# OSCCAR: Ocean State Crohn's and Colitis Area Registry

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**Epidemiology studies describe population** characteristics of disease states. The results are important for determining the allocation of healthcare resources, developing preventative measures, identifying risk factors for disease and predicting outcomes of disease. The **Ocean State Crohn's and Colitis Area Registry** (**OSCCAR**) is a population-based cohort of newly diagnosed patients to be followed prospectively to determine the epidemiologic characteristics of **Crohn's disease** (**CD**) and **ulcerative colitis** (**UC**). This study has used the population of Rhode Island as a defined base.

Much of what we know about IBD in the US population comes from studies conducted in Canada and Olmsted County, MN.[1-6] Data from these studies may not be applicable to the more diverse population of the **United States** (**US**). In addition to a homogenous population, residents of Olmsted County are 3 times more likely to be employed in health care services and 1.5 times more likely to have completed college compared to the general population.[4] The Olmsted results may also be limited by misclassification bias due to retrospective data acquisition.[3]

Several population-based studies have used hospital admission data,[7-11] but because the majority of patients with IBD are treated as outpatients, the incidence and prevalence rates may be underestimated. Sonnenberg et al. reviewed admission data for patients with the Veterans Administration to determine the incidence and prevalence of IBD,[12] but the VA has a very specific, largely male, patient population. The resulting data may not be generalizable to the US population.

More recent studies have used HMO and insurance claims data to determine incidence and prevalence of IBD.[11,13-16] These studies have several limitations. The populations sampled are not random. Health plans do not represent all age groups or uninsured patients. Most plans do not collect detailed demographic patient information, such as ethnicity or race. There may also be misclassification or coding inconsistencies. Claims data lack sufficient clinical evidence to confirm diagnosis.

Due to the fragmented nature of the health care system, epidemiologic studies of the general population of the US are costly and difficult. Studies of patients seen at referral centers likely reflect the outcomes of the most severely affected individuals, who may not reflect the broad population of individuals with these diseases. These differences are critical to understanding why the course of these diseases is so highly variable and, at the present time, unpredictable. The ability to identify otherwise unselected Americans with new diagnoses of IBD, and to track their outcomes over time would greatly enhance our understanding of these diseases and their effect.

The lack of a well-defined, prospectively evaluated, population-based inception cohort in the US is a critical impediment to developing generalizable prognostic markers and models of disease progression in IBD. OSCCAR is necessary for several reasons: (1) To date, population-based studies designed to evaluate IBD have been limited to small relatively homogeneous populations; (2) Incidence rates of IBD continue to rise – an increase not completely attributable to increased awareness and advances in disease diagnosis; (3) The natural history of IBD is incompletely described. While studies have helped to define the natural history of IBD in aggregate, they do not allow prediction of the individual course of disease or prognosis. None reflect treatment practices in the US, with increasing use of immunomodulators and anti-TNF antibodies;(4) Determinants of prognosis are poorly understood. Little is known about the clinical implications of genetic

*Table 1: Census Bureau Data for Rhode Island for the Year 2006* [24]

| | |
|---|---|
| Population | 1,067,610 |
| Females | 51.6% |
| Males | 48.4% |
| Age Distribution | |
| < 5 years old | 5.8% |
| 5-17 | 22.2% |
| 18-64 | 58.1% |
| ≥ 65 | 13.9% |
| Caucasian | 79.6% |
| Hispanic | 11% |
| African-American | 6% |
| Asian or Pacific Islander | 2.8% |
| Native American | 0.6% |

*Table 2: Diagnosis of IBD According to The NIDDK IBD Genetics Consortium Phenotype Operating Manual* [21]

A Symptoms including one or more of: diarrhea, rectal bleeding, abdominal pain, fever, complicated perianal disease, extraintestinal manifestations, weight loss or failure to thrive; and

