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Construction and validation of a web-based epidemiological database for inflammatory bowel diseases in Europe
An EpiCom study

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KEYWORDS
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Eastern Europe;
Western Europe;
Environmental factors;
Quality of life

Abstract

Background: The EpiCom-study investigates a possible East-West-gradient in Europe in the incidence of IBD and the association with environmental factors. A secured web-based database is used to facilitate and centralize data registration.
Aim: To construct and validate a web-based inception cohort database available in both English and Russian language.
Method: The EpiCom database has been constructed in collaboration with all 34 participating centers. The database was translated into Russian using forward translation, patient questionnaires were translated by simplified forward-backward translation. Data insertion implies fulfillment of international diagnostic criteria, disease activity, medical therapy, quality of life, work productivity and activity impairment, outcome of pregnancy, surgery, cancer and death. Data is secured by the WinLog3 System, developed in cooperation with the Danish Data Protection Agency. Validation of the database has been performed in two consecutive rounds, each followed by corrections in accordance with comments.
Results: The EpiCom database fulfills the requirements of the participating countries' local data security agencies by being stored at a single location. The database was found overall to be "good" or "very good" by 81% of the participants after the second validation round and the general applicability of the database was evaluated as "good" or "very good" by 77%. In the inclusion period January 1st –December 31st 2010 1336 IBD patients have been included in the database.
Conclusion: A user-friendly, tailor-made and secure web-based inception cohort database has been successfully constructed, facilitating remote data input. The incidence of IBD in 23 European countries can be found at www.epicom-ecco.eu.
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1. Introduction

The Epidemiology Committee (EpiCom) web-based study (EpiCom, www.epicom-ecco.eu) was initiated during the period 2006–2010, when Pia Munkholm was chairing the EpiCom in ECCO. Johan Burisch was elected as the first EpiCom PhD-student at the University of Copenhagen, being the lead figure in the database construction and the subsequent inception cohort studies.

The study was initiated to better define the burden of illness of inflammatory bowel disease (IBD), to explore the mechanism of association of IBD with environmental factors, as well as to identify new risk factors in the environment across the borders. The EpiCom-study will create a new prospective, uniformly diagnosed, population-based inception cohort of patients diagnosed with IBD in a one-year period, 01.01.2010–31.12.2010 within well-defined geographical areas in both Western and Eastern Europe. The follow-up period (FU) will last from inclusion until 31.12.2011.

For the first time in Europe, scientists will be able to describe differences among geographical regions across Europe and to demonstrate the impact of lifestyle on the incidence of IBD. 34 centers from 23 countries representing adult and pediatric inception cohorts from 15 Western European countries, 8 Eastern European countries and 1 Asian country, Wuhan city in China, are participating (Table 1).

The overall aim of the EpiCom-study is to investigate whether there is an East–West-gradient in the incidence of IBD in European countries and, in addition, whether the difference in IBD incidence is associated with dissimilarities in environmental exposure. One year after the project start, a follow-up stage will be launched to analyze whether there are differences throughout Europe in respect of:

- Vitamin D levels
- Quality of life and quality of care gradient
- Prognosis in terms of disease progression, surgery, mortality, cancer and pregnancy out-come
- Work Productivity and Activity impairment
- The prevalence of extra-intestinal manifestation
- The effect of different economic considerations on choice of treatment strategies
- Geographical effect on disease severity
- The impact of migration
- The incidence of primary sclerosing cholangitis
- The incidence of chronic viral hepatitis B and C and of HIV infection in IBD

Table 1 List of participants.

