Applying Grid Computation for Evaluating Potentially Inappropriate Medication Use in Elderly Patients

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Abstract

Objectives: The nationwide health claims data stored in the National Health Insurance Research Database (NHIRD) in Taiwan have been used to analyze potentially inappropriate medication use in elderly patients. To access the huge data of NHIRD, we applied the Grid-computing technology to develop a Grid-based data analysis system in this study.
Methods: Globus Toolkit was used to integrate 12 Mac Mini computers and 4 disk arrays for building the Grid system. Prevalence and drug duration score (DDS) of 28 potentially inappropriate medication uses from 2000 to 2002 were calculated.
Results: In 2000 – 2002, 68.79% of elderly patients received at least one of 28 inappropriate medications. 14.88% of elderly patients received at lease one of 9 drugs classified by an expert panel as "should always be avoided"; 40.45% of elderly patients received at least one of 6 drugs that would rarely be considered appropriate; and 51.70% of elderly patients received at least one of 13 medications that have some indications but are often misused. The DDS of chlorpropamide and carisoprodol was 23.01 and 13.83 respectively, which were the highest scores in the "should always be avoid" and "are rarely appropriate" category.
Conclusions: For the task of huge data analysis, the Grid is an appropriate and robust approach to facilitate the analytical process. The inappropriate medication analysis results of this study can be represented as practical observations of potentially inappropriate medication conditions of elderly patients in Taiwan; moreover they can also serve as basic references for further inappropriate medication studies.

1. Introduction

Inappropriate medication use is one of major patient safety and public health concerns, especially for elderly patients [1, 2]. Elderly patients who often take polypharmacy are at increased risk of adverse drug effects and drug toxicity [3]. Many researchers studied the prevalence of potentially inappropriate medication use in elderly by analyzing retrospective data [4, 5]. Much of their work has been limited to particular medical facilities or communities.

In this study, we used 3 years (2000 - 2002) complete data of the National Health Insurance Research Database (NHIRD) in Taiwan to extract prescriptions for inappropriate medication identification in elderly outpatients. Nowadays, this database was frequently used to investigate and resolve health and epidemiologic problems [6, 7]. The complete dataset of the NHIRD is too huge to be processed by a personal computer or even a powerful server; therefore most researchers have only used subsets of sampled data for their studies. The two major benefits of using complete data are: (1) the analytical results can be used to represent the entire population with no inferential statistics, and (2) sampling methods may influence analytical results, therefore using complete data can avoid errors due to applying inappropriate or incorrect sampling methods.

Recently lots of claims data, medical records, images, and gene and protein sequence data have been digitized. Traditional data analysis approaches have gradually been rendered incapable of dealing with large datasets. Because the Grid technology [8, 9] is usually used to resolve very complicated problems, which cannot be handled with limited computing resources, this technology has been widely applied in health and biomedical research and projects [10-13]. In general, the Grid is a service for computing resource sharing over the Internet. It can turn computers in different places into one vast computational power to process difficult computational problems.

In this study, we only used part of NHIRD including data of ambulatory care expenditures by visits and details of ambulatory care orders. These data exceeded 200 GB of storage space for 1 year on average. To be capable of analyzing this huge amount of data, we applied the Grid architecture to design the identification procedure for potentially inappropriate medication use in elderly patients.

2. Methods

2.1. Data sources

In Taiwan, the nationwide health claims data including disease diagnosis, treatment, inpatient and outpatient claims, and details of prescriptions dispensed are stored in the NHIRD hosted by the National Health

Research Institute. The NHIRD for a 3-year period (2000 - 2002) was used to retrieve inappropriate medication information in this study. In the NHIRD, we only used the data of ambulatory care expenditures by visits and details of ambulatory care orders including prescription, patient's ID, gender and age.

An inappropriate medication database for elderly was created based on the study of Zhan et al [14]. Regardless of drug dosage, frequency, and duration of administration, they referred 1997 Beers criteria [15] and restricted their analysis to a subset of 33 drugs. They recruited an medical expert panel and used a modified Delphi method to classify these 33 drugs into 3 categories of drugs that (1) should always be avoided, (2) are rarely appropriate, and (3) have some indications but are often misused. In the Beers criteria, all drugs are classified as high severity or not for elderly persons. That is not sufficient for clinical use. Therefore we followed Zhan's classifications and created the inappropriate medication database to identify potentially inappropriate medications from elderly outpatient's prescription claims data.