B Symptoms on two or more occasions separated by at least 8 weeks or ongoing symptoms of at least 6 weeks duration. When there has been a single episode of colitis (in some instances less then 6 weeks duration) resulting in colectomy and resolution of disease symptoms, pathology on the colectomy specimen should be consistent with idiopathic IBD and microbiology studies should be negative; and

C One or more of the following providing *objective* evidence of inflammation:

1.C Endoscopic: Mucosal edema, erythema, loss of normal submucosal vasculature, friability, ulceration, stricture formation, pseudopolyps. *Where there are only minor changes (mucosal edema, erythema, loss of normal submucosal vasculature, friability) mucosal biopsies should have been done to confirm the presence of IBD; and/or*

2.C Radiologic: Mucosal thickening and/or nodularity, ulceration, stricture, pseudopolyps, fistula formation, pseudosacculation. Minor changes alone (mucosal thickening and/or nodularity) should not be sufficient to make a diagnosis of IBD; and/or

3.C Histologic: Mucosal erosion or ulceration, architectural changes of crypts, Paneth cell metaplasia (in colon), transmural inflammatory infiltrate*, fibrosis of muscularis propria*, noncaseating granuloma*. (*Crohn's disease only)

profiles on prognosis, with regard to the correlation of genotype and phenotypic presentation of disease.[17-19] Few environmental risk factors have been established, and these risk factors do not completely explain the occurrence of IBD and the rising incidence rates of CD.

Rhode Island, with a diverse population of over 1 million, provides an ideal base for a prospective inception cohort of IBD patients, limiting referral bias in estimates of prognosis, and enhancing generalizability of predictive models. (Table 1) Based on American estimates of incidence rates of CD (7-8 cases per 100,000 person-years) and UC (8-9 cases per 100,000 person-years),[20] approximately 70 and 80 cases of CD and UC will be diagnosed annually, respectively.

## Description

OSCCAR is a population-based study designed to capture each new case of inflammatory bowel disease diagnosed in Rhode Island. This is the first of its kind and one of very few such cohorts in the world. The goals of the study include: 1) describing the incidence rates of CD and UC; 2) describing disease outcomes; and 3) identifying factors that predict disease outcomes. In the coming years, we anticipate enrolling between 150 and 250 newly diagnosed individuals annually. As we track the diversity of backgrounds and exposures, we expect to describe the outcomes of these diseases with great detail and precision. More important, we expect to begin to unravel the reasons for these diverse outcomes, and eventually to predict the course of the disease with increasing accuracy.


## Funding Source

The **Centers for Disease Control and Prevention (CDC)** has granted funds to the **Crohn's & Colitis Foundation of America (CCFA)** to support OSCCAR (Project # 1 UO1 DP000340-03). In addition, the **National Institutes of Health (NIH)** has granted funds to subsidize OSCCAR (NIH grant # 5R21DK078555-02). This study is being conducted jointly by investigators at the Harvard Medical School and the Warren Alpert Medical School of Brown University.


## Objectives

The initial study objectives include: (1) establishing study procedures to develop and maintain a population based, prospective inception cohort of IBD patients in the state of Rhode Island; (2) determining the incidence rates of CD and UC in Rhode Island and extrapolating these rates to the general US population; (3) defining the natural history of IBD in the setting of contemporary treatment practices in the US, and obtaining preliminary data to identify clinical and subclinical factors associated with disease progression in CD and UC; and (4) identifying clinical and subclinical (including genetic) risk factors for steroid resistance in IBD.