Western Europe [14 countries]	
Cyprus	John Kaimakliotis
	Michael Tryphonos
Denmark	Soeren Avnstroem
	Lisbet Ambrosius Christensen
	Jens F. Dahlerup
	Vibeke Andersen
	Jens Kjeldsen
	Johan Burisch
	Pia Munkholm
	Natalia Pedersen
	Ebbe Langholz
	Margarita Elkjaer
	Anders Pærregaard
	Niels Thorsgaard Pedersen
Faroe Islands	Kári R. Nielsen
Finland	Pekka Collin
	Pia Manninen
	Kaija-Leena Kolho
	Matti Verkasalo
Greece	Epameinondas V. Tsianos
	Konstantinos H. Katsanos
	Ioannis Vagias
Greenland	Karin Ladefoged
Iceland	Einar Bjoernsson
	Sjöfn Kristjansdottir
Ireland	Colm O'Morain
	Mary Shuhaibar
Israel	Selwyn Odes
	Ohad Etzion
Italy	Sergio Gullini
	Angelo Zelante
	Loredana Simone
	Reinhold Stockbrugger
	Matteo Martinato
	Renata D'Incà
	Giovanni Fornaciari
	Marina Beltrami
	Daniela Valpiani
	Monica Milla
Portugal	Fernando Magro
	Luisa Manuela Barros
Spain	Alberto Fernandez Villaverde
	David Martinez Ares
	Vicent Hernandez Ramirez
	Santos Pereira
	Guillermo Bastida
	Joan Clofent
Sweden	Sven Almer
	Jonas Halfvarson
	Curt Tysk
	Erik Hertervig
United Kingdom	Ailsa Hart
	Warren Hyer
	Naila Arebi
	Shaji Sebastian
Eastern Europe [8 countries]	
Croatia	Boris Vucelic
	Silvija Cukovic-Cavka
Czech Republic	Olga Shonová
	Zdenka Krocáková
	Martin Bortlik
	Milan Lukas
	Dana Duricova
	Miroslava Adamcova
Hungary	Peter Lakatos
Lithuania	Limas Kupcinskas
	Gediminas Kiudelis
	Ruta Kucinskien
Moldova	Ion Mihu
	Olga Tighineanu
	Viorica Pleşca
	Svetlana Turcan
Romania	Adrian Goldis
Russia	Elena Belousova
	Inna Nikulina
Asia [1 country]	
China	Siew Ng
	Michael Kamm
	Joseph Sung
	Bing Xia
	Pinjin Hu

In order to facilitate data acquisition, to ensure data quality, as well as to enable centralization of data storage, a secure web-based database was constructed with the purpose of providing a basis for completing the aims of the EpiCom-study. The web-based database was optimized with respect to accuracy, functionality, cost-effectiveness and visual presentation. The Copenhagen diagnostic criteria were used,[1–4] to increase the internal validity. In addition, the database should give the users online reporting of current inclusion and incidence rates for each cohort involved.

The aim of this paper is to describe the construction and validation of the web-based inception cohort database, available in both English and Russian language. Future papers will address the inclusion process as well as the incidences of IBD in Europe.

2. Methods

2.1. Database Construction in English

The development of the web-based EpiCom database application was carried out by HD-support LLC, Denmark, over a period of approximately two years. The construction of the database required a series of interviews by HD-support with the project steering group regarding the content and structure of the database, as well as agreeing on an initial feature list for the prototype construction. These issues were then discussed with all EpiCom-members and comments and additional suggestions were implemented. Since 2006 EpiCom members had been meeting regularly at international congresses: European Crohn's and Colitis Organization congress, Digestive Disease Week, United European Gastroenterology Week and Nordic Gastroenterology Congress.

The database was programmed at the same time as being continually released to the steering group for testing, which reported defects and requested new features or amendments to those already existing. In addition, there was an ongoing internal testing by the developers. After having secured a certain number of features, a validation release was provided for all participants, allowing them to test the database, offer comments on the design, and report defects. The validation process was repeated twice (December 2008–June 2009), followed by corrections of reported defects. After a satisfactory validation of the project, the feature list was frozen, preventing further changes/additions to the feature list.

A website, www.epicom-ecco.eu, was created for this project, permitting access to the database and containing contact information as well as the EpiCom-project protocol, available to anyone in the world for the purpose of transparency. In addition, an inclusion chart was created on the front page of the website showing both the current number of patients included in the database as well as the current incidence for each participating center. Thereby the inclusion of patients can be followed live, Fig. 1.

