Published by Oxford University Press on behalf of the International Epidemiological Association
© The Author 2008; all rights reserved. Advance Access publication 9 September 2008

International Journal of Epidemiology 2009;**38**:922–931
doi:10.1093/ije/dyn180

COHORT PROFILE

Cohort Profile: The Swiss Inflammatory Bowel Disease Cohort Study (SIBDCS)

Valérie Pittet,[1]* Pascal Juillerat,[2] Christian Mottet,[2] Christian Felley,[2] Pierluigi Ballabeni,[1] Bernard Burnand,[1] Pierre Michetti,[2] John-Paul Vader[1] and the Swiss IBD Cohort Study Group[†]

Accepted 6 August 2008

How did the study come about?

Background

Crohn's disease, ulcerative colitis and indeterminate colitis are the three subtypes of disease collectively known as inflammatory bowel diseases: relapsing and remitting conditions characterized by chronic inflammation which is limited to the colon in ulcerative colitis, whereas it can involve various sites in the gastrointestinal tract in Crohn's disease.[1] The pathogenesis of inflammatory bowel disease is currently still unclear, although humoral and cell-mediated immune system, as well as environmental [hygiene, smoking, non-steroidal anti-inflammatory drugs (NSAIDs) use, geographic location] and genetic factors are known to be involved in the occurrence of these diseases.

Patients often require continuous medication as well as one or more intestinal resections. The care of these patients is evolving rapidly with the introduction of novel therapies and treatment plans.[2,3] Some of these new treatments are expensive and their efficacy is usually limited to 30–50% of patients. In the absence of markers able to predict response to specific therapies, all eligible patients currently receive several of these drugs. They are thus exposed to side-effects which contribute to the high overall cost of these therapies—half the average medical costs associated with the disease,[4,5]—while only a fraction of those treated will benefit at each stage.

Impact on patient quality of life is often considerable, especially because disease onset can occur already in the first or second decade of life, while patients are either in full-time education or just entering the workforce. The negative impact on social life or ability to achieve, either scholastically or professionally, can severely affect professional as well as family life. Indeed, >50% of patients with Crohn's disease indicate that their disease has an influence on their professional and personal life.[6] The course of the disease is often characterized by progressive worsening of the patient's condition, with increasing frequency of hospitalization and considerable indirect costs through absenteeism and disability allowances.[7] Disease activity is known to be influenced by psychological factors.[8–10]

Pilot study

In a first phase, an adult, population-based cohort was established in the Canton of Vaud (Switzerland) between July 2003 and December 2004 in order to make an estimation of the prevalence of inflammatory bowel disease patients. Among this population of 650 000 inhabitants (about a tenth of the Swiss population, with similar age and sex distribution), 1016 adult inflammatory bowel disease patients were identified,[11] corresponding to an age- and sex-adjusted prevalence of 206 inflammatory bowel disease cases per 10^5 inhabitants. Extrapolating from these figures to the whole of Switzerland, the number of adults with inflammatory bowel disease could be estimated to be about 12 000, i.e. rather high compared with reported rates in Europe and North America over the last 20 years.[12–18]

The study was extended to all of Switzerland in 2006, in a collaborative and multidisciplinary effort by gastroenterologists, pathologists, psychologists and methodologists, and with the financial support of the Swiss National Science Foundation (SNSF).

What does it cover?

The general aim of the SIBDCS is to provide the Swiss and international scientific, public health and medical community with a disease-oriented prospective cohort

[1] Institute of Social and Preventive Medicine, Centre Hospitalier Universitaire Vaudois and University of Lausanne, Lausanne, Switzerland.
[2] Department of Gastroenterology and Hepatology, Centre Hospitalier Universitaire Vaudois and University of Lausanne, Lausanne, Switzerland.
* Corresponding author. Healthcare Evaluation Unit, Institute of Social and Preventive Medicine (IUMSP), Bugnon 17, CH-1005 Lausanne, Switzerland. E-mail: Valerie.Pittet@chuv.ch
[†] See Appendix 1 for list of participating centres.

of inflammatory bowel disease patients. Data from the Swiss IBD cohort (SIBDC) will (i) provide up-to-date epidemiological data (e.g. prevalence, incidence, clinical course of inflammatory bowel diseases) and to investigate risk factors associated with favourable or unfavourable evolution of the course of the disease; (ii) document medical care given to the patient in order to assess appropriateness of care; (iii) evaluate current health resource consumption (direct and indirect costs) for inflammatory bowel disease patients and the influence of new biological therapies, in order to optimize costs and public health policies for chronic diseases; and (iv) study psychosocial aspects linked to the disease, by seeking predictors associated with inflammatory bowel disease exacerbation, as well as investigating the role of cytokines in the pro-inflammatory response to stress.

A biobank has been set up to collect serum, blood lymphocyte and DNA samples to allow better identification of clinical or biological markers able to predict response to specific therapies.