## Subject Selection

All adults and children living in Rhode Island, and newly diagnosed with CD, UC, or indeterminate colitis, will be invited to join the study. As there are no gold standard tests for diagnosing Crohn's disease and ulcerative colitis, new diagnoses of IBD depend upon signs and symptoms consistent with the diagnosis and confirmed on endoscopy, pathology, or imaging. Histopathologic confirma-

*Table 3: Categorization of IBD into Subtypes According to The NIDDK IBD Genetics Consortium Phenotype Operating Manual* [21]

| | |
|---|---|
| Crohn's Disease (CD) | |
| 1 | Evidence of small intestinal inflammation with endoscopically, radiologically or histologically demonstrated ulcerations, fistulization, mucosal fissuring, nodularity or cobblestoning, stricture formation or histologically demonstrated transmural inflammation with or without granuloma formation. |
| 2 | Isolated esophageal, gastric or duodenal inflammation with the finding of noncaseating granuloma. |
| 3 | Colonic inflammation which is patchy (normal segments separating areas of inflammation, as described above) or associated with one or more of the following features: complete rectal sparing, multiple (>10) aphthoid ulcers, deep ulceration (into the muscularis propria), transmural inflammation, extensive fibrosis and wall thickening, fistulization, non-caseating granuloma. |
| 4 | The presence of complex suppurative perianal disease (i.e. more than a superficial fistula or uncomplicated superficial abscess). |
| 5 | If there are fewer than 10 aphthoid ulcers in the cecum (and the rest of the colon appears normal) in a patient with small bowel disease then this should be called small bowel disease only. Similarly, if the colon is normal except for the presence of a fistula extending from inflamed small bowel, the patient should be said to have small bowel disease alone. If the cecum is involved with ulcers larger than aphthoid ulcers or ulcers that are deep or if the involvement has resulted in deformity of the cecum this would be considered to be colonic involvement. |
| Ulcerative Colitis (UC) | |
| 1 | Superficial inflammation and/or ulceration (involving only the mucosa and submucosa) of the colon which is continuous from the rectum extending proximally without skip lesions or complete rectal sparing (N.B. Relative rectal sparing is allowed for patients receiving topical rectal therapy). |
| 2 | No inflammation of the small intestine ("backwash ileitis" is allowed - nonstenosing superficial inflammation of the terminal ileal mucosa associated with severe pancolitis which resolves following medical or surgical treatment of the colitis). |
| 3 | No features of Crohn's disease listed above. |
| Indeterminate Colitis (IC) | |
| 1 | Confirmed IBD by A, B and C above (Table 2). |
| 2 | Physician unable to classify individual into either CD or UC based on above criteria and/or patient has features of both CD and UC with none of the features diagnostic of one or the other. |

tion is usually possible-based on review of endoscopic biopsies. For this study, a diagnosis of IBD is made according to the NIDDK IBD genetics consortium criteria as described in their phenotype operating manual (May 10, 2006).[21] (Tables 2 and 3)

Individuals diagnosed with CD, UC, or indeterminate colitis prior to the study start date (i.e., prevalent cases), those unwilling to provide informed consent, those who are prisoners at the time of diagnosis and pregnant women will not be permitted to enroll.

## Subject Enrollment

We believe that the majority of patients suspected of having IBD are evaluated by a gastroenterologist or colorectal surgeon to establish a diagnosis. The clinician will present OSCCAR to the patient at anytime up to 6 months from diagnosis. Patients who agree to be contacted will complete a referral form, which is available in pamphlets distributed to all gastroenterology and colorectal surgery practices in the state, and in practices in Southeastern Massachusetts along the eastern border of Rhode Island. The referral forms are faxed to the study office. Alternatively, online referrals can be made through the study website at http://www.osccar.org.

*Table 4: Summary of Data Being Collected*

1. General subject information (date of birth, place of residency, contact information)
2. Demographic data (age, gender, race, ethnicity, occupation, marital status, education level)
3. Symptoms at diagnosis
4. Tobacco history
5. Family history of IBD
6. History of immune-related conditions and cancer (patient and family history)
7. Pediatric growth and development
8. Laboratory and serology results at diagnosis
9. Endoscopy findings
10. Surgical findings and procedures
11. Pathology findings
12. Radiology findings
13. Past and present medication use for the treatment of IBD
14. Interval history at 3, 6 and 9 months, and annually, including development of extraintestinal manifestations, medication use, hospitalizations, endoscopic procedures, imaging studies, and/or surgery
15. Disease activity indices: Harvey Bradshaw Index (CD) or Simple Clinical Colitis Activity Index (UC or IC) [25,26], Pediatric Crohn's Disease Activity Index (PCDAI) or Pediatric Ulcerative Colitis Activity Index [27,28]
16. Dietary history using the Food Frequency Questionnaire [29,30]

