

Research on the construction of a knowledge graph of COVID-19 based on Chinese medicine prescriptions

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Abstract. In order to explore the method and general steps of knowledge mapping for mining the prescriptions of novel coronavirus, and to verify the applicability of knowledge mapping in the diagnosis and treatment of novel coronavirus. In this paper, we collected 75 TCM prescriptions published by national and local TCM administrations, and obtained data on the names, tongues and pulses of TCM. The data were analyzed based on the Neo4j database, and the knowledge graphs were constructed based on the rules of association. The research results, on the one hand, achieved explicit expression of the implicit knowledge of Chinese medicine in the prevention and treatment of neocrown pneumonia, such as drugs, symptoms and correlations, and provided a basis for the future construction of an intelligent auxiliary information system based on knowledge mapping, and provided ideas for the application of knowledge mapping in other public health events.

Keywords: COVID-19; Neo4j; Traditional Chinese medicine; Knowledge graph; Prescription.

1 Introduction

In December 2019, several cases of unexplained pneumonia with a history of exposure to seafood markets in South China were identified in some hospitals in Wuhan, Hubei Province, and the disease developed rapidly and spread nationwide. The outbreak and spread of the disease was also reported in several countries and regions worldwide. After the outbreak of the new coronavirus epidemic, the national and provincial health committees and TCM administrations organized experts and scholars in the field of TCM to prepare a prevention and treatment protocol for the new coronavirus pneumonia, which was revised several times. Based on the national program, each province and some regions have also issued "localized" and "individualized" TCM prevention and treatment programs for new coronavirus pneumonia, taking into account the characteristics of the population in each region. As of March 2022, the national program has been updated from the third edition to the ninth edition, and the provinces and regions have been continuously updated and revised. After the release of the TCM and prevention and treatment protocols, all provinces and municipalities have been actively exploring the strategies of TCM to prevent and treat NCCP and applying them to clinical treatment. Because TCM experts in different provinces and municipalities have different criteria for judging and using the evidence and medication, the public does not have access to comprehensive TCM treatment protocols for NCCP, and there is an urgent need for a way to synthesize the treatment protocols of individual provinces and municipalities to better visualize the invisible knowledge of TCM in the prevention and treatment of NCCP. Therefore, this paper aims to collect the TCM prescriptions published by national and local TCM administrations, standardize the data of TCM names, tongues and pulses, and construct a knowledge graph with the help of Neo4j to systematically and comprehensively express the invisible knowledge of TCM in the prevention and treatment of neoconjunctivitis, and provide support for TCM practitioners in the treatment and decision-making of neoconjunctivitis.

2 Related Studies

2.1 TCM Industry Knowledge Map

The research and application of medical knowledge mapping in several aspects of TCM, such as basic theory, clinical support, and prescription and medication, is developing rapidly ^[1]. Research on knowledge mapping in TCM ^[2] is roughly divided into two categories, namely, scientific knowledge mapping and semantic knowledge mapping, which differ in their conceptual aspects; one is a visual analysis of the literature, while the other aims to describe the relationships between entities.

2.1.1 Application of scientific knowledge mapping.

Scientific knowledge mapping belongs to bibliometrics, which is evolved from scientific knowledge maps and extended and extended by Liu Zeyuan et al. in 2004 ^[3], among which Citespace, VOSviewer, Ucinet NetDraw, etc., which are often used to measure the field of TCM, are all tools of scientific knowledge mapping. The above methods can be used in the mapping of TCM science to complete the mapping through eight steps: retrieval, pre-processing, selection of knowledge units, construction of unit relationships, data standardization, data analysis, knowledge visualization, and mapping interpretation.

In this paper, we use KY=('Citespace'+'Histcite'+'VOSviewer'+'Ucinet'+ 'Bibexcel'+'SPSS'+'TDA'+'Sci2Tools'+'WordSmith'+'Knowledge map') AND TKA=('ZhongYi'+'ZhongYao'+'ZhongYiyao') as the search formula, and 436 valid journals were obtained by searching the journal literature in the China Knowledge Network database (CNKI), and bibliometric analysis was performed on these journals. The analysis results show that scientific knowledge mapping is more commonly applied in the analysis of hotspots and trends of diseases such as novel coronavirus, diabetes and hypertension. In terms of analysis tools, Hongzheng Lu^[4], Rongquan Xu^[5], and Zhong Li^[6] used Citespace to analyze chronic urticaria, osteoporosis, and new coronavirus pneumonia, and Fumin Wang, Yuanzhang Hu, Man Jin, Sihan Sun, Menglin Wang, and Xiaoen Cheng ^[7] used VOS viewer to study the field of Chinese medicine against respiratory infectious diseases.

