Title: METHOD AND SYSTEM FOR MANAGING REMOTE DATA COLLECTION IN A CLINICAL TRIAL

Abstract: ABSTRACTA method and system for managing remote data collection in a clinical trial are disclosed. The system comprises a central server and a database of trial information and treatment data. A number of portable computing devices run client software which permits them to upload data to and download data from the server via a public network. The client application controls registration of patients in the trial by a registered user of each portable computing device and the collection of patients’ data. The random allocation of a treatment regime to each patient is done by the client software in the portable computing device, utilising treatment data downloaded from the central server. From time to time, patient data is uploaded to the central server and recorded in the central database, thus maintaining a central record of the clinical trial.
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METHOD AND SYSTEM FOR MANAGING REMOTE DATA COLLECTION IN A CLINICAL TRIAL

BACKGROUND OF THE INVENTION

This invention relates to a method and system for managing remote data collection in a clinical trial.

Traditionally, large multi-centre randomised clinical trials are used extensively to test efficacy claims for new drugs. The process generally relies on manual methods of data collection. However, this is arduous and error-prone. In addition, the process of randomisation can be compromised, resulting in biased results. There is also little opportunity in such a situation for feedback during the project, should skewing be uncovered during the trial.

While computerised applications have been developed for routine data administration and randomised clinical trial management, there is a need for a method and system which provide enhanced management of such trials.
SUMMARY OF THE INVENTION

According to the invention of a method of managing remote data collection in a clinical trial comprises:

- providing a central server and a database of trial information and treatment data defining a plurality of predetermined treatment regimes;
- registering a plurality of portable computing devices and respective authorised users thereof with the central server and recording details thereof in the database;
- downloading treatment data from the central server to each portable computing device;
- registering a plurality of patients in the trial via the portable computing devices and recording corresponding patient data;
- automatically allocating a predetermined treatment regime to each registered patient according to the downloaded treatment data and recording corresponding allocation data;
- uploading the patient data and associated allocation data to the central server; and
- recording the uploaded patient data and associated allocation data in the database, thereby to generate a central record of the clinical trial.

Each treatment regime will typically comprise an allocation of drugs to be dispensed to a patient, in which case the treatment data will typically comprise a code corresponding to a pre-prepared package of drugs.
For example, the code may correspond to a barcode on the package of drugs.

However, it is also possible that the treatment regime may comprise another form of treatment or intervention.

Preferably, the method includes downloading data to each portable computing device from the central server which comprises a client application adapted to run on the portable computing device and to facilitate data entry for a predetermined clinical trial.

The client application preferably generates prompts to the authorised user of each portable computing device to enter required data, for example, patient data.

The random allocation of a predetermined randomised drug allocation to each registered patient is preferably controlled by the client application, the client application flagging each predetermined drug allocation as having been used on allocation thereof.

The method preferably includes recording clinical data for each registered patient from time to time, and uploading the clinical data to the central server for storage in the database.

The method may further include, in the event that the need arises, recording adverse effects experienced by a patient.

In such a case, the method may include breaking the trial by decrypting and displaying the randomised drug allocation assigned to a particular patient and irreversibly flagging the relevant patient record.
Further according to the invention there is provided a system for managing remote data collection in a clinical trial comprising:

a central server;

a database associated with the central server, the database comprising trial information and treatment data defining a plurality of treatment regimes; and

a plurality of portable computing devices registered with the central server together with respective authorised users thereof, details of the registrations being recorded in the database,

each portable computing device being connectable to the central server from a remote location to download treatment data from the central server to the portable computing device, to register a plurality of patients in the trial via the portable computing devices and record corresponding patient data, to allocate automatically a predetermined treatment regime to each registered patient according to the downloaded treatment data and to record corresponding allocation data, to upload the patient data and associated allocation data to the central server, and to record the uploaded patient data and associated allocation data in the database, thereby to generate a central record of the clinical trial.

The database may comprise a central data structure to contain all patient and clinical information, and individual data structures to hold patient and clinical information for individual users or data administrators.

Preferably, each portable computing device is connectable to the central server via a public network such as a telephone network.
Each portable computing device may be loaded with a client application which controls downloading of data from and uploading of data to the central server, entry of patient data, and allocation of a treatment regime to a patient.

**BRIEF DESCRIPTION OF THE DRAWINGS**

**Figure 1**
is a simplified block diagram illustrating the basic architecture of a system for managing remote data collection in a clinical trial according to the invention;

**Figure 2**
is a simplified flow diagram illustrating major steps in the overall method of the invention;

**Figure 3**
is a simplified flow diagram illustrating the major steps involved in the initiation of a clinical trial according to the method of the invention;

**Figure 4**
is a simplified flow diagram illustrating the major steps involved in patient and trial data collection according to the method of the invention;

**Figure 5**
is a simplified flow diagram illustrating the major steps involved in a data synchronization process used in the method of the invention;

**Figure 6**
is a simplified flow diagram illustrating the major steps involved in breaking a trial for a patient according to the method of the invention; and
Figures 7 to 11 are diagrams in Unified Modelling Language (UML) illustrating the method of the invention in detail.

