient safety and quality improvement project monies.

··· RESULTS ···

There were 382 Olmsted county residents who were anti-Hepatitis C virus-positive or had a physician diagnosis of hepatitis C. Of these, 27 were considered to be false positives, including 13 individuals with negative RIBA, 13 with indeterminate RIBA, and 1 in whom RIBA was not performed. None of the 27 individuals had any documented risk factors for hepatitis C and all had normal liver function tests and the absence of other abnormal liver findings at the time of hepatitis C screening.

Almost twice as many men as women were identified for the registry. The subjects' demographic data, including hepatitis C risk factors as documented in the medical record, are displayed in the **Table**.

Both the REP data and the laboratory summary data were important in the identification of subjects for the registry. Using the specific hepatitis C codes listed in the "Methods" section identified 309 (87%) of the 355 subjects. The inclusion of codes for nonspecific hepatitis and viral hepatitis not otherwise specified (155.0) was not helpful. The addition of the nonspecific code more than tripled the number of people identified as potential cases, without adding any whom were not identified by the more specific hepatitis C codes. Of the 46 (13%) subjects identified only by laboratory data, two thirds (31) were patients who had their first screening and diagnosis during a hospitalization or ED visit for another non–liver-related problem. The rest (15) were diagnosed within the 9 months prior to the latest medical records abstraction, and physician diagnostic codes did not yet appear in the REP diagnostic database. For those diagnosed in the hospital without a hepatitis C diagnostic code recorded on the hospital discharge summary, the diagnosis of hepatitis C was usually made and confirmed by a consulting hepatologist in a patient with other serious medical problems. Laboratory information data is available within 24 hours of completion of the blood testing. Death tapes from the Minnesota Department of Health and the National Center for Health Statistics were the only data sources to identify 2 of the 10 deaths.

The number of new diagnoses of hepatitis C each year varied little after 1992 (**Figure 1**). The yearly rate of new diagnoses decreased slightly over that time period because the denominator (the county population) increased slightly, from about 127,000 to 130,000 over the 10 years from 1990 to 2000.

Data on comorbidities such as HIV status, active injecting drug use (IDU), and other chemical dependency, such as alcoholism, were available in many charts. Of the 177 persons with documented IDU, 43 had been tested for HIV and 5 were positive. In total, 58 (17%) of the 355 subjects (including 10 without a history of IDU) were screened for HIV. In addition, 331 (95%) had screening tests for hepatitis B, of which 2 had tests suggestive of active or chronic active hepatitis B disease. Overall, 57% (n = 202) of the population had a diagnostic visit code or medical record notation consistent with active and ongoing chemical abuse. Of these, 43 had specific notation of alcohol abuse that affected treatment decisions and 5 participated in some type of chemical-dependency treatment during the observation period.

Laboratory evaluation of liver function status was easy to identify in the medical records, as were visits to hepatology specialists, applications for liver transplantation, and deaths. However, visit or billing diagnostic codes did not identify all visits in which primary

Table. Demographic and Natural History Data (n = 355)

Sex	**N (%)**		
Male	219 (62%)		
Female	136 (38%)		
Risk factors recorded at diagnostic visit or within 3 months of diagnosis			
History of intravenous drug use	177 (50%)		
Sexual exposure	128 (36%)		
Immigrant	47 (13%)		
Tattoos	60 (17%)		
History of blood transfusion	107 (30%)		
Occupational risks	44 (22%)		
Actual needle sticks	4 (1%)		
Age at diagnosis			
Mean	42.3 y		
Standard deviation	14.6 y		
Range	2 d to 86 y		
Complications	**3 y before or at time of diagnosis**	**After diagnosis**	**Total**
Jaundice	9	7	16
Cirrhosis	23	15	38
Ascites	13	10	23
Gastrointestinal bleeding	5	8	13
Enchephalopathy	1	7	8
Hepatocellular carcinoma	2	6	8

care hepatitis C follow-up care was given. Notes for primary care visits for other reasons, such as preventive care or acute illnesses, often contained information regarding hepatitis C care, but the visit diagnostic and billing codes failed to mention hepatitis C.