A number of nested projects on various specific aspects linked to inflammatory bowel disease and the cohort study are proposed each year. The most promising projects will be funded within the framework of the cohort, but additional, independently funded projects may be proposed as well.

Who is in the sample?

Because access to patient chart data from all of the 250 gastroenterologists in Switzerland is difficult to obtain, there is no intention to recruit all patients with inflammatory bowel disease in the whole of Switzerland. In addition, there is no centralized administrative database that could assist in case identification. There is no financial incentive for the gastroenterologists to participate in the cohort; participation is voluntary, relying on individual motivation, especially for those working in private practice and outside the university hospital setting. Despite these obstacles, we plan to be able to assemble a large clinical cohort in Switzerland.

Within this framework, we will also assemble a population-based clinical cohort and recruit all patients with inflammatory bowel disease in two specific geographic regions corresponding to the cantons of Vaud and Solothurn (910 000 total inhabitants at the end of 2006). Indeed, a pilot study has already taken place in the Canton of Vaud, meaning that coverage is thus virtually complete.

Participation is not restricted by age or sex. Permanent residence status in Switzerland or having contracted Swiss health insurance and being treated on a regular basis in Switzerland are, however, a requirement for study inclusion. This means that individuals who are treated in Switzerland, but who are not residents, most commonly cross-border workers from France, are included in the cohort. To be included, patients must have a diagnosis established at least 4 months prior to inclusion or have had at least one recurrence of the symptoms. Diagnosis, based on Lennard-Jones criteria,[19] can be confirmed by radiological, endoscopic and histological findings, or surgery.

One thousand and twenty patients have been recruited as of June 30, 2008, the goal being to include, within 3 years, 3000 patients from anywhere in Switzerland with any diagnosis of Crohn's disease, ulcerative colitis or indeterminate colitis. Given the diversity of projects included in the cohort study (appropriateness of care; economics of IBD; psychosocial correlates of relapse; in addition to smaller nested projects), it is not possible to calculate a unique cohort sample size, as this would be linked to the research hypothesis of each of these projects. For example, a sample size of 950 patients with Crohn's disease would be needed to detect a 10% difference in proportion of patients having appropriate therapy, depending on whether they were being treated with steroids or biologicals, to maintain disease remission.

Recruitment first began in the six major inflammatory bowel disease centres of the university-based tertiary hospitals. Each participating centre has a local coordinator and a study nurse/clinical research assistant, who is responsible for recruitment organization in a defined region (Figure 1), called working areas. The working areas were defined according to affinities between regional gastroenterology networks and university centres. Recruitment is fostered by providing information about the study and contacting gastroenterologists by mail or through informational meetings, either in regional or canton hospitals or in private practices. The local coordinator organizes biosample collection and processing in collaboration with the central biobank and is responsible for quality control of information provided on biosample tube labels and forms sent with the specimens. Recruitment of inflammatory bowel disease patients is carried out by their gastroenterologist, either during a routine visit or by mail invitation. A further channel of information about the study exists through patient organizations [ASMCC (Association Suisse de la Maladie de Crohn et de la Colite ulcéreuse)/SMCCV (Schweizerische Morbus Crohn/Colitis ulcerosa Vereinigung)], so that patients can be recruited independently, for example those who have been in remission for a long time and who do not currently require any medical attention.

The study required approval by all ethics committees in Switzerland. In all, 14 cantonal or regional ethics committees had to be contacted in the 26 Swiss cantons, to cover the whole country. Eight cantons had their own local committee and the other 18 were covered by 6 committees serving regions comprising 2–6 cantons. Approval has so far been obtained in all but four cantons.

Figure 1 Location of the six major centres of inclusion and their working areas

How often is the follow-up?

All patients (adult and paediatric) are followed up once a year. An annual medical examination is planned with the gastroenterologist for this purpose, in order to update the patient's medical record with any changes that have occurred during the previous year. In addition, an annual questionnaire is sent to the patient to collect information about events that have occurred during the previous year (hospitalization, new therapies) and to update the psychosocial situation (repeat measurements of quality of life, depression and anxiety) and clinical evolution (disease activity). Gastroenterologists are also encouraged to report any relevant events occurring at any time, by completing an 'unscheduled event' form, a one-page document referring to any incident in the patient's disease evolution (flare, hospitalization) or significant treatment modifications.

For the paediatric part of the cohort, physician questionnaires have been adapted for paediatric patients, i.e. using severity scores of disease specially developed for this population, and the patient questionnaires were divided into two parts, one that will be completed with the child during a structured interview conducted by a research assistant and one to be completed by the parents.

What is being measured?

