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A pragmatic method for electronic medical record-based observational studies: developing an electronic medical records retrieval system for clinical research

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ABSTRACT

Objective: Utilising data collected via electronic medical records (EMRs) is necessary to improve clinical research efficiency. However, it is not easy to identify patients who meet research eligibility criteria and collect the necessary information from EMRs, as the data collection process must integrate various techniques, including developing a data warehouse and translating eligibility criteria into computable criteria. This research aims to establish a pragmatic method optimised for patient identification and collect necessary clinical research information from EMRs. **Design**: Qualitative analyses. **Participants**: At our hospital, 800,000 cases of clinical information have been stored in EMRs. **Primary and secondary outcome measures**: To evaluate the feasibility and usefulness of the ERS, the method to convert text form eligible criteria to computable criteria, and a reconfirmation method to increase research data accuracy. **Results:** To comprehensively and efficiently collect information from patients participating in clinical research, we developed an EMR retrieval system (ERS). To design the ERS database, we modified the star schema and designed a new multi-dimensional data model optimised for patient identification. We also devised practical methods to translate narrative eligibility criteria into computable parameters. We applied the system to an actual hospital-based cohort study performed at our hospital. We converted the test results into computable criteria. Based on this information, we identified eligible patients and extracted data necessary for confirmation by our investigators and statistical analyses with our ERS.

Conclusion: We propose a pragmatic methodology to identify patients from EMRs who met clinical research eligibility criteria. Our ERS allowed for the efficient collection of information on the eligibility of a given patient. The method proposed here reduces the labour required from the investigators. We believe an efficient ERS is essential to facilitate clinical research that utilises EMRs.

ARTICLE SUMMARY

Article focus

To establish a pragmatic methodology to efficiently collect information from patients who meet clinical research eligibility criteria from EMRs.

Key messages

Utilising data collected as electronic medical records (EMRs) is necessary to improve clinical research efficiency. However, it is not easy to identify patients who meet research eligibility criteria and collect necessary data from EMRs, as the data collection process must integrate various techniques, including developing a data warehouse and translating eligibility criteria into computable criteria. An efficient ERS that integrates these techniques is essential to facilitate clinical research that utilises EMRs.

Strengths and limitations of this study

- The strengths of our method include using a specialised data model for patient identification in clinical research and efficient data conversion without being conscious of the EMR database structure when converting narrative criteria to computable criteria.

- Our ERS cannot retrieve information that is not in the data model. It is thus necessary to create eligibility criteria assuming the use of our ERS in the protocol development stage.

- Enabling ERS use in multiple institutions is an important future task.

BACKGROUND

Medical information technology has recently advanced in many countries, and enormous amounts of clinical data are already stored as electronic medical records (EMRs). Utilising the data collected in EMRs is necessary to improve clinical research efficiency. An EMR is a large database of patient data and is used in observational research investigating the relationships among diseases, treatments, and outcomes; conducting surveillance for rare drug reactions; and recruiting patients for clinical trials [1-10]. However, it is not easy to identify patients who meet research eligibility criteria and collect necessary information from EMRs. Herein, we describe three major issues concerning EMR-based observational studies: EMR patient data retrieval function, eligibility criteria protocol representation, and EMR data accuracy. [11-14]

To identify patients who meet research eligibility criteria, it is necessary to obtain various types of information stored in EMRs by subject, e.g., diagnosis and prescribed medications. However, because the EMR database structure is designed to facilitate online transaction processing to enable rapid and detail-oriented clinical information searches and updates on individual patients [12-13], current EMR system do not facilitate this retrieval function [11-13, 15]. Data warehouses are essential components of data-driven decision support. To allow efficient research analyses, EMR data must first be warehoused to allow data analyses across patient populations [16-23]. However, health care data modelling is difficult and time-consuming because of the complexity of the medical knowledge involved. Thus, the most common approaches to clinical data warehouse modelling are variations on the entity-attribute-value (EAV) model [24-30], where data are stored in a single table with three columns: entity identification, attribute, and attribute value. The EAV design has advantages, including flexibility and ease of storage; however, it requires transforming EAV data into another analytical format before analysis [25-30]. Online analytical processing (OLAP), which facilitates flexible data navigation and analyses, is most frequently used for searching data stored in the data warehouse [16-19, 31-34]. OLAP systems in relational databases are typically designed based on Kimball's star or snowflake schemas [16-19, 31, 33]. However, the star schema was devised to facilitate online measurement analyses [16-19, 31, 33]. In health care, this method can be used to dynamically gather online analyses of numeric data (e.g., a specific dose of a drug for a specific disease or the time required for a specific operation) in clinical practice. It is thus not suitable for identifying patients who meet the complicated eligibility criteria for a given clinical research.

Current eligibility criteria are written in a text format that cannot be computationally processed. Several investigations have sought to establish computable eligibility criteria [35-42]. However, eligibility criteria are not yet completely standardised. Using natural language processing (NLP) technologies, converting the text format of eligibility criteria to a computer or extracting patient identifications from EMRs is far from perfect without human intervention [13, 43-44].

Current EMRs have been used to support claims for medical service fees and the treatments administered to each patient; therefore, data gathered specifically for research purposes may be incomplete and unreliable [12-13].

Although various investigations on each technique are executed individually, standardised methods must still be established that integrate these techniques, facilitate identifying patients who are eligible for clinical research, and collect necessary information from EMRs.

Objective

To utilise EMRs efficiently in clinical research, we considered it necessary to develop an EMR retrieval system (ERS) to collect data from patients who meet the eligibility criteria for a study and establish practical methods to utilise the system.

This research aims to establish a pragmatic method optimised for patient identification and collect necessary information from EMRs for clinical research. These tools are implemented as an ERS. We apply the system to an actual hospital-based cohort study and conduct qualitative analyses to evaluate the feasibility and usefulness of the ERS, the method to convert text form eligible criteria to computable criteria, and a reconfirmation method to increase research data accuracy.

MATERIALS AND METHODS

EMR retrieval system

In our hospital, EMR use was introduced in 2005; approximately 800,000 cases of clinical information have already been stored. To collect information for patients participating in clinical research comprehensively and efficiently, we developed an ERS [45].

We identified nine data categories (i.e., entities) from EMRs that are useful for clinical research: demographic characteristics, physical findings, diagnostic studies, laboratory tests, diagnoses, progress reports on an EMR template [46-50], medications and injections, operation records, and other treatments.

In designing the ERS database, we designed a new data model based on the star schema, optimised for patient identification in clinical research. Figure 1 presents our data model. In our data model, all entities in a given schema are independent and complete; this allows for logical operations and creating eligible patient lists for each respective parameter in a study [51]. The target patient list is made by combining these patient lists. The data model also supports the inferrence of medical concepts expressed in eligibility criteria in reference to corresponding patient data accumulated in EMRs [35].

To ensure that the data retrieval process is practical and independent of the EMR system structure, a data warehouse (i.e., data mart [52]) was created on a relational database management system by extracting, transforming, and loading information from the EMR system [16-23].

An OLAP tool was installed to efficiently search through data from multiple patients [16-19, 31-34]. The OLAP tool runs in an Internet browser and can generate structured query language (SQL) based on predefined metadata (i.e., a data model) by defining logical queries (i.e., programs) using a graphical user interface (GUI) [16-19, 31-34]. Moreover, it allows reports on information retrieved from the browser to be transcribed using hypertext markup language (HTML). The reports are created in various formats, including portable document format (PDF), comma separated values (CSV), and extensible markup language (XML).

To protect personal information in medical records at our hospital, the EMR network is separated physically from other networks. Our data warehouse and OLAP servers are deployed in the same EMR network and managed using the same EMR security policies. Additionally, using our ERS is limited only to clinical research approved by the ethics committee at our hospital. Only designated staff member at our centre are allowed to retrieve data. Our centre creates and manages ERS user identification separate from the EMRs. For the external output of CSV and other data, permission must be obtained from our department of medical informatics and data extraction must be executed in the presence of supervisors who are responsible for protecting personal information at our hospital.

Application to clinical research

We applied the system to a hospital-based cohort study performed at our hospital, titled 'Risk of osteomyelitis of the jaw induced by oral bisphosphonates (BP) in patients taking medications for osteoporosis: a hospital-based cohort study in Japan', in which we identified eligible patients, extracted research data, and evaluated the feasibility of our system. The ethics committee at Kyoto University Hospital approved this research. A different paper details the purpose, methods, results, and discussion of this research.

This research aims to estimate the risks for osteomyelitis of the jaw in osteoporosis patients at our hospital who had been exposed to oral BP compared to those who had not [53-54].

The eligibility criteria were as follows.

Inclusion criteria

- Patients diagnosed with osteoporosis and treated with osteoporosis medications at Kyoto University Hospital between November 2000 and October 2010.
- Patients aged 20 years or older.

Exclusion criteria

- Patients with a history of treatment with radiation therapy to the maxillofacial region.

- Patients with primary or metastatic tumours in the maxillofacial region.
- Patients treated with intravenous BP.

The data collected were diagnosis, date of diagnosis, sex, birthday, and the doses and dates when osteoporosis medications, steroids, biopharmaceuticals in rheumatic diseases, disease modifying antirheumatic drugs, anticancer drugs, diabetes drugs and HbA1c test were administered.

Patient identification and data collection using our ERS

To identify patients who meet the eligibility criteria for the clinical research in question, data were collected using the ERS in the following ways:

1) Convert the text form of the narrative criteria into computable criteria.

2) Create a targeted patient list.

3) Add a flag for investigators to confirm the targeted patient list.

4) Create reports for the investigators to confirm.

We show the details below.

Convert the text form of the narrative criteria to computable criteria

To identify eligible patients and collect the necessary data from EMRs, narrative criteria and data must be converted to computable criteria. Such computable criteria include entities, attributes, logical operators (i.e., 'and' and 'or'), codes, and parameters [35-42]. The clinical research purpose and clinical practice demands made it necessary to perform this task.

As an example of conversion from narrative criteria to computable criteria, we present the following two-step conversion procedure.

Step 1: Convert narrative criteria into entity-level criteria.

Medical concepts expressed as narrative criteria are mapped onto entities in the data model and converted into entity-level criteria. For each entity, a criterion is created to extract patients who meet each condition. If exclusive conditions for the same entity must be defined, a different criterion is created. In this study, we mapped 'osteoporotic patients' onto two entities (i.e., 'diagnosis' and 'medications and injections') and converted it to a combination of two criteria (i.e., 'diagnosis of osteoporosis' and 'osteoporosis drug administration'). This process reflects that the test research aims to estimate some risks of osteomyelitis of the jaw with BP administration instead of diagnosing osteoporosis patients accurately. The recorded diagnosis in the EMR was typically designed to ensure payment for medical claims. We thus sought to reduce the number of false-positives by extracting patients with a given treatment type. This task was performed at the protocol development stage of the study.

Step 2: Convert entity-level criteria into attribute-level criteria (i.e., computable criteria).

Medical concepts expressed in the entity-level criteria are mapped onto attributes in the data model; these become computable criteria by specifying the corresponding date and codes [55]. For this study, Table 1 presents a "diagnosis of osteoporosis and osteoporosis drug administration and no intravenous BP administration (i.e., exclude 'intravenous BP administration')".

Table 1. Example of computable criteria to create the targeted patient list

Criterion	Entity	Operator symbol	Attribute	Operator symbol	Parameter	SQL
Inclusion: Osteoporosis diagnosis	Diagnosis	-	ICD10Code	in	(ICD10 code list)	Select PatientId From Diagnosis Where ICD10Code in (ICD10 code list) and DiagnosisDate >= '10/01/2000' and DiagnosisDate <= '09/30/2010'and SuspectedFlag = 'Fixed'
		and	DiagnosisDate	>=	'10/01/2000'	
		and	DiagnosisDate	<=	'09/30/2010'	
		and	SuspectedFlag	=	Fixed	
Inclusion: Osteoporosis drug administrations	Medications and Injections	-	DrugCode	in	(drug code list)	Select PatientId From MedicationsAndInjections Where DrugCode in (drug code list) and ExecuteDate >= '10/01/2000' and ExecuteDate <= '09/30/2010'
		and	ExecuteDate	>=	'10/01/2000'	
		and	ExecuteDate	<=	'09/30/2010'	
Exclusion: Intravenous BP	Medications and	-	DrugCode	in	(drug code list)	Select PatientId From MedicationsAndInjections
		and	ExecuteDate	>=	'10/01/2000'	

administrations	Injections	and	ExecuteDate	<=	'09/30/2010'	Where DrugCode in (drug code list) and ExecuteDate >= '10/01/2000' and ExecuteDate <= '09/30/2010'

BP: bisphosphonates; ICD: International Classification of Diseases; ID: identifications; SQL: structured query language.

Creating a targeted patient list

A targeted patient list is created from the entire set of patients for whom EMRs have been obtained by defining logical queries (i.e., programs defined by the GUI) based on the computable criteria included in the ERS.

Logical queries are first defined in the ERS to identify patients who meet the conditions for each criterion. The ERS automatically generates the SQL necessary for data extraction according to the logical queries. Logical queries are then defined to include or exclude eligible patients who meet each criterion for the demographic entity. The targeted patient list is created by executing the logical query. Figure 2 presents an example of SQL automatically generated by the ERS.

