http://jhmi.sums.ac.ir
Health Man & Info Sci 2021, 8(3), 149–158

HMIS
Health Management and Information Science

Review Article

Drug Classification Systems: Applications and Characteristics

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Abstract

Introduction: The quality management and financial control of drugs have been considered as a priority for healthcare managers. The drug classification and coding systems, as an information management tool, could be beneficial. The review aims to extract the characteristics of the drug classification systems and identify their main applications in the drug management processes. **Methods:** For this purpose, the library sources including e-databases PubMed, Scopus, Web of Science, and Google Scholar search engine, e-files, and specialized websites were searched using keywords "Drug", "Classification system", "Coding system", and "Terminology" alongside their synonyms. The search results were limited to the drug classification systems that categorize drugs and pharmaceutical information using code sets with an appropriate granularity level.

Results: Twenty-eight drug classification systems were included. Half of these systems are used internationally, and the others are used nationally. All included systems were divided into three categories, based on their features. The domain classification of systems includes human drugs, animal drugs, herbal medicines, dosage forms, drug side effects, and ingredients of medicinal products. Most of them are hierarchically designed. The code structure of these systems was mainly numerical, and some of them were alphabetical-numeric or alphabetical. They are mostly applied for unique identification, interoperability, statistics, pharmacovigilance and drug-related problems, marketing, and artificial intelligence methods.

Conclusion: The drug classification systems are designed in different ways with respect to their applications. The development of multipurpose systems and provision of efficient mapping among these systems could be beneficial to improve the drug management processes.

Keywords: Drug, Coding, Classification, Terminology, Information management.

Article History:
Received: 24 April 2021
Accepted: 20 September 2021

Please cite this paper as:
Safdari R, Esmaeili M, Marashi Shooshtari SS, Javanmard Z. Drug Classification Systems: Applications and Characteristics. Health Man & Info Sci. 2021; 8(3): 149-158. doi: 10.30476/jhmi.2022.91329.1083.

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Introduction

According to Statista's report, drug costs which account for a large portion of the costs of the healthcare industry have been increased around the world and are predicted to reach 1.52 trillion dollars by 2023 (1). The growth of the drug costs could be due to factors related to the growth of aging, increasing demand, increasing life expectancy, increasing chronic diseases, medical advancements, and production of new drugs for treating special diseases, as well as drug errors and their side effects (2-5).

Therefore, the quality management and financial control of drugs have been considered as a priority for healthcare managers. Medical information classification and coding systems as an information management tool (6), could facilitate the exchange of this information for research, statistics and reimbursement purposes through transforming medical information into structured codes, (7, 8). Thus, these tools could be applied for managing the drugs.

There are diverse tools including classification systems, terminologies, dictionaries, thesauruses, and ontologies related to drugs that have been developed at the international or national levels and are widely used in different countries (9). The classification systems have been designed to classify drug products and information into the predefined levels, so comparing the gathered information about drug usages would be possible (10). Besides, the terminologies have been developed to identify drug products uniquely and can facilitate interoperability among different systems (11, 12). The drug classification systems are designed with different structures since they are utilized for various purposes. For example, the USC, as a drug classification system, has been developed in North America to provide information to drug manufacturers about the state of the drug markets and their competitors (13). Another one, the AMT as a drug terminology, has been developed in Australia to identify and describe drug products nationally (14).

There are several studies (7, 15-17) that have addressed the drug classification system from various aspects. In a study (15) on evaluation of the terminologies used in coding allergy information, five drug terminologies including SNOMED-CT, NDF-RT, MedDRA, UNII, and RxNorm were studied and compared. Also, in an other study (16), the challenges of mapping among drug terminologies, their applications, and characteristics such as information domain and structure were investigated.

Although several studies have addressed the drug classification systems, due to the multiplicity of the drug classification systems developed nationally and internationally and in order to have a comprehensive picture of them, this study aimed to review the common drug classification systems, their characteristics and applications in the drug management process at international and national levels.