At the initial visit, the patient's gastroenterologist checks the eligibility of the patient for the study (screening form) and then completes the enrolment form. The gastroenterologist fills in the current disease status part of the enrolment questionnaire, but can request the assistance of a study nurse to complete the part concerning past medical history. Variables collected include severity and location of the disease, current and past therapies, factors that may play a role in the pathogenesis of the disease (smoking status, non-steroidal anti-inflammatory drugs), complications and surgery.

By signing the appropriate informed consent form, eligible patients confirm their participation in the cohort study at the time of enrolment and give their consent to blood and tissue sample collection for research purposes. If the patient agrees to biosample collection, blood samples and biopsies are collected within 3 weeks of enrolment and sent to the SIBDCS biobank to be stored and processed for specific research projects.

A questionnaire, in French or German, is then sent to the patient in order to collect socio-demographic data as well as information about ethnicity, disability, hospital stays, medical consultations and history of joint pain. Elements concerning psychosocial well-being, which are presumed to be related to or to influence the exacerbation of the disease are also collected through 10 specific standardized questionnaires which focus on areas such as quality of life, social environment, stress, mood and personality.

If the patient is hospitalized, a short supplementary questionnaire concerning hospital resource consumption is completed by the study nurse.

The questionnaires used for the study are listed in Table 1. A summary of the variables collected and frequency of data collection is given in Table 2,

Table 1 SIBDCS questionnaires and person responsible for providing the information

Questionnaire nme	Responsible for completion
Screening sheet (S)	Physician
Enrolment (E)	Physician/Study nurse
Initial patient questionnaire (P1/F[a]or G[a])	Patient
Biosamples (B)	Physician/Study nurse
Unscheduled event sheet (UE)	Physician
Hospital resources consumption (H)	Study nurse
Annual follow-up (AF)	Physician/Study nurse
Annual follow-up qestionnaire (FUP/F[a]or G[a])	Patient
Stop Form	Physician

[a]F, French version; G, German version.

with indications concerning the related questionnaires and frequency of collection (unique/repeated measurements).

What will be the major areas of research?

Firstly, we aim to provide up-to-date epidemiological data (e.g. prevalence, incidence, clinical course of inflammatory bowel diseases) and investigate risk factors associated with favourable or unfavourable evolution of the course of the disease. We also plan to be able to investigate risk factors associated with disease by comparison with an external population-based cohort, the CoLaus study,[20] which studies cardio-vascular risk factors and new genetic determinants in the population of Lausanne, Canton of Vaud, Switzerland.

Appropriateness of care

Information on appropriateness of care and the impact of medical management on medium- to long-term general patient outcome is lacking in inflammatory bowel diseases. Existing observational long-term follow-up data has been limited to specific therapies or to specific complications such as the development of cancer.[21–23] As a result, decision-making on the use of the various available therapies is based mainly on results of randomized trials that include a limited number of patients, with little knowledge as to whether the treatment favourably modifies disease outcome and overall patient health. In addition to being crucial for individual patient management, global long-term outcome information is central to decision-making in health economics and this project will thus fill gaps in our scientific knowledge in a timely fashion.

Up-to-date criteria on appropriateness of care for Crohn's disease patients were recently developed using the RAND/UCLA Appropriateness Method.[24,25] Applying these criteria as an observational tool allows assessment of appropriateness of care at baseline and examination of the possibilities for its systematic improvement prospectively.[26] Moreover, various pharmaceutical agents will be compared to each other in terms of safety and effectiveness, and overall management strategies applied to patient groups within the cohort. The role of surgery in the care of these patients is changing[27] and its current use will be documented in comparison to medical therapy.

Economic aspects

The second core project evaluates resource consumption (direct and indirect costs) and cost of new biological therapies.[4,5,7] Indeed, studies exist which show a significant influence of these novel drugs on hospitalization and surgical procedures with possible cost-saving effects.[28–30] There is also a possible shift of the resource demand from inpatient-based management to outpatient care. We will analyse the cost of the disease and study the cost-effectiveness of different interventions, in order to re-assess the economic impact of inflammatory bowel disease. A better understanding of these changes is essential to optimize both individual patient care, resource allocation by the healthcare system, and impact on social insurance. The data collected will further provide valuable information and tools for the development of a common model for socio-economic evaluation vs prediction of medical and social resource consumption in chronic inflammatory disease in general.