We thus designed our data model to enable creating the targeted patient list by defining the patients extracted from each criterion (i.e., 'in' or 'not in') as conditions for the demographic entity that was the unique patient list for the entire hospital. If logical queries are defined using our method, even if the eligibility criteria are complicated, it is not necessary to dramatically change the SQL structure generated in the ERS.

Flagging entries for investigators to confirm

To improve research data accuracy, confirmation by the investigators was necessary. When confirmation is required, additional information is linked.

For the targeted patient list, logical queries are defined to flag certain items according to the investigators' interest. Necessary logical queries are first defined for each criterion. Logical queries are then defined for addition to the patient list as ‘1’ if the data correspond or ‘0’ if they do not. Data sets created by these operations are joined by ‘union’ and pivoted on a cross-tabulation list using statistical analysis software. We show an example of computable criteria that contain two criteria (i.e., ‘oral BP administration’ and ‘diagnosis of osteomyelitis of the jaw’) in Table 2 and SQL generated by the ERS in Figure 3. We also present the dataset image created by these operations in Figure 4.

Table 2. Example of computable criteria to be flagged for confirmation by investigators

Criterion	Entity	Operator symbol	Attribute	Operator symbol	Parameter	SQL
Oral BP administrations	Medications and Injections	-	DrugCode	in	（drug code list）	Select PatientId From MedicationsAndInjections Where DrugCode in （drug code list）and
		and	ExecuteDate	>=	'10/01/2000'	
		and	ExecuteDate	<=	'09/30/2010'	

						ExecuteDate >= '10/01/2000' and ExecuteDate <= '09/30/2010'
Diagnosis of inflammatory conditions of jaws	Diagnosis	-	ICD10Code	in	(ICD10 code list)	Select PatientId From Diagnosis Where ICD10Code in（ICD10 code list）and DiagnosisDate >= '10/01/2000' and DiagnosisDate <= '09/30/2010' and SuspectedFlag = 'Fixed'
		and	DiagnosisDate	>=	'10/01/2000'	
		and	DiagnosisDate	<=	'09/30/2010'	
		and	SuspectedFlag	=	Fixed	

BP: bisphosphonates; ICD: International Classification of Diseases; ID: identifications; SQL: structured query language.

Create reports for investigators to confirm

To help investigators confirm the targeted patient list, reports are created by linking the findings for diagnostic imaging, pathological diagnosis, operations, and others. Investigators confirm these entries using the reports and EMR information, including progress notes and images. When the diagnosis history, medication, laboratory results, progress notes, and other information are necessary, the same operation is executed for each instance. We present the dataset image generated by this operation in Figure 5. The reports may improve the investigators' confirmation efficiency, because it prevents referring to the medical records for each patient who needs confirmation.

Systemic evaluation

To evaluate our system, we collected information about the research period using the recall method. For the accuracy of the data collected by the ERS, we evaluated the results after investigator confirmation. We also asked the investigators to evaluate the system in a questionnaire.

RESULTS

Computable criteria, datasets, and system evaluation

We present the computable criteria in Table 3. To increase data accuracy, we collected all exclusion criteria for the investigators to confirm. As Table 3 shows, we extracted information from EMRs. For investigator confirmation, we also reported all targeted patients using the following lists: osteoporosis drugs administered, oral BP administered, intravenous BP administered, diabetes drugs administered, anticancer drugs administered, biopharmaceuticals in rheumatic diseases administered, disease-modifying antirheumatic drugs, steroid drugs administered, osteoporosis diagnoses, oral cancer diagnoses, patients diagnosed with inflammation of the jaw, patients diagnosed with other suspicious diseases, patients diagnosed with diabetes, patients diagnosed with rheumatoid arthritis, patients diagnosed with Sjogren's syndrome, HbA1c values, radiological findings, pathological findings, and radioisotope findings. These data were extracted from the ERS for statistical analyses, presented in CSV format, and analysed using statistics software.

Table 3. Computable criteria for our test research

Criterion	Entity	Operator symbol	Attribute	Operator symbol	Parameter
Create a targeted patient list					
Inclusion criteria: Osteoporosis diagnosis	Diagnosis	-	ICD10Code	in	(osteoporosis ICD10 code list)
		and	DiagnosisDate	>=	'10/01/2000'
		and	DiagnosisDate	<=	'09/30/2010'
		and	SuspectedFlag	=	Fixed
Inclusion criteria: Osteoporosis drug administrations	Medications and Injections	-	DrugCode	in	(osteoporosis drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Add a flag for investigators to confirm the targeted patient list					
Exclusion criteria: Oral cancer diagnosis	Diagnosis	-	ICD10Code	in	(oral cancer ICD10 code list)
		and	DiagnosisDate	>=	10/01/2000'
		and	DiagnosisDate	<=	09/30/2010'
		and	SuspectedFlag	=	Fixed
Exclusion criteria: Intravenous BP administrations	Medications and Injections	-	DrugCode	in	(intravenous BP drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Oral BP administrations	Medications and Injections	-	DrugCode	in	(oral BP drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Inflammatory jaw condition diagnosis	Diagnosis	-	ICD10Code	in	(inflammatory conditions of jaws ICD10 code list)
		and	DiagnosisDate	>=	'10/01/2000'
		and	DiagnosisDate	<=	'09/30/2010'
		and	SuspectedFlag	=	Fixed
Other suspicious disease diagnosis	Diagnosis	-	ICD10Code	in	(other suspicious disease ICD10 code list)
		and	DiagnosisDate	>=	'10/01/2000'
		and	DiagnosisDate	<=	'09/30/2010'
		and	SuspectedFlag	=	Fixed
Rheumatoid arthritis diagnosis	Diagnosis	-	ICD10Code	in	(rheumatoid arthritis ICD10 code list)
		and	DiagnosisDate	>=	'10/01/2000'
		and	DiagnosisDate	<=	'09/30/2010'

		and	SuspectedFlag	=	Fixed
Sjogren's syndrome diagnosis	Diagnosis	-	ICD10Code	in	(sjogren's syndrome ICD10 code list)
		and	DiagnosisDate	>=	'10/01/2000'
		and	DiagnosisDate	<=	'09/30/2010'
		and	SuspectedFlag	=	Fixed
Diabetes diagnosis	Diagnosis	-	ICD10Code	in	(diabetes ICD10 code list)
		and	DiagnosisDate	>=	'10/01/2000'
		and	DiagnosisDate	<=	'09/30/2010'
		and	SuspectedFlag	=	Fixed
Steroid drug administrations	Medications and Injections	-	DrugCode	in	(steroid drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Biopharmaceuticals in rheumatic diseases administrations	Medications and Injections	-	DrugCode	in	(biopharmaceuticals in rheumatic diseases code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Disease-modifying antirheumatic drug administrations	Medications and Injections	-	DrugCode	in	(disease modifying antirheumatic drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Anticancer drug administrations	Medications and Injections	-	DrugCode	in	(anticancer drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Diabetes drug administrations	Medications and Injections	-	DrugCode	in	(diabetes drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
HbA1c test execution	Laboratory Test	-	LaboratoryTestCode	in	(HbA1c test code)
		and	TestDate	>=	'10/01/2000'
		and	TestDate	<=	'09/30/2010'
Create reports for confirmation by the investigators					
Radiological finding reports	Diagnostic Studies	-	ReportName	in	(report name list of oral region)
Pathologic finding reports	Diagnostic Studies	-	SampleName	contains	'bone'
		or	SampleName	contains	'jaw'

Radio isotope finding reports	Diagnostic Studies	-	-	-	-

BP: bisphosphonates; ICD: International Classification of Diseases; ID: identifications

Among the approximately 800,000 cases at our hospital, 8,772 were categorised using the terms 'Inclusion criteria: Osteoporosis diagnosis'; among this group, 7,195 were further categorised using 'Inclusion criteria: Osteoporosis drug administration'. We then calculated the time that had elapsed since the osteoporosis diagnosis, determined that 7,062 patients were aged 20 years or older and created a targeted patient list. Among those on the targeted patient list, 23 were placed under the heading 'Exclusion criteria: Oral cancer diagnosis', 110 under 'Exclusion criteria: Intravenous BP administration', 4,200 under 'Oral BP administration', 84 under 'Inflammatory jaw condition diagnosis', 2,064 as 'Other suspicious disease diagnosis', 1,176 as 'Rheumatoid arthritis diagnosis', 394 as 'Sjogren's syndrome diagnosis', 1,700 as 'Diabetes diagnosis', 4,551 as 'Steroid drug administration', 186 as 'Biopharmaceuticals in rheumatic diseases administrations', 1,279 as 'Disease-modifying antirheumatic drug administrations', 904 as 'Anticancer drug administrations', 1,055 as 'Diabetes drug administrations', and 3,641 as 'HbA1c test execution'. Because of the end point considered, patients who were classified under 'Inflammatory jaw condition diagnosis' or 'Other suspicious disease diagnosis' were confirmed by investigators, who performed the statistical analyses and arranged the research results.

The accuracy of the data extracted by the ERS was characterised as follows. Reviewing the medical records revealed that 2,817 patients were not labelled as 'Oral BP administration', including seven (one who received intravenous BP) treated at other hospitals. Six patients had been treated with radiation therapy to the oral and maxillofacial regions. Among 72 classified under 'Inflammatory jaw condition diagnosis', 35 cases and 37 non-cases were identified.

We present the timeline required for the test research. The data extraction period lasted approximately three months. Ten meetings were held to create and validate the computable criteria and the list of codes for various drugs and diagnoses (i.e., International Statistical Classification of Diseases (ICD)-10 [56]). The time required for logical query definition when using the ERS was approximately 20 hours. The investigator confirmations and statistical analyses took approximately four months.

The investigators evaluating the system mentioned that 1) it enabled them to extract the necessary data for diagnosis and drug administration without exception; 2) by screening the entire patient population at the hospital using the ERS, they could identify not only eligible patients in the department of oral and maxillofacial surgery but also all eligible patients, which reduced the study bias; and 3) by creating reports for confirmation, it enabled investigators to devote their time to reading images, thus effectively reducing the time required for reviewing medical records.

DISCUSSION

We identified eligible patients for this research and extracted the data necessary for confirmation by investigators and statistical analyses. Using the ERS allowed the collection of information on patient eligibility by efficiently combining clinical information. Our proposed method also reduced the labour required from investigators, indicating that it was useful.

To design the ERS database, we modified the star schema and designed a new data model optimised for patient identification. To compare our data model with the star schema, we present an example of a clinical data model designed based on the star schema [34] in Figure 6. The main differences between our data model and the star schema were 1) demographic data, which were presented in list form in our EMR system, were presented as a fact-less fact table, and 2) date and time, measurements (i.e., facts) and text information were presented in dimension tables [43]. The most significant characteristic of our method for patient identification is using a specialised data model for patient identification in clinical research. Data can be converted efficiently without being conscious of the EMR database structure when converting narrative criteria to computable criteria. In this research, we considered whether data were extracted directly from EMRs at the protocol development stage. However, EMR data were recorded in a sequential format for every medical practice, and the database structure was complicated. Comprehending the location and meaning of the necessary data thus required tremendous effort. It was difficult to make precise logical queries for patient identification. However, because our ERS data model was arranged by subjects (e.g., tests, diagnosis, or medications), it was easy to interpret the available information. Due to the standardisation of computable criteria and SQL possible with the ERS, it was also possible to create computable criteria in little time. Additionally, verifying the patient identification accuracy was easy because it was possible to test each individual criterion.

The SQL generated by our ERS does not reduce the time required for data retrieval. Our ERS also cannot retrieve information that is not in the data model. It is thus necessary to create eligibility criteria assuming the use of our ERS from the protocol development stage. Current EMRs do not store all necessary data for clinical research, including information related to pregnancy, performance status, cancer stage, availability of transportation to the hospital, specific tests that are not typically performed, drug regimen, outcomes including death, and adverse events. Additionally, all tests are not administered to all patients, and necessary information may have been recorded in medical records at another hospital [12-13]. To facilitate EMR use in clinical research, it is necessary to accumulate as much of this information as possible. In the hospital, much information does not integrate well with EMRs, including test reports stored only in the departmental system and departmental research databases [57]. It is important to utilise this information. Additionally, enabling ERS use in multiple institutions is also an important future task.

Our conversion method depends on high-level medical decisions by investigators. Some medical concepts may be interpreted differently depending on the research and the investigator caring for the patients. It is necessary both to change the tacit knowledge of the investigators about converting computable criteria to explicit knowledge and to standardise this knowledge [58-63]. To reduce criteria conversion and investigator confirmation, it may be useful to apply NLP or decision support technology in combination with our system. Moreover, it is important to further discuss computable eligibility criteria standardisation. The attribute-level criteria that describe the search conditions in detail may be useful in global studies that address diseases that vary according to the diagnostic criteria used in each country.

