Review of the use of defined daily dose concept in drug utilisation research in China

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ABSTRACT

Purpose This study aimed to understand the characteristics of drug utilisation researches (DURs) using concepts of defined daily dose in China and to provide further suggestion for future DURs in China.

Methods DURs using concepts of defined daily dose published in China were identified from China Journal Full-text Database, and in-depth data analysis was conducted for DURs published in every even-numbered year.

Results In total, 2,911 DURs published between 1989 and 2009 were identified, of which 1,268 were included for further data analysis. All studies were hospital-based. Types of drugs commonly assessed in DURs were Anti-infectives for systemic use (34.1%), drugs for Nervous system (25.5%) and drugs for Alimentary tract and metabolism (14.3%). In addition, 63 DURs published in even-numbered year focusing on Chinese Herbal Medicine (CHM) were identified. Commonly used sources of defined dose were Xin Bian Yao Wu Xue/New Materia Medica (83.9%), drug information leaflets (66.8%) and Chinese Pharmacopoeia (52.0%). Common indicators used in DURs include defined daily doses (DDDs), drug utilisation index (DUI) and daily dose cost (DDC).

Conclusion DUR is a popular method to explore the use of both pharmaceutical drugs and CHM in China. The definition of defined daily dose and its related indicators presented in the DURs were highly varied. From this, it follows that DURs with more consistent methodology are highly needed for a thorough understanding of drug utilisation in China. Apart from DURs focusing on the hospital setting, more DURs from other health settings are needed. Copyright © 2012 John Wiley & Sons, Ltd.

KEY WORDS drug utilisation research; defined daily dose; ATC/DDD

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INTRODUCTION

The idea of drug utilisation research (DUR) was initiated in Europe in early 1960s[1,2]. The explanation of DUR given by the World Health Organization (WHO) is “the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences.”[1] Another common description by Wettermark et al. is “an eclectic collection of descriptive and analytical methods for the quantification, understanding and evaluation of the processes of prescribing, dispensing, and consumption of medicines, and for the testing of interventions to enhance the quality of these processes.”[3]

Drug utilisation research is an essential research approach in health services research to understand the drug use pattern (e.g., the extent of use of a certain drug in a certain period of time), to identify early signals of irrational drug use, and to improve the quality of drug use.[1] DUR has been associated with several relevant fields such as pharmacoepidemiology and pharmacovigilance for a better understanding of drug use from a safety perspective[3].

To compare drug use statistics at a general level, a common classification system for drugs and a common unit of measurement are needed. In 1981, the WHO adopted the ATC/DDD system for DUR, which is known as Anatomical Therapeutic Chemical (ATC) classification and Defined Daily Dose (DDD).[2] The abbreviation DDD in block capital is usually referred
to the WHO value. The ATC classification system assigns a unique code to each drug product based on its major specific therapeutic purpose as well as a DDD, which is defined as “the assumed average maintenance dose per day for a drug used for its main indication in adults.” Each DDD links to a specific ATC code and provides common dosage allowance for each drug under one administration route. The value of DDD is decided by the WHO International Working Group for Drug Statistics Methodology. Further details can be found from *WHO Guidelines for ATC classification and DDD assignment* and the Web site of the WHO Collaborating Centre for Drug Statistics Methodology.4

In China, DUR and ATC/DDD were introduced in the late 1980s. Since then, several articles have been published to introduce the concepts of DUR and ATC/DDD.5–7 The first well-recognised DUR in China was conducted by Zou et al. in 1996,8 which used a defined dose system to assess the consumption of drugs in 10 military hospitals in China between 1992 and 1994. The concept of the WHO ATC/DDD was introduced, but the WHO value was not applied for the data analysis. Defined doses were calculated based on the dose recommendations in the *Chinese Pharmacopoeia*9 and/or *New Materia Medica*10.

The information referred in Chinese sources may differ from WHO value. For example, the daily dose for oral administration of paracetamol (WHO ATC Code N02BE01; DDD = 3 g) is documented as “0.3–0.6 g every four hours or four times per day, no more than 2 g per day” in the *Chinese Pharmacopoeia*9 and “0.3–0.6 g per dose, 0.6–0.8 g per day, no more than 2 g per day” in the *New Materia Medica*.10

In China, most DURs are performed at hospitals, and they are based on data including both sales to inpatients and outpatients. This issue was addressed in a well-conducted DUR, which compared 5-year antibiotic use in five children’s hospitals in different cities.11,12 It indicated a problem in gathering population-based data for DUR, which could be due to the lack of a comprehensive drug management system in China. However, there is a lack of detailed investigation on this aspect.