2.2. Database Cost

The EpiCom database was constructed by HD-support for a price of € 75.000 funded by a private organization and the pharmaceutical industry. Each participating center has to pay a yearly fee of € 2.200 for 2010 and €1.500 for 2011 in order to use the database. This fee covers the expenses for user administration, user support, continuous correcting of minor logistical errors in the database as well as the hosting of the EpiCom-server (Backup, hardware maintenance, and software maintenance) by HD-support. In the future, after the end of the EpiCom-study in 2012, the database will be available for everyone interested in gaining access.

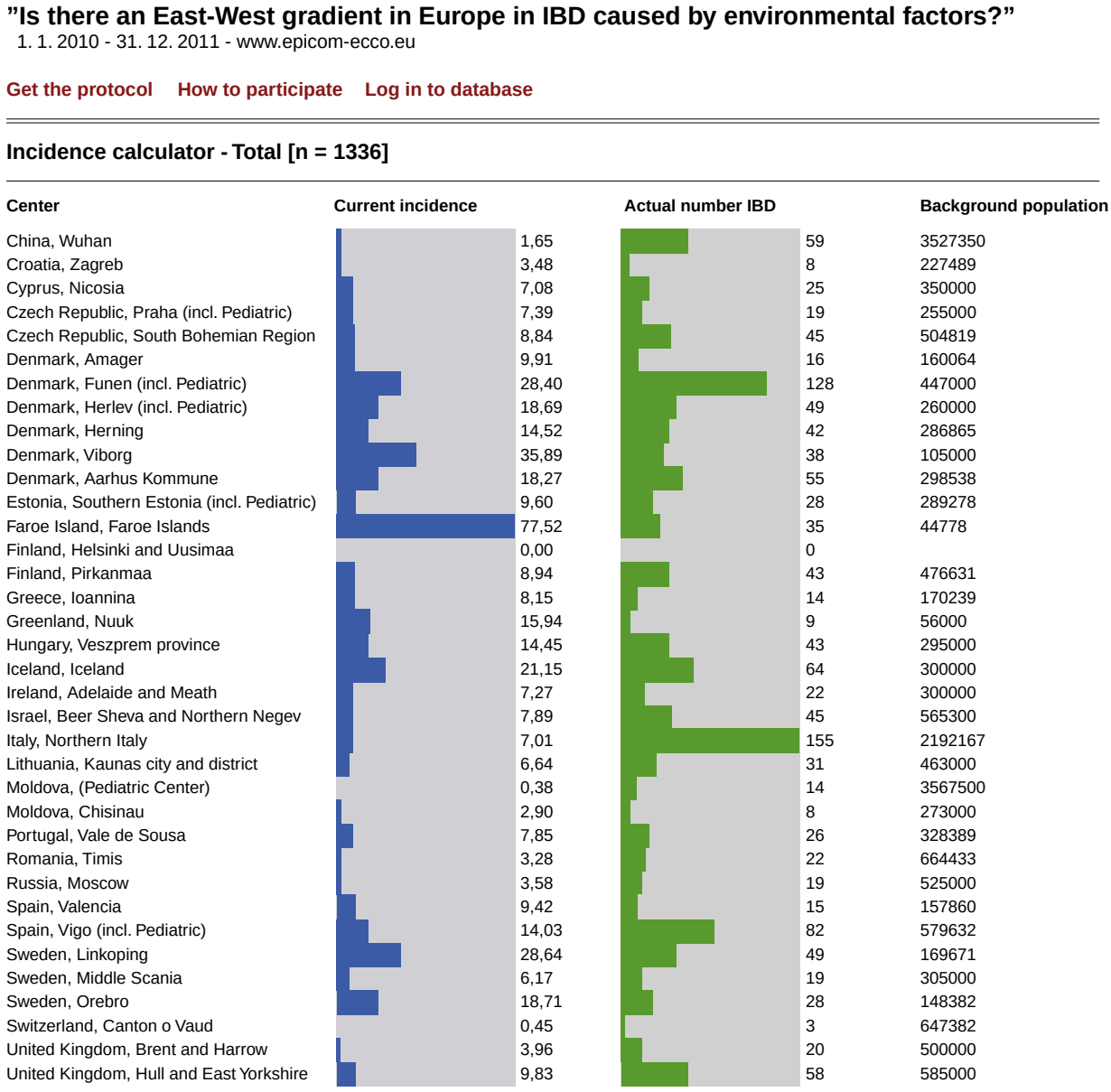

Figure 1 The front page of www.epicom-ecco.eu, displaying current numbers of IBD patients included per center and current calculated incidence, as of December 31st 2010.