Concerning EMR data accuracy, the ICD10 code (osteomyelitis of the jaw) sensitivity was 48.6% (35/72). The investigators reported six simple diagnosis errors, seven oral BP administrations at other hospitals, and six patients who were treated with radiation therapy in the oral and maxillofacial region. For the accuracy of current EMRs, the investigators had to confirm the information. However, the EMRs provided rich confirmation data and were useful in improving research data accuracy. In this study, we checked the data from actual EMRs manually and identified patients precisely and extensively using coded information, narrative information, and images. However, only information from existing EMRs was available. Current EMRs have a high degree of flexibility in data entry and are not currently managed for research purposes, which decreases their reliability [12-13]. It is necessary to improve data quality through quality control without placing too much of a burden on clinical practice. Alternatively, it may be possible to organise data sufficiently before research use [64-66]. Standardising terminology and exchange formats characteristic of healthcare has facilitated international discourse [56, 67-73]. It is necessary to further discuss not only clinical practice but also research purposes, particularly how to utilise such various standards when using EMRs beyond the hospital setting.

CONCLUSION

We proposed a pragmatic method for EMR-based observational studies. Our ERS is already used to support hospital-based cohort studies, clinical trial recruitment, and the eClinical trial infrastructure [45] at our centre. We believe an efficient ERS is essential to facilitate clinical research that utilises EMRs.

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Competing interests

None.

Contributors

KY designed the study, developed the ERS system, identified the computable eligibility criteria, wrote logical queries, collected data, and wrote the manuscript. ES is grant holder, designed the study, developed the ERS system, and wrote and edited the manuscript. TY designed and conducted the 'Risk of osteomyelitis of the jaw induced by oral bisphosphonates in patients taking medications for osteoporosis: a hospital-based cohort study in Japan' (BRONJ study) study and this study, identified the computable eligibility criteria, and wrote and edited the manuscript. KA and MY designed and conducted the BRONJ study. ST is designed the study and provided comments and feedback on the study. KB is the principal investigator of the BRONJ study. MY is the owner of the ERS system and supervised the study. MF supervised the study and provided comments and feedback on the study. All of the authors read and approved the final manuscript.

Provenance and peer review

Not commissioned; externally peer reviewed.

Data sharing statement

No other data are available to share.

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FIGURE CAPTIONS

Figure 1. Data model for our EMR retrieval system.

Figure 2. Example SQL to create the target patient list.

Figure 3. Example SQL to flag the target patient report for investigator confirmation.

Figure 4. Sample data were flagged on the target patient report for investigator confirmation. The left table is extracted from logical queries, which were defined to add patients as '1' on the list if a correspondence was observed or as '0' if no correspondence was observed. The table was pivoted on a cross-tabulation list using statistical software.

Figure 5. Dataset image set aside for investigator confirmation. This is a sample of the list of radiological findings.

Figure 6. Example of a star schema for clinical information.

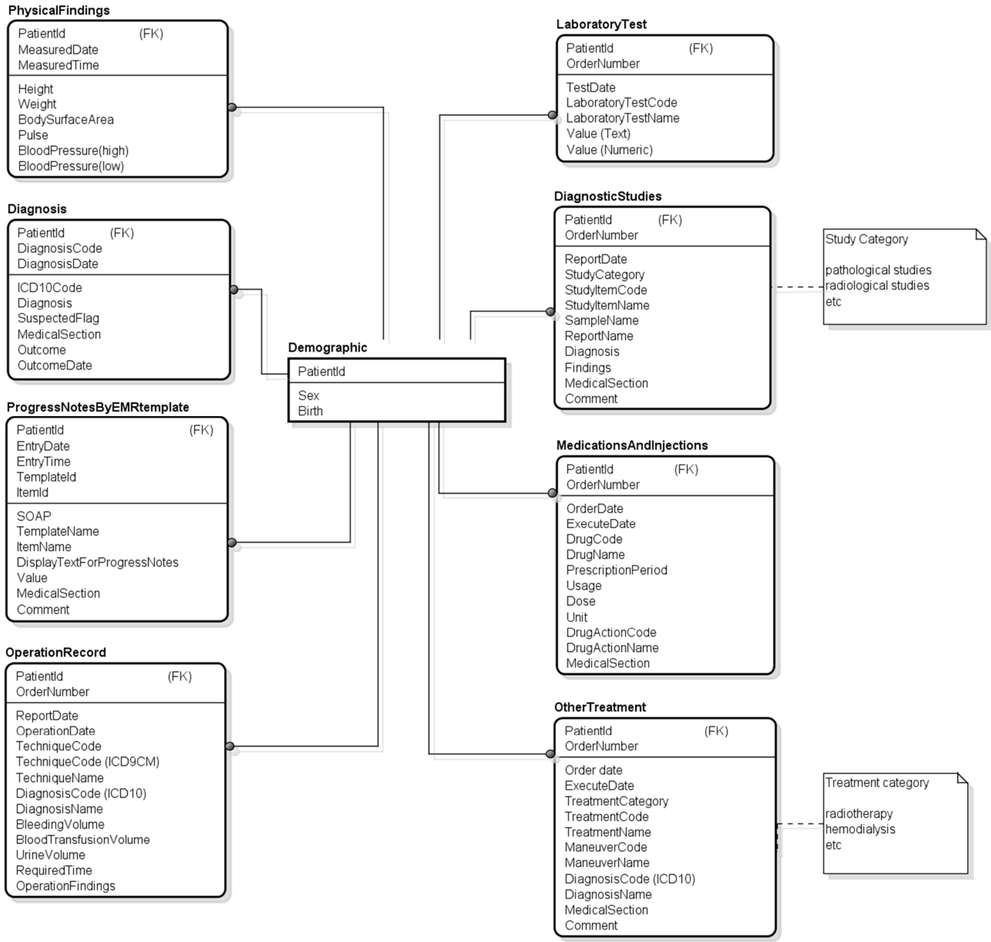


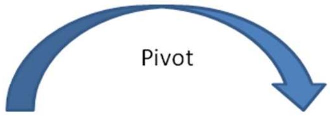
Figure 1. Data model for our EMR retrieval system.
109x104mm (300 x 300 DPI)

```
Create View_PatientsList as
Select PatientId From Demographic a
Where
a. PatientId in (
  Select PatientId From Diagnosis
  Where ICD10Code in (osteoporosis ICD10 code list) and
    DiagnosisDate >= '10/01/2000' and DiagnosisDate <= '09/30/2010' and
    SuspectedFlag = 'Fixed' )
and
a. PatientId in (
  Select PatientId From MedicationsAndInjections
  Where DrugCode in (osteoporosis drugs code list) and
    ExecuteDate >= '10/01/2000' and ExecuteDate <= '09/30/2010' )
and
a. PatientId not in (
  Select PatientId From MedicationsAndInjections
  Where DrugCode in (intravenous BP drug code list) and
    ExecuteDate >= '10/01/2000' and ExecuteDate <= '09/30/2010' )
```

Figure 2. Example SQL to create the target patient list.
81x60mm (300 x 300 DPI)

```
Select PatientId, 'Oral BP administrations', 1 From View_PatientsList a
Where a. PatientId in (
    Select PatientId From MedicationsAndInjections
    Where DrugCode in (oral BP drugs code list) and
      ExecuteDate >= '10/01/2000' and ExecuteDate <= '09/30/2010 ' )
Union all
Select PatientId, 'Oral BP administrations', 0 From View_PatientsList a
Where   a. PatientId not in (
    Select PatientId From MedicationsAndInjections
    Where DrugCode in (oral BP drugs code list) and
        ExecuteDate >= '10/01/2000' and ExecuteDate <= '09/30/2010')
Union all
Select PatientId, 'Inflammatory jaw condition diagnosis', 1 From View_PatientsList a
Where   a. PatientId in (
    Select PatientId From Diagnosis
    Where ICD10Code in (inflammatory conditions of jaws ICD10 code list) and
        DiagnosisDate >= '10/01/2000' and DiagnosisDate <= '09/30/2010' and  SuspectedFlag = 'Fixed')
Union all
Select PatientId, 'Inflammatory jaw condition diagnosis', 0 From View_PatientsList a
Where   a. PatientId not in (
    Select PatientId From Diagnosis
    Where ICD10Code in (inflammatory conditions of jaws ICD10 code list ) and
        DiagnosisDate >= '10/01/2000' and DiagnosisDate <= '09/30/2010' and  SuspectedFlag = 'Fixed')
```

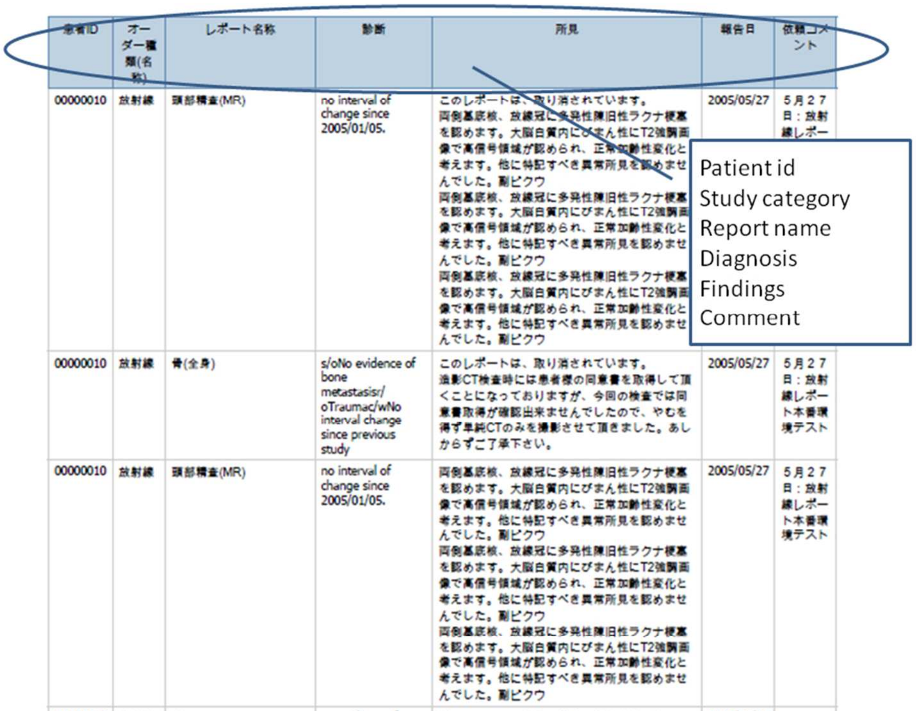
Figure 3. Example SQL to flag the target patient report for investigator confirmation.
81x60mm (300 x 300 DPI)



Patient Id	Criteria	Value
1	Oral BP administrations	0
1	Inflammatory jaw condition diagnosis	0
2	Oral BP administrations	1
2	Inflammatory jaw condition diagnosis	1
3	Oral BP administrations	0
3	Inflammatory jaw condition diagnosis	0
4	Oral BP administrations	1
4	Inflammatory jaw condition diagnosis	0
5	Oral BP administrations	0
5	Inflammatory jaw condition diagnosis	1
6	Oral BP administrations	0
6	Inflammatory jaw condition diagnosis	1
7	Oral BP administrations	0
7	Inflammatory jaw condition diagnosis	0
8	Oral BP administrations	1
8	Inflammatory jaw condition diagnosis	1

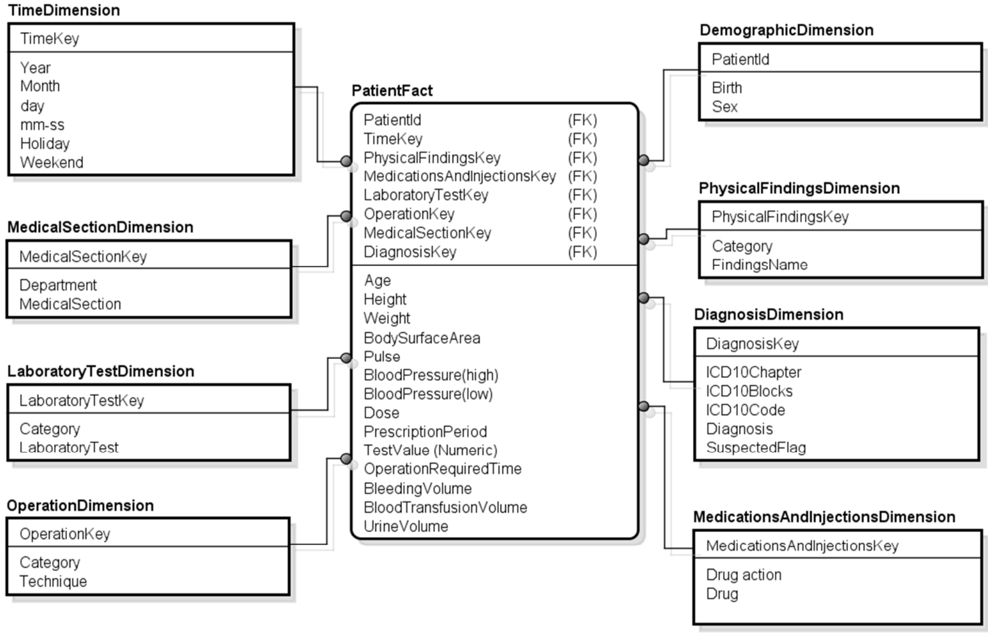
Patient Id	Oral BP administrations	Inflammatory jaw condition diagnosis
1	0	0
2	1	1
3	0	0
4	1	0
5	0	1
6	0	1
7	0	0
8	1	1