About half of the subjects (n = 174, 49%) had data available from the date of diagnosis through the last date of data abstraction (January 2001). The average number of years of follow-up data was 3.1 years, and 20% of the subjects were lost to follow-up before December 31, 2000. Thirty-five patients (10%) died during the follow-up period. Survival data is displayed in **Figure 2**.

··· DISCUSSION ···

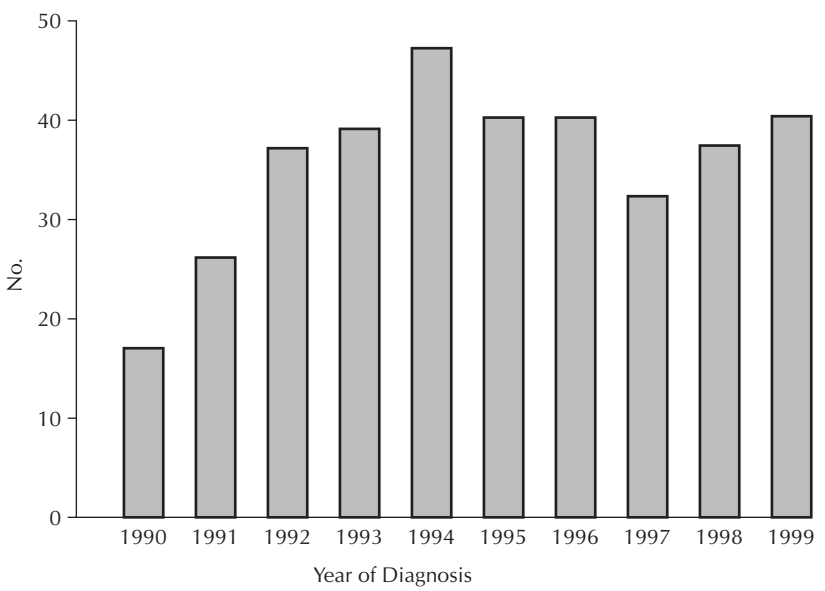
Although a unique community-population-based database (the REP database) made this registry possible, the process identifies important considerations for the development of registries using other combinations of community provider or health systems information resources. The use of laboratory data increased the capture rate of cases identified from the medical diagnostic summary (REP) and should be included as an important identification tool in any registry based on medical information. Laboratory data were more quickly available than data from the administrative database but did not identify those people with testing outside the county, or in the blood bank. Vital statistics data or death tapes identified 2 deaths not reported in the medical records. The definition of a hepatitis C case had to be tailored to clinical practice. Clinical trial definitions that require PCR testing or liver biopsy were considered too rigid and did not reflect recent expert opinion or guidelines for diagnosis of hepatitis C. Despite the potentially sensitive nature of information in these subjects' medical records, less than 3% refused research access to their data. The percentage that would refuse inclusion in a nonresearch registry is unknown.

About 15 % of the cases in this registry were identified through laboratory data, not from the diagnostic summary. The missing data were based on a time lag for residency and diagnostic verification done before transferring data from billing tapes into the REP, and on diagnoses missing from hospitalization and ED visit records. Hospital discharge codes are based on the billing summary codes. These codes are selected to maximize the reimbursement for the hospitalization and may include only codes that add complexity to the care of the primary diagnosis. Several of the subjects whose hepatitis C was found only on laboratory records had hepatitis C evaluations during hospitalization for other major medical problems unrelated to the hepatic system. The hepatitis C test results were reported in a progress note or consultation but hepatitis C was not included among the final diagnoses at the time of hospital discharge.