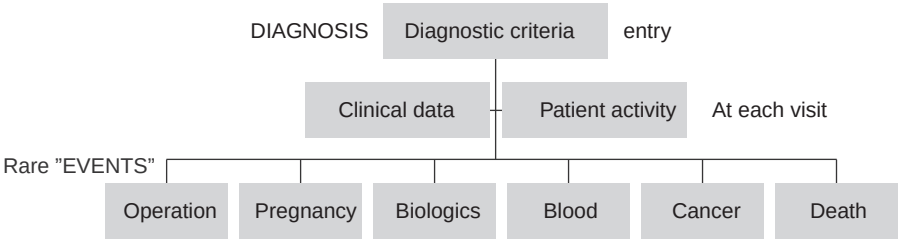

Figure 2 Schematic outline of the schemes used in the database.

2.3. Database Design and Content

The web-based EpiCom Database application has been designed on the basis of the Danish Crohn Colitis Database (DCCD), www.dccd-ibd.dk, aiming strictly to be an epidemiological database focusing on academic and epidemiological content in contrast to clinical applicability. The database was used for online registration of the various forms used in the EpiCom-project. In order to be able to follow and document the clinical course of patients included in the project, the database was built up around 9 clinical schemes covering all aspects of the course of the disease. The clinical schemes were divided into entry schemes, schemes used for each patient visit, and schemes used for rare events, Fig. 2.

The entry schemes include a *diagnostic criteria scheme*, containing data regarding diagnosis, disease extent and behavior, performed examinations and patient demographic details. The schemes used at each patient visit include a *disease activity scheme*, a *blood sample scheme* for registration of blood analysis including vitamin D as well as a *clinical assessment scheme* regarding disease status, treatment, and examinations performed since last visit. To measure the disease activity, the EpiCom-database uses the internationally validated Harvey–Bradshaw index (HB)[5] for CD and Simple Clinical Colitis Activity Index (SCCAI) [6] for UC. For pediatric patients' disease activity the Pediatric Ulcerative Colitis Activity Index (PUCAI)[7] and the Pediatric Crohn's Disease Activity Index (PCDAI)[8] are being used. The *rare event schemes* include specific schemes regarding surgery, death and cancer using ICD-10 codes as well as schemes regarding pregnancy outcome and the use of biological treatment.

For the purpose of answering the questions of the EpiCom-project regarding quality of care (QoC), quality of life (QoL), work productivity and activity impairment (WPAI) as well as to investigate the role of environmental factors in incidence of IBD, internationally validated questionnaires and schemes were implemented in the EpiCom-database. Regarding environmental factors in IBD, the questionnaire proposed by the IOIBD (International Organization of Inflammatory Bowel Disease) is used.[9] To measure patients' health-related quality of life, the short Inflammatory Bowel Disease Questionnaire (s-IBDQ)[10] is used, while the Health Survey SF-12[11,12] is used for measuring general wellbeing.

To describe the quality of health care in Eastern and Western European countries, a questionnaire with particular regard to the physician's background, physician's education in IBD, patient's level of information on treatment, monitoring of drug adverse events and colorectal cancer surveillance was developed. The questionnaire was created on the basis of the ECCO consensus about IBD patients' needs in health quality of care.[13] The Nurse EpiCom group in 10 countries was formed and a QoC questionnaire focusing on nursing was constructed. To measure the effect of overall health and specific symptoms on productivity at work and outside of it, the WPAI Questionnaire[14] has been implemented.