Figure 4. Sample data were flagged on the target patient report for investigator confirmation. The left table is extracted from logical queries, which were defined to add patients as '1' on the list if a correspondence was observed or as '0' if no correspondence was observed. The table was pivoted on a cross-tabulation list using statistical software.
79x41mm (300 x 300 DPI)



患者ID	オーダー種類(名称)	レポート名称	診断	所見	報告日	依頼コメント
00000010	放射線	頭部精査(MR)	no interval of change since 2005/01/05.	このレポートは、取り消されています。 両側基底核、放線冠に多発性陳旧性ラクナ梗塞を認めます。大脳白質内にびまん性にT2強調画像で高信号領域が認められ、正常加齢性変化と考えます。他に特記すべき異常所見を認めませんでした。副ピクウ 両側基底核、放線冠に多発性陳旧性ラクナ梗塞を認めます。大脳白質内にびまん性にT2強調画像で高信号領域が認められ、正常加齢性変化と考えます。他に特記すべき異常所見を認めませんでした。副ピクウ 両側基底核、放線冠に多発性陳旧性ラクナ梗塞を認めます。大脳白質内にびまん性にT2強調画像で高信号領域が認められ、正常加齢性変化と考えます。他に特記すべき異常所見を認めませんでした。副ピクウ	2005/05/27	５月２７日：放射線レポー
00000010	放射線	骨(全身)	s/oNo evidence of bone metastasisr/oTraumac/wNo interval change since previous study	このレポートは、取り消されています。 造影CT検査時には患者様の同意書を取得して頂くことになっておりますが、今回の検査では同意書取得が確認出来ませんでしたので、やむを得ず単純CTのみを撮影させて頂きました。あしからずご了承下さい。	2005/05/27	５月２７日：放射線レポート本番環境テスト
00000010	放射線	頭部精査(MR)	no interval of change since 2005/01/05.	両側基底核、放線冠に多発性陳旧性ラクナ梗塞を認めます。大脳白質内にびまん性にT2強調画像で高信号領域が認められ、正常加齢性変化と考えます。他に特記すべき異常所見を認めませんでした。副ピクウ 両側基底核、放線冠に多発性陳旧性ラクナ梗塞を認めます。大脳白質内にびまん性にT2強調画像で高信号領域が認められ、正常加齢性変化と考えます。他に特記すべき異常所見を認めませんでした。副ピクウ 両側基底核、放線冠に多発性陳旧性ラクナ梗塞を認めます。大脳白質内にびまん性にT2強調画像で高信号領域が認められ、正常加齢性変化と考えます。他に特記すべき異常所見を認めませんでした。副ピクウ	2005/05/27	５月２７日：放射線レポート本番環境テスト

Figure 5. Dataset image set aside for investigator confirmation. This is a sample of the list of radiological findings.
81x60mm (300 x 300 DPI)



Example of a star schema for clinical information.
90x58mm (300 x 300 DPI)

A pragmatic method for electronic medical-record-based observational studies: developing an electronic medical records retrieval system for clinical research

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A pragmatic method for electronic medical-record-based observational studies: developing an electronic medical records retrieval system for clinical research

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ABSTRACT

Objective: The use of electronic medical record (EMR) data is necessary to improve clinical research efficiency. However, it is not easy to identify patients who meet research eligibility criteria and collect the necessary information from EMRs because the data collection process must integrate various techniques, including the development of a data warehouse and translation of eligibility criteria into computable criteria. This research aimed to demonstrate an electronic medical records retrieval system (ERS) and an example of a hospital-based cohort study that identified both patients and exposure with an ERS. We also evaluated the feasibility and usefulness of the method. **Design**: The system was developed and evaluated. **Participants:** In total, 800,000 cases of clinical information stored in EMRs at our hospital were used. **Primary and secondary outcome measures:** The feasibility and usefulness of the ERS, the method to convert text from eligible criteria to computable criteria, and a confirmation method to increase research data accuracy. **Results:** To comprehensively and efficiently collect information from patients participating in clinical research, we developed an ERS. To create the ERS database, we designed a multi-dimensional data model optimised for patient identification. We also devised practical methods to translate narrative eligibility criteria into computable parameters. We applied the system to an actual hospital-based cohort study performed at our hospital and converted the test results into computable criteria. Based on this information, we identified eligible patients and extracted data necessary for confirmation by our investigators and for statistical analyses with our ERS. **Conclusion:** We propose a pragmatic methodology to identify patients from EMRs who meet clinical research eligibility criteria. Our ERS allowed for the efficient collection of information on the eligibility of a given patient, reduced the labour required from the investigators, and improved the reliability of the results.

ARTICLE SUMMARY

Article focus

The focus of this work was to establish a pragmatic methodology to efficiently collect information from EMRs about patients who meet clinical research eligibility criteria.

Key messages

The use of electronic medical record (EMR) data is necessary to improve clinical research efficiency. However, it is not easy to identify patients who meet research eligibility criteria and collect necessary data from EMRs because the data collection process must integrate various techniques, including the development of a data warehouse and the translation of eligibility criteria into computable criteria. An efficient ERS and a standardised data processing model that integrates these techniques are essential to facilitate clinical research that utilises EMRs.

Strengths and limitations of this study

- Our method uses a specialised data model for patient identification in clinical research and efficient data conversion that does not depend on the EMR database structure when converting narrative criteria to computable criteria.

- We propose that computable criteria should not be a result of the automated conversion of narrative criteria but rather a result of research preparation involving medical concepts that are not expressed logically or explicitly in the narrative criteria. Therefore a large amount of the conversion of the eligibility criteria to computable criteria should be executed at the protocol development stage.

- It is important to further discuss protocol standardisation, including eligibility criteria representation for computable use.

- Enabling ERS use in and across multiple institutions is an important future task.

BACKGROUND

Medical information technology has recently advanced in many countries, and enormous amounts of clinical data are already stored as electronic medical records (EMRs). Utilising the data collected in EMRs is necessary to improve clinical research efficiency [1-3]. An EMR is a large database of patient data and is used in observational research to investigate the relationships among diseases, treatments, and outcomes [4-7], to conduct surveillance for rare drug reactions [4, 8], and to recruit patients for clinical trials [9-13]. However, it is not easy to identify patients who meet research eligibility criteria and collect necessary information from EMRs [2-3]. Herein, we describe three major issues concerning EMR-based observational studies: EMR patient data retrieval function, eligibility criteria protocol representation, and EMR data accuracy.

To identify patients who meet research eligibility criteria, it is necessary to obtain various types of information stored in EMRs by subject, e.g., diagnosis and prescribed medications. However, the EMR database is designed to facilitate online transaction processing for rapid and detail-oriented clinical information searches on individual patients, and the current EMR system does not facilitate this retrieval function [2-3, 14]. Data warehouses are essential components of data-driven decision support. To allow for efficient research analyses, EMR data must first be warehoused to enable data analyses across patient populations [15-21]. However, health care data modelling is difficult and time-consuming because of the complexity of the medical knowledge involved. Thus, the most common approaches to clinical data warehouse modelling are variations on the entity-attribute-value (EAV) model [22-28], where data are stored in a single table with three columns: entity identification, attribute, and attribute value. The EAV design has advantages, including flexibility and ease of storage; however, it requires transforming EAV data into another analytical format before analysis [25, 28]. Online analytical processing (OLAP) is most frequently used for searching data stored in the data warehouse [29-31]. OLAP systems in relational databases are typically designed based on Kimball's star schema [32]. However, the star schema was devised to facilitate online measurement analyses. In health care, this method can be used to dynamically gather online analyses of numeric data (e.g., a specific dose of a drug for a specific disease) in clinical practice. Therefore, this method is not suitable for identifying patients who meet the complicated eligibility criteria for a given clinical research study. Data-modelling methods that facilitate the identification of patients and enable the collection of necessary information from EMRs remain to be established [28].

Current eligibility criteria are written in a text format that cannot be computationally processed. Additionally, to be applied in actual EMR, eligible criteria need to be integrated with the data model of EMRs [33]. Several investigations have sought to establish computable eligibility criteria [34-41]. However, there is no consensus regarding a standard patient information model [33], and the eligibility criteria are not yet completely standardised.

Using natural language processing (NLP) technologies to convert the text format of eligibility criteria to a computer or to extract patient identifications from EMRs is far from perfect without human intervention [3, 42-43].

Current EMRs have been used to support claims for medical service fees and the treatments administered to each patient; therefore, data gathered specifically for research purposes may be incomplete and unreliable [2-3, 44].

Although various investigations on each technique are executed individually, standardised methods must still be established that integrate these techniques, facilitate the identification of patients who are eligible for clinical research, and collect necessary information from EMRs.

OBJECTIVE

We designed a pragmatic data processing model optimised for patient identification and for the collection of necessary information from EMRs for clinical research. These tools are implemented as an electronic medical records retrieval system (ERS) [44].

This research aimed to demonstrate an ERS and an example of a hospital-based cohort study that used the ERS to identify both patients and exposure. Another aim was to evaluate the feasibility and usefulness of the ERS, the method to convert text form eligible criteria to computable criteria, and a confirmation method to increase research data accuracy.

MATERIALS AND METHODS

Outline of our procedure for patient identification and data collection from the EMR

To identify patients who met the eligibility criteria for the clinical research in question, data were collected in the following ways:

1) The text form of the narrative criteria was converted into computable criteria.

2) A targeted patient list was created.

3) A flag was added for investigators to confirm the targeted patient list.

4) Reports were created for the investigators to confirm.

5) After confirmation by the investigator, the statistical analyses were executed.

EMR retrieval system

In our hospital, EMR use was introduced in 2005; approximately 800,000 cases of clinical information have already been stored. To comprehensively and efficiently collect information about patients participating in clinical research, we developed an ERS [44].

EMRs store various types of information, integrating billing, pharmacy, radiology, laboratory information, and others [4]. In creating the ERS database, we designed a new data model based on the star schema that was optimised for patient identification in clinical research. We identified nine data categories from EMRs that are useful for clinical research: demographic characteristics, physical findings, diagnostic studies, laboratory tests, diagnoses, progress reports on an EMR template [44-45], medications and injections, operation records, and other treatments. We then designated these categories to 'entities'. In our hospital, the diagnosis is managed by codes that were originally defined by our hospital and mapped with International Statistical Classification of Diseases (ICD) 10 codes [46] for medical insurance purposes. Operations codes were also managed by codes that originally were defined by our hospital and mapped with ICD-9 Clinical Modification codes. We identified available columns (e.g., ICD code, diagnosis date) from the EMR data model and designated these columns as 'attributes' of the entities.

Figure 1 presents our data model. In our model, all entities in a given schema are independent and complete; this allows for logical operations and for the creation of eligible patient lists for each respective parameter in a study. The target patient list is generated by combining these patient lists. The data model also supports the inference of medical concepts expressed in the eligibility criteria in reference to corresponding patient data accumulated in EMRs [33-34].

In our hospital, a replicate of the EMR database known as 'Open DB' was established for the secondary use of accumulated EMR data [7]. A data mart for our ERS was created to ensure that the data retrieval process was practical and independent of the EMR system structure; the data mart was created on the relational database management system by extracting, transforming, and loading (ETL) information from the Open DB [7, 44]. The ETL process is performed automatically once nightly except for the ‘Progress notes by EMR template’ entity, which is referred directly from the Open DB to ensure real-time visibility for the eClinical trial [44].

An OLAP tool was installed to efficiently search through data from multiple patients [44]. The OLAP tool runs in an Internet browser and can generate structured query language (SQL) based on predefined metadata (i.e., a data model) by defining logical queries (i.e., programs) using a graphical user interface (GUI). Moreover, this tool allows reports on information retrieved from the browser to be transcribed using hypertext markup language (HTML). The reports are created in various formats, including portable document format (PDF), comma separated values (CSV), and extensible markup language (XML) [44].

To protect personal information in medical records at our hospital, the EMR network is separated physically from other networks. Our data mart and OLAP servers are deployed in the same EMR network and managed using the same EMR security policies. Additionally, the use of our ERS is limited to clinical research approved by the ethics committee at our hospital, and only designated staff members at our centre are allowed to retrieve data. Our centre creates and manages ERS user identification separate from the EMRs. For the external output of CSV and other data, permission must be obtained from our department of medical informatics, and data extraction must be executed in the presence of supervisors who are responsible for protecting personal information at our hospital.

Application to clinical research

We applied the system to a hospital-based cohort study performed at our hospital titled 'Risk of osteomyelitis of the jaw induced by oral bisphosphonates (BP) in patients taking medications for osteoporosis: A hospital-based cohort study in Japan' [47], in which we identified eligible patients, extracted research data, and evaluated the feasibility of our system. The ethics committee at Kyoto University Hospital approved this research. A different paper details the purpose, methods, results, and discussion of this research [47].

This research aimed to estimate the risks for osteomyelitis of the jaw in osteoporosis patients at our hospital who had been exposed to oral BP compared to those who had not [48-49].