DESCRIPTION OF AN EMBODIMENT

Referring first to Figure 1, the basic architecture of a clinical trial data management system according to the present invention comprises a central server 10 with an associated central database 12.1 and many individual user databases 12.2 which is connected either directly or via a public or private network 14 (for example, the public telephone network, the Internet or a local or wide area network) to a number of portable computing devices 16. The server controls the operation of a clinical trial which is administered by authorised users utilising the portable computing devices, and the associated databases store the relevant data gathered by the trial.

In the prototype system, a Palm Pilot Vx was the portable computing device of choice, but various other devices could be used instead. The main requirement is a convenient data entry interface and suitability for running third party client applications of the kind utilised, as well as a communication facility to allow downloading and uploading of data from and to the central server.

A client software application was written utilising Code Warrior (a Palm specific programming environment that generates C++ code). The application generates data capture fields, allowing the user to enter data directly into a back-end database running on the Palm device. A database software application was also provided, that runs on the server and contains all the data structures to receive data stored temporarily on the Palm device during the clinical trial, as well as the initial setup information during the setup phase of the trial. This latter information includes the important codes and/or numbers used to identify drug packs allocated to patients, and an algorithm that
randomly assigns drug packs to records in the data structure prior to downloading to the Palm Pilot.

Operation of the method and system of the invention is illustrated graphically in the simplified flow diagrams of Figures 2 to 6 and, in greater detail, in the UML diagrams of Figures 7 to 11.

As indicated in Figure 3, the trial is initialized by central and individual user databases 12.1 and 12.2 with data structures corresponding to the trial information that needs to be collected as well as other administrative information. A randomization algorithm is then used to create a table of randomized drug allocations matched with other information, e.g. drug package bar codes.

Each individual trial administrator (i.e. authorised user) is provided with a Palm Pilot device and the trial co-ordinator registers both the user and the unique serial number of the respective Palm device in the trial database. Thereafter, the device is synchronised with the server from time to time, utilising the proprietary Palm "hot-sync" cradle. This can be done over a network such as the Internet, a local or wide area network, or a public telephone network, for example, in which latter case a modem would normally be needed.

When the user connects to the server for the first time, the client application, data structure and a set of encrypted, randomly assigned drug allocation codes or numbers are downloaded to the Palm device.

As indicated in Figure 4, once the client application has been loaded on the Palm device, the user can log in and select two basic sets of menu options. The first option relates to the registration of a patient and the recording of clinical observations, while the second option relates to collecting ongoing follow-up information.
To register a patient, the appropriate menu option is selected, and the client application then generates prompts to the user, to insure that the necessary patient data is entered. The patient details are encrypted and stored in the database on board the device.

The client application validates the patient data and then assigns a random drug allocation or treatment package to the patient.

The patient registration process involves activation of a user interface by means of which the user can enter textual details or select predefined options from single- or multi-select lists. In addition, questions are presented according to a pre-programmed flow structure that results in the user inputting appropriate data only. The default condition is "NOT ENTERED". The user continues to the end of the electronic questionnaire and reaches a system-defined rejection or acceptance, at which point the system assigns the next available random drug allocation from the encrypted data set and, if required, waits for bar code validation.

The patient validation is done by comparing the patient and clinical details against a predetermined set of criteria for determining whether a patient is eligible for inclusion in the trial, for example blood pressure range, clinical history etc.

During the trial setup, a large number of drugs in packages are accumulated for distribution to the trial data collection centres. These drug packages all have bar code identifiers. This information can be obtained beforehand and loaded into the data structure and downloaded with the rest of the drug information to the handheld device. Once the random drug allocation has been assigned to the patient, the bar code in the database can be checked
against the bar code on the package given to the patient as a further check that the correct allocation has been made.

The number or code representing the drug allocation or treatment package is then flagged as having been used, so that it cannot be re-used, and so that its use can be logged when the device is next hot-synced with the server. It will be appreciated that this feature of the invention is important, as it ensures that the random allocation of treatment to patients is centrally controlled and monitored. Inter alia, this means that remedial action can be taken in certain circumstances which might otherwise compromise the clinical trial. For example, if the contents of the treatment package were to be exposed (say, in an emergency situation) the relevant patient record can be irreversibly flagged to indicate that the randomisation has been broken, and this record can then be excluded from the trial.

From time to time, the trial administrator will make clinical observations on each patient, which are stored in an encrypted form in the on-board database of the Palm Pilot. These entries are uploaded to the server whenever the Palm device is hot-synced with the server.

As indicated in Figure 5, data synchronization begins with a user connecting the device to a communications interface such as a serial or infrared port on a network computer, a modem connection to a telephone network or an infrared connection to a cellular telephone network. The data synchronization function is activated and the device makes a connection with the host computer. Once the connection has been made, device and user authentication and validation occurs. Once the user has been validated, the data is uploaded to the user database and validated. Data in the user database is uploaded to the central database either manually or via an automated program.
Once the initial allocation of treatment package codes has been utilised, the user needs to hot-sync with the server to obtain additional codes. This happens automatically as part of the bidirectional hot-sync process. Each time the user connects to the server, new patent information is uploaded to the server, and additional random treatment allocations, messages from the trial co-ordinator, newsletters, or other data or are downloaded to the Palm device.