All used questionnaires will be available in English and Russian language in the database. The SF-12, s-IBDQ and WPAI are available in a number of validated translations and the participants will be able to use versions in their local language. The IOIBD environmental factors scheme is only available in English and in a validated Danish version.[15]

The database has built-in control and validation tests in the schemes used, thereby making sure to avoid missing data and inconsistencies. It is impossible to enter invalid data, particularly in the form of patients who do not fulfill the required Copenhagen Diagnostic Criteria for CD and UC. To ensure anonymity, patients are only registered by date of birth and by a unique patient-ID number. The patient-ID consists of five elements: patient inclusion number (six digits); date of birth (six digits); gender (M/F); center number (three digits); and country number (three digits).

To answer the questions of the EpiCom-study, 13 work packages were created by the participant teams with elected leaders responsible for carrying out the work packages, Table 2.

2.4. Database Security

The EpiCom Database is located on a central secure server in the professional hosting center Athena Hosting in Denmark, located in a former regional branch of the National Bank of Denmark. The data is stored in a secure database engine, including backup. The entered data is secured by the WinLog3 Security System, which has been developed in cooperation with the Danish Data Protection Agency. It is thereby possible for all participants to share data across their borders while those same data are stored at a single location. Participating centers will only be able to view patient data from their own center, as they have no access to data from other centers, apart from the calculation of the cumulative patient inclusion at the front page.

2.5. Database Validation

A validation scheme was created for the purpose of the database validation. The validation scheme contained questions regarding general use of the database, time consumption, the overall impression and satisfaction, as well as the relevance and applicability of the questionnaires and schemes used in the database. Furthermore, participants were asked about their previous experience with inception cohort studies as well as their catchment area. Fictional patient cases were created, involving both CD and UC. Participants were also encouraged to invent their own cases or clinical scenarios in order to test all features of the database.

The validation underwent two rounds. All participants in the EpiCom-project were invited to take part in the validation process. They were provided with two IBD cases and the validation scheme and were encouraged to comment on the content and usability of the database. Comments, reported defects and requests for changes in/additions to the feature list were taken into consideration and implemented in the database. The process was then repeated with two new IBD cases, followed by further corrections and changes.

Table 2 EpiCom work packages.

Work package	Leader
WP 1: Inception group construction, environmental factors	JB, NP, PM (Denmark)
WP 2: Database construction and data management	BD (Denmark)
WP 3: IBD diagnostics	JB, NP, PM, Peter Lakatos (Hungary)
WP 4: Quality of care	JB, NP, PM — nurses Birgit Laugesen, Dorte Marker, Hanne Scherfig (Denmark)
WP 5: Quality of life	JB, NP, PM, Mary Shuhaibar (Ireland)
WP 6: Surgery	JB, NP, PM
WP 7: Cancer, survival	Epameinondas V. Tsianos, Kostas Katsanos (Greece), Peter Lakatos (Hungary), Vicent Hernandez (Spain)
WP 8: Pediatrics (<15 years), pregnancy outcome	JB, NP, PM, Pia Manninen (Finland), Dana Duricova (Czech Republic)
WP 9: Health care costs	Selwyn Odes (Israel), Limas Kupcinskas (Lithuania)
WP 10: Biologicals	JB, NP, PM
WP 11: Primary sclerosing cholangitis	Einar S. Björnsson (Iceland)
WP 12: Europe–China gradient	Siew Chien Ng (China)
WP 13: Chronic viral hepatitis B and C and HIV	Epameinondas V. Tsianos, Kostas Katsanos (Greece)

JB: Johan Burisch; NP: Natalia Pedersen; PM: Pia Munkholm; and BD: Birger Dinesen — Denmark.

2.6. Database Translation into Russian

The majority of the Eastern parts of Europe does understand the Russian language to some extent. Therefore a Russian version of the database was developed to ease inclusion of data as well as the patients' understanding of the questionnaires. The EpiCom-database, including schemes constructed by the steering group (diagnostic criteria, clinical assessment, blood samples and rare event scheme) as well as disease activity schemes, was translated from English into Russian by three health care professionals together with the steering group. While being translated, the database underwent continuous testing as well as qualitative and quantitative evaluations by the translators to ensure semantic equivalence.