Psychosocial aspects

Psychiatrists have studied patients with inflammatory bowel disease since the beginning of the 20th century. Before the introduction of the autoimmune hypothesis in the 1960s and the success of corticosteroids in inflammatory bowel disease therapy, it was largely considered to be a psychosomatic disorder.[31] Interest in the role of psychosocial stress in the pathogenesis and course of these diseases lead to a revival in behavioural medicine in the last 10 years, with the advent of the field of psycho-neuro-immunology (PNI).[32] PNI is seen as an interdisciplinary field studying and integrating interactions between behavioural, neural and endocrine, and immune processes and appears to be a promising approach to unravelling the contribution of psychosocial stress to immunological diseases such as inflammatory bowel disease.[33]

This major objective of the project is thus based on the relationship between psychosocial risk factors and steady-state inflammatory activity in inflammatory bowel disease patients. Secondly, stress reactivity of pro-inflammatory markers in such patients will be

Table 2 SIBDCS variables and informants [Physician, Patient or specific questionnaires] at inclusion, at annual follow-up or linked to specific unscheduled events

	Questionnaire			Frequency of data collection		
Measurements	**Physician**	**Patient**	**Specific**	**At inclusion**	**Annual FU**	**Unscheduled event**
Inclusion and exclusion criteria			S	X		
Diagnosis	X	X	S	X	X	
Diagnosis (duration of symptoms, duration of disease)	X	X		X		
Clinical course	X				X	
Current disease location	X			X	X	
Initial disease location and methods of assessment	X			X		
Severity of disease	X			X	X	
Laboratory values	X			X	X	
Current therapy (Specific to IBD; dietary supplementation; alternative medicine)	X	X	UE	X	X	
Previous therapies	X	X		X		
Adverse events report	X				X	
Clinical situation (working hypothesis)	X		UE	X	X	X
Management decision	X		UE	X	X	X
Previous medical visits and exams		X		X		
New exams	X		UE		X	X
Current smoking status	X	X		X	X	
Smoking status at diagnosis	X	X		X		
NSAIDs consumption at diagnosis	X	X		X		
Family history of IBD	X	X		X		
Complications	X		UE	X	X	X
Extraintestinal manifestations	X			X	X	
Fistula/Abscess	X			X	X	
Stenosis	X			X	X	
New hospitalization	X		UE, H		X	X
Previous hospitalization	X	X		X		
Previous rehabilitation clinic stays		X		X		
Surgery	X	X	UE, H	X	X	X
Specific questions about medical history (TBC vaccination, appendicectomy, coeliac disease, psoriasis)	X			X		
Indication for colonoscopy			B	X	X	X
Endoscopy findings			B	X	X	X
Disease activity			B	X	X	X
Demographic data/ethnicity		X		X		
Socioeconomic data (education, occupation)		X		X	X	
Degree of disability		X				
Life-habits (Jenkins Sleep Questionnaire, sport, alcohol consumption)		X		X	X	
Rheumatological pain		X		X	X	
Psychosocial Questionnaires						
Inflammatory Bowel Disease Quality of life Questionnaire (IBDQ)		X		X	X	

(continued)

Table 2 Continued

Measurements	Questionnaire			Frequency of data collection		
	Physician	Patient	Specific	At inclusion	Annual FU	Unscheduled event
SF-36		X		X	X	
Hospital Anxiety and Depression Scale (HADS)		X		X	X	
Enhancing Recovery in Coronary Heart Disease Patients Social Support Inventory (ENRICHD SSI)		X		X		
Type D Personality (DS-14)		X		X		
Over-commitment Questionnaire		X		X		
Coping Inventory for Stressful Situations short form (CISS)		X		X		
Perceived Stress Questionnaire (PSQ)		X		X		
Post-traumatic Diagnostic Scale (PDS)		X		X		
Effort-Reward-Imbalance questionnaire (ERI)		X		X		

S, screening sheet; UE, unscheduled event sheet; H, hospital resource consumption; B, biosample form.

compared with controls in order to identify the predictors of disease exacerbation. This will constitute an important step towards better understanding of some of the bio-behavioural links between stress and disease activity in humans. Understanding the basic psychophysiology of human diseases requires rigorous inclusion criteria to prevent confounding of biological measures (e.g. cytokines) by many factors, including pre-analytical factors.[34,35] The recruitment of a sub-cohort of selected patients to perform cytokine and stress studies with negligible confounding will be possible because of the large number of patients included in the cohort study.

Biobank

In addition to clinical and patient-reported data, a central biobank collects serum, blood lymphocyte and DNA samples. As the biobank is closely linked to the large volume of patient information, unique genetic and immunological correlations with patient phenotype, response to therapy, clinical course and outcome are foreseen. The recognition of the crucial role of genetically encoded variants of proteins critically involved in bacterial antigen recognition, such as the products of Crohn's disease-associated NOD2/CARD15 mutations, is now regarded as a central event in the immunopathological cascade that characterizes Crohn's disease. In ulcerative colitis, the genetic base is less well characterized, but gene involvement, in particular in HLA-compatibility genes, may contribute to disease pathogenesis.

Nested projects

Two nested projects are currently linked to the SIBDCS. The first examines the pharmacogenetics of drug transporters and nuclear receptors in inflammatory bowel disease. The aim of this project is to analyse the role of genetic variants of drug transporters and nuclear receptor genes in determining disease phenotype and response to pharmacological treatment in patients with inflammatory bowel disease.[36–38]

The second nested project concerns the association of clinical subgroups of inflammatory bowel disease patients with Mannan-binding lectin (MBL) genotypes and humoral immune responses.[39] The objective is to obtain further information on the clinical significance of MBL deficiency using a nationwide cohort of inflammatory bowel disease patients.