2.1.2 Application of Semantic Knowledge Graph.

In the perspective of TCM, knowledge can be discovered and problems can be analvzed from relationships, where Neo4j graph database is an important tool for semantic knowledge mapping. When constructing semantic knowledge graphs in TCM, there are four main processes: knowledge extraction, representation, fusion, and knowledge computation and inference. Data are extracted from unstructured, semi-structured as well as structured data sources, knowledge representation is performed using RDF triples, and integration and fusion work is performed on knowledge from different sources and forms to facilitate knowledge inference, so that more knowledge can be obtained and the knowledge base can be extended [7-8]. Semantic knowledge graphs are less applied compared to scientific knowledge graphs and are still in the exploration stage, among which RDF datasets are generally represented in the form of triads in the field of Chinese medicine, and the most applied in semantic knowledge graphs is the graph database Neo4i. Neo4i has a wide range of applications in the field of Chinese medicine such as scripture mining, adjuvant therapy, and medical case mining, e.g., Chen Shanda, Xia Shuaihua, Deng Wenxiang, Li Liang, Yan Junfeng^[9] et al. studied coronary heart disease in the field of TCM by Neo4j, and Zhao Yanhua, Li Yue, Zhang Jianxun^[10] used Neo4j to analyze and study the TCM-like influenza.

Comprehensive current research status shows that research work on knowledge graphs has been widely penetrated into the field of TCM research, and a stable development vein has been gradually formed. By studying the application of knowledge graphs in the field of TCM, we can better break the barriers of interdisciplinary research and inject a strength to the inheritance of TCM culture.

3 Data selection and processing

3.1 Data sources for knowledge graphs

The data of this study were obtained from the prevention and treatment protocols of novel coronaviruses included in the national and provincial health care committees and TCM administrations. Due to the difference in the number and time of revision of prevention and treatment protocols by provinces, cities and regions, this study included protocols collected after August 2021, and the included protocols did not include the prevention and treatment protocols collected in Inner Mongolia and Xinjiang for non-TCM (Mongolian and Tibetan) categories, including provinces and regions in Northeast China (Heilongjiang Province), East China (Shandong Province, Zhejiang Province, Anhui Province), North China (Hebei, Tianjin, Shanxi), Central China (Henan, Hubei, Hunan), South China (Guangxi, Hainan), Southwest China (Sichuan, Guizhou, Chongqing), Northwest China (Qinghai, Shaanxi, Gansu). The publication dates of the revisions of the partially incorporated programmes are shown in Table 1.

Province & Re- gion	Program Name	Release Time
Henan	Chinese Medicine Treatment and Prevention Program for New Coronary Pneumonia in Henan Province	2022.01.08
Hubei	Chinese Medicine Treatment Plan for New Coronary	2021.08.05
Hubei	Pneumonia in Hubei Province (2021 Edition) Chinese Medicine Treatment Plan for New Coronary Pneumonia in Hubei Province (2022 Edition)	2021.08.05

Table 1. Incorporate the program name and revise the publication date.

3.2 Data inclusion and exclusion criteria

The inclusion of the protocols was limited to the TCM prevention and treatment protocols in Table 1 (due to the different names of the protocols in each province and city, they are referred to as "treatment protocols" hereafter). The treatment protocols mentioned in Table 1 were obtained, and the data were extracted by two researchers using an Excel database. Since tongue diagnosis and pulse diagnosis play an important role in TCM dialectical treatment, the data extracted included: province and region where the treatment protocol was published, type of infection, applicable population, type of Chinese medicine, tongue texture, tongue coating, pulse, TCM prescription and medication. After the data were extracted, two researchers checked them several times by:

