

Utilization of Electronic Health Information in Pharmacovigilance

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Global concern on safety of drugs

- Vioxx, IOM Report
- MHLW Committee on HCV Infection by Blood preparation

Difficulty of evaluation of post-approval safety of drugs

- Tamiflu, Anti-depressants

Limitation of spontaneous ADR reporting in safety evaluation

International harmonization

- Implementation of E2E

New technologies for drug safety

- Data mining
- Regulatory epidemiology

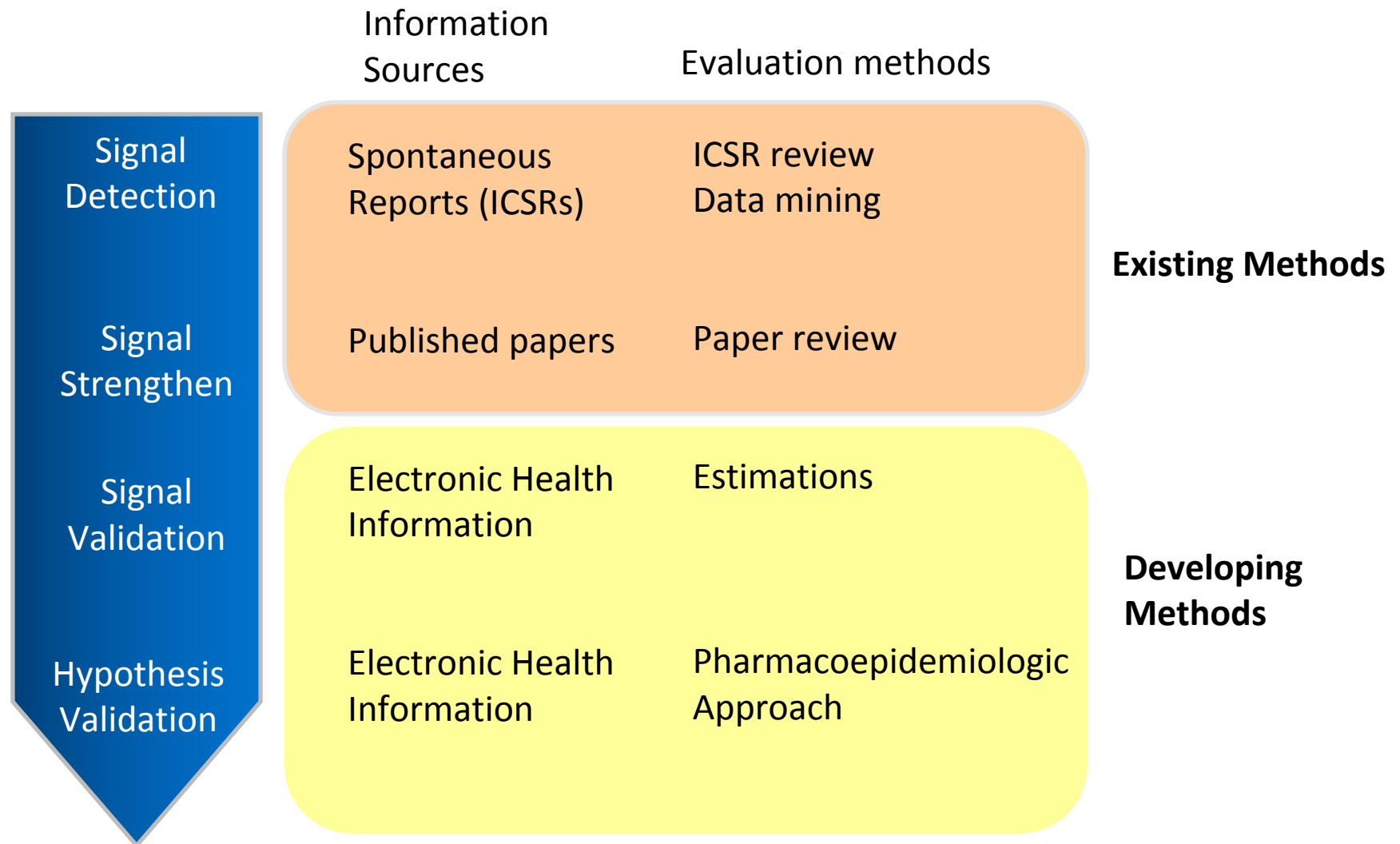


**NEED TO MODERNIZE DRUG SAFETY PROGRAM :
USE OF ELECTRONIC HEALTH DATABASE**

Reinforcement and enhancement of the system for safety information collection and evaluation