The questionnaires to be completed by the patients themselves (s-IBDQ, SF12, WPAI, Quality of care and environmental factors) were translated using a simplified forward–backward translation.[16] The questionnaires were translated forward by a bilingual non-health care professional into Russian. Problematic items and response choices were discussed with a bilingual health care professional. The questionnaires were then completed by 10 healthy Russian subjects. Difficulties with understanding the questions were assessed and problems were identified. The questionnaires were then translated backwards into English by an independent translator and that translation was then compared with the original English version. Finally, the steering group and all translators involved agreed upon a final Russian version.

3. Results

3.1. Database Construction and Translation into Russian

The web-based inception cohort database was created by implementing clinical schemes as well as internationally validated questionnaires. Schemes and questionnaires are available from the menu in the database and sorted in the following categories for ease of access: inclusion and yearly status, visit event, pediatric patients and special events.

The security of the EpiCom database fulfills the requirements of the participating countries' local data security agencies by being stored at a single location. All questionnaires and schemes used in the database are available for download in pdf-format to be used in case record forms by the participants. The database is available online at www.epicom-ecco.eu and between January 1st and December 31st 2010 1336 patients were included. The incidence of the participating centers can be viewed online on the inclusion chart on the project website.

3.2. Database Validation

Participants from 39 centers representing 24 countries were invited to take part in the validation process. 36 (92%) centers from 13 Western European countries (26 centers) and 10 Eastern European countries (10 centers) took part in the first round of validation. In the second round 23 (59%) centers from 11 Western European countries (18 centers) and 5 Eastern European countries (5 centers) participated. Half of the participants stated that they had never been involved in inception cohort studies before.

At the first validation, the participants found a number of errors in the questionnaires (e.g. it was impossible to correct wrong entries in some questionnaires and the internal validation of the diagnostic criteria did not work in some scenarios), and in the presented proposals for changes in the design and setup of the database (e.g. additional options in some questionnaires making it more suitable for daily use and deletion of unimportant parameters). All comments were taken into consideration and implemented in the database. No further errors were reported or comments given on the database at the second validation.

After the second validation 81% of the participants found the database overall to be "good" or "very good" compared to 68% after the first round, Fig. 3. The general applicability of the database for the project was evaluated as "good" or "very good" by 77% after the second round compared to 70% after the first, Fig. 4. However the changes between the validation rounds were not significant ($p=0.27$ and $p=0.58$ respectively). The participants did not find the database less or more time-consuming after the second validation round. However, the database being time-consuming was certainly an issue for the participants as a majority found the database time-consuming and approximately 30% found it too time-consuming, as depicted in Fig. 5.

3.3. Database Translation into Russian

The 10 healthy Russian subjects reported no obvious problems with understanding the Russian translation of the questionnaires. The

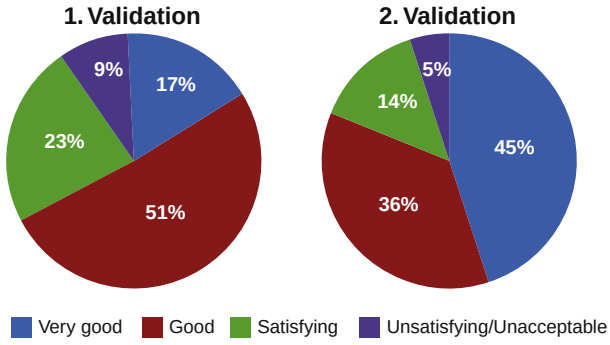

Figure 3 Overall satisfaction, 1st validation vs. 2nd validation.

backward translations were very similar to the original questionnaires, differing only in the syntax. The EpiCom database was thus translated successfully and the desired language can easily be chosen in the log-in window.

4. Discussion

We have constructed a user-friendly, tailor-made and secure web-based inception cohort database, facilitating remote data input from around the world. The database is protected against invalid data entry by built-in controls and validation tests and the incidence of IBD in all 23 participating countries can be seen online on the project website, www.epicom-ecco.eu.

