

European-wide Validation of the Web-based Documentation Standard IBDIS by Inter-observer Analysis

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1 Background

Inflammatory bowel diseases (IBD) comprise as a heterogeneous family of disorders a variety of complex clinical patterns. Diagnosis of IBD relies on clinical evaluation and a combination of endoscopic, histological, radiological, and/or biochemical investigations. Hence, the lack of a gold standard for diagnosis may lead to diagnostic pitfalls.¹ In order to minimize diagnostic uncertainties disease relevant parameters shall be assigned strict definitions, which need to be validated by inter-observer agreement.² Silverberg et al. reported a change of diagnosis in 6.2% of patients within a cohort reviewed for an IBD genetics program and calculated that a 10% diagnostic misclassification rate in IBD results in an up to 40% loss of power to detect a true linkage for a presumed IBD locus in genetic studies.³ Therefore, precise disease description and classification may influence tremendously the revelation of environmental and genetic determinants.

Several attempts have been made to consolidate the complexity of Crohn's disease (CD) within the frame of a disease classification. By revealing only fair inter-rater agreement of disease behaviour as adapted from the disease classification proposed by Greenstein and Sachar, Steinhart et al. pinpointed the issue of lacking precise definitions for disease relevant parameters in CD and raised concerns specifically in respect of the applicability of behaviour in ongoing studies. Subsequently, the Vienna Classification of CD was developed as a simple tool to categorize CD based on objective and reproducible clinical variables and has been replaced by Montreal Classification lately.^{4,5} However, as a matter of fact, neither of those classifications has been formally subjected to a validation process.

Recently, we have shown that inter-observer agreement for the current definitions of location and behaviour in CD are 70% and 95%, respectively. Providing the assumption of a genotype/phenotype

association the proportion of non-significant studies ($p > 0.05$) due to the observed misclassification of location and behaviour was ranging from 13.3 to 63.8 % and from 0.2 to 22.2 %, respectively, depending on the study sample size.⁶ We concluded from these findings that insufficiently defined disease parameters may obscure true associations of certain disease phenotypes with environmental or genetic susceptibilities and delineated the necessity for the development of valid and reproducible definitions of disease-relevant variables in IBD upfront their application in scientific studies. Furthermore, a move towards individualized healthcare systems whereby patients are intended to receive personalized, targeted treatment solutions specific for their individual disease states as well as their individual genetic and metabolic parameters can be only envisioned on the basis of qualified phenotype definitions.

2 Introduction

In 1999, Walter Reinisch from the General Hospital in Vienna and Nikolaus Pedarnig, founder and owner of UNIDATA GEODESIGN, started to outline the concept of a standardized documentation on IBD patients. A close cooperation between science and technology was established to realize a project, which aims to result in the development of a validated and reliable catalogue of parameters relevant for scientific approaches and daily practise in inflammatory bowel diseases.

Initially, for the establishment of a standardized documentation system (Inflammatory Bowel disease information system, IBDIS) 186 IBD-relevant parameters were selected by 27 members of the Austrian IBD working group according to the Delphi method between 1999 and 2002. The parameters which were related to demographics, diagnosis, complications, risk factors, pregnancy, surgical and conservative therapy were incorporated into a data sheet. Variability of parameters was defined and expressed as date, binary, continuous, nominal, and ordinal data. The

validity of IBDIS as a data sheet was studied by nation-wide inter-observer agreement (IOA) analysis. Data from 16 charts of IBD patients provided from centres in Austria were captured by 18 observers by means of the IBDIS data sheet. The strength of agreement was determined using Cohen's Kappa statistic and considered to be poor if $\kappa < 0.2$, fair if $0.21 < \kappa < 0.4$, moderate if $0.41 < \kappa < 0.6$, good if $0.61 < \kappa < 0.8$ and very good if $\kappa > 0.8$. For 70% of evaluated parameters IOA was good to very good e.g. diagnosis, ileocolonoscopy, or enteroclysis. Moderate to fair IOA was obtained especially for parameters subjected to potential irregularities of retrospective data collection, such as nicotine consume or joint involvement. Sonography was the single parameter resulting in poor IOA. Our result of very good IOA for CD behavior ($\kappa = 0.920$; SEM = 0.068) by predefined IBDIS succeeds in overcoming the difficulties in documentation of this single parameter as previously tested by Steinhart et al. ($\kappa = 0.353$, SEM = 0.021).⁷ From the results of the nation-wide IOA we re-evaluated parameters from the data sheet and adapted a web-based electronic version of IBDIS. The IBDIS software provides integrated and automated plausibility checks, a permanent Audit Trail, record retention and archiving tools to maintain the best quality of data. Every application of IBDIS is equipped with an online support and information system (IBDIS Knowledgebase).