The second gap in the administrative data was seen in the ED. Sometimes, hepatitis C screening tests were ordered as part of a battery of tests during an ED visit and were to be addressed in follow-up visits that never occurred. The hepatitis C tests were reviewed and the diagnosis was made in the medical record but the patient failed to return for the follow-up appointment. Therefore, the diagnosis of hepatitis C was not attached to a visit and was not included in the diagnostic summary or administrative billing database.

This registry was also designed to allow longitudinal study of

Figure 1. Number of New Diagnoses per Year*



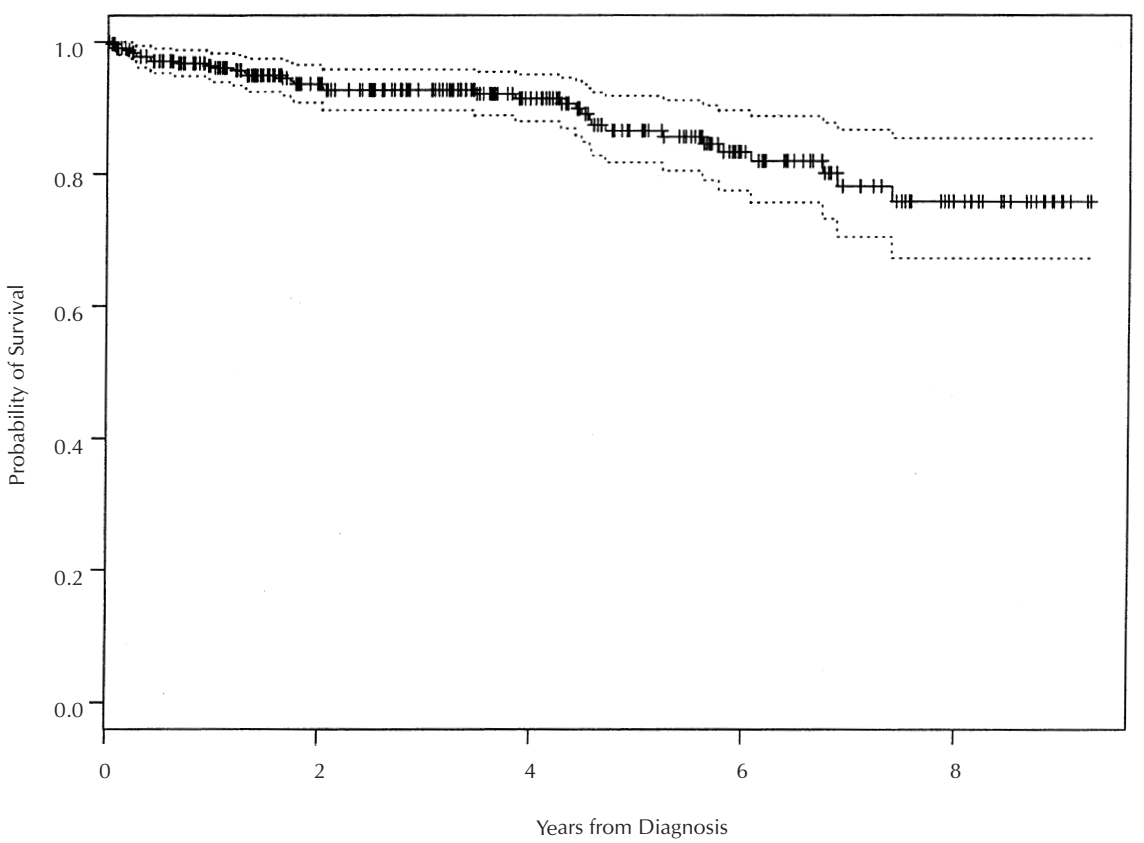
*Population denominator varies slightly from 127,000 in 1990 to 130,000 in 2000.

hepatitis C follow-up care and the course of disease in diagnosed hepatitis C. Visit summary diagnoses from administrative databases can identify visits but often fail to reflect all of the medical problems or concerns addressed at each visit.[30] Therefore, accurate reporting of all documented discussion and testing related to hepatitis C required review of the medical record. Only review of the medical record provided information on physician's choices not to offer or recommend hepatitis C treatment. We could not determine whether other methods, such as patient surveys or periodic physician summaries,[24,25] can be substituted for the medical record review.