The database has been tested, validated and changed in accordance with comments and errors found by the participants of the EpiCom-project, thus involving the participants from the beginning and introducing them gradually to the concept. No significant positive change in the general satisfaction and applicability after the implementation of changes was found at the second validation round. However, these variables were very positive after the first validation, thus leaving little room for improvement. Also, a number of participant centers dropped out of the validation process after the first round, thereby making a comparison difficult. Nonetheless, there was a general trend of increased satisfaction with the database.

Between January 1st and December 31st 2010, 1336 patients were included in the database. Despite web-based registration it is still very time-consuming to carry out inception cohort studies, as the varying inclusion rates of the participating centers show (Fig. 1). In some cases, participants lack the time to continually enter the included patients in the database, thus partly explaining the low numbers of included patients at some centers. After establishing the EpiCom Nurse project regarding health quality of care, we have observed that in centers where nurses are involved in EpiCom,

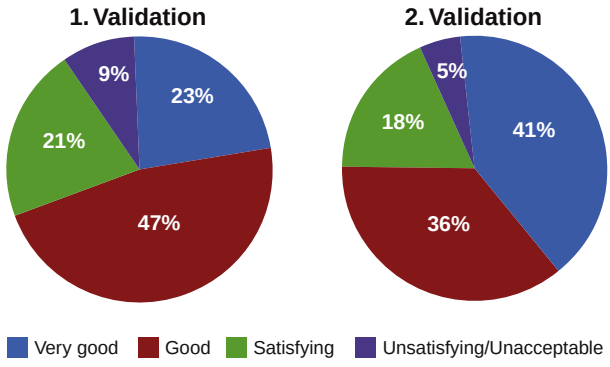

Figure 4 General applicability, 1st validation vs. 2nd validation.

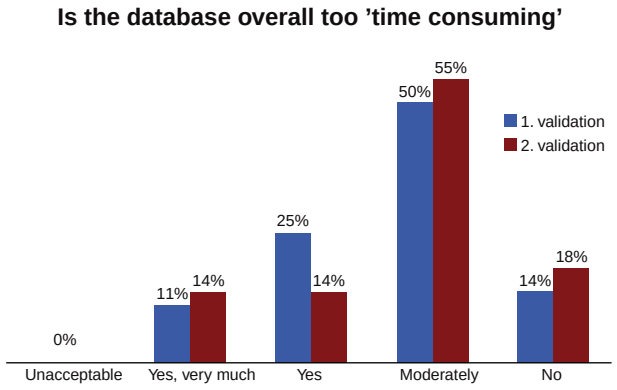

Figure 5 Time consumption, 1st validation vs. 2nd validation.

patient inclusion is improved (data not shown). Thus, the combined efforts of doctors and nurses are recommended.

In future the database will be translated into the respective languages of participating countries following the methods described above or by using already translated and validated questionnaires available in those languages. A Spanish version of EpiCom is in progress. This will facilitate data entry and make the database a useful tool for future studies. Furthermore, a patient-oriented addition to the database is in progress, offering an overview of medication and disease activity for the patients. Web-based questionnaires not only offer a range of benefits for the investigator[17] but may also enhance the patient's compliance.

In conclusion, this concept of a secure web-based database has great potential for performing inception cohort studies and may serve as a template for future multi-national follow-up studies. Furthermore, the database can be used as a clinical assessment for imminent biobanking in ECCO and Europe. Upcoming papers will address the East–West-gradient in the incidence of IBD in the participating countries and as well as the patient data from 1 to 2 years follow-up after diagnosis (medical treatment, surgery, cancer, biological treatment etc.). Future EpiCom trials will address the long-term outcome in the included IBD patients.

Acknowledgements

All authors have made significant contributions to the research described in this manuscript. JB carried out the study, collected and analyzed data and drafted the manuscript. SCC, IK, OS, VA, JFD, ME, EL, NP, RS, KLK, PLL, PMa, MS, SO, YC, MM, IM, FM, EB, AF, SA, JH and AH took part in the validation process and revised the draft of the manuscript. ME and EB carried out the Russian translation of the database. PMu took part in the planning and designing of the study and revised the draft of the manuscript. All authors read and approved the final manuscript.

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