The eligibility criteria were as follows:

Inclusion criteria

- Patients diagnosed with osteoporosis and treated with osteoporosis medications at Kyoto University Hospital between November 2000 and October 2010.
- Patients aged 20 years or older.

Exclusion criteria

- Patients with a history of treatment with radiation therapy to the maxillofacial region.
- Patients with primary or metastatic tumours in the maxillofacial region.
- Patients treated with intravenous BP.

The data collected were diagnosis, date of diagnosis, sex, birthdate, and the doses and dates when osteoporosis medications, steroids, anticancer drugs, diabetes drugs and HbA1c tests were administered.

Conversion of the text form of the narrative criteria to computable criteria

To identify eligible patients and collect the necessary data from the EMRs, narrative criteria and data must be converted to computable criteria. Such computable criteria include entities, attributes, logical operators (i.e., 'and' and 'or'), codes, and parameters [33-37]. The clinical research purpose and clinical practice demands made it necessary to perform this task.

We manually executed the conversion from text eligibility criteria to computable criteria. As an example of the conversion from narrative criteria to computable criteria, we present the following two-step conversion procedure:

Step 1: Convert the narrative criteria into entity-level criteria.

Medical concepts expressed as narrative criteria are mapped onto entities in the data model and converted into entity-level criteria. This task is manually performed at the protocol development stage of the study by the investigators. For each entity, a criterion is created to extract patients who meet each condition. If exclusive conditions for the same entity must be defined, a different criterion is created. Additionally, the list of codes for drugs and diagnoses (i.e., ICD-10) is created, and the period of treatments and others are defined by investigators. In this study, we mapped 'osteoporotic patients' onto two entities (i.e., 'diagnosis' and 'medications and injections') and converted it to a combination of two criteria (i.e., 'diagnosis of osteoporosis' and 'osteoporosis drug administration'). In the test research, we defined the entity-level criteria according to the entered diagnosis and ordered treatments rather than the diagnostic criteria of the disease. This process reflects that the test research aimed to estimate some risks of osteomyelitis of the jaw with BP administration instead of diagnosing osteoporosis patients accurately. The recorded diagnosis in the EMR was typically designed to ensure payment for medical claims. We thus sought to reduce the number of false positives by extracting patients with a given treatment type.

Step 2: Convert entity-level criteria into attribute-level criteria (i.e., computable criteria).

The abovementioned corresponding codes, date and parameters are mapped onto attributes of the entity-level criteria, and these factors become computable criteria.

Creating a targeted patient list

A targeted patient list is created from the entire set of patients for whom EMRs have been obtained by defining logical queries (i.e., programs defined by the GUI) based on the computable criteria included in the ERS.

Logical queries are first defined in the ERS to identify patients who meet the conditions for each criterion. The ERS automatically generates the SQL necessary for data extraction according to the logical queries. Logical queries are then defined to include or exclude eligible patients who meet each criterion for the demographic entity. The targeted patient list is created by executing the logical query. Figure 2 presents an example of an SQL automatically generated by the ERS.

We thus designed our data model to enable the creation of a targeted patient list by defining the patients extracted from each criterion (i.e., 'in' or 'not in') as conditions for the demographic entity that was the unique patient list for the entire hospital. If logical queries are defined using our method, even if the eligibility criteria are complicated, it is not necessary to dramatically change the SQL structure generated in the ERS.

Flagging entries for investigators to confirm

To improve research data accuracy, confirmation by the investigators is necessary. When confirmation is required, additional information is linked.

For the targeted patient list, logical queries are defined to flag certain items according to the investigators' interest. Necessary logical queries are first defined for each criterion. Logical queries are then defined for addition to the patient list as ‘1’ if the data correspond or ‘0’ if they do not. Data sets created by these operations are joined by ‘union’ and pivoted on a cross-tabulation list using statistical analysis software. We show an example of an SQL generated by the ERS in Figure 3.

Create reports for investigators to confirm

To help investigators confirm the targeted patient list, reports are created by linking the findings for diagnostic imaging, pathological diagnosis, operations, and other findings. Investigators confirm these entries using the reports and EMR information, including progress notes and images. When the diagnosis history, medication, laboratory results, progress notes, and other information are necessary, the same operation is executed for each instance. For example, the list of radiological findings involves ‘patient id’, ‘study category’, ‘report name’, ‘diagnosis’, ‘findings’, and ‘comment’. The reports may improve the investigators' confirmation efficiency because they prevent the need to refer to the medical records for each patient who needs confirmation.

Confirmation by the investigator and execution of the statistical analyses.

The investigators confirm the accumulated data and execute the statistical analysis. In this test research, two oral and maxillofacial surgeons diagnosed cases by a chart review with an observation of imaging findings [47].

Systemic evaluation

To evaluate our system, we collected information about the research period using the recall method. For the accuracy of the data collected by the ERS, we evaluated the results after they were confirmed by the investigator.

RESULTS

Computable criteria, datasets, and system evaluation

We present the computable criteria in Table 1. To increase data accuracy, we collected all of the exclusion criteria for the investigators to confirm. As Table 1 shows, we extracted information from EMRs. For investigator confirmation, we also reported all targeted patients using the following lists: osteoporosis drugs administered, oral BP administered, intravenous BP administered, diabetes drugs administered, anticancer drugs administered, steroid drugs administered, osteoporosis diagnoses, oral cancer diagnoses, patients diagnosed with inflammation of the jaw, patients diagnosed with other suspicious diseases, patients diagnosed with diabetes, HbA1c values, radiological findings, pathological findings, and radioisotope findings. These data were extracted from the ERS for statistical analyses, presented in CSV format, and analysed using statistics software.

Table 1. Computable criteria for our test research

Criterion	Entity	Operator symbol	Attribute	Operator symbol	Parameter
Created a targeted patient list					
Inclusion criteria: Osteoporosis diagnosis	Diagnosis	-	ICD10Code	In	(osteoporosis ICD10 code list)
		and	DiagnosisDate	>=	'10/01/2000'
		and	DiagnosisDate	<=	'09/30/2010'
		and	SuspectedFlag	=	Fixed
Inclusion criteria: Osteoporosis drug administrations	Medications and Injections	-	DrugCode	in	(osteoporosis drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Added a flag for investigators to confirm the targeted patient list					
Exclusion criteria: Oral cancer diagnosis	Diagnosis	-	ICD10Code	in	(oral cancer ICD10 code list)
		and	DiagnosisDate	>=	10/01/2000'
		and	DiagnosisDate	<=	09/30/2010'
		and	SuspectedFlag	=	Fixed
Exclusion criteria: Intravenous BP administrations	Medications and Injections	-	DrugCode	in	(intravenous BP drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Oral BP administrations	Medications and Injections	-	DrugCode	in	(oral BP drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Inflammatory jaw condition diagnosis	Diagnosis	-	ICD10Code	in	(inflammatory conditions of jaws ICD10 code list)
		and	DiagnosisDate	>=	'10/01/2000'
		and	DiagnosisDate	<=	'09/30/2010'
		and	SuspectedFlag	=	Fixed
Other suspicious disease diagnosis	Diagnosis	-	ICD10Code	in	(other suspicious disease ICD10 code list)
		and	DiagnosisDate	>=	'10/01/2000'
		and	DiagnosisDate	<=	'09/30/2010'
		and	SuspectedFlag	=	Fixed
Diabetes diagnosis	Diagnosis	-	ICD10Code	in	(diabetes ICD10 code list)
		and	DiagnosisDate	>=	'10/01/2000'
		and	DiagnosisDate	<=	'09/30/2010'
		and	SuspectedFlag	=	Fixed

Steroid drug administrations	Medications and Injections	-	DrugCode	in	(steroid drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Anticancer drug administrations	Medications and Injections	-	DrugCode	in	(anticancer drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Diabetes drug administrations	Medications and Injections	-	DrugCode	in	(diabetes drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
HbA1c test execution	Laboratory Test	-	LaboratoryTestCode	in	(HbA1c test code)
		and	TestDate	>=	'10/01/2000'
		and	TestDate	<=	'09/30/2010'
Created reports for confirmation by the investigators					
Radiological finding reports	Diagnostic Studies	-	ReportName	in	(report name list of oral region)
Pathologic finding reports	Diagnostic Studies	-	SampleName	contains	'bone'
		or	SampleName	contains	'jaw'
Radio isotope finding reports	Diagnostic Studies	-	-	-	-

BP, bisphosphonates; ICD, International Classification of Diseases; ID, identifications

Among the approximately 800,000 cases at our hospital, 8,772 were categorised using the terms ‘Inclusion criteria: Osteoporosis diagnosis’; among this group, 7,195 were further categorised using ‘Inclusion criteria: Osteoporosis drug administration’. We then calculated the time that had elapsed since the osteoporosis diagnosis, determined that 7,062 patients were aged 20 years or older, and created a targeted patient list. Among those on the targeted patient list, 23 patients were placed under the heading ‘Exclusion criteria: Oral cancer diagnosis’, 110 under ‘Exclusion criteria: Intravenous BP administration’, 4,200 under ‘Oral

BP administration', 84 under 'Inflammatory jaw condition diagnosis', 2,064 as 'Other suspicious disease diagnosis', 1,700 as 'Diabetes diagnosis', 4,551 as 'Steroid drug administration', 904 as 'Anticancer drug administrations', 1,055 as 'Diabetes drug administrations', and 3,641 as 'HbA1c test execution'. Because of the end point considered, patients who were classified under 'Inflammatory jaw condition diagnosis' or 'Other suspicious disease diagnosis' were confirmed using predefined hierarchical diagnostic criteria by investigators who performed the statistical analyses and arranged the research results. We show the schema of data collection and confirmation as Figure 4 [47].

The accuracy of the data extracted by the ERS was then characterised. Reviewing the medical records revealed that 2,817 patients were not labelled as 'Oral BP administration', including 7 (1 who received intravenous BP) treated at other hospitals. 6 patients had been treated with radiation therapy to the oral and maxillofacial regions. Among the 72 patients classified under 'Inflammatory jaw condition diagnosis', 35 cases and 37 non-cases were identified.

The data extraction period lasted approximately three months. Ten meetings were held during the protocol development stage to create and validate the computable criteria and the list of codes for various drugs and diagnoses (i.e., ICD-10). The time required for logical query definition when using the ERS was approximately 20 hours. The investigator confirmations and statistical analyses took approximately four months.

DISCUSSION

We identified eligible patients for this research and extracted the data necessary for confirmation by investigators and for statistical analyses.

We asked the chart reviewers to evaluate the system in a questionnaire about 'the effect of computer programming support for data retrieval from the EMR', 'the result of the data retrieval', 'the positive and negative aspects of our ERS use', and 'the aspects of our method that should be improved'. The investigators evaluating the system mentioned that the following points: 1) the method enabled them to extract the necessary data for diagnosis and drug administration without exception; 2) by screening the entire patient population at the hospital using the ERS, they could identify not just eligible patients in the department of oral and maxillofacial surgery but all eligible patients, which reduced the study bias; and 3) by creating reports for confirmation, it enabled investigators to devote their time to reading images, thus effectively reducing the time required for reviewing medical records. The aspects of our method that should be improved are the 'lack of claim data' and the 'administrative complexity of EMR data use'. No negative aspects of our ERS use were noted.

The ERS allowed for the collection of information on patient eligibility by efficiently combining clinical information. Although we did not compare our method with other methods, our proposed method reduced the labour normally required from investigators and improved the reliability of test research results, which indicated that it was useful.

To design the ERS database, we designed a new data model optimised for patient identification. The main differences between our data model and the star schema were as follows: 1) demographic data, which were presented in list form in our EMR system, were presented as a fact-less fact table, and 2) date, time, measurements and text information were presented in dimension tables [32]. The most significant characteristic of our method for patient identification is the use of a specialised data model in clinical research and the ability to execute a large number of conversion tasks at the protocol development stage. Data can be converted efficiently in a way that does not depend on the EMR database structure when converting narrative criteria to computable criteria. In this research, we considered whether data were extracted directly from EMRs at the protocol development stage. However, EMR data were recorded in a sequential format for every medical practice, and the database structure was complicated. Comprehending the location and meaning of the necessary data thus required tremendous effort. It was difficult to make precise logical queries for patient identification. However, because our ERS data model was arranged by subjects (e.g., tests, diagnosis), it was easy to interpret the available information. Due to the standardisation of computable criteria and SQL possible with the ERS, it was also possible to create computable criteria in little time. Additionally, verifying the patient identification accuracy was easy because it was possible to test each individual criterion.

The SQL generated by our ERS does not reduce the time required for data retrieval. Our ERS also cannot retrieve information that is not in the data model. Current EMRs do not store all necessary data for clinical research, including information related to pregnancy, performance status, cancer stage, availability of transportation to the hospital, specific tests that are not typically performed, drug regimen, outcomes (including death), and adverse events. Additionally, all tests are not administered to all patients, and necessary information may have been recorded in medical records at another hospital [44]. To facilitate EMR use in clinical research, it is necessary to accumulate as much of this information as possible. In the hospital, much of this information does not integrate well with EMRs, including test reports stored only in the departmental system [50]. However, it is important to utilise this information. Additionally, enabling ERS use in and across multiple institutions is also an important future task.