At present, DUR is a common technique in China to assess drug use, and defined daily dose is a popular concept adopted in most DURs. Due to a large population with considerably huge drug consumption, the rational drug use in China has a strong impact on ensuring drug safety. However, little is known regarding the DUR conducted in China from an international perspective, as most studies were published in the Chinese language. There is a lack of information on the characteristics of these DURs and, in particular, to what extent the WHO ATC/DDD concept has been applied. Understanding these characteristics may help to identify the factors that may influence the quality of DUR in China and provide further advice for policy making of rational drug uses.

Against this background, this study aimed to identify DURs that used a concept of defined daily dose published in China, to understand the characteristics of these DURs, and to provide future suggestions, if any, for DURs in China.

**METHODS**

Full-text search was conducted on the China Journal Full-Text Database, the largest online database of Chinese academic journals established by the China National Knowledge Infrastructure (http://cnki.nlic.net.cn/kns50/Navigator.aspx?ID=CJFD).

A search strategy, “Xian Ding Ri Ji Liang or (DDD and (ATC or Jie Pou Zhi Liao Hua Xue Dai Ma))” was developed for collecting potential studies, where “Xian Ding Ri Ji Liang” stands for DDD and “Jie Pou Zhi Liao Hua Xue Dai Ma” stands for ATC codes. Chinese language terms were input by using Chinese characters because Chinese alphabet is only used for pronunciation.

Articles published between 1960 and 2009 were searched. DURs using a concept of defined daily dose were selected by browsing their titles and abstracts; where necessary, full-text was also browsed.

Because there were a large number of publications, to narrow down the number for in-depth analysis, the randomisation approach could be good to reduce the selection bias. However, in this study, full-text articles published in even-numbered year were obtained, as the selection procedure was conducted via online database, and it was considered more time-saving to simultaneously download the articles of interest published in a year during browsing articles.

Types of drugs presented in identified DURs were classified according to the WHO ATC system main groups in the *WHO Guidelines for ATC classification and DDD assignment 2010*.2 Data were analysed via Microsoft Excel 2007. Descriptive statistics (e.g., the frequency of occurrences of each characteristic) were applied for summarising the data.

This is a review article assessing the published literatures of original studies. An ethical approval for human research is not applicable for this study.

Meanwhile, it is important to note that although this study aimed to understand to what extent the WHO DDD concept has been applied, DUR using a concept of defined daily dose does not necessarily mean DUR
that used the WHO DDD value. Defined daily dose may refer to the recommended daily dose published in some authorised references such as Pharmacopoeia or an estimated appropriate daily dose calculated from other clinical practice reference books.

**RESULTS**

In total, 2911 DURs using a concept of defined daily dose were identified. The first available DUR was published in 1989. The number of identified studies in each year varied from 1 to 642 between 1989 and 2009. Figure 1 shows the number of DURs against publication year. All studies were in Chinese language, some of which contain an English abstract. In total, 1268 (43.6%) studies published in even-numbered year starting from 1990 were selected for further data analysis.

**Characteristics of identified studies**

All identified 1268 DURs assessed were obtained from hospital settings. In total, 21.8% (n = 277) studies analysed drugs used in hospitalised patients (different types of wards), 21.7% (n = 274) analysed drugs used in outpatients, and 56.5% (n = 717) analysed the data of both groups. Only a small number (n = 52) of DURs

