Objectives. Most clinical studies use paper case record forms (CRFs) to collect data. In the Dutch multi-centre observational study on biologicals we encountered several disadvantages of using the paper CRFs. These are delay in data collection, lack of overview in collected data and difficulties in obtaining up-to-date interim reports. Therefore, we wanted to create a more effective method of data collection compared with CRFs on paper in a multi-centre study.

Methods. We designed a web-based register with the intention to make it easy to use for participating physicians and at the same time accurate and up-to-date. Security demands were taken into account to secure the safety of the patient data.

Results. The web-based register was tested with data from 161 juvenile idiopathic arthritis patients from nine different centres. Internal validity was obtained and user-friendliness guaranteed. To secure the completeness of the data automatically generated e-mail alerts were implemented into the web-based register. More transparency of data was achieved by including the option to automatically generate interim reports of data in the web-based register. The safety was tested and approved.

Conclusions. By digitalizing the CRF we achieved our aim to provide easy, rapid and safe access to the database and contributed to a new way of data collection. Although the web-based register was designed for the current multi-centre observational study, this type of instrument can also be applied to other types of studies. We expect that especially collaborative study groups will find it an efficient tool to collect data.

Key words: Web-based register, Data collection, Multi-centre study, Juvenile idiopathic arthritis, Biologicals.

Introduction

Biologicals are a recent development in the treatment of juvenile idiopathic arthritis (JIA) [1–5]. The efficacy and safety of etanercept and other biologicals (infliximab, adalimumab and anakinra) is, since the introduction in the Netherlands, investigated in a prospective observational study [6]. This nation-wide survey is coordinated by the Erasmus MC Sophia Children’s Hospital in Rotterdam and based on collaboration of the ‘Arthritis and Biologicals in Children’ (ABC) working group members. As result of this collaboration all Dutch JIA patients treated with biologicals since 1999 are included. The database from the central evaluation board that had to approve treatment for each individual patient was used to insure completeness.

Data were documented by the treating physician on paper case record forms (CRFs). The investigator had to collect the CRFs at the local centres and import the data into a database. In time, data collection became more difficult because of the rapidly increasing group of patients using etanercept and the increased use of other biologicals. As data accumulate, lack of overview may occur and as a result side-effects of medication and significant events may remain underreported [7, 8].

In contrast to paper CRFs, a web-based register is a tool to collect data on a long-term continuous basis with more accuracy and completeness [8]. Since a web-based register is thought to be more up-to-date and less time-consuming, data can be collected with the shortest possible delay and lower costs in the long-term [8–10]. In addition, it creates an opportunity for interim reports.

The aim of the web-based register is to provide easy and safe access to the database for the participating physicians, which also produces automatically generated interim reports, and provides an accurate and up-to-date database for the investigators.

Methods: webdesign and structured data entry

Data collected in the ABC register

The data collected in the register include patient and disease characteristics as: date of birth, gender, length, weight, onset of the disease, JIA onset type, medical therapy in the past and current co-medication (NSAIDs, glucocorticoids and DMARDs). Furthermore, detailed data are collected regarding the use of biologicals (type, dose, frequency), disease activity conform the JIA core set of response variables and adverse events [11].

All treating physicians are defined as ‘users’, the investigators from the coordinating centre are defined as ‘investigators’. On conforming to the study protocol, data will be collected at fixed follow-up moments. The users are invited by an automatically generated e-mail message to assure data collection at each follow-up moment. In case of unforeseen events such as side-effects or disease flaring, the users are asked to add the data on their own initiative.

Web-based register design

The screens used in the web-based register are presented in a logical sequence. The user logs in to the administrative section,
and is then offered different selection buttons from the menu. With the button ‘new patient’ the user enters the initial data. Under ‘known patient’ the user has several options besides entering the usual follow-up data, such as adverse events or disease flaring. With the button ‘results’, an overview is shown of the combined general information of all patients included nationwide as well as a summary of the specific data of the centre that has logged in. This summary includes the total number of patients included, division in JIA subtypes, gender distribution, the outcome of the JIA core set, reported side-effects and a Kaplan–Meier curve on the continuation of use of the diverse biologicals. The button ‘current status’ presents a summary of a specific patient (Figs 1 and 2).

As an extra the user can download several forms, such as the Childhood HAQ form, the joint-score form and the informed-consent form [12].

User-friendliness of the design was tested by most users in a joined meeting addressing the practical use of the register. An example was given entering ‘new patient’ as well as a ‘follow-up’ data. After this, the inexperienced users were asked to enter data while recording the time needed. Comments on user-friendliness were processed.

Data saving and retrieval

Data entered are saved automatically as the user goes to the next screen, herewith preventing the risk of data loss. Imported data are automatically checked for major erroneous and completeness at the end of each step. At the end of the data entry process, a summary is presented and the user has to confirm the correctness of data. The user is able to change the data up to a month. Thereafter, the imported data are checked on inconsistencies and potential missing values by the investigators and secured. Thereafter, changes can only be made by contacting the investigator.

Safety of privacy and security

The change from paper CRFs to a web-based register was approved by the Medical Ethical Committee of Erasmus MC, Rotterdam. Privacy and security measures were taken to comply with the requirements of the Dutch privacy law and the Dutch law on medical treatment. Data of patients were made anonymous before they are stored in a central database. All participating centres will sign a contract regarding their responsibility over the implemented data.