Currently, most clinical research studies that use data from EMRs are planned according to the concept that the primary use of EMRs is for clinical practice and a secondary use is for clinical research [44]. Therefore, most investigators attempt to convert the text form eligibility criteria that already have been defined on a protocol to computable criteria at the data collecting stage [35. 36]. However, we propose that computable criteria should not be a result of the automated conversion of narrative criteria but rather a result of research preparation involving medical concepts that are not expressed logically or explicitly in the narrative criteria. Some medical concepts may be interpreted differently depending on the research and the investigator caring for the patients. Additionally, current eligibility criteria are vague or complex, and they do not consider the use of the actual EMR. To convert computable criteria appropriately, high-level medical decisions to answer the research question are required. Therefore, we thought that a large amount of the conversion of the eligibility criteria to computable criteria should be executed at the protocol development stage. In addition, the conversion process should be divided into entity-level conversions that require higher medical decisions and attribute-level conversions. To reduce the burden of conversion, it may be useful to apply NLP technology for the conversion from entity-level criteria to attribute-level criteria. Moreover, it is important to further discuss protocol standardisation, including eligibility criteria representation for computable use. For instance, the attribute-level criteria that describe the search conditions in detail may be useful in global studies to address diseases that vary according to the diagnostic criteria used in each country.

Concerning EMR data accuracy, the ICD10 code (osteomyelitis of the jaw) sensitivity was 48.6% (35/72). The investigators reported 6 simple diagnosis errors, 7 oral BP administrations at other hospitals, and 6 patients who were treated with radiation therapy in the oral and maxillofacial region [47]. For the accuracy of current EMRs, the investigators had to confirm the information. However, the EMRs provided rich confirmation data and were useful in improving research data accuracy. In this study, we checked the data from actual EMRs manually and identified patients precisely and extensively using coded information, narrative information, and images. However, only information from existing EMRs was available. Current EMRs have a high degree of flexibility in data entry and are not currently managed for research purposes, which decreases their reliability. It is necessary to improve data quality through quality control without placing too much of a burden on clinical practice. Alternatively, it may be possible to organise data sufficiently before research use [51-53]. Standardising the terminology and exchange formats used in the healthcare setting has facilitated international discourse [46, 54-58]. It is necessary to further discuss not only clinical practice but also research purposes, particularly how to utilise various standards when using EMRs beyond the hospital setting.

CONCLUSION

We propose a pragmatic method for EMR-based observational studies. Our ERS is already used to support hospital-based cohort studies, clinical trial recruitment, and the eClinical trial infrastructure [44] at our centre. We believe an efficient ERS and standardised data processing model are essential to facilitate clinical research that utilises EMRs.

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Competing interests

None.

Contributors

KY designed the study, developed the ERS system, identified the computable eligibility criteria, wrote logical queries, collected data, and wrote the manuscript. ES is grant holder who designed the study, developed the ERS system, and wrote and edited the manuscript. TY designed and conducted the 'Risk of osteomyelitis of the jaw induced by oral bisphosphonates in patients taking medications for osteoporosis: A hospital-based cohort study in Japan' (BRONJ study) study and the current study, identified the computable eligibility criteria, and wrote and edited the manuscript. KA and MY designed and conducted the BRONJ study. ST designed the study and provided comments and feedback. KB is the principal investigator of the BRONJ study. MY owns the ERS system and supervised the study. MF supervised the study and provided comments and feedback. All of the authors read and approved the final manuscript.

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FIGURE CAPTIONS

Figure 1. Data model for our EMR retrieval system.

Figure 2. Example SQL to create the target patient list.

Figure 3. Example SQL to flag the target patient report for investigator confirmation.

Figure 4. Schema of data collection and confirmation.

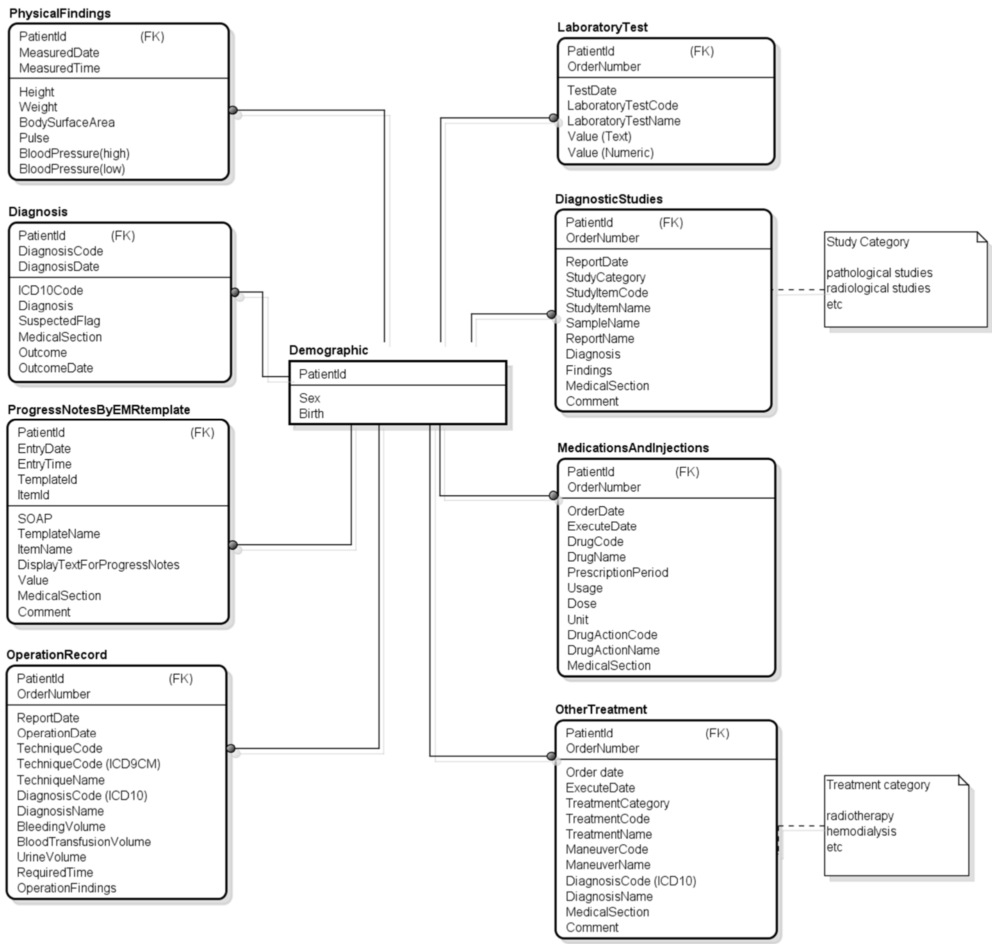

Figure 1. Data model for our EMR retrieval system.
109x104mm (300 x 300 DPI)

```
Create View_PatientsList as
Select PatientId From Demographic a
Where
a. PatientId in (
  Select PatientId From Diagnosis
  Where ICD10Code in (osteoporosis ICD10 code list) and
     DiagnosisDate >= '10/01/2000' and DiagnosisDate <= '09/30/2010' and
     SuspectedFlag = 'Fixed' )
and
a. PatientId in (
  Select PatientId From MedicationsAndInjections
  Where DrugCode in (osteoporosis drugs code list) and
     ExecuteDate >= '10/01/2000' and ExecuteDate <= '09/30/2010' )
and
a. PatientId not in (
  Select PatientId From MedicationsAndInjections
  Where DrugCode in (intravenous BP drug code list) and
     ExecuteDate >= '10/01/2000' and ExecuteDate <= '09/30/2010' )
```

Figure 2. Example SQL to create the target patient list.
81x60mm (300 x 300 DPI)

```
Select PatientId, 'Oral BP administrations', 1 From View_PatientsList a
Where a. PatientId in (
  Select PatientId From MedicationsAndInjections
  Where DrugCode in (oral BP drugs code list) and
    ExecuteDate >= '10/01/2000' and ExecuteDate <= '09/30/2010 ' )
Union all
Select PatientId, 'Oral BP administrations', 0 From View_PatientsList a
Where   a. PatientId not in (
  Select PatientId From MedicationsAndInjections
  Where DrugCode in (oral BP drugs code list) and
    ExecuteDate >= '10/01/2000' and ExecuteDate <= '09/30/2010')
Union all
Select PatientId, 'Inflammatory jaw condition diagnosis', 1 From View_PatientsList a
Where   a. PatientId in (
  Select PatientId From Diagnosis
  Where ICD10Code in (inflammatory conditions of jaws ICD10 code list) and
    DiagnosisDate >= '10/01/2000' and DiagnosisDate <= '09/30/2010' and  SuspectedFlag = 'Fixed')
Union all
Select PatientId, 'Inflammatory jaw condition diagnosis', 0 From View_PatientsList a
Where   a. PatientId not in (
  Select PatientId From Diagnosis
  Where ICD10Code in (inflammatory conditions of jaws ICD10 code list ) and
    DiagnosisDate >= '10/01/2000' and DiagnosisDate <= '09/30/2010' and  SuspectedFlag = 'Fixed')
```

Figure 3. Example SQL to flag the target patient report for investigator confirmation.
81x60mm (300 x 300 DPI)

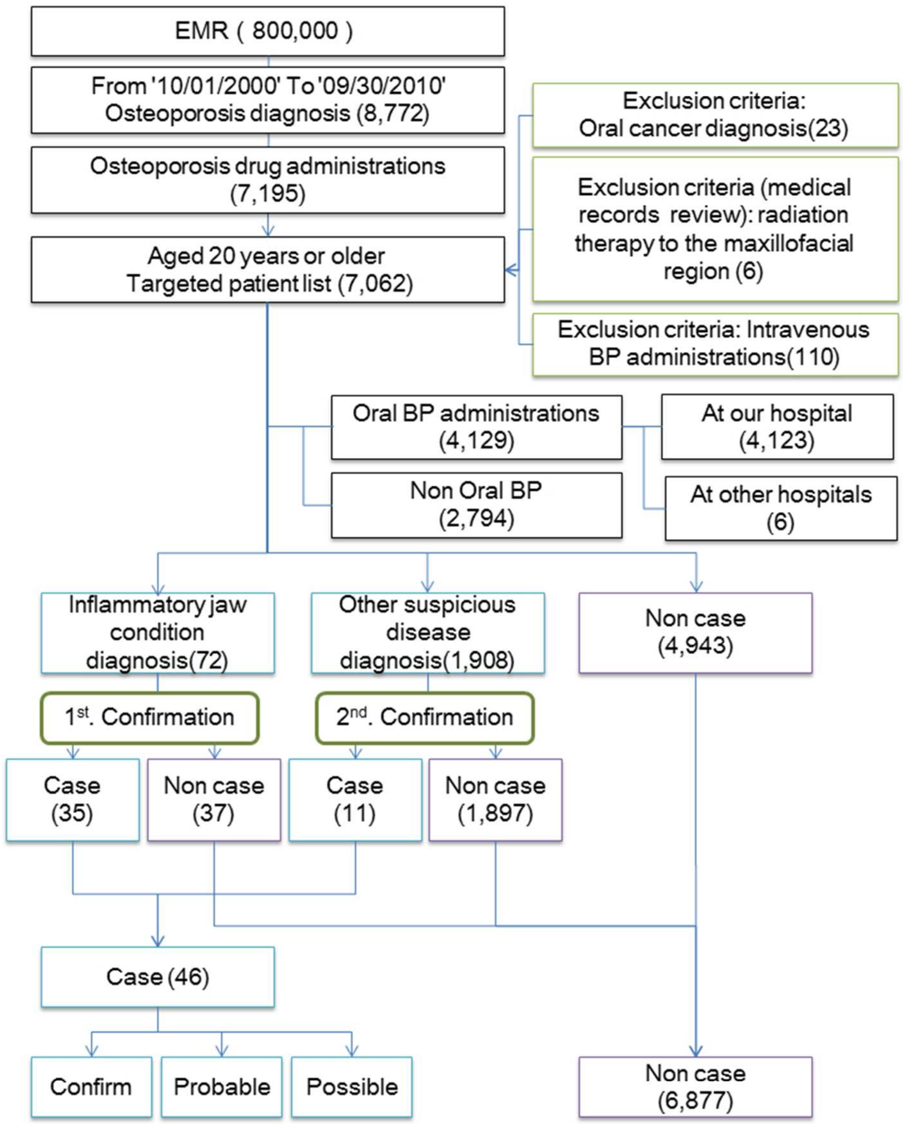

Figure 4. Schema of data collection and confirmation.
60x81mm (300 x 300 DPI)

A pragmatic method for electronic medical-record-based observational studies: developing an electronic medical records retrieval system for clinical research

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ABSTRACT

Objective: The use of electronic medical record (EMR) data is necessary to improve clinical research efficiency. However, it is not easy to identify patients who meet research eligibility criteria and collect the necessary information from EMRs because the data collection process must integrate various techniques, including the development of a data warehouse and translation of eligibility criteria into computable criteria. This research aimed to demonstrate an electronic medical records retrieval system (ERS) and an example of a hospital-based cohort study that identified both patients and exposure with an ERS. We also evaluated the feasibility and usefulness of the method. **Design**: The system was developed and evaluated. **Participants**: In total, 800,000 cases of clinical information stored in EMRs at our hospital were used. **Primary and secondary outcome measures**: The feasibility and usefulness of the ERS, the method to convert text from eligible criteria to computable criteria, and a confirmation method to increase research data accuracy. **Results:** To comprehensively and efficiently collect information from patients participating in clinical research, we developed an ERS. To create the ERS database, we designed a multi-dimensional data model optimised for patient identification. We also devised practical methods to translate narrative eligibility criteria into computable parameters. We applied the system to an actual hospital-based cohort study performed at our hospital and converted the test results into computable criteria. Based on this information, we identified eligible patients and extracted data necessary for

confirmation by our investigators and for statistical analyses with our ERS. **Conclusion:** We propose a pragmatic methodology to identify patients from EMRs who meet clinical research eligibility criteria. Our ERS allowed for the efficient collection of information on the eligibility of a given patient, reduced the labour required from the investigators, and improved the reliability of the results.