## Study Procedures

Once a referral is received, study personnel will contact the patient to schedule an intake visit, in either the patient's home or in a place of their choosing. In the case of children, the intake visit takes place at the Hasbro Children's Hospital. During that visit, lasting approximately 2 hours, personnel obtain informed consent (available in English, Spanish, and Portuguese) and provide detailed education regarding the diagnosis of IBD. Personnel record demographic data, past medical history and disease-related information, administer quality of life and disease activity questionnaires (Tables 4 and 5), and collect blood, urine and stool samples. Later, study personnel obtain additional data elements by standardized chart review of the subject's medical record.

Study personnel will contact subjects by telephone at months 3, 6 and 9 for a brief follow up interview. Patients (or their parents, in the case of children under age 18) are queried about their disease activity, the medical and surgical treatments or procedures they have received since their most recent interview, and reasons for discontinuing any medical therapies. In addition, personnel will administer the **Short Inflammatory Bowel Disease Questionnaire (SIBDQ)** , a measure of disease activity for adults, or the **IBD Quality of Life Survey (IMPACT-35 Questionnaire)**, for children. [21,22]

One year from diagnosis, study personnel will arrange a return visit. Personnel will re-obtain the initial data elements (except for demographic data), will abstract interval data from the medical record, and will collect blood, urine, and stool samples. Personnel will schedule return visits annually.

Subjects will be compensated: Each subject will receive a one-hundred dollar stipend upon enrollment, and a fifty dollar stipend for each annual visit completed.

## Procedure for Missed Cases

Initial experience since the start of the study suggests that the capture rate of newly diagnosed patients by initial referral by a gastroenterologist or colorectal surgeon has been good; but to improve the capture rate, we have asked each prac-

| *Table 5: Quality of Life Questionnaires* | *Acronym* | *Description* |
|---|---|---|
| Inflammatory Bowel Disease Questionnaire[31] and Short Inflammatory Bowel Disease Questionnaire[23] | IBDQ SIBDQ | Health-related quality of life questionnaire specific for adults with IBD |
| IBD quality of Life Interview (IMPACT-35)[22] | IMPACT-35 | Health-related quality of life questionnaire specific for pediatric population with IBD |
| SF-36[32] | SF-36 | Generic quality of life questionnaire |
| EuroQol [33,34] | EQ-5D | Generic quality of life questionnaire for adults |
| Work Productivity and Activity Impairment Questionnaire[35] | WPAI:SHP | Generic questionnaire assessing the effects of a condition on ability to work or perform regular activities (adults) |
| Functional Assessment of Chronic Illness Therapy[36] | FACIT | Generic questionnaire assessing patent fatigue level related to a health condition (adults) |

**Patient self referral form**

# Enrollment Contact Form

Fax to: 401-444-4283
Date: ____/____/_____
Diagnosis: Crohn's Ulcerative Colitis
(circle one)
Referring Physician: _____

The Ocean State
Crohn's & Colitis
Area Registry

We are asking your permission to contact you to answer any questions you may have about participating in OSCCAR and to arrange a visit.

By filling out this form, you agree to allow a member of the study staff to contact you. Submitting this form does not obligate you to participate in the study and does not change or decrease the health care you usually receive.;

We are delighted with your interest and look forward to speaking with you soon.

First Name: _____

Last Name: _____

How would you like us to reach you?