Disease registries are a potential source of concern regarding patient confidentiality. The high-risk personal behaviors association with acquiring hepatitis C might make a registry of people with hepatitis C a source for increased concern. The rate of patient refusal of general research authorization (2.6%) in this group of subjects with hepatitis C is no higher than the rate of research authorization refusal for the total Olmsted County population.[31,32] This apparent lack of additional concern by people with hepatitis C and documented risk factors, such as IDU, provides some assurance that hepatitis C registries are possible and can provide healthcare utilization data on most people with physician-diagnosed hepatitis C. However, general research authorization allowing subjects to be included in this research registry does not assure that the same subjects would be willing to be included in a more traditional disease registry that involved patient contact or reporting to health authorities.

Selection of the data elements included in this registry was based on the purposes of the registry and the data sources available. Data such as liver function test results, signs of liver decompensation, risk factors directly related to hepatitis C natural history, and complications are obvious choices. In addition, the course of hepatitis C and its progression are believed to be affected by factors such as alcohol

Figure 2. Survival from Date of Diagnosis of Hepatitis C



consumption,[33-36] making it important to collect this type of exposure data. Registries for other conditions—sports injuries, using game and practice exposure data in paticular[15]—provide useful examples. In some cases, there were no documented diagnoses of alcoholism; however, several medical records had repeated documentation of alcohol intake ≥ 6 drinks per day or ≥ 3 recorded visits to the ED for alcohol-related injuries during a single 12-month period, which are compatible with a diagnosis of alcohol abuse. Extension of the definition of data elements (alcoholism) to include documented behaviors (heavy drinking or repeated injuries related to intoxication) can facilitate incorporation of this vital information into the registry.

The type of registry data described here has many potential uses beyond the traditional delineation of the disease course of hepatitis C. Unlike clinical trial data, this community practice data can provide effectiveness, as opposed to efficacy, information on hepatitis C treatment. Published estimates or projections of future healthcare costs,[37] utilization, or treatment outcomes should be validated against such "real-world" effectiveness data. Information from this type of community-based registry could also be used for clinical purposes, such as evaluating physicians' practices or supporting a quality improvement (QI) process. The New Hampshire Mammography Network registry has been used to identify practice variations and develop systems to address the variations.[17] Variations in disease monitoring or use of secondary prevention strategies (Hepatitis B virus immunization or alcoholism identification and referral for treatment) could be addressed in QI programs designed and implemented across providers, rather than those traditionally limited to a single hepatology clinic or provider. The registry could also be used to identify potential subjects for clinical trials.

The appropriate common set of core variables must be determined for optimal use of hepatitis C registries. For example, the definition of whom is included as a case of hepatitis C must be standardized. Clinical trials often require a subject to have a positive PCR or liver biopsy.[38] Clinical review articles suggest that a PCR may not be necessary in the case of a positive or indeterminate RIBA in a person with risk factors and normal liver function tests.[39-41] Until national standards for essential data elements and data definitions are developed, linking regional registries or developing a national registry will be difficult. The ability to follow subjects across registries will require careful consideration of how to collect and code subject identification data. Articles regarding immunization registries may help inform these attempts.[13]

Future uses of the registry database can only be hypothesized. We know that the genotype of the virus is important in determining response to therapy and possibly progression.[2,38] In the future, we may be able to determine the role of the subject's genotype in the progression or regression of hepatitis C.[14,42]

Our registry study has limitations. Using healthcare encounter data for subject identification will not identify everyone in the community with hepatitis C and therefore cannot provide public health estimates of disease prevalence. However, the registry can provide information to estimate the proportion of existing cases that are recognized. For example, estimates of the prevalence of hepatitis C in the US population varies from 3 to 10 million cases, or 1.8% to 3.8% of all Americans, depending on the source of data used.[1-3] The estimated prevalence of the Midwestern white population is 1.8%,[4] compared to the 1998 Olmsted County, physician-diagnosed prevalence of approximately 270/100,000 (0.27%). This comparison suggests new avenues of research, including methods to enhance case identification and physicians' hepatitis C screening strategies. Conversely, the ability to review and record all of the hepatitis C care allows unique opportunities for studies of current medical practice. The relatively modest sample size will require long-term observation to allow study of rare outcomes.