**Table 1. Number of identified DURs classified by the WHO ATC system main groups**

<table>
<thead>
<tr>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>J Anti-infectives for systemic use</td>
<td>0</td>
<td>0</td>
<td>12</td>
<td>17</td>
<td>28</td>
<td>31</td>
<td>62</td>
<td>103</td>
<td>180</td>
<td>433</td>
<td>(34.1%)</td>
<td></td>
</tr>
<tr>
<td>N Nervous system</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>7</td>
<td>11</td>
<td>36</td>
<td>57</td>
<td>78</td>
<td>123</td>
<td>(25.5%)</td>
<td></td>
</tr>
<tr>
<td>A Alimentary tract and metabolism</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td>12</td>
<td>33</td>
<td>51</td>
<td>74</td>
<td>(14.3%)</td>
<td></td>
</tr>
<tr>
<td>C Cardiovascular system</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>7</td>
<td>3</td>
<td>12</td>
<td>22</td>
<td>54</td>
<td>49</td>
<td>(11.7%)</td>
<td></td>
</tr>
<tr>
<td>M Musculoskeletal system</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>12</td>
<td>6</td>
<td>23</td>
<td>(1.8%)</td>
<td></td>
</tr>
<tr>
<td>L Antineoplastic and immunomodulating agents</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>14</td>
<td>19</td>
<td>(1.5%)</td>
<td></td>
</tr>
<tr>
<td>R Respiratory system</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>10</td>
<td>17</td>
<td>(1.3%)</td>
<td></td>
</tr>
<tr>
<td>H Systemic hormonal preparations, excluding sex hormones and insulins</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>(0.9%)</td>
<td></td>
</tr>
<tr>
<td>P Antiparasitic products, insecticides, and repellents</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>(0.9%)</td>
<td></td>
</tr>
<tr>
<td>B Blood and blood forming organs</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>(0.2%)</td>
<td></td>
</tr>
<tr>
<td>G Genitourinary system and sex hormones</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>(0.1%)</td>
<td></td>
</tr>
<tr>
<td>S Sensory organs</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>(0.1%)</td>
<td></td>
</tr>
<tr>
<td>D Dermatologicals</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>(0.0%)</td>
<td></td>
</tr>
<tr>
<td>Chinese herbal medicine*</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>6</td>
<td>12</td>
<td>40</td>
<td>(5.0%)</td>
<td></td>
</tr>
<tr>
<td>Miscellaneous†</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>8</td>
<td>16</td>
<td>(3.6%)</td>
<td></td>
</tr>
<tr>
<td>Total (%)</td>
<td>2</td>
<td>2</td>
<td>6</td>
<td>19</td>
<td>34</td>
<td>54</td>
<td>102</td>
<td>199</td>
<td>335</td>
<td>515</td>
<td>(100.0%)</td>
<td>1268</td>
</tr>
</tbody>
</table>

WHO, World Health Organization; ATC, Anatomical Therapeutic Chemical; DUR, drug utilisation research.

*DURs of Chinese herbal medicine used in China that was not classified by the WHO ATC system.

†Miscellaneous types of drugs assessed in a single study (e.g., all drugs used in a certain patient group).
compared the drug uses amongst different geographic areas. Most studies aimed at providing a finance-based analysis of the drugs used.

Types of drugs assessed in identified studies were classified using the WHO ATC system main groups. Types of drugs commonly evaluated are anti-infectives for systemic use, drugs for nervous system, drugs for alimentary tract and metabolism, and drugs for cardiovascular system. Table 1 lists the number of published DURs according to the WHO ATC main group classification. Drugs for pediatric uses were analysed in 26 studies.

In total, 5% \( (n = 63) \) were DURs for Chinese herbal medicine (CHM), the number of which increased with years. Types of CHMs include manufactured herbal products and single crude herbs. Moreover, the use of Chinese herbal injections (prepared from herbal extracts) was often assessed (e.g., 27 of 40 DURs for CHM published in 2008 analysed the utilisation of herbal injection).

**Sources of the defined daily dose**

Of all 1268 identified studies, 89.4% \( (n = 1134) \) addressed the sources of defined daily dose used in data analysis, which included Chinese original sources and/or the WHO source (DDD by the WHO Collaborating Centre for Drug Statistics Methodology). In total, 72.9% \( (n = 924) \) of the studies used sources originating from China (i.e., the recommended dose defined by Chinese Pharmacopoeia or other Chinese authoritative reference books), 12.0% \( (n = 152) \) used both the Chinese original and the WHO sources, whereas 4.6% \( (n = 58) \) used only the WHO source.

In most studies, the value of defined daily dose was referred and calculated from multiple Chinese sources. Of all 1076 studies that used Chinese sources, the most common one were Xin Bian Yao Wu Xue (New Materia Medica, 10 83.9%, \( n = 903 \)), drug information leaflets (66.8%, \( n = 719 \)), Chinese Pharmacopoeia \( ^9 \) (52.0%, \( n = 559 \)), and clinical practice experience (44.4%, \( n = 478 \)). Figure 2 presents the number of studies using different sources. In addition, Lin Chuang Yong Yao Xu Zhi (Clinical Guide to the Chinese Pharmacopoeia), an authoritative supplement of Chinese Pharmacopoeia was used in some identified DURs, which was included and counted as a part of source belonging to Chinese Pharmacopoeia.