Methods

This study was conducted to identify the drug classification systems and compare their characteristics and applications in 2020. A comprehensive search was done without any time limits through different sources including e-databases, journals, books, reports, electronic files as well as specialized websites and websites related to the ministry of health of some developed countries. At first, the e-databases PubMed, Scopus, Web of Science, as well as Google Scholar search engine were searched to retrieve papers that introduce one (or more) drug coding and classification system. Then, other sources were searched to find more related systems. The search consists of the keywords including "Drug", "Classification system", "Coding system", and "Terminology" alongside their synonyms, such as "Pharmaceutical Products", "Pharmaceuticals", "Taxonomy", "Dictionary", "Clinical coding", and "Nomenclature". The drug classification systems were selected based on the criteria including having code sets for the categorized drugs and classifying the drugs in precise classes with the appropriate granularity level. Then, their features were extracted. The ones about which we could not obtain sufficient information, even after making correspondence with their respective organizations, were excluded from this review. Afterward, to compare the included systems, their characteristics and applications were tabulated. These features contain release date, updating period, developer organization, application level, classification domain, basic framework, general structure, and code structure.

Results

Thirty-two drug coding systems were identified from searching for the library sources. Most of the systems (twenty-two) were found through the review of about 125 articles, while the others were identified from other sources.

At first, these systems consisted of 11 drug-specific classification systems, 12 drug-specific terminologies, and 9 non-drug-specific coding systems. After that, 2 drug-specific classification systems (GPI and BNF) and 2 drug-specific terminologies (SDD and WHODrug Global) were excluded from the study due to the lack of access to the desired information. Finally, 28 drug coding systems were included to be investigated and compared to each other.

All included systems were divided into three categories: drug-specific classification systems, drug-specific terminologies, and non-drug-specific coding systems; their characteristics are shown in Tables 1, 2, and 3, respectively.

Drug-specific Classification Systems

The results showed that most of the Drug-specific classification systems (7 of 9 systems, about 78%) were accepted internationally. Two classification systems are just used at the national level. These systems are hierarchically designed in a multilevel structure. In addition to the classification of human medicines, the classification domain of the systems includes veterinary medicines, herbal medicines, dosage forms, and drug-related problems (DRPs).

Table 1: The characteristics of drug-specific classification systems

Abbreviated Name	Release Date (Updating Period)	Developer Organization	Application Level	Classification Domain	Basic Framework	General Structure	Code Structure
ATC/DDD (18)	1976 (Annually)	WHO Collaborating Centre for Drug Statistics Methodology (WHOCC)	International	Human Medicines	AT-EphMRA	Hierarchical, 5 levels	Alpha-numeric, 7 Characters
ATCvet (19, 20)	1989 (Annually)	WHOCC	International	Veterinary Medicines	ATC-WHO	Hierarchical, 5 levels	Alpha-numeric, 7 Characters
HerbalATC (21)	Not available (Twice a year)	Uppsala Monitoring Centre (UMC)	International	Herbal Medicines	ATC-WHO	Hierarchical, 5 levels	Alpha-numeric, 7 Characters)Expandable to 9 characters(
AT-EphMRA (22)	1971 (Annually)	European Pharmaceutical Market Research Association (EphMRA)	International	Human Medicines	Does not have	Hierarchical, 3 levels (sometimes 4 levels)	Alpha-numeric, maximum 5 characters
NFC (23)	1985 (Annually)	The EphMRA NFC Committee	International	Dosage Forms	the Three Letter Code (TLC)	Hierarchical, 3 levels (with set of rules)	Alphabetic, 3 letters
AHFS (24)	1959 (Annually)	American Society of Health-System Pharmacists (AHSP)	International	Human Medicines	Drug classification system used in the University of Michigan's Hospital Formulary	Hierarchical, 4 levels	Numeric, 6 digits
USC (13)	1975 (Not available)	IQVIA company	National (America)	Human Medicines	No basic framework	Hierarchical, 4 levels	Numeric, 5 digits
CFT (7)	Not available	Ministry of Health	National (Portugal)	Human Medicines	ATC-WHO	Hierarchical, 4 levels (Expandable to 5 levels)	Numeric, maximum 6 digits
PCNE (25)	1999 (Not available)	Pharmaceutical Care Network Europe	International	Drug Related Problems (DRPs)	No basic framework	Hierarchical, 2 levels	Alpha-numeric, 3 Characters