In conclusion, this community-based hepatitis C registry highlights some of the benefits and shortcomings common to any chronic disease registry. We confirm the ability to include clinical practice data that facilitate new uses of registry data.

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··· REFERENCES ···

1. Armstrong GL, Alter MJ, McQuillan GM, Margolis HS. The past incidence of hepatitis C virus infection: Implications for the future burden of chronic liver disease in the United States. *Hepatology* 2000;31:777-782.

2. Muir AJ. The natural history of hepatitis C viral infection. *Semin Gastrointest Dis* 2000;11:54-61.

3. Alter M, Kruszon-Moran D, Nainan OV, et al. The prevalence of hepatitis C virus infection in the United States, 1988 through 1994. *N Engl J Med* 1999;341:556-562.

4. *Third National Health and Nutrition Examination Survey, 1988-1994 (NHANES III).* Hyattsville, MD: National Center for Health Statistics; 1996.

5. Poynard T, Bedossa P, Opolon P, et al. Natural history of liver fibrosis progression in patients with chronic hepatitis *C. Lancet* 1997;346:825-832.

6. Seeff LB, Miller RN, Rabkin CS, et al. 45-year follow-up of hepatitis C virus infection in healthy young adults. *Ann Intern Med* 2000;132:105-111.

7. Villano SA, Vlahov D, Nelson K, et al. Persistence of viremia and the importance of long-term follow-up after acute hepatitis C infection. *Hepatology* 1999;29:908-914.

8. Alter MJ. Epidemiology of hepatitis C in the West. *Semin Liver Dis* 1995;15:5-14.

9. Alter MJ. Epidemiology of hepatitis C. *Hepatology* 1997;26(3 suppl 1):62S-65S.

10. Minello A, Boschi F, Harb M, et al. Creation of a viral hepatitis B and C in the Cote [in French]. *Gastroenterol Clin Biol* 1998;22:
766-771.

11. McQuillan G, Alter M, Moyer L, Lambert S, Margolis H. A population-based serologic study of hepatitis C virus infection in the United States. *Am J Epidemiol* 1996;143(suppl):S32.

12. Crowe J, Doyle C, Fielding JF, et al. Presentation of hepatitis C in a unique uniform cohort 17 years from inoculation [abstract]. *Gastroenterology* 1995;108:A1054.

13. Woods DR, Saarlas KN, Inkelas M, Matyas BT. Immunization registries in the United States: Implications for the practice of public health in a changing healthcare system. *Annu Rev Public Health* 1999;20:231-255.

14. Tull ES, Christian CLE, Roseman JM. Development of a registry for diabetes in persons 0-19 years of age in the US Virgin Islands. *Bull Pan Am Health Organ* 1991;25:218-228.

15. Meeuwisse WH, Love EJ. Development, implementation, and validation of the Canadian Intercollegiate Sport Injury Registry. *Clin J Sport Med* 1998;8:164-177.

16. Hollander JE, Singer AJ, Valentine S, Henry MC. Wound registry: Development and validation. *Ann Emerg Med* 1995;25:675-685.

17. Carney PA, Poplack SP, Wells WA, Littenbert B. The New Hampshire Mammography Network: The development and design of a population-based registry. *AJR* 1996;167:367-372.

18. Brown LJ, Scott RS. A population-based diabetes register-development & applications. *Community Health Study* 1988;12:437-443.