In total, 9.5% \( (n = 120) \) of the studies used only a single source (i.e., either one of each Chinese source or the WHO source). Multiple sources including drug information leaflets and clinical experiences were used when the information on the defined daily dose was not available from common authoritative sources such as Chinese Pharmacopoeia.

**Indicators relating to defined daily dose used in DURs**

Several different indicators (Table 2) relating to defined daily dose were presented in identified DURs for data analysis. In some studies, data were presented using the ratio of ranking numbers. Detailed calculation methods are presented in Table 2 with the number of studies that used these indicators.

Defined daily doses (DDDs) was used as a basic indicator for data analysis by all identified studies. Other indicators were calculated based on the DDDs value when more than one indicator apart from DDDs was applied (Table 2). In total, 30.8% of identified studies used DDDs as the only indicator. Figure 3 presents the number of studies using different indicators.

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**Figure 2. Number of drug utilisation researches using different sources of defined daily dose**

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Pharmacoepidemiology and Drug Safety, 2012 DOI: 10.1002/pds
DISCUSSION

Since 1989, the increased number of DURs in China may imply that there is an increasing awareness of the importance of studies on drug use patterns. The large number of DURs could provide valuable data for understanding the current utilisation patterns and for reviewing DUR behaviour to instigate better future interventions in China.

Most identified DURs provided useful information and suggestions on rational drug use in China. However, these were conducted using only practice setting data from hospitals, and no study focused on other sources such as community settings, regulatory agency, or drug distributors. This may be due to the feature that a majority of DURs in China were conducted by hospital pharmacy departments. In addition, because the drug management system is currently insufficient, this makes it difficult to undertake population-wide studies.

Other sources of data cannot be neglected to understand the full picture of drug exposure in a particular geographical area. The European Surveillance of Antimicrobial Consumption project14–16 could be a good model of DUR, which has collected data on antibiotic use in different settings in 34 countries in Europe such as ambulatory care,14 hospital care,15 and nursing homes16. Another well-recognised DUR is a comparison study analysing antibiotic use in 1997 amongst 15 European countries by Cars et al.,17 where data were obtained from other sources.

Moreover, future study is necessary to understand the reason there is a lack of DUR using other types of data sources in China. Apart from community healthcare centres/clinics, the initiatives on assessing the utilisation amongst community pharmacies could be considerable to provide a comprehensive picture in China.

In many identified DURs, DDD was used as an abbreviation of the term defined daily dose, irrespective of whether the values of defined dose used in the study were from the WHO ATC/DDD Index. DDD in block capital is a defined abbreviation used by the WHO ATC/DDD system, and it is inappropriate to directly use the term “DDD” when the defined dose was calculated from other sources.

Sources for calculating defined daily dose varied. Most were Chinese originals and in Chinese language. The concept of the WHO ATC/DDD index was commonly introduced, but the value of the WHO DDD was rarely applied, despite the fact that a Chinese

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Calculation method</th>
<th>Number of studies (%, n = 1268)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDDs</td>
<td>DDDs = overall amount used in a certain period of time/defined daily dose</td>
<td>390 (30.8%) using only DDDs</td>
</tr>
<tr>
<td>DUI</td>
<td>DUI = DDDs/number of days of drug usage</td>
<td>453 (35.7%)</td>
</tr>
<tr>
<td>DDC</td>
<td>DDC = total cost of drug in a certain period of time/DDDs</td>
<td>392 (30.9%)</td>
</tr>
<tr>
<td>Ratio of ranking number</td>
<td>For example, the ratio of sales ranking number to DDDs ranking number</td>
<td>105 (8.3%)</td>
</tr>
<tr>
<td>AARG</td>
<td>AARG = [(data for the ending year / data for the beginning year)^(ending year - beginning year) - 1] × 100%; data may represent either cost of drug or amount of drug</td>
<td>33 (2.6%)</td>
</tr>
</tbody>
</table>

DUR, drug utilisation research; DDDs, defined daily doses; DUI, drug utilisation index; DDC, daily dose cost (sometimes referred as DDDc: defined daily dose cost); AARG, average annual rate of growth.

Figure 3. Number of drug utilisation researches using different indicators
language version of the WHO ATC/DDD index was published in China in 2003.18 Furthermore, the process of assigning a defined daily dose was not transparent in most of the studies. For example, the value of defined daily dose based on the clinical experience could differ, which could cause difficulties when comparing utilisation in different regions.