Drug-specific Terminologies

This category includes ontologies, terminologies, dictionaries, and vocabularies related to drugs that are named in this study as the drug-specific terminologies. Most of them (8 of 10 systems, 80%) are developed and used nationally. The structure of the drug-specific terminologies is also hierarchical and multilevel, and about 60% of them are based on a model. These models are made of two main elements - concepts and their relationships - to describe drug substances in various levels including medicinal/generic product, trade product, unit of use, medicinal/generic product pack, and trade product pack (14, 26, 27). The NDF-RT terminology has an ontological structure in addition to the hierarchical structure and consider multiple axes such as chemical structure, mechanism of action, physiologic effect, therapeutic intent, pharmacokinetics, VHA drug class, and dosage form for identifying the drugs completely (12). It is worth mentioning that NDF-RT has been replaced with MED-RT terminology in 2018 (28). The MED-RT, as a developed replacement, has been designed based on the same concepts and relationships of NDF-RT (29).

Non-drug-specific Coding Systems

This category contains the coding systems that classify the concepts in other healthcare industry; however, some chapters or sections are included in

Table 2: The characteristics of drug-specific terminologies

Abbreviated Name	Release Date (Updating Period)	Developer Organization	Application Level	Classification Domain	Basic Framework	General Structure	Code Structure
AMT (14)	2009 (Monthly)	The National Clinical Terminology Service (NCTS)	**National (Australia)**	Human Medicines	SNOMED-CT	Hierarchical, Based on AMT relational model)As a part of SNOMED-CT-AU)	**Numerical identifiers,** 17 digits
NZMT(26, 30)	2011 (Not available**)**	New Zealand Ministry of Health	National (New Zealand)	Human Medicines	SNOMED-CT	Hierarchical, Based on the NZMT Model (As a part of NZ Universal List of Medicines-NZULM)	**Numerical identifiers,** 17 digits
TMT (27, 31)	2013 (Twice a month)	Thai Health Information Standards Development Center (THIS)	National (Thailand)	Human Medicines	SNOMED-CT	Polyhierarchical, Based on TMT model	Numerical identifiers, 6 digits (TMTID)
HKMTT (32)	2013 (Monthly)	The eHR Information Standards Office (eHRISO)	National (Hong Kong)	Human Medicines	SNOMED-CT	Multi-Hierarchical, Based on HKMTT model (As a part of Hong Kong Clinical **Terminology Table (HKCTT))**	Numeric identifier (ConceptID), 5 digits + SNOMED-CT Identifiers
DM&D (33)	Not available (Annually)	NHS Business Service Authority (NHSBSA)	National (England)	Human Medicines	SNOMED-CT	Based on DM&D Model	SNOMED-CT Identifiers
RxNorm (34)	2004 (Monthly)	U.S National Library of Medicine (NLM)	National (America)	Human Medicines	No basic framework	Based on RxNorm Model	**RxNorm concept unique identifier (RXCUI)**
MedDRA (35, 36)	1999 (**Twice a year)**	**The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)**	International	Adverse Drug Reactions (ADRs)	**Medical Dictionary for Drug Regulatory Affairs (MEDDRA)**	**Multiaxial, Hierarchical, 5level**s	**Numerical, 8 digits**
WHO-ART (37, 38)	1968 (Once every three months)	Uppsala Monitoring Centre (UMC)	International	Adverse Drug Reactions (ADRs)	No basic framework	**Hierarchical, 4levels**	**Numerical, 7 digits**
NDF-RT*(39)	2003-2018 (Monthly) *Replaced with MED-RT	**U. S Department of Veterans Affairs, Veterans Health Administration (VHA)**	National (America)	Human Medicines	**VHA National Drug File (NDF)**	**Multiaxial, Hierarchical**	Alpha-numeric, 5 Characters (VA Class)
NDC (40)	1972 (Daily)	Food and Drug Administration (FDA)	National (America)	Human Medicines	No basic framework	As a part of NDC Directory	Numerical, 10 digits (Three-Segments)