- creating a database using Excel to store the current treatment protocols,
- classifying the prevention and treatment methods into dietary treatment, aromatherapy (plague prevention) treatment, foot bath treatment, and soup treatment according to the different prevention and treatment methods. At the same time, the treatment plan was divided into three stages: observation period, treatment period, and recovery period,
- since the characteristics of the treatment plan differed from province to province and region to region, for example, the treatment plan for food therapy, aromatherapy, and foot bath may not exist in each region, the author mainly analyzed the treatment plan for the soup category. Among the 26 treatment protocols, children's treatment protocols had less data, and some of them only listed the names of Chinese medicine prescriptions without mentioning the composition and symptoms of Chinese medicine, so children's treatment protocols and protocols without mentioning the composition and symptoms of drug ingredients in the treatment plan but did not mention the addition or subtraction of drug ingredients in the treatment plan but did not mention the addition or subtraction of specific tongue and pulse symptoms were counted according to one prescription; the prescriptions of proprietary Chinese medicines suggested in the treatment plan were not included in the collection of the treatment plan.

3.3 Storage data normalization process

The data on tongue texture, tongue coating, pulse and drugs were obtained by extracting the data from the treatment protocols revised and published by the National and Provincial Health and Health Commissions and the Chinese Medicine Administration (the included data did not include the dosage of drugs, the recommended proprietary Chinese medicines in the protocols, and other clinical symptoms other than tongue and pulse), based on which the Pharmacopoeia of the People's Republic of China (Chinese Pharmacopoeia) 2020 The latest edition and the ancient and modern cloud medical case platform were used to standardize the names, tongue texture and tongue coating of the included Chinese medicines and to disambiguate the semantics, as well as to conduct statistics on the four gi, five tastes and attribution of each Chinese medicine. In this paper, the following data standardization criteria were adopted: for example, raw Coix seed, raw barley, and rice kernel were unified as "raw Coix seed"; Dabei mother and Zhebei mother were unified as (some of the medicines in this paper are not combined because of the difference in the method of preparation and the way of preparation affects to some extent the efficacy, four qi, five flavors, and the generalization of the drug); the tongue is divided into "light tongue", "dark red tongue", "dark red tongue", and "dark red tongue". "(The tongue and pulse symptoms in this article are derived from the treatment protocols of different provinces and cities in China. (The tongue and pulse symptoms in this article are taken from the treatment protocols of different provinces and cities in China, and the understanding and judgment of tongue and pulse symptoms vary from region to region, therefore, the detailed division of tongue color and moss color is not made.)

After normalizing the data of drugs, tongue and pulse, the de-duplication function in Excel tool was used to de-duplicate each of the included data. If the contents of tongue, pulse and drugs are identical, they are marked as duplicate items and only one item is retained (in this paper, the dosage of drugs is not considered, so as long as the ingredients of drugs are the same, they are recorded as the same drugs; if the order of drugs is different, they are recorded as different treatment plans).

4 Building Knowledge Graphs with Neo4j

4.1 Entity-relationship extraction and property setting

4.1.1 Related Named Entity Extraction.

By parsing the data after data normalization, entities such as various types of Chinese medicine, tongue texture, tongue coating and pulse are extracted in the data source. After the entities are extracted, the entities are checked for consistency with the source data to ensure the accuracy of the extracted entities. After the statistical and de-duplication process of the Excel database, the three entities of tongue texture, tongue coating and pulse were obtained; after the statistical, standardization and de-duplication process of the Chinese medicine names contained in 75 different prescriptions, the prescriptions and the Chinese medicine entities were obtained; since the four qi, five tastes and the

attribution of the Chinese medicine can help Chinese medicine practitioners in the clinical use of medicine, this study was conducted to obtain the Chinese medicine entities. In this study, we obtained three types of Chinese medicine entities, namely, the four qi, five tastes, and the five aptitudes, and the aptitudes, by using the latest version of the Pharmacopoeia of the People's Republic of China (Chinese Pharmacopoeia) 2020 and the ancient and modern cloud medical case platform to summarize and de-duplicate the four qi, five tastes, and the aptitudes of each Chinese medicine.

4.1 2 Extraction of relations and setting of attributes.

The knowledge graph is a semantic type network, and the setting of entity relationships and attributes is its focus. The relationship between entities in this study is determined by the knowledge system of novel coronary pneumonia prevention and treatment, and since there are various types of entities such as Drug, Tongue and Mossy in this knowledge graph, the association between various types of entities is more complicated. The overall entity relationship pattern diagram studied in this paper is shown in Figure 1.