- Introduction of safety assessment team system according to therapeutic categories to realize advanced and specialized assessment of adverse drug reactions (ADRs). Stepwise increase of the number of teams.
- Utilization of data-mining methodology in safety assessment to enable early detection of ADRs and proactive safety measures to minimize risks .
- **Securing access to electronic medical record database including claim data to assess drug safety through ADR incidence survey and using a pharmacoepidemiological approach**
- Rationalization and effective implementation of PMS and surveys required by approval conditions including their timely review. Continuous evaluation of effectiveness and efficiency of PMS and post-approval surveys.
- Stepwise implementation of PMDA follow-up to ADR reporting by HCP.

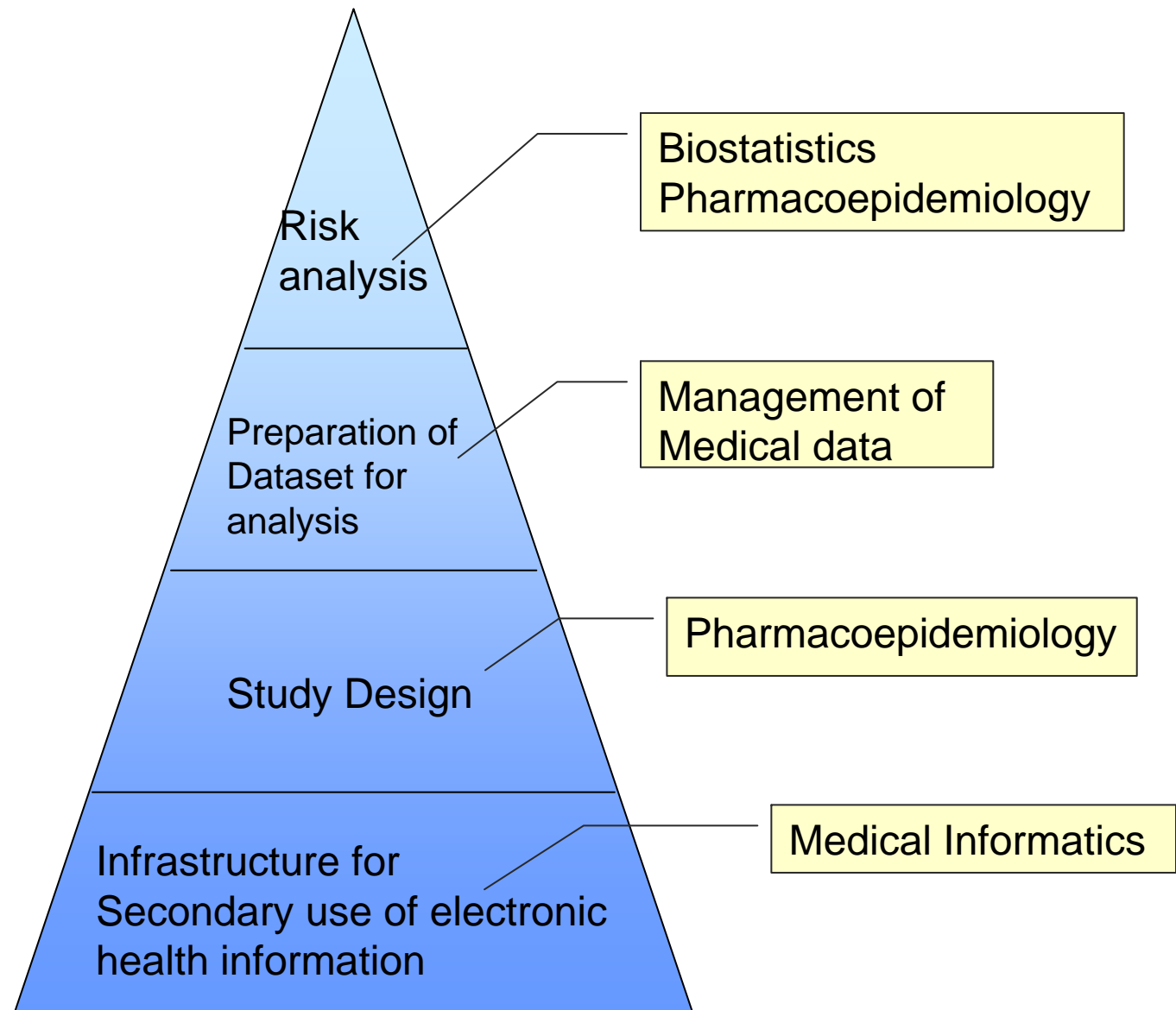
Introduction of new methods to drug safety evaluation process