Table 3: The characteristics of non-drug-specific coding systems

Abbreviated Name	Release Date (Updating Period)	Developer Organization	Application Level	Classification Domain	Basic Framework	General Structure	Code Structure	Drug-related parts
ICD-10 (44)	1990 (Annually)	World Health Organization (WHO)	International	Diseases & Health Related Problems (Including medicines and adverse drug reactions)	Previous Versions	Three volumes, Hierarchical	Alpha-numeric, Up to 5 digits	Chapter 19: T36-T50: Poisoning by drugs, medicaments and biological substances Chapter 20: Y40-Y59: Drugs, medicaments and biological substances causing adverse effects in therapeutic use
ICPM (48)	1978 (No updates)	World Health Organization (WHO)	International	Medical procedures (Chapters 6 & 7: Coding of drugs used in prescriptions)	ICD-9 (Section: 960-979)	Two volumes (Chapters 1,2,4,5,8 and 9 in volume 1 and chapters 3,6 and 7 in volume2)	Numeric, Up to 6 digits	Chapters 6 & 7: Drug medicaments and biological agent (Range of Codes: 6-00 to 6-99 and 7-00 to 7-99)
UNSPSC (43)	1998 (At least once a year)	GS1 US™ for the UN Development Programme (UNDP)	International	Products and Services (Including medicines)	No basic framework	Hierarchical, 5 levels	Numeric, Up to 10 digits	Segment 51: Drugs and Pharmaceutical Products
JSCC (42)	Not available (No updates)	the Ministry of Internal Affairs and Communication	National (Japan)	Products and Services (Including medicines)	No basic framework	Hierarchical, 6 levels	Numeric, 5 or 6 digits	Subclass "87": Drugs and related commodities
CPV (41)	1993 (There is no specific update plan yet.)	The Office for Official Publications of the European Communities)OPOCE)	International	Products and Services (Including medicines)	Classification of Products by Activity (CPA)	**Consists of a main vocabulary** (5 Levels) **and a supplementary vocabulary (3 Levels)**	**Main vocabulary has Numeric codes with 9digits. Supplementaryvocabulary has Alphanumeric codes with 5characters**	**Division 33: Medical equipment, pharmaceuticals and personal care products. Group 336: Pharmaceutical products**
NHS-eCl@ss (49)	Not available (Not available)	**NHS Shared Business Services**	National (England)	Products and Services (Including medicines	No basic framework	Hierarchical, 3 levels	Alphabetical, 3 letters	Category D: **Pharmaceuticals Blood Products &Medical Gases**
SNOMED-CT (50)	1999 (Twice a year)	SNOMED International	International	Collection of Clinical Concepts (Including pharmaceutical concepts)	Read Codes & SNOMER-RT	**Poly Hierarchy, Consists of:** Concepts, Descriptions and Relationship	Numerical identifiers (SCTID), Between 6 to 18 digits	**Pharmaceutical / biologic product (product) SCTID: 373873005**
UNII (46)	2006 (As required)	Food and Drug Administration (FDA)	National (America)	ingredients in FDA-regulated products	No basic framework	As a part of FDA's Global Substance Registration System	Alpha-numeric, 10 Characters (Identifier)	substances within medicinal products
NCIt (47)	2000 (Monthly)	National Cancer Institute	National (America)	concepts used in cancer research	No basic framework	**Hierarchical, Up to 8levels**	Alpha-numeric, Up to 7 Characters	Section: Drug, Food, Chemical or Biomedical Material

them to code the drugs for different purposes.

The results showed about half of the non-drug-specific systems (4 of 9 systems, 45%) were used in coding products including health products such as medicines and also applied in marketing, e-business, and statistics (41-43). Chapters 19 and 20 of the ICD-10 classification system code the drugs that are related to drug poisoning and drug side effects (44). The classification of drug substances in the ICPM system is used to identify the prescribed drugs in the prescription drug interventions (45). The UNII system that is part of the FDA's Global Substance Registration System can code the drug substances containing the FDA-regulated products (46). The other system that is applied in the cancer research area is the NCIt and a part of this system has identified and coded the drugs (47).