A major benefit of the invention is the fact that the trial coordinators can manipulate the data collection process to even out biases in the data collection procedure. For example, if too many patients of a certain racial group are being obtained, the trial coordinators can correct this after examining the data.

As indicated in Figure 6, the method of the invention contains a method for rapidly displaying the drug allocation for a particular patient and irreversibly flagging the record in the database to ensure that the patient is removed from the trial. The software application warns the user before displaying the data.

The detailed flow diagrams of Figures 7 to 11 show the specific steps of the method in greater detail.

The invention provides a method and computer-implemented system for conveniently administering remote data collection in a clinical trial. Patients can be screened for eligibility, rapidly registered on a trial and a random drug allocation made to them. Trial information is collected on an ongoing basis in a convenient and cost-effective way and communicated to the central trial database. The system also provides feedback to end users and controls the security of random number allocations by restricting access to the numbers.

The invention includes a mechanism for breaking a trial if necessary, for rapidly displaying a patient’s drug allocation and, at the same time, marking the record such that the patient is irreversibly removed from the trial.
Although the invention has been described with reference to treatment regimes comprising the allocation of packages of drugs to patients, it will be appreciated that other treatment regimes comprising a medical treatment or other intervention could be used, in which case the treatment data downloaded to the Palm Pilots would alter correspondingly to define such treatment or intervention.
CLAIMS

1. A method of managing remote data collection in a clinical trial comprising:

   providing a central server and a database of trial information and treatment data defining a plurality of predetermined treatment regimes;

   registering a plurality of portable computing devices and respective authorised users thereof with the central server and recording details thereof in the database;

   downloading treatment data from the central server to each portable computing device;

   registering a plurality of patients in the trial via the portable computing devices and recording corresponding patient data;

   automatically allocating a predetermined treatment regime to each registered patient according to the downloaded treatment data and recording corresponding allocation data;

   uploading the patient data and associated allocation data to the central server; and

   recording the uploaded patient data and associated allocation data in the database, thereby to generate a central record of the clinical trial.
2. A method according to claim 1 wherein each treatment regime comprises an allocation of drugs to be dispensed to a patient.

3. A method according to claim 2 wherein the treatment data comprises a code corresponding to a pre-prepared package of drugs.

4. A method according to claim 3 wherein code corresponds to a barcode on the package of drugs.

5. A method according to claim 2 including downloading data to each portable computing device from the central server which comprises a client application adapted to run on the portable computing device and to facilitate data entry for a predetermined clinical trial.

6. A method according to claim 5 wherein the client application generates prompts to the authorised user of each portable computing device to enter required data.

7. A method according to claim 6 wherein the required data includes patient data.

8. A method according to claim 5 wherein the random allocation of a predetermined randomised drug allocation to each registered patient is controlled by the client application, the client application flagging each predetermined drug allocation as having been used on allocation thereof.

9. A method according to claim 1 including recording clinical data for each registered patient from time to time, and uploading the clinical data to the central server for storage in the database.
10. A method according to claim 9 including recording adverse effects experienced by a patient.

11. A method according to claim 10 including breaking the trial by decrypting and displaying the randomised drug allocation assigned to a particular patient and irreversibly flagging the relevant patient record.

12. A system for managing remote data collection in a clinical trial comprising:

   a central server;

   a database associated with the central server, the database comprising trial information and treatment data defining a plurality of treatment regimes; and

   a plurality of portable computing devices registered with the central server together with respective authorised users thereof, details of the registrations being recorded in the database,

   each portable computing device being connectable to the central server from a remote location to download treatment data from the central server to the portable computing device, to register a plurality of patients in the trial via the portable computing devices and record corresponding patient data, to allocate automatically a predetermined treatment regime to each registered patient according to the downloaded treatment data and to record corresponding allocation data, to upload the patient data and associated allocation data to the central server, and to record the uploaded patient data and associated allocation data in the database, thereby to generate a central record of the clinical trial.
13. A system according to claim 12 wherein the database comprises a central data structure to contain all patient and clinical information, and individual data structures to hold patient and clinical information for individual users or data administrators.

14. A system according to claim 12 wherein each portable computing device is connectable to the central server via a public network such as a telephone network.

15. A system according to claim 12 wherein each portable computing device is loaded with a client application which controls downloading of data from and uploading of data to the central server, entry of patient data, and allocation of a treatment regime to a patient.
Connect Device to Communications Interface

Direct

Activate Hot Synch

Network

Establish Connection

Activate Hot Synch

Validate User and Open Individual User Database

Insert or Update Data Records

Validate Data Transfer

Send OK Message

Upload to Central Database
Figure 6

1. Display Menu
2. Select Break Trial Option
3. Validate Selection
4. Warning of Irreversible Step
5. OK
   - Irreversibly Mark Record for Exclusion
     - Display Drug Allocation
     - Display Exclusion Message
6. Cancel