- Detection of unknown ADR
- Estimation and evaluation of risk of drugs
- Evaluation of risks in subgroup and special population
- Comparison of AE incidence between new and existing drugs
- Comparison of AE incidence between use and non-use of a drug
- Analysis of impact and effectiveness of safety measures

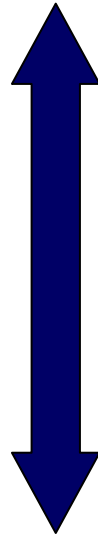
- First Meeting in July 2009
- Main objectives: to identify:
 - necessary infrastructure to ensure access to electronic health information such as e-medical records and e-insurance claim data.
 - methodology and technique to use electronic health information for quantitative risk evaluation of pharmaceuticals employing pharmacoepidemiology analysis.
 - methodology and technique to use electronic health information for evaluation of impact of regulatory actions for drug safety.

Academic Areas pertinent to Utilization of Electronic Health Information for Pharmacovigilance



MHLW: Consultation Meeting on the Utilization of Medical-area Database for Drug Safety Measures

Cooperation



MHLW-granted Research : Research on Creation of Pharmacoepidemiology Database Using medical Claim Data

Research results



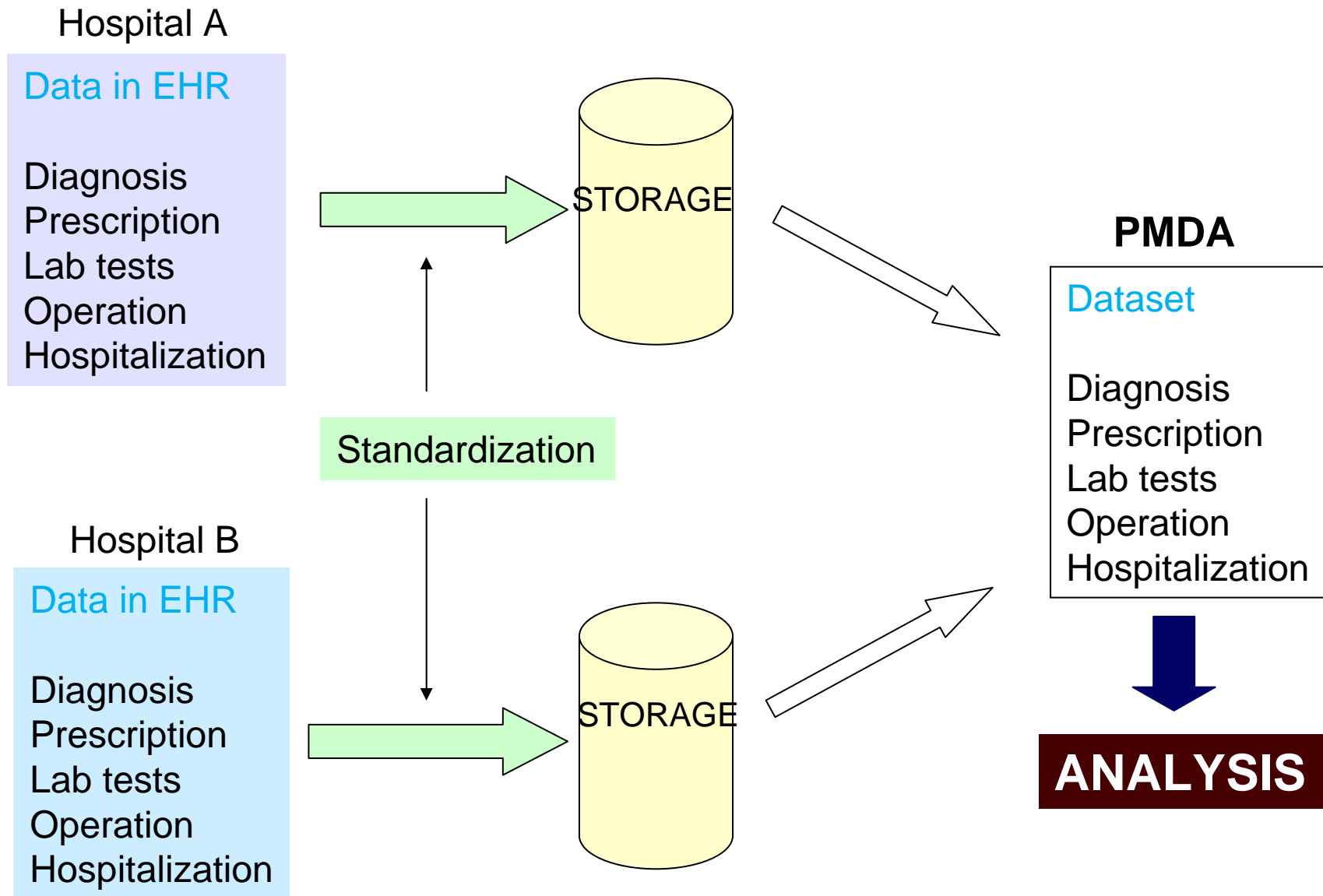
Research results



PMDA: Expert Committee on Utilization of Electronic Health Database for Pharmacovigilance