Applications of the Drug Classification Systems

The drug classification systems could be applied in various areas, as shown in Figure 1. Pharmacovigilance (PV) and drug safety monitoring are the two most significant applications of these systems. For these purposes, the coding systems such as MedDRA and WHO-ART that are used for coding drug side effects are widely applicable (51). The systems that have been mentioned in the e-prescribing area are NDC and RxNorm (52, 53). Besides, the drug classification systems and terminologies have been recently applied in processing the texts containing medical information, using text mining and natural language processing (NLP) techniques. The terminologies could be helpful in named entity recognition (NER) and disambiguation. The extracted data through processing the texts could be used for developing clinical decision support systems (CDSS) and computerized physician order entry (CPOE) (54-56). In this review, the study about the applications and characteristics of the drug classification systems reveals that these systems, especially drug terminologies, are beneficial in the unique identification of the drug products and facilitation of information exchange.

Discussion

The aim of this review is to identify and compare the drug classification systems at international

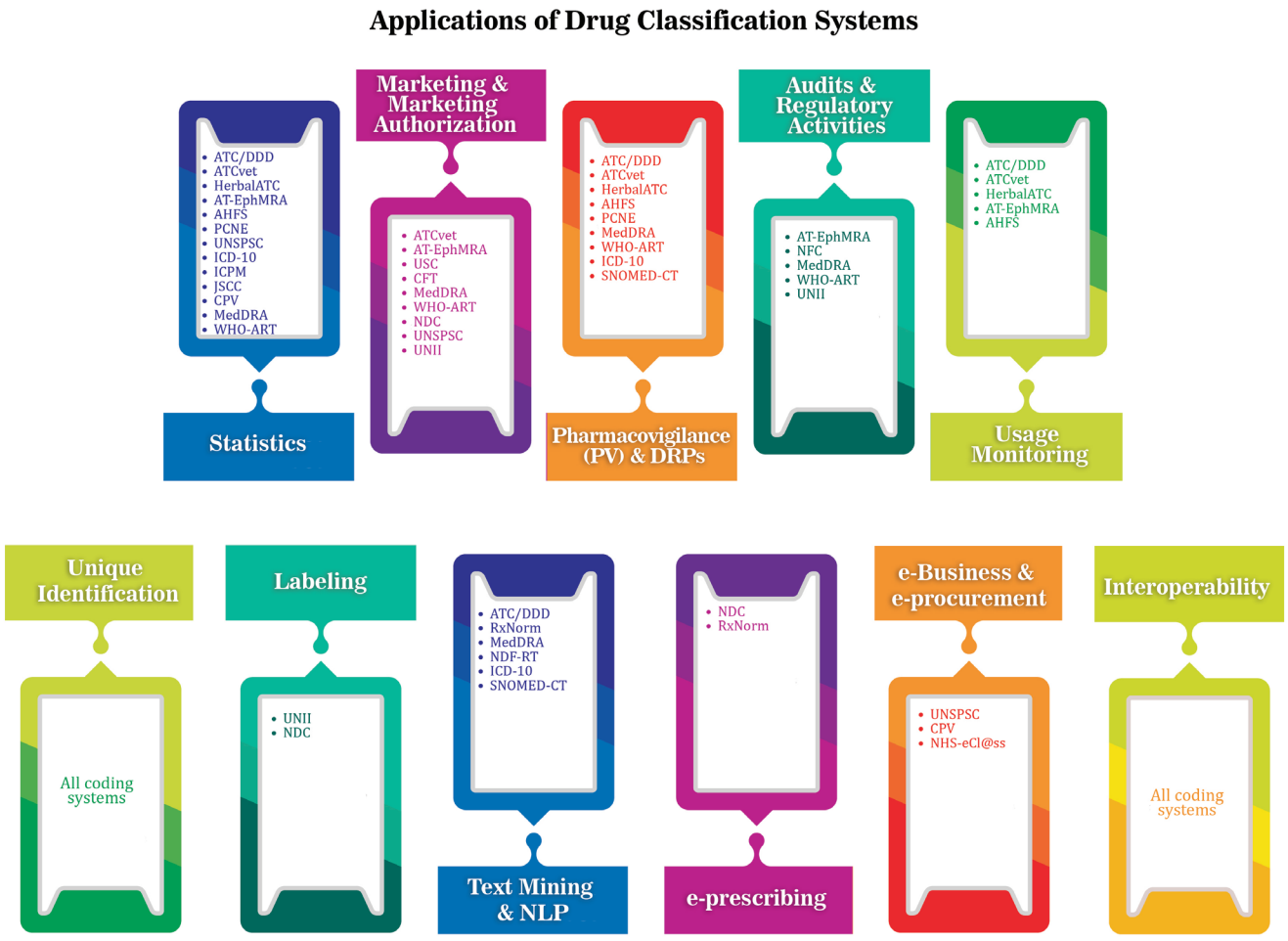

Figure 1: The applications of drug classification systems

and national levels. The most important resources were the websites and articles for identifying the systems, published guidelines from their developer organizations for extracting their characteristics, and the articles. For informing about their applications. Moreover, the coding structure of some systems, such as the CFT, was extracted by reviewing the available codes due to the inaccessibility of the information resources. Therefore, the files related to system codes were also used to extract some features. In (17), MEDLINE and Yahoo were searched, as information resources, to identify and compare DRP classification systems.

A number of the drug classification systems found through the search were excluded from this study. Some of them were used to classify the drugs but did not have a set of codes, so they were not included. For instance, the Australian categorization system for prescribing medicines in pregnancy is part of the prescribing medicines in pregnancy database and classifies the drugs according to their risk during pregnancy in seven categories (57). Also, the NbN nomenclature categorizes the drugs related to neurological diseases, according to their features (58). The other classification systems, that were excluded from this study, classify the drugs generally and sporadically, such as the Canadian NAPCS classification system (59) and the GPC classification system (60), which classify products including goods and services.

The international classification systems could be used in the drug databases and registries, to identify the drugs, such as the DrugBank database, which provides ATC/DDD and AHFS codes of the drugs in addition to the relevant information about them (61). Furthermore, some of the drug databases assign identifiers to the drugs in addition to the international codes, for various goals, for example the Canadian Drug Product Database, which assigns the national drug identification numbers (DIN) to the drugs. These identifiers could be used to identify the drugs that are licensed to sell in Canada (62).