Extensive security tools have been implemented to protect the register against unauthorized use. These include, among others, individual logins and passwords for users and investigators. Users can only access patients from their own centre; investigators have access to all patients. When logged in incorrectly three times, the account will be blocked and the user has to contact the webmaster. The system also registers as to which user logs in and can link this to the imported data.

To reduce the risk of data loss due to browser or PC failure, data entered by the user are saved as each screen is completed. Facilities were made for backup of data for at least 10 yrs. Anti-virus software is installed, and will be updated on a regular basis. Security experts from Erasmus MC insured that all requirements concerning the protection of patient data were met. The security demands of the service provider and the web application

FIG. 1. Entering and retrieving data; the upper left side of the screen shows the menu, in which the user can choose the options ‘About ABC’, ‘Forms/Downloads’, ‘New patient’, ‘Known patient’, ‘Results’, ‘Questions/Remarks’ or ‘Log out’. The right side of the screen displays an entry form for follow-up data. The imported data from the last follow-up are shown in brackets and italic font style on the screen as a reminder for the user.
were all checked. A security risk analysis was performed to anticipate possible safety risks.

Software
The following programs were used: Dreamweaver (for the design and realization of the webpages), MySql (for the database) and PHP (for the link between database and webpages). The web server was installed and coordinated by external companies specialized in medical multimedia. The ABC logo and layout of the site was designed using QuarkXPress and Adobe Photoshop. The register Internet domain is made available at www.abc-register.nl

Results
The web-based register was first tested by the investigators with the data from all 41 study patients from the Erasmus MC Sophia Children’s Hospital. After data entry several issues in usability were encountered and successfully adjusted. For instance, we discussed as to what to do with patients who discontinued a biological. We decided to keep these patient cases open for data entry as follow-up data of these cases are highly desired. To prevent confusion these patients would be marked with ‘stop’ in the overview unless they restart a biological. Other issues concerned time frame calculations to appoint follow-up data to fixed time points and minor adjustments in the layout to improve user-friendliness.

All imported data from the register could be automatically converted into an SPSS file. Since the original database (in which the data from the paper CRFs was imported) consisted of an SPSS file as well, data could be easily compared. Some errors were detected and correction of false couplings was needed and performed.

Next, the investigators tested the ABC register with the data from all 161 included patients from nine different centres. In order to check if all information about the centre was given correctly and to verify if data from other centres were not accessible, we logged into the register using the specific password of a user of that centre.

User implications
The users were positive about the layout, readability and order in which data had to be entered. They all judged the amount of entered data as sufficient and saw no need in adding extra. The mean duration of data entry in the web-based register on a new patient was 4 min 33 s vs 4 min 25 s on paper CRF. The follow-up assessment entry took an average of 2 min 22 s vs 2 min 40 s on paper CRF. The users judged the time needed for data entry acceptable. No errors were found in the imported data.

At first all data regarding a specific patient had to be entered at once. This was judged as a disadvantage by the users as some data are not known immediately. Now the user is notified if data are missing, but may proceed data entry despite missing data. The investigator will contact the user if the data are still missing after 30 days.

A user suggested providing a paper overview of data needed for the web-based register as a reminder. We therefore designed a mousepad with an overview of the data needed, an email address to be used for help and the website address of the register.

Safety tests
The inaccessibility to patient data for unauthorized visitors was tested when the Computer Emergency Response Team (CERT) tried to hack into the ABC register unsuccessfully. After multiple
safety tests the CERT as well as the security officer and the officer for protection of personal information of the information department concluded that the web-based ABC register was safe to use as a data collection tool.

Discussion

By developing a web-based register we have digitalized the CRF and achieved our aim to provide easy and rapid access to the database. As most scientific clinical studies use paper CRFs to collect data, such a web-based register can also be used for other type of studies, like clinical trials or cohort studies [8–10]. An advantage for the users is the possibility to check own data at any given moment and the general data of all participating centres combined. Continuous accurate output and reports will improve the collaboration between the centres and promote involvement [8–10]. The advantage for the investigator is the continuous access to a complete, up-to-date, multi-centre database. In addition, it saves the investigators time since data collection has been automated and visits to local centres are reduced.

The velocity and simplicity of data entry, has to stimulate the physician to use the register [5, 6]. At the fixed follow-up moments for each patient, physicians will automatically be reminded through an e-mail to update the patient data into the register.

Nevertheless, the register does request physicians to be alert and report side-effects, flares, therapy withdrawals and therapy changes, since automatic reminders are not possible for these situations. Connecting the register to the electronic medical records of each centre would improve completeness of the database and increase user-friendliness [7]. This is certainly a recommendation for the future.

A potential drawback of a web-based register is that it brings the risk of losing entered data or problems with data entry due to browser or PC failure. Therefore, it is essential to provide an excellent back-up system to prevent loss of data.

In addition, when the register is not designed properly it may lead to the production of misleading data [8]. For this reason, testing of the register by investigators and users is important to secure internal validity.

We expect that the use of web-based registers will greatly expand over the next decade and that especially collaborative study groups will find it an efficient tool to collect data.

By reporting the process of developing a web-based register for biologicals in JIA (the ABC register) and the advantages of using such a register, we hope to have contributed to a new way of data collection for clinical research.

Rheumatology key messages

- Web-based registers are a new and adequate tool in clinical studies, especially when multiple centres are involved.
- It is user-friendly and improves the adherence of the participants in the study.

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References