- Health insurance claim data
 - National database
- Diagnosis procedure combination (DPC)
 - Health insurance claim data for in patients
- Medical information system
 - Comprehensive system in hospital including EHR
- Drug Use Result Survey Data
 - Post-market drug survey
- Adverse Drug Reaction Report (ICSR) Database
 - ADR reports from hospitals and companies
- Existing databases
 - Large databases in abroad (e.g. GPRD)

Possible use of EHR for safety analysis



Pilot Study: Summary (1)



Objective	To assess electronic health information whether it could be a innovative tool to strengthen our pharmacovigilance activities through characterization of electronic health information from two different data sources, investigation for the method to extract data regarding drug adverse reactions, and analysis of the data to estimate risks.	
Study name	Medical Information System (MIS) study	DPC study
Data source	Medical records	DPC (Claim data)
Investigation event	<p>A) Pseudomembranous colitis / Antibiotics</p> <p>B) Stevens Johnson Syndrome / Antibiotics</p> <p>C) Rhabdomyolysis / Statins</p>	A) Pseudomembranous colitis / Antibiotics
Investigation period	January 1, 2007 – December 31, 2007	April 1, 2007 – December 1, 2007
Number of participated hospital	1 (The same hospital for MIS study and DPC study)	

Pilot Study: Summary (1)