2.2. Inappropriate medication identification

To identify inappropriate medication use in elderly from prescription data of NHIRD, we have developed an application for inappropriate medication information retrieval. The application procedure is shown in Figure 1. In Figure 1, elderly patient's prescription sheet data is obtained from NHIRD and every drug in a prescription sheet is checked for an inappropriate medication according to the inappropriate medication database. If a drug is identified as an inappropriate medication, the drug name and code are outputted and saved in the result repository. Furthermore, the patient's ID, gender, age, and drug duration of administration are also retrieved from NHIRD.

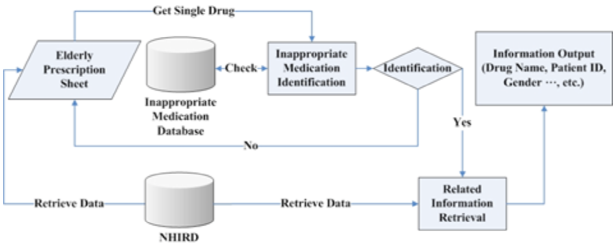

Figure 1: Inappropriate medication identification procedure

2.3. Inappropriate medication data analysis

To measure the drug duration of a specific inappropriate medication, we calculated a drug duration score (DDS) for inappropriate medication defined by formula (1):

$$DDS_j = \frac{\sum n_{D_i \in IM_j}}{N_{PS_j}}, \quad (1)$$

where IM_j is a specific inappropriate medication and N_{PS_j} is the total number of prescription sheets contained a specific IM_j, and $n_{D_i \in IM_j}$ represents the drug duration administration (days) of IM_j. That is, the DDS is an averaged IM weighted by the drug duration of each administration.

Simply, DDS is the average drug duration of an inappropriate medication for each prescription sheet. For example, the DDS of the inappropriate medication, dicyclomine, is representing the average days that dicyclomine effected an elderly patient when he received a prescription containing dicyclomine.

2.4. Grid-based data analysis system

In Taiwan, there are 533 million hospital visits and 529 million prescription sheets every year on average. These data with patient's profile, diagnosis and other related claims data take up over 200 GB of storage space for one year. To efficiently analyze this huge health claims data, we have developed a Grid-based data analysis system for inappropriate medication identification and analysis.

In the Grid architecture, distributive computing resources can be integrated into a single powerful computational unit. Because the number of computers included in the Grid system is unlimited, it is possible to obtain more computational power by just increasing the hardware. In this study, we used Globus Toolkit [16], which is a popular Grid middleware to integrate 12 Mac Mini computers with a total of 720 GB of storage for building the Grid system. In addition, the MySQL DBMS was used to manage the data of NHIRD and to establish the data center. The system architecture is shown in Figure 2.

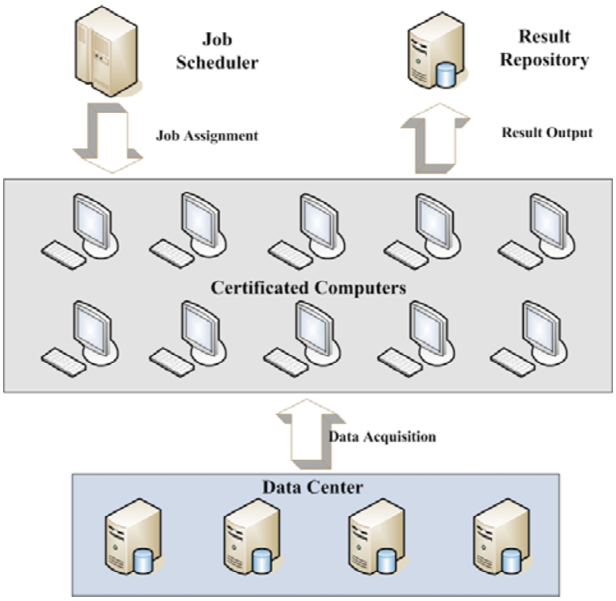

Figure 2: Architecture of the Grid-based data analysis system

In Figure 2, the job scheduler that controls program allocation, job submission, error detection and correction manages the processes of inappropriate medication identification and data analysis. NHIRD data are stored and organized in the data center, which consists of 4 database servers for load sharing. The analytical results calculated by all computers are saved in the result repository.