19. Ortiz A. Development of a system for registry of information on drug use in Mexico. *Bull Pan Am Health Organ* 1990;24:46-52.

20. Rothwell AG. Development of the New Zealand Joint Register. *Bull Hosp Jt Dis* 1999;58:148-160.

21. Alter MJ, Margolis HS, Krawczynski K, et al. The natural history of community-acquired hepatitis C in the United States. *N Engl J Med* 1992;327:1899-1905.

22. Hoofnagle JH. Hepatitis C: The clinical spectrum of disease. *Hepatology* 1997;26(suppl):15S-20S.

23. Takahashi M, Yamada G, Miyamoto R, et al. Natural course of chronic hepatitis C. *Am J Gastroenterol* 1993;88:240-243.

24. CDSC. Hepatitis C and blood transfusion. *Commun Dis Rep CDR Wkly* 1995;5:9.

25. A national register of hepatitis C virus infections with known dates of acquisition [editorial]. *CDR Weekly* 1998;8:18.

26. Department of Health. Hepatitis C and Blood Transfusion Look Back. London: HMSO; 1995. [PL CMO](95)1].

27. Kurland LT, Molgaard CA. The patient record in epidemiology. *Sci Am* 1981;245:54-63.

28. Melton LJ III. History of the Rochester Epidemiology Project. *Mayo Clin Proc* 1996;71:266-274.

29. Medicode, Inc. *Physician ICD-9 CM.* Volumes 1 and 2. Salt Lake City, Utah: Medicode, Inc; 1998.

30. Jaen CR, Stange KC, Nutting PA. Competing demands of primary care: A model for the delivery of clinical preventive services. *J Fam Pract* 1994;38:166-171.

31. Yawn BP, Yawn RA, Geier GR, Xia Z, Jacobsen SJ. The impact of requiring patient authorization for use of data in medical records research. *J Fam Pract* 1998;47:361-365.

32. Jacobsen SJ, Xia Z, Campion ME, et al. Potential effect of authorization bias on medical record research. *Mayo Clin Proc* 1999;74:330-338.

33. Gordon SC, Elloway RS, Long JC, Dmuchowski CF. The pathology of hepatitis C as a function of mode of transmission: Blood transfusion vs intravenous drug use. *Hepatology* 1993;18: 1338-1343.

34. Desmet VJ, Gerber M, Hoofnagle JH, Manns M, Scheuer PJ. Classification of chronic hepatitis: Diagnosis, grading and staging. *Hepatology* 1994;19:1513-1520.

35. Jenkins PJ, Cromie SL, Roberts SK, et al. Chronic hepatitis C, alcohol and hepatic fibrosis [abstract]. *Hepatology* 1996;24:153A.

36. Bellentani S, Pozzato G, Saccoccio G, et al. Clinical course and risk factors of HCV related liver disease in the general population: Report from the Dionysos study. *Gut* 1999;44:874-880.

37. Kim WR, Gross JB Jr, Poterucha JJ, et al. Outcome of hospital care of liver disease associated with hepatitis C in the United States. *Hepatology* 2001;33:201-206.

38. Whitehead JM, Patterson AP, Moulton A. Development of databases and registries. *Ann N Y Acad Sci* 1998;862:217-221.

39. Gross JB Jr. Clinician's guide to hepatitis C. *Mayo Clin Proc* 1998;73:355-360; quiz 361.

40. Shaib YH, Vega KH, Jamal MM. Approach to patients with hepatitis C and persistently normal alanine aminotransferase levels. *Clin Perspect Gastroenterol* 2000;5:252-258.

41. Farrell GC, Liaw YF. Consensus statements on the prevention and management of hepatitis B and hepatitis C in the Asia-Pacific region. *J Gastroenterol Hepatol* 2000;8:825-841.

42. Silini E, Bono F, Civicini A, et al. Differential distribution of hepatitis C virus genotypes in patients with and without liver function abnormalities. *Hepatology* 1995;21:285-290.