Phone: ☐☐☐ ☐☐☐ ☐☐☐☐

Email: _____

What times of day work best? _____

When were you diagnosed? ☐☐ ☐☐ ☐☐☐☐

Rhode Island Hospital Liver Research Center 55 Claverick Street, Rm 333 Providence, RI
Phone: 401-444-3381 / Fax: 401-444-4283 / email: osccar@lifespan.org / www.osccar.org

**Health care professional referral form**

# Enrollment Contact Form

Fax to: 401-444-4283
Today's Date: __/__/_____
Diagnosis: Crohn's Disease Ulcerative Colitis (circle one)
Referring Physician, RN, or NP:

_____

Completed by: _____

The Ocean State Crohn's & Colitis Area Registry

Please complete this form once you have spoken with your patient (or their guardians if patient is a child) about OSCCAR and he/she has indicated it would be ok for someone from the study to contact them.

When we call your patient, we will answer any questions they may have about participating in OSCCAR and if they are interested, we will schedule a visit.

By providing your patient's information below, he/she is in no way obligated to participate in the study.

Patient's
First Name: _____

Patient's
Last Name: _____

Guardian's Name
(if patient is a minor): _____

Estimated date
of diagnosis: _____/_____/_____

Patient/Guardian's
Phone Number: | | | | | | | | | | |

Rhode Island Hospital Dept. Pedi GI 593 Eddy Street MPS 148 Providence, RI 02903
Phone: 401-444-4143 / Fax: 401-444-4283 / email: osccar@lifespan.org / www.osccar.org

*Table 6: Enrollment Table as of January 15, 2009*

| | Adult | | Pediatric | | Total |
|---|---|---|---|---|---|
| | Male | Female | Male | Female | |
| Enrolled | 21 | 34 | 9 | 8 | 72 |
| Pending | 4 | 0 | 0 | 1 | 5 |
| Ineligible | 5 | 5 | 0 | 0 | 10 |
| Unresponsive/ Declined | 3 | 2 | 0 | 1 | 6 |

tice to search billing data for a defined period of time by ICD-9 codes mapping to IBD. Any patients discovered during this process and not previously referred to the study may be contacted by their gastroenterologist and referred at that time with the patient's permission. Each practice will undergo a diagnostic review every 4 months. Diagnostic review has resulted in an increased overall capture rate.

## Use of Specimens

Blood samples are collected during the intake and annual study visits. Peripheral blood is collected for isolation of messenger RNA (mRNA) for gene expression arrays. Plasma is collected for proteomics studies, and serum for serologic studies. DNA is being isolated for studies of genetic susceptibility and genetic determinants of phenotype and prognosis.

Urine is collected and stored for future metabolomics studies.

Stool samples are collected for speciation of fecal flora by non-classical bacteriologic methods, such as 16S ribosomal RNA speciation or multiplex PCR of IS900 integration loci. Ultimately we intend to apply high-throughput novel technologies to elucidate factors and/or profiles associated with phenotype of disease and prognosis. Steroid dependence remains an increasing problem in IBD and this will be the first focus of the laboratory effort.

## Current Status of OSCCAR

OSCCAR has been open to enrollment since January 1, 2008. Ninety-seven gastroenterologists/colorectal surgeons from 22 practices have agreed to refer patients. Study staff and the principal investigators visited each practice prior to initiation and the study was gradually rolled out to each practice. Brochures describing OSCCAR and IBD educational booklets have been distributed to each practice. (Table 6)

## Contribution of OSCCAR

Initially, each subject will benefit from individual and private education about their new diagnosis of IBD. It is hoped that OSCCAR will provide an accurate incidence rate applicable to the US population. In addition, the results will provide information regarding determinants of steroid resistance, describe disease outcomes and identify predictors of disease, such as environmental and genetics risk factors. The knowledge gained from OSCCAR will assist with the creation of treatment algorithms for IBD and provide insight into areas of future research.

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### Disclosure of Financial Interests

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