3. Results

We used 12 Mac Mini computers, 4 disk raids to store the NHIRD, and one result repository database to build the Grid system. In this system, it took about 2 hours to retrieve medication information of patients aged 65 years and older from every single prescription sheet and calculate inappropriate medication events for 1 year of NHIRD data, which contained more than 1.2×10^9 prescriptions. Table 1 shows the number of prescription sheet received by elderly patients and by the whole population of patient from 2000 to 2002. In Taiwan, elderly people (n = 1,975,322) are 8.82% of total population (n = 22,401,005) on average, however elderly patient received 17.94% of total prescription sheets on average.

Table 1: Prescription sheet (PS) distribution of elderly patients and the patient population from 2000 to 2002.

Year	No. of PS received by elderly patient	No. of PS received by all patient	%
2000	93,236,719	568,843,314	16.39
2001	93,223,821	511,190,370	18.24
2002	97,323,170	506,940,349	19.20

Although Zhan et al selected 33 drugs from 1997 Beers criteria as potentially inappropriate medications; we only found 28 inappropriate medications in the NHIRD. Table 2 shows the numbers, rates and DDSs of use in elderly patients of the 28 potentially inappropriate medications in Taiwan from 2000 to 2002. There were 68.79% of elderly patients on average received at least one of 28 drugs identified as inappropriate medications. For the 3 categories of inappropriate medication defined by Zhan et al, there were 14.88% of elderly patients on average received at lease one of 9 drugs classified as "should always be avoided"; 40.45% of elderly patients on average received at least one of 6 drugs classified as "are rarely appropriate"; and 51.70% of elderly patients on average received at least one of 13 medications that may "have some indications". In the "should always be avoid" category, dicyclomine was the drug that the most elderly patients (10.09% on average) received. Diazepam (23.36% on average) and chlorzoxazone (23.05% on average) were the medications that the most frequently used by elderly patients in the "are rarely appropriate" category. Furthermore, 31.11% of elderly patients on average received chlorpheniramine that was the most frequently used drug in the "have some indications" category.

Drug duration information is also shown as DDS column in Table 2. The mean value of DDS for chlorpropamide and carisoprodol was 23.01 and 13.83 respectively, which were the highest in the "should always be avoid" and "are rarely appropriate" category. In the "have some indications" category, the top five medications with higher mean DDS values are methyldopa, ticlopidine, dipyridamole, amitriptyline, and doxepin. The mean DDS value of methyldopa was 24.55, which was much higher than the others.

Overall mean rates of any 28 potentially inappropriate medication uses were higher in women (68.03%) than that in men (65.02%). In addition, overall rates of potentially inappropriate medication uses classified by 5 age subgroups are shown in Table 3. The mean rate of use any 28 potentially inappropriate medication was 66.73% in patients aged 65 to 69 years, 68.51% in those aged 70 to 74 years, 68.66% in those aged 75 to 79 years, 66.41% in those aged 80 to 84 years, and 54.39% in those aged 85 years and older. There was 15.44% of patients aged 65 to 69 years received one of medications that should always be avoided, compared with 14.56% of those aged 70 to 74 years, 14.14% of those aged 75 to 79 years, 13.21% of those 80 to 84 years, and 10.31% of those aged 85 years and older.

Table 2: Numbers, rates and DDSs of use in elderly patients of the 28 potentially inappropriate medications in Taiwan from 2000 to 2002.