ARTICLE SUMMARY

Article focus

The focus of this work was to establish a pragmatic methodology to efficiently collect information from EMRs about patients who meet clinical research eligibility criteria.

Key messages

The use of electronic medical record (EMR) data is necessary to improve clinical research efficiency. However, it is not easy to identify patients who meet research eligibility criteria and collect necessary data from EMRs because the data collection process must integrate various techniques, including the development of a data warehouse and the translation of eligibility criteria into computable criteria. An efficient ERS and a standardised data processing model that integrates these techniques are essential to facilitate clinical research that utilises EMRs.

Strengths and limitations of this study

- Our method uses a specialised data model for patient identification in clinical research and efficient data conversion that does not depend on the EMR database structure when converting narrative criteria to computable criteria.
- We propose that computable criteria should not be a result of the automated conversion of narrative criteria but rather a result of research preparation involving medical concepts that are not expressed logically or explicitly in the narrative criteria. Therefore a large amount of the conversion of the eligibility criteria to computable criteria should be executed at the protocol development stage.
- It is important to further discuss protocol standardisation, including eligibility criteria representation for computable use.
- Enabling ERS use in and across multiple institutions is an important future task.

BACKGROUND

Medical information technology has recently advanced in many countries, and enormous amounts of clinical data are already stored as electronic medical records (EMRs). Utilising the data collected in EMRs is necessary to improve clinical research efficiency [1-3]. An EMR is a large database of patient data and is used in observational research to investigate the relationships among diseases, treatments, and outcomes [4-7], to conduct surveillance for rare drug reactions [4, 8], and to recruit patients for clinical trials [9-13]. However, it is not easy to identify patients who meet research eligibility criteria and collect necessary information from EMRs [2-3]. Herein, we describe three major issues concerning EMR-based observational studies: EMR patient data retrieval function, eligibility criteria protocol representation, and EMR data accuracy.

To identify patients who meet research eligibility criteria, it is necessary to obtain various types of information stored in EMRs by subject, e.g., diagnosis and prescribed medications. However, the EMR database is designed to facilitate online transaction processing for rapid and detail-oriented clinical information searches on individual patients, and the current EMR system does not facilitate this retrieval function [2-3, 14]. Data warehouses are essential components of data-driven decision support. To allow for efficient research analyses, EMR data must first be warehoused to enable data analyses across patient populations [15-21]. However, health care data modelling is difficult and time-consuming because of the complexity of the medical knowledge involved. Thus, the most common approaches to clinical data warehouse modelling are variations on the entity-attribute-value (EAV) model [22-28], where data are stored in a single table with three columns: entity identification, attribute, and attribute value. The EAV design has advantages, including flexibility and ease of storage; however, it requires transforming EAV data into another analytical format before analysis [25, 28]. Online analytical processing (OLAP) is most frequently used for searching data stored in the data warehouse [29-31]. OLAP systems in relational databases are typically designed based on Kimball's star schema [32]. However, the star schema was devised to facilitate online measurement analyses. In health care, this method can be used to dynamically gather online analyses of numeric data (e.g., a specific dose of a drug for a specific disease) in clinical practice. Therefore, this method is not suitable for identifying patients who meet the complicated eligibility criteria for a given clinical research study. Data-modelling methods that facilitate the identification of patients and enable the collection of necessary information from EMRs remain to be established [28].

Current eligibility criteria are written in a text format that cannot be computationally processed. Additionally, to be applied in actual EMR, eligible criteria need to be integrated with the data model of EMRs [33]. Several investigations have sought to establish computable eligibility criteria [34-41]. However, there is no consensus regarding a standard patient information model [33], and the eligibility criteria are not yet completely standardised.

Using natural language processing (NLP) technologies to convert the text format of eligibility criteria to a computer or to extract patient identifications from EMRs is far from perfect without human intervention [3, 42-43].

Current EMRs have been used to support claims for medical service fees and the treatments administered to each patient; therefore, data gathered specifically for research purposes may be incomplete and unreliable [2-3, 44].

Although various investigations on each technique are executed individually, standardised methods must still be established that integrate these techniques, facilitate the identification of patients who are eligible for clinical research, and collect necessary information from EMRs.

OBJECTIVE

We designed a pragmatic data processing model optimised for patient identification and for the collection of necessary information from EMRs for clinical research. These tools are implemented as an electronic medical records retrieval system (ERS) [44].

This research aimed to demonstrate an ERS and an example of a hospital-based cohort study that used the ERS to identify both patients and exposure. Another aim was to evaluate the feasibility and usefulness of the ERS, the method to convert text form eligible criteria to computable criteria, and a confirmation method to increase research data accuracy.

MATERIALS AND METHODS

Outline of our procedure for patient identification and data collection from the EMR

To identify patients who met the eligibility criteria for the clinical research in question, data were collected in the following ways:

1) The text form of the narrative criteria was converted into computable criteria.

2) A targeted patient list was created.

3) A flag was added for investigators to confirm the targeted patient list.

4) Reports were created for the investigators to confirm.

5) After confirmation by the investigator, the statistical analyses were executed.

EMR retrieval system

In our hospital, EMR use was introduced in 2005; approximately 800,000 cases of clinical information have already been stored. To comprehensively and efficiently collect information about patients participating in clinical research, we developed an ERS [44].

EMRs store various types of information, integrating billing, pharmacy, radiology, laboratory information, and others [4]. In creating the ERS database, we designed a new data model based on the star schema that was optimised for patient identification in clinical research. We identified nine data categories from EMRs that are useful for clinical research: demographic characteristics, physical findings, diagnostic studies, laboratory tests, diagnoses, progress reports on an EMR template [44-45], medications and injections, operation records, and other treatments. We then designated these categories to 'entities'. In our hospital, the diagnosis is managed by codes that were originally defined by our hospital and mapped with International Statistical Classification of Diseases (ICD) 10 codes [46] for medical insurance purposes. Operations codes were also managed by codes that originally were defined by our hospital and mapped with ICD-9 Clinical Modification codes. We identified available columns (e.g., ICD code, diagnosis date) from the EMR data model and designated these columns as 'attributes' of the entities.

Figure 1 presents our data model. In our model, all entities in a given schema are independent and complete; this allows for logical operations and for the creation of eligible patient lists for each respective parameter in a study. The target patient list is generated by combining these patient lists. The data model also supports the inference of medical concepts expressed in the eligibility criteria in reference to corresponding patient data accumulated in EMRs [33-34].

In our hospital, a replicate of the EMR database known as 'Open DB' was established for the secondary use of accumulated EMR data [7]. A data mart for our ERS was created to ensure that the data retrieval process was practical and independent of the EMR system structure; the data mart was created on the relational database management system by extracting, transforming, and loading (ETL) information from the Open DB [7, 44]. The ETL process is performed automatically once nightly except for the 'Progress notes by EMR template' entity, which is referred directly from the Open DB to ensure real-time visibility for the eClinical trial [44].

An OLAP tool was installed to efficiently search through data from multiple patients [44]. The OLAP tool runs in an Internet browser and can generate structured query language (SQL) based on predefined metadata (i.e., a data model) by defining logical queries (i.e., programs) using a graphical user interface (GUI). Moreover, this tool allows reports on information retrieved from the browser to be transcribed using hypertext markup language (HTML). The reports are created in various formats, including portable document format (PDF), comma separated values (CSV), and extensible markup language (XML) [44].

To protect personal information in medical records at our hospital, the EMR network is separated physically from other networks. Our data mart and OLAP servers are deployed in the same EMR network and managed using the same EMR security policies. Additionally, the use of our ERS is limited to clinical research approved by the ethics committee at our hospital, and only designated staff members at our centre are allowed to retrieve data. Our centre creates and manages ERS user identification separate from the EMRs. For the external output of CSV and other data, permission must be obtained from our department of medical informatics, and data extraction must be executed in the presence of supervisors who are responsible for protecting personal information at our hospital.

Application to clinical research

We applied the system to a hospital-based cohort study performed at our hospital titled 'Risk of osteomyelitis of the jaw induced by oral bisphosphonates (BP) in patients taking medications for osteoporosis: A hospital-based cohort study in Japan' [47], in which we identified eligible patients, extracted research data, and evaluated the feasibility of our system. The ethics committee at Kyoto University Hospital approved this research. A different paper details the purpose, methods, results, and discussion of this research [47].

This research aimed to estimate the risks for osteomyelitis of the jaw in osteoporosis patients at our hospital who had been exposed to oral BP compared to those who had not [48-49].

The eligibility criteria were as follows:

Inclusion criteria

- Patients diagnosed with osteoporosis and treated with osteoporosis medications at Kyoto University Hospital between November 2000 and October 2010.
- Patients aged 20 years or older.

Exclusion criteria

- Patients with a history of treatment with radiation therapy to the maxillofacial region.
- Patients with primary or metastatic tumours in the maxillofacial region.
- Patients treated with intravenous BP.

The data collected were diagnosis, date of diagnosis, sex, birthdate, and the doses and dates when osteoporosis medications, steroids, anticancer drugs, diabetes drugs and HbA1c tests were administered.

Conversion of the text form of the narrative criteria to computable criteria

To identify eligible patients and collect the necessary data from the EMRs, narrative criteria and data must be converted to computable criteria. Such computable criteria include entities, attributes, logical operators (i.e., 'and' and 'or'), codes, and parameters [33-37]. The clinical research purpose and clinical practice demands made it necessary to perform this task.

We manually executed the conversion from text eligibility criteria to computable criteria. As an example of the conversion from narrative criteria to computable criteria, we present the following two-step conversion procedure:

Step 1: Convert the narrative criteria into entity-level criteria.

Medical concepts expressed as narrative criteria are mapped onto entities in the data model and converted into entity-level criteria. This task is manually performed at the protocol development stage of the study by the investigators. For each entity, a criterion is created to extract patients who meet each condition. If exclusive conditions for the same entity must be defined, a different criterion is created. Additionally, the list of codes for drugs and diagnoses (i.e., ICD-10) is created, and the period of treatments and others are defined by investigators. In this study, we mapped ‘osteoporotic patients’ onto two entities (i.e., ‘diagnosis’ and ‘medications and injections’) and converted it to a combination of two criteria (i.e., ‘diagnosis of osteoporosis’ and ‘osteoporosis drug administration’). In the test research, we defined the entity-level criteria according to the entered diagnosis and ordered treatments rather than the diagnostic criteria of the disease. This process reflects that the test research aimed to estimate some risks of osteomyelitis of the jaw with BP administration instead of diagnosing osteoporosis patients accurately. The recorded diagnosis in the EMR was typically designed to ensure payment for medical claims. We thus sought to reduce the number of false positives by extracting patients with a given treatment type.

Step 2: Convert entity-level criteria into attribute-level criteria (i.e., computable criteria).

The abovementioned corresponding codes, date and parameters are mapped onto attributes of the entity-level criteria, and these factors become computable criteria.

Creating a targeted patient list

A targeted patient list is created from the entire set of patients for whom EMRs have been obtained by defining logical queries (i.e., programs defined by the GUI) based on the computable criteria included in the ERS.

Logical queries are first defined in the ERS to identify patients who meet the conditions for each criterion. The ERS automatically generates the SQL necessary for data extraction according to the logical queries. Logical queries are then defined to include or exclude eligible patients who meet each criterion for the demographic entity. The targeted patient list is created by executing the logical query. Figure 2 presents an example of an SQL automatically generated by the ERS.

We thus designed our data model to enable the creation of a targeted patient list by defining the patients extracted from each criterion (i.e., 'in' or 'not in') as conditions for the demographic entity that was the unique patient list for the entire hospital. If logical queries are defined using our method, even if the eligibility criteria are complicated, it is not necessary to dramatically change the SQL structure generated in the ERS.

Flagging entries for investigators to confirm

To improve research data accuracy, confirmation by the investigators is necessary. When confirmation is required, additional information is linked.

For the targeted patient list, logical queries are defined to flag certain items according to the investigators' interest. Necessary logical queries are first defined for each criterion. Logical queries are then defined for addition to the patient list as '1' if the data correspond or '0' if they do not. Data sets created by these operations are joined by 'union' and pivoted on a cross-tabulation list using statistical analysis software. We show an example of an SQL generated by the ERS in Figure 3.