Response rate and expected attrition

The response rate of patients to the initial patient questionnaire is currently about 76% ($n = 851$ as of June 30, 2008), but this proportion will, in fact, probably be slightly greater as mailings and reminders are sent throughout the year. This point estimation takes into account those who only received the questionnaire a short time ago, as well as those who received a first reminder. In case of non-response after 3 months, a first reminder is sent, followed by a second one in which it is suggested that the patient contacts a study nurse to help them fill in the questionnaire if necessary. If the patient does not respond to the second reminder, the study nurse attempts to make contact by telephone, in order to be able to ascertain the reason for non-response as a minimum. Based on current returns following two reminders, it is anticipated that close to 90% of patients will return the patient questionnaire. Patients who did not reply to the two reminders or who could not be contacted by telephone by the study nurse, will be considered as lost to follow-up. Patients can be considered as excluded or withdrawn for several reasons, such as change of diagnosis (no more inflammatory bowel disease), withdrawal of consent or emigration.

The SIBDCS will encourage and maintain the participation by physicians and patients by providing them with annual information and feedback. In addition, it is planned that a physician- and patient-newsletter will be sent to them, as well as posting it on the study website.

Each year, gastroenterologists who enrol patients will receive a certificate of participation in the SIBDCS, and since November 1, 2007, a cohort member card has been sent to patients, with a unique cohort number to be shown each time they visit the gastroenterologist or in case of hospitalization, which will also assist in avoiding double-entry. Furthermore, a 'Swiss IBD Day' conference has been introduced to encourage participation by providing appropriate content for practitioners, researchers and patients.

What has been found so far?

Since November 2006, the six major inflammatory bowel disease university centres have begun to recruit patients. Figure 2 shows the number of patients enrolled per month up to June 2008 and the cumulative number of patients enrolled. For the first year, the expected number of patients enrolled was 1000, corresponding to a mean of 83 per month. A total of 1120 patients were enrolled as of end June 2008, 670 (59.8%) suffering from Crohn's disease, 419 (37.4%) from ulcerative colitis and 31 (2.8%) with the diagnosis of an indeterminate colitis. The proportion of cases according to gender and type of disease is given in Table 3. Globally, there is an equal gender proportion for both Crohn's disease and ulcerative colitis patients.

The mean age of the cohort population is 43 years (±15), ranging from 7 to 89 years. The diagnosis of the Crohn's disease patients was established at least 4 months prior to inclusion in 95% of cases; 66% were diagnosed after at least one recurrence. The method of diagnostic assessment for Crohn's disease or ulcerative colitis was endoscopy with biopsies in the majority of patients (96%, 99%, respectively), and/or surgery (29%, 8%, respectively) or radiological studies (26%, 12%, respectively).

Seventy-six percent of patients have already responded and 13% are currently expected to respond, i.e. they received the questionnaire <3 months ago. Only 11% of patients did not reply to the first reminder, and it is planned that the local study nurse will contact them in the near future.

Figure 2 shows a slight tendency towards a decrease in the number of patients enrolled. This is linked to the fact that during the first year most patients were enrolled in the major centres and less in regional hospitals and in private practices. It is planned that regular information meetings conducted by study nurses and local clinical investigators to give up-to-date information on the cohort study will bring other gastroenterologists and patients into the study.

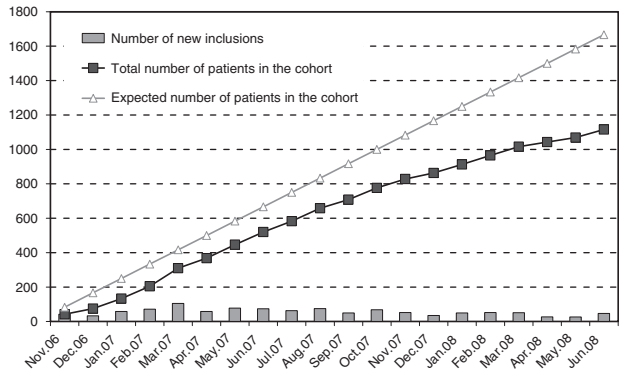

Figure 2 Cumulative number of SIBDCS patients included from November 2006 to June 2008

Table 3 Type of disease according to gender

	Gender		
Type of diagnosis	**Male**	**Female**	**Total**
Crohn's disease	218 (47%)	244 (53%)	462 (62%)
Ulcerative colitis	138 (50%)	137 (50%)	275 (36%)
Indeterminate colitis	9 (53%)	8 (47%)	17 (2%)
Inflammatory bowel disease	365 (48%)	389 (52%)	754

What are the main strengths and weaknesses?