Drugs	No. of elderly patient			% of total elderly patient receiving drugs			DDS		
	2000	2001	2002	2000	2001	2002	2000	2001	2002
Always avoid	281,178	269,523	270,395	14.91%	13.83%	13.43%	5.96	6.45	6.55
Barbiturates	41,338	31,689	26,696	2.19%	1.63%	1.33%	4.50	5.04	5.41
Flurazepam	11,849	12,641	11,593	0.63%	0.65%	0.58%	15.06	14.95	14.80
Meprobamate	789	776	715	0.04%	0.04%	0.04%	3.12	3.61	3.92
Chlorpropamide	2,006	1,841	1,614	0.11%	0.09%	0.08%	22.72	23.03	23.28
Meperidine	18,963	19,575	22,091	1.01%	1.00%	1.10%	4.83	4.86	4.83
Belladonna	15,455	10,954	10,657	0.82%	0.56%	0.53%	5.21	11.00	6.62
Dicyclomine	195,841	195,363	198,660	10.38%	10.03%	9.87%	5.20	5.53	5.58
Hyoscyamine	6,652	9,750	19,271	0.35%	0.50%	0.96%	3.10	4.51	6.13
Propantheline	33,617	27,943	22,034	1.78%	1.43%	1.09%	7.65	8.89	9.06
Rarely appropriate	786,377	780,802	797,191	41.69%	40.08%	39.60%	8.49	9.30	9.85
Chlordiazepoxide	56,539	45,599	40,725	3.00%	2.34%	2.02%	5.76	6.08	6.46
Diazepam	468,514	447,239	448,760	24.84%	22.96%	22.29%	9.63	10.73	11.53
Propoxyphene	1,359	887	5,553	0.07%	0.05%	0.28%	11.07	5.36	5.89
Carisoprodol	29,118	31,481	33,010	1.54%	1.62%	1.64%	12.88	13.94	14.68
Chlorzoxazone	441,270	448,021	458,444	23.39%	23.00%	22.77%	6.90	7.39	7.64
Methocarbamol	34,831	37,304	39,802	1.85%	1.91%	1.98%	12.69	12.81	13.61
Some indications	1,004,976	1,000,980	1,015,627	53.27%	51.38%	50.45%	11.07	12.00	12.48
Amitriptyline	17,365	17,191	18,012	0.92%	0.88%	0.89%	15.04	15.98	17.11
Doxepin	19,200	29,019	36,570	1.02%	1.49%	1.82%	14.95	14.47	16.61
Indomethacin	154,162	144,289	140,066	8.17%	7.41%	6.96%	7.79	8.32	8.20
Dipyridamole	340,075	329,340	316,144	18.03%	16.91%	15.70%	18.06	19.15	20.00
Ticlopidine	35,092	37,714	38,241	1.86%	1.94%	1.90%	23.06	24.22	24.89
Methyldopa	4,432	3,914	3,302	0.23%	0.20%	0.16%	23.92	24.78	24.95
Reserpine	84,787	77,187	71,762	4.49%	3.96%	3.56%	12.13	13.31	14.38
Disopyramide	464	400	559	0.02%	0.02%	0.03%	10.79	12.26	13.51
Oxybutynin	38,233	43,903	48,122	2.03%	2.25%	2.39%	13.31	14.61	15.97
Chlorpheniramine	610,511	597,087	610,447	32.36%	30.65%	30.32%	5.00	5.40	5.60
Cyproheptadine	174,618	172,985	178,011	9.26%	8.88%	8.84%	5.87	6.10	6.39

Diphenhydramine	2,536	2,474	2,307	0.13%	0.13%	0.11%	3.01	2.96	2.98
Promethazine	2,685	1,181	879	0.14%	0.06%	0.04%	5.92	6.83	8.19
Any class	1,317,155	1,330,676	1,362,262	69.82%	68.30%	67.67%			

Table 3: Overall rates of potentially inappropriate medication use classified by 5 age subgroups in Taiwan from 2000 to 2002.

Age	Always avoid n / %			Rarely appropriate n / %			Some indications n / %			Any class n / %		
	2000	2001	2002	2000	2001	2002	2000	2001	2002	2000	2001	2002
65-69	105,276	99,081	98,729	269,713	258,736	260,380	327,207	312,102	309,450	443,668	432,301	434,020
	16.14%	15.22%	14.95%	41.36%	39.75%	39.44%	50.17%	47.94%	46.87%	68.03%	66.41%	65.74%
70-74	90,917	82,363	86,490	245,403	241,805	241,431	311,023	306,545	302,602	407,480	407,561	407,427
	15.51%	13.79%	14.38%	41.87%	40.50%	40.14%	53.06%	51.34%	50.31%	69.52%	68.26%	67.74%
75-79	57,711	56,574	58,148	158,563	162,071	168,631	208,466	213,981	222,812	267,858	278,314	291,978
	14.95%	13.90%	13.58%	41.06%	39.85%	39.37%	53.98%	52.62%	52.02%	69.37%	68.44%	68.17%
80-84	26,685	28,272	29,938	75,641	80,018	85,936	104,413	111,860	119,808	133,356	143,973	155,072
	13.82%	12.98%	12.82%	37.76%	36.81%	36.81%	52.13%	51.46%	51.31%	66.58%	66.23%	66.42%
>=85	14,712	14,354	14,975	38,637	39,479	4,2082	56,730	5,8984	63,351	73,405	76,725	82,405
	10.73%	10.18%	10.03%	28.19%	28.01%	28.18%	41.39%	41.84%	42.42%	53.56%	54.43%	55.17%