The drug classification systems encode different types of information about the drugs, depending on the purpose and domain of usage. Therefore, in the health system of a country, several drug classification systems may be used simultaneously based on their needs. In addition, numerous classification systems are also applied in different countries or may be used nationally. These issues lead to the allocation of different codes to the drugs and the lack of integrity of the drug coding. Since data integration is essential for exchanging information and providing statistics about the rate of drug consumption and prescription, mapping among these systems is required. Developing the mapping methods could eliminate the barriers to adoption of new classification systems (8). Currently, the possibility of mapping across a number of drug classification systems has been provided through the Unified Medical Language System (UMLS) and the RxNorm system (45, 63). The SNOMED-CT, ATC/DDD, MedDRA, and ICD-10 have been used in these systems as the source vocabularies (34, 64).

Conclusions

We concluded that the drug classification systems are designed in different ways with respect to their applications. However, it would be efficient to develop a comprehensive, integrated classification system with granularity and additional axes along with the advancements of mapping methods. It would be possible to improve the process of drug management using integrated drug classification systems. Therefore, it is recommended to design a multipurpose electronic system to widely classify the drugs and relevant information. Also, instead of developing a separate system for missing information such as traditional medicine drugs, it is suggested that a system such as the ATC/DDD classification which is highly accepted should be added and integrated with it More over, providing comprehensive drug information is efficient for improving vocabulary-based text mining algorithms.

Limitations

Although the comprehensive search was conducted through many pertinent resources, it might be possible that many drug classification systems have been missed or excluded. Some of them have been nationally developed in different countries and their descriptions are written in non-English languages. Also, lack of access to complete information about the characteristics of a number of systems is the second limitation of the present study.

Acknowledgements

This study was part of a MSc thesis supported by Tehran University of Medical Sciences under grant no. 280/3/F/104. The authors would like to gratefully acknowledge all those who contributed to this study.

Authors' Contributions

R.S. and Z.J. contributed to the study concept and design. Also, Z.J. contributed to the literature search, screening, and data extraction. The methodology was examined and approved by other authors. The first

draft of the manuscript was written by Z.J. and M.E.; they critically revised it. Finally, all authors revised the final manuscript and approved it.

Conflict of Interest: None declared.

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