The SIBDC is a disease-oriented prospective cohort. It will not be entirely population-based, except for specific geographic regions, e.g. the Cantons of Vaud and Solothurn. This is a limitation of the study because comparisons with non-inflammatory bowel disease cases would only be possible using data from external research groups. The decentralized organization of the Swiss healthcare system precludes achieving comprehensive coverage of all cases in the country for inflammatory bowel disease, whereas broader coverage was achieved by the Swiss HIV cohort[40] because almost all cases are referred to dedicated specialist clinics.

Our study includes both children and adult patients, and specific questionnaires were designed for each category, specifically taking into account severity-of-disease measurements, psycho-social factors and quality of life. The inclusion of patients of all ages constitutes a strength of the study of these chronic diseases which not infrequently begin in adolescence and early adulthood.

The SIBDCS encompasses research input from different fields and medical disciplines

(gastroenterology, internal medicine, psychiatry, public health, health economics, paediatrics, genetics and genomics). This is one of its strengths and a source of mutual enrichment. On the clinical side, the team of gastroenterologists includes physicians working in university hospitals as well as in private practice. This variety of experience was taken into account in the design of questionnaires (time available for completion, parts that could be completed either by the physician or by a nurse), organization and logistics of enrolment and follow-up. Other researchers involved at the data centre are statisticians, epidemiologists and computer scientists. Pathologists have set up a biobank for collecting samples that can be stored for specific genetic analysis.

Can I have access to the data? Where can I find out more about the study?

All data are organized and centralized at the data centre, attached to the Lausanne Institute of Social and Preventive Medicine. All logistic aspects of the data flow are managed through the centre, as well as data control and statistical analyses. Information and summary results are provided to the participating gastroenterologists in the form of a report which comprises three parts: (i) an individual feedback sheet, established for each patient, which contains a summary of the information collected via physician questionnaires over the past year; (ii) a summary and basic descriptive analysis of the physician's group of patients and for the whole cohort; and (iii) it is planned that the global results giving summary information on the whole cohort will be accessible on the website of the SIBDCS, currently under construction (http://www.ibdcohort.ch).

A manual of Guidelines for Submission and Evaluation of Project Proposals has been prepared by the Scientific Board of SIBDCS and it is thus possible to submit proposals for specific projects that might benefit from access to anonymous data from the cohort study, within the limits of ethical considerations, the consent given by the participating patients and the judicious use of the cohort resources. All submitted projects are peer-reviewed and subject to a final decision by the Scientific Board and the Executive Board.

An external International Scientific Advisory Committee has been constituted (see appendix) to provide input on the current state and future development of the cohort.

Funding

Swiss National Science Foundation (N 3347CO-108792/1).

Conflict of interest: None declared.

References

[1] Baumgart DC, Carding SR. Inflammatory bowel disease: cause and immunobiology. *Lancet* 2007;**369:**1627–40.

[2] Rutgeerts P, Feagan BG, Lichtenstein GR *et al*. Comparison of scheduled and episodic treatment strategies of infliximab in Crohn's disease. *Gastroenterology* 2004;**126:**402–13.

[3] Rutgeerts P, Sandborn WJ, Feagan BG *et al*. Infliximab for induction and maintenance therapy for ulcerative colitis. *N Engl J Med* 2005;**353:**2462–76.

[4] Bassi A, Dodd S, Williamson P, Bodger K. Cost of illness of inflammatory bowel disease in the UK: a single centre retrospective study. *Gut* 2004;**53:**1471–78.

[5] Bodger K. Cost of illness of Crohn's disease. *Pharmacoeconomics* 2002;**20:**639–52.

[6] Boonen A, Dagnelie PC, Feleus A *et al*. The impact of inflammatory bowel disease on labor force participation: results of a population sampled case-control study. *Inflamm Bowel Dis* 2002;**8:**382–89.

[7] Cohen RD. IBD indirect costs: the sleeping giant? *Gastroenterology* 2003;**125:**982–84.

[8] Levenstein S, Prantera C, Varvo V *et al*. Stress and exacerbation in ulcerative colitis: a prospective study of patients enrolled in remission. *Am J Gastroenterol* 2000;**95:**1213–20.

[9] Bitton A, Sewitch MJ, Peppercorn MA *et al*. Psychosocial determinants of relapse in ulcerative colitis: a longitudinal study. *Am J Gastroenterol* 2003;**98:**2203–8.

[10] Bitton A, Dobkin P, Edwardes MD *et al*. Predicting relapse in Crohn's disease: a biopsychosocial model. *Gut* 2008, doi:10.1136/gut.2007.134817.

[11] Juillerat P, Pittet V, Bulliard J-L *et al*. Prevalence of inflammatory bowel disease in the Canton of Vaud (Switzerland): a population-based cohort study. *J Crohn's Colitis* 2008;**2:**131–41.