Amongst identified indicators, daily dose cost (DDC) were originally initiated in China in a large-scale study by Zou et al. in 19968. Since then, DDC has been applied in nearly one third of DURs in China. The possible reason for using this indicator could be that it could provide advices for price policies of pharmaceutical products on the market.8 In most studies, the population denominator for indicators was not recognised (e.g., in some inpatient studies, DDDs were not found to be presented as DDDs per 100 bed-days).

Other problems include inconsistent definition of defined daily dose, different or unclear calculation approaches (based on various domestic or unauthorised sources) to defining a daily dose, and diverse methodologies to generate indicators for data analysis. Similar methodological problems have been found in a European study conducted by Rønning et al. in 2003.19 The study showed that the assignments of defined daily dose were divergent and that unofficial defined daily dose and different versions of ATC/DDD were used in the DURs of antibacterials in Europe. This may indicate that potential similar problems exist in DURs across different countries, and the inconsistency of study methodologies could make interregional or international comparisons of drug utilisation difficult.

Apart from pharmaceutical drugs, DUR has been applied to CHM, in particular, to evaluate the safety of Chinese herbal injections20,21 because there is an increasing awareness of high-profile safety problems associated with these injections in China.20–22 However, most conducted DURs of CHM were limited to a small-scale comparison, and the value of defined daily dose was self-made by using drug information leaflets and clinical experiences without presenting a clear calculation process.

The official WHO DDD is only applicable for a drug when an ATC code is assigned.4 Currently, there is no feasible international standard for DDD for traditional medicines including CHM due to the difficulties of ATC assignment. The Uppsala Monitoring Centre (UMC; the WHO Collaborating Centre for International Drug Monitoring) launched a herbal ATC (HATC) project in 2002 and published a guideline of herbal ATC index in 200423. Certain ATC codes were assigned for common medicinal herbal species used in the Western countries.

At present, there is no consistent HATC coding system amongst East Asian countries, although most of their traditional formulae are derivatives of ancient CHM. In Japan, an attempt was made to assign ATC classification on Japanese traditional medicine (Kampo), where a provisional HATC coding system of 228 Kampo formulae was developed24. This project revealed that one unique code according to the Western medical ATC categories could be assigned to only 20% of the formulae (traditional therapeutic classification was required for the rest of the formulae). Herbs used in East Asia are employed for different traditional indications, and Western ATC classification may not be completely feasible for coding traditional East Asian medicines. Developing a convincing classification and coding system for East Asian herbal medicine is necessary via harmonisation and collaboration within these countries.

Overall, this study is the first of its kind in describing major characteristics of DURs conducted and published in China. As this study mainly focused on the concepts of defined daily dose, it did not look into the details of the other characteristics including exact types of patients, the number of patients, and types of wards such as medical surgical wards and intensive care unit. Future studies are recommended to improve these issues.

This study involved DURs that adopted a defined daily dose concept rather than DURs using the other methods, which may present a limitation of understanding a complete view of methodologies used in DURs in China. Future study is necessary to estimate the popularity of defined daily dose concept as well as other methods amongst DURs in China.

Nevertheless, this study has identified several factors that could affect the quality of DUR in China. For future feasible cross-national studies between China and other countries, it is necessary to avoid the confusion of using various versions of defined doses. To make each DUR more applicable for comparison uses of drugs, it is important to encourage the use of WHO DDD as one standard in China. Future actions such as educational course are suggested to introduce the use of WHO concepts amongst Chinese healthcare professionals.

CONCLUSION

In China, DUR has become a popular research tool used for exploring the use of drugs. However, apart from hospital-based data, there is a lack of DURs in other settings. Methodologies used to assess drug utilisation are inconsistent, as the definition of defined daily dose varied by using unauthorised sources or
sources based on personal experiences. Future high-quality DURs with consistent methodology are needed for DURs conducted in China to reach an international capacity.

In addition, DUR has been recognised as a scientific approach to evaluate the use of CHM, which may imply that it is necessary to develop of a feasible classification and coding system for traditional medicines.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

KEY POINTS

- This study is the first of its kind in presenting the characteristics of drug utilisation researches (DURs) that used defined daily dose concepts in China.
- Drug utilisation studies in China tend to focus on practice setting data from only hospitals including inpatients and/or outpatients data.
- Main factors that affect the quality of DURs in China were inconsistent methodologies including using various definitions of defined daily dose.
- Future high-quality DURs are needed, particularly DURs using different types of data sources.

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REFERENCES