Method	Study target populations prescribed antibiotics or statins were identified according to the criteria. Case patients were identified by the criteria of the events (A, B, or C). The extracted data was calculated, and exploratory analysis was adopted to Pseudomembranous colitis / antibiotics (event A) in MIS study.
Result	<p>From MIS study, target populations were identified as 7,259 for antibiotics and 1,920 for statins. There were 55 cases of Pseudomembranous colitis, 1 case of Stevens Johnson Syndrome, and 1 case of Rhabdomyolysis. Proportion of the events were 0.76 %, 0.01 %, and 0.30 %, respectively.</p> <p>From DPC study, target population was identified as 3,335 and there were 10 cases of Pseudomembranous colitis, therefore, the event proportion was 0.30 %.</p>

Ethical consideration

This study followed 'Ethical guideline for epidemiological studies' which was provided by MHLW. As the guideline indicated, informed consent was not required in this study since it was an observation study only using existing documents.

The study plan was approved by ethical committee in the hospital where the study was conducted. The notice about this study had been posted at the hospital during the study period so that the people visiting doctors could have an opportunity to decline using their data.

- Only one hospital participated in this study, however, some progresses were made :
 - ADR information could be identified from both medical records (Medical Information System) and DPC
 - A framework to characterize medical records and DPC was successfully developed
 - The health records have potential to become a useful tool for pharmacovigilance
- The level of available information depends on data sources, therefore, the way we use each data source should be different. Further investigation is needed in order to establish procedures that will help us to utilize electronic health records as a new tool to strengthen pharmacovigilance in PMDA

<Claim data>

- > Small scale pilot study using commercially available claim DB (relatively small number of subjects).
- > To conduct actual analysis on an AE and a medicine on DB.
- > To identify characteristic and usability of claim data.

<Medical Information System>

- > To obtain medical records in a standardized format from a small number of hospitals.
- > To conduct actual analysis of a specific AE and a specific medicine on HIS data.
- > To identify characteristic and usability of MIS data.

<Existing DB abroad>

- > To study existing DB in the US and Europe.
- > Also to study how regulatory agencies such as FDA/EMA use those DB for epidemiological analysis and for regulatory consideration and action.

<ADR Database>

- > To start consideration of
 - improving content and presentation of ADR line listing on PMDA website.
 - providing ADR data available for researchers etc. for data-mining and other analysis

<Drug Use Result Survey Data>

- > To start consideration of
 - promoting feedback and use of drug use result survey data including provision of a database

Thank you!

Back up

Health Insurance Claim Data

- Japan has a national health insurance system.
- On-line electronic claim for reimbursement will be made obligatory by 2011.
- A National claim database is planned to be constructed. The DB will be used primarily for research and analysis of medical economy.
- MHLW committee report discusses secondary use of DB by entities other than national government: pending: PMDA to be a secondary user of DB for drug safety analysis.
- **MHLW committee on reviewing hepatitis C cases and developing new regulatory structure to prevent relapse of ADR tragedies** recommended use of a national claim data DB for pharmacovigilance.

Diagnosis Procedure Combination (DPC)

- Inclusive reimbursement system for hospitalized patients with acute diseases.
- Electronic claim data with standardized data elements and codes are collected and populated to DB by MHLW.
- DPC system started in 2003 with 82 hospitals.
- Number of DPC hospitals has been increasing.
- According to 2007 survey,

	Number of hospitals	Number of beds
DPC	1,283	434,231
All hospitals	8,862	913,234

Medical Information System

2001 Grand Design for IT introduction in medical area (MHLW)

Target: Installation of electronic medical record system in 60% of hospitals with more than 400 beds by 2006

2005 Medical Institution Survey (9026 hospitals)

- Installation of electronic medical record system

(All hospitals) Full installation 470 hospitals (5.2%)

Partial installation 156 hospitals (1.7%)

(Hospitals with more than 400 beds (722 hospitals))

Full installation 129 hospitals (17.9%)

Partial installation 23 hospitals (3.2%)

2006 New IT Renovation Strategy (Cabinet Office)

- Installation of integrated MIS (medical records and ordering system) in most hospitals with more than 200 beds by 2010