4. Discussion

Many researchers reported their study results about potentially inappropriate medication use in elderly people. Based on 1997 Beers criteria, Rigler et al. [17] analyzed claim data from May 2000 to April 2001 for 3 cohorts of older Medicaid recipients. The rate of any inappropriate medication use ranged from 21% to 48% across the 3 cohorts. Another similar study was done by Simon et al. [18]. They used medication-dispensing data from 10 HMOs to determine rates of potentially inappropriate medication use in elderly persons in the U.S. in 2000 – 2001. Their study was also based on the Zhan's 33 inappropriate medication classifications and found 28.8% of elderly persons received at least one of 33 inappropriate medications. Compared the overall rate of potentially inappropriate medication use estimated in this studies (68.79%) with others, the prevalence of potentially inappropriate medication used by elderly patients in Taiwan was obviously very high.

In Taiwan, it is very easy for patients to seek medical advice and obtain prescription in the outpatient service. From the data of NHIRD in 2000 - 2002, there were 528,991,344 hospital visits and 533,515,227 prescription sheets on average. For a single elderly person, there were 46.87 hospital visits and received 46.80 prescription sheets on average in one year. In addition, elderly people usually suffered multiple diseases and received polypharmacy at the same time from different doctors or even different medical service units. This may provide a reason for that the prevalence of potentially inappropriate medication use in elderly people was comparatively high in Taiwan.

Drugs with the same chemical components may have different brand names and codes in the NHIRD. For examples, dicyclomine has 69 different names and codes in the database. Other drugs that have similar effects may not be included in Zhan's inappropriate medication categories and Beers criteria. For examples, phenobarbital, pyrabital, and amobarbital etc. have the same effect as barbiturates and only barbiturates was listed in Beers criteria. More examinations are necessary to decide if we should include the other medicines. This would cause errors in our calculation. Thus, more analysis may need to perform for solving these problems.

The updated version of 2002 Beers criteria [19] included several new drugs that were not included in the 1997 list. Further analysis should perform to evaluate these drugs used by elderly people. In this study, we followed Zhan's inappropriate medication categories and didn't assess other domains of potentially inappropriate prescribing, such as drug-drug interactions, drug-disease

interactions, and dosage. According to our previous study result, the frequency of drug-drug interaction in one single prescription sheet for elderly patients was 12.76% in one year, which was much higher than other age groups. Thus, it will be very interesting if we can combine drug-drug interaction into the analysis of potentially inappropriate medication use in the future.

The strength of this study is that we are capable of analyzing the nationwide health claims data by the help of Grid. The study result could be a true representation of the potentially inappropriate medication use status of the whole elderly population in our country.

5. Conclusions

The Grid is an appropriate architecture for the task of large-scale data analysis. By the help of the Grid technology, we were capable of using nationwide health claim data to identify and analyze potentially inappropriate medication use in elderly patients. There have been many Grid-based systems and applications for huge data analysis [20-22]. The major benefit of applying the Grid technology is that computational power can be increased without any restriction. Computational units such as personal computers, workstations, or servers are not necessary located at the same place. They can be integrated by the Grid system via Internet. Nakagawa et at. [23] developed a Grid environment includes many PC clusters at different facilities for Magnetoencephalography (MEG) data analysis. Although we only used 12 Mac Mini computers to process the data analysis procedure in this study, we efficiently solved the complicated problem by spending lower costs.

We have successfully applied the Grid technology to analyze the huge health claims data for the task of inappropriate medication identification. The analytical results can serve as a brief representation of inappropriate medication use conditions in elderly people in Taiwan; moreover they can also serve as basic references for further inappropriate medication studies. In addition, although we cannot evaluate the adverse drug event when elderly patients received inappropriate medications, our analytical results can be used as knowledge references to develop a reminding system to improve safety for elderly patient.

6. Acknowledgement

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