[12] Loftus EV Jr, Silverstein MD, Sandborn WJ, Tremaine WJ, Harmsen WS, Zinsmeister AR. Crohn's disease in Olmsted County, Minnesota, 1940-1993: incidence, prevalence, and survival. *Gastroenterology* 1998; **114:**1161–68.

[13] Loftus EV Jr, Silverstein MD, Sandborn WJ, Tremaine WJ, Harmsen WS, Zinsmeister AR. Ulcerative colitis in Olmsted County, Minnesota, 1940-1993: incidence, prevalence, and survival. *Gut* 2000;**46:**336–43.

[14] Loftus CG, Loftus EV Jr, Harmsen WS *et al*. Update on the incidence and prevalence of Crohn's disease and ulcerative colitis in Olmsted County, Minnesota, 1940-2000. *Inflamm Bowel Dis* 2007;**13:**254–61.

[15] Bernstein CN, Blanchard JF, Rawsthorne P, Wajda A. Epidemiology of Crohn's disease and ulcerative colitis in a central Canadian province: a population-based study. *Am J Epidemiol* 1999;**149:**916–24.

[16] Rubin GP, Hungin AP, Kelly PJ, Ling J. Inflammatory bowel disease: epidemiology and management in an English general practice population. *Aliment Pharmacol Ther* 2000;**14:**1553–59.

[17] Lapidus A. Crohn's disease in Stockholm County during 1990-2001: an epidemiological update. *World J Gastroenterol* 2006;**12:**75–81.

[18] Daiss W, Scheurlen M, Malchow H. Epidemiology of inflammatory bowel disease in the county of Tubingen (West Germany). *Scand J Gastroenterol Suppl* 1989; **170:**39–43.

[19] Lennard-Jones JE. Classification of inflammatory bowel disease. *Scand J Gastroenterol Suppl* 1989;**170:**2–6.

[20] Firmann M, Mayor V, Vidal PM *et al*. The CoLaus study: a population-based study to investigate the epidemiology and genetic determinants of cardiovascular risk factors and metabolic syndrome. *BMC Cardiovasc Disord* 2008;**8:**6.

[21] Faubion WA Jr, Loftus EV Jr, Harmsen WS, Zinsmeister AR, Sandborn WJ. The natural history of corticosteroid therapy for inflammatory bowel disease: a population-based study. *Gastroenterology* 2001;**121:**255–60.

[22] Halfvarson J, Bodin L, Tysk C, Lindberg E, Jarnerot G. Inflammatory bowel disease in a Swedish twin cohort: a long-term follow-up of concordance and clinical characteristics. *Gastroenterology* 2003;**124:**1767–73.

[23] Langholz E. Ulcerative colitis. An epidemiological study based on a regional inception cohort, with special reference to disease course and prognosis. *Dan Med Bull* 1999;**46:**400–15.

[24] Naylor CD. What is appropriate care? *N Engl J Med* 1998;**338:**1918–20.

[25] Vader JP, Froehlich F, Juillerat P *et al*. Appropriate treatment for Crohn's disease: methodology and summary results of a multidisciplinary international expert panel approach–EPACT. *Digestion* 2006;**73:**237–48.

[26] Guessous I, Juillerat P, Pittet V *et al*. Evaluating appropriateness of treatment for Crohn's disease: feasibility of an explicit approach. *Digestion* 2007; **75:**46–52.

[27] Polle SW, Slors JF, Weverling GJ, Gouma DJ, Hommes DW, Bemelman WA. Recurrence after segmental resection for colonic Crohn's disease. *Br J Surg* 2005; **92:**1143–49.

[28] Cohen RD, Larson LR, Roth JM, Becker RV, Mummert LL. The cost of hospitalization in Crohn's disease. *Am J Gastroenterol* 2000;**95:**524–30.

[29] Feagan BG, Vreeland MG, Larson LR, Bala MV. Annual cost of care for Crohn's disease: a payor perspective. *Am J Gastroenterol* 2000;**95:**1955–60.

[30] Lichtenstein GR, Yan S, Bala M, Blank M, Sands BE. Infliximab maintenance treatment reduces hospitalizations, surgeries, and procedures in fistulizing Crohn's disease. *Gastroenterology* 2005;**128:**862–69.

[31] Aronowitz R, Spiro HM. The rise and fall of the psychosomatic hypothesis in ulcerative colitis. *J Clin Gastroenterol* 1988;**10:**298–305.

[32] Levenstein S. Stress and ulcerative colitis: convincing the doubting Thomases. *Am J Gastroenterol* 2003;**98:** 2112–15.

[33] Ader R. On the development of psychoneuroimmunology. *Eur J Pharmacol* 2000;**405:**167–76.