As next step, an inter-observer analysis of IBDIS in cooperation with European IBD experts under the umbrella of the European Crohn's and Colitis Organisation (ECCO) is conceived.

3 Aim(s)

The present study is aimed to validate IBDIS as a web-based documentation standard for patients with inflammatory bowel diseases.

The study is designed to obtain robust data on each of the disease relevant parameters captured by IBDIS.

The potential applicability of IBDIS is manifold and designed to support several potential applications. From a ready-to-use tool for scientific analysis to an electronic patient record with integration into the clinical routine, or an electronic case report form, as applied in clinical trials, registries, biobanks or health economic studies.

4 Methods, materials and scientific procedures

Cases

To investigate the validity of IBDIS by inter-observer agreement analysis, members of ECCO were asked to provide anonymous records on IBD patients adhering to the following criteria:

- A specific disease history not exceeding 5 years
- A complex course of disease (e.g., a positive family history, perianal fistula, extraintestinal manifestations, complications, intestinal resections, immunosuppressive therapy)
- A concise review of the patient's medical history including patient demographics
- Translations of original reports (e.g., x-rays, endoscopy, pathology, surgical report) omitting final diagnosis
- Avoidance of an exhaustive account on laboratory value
- Providing generic names of drugs
- Providing the start and concluding date of drug treatment, possible intolerances, and concomitant medications
- Description of the patient's course of disease according to notes from the patient's file in a way that the reader is able to understand the physician's therapeutic decisions and actions
- Providing details on co-morbidities, pregnancies, nicotine abuse, NSAID intake and contraceptives

Documentation and Data

ECCO members from 14 European countries provided patient files which are made available as PDF-files in the member's area of the IBDIS homepage (documentation.ibdis.net). At least 20 observers, particularly members of Young ECCO (YECCO) will be asked to capture the data from the provided patient files by means of web-based IBDIS. One rater (W.R.) is selected as reference observer. He is most experienced in the use of IBDIS.

To investigate intra-observer agreement (retest reliability) one third ($n = 7$) of the observers will be asked to re-evaluate 7 medical records after another 12 weeks. Both observers and charts will be selected randomly by the statistician (O.E).

Statistics

Interobserver agreement (IOA) analysis is an accuracy analysis that calculates the percentage (standard deviation, SD, or the 95% confidence interval, CI) of observer agreement with a predetermined reference observer. The agreement between the mode (the most frequently assessed value) and the reference is expressed as a percentage. Statistical characterization of the strength of interobserver agreement will be determined using Cohen's kappa (κ). In the study each patient file will be considered as an independent observation. The strength of agreement is considered poor with a κ statistic of less than 0.2, fair with a κ of 0.21 to 0.4, moderate with a κ of 0.41 to 0.6, good with a κ of 0.61 to 0.8, and very good with a κ of more than 0.8.

Intra-observer agreement analysis

The intra-observer agreement analysis (retest reliability) is an accuracy analysis calculating the percentage of agreement between first and second observation of the 7 selected observers.

Furthermore, different tests as e.g. test of homogeneity, test of coincidence, chi-square-tests, odds-ratio and pooled kappa-tests will be used to detect influences of geographical and lingual regions.

Organisational issues

During the study, the IBDIS staff (N.P.) will contact each observer several times for service and support.

The applicants of this project proposal and all observers who agree to perform the second evaluation as part of the intra-observer agreement analysis will co-author the manuscript. Each observer and each provider of a patient file will be named in the acknowledgement of the publication. Manuscripts deriving from the study will name ECCO as sponsor and ought to be submitted to the Journal of Crohn's and Colitis (JCC) as original contribution.

5 Expected results

All the parameters included in the IBDIS software and subjected to the inter-observer and intra-observer agreement study are expected to reach the bar of a κ -value beyond 0.8.

6 Justification for the requested support

The proposed project is supposed to result in a unique, validated and harmonized standard in the documentation of IBD in Europe. Due to this challenge, a qualified team of experts is needed to realise all specifications of this project. The applicants possess the required expertise in the medical, statistical and technical areas as requested by the protocol. The

organisational and financial support of ECCO is key for the success of the project.

7 Timelines

Date	Issue
Step 1: Month 1	<ul style="list-style-type: none">• Contacting observers• Confidentiality agreements• Online training sessions• Begin of data capture process• Begin of reminder schedule
Step 2: Month 2 to Month 8	<ul style="list-style-type: none">• Data capture process• Support services by IBDIS staff
Step 3: Month 9	<ul style="list-style-type: none">• Closing of data capture process• Begin of analysis issues
Step 4: Month 10	<ul style="list-style-type: none">• analysis• discussion process
Step 5: Month 11 to 12	<ul style="list-style-type: none">• Final report• press conference• publication

8 References

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