Create reports for investigators to confirm

To help investigators confirm the targeted patient list, reports are created by linking the findings for diagnostic imaging, pathological diagnosis, operations, and other findings. Investigators confirm these entries using the reports and EMR information, including progress notes and images. When the diagnosis history, medication, laboratory results, progress notes, and other information are necessary, the same operation is executed for each instance. For example, the list of radiological findings involves 'patient id', 'study category', 'report name', 'diagnosis', 'findings', and 'comment'. The reports may improve the investigators' confirmation efficiency because they prevent the need to refer to the medical records for each patient who needs confirmation.

Confirmation by the investigator and execution of the statistical analyses.

The investigators confirm the accumulated data and execute the statistical analysis. In this test research, two oral and maxillofacial surgeons diagnosed cases by a chart review with an observation of imaging findings [47].

Systemic evaluation

To evaluate our system, we collected information about the research period using the recall method. For the accuracy of the data collected by the ERS, we evaluated the results after they were confirmed by the investigator.

RESULTS

Computable criteria, datasets, and system evaluation

We present the computable criteria in Table 1. To increase data accuracy, we collected all of the exclusion criteria for the investigators to confirm. As Table 1 shows, we extracted information from EMRs. For investigator confirmation, we also reported all targeted patients using the following lists: osteoporosis drugs administered, oral BP administered, intravenous BP administered, diabetes drugs administered, anticancer drugs administered, steroid drugs administered, osteoporosis diagnoses, oral cancer diagnoses, patients diagnosed with inflammation of the jaw, patients diagnosed with other suspicious diseases, patients diagnosed with diabetes, HbA1c values, radiological findings, pathological findings, and radioisotope findings. These data were extracted from the ERS for statistical analyses, presented in CSV format, and analysed using statistics software.

Table 1. Computable criteria for our test research

Criterion	Entity	Operator symbol	Attribute	Operator symbol	Parameter
Created a targeted patient list					
Inclusion criteria: Osteoporosis diagnosis	Diagnosis	-	ICD10Code	In	(osteoporosis ICD10 code list)
		and	DiagnosisDate	>=	'10/01/2000'
		and	DiagnosisDate	<=	'09/30/2010'
		and	SuspectedFlag	=	Fixed
Inclusion criteria: Osteoporosis drug administrations	Medications and Injections	-	DrugCode	in	(osteoporosis drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Added a flag for investigators to confirm the targeted patient list					
Exclusion criteria: Oral cancer diagnosis	Diagnosis	-	ICD10Code	in	(oral cancer ICD10 code list)
		and	DiagnosisDate	>=	10/01/2000'
		and	DiagnosisDate	<=	09/30/2010'
		and	SuspectedFlag	=	Fixed
Exclusion criteria: Intravenous BP administrations	Medications and Injections	-	DrugCode	in	(intravenous BP drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Oral BP administrations	Medications and Injections	-	DrugCode	in	(oral BP drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Inflammatory jaw condition diagnosis	Diagnosis	-	ICD10Code	in	(inflammatory conditions of jaws ICD10 code list)
		and	DiagnosisDate	>=	'10/01/2000'
		and	DiagnosisDate	<=	'09/30/2010'
		and	SuspectedFlag	=	Fixed
Other suspicious disease diagnosis	Diagnosis	-	ICD10Code	in	(other suspicious disease ICD10 code list)
		and	DiagnosisDate	>=	'10/01/2000'
		and	DiagnosisDate	<=	'09/30/2010'
		and	SuspectedFlag	=	Fixed
Diabetes diagnosis	Diagnosis	-	ICD10Code	in	(diabetes ICD10 code list)
		and	DiagnosisDate	>=	'10/01/2000'
		and	DiagnosisDate	<=	'09/30/2010'
		and	SuspectedFlag	=	Fixed

Steroid drug administrations	Medications and Injections	-	DrugCode	in	(steroid drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Anticancer drug administrations	Medications and Injections	-	DrugCode	in	(anticancer drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
Diabetes drug administrations	Medications and Injections	-	DrugCode	in	(diabetes drugs code list)
		and	ExecuteDate	>=	'10/01/2000'
		and	ExecuteDate	<=	'09/30/2010'
HbA1c test execution	Laboratory Test	-	LaboratoryTestCode	in	(HbA1c test code)
		and	TestDate	>=	'10/01/2000'
		and	TestDate	<=	'09/30/2010'
Created reports for confirmation by the investigators					
Radiological finding reports	Diagnostic Studies	-	ReportName	in	(report name list of oral region)
Pathologic finding reports	Diagnostic Studies	-	SampleName	contains	'bone'
		or	SampleName	contains	'jaw'
Radio isotope finding reports	Diagnostic Studies	-	-	-	-

BP, bisphosphonates; ICD, International Classification of Diseases; ID, identifications

Among the approximately 800,000 cases at our hospital, 8,772 were categorised using the terms 'Inclusion criteria: Osteoporosis diagnosis'; among this group, 7,195 were further categorised using 'Inclusion criteria: Osteoporosis drug administration'. We then calculated the time that had elapsed since the osteoporosis diagnosis, determined that 7,062 patients were aged 20 years or older, and created a targeted patient list. Among those on the targeted patient list, 23 patients were placed under the heading 'Exclusion criteria: Oral cancer diagnosis', 110 under 'Exclusion criteria: Intravenous BP administration', 4,200 under 'Oral

BP administration’, 84 under ‘Inflammatory jaw condition diagnosis’, 2,064 as ‘Other suspicious disease diagnosis’, 1,700 as ‘Diabetes diagnosis’, 4,551 as ‘Steroid drug administration’, 904 as ‘Anticancer drug administrations’, 1,055 as ‘Diabetes drug administrations’, and 3,641 as ‘HbA1c test execution’. Because of the end point considered, patients who were classified under ‘Inflammatory jaw condition diagnosis’ or ‘Other suspicious disease diagnosis’ were confirmed using predefined hierarchical diagnostic criteria by investigators who performed the statistical analyses and arranged the research results. We show the schema of data collection and confirmation as Figure 4 [47].

The accuracy of the data extracted by the ERS was then characterised. Reviewing the medical records revealed that 2,817 patients were not labelled as ‘Oral BP administration’, including 7 (1 who received intravenous BP) treated at other hospitals. 6 patients had been treated with radiation therapy to the oral and maxillofacial regions. Among the 72 patients classified under ‘Inflammatory jaw condition diagnosis’, 35 cases and 37 non-cases were identified.

The data extraction period lasted approximately three months. Ten meetings were held during the protocol development stage to create and validate the computable criteria and the list of codes for various drugs and diagnoses (i.e., ICD-10). The time required for logical query definition when using the ERS was approximately 20 hours. The investigator confirmations and statistical analyses took approximately four months.

DISCUSSION

We identified eligible patients for this research and extracted the data necessary for confirmation by investigators and for statistical analyses.

We asked the chart reviewers to evaluate the system in a questionnaire about ‘the effect of computer programming support for data retrieval from the EMR’, ‘the result of the data retrieval’, ‘the positive and negative aspects of our ERS use’, and ‘the aspects of our method that should be improved’. The investigators evaluating the system mentioned that the following points: 1) the method enabled them to extract the necessary data for diagnosis and drug administration without exception; 2) by screening the entire patient population at the hospital using the ERS, they could identify not just eligible patients in the department of oral and maxillofacial surgery but all eligible patients, which reduced the study bias; and 3) by creating reports for confirmation, it enabled investigators to devote their time to reading images, thus effectively reducing the time required for reviewing medical records. The aspects of our method that should be improved are the ‘lack of claim data’ and the ‘administrative complexity of EMR data use’. No negative aspects of our ERS use were noted.

The ERS allowed for the collection of information on patient eligibility by efficiently combining clinical information. Although we did not compare our method with other methods, our proposed method reduced the labour normally required from investigators and improved the reliability of test research results, which indicated that it was useful.

To design the ERS database, we designed a new data model optimised for patient identification. The main differences between our data model and the star schema were as follows: 1) demographic data, which were presented in list form in our EMR system, were presented as a fact-less fact table, and 2) date, time, measurements and text information were presented in dimension tables [32]. The most significant characteristic of our method for patient identification is the use of a specialised data model in clinical research and the ability to execute a large number of conversion tasks at the protocol development stage. Data can be converted efficiently in a way that does not depend on the EMR database structure when converting narrative criteria to computable criteria. In this research, we considered whether data were extracted directly from EMRs at the protocol development stage. However, EMR data were recorded in a sequential format for every medical practice, and the database structure was complicated. Comprehending the location and meaning of the necessary data thus required tremendous effort. It was difficult to make precise logical queries for patient identification. However, because our ERS data model was arranged by subjects (e.g., tests, diagnosis), it was easy to interpret the available information. Due to the standardisation of computable criteria and SQL possible with the ERS, it was also possible to create computable criteria in little time. Additionally, verifying the patient identification accuracy was easy because it was possible to test each individual criterion.

The SQL generated by our ERS does not reduce the time required for data retrieval. Our ERS also cannot retrieve information that is not in the data model. Current EMRs do not store all necessary data for clinical research, including information related to pregnancy, performance status, cancer stage, availability of transportation to the hospital, specific tests that are not typically performed, drug regimen, outcomes (including death), and adverse events. Additionally, all tests are not administered to all patients, and necessary information may have been recorded in medical records at another hospital [44]. To facilitate EMR use in clinical research, it is necessary to accumulate as much of this information as possible. In the hospital, much of this information does not integrate well with EMRs, including test reports stored only in the departmental system [50]. However, it is important to utilise this information. Additionally, enabling ERS use in and across multiple institutions is also an important future task.

Currently, most clinical research studies that use data from EMRs are planned according to the concept that the primary use of EMRs is for clinical practice and a secondary use is for clinical research [44]. Therefore, most investigators attempt to convert the text form eligibility criteria that already have been defined on a protocol to computable criteria at the data collecting stage [35. 36]. However, we propose that computable criteria should not be a result of the automated conversion of narrative criteria but rather a result of research preparation involving medical concepts that are not expressed logically or explicitly in the narrative criteria. Some medical concepts may be interpreted differently depending on the research and the investigator caring for the patients. Additionally, current eligibility criteria are vague or complex, and they do not consider the use of the actual EMR. To convert computable criteria appropriately, high-level medical decisions to answer the research question are required. Therefore, we thought that a large amount of the conversion of the eligibility criteria to computable criteria should be executed at the protocol development stage. In addition, the conversion process should be divided into entity-level conversions that require higher medical decisions and attribute-level conversions. To reduce the burden of conversion, it may be useful to apply NLP technology for the conversion from entity-level criteria to attribute-level criteria. Moreover, it is important to further discuss protocol standardisation, including eligibility criteria representation for computable use. For instance, the attribute-level criteria that describe the search conditions in detail may be useful in global studies to address diseases that vary according to the diagnostic criteria used in each country.

Concerning EMR data accuracy, the ICD10 code (osteomyelitis of the jaw) sensitivity was 48.6% (35/72). The investigators reported 6 simple diagnosis errors, 7 oral BP administrations at other hospitals, and 6 patients who were treated with radiation therapy in the oral and maxillofacial region [47]. For the accuracy of current EMRs, the investigators had to confirm the information. However, the EMRs provided rich confirmation data and were useful in improving research data accuracy. In this study, we checked the data from actual EMRs manually and identified patients precisely and extensively using coded information, narrative information, and images. However, only information from existing EMRs was available. Current EMRs have a high degree of flexibility in data entry and are not currently managed for research purposes, which decreases their reliability. It is necessary to improve data quality through quality control without placing too much of a burden on clinical practice. Alternatively, it may be possible to organise data sufficiently before research use [51-53]. Standardising the terminology and exchange formats used in the healthcare setting has facilitated international discourse [46, 54-58]. It is necessary to further discuss not only clinical practice but also research purposes, particularly how to utilise various standards when using EMRs beyond the hospital setting.

CONCLUSION

We propose a pragmatic method for EMR-based observational studies. Our ERS is already used to support hospital-based cohort studies, clinical trial recruitment, and the eClinical trial infrastructure [44] at our centre. We believe an efficient ERS and standardised data processing model are essential to facilitate clinical research that utilises EMRs.

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Competing interests

None.

Contributors

KY designed the study, developed the ERS system, identified the computable eligibility criteria, wrote logical queries, collected data, and wrote the manuscript. ES is grant holder who designed the study, developed the ERS system, and wrote and edited the manuscript. TY designed and conducted the 'Risk of osteomyelitis of the jaw induced by oral bisphosphonates in patients taking medications for osteoporosis: A hospital-based cohort study in Japan' (BRONJ study) study and the current study, identified the computable eligibility criteria, and wrote and edited the manuscript. KA and MY designed and conducted the BRONJ study. ST designed the study and provided comments and feedback. KB is the principal investigator of the BRONJ study. MY owns the ERS system and supervised the study. MF supervised the study and provided comments and feedback. All of the authors read and approved the final manuscript.

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No other data are available to share.

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FIGURE CAPTIONS

Figure 1. Data model for our EMR retrieval system.

Figure 2. Example SQL to create the target patient list.

Figure 3. Example SQL to flag the target patient report for investigator confirmation.

Figure 4. Schema of data collection and confirmation.