[34] von Kaenel R, Kudielka BM, Preckel D, Hanebuth D, Fischer JE. Delayed response and lack of habituation in plasma interleukin-6 to acute mental stress in men. *Brain Behav Immun* 2006;**20:**40–48.

[35] Kudielka BM, von KR, Preckel D, Zgraggen L, Mischler K, Fischer JE. Exhaustion is associated with reduced habituation of free cortisol responses to repeated acute psychosocial stress. *Biol Psychol* 2006;**72:**147–53.

[36] Wusk B, Kullak-Ublick GA, Rammert C, von Eckardstein A, Fried M, Rentsch KM. Therapeutic drug monitoring of thiopurine drugs in patients with inflammatory bowel disease or autoimmune hepatitis. *Eur J Gastroenterol Hepatol* 2004;**16:**1407–13.

[37] Wusk B, Kullak-Ublick GA, Rammert C, von Eckardstein A, Fried M, Rentsch KM. Thiopurine S-methyltransferase polymorphisms: efficient screening method for patients considering taking thiopurine drugs. *Eur J Clin Pharmacol* 2004;**60:**5–10.

[38] Newman B, Gu X, Wintle R *et al*. A risk haplotype in the Solute Carrier Family 22A4/22A5 gene cluster influences phenotypic expression of Crohn's disease. *Gastroenterology* 2005;**128:**260–69.

[39] Seibold F, Konrad A, Flogerzi B *et al*. Genetic variants of the mannan-binding lectin are associated with immune reactivity to mannans in Crohn's disease. *Gastroenterology* 2004;**127:**1076–84.

[40] Sudre P, Rickenbach M, Taffe P, Janin P, Volkart AC, Francioli P. Clinical epidemiology and research on HIV infection in Switzerland: the Swiss HIV Cohort Study 1988-2000. *Schweiz Med Wochenschr* 2000;**130:** 1493–500.

Appendix 1

Members of the SIBDCS study group

Main project coordinator: Prof. Pierre Michetti (Department of Gastroenterology, University of Lausanne) – Data centre: Prof. John-Paul Vader, Prof. Bernard Burnand, Dr Valérie Pittet, Dr Pierluigi Ballabeni (Institute of Social and Preventive Medicine, Lausanne) – Biobank: Prof. Christoph Mueller, Ms Silvia Rihs (Institute of Pathology, Bern) – Paediatric cohort: Prof. Christian Braegger (Division of Gastroenterology, University of Zürich) – Participating centres: Prof. Pierre Michetti, Dr Christian Mottet, Dr Pascal Juillerat, Dr Christian Felley (Department of Gastroenterology, University of Lausanne), Prof. Christoph Beglinger, Dr Florian Froehlich, Dr Stephan Vavricka (Division of Gastroenterology, University of Basle), Prof. Frank Seibold, Dr Alain Schoepfer (Division of Gastroenterology, University of Bern), Prof. Roland von Kaenel, Dr Stephan Begré (Division of Psychosomatic Medicine, University of Bern), Dr Philippe de Saussure (Division of Gastroenterology, University of Geneva),

Prof. Christa Meyenberger, Dr Markus Sagmeister (Division of Gastroenterology, University of St-Gallen), Prof. Gerhard Rogler, Prof. Gerd A. Kullak-Ublick (Division of Gastroenterology, University of Zürich), Dr Remy Meier (Cantonal Hospital Liestal), Dr Alex Straumann (Private Gastroenterologist, President of IBD-Net, Olten), Dr Dominique Criblez, Dr Matthias Engelmann (Cantonal Hospital Lucerne).

Scientific committee

Prof. Pierre Michetti, Prof. Christoph Mueller, Prof. Frank Seibold, Prof. Christoph Beglinger, Dr Philippe de Saussure, Prof. Christa Meyenberger, Prof. Gerd A. Kullak-Ublick, Dr Alex Straumann, Prof. John-Paul Vader, Prof. Christian Braegger, Prof. Roland von Kaenel, Dr Christian Mottet, Dr Markus Sagmeister, Dr Florian Froehlich, Dr Pascal Juillerat, Dr Christian Felley, Dr Valérie Pittet, Dr Stephan Begré, Dr Alain Schoepfer, Dr Stephan Vavricka, Ms Mirjam Schenk (Institute of Pathology, Bern).

Members of the external International Scientific Advisory Committee

Prof. Henrik Toft Sorensen (Department of Clinical Epidemiology, Aarhus University Hospital, Denmark), Prof. Daan W. Hommes (Department of Gastroenterology and Hepatology, University of Amsterdam, The Netherlands), Prof. Susan Levenstein (Aventino Medical Group, Rome, Italy), Prof. Séverine Vermeire (Division of Gastroenterology, University of Leuven, Belgium) Prof. Markus F. Neurath (Laboratory of Immunology, University of Mainz, Germany).