Fig. 1. Overall Entity-Relationship Model Diagram.

For example, the entity "Drug" can be connected to the entity "Tongue" or "Mossy" or "Pulse" by "drug_with_symptom". "Mossy" or "Pulse", or "have_four_qi" or "have_five_flavors" or "have_meridians" ifve_flavors" or "have_meridians" with "Four_Qi", "Five_Flavors" and "Meridians" respectively. " and "Meridians" entities respectively, and can also be connected to the "Prescription" entity via "have_drug". " entity. Therefore, this study contains 8 types of nodes, 8 types of labels, and 10 types of basic relationship types. Among the eight types of attribute labels: id represents the node number; name represents the ranking of the number of occurrences of a node; pro1 represents the antecedent or superior term of a node; pro2 represents the posterior or inferior term of a node; support represents the support between two nodes; confidence represents the confidence between two nodes [11].

For example, in the treatment of neoconjunctivitis, doctors often look up the relevant drugs based on the patient's tongue or pulse. The relationship "drug_with_symptom" shows that when the tongue is "dark", the system recommends drugs such as Wu Wei Zi, Angelica Sinensis, Mai Dong, Almond and Roasted Loquat Leaf. By clicking on the node of "almond", we could learn that the frequency (fre) of almond in 75 prescriptions was 24; the number of occurrences (number) was 1, which was the most used Chinese medicine among the 75 prescriptions; "dark tongue The support between the node of "dark tongue" (pro1) and the node of "almond" (pro2) is 4, that is, the symptom of "dark tongue" and the drug "almond" appear at the same time. The probability that the symptom "dark tongue" (pro1) and the node "almond" (pro2) is 100, i.e., the probability that the recommended prescription contains "almond" based on the presence of "dark tongue" is 100%.

In this study, the attributes of support and confidence contained in each type of entity relationship are calculated by the association rule algorithm of SPSS Modeler18. The difference between the support and confidence values in the above examples can also be seen. Support is often used to indicate the probability that two nodes with no direction occur simultaneously. Confidence is used to indicate the probability of the occurrence of a node based on the occurrence of another node. In the knowledge graph constructed in this study, support and confidence are commonly used to discover the association between different clinical symptoms, between different drugs, and between symptoms and drugs. The values of both are obtained to assist TCM practitioners in their drug recommendation work. The table of association rules between some symptoms and drugs is shown in Table 2.

Table 2. Table of association rules between some symptoms and drugs.

Posterior term (pro2)	Pre-item (pro1)	Support	Confidence
Bai Qian Bianxia	Dark tongue dark red tongue	4 9.333333333	33.33333333 28.57142857

4.2 Building a knowledge map of neocoronavirus pneumonia

4.2.1 Entry and storage of relevant data.

The relationship information between the various types of entities and entities mentioned in 3.1 was organized into structured data by Excel, and the relevant attributes and labels of each entity and relationship were set, and the data were stored using the .CSV format. The information of the five flavors of the drugs in this study is shown in Table 3, and the relationship information of the concurrent symptoms is shown in Table 4.

Table 3. The storage format of "Five Flavors" entity in. CSV file.

id	name	fre	number	label
12	Xin	77	1	five_flavors
			•••	

from name	pro l	pro2	to name	support	confidence
Yellowish	Yellowish	Purple-red	Purple-red		
brown moss	brown	tongue	tongue	0.384615385	100
	moss				
					•••

Table 4. The storage format of "with_symptom" relation in. CSV file.

4.2.2 Neo4j-based implementation.

This study uses Neo4j graph database to store entities, relations and attribute properties, and presents the data storage process in the form of a simple graph structure. After storing the data in ".CSV" format, simple code was written to create the entities and relationships (shown in Tables 2 and 3) involved in the tongue and pulse of the novel coronavirus cases using the Cypher language provided by the graphical database for the relationships and attribute statements of the nodes. Neo4j data entry methods include code writing (Cypher Load XXX.CSV statement, Cypher Create statement direct creation) and import bulk import operation in Neo4j. CSV and import bulk import operations (the prepared triad type .CSV data files of entities, relationships, etc. are stored in the import folder of the Neo4j installation directory) ^[12-16]. For example, to build the "Drug" node, the Cypher statement is LOAD CSV WITH HEADERS FROM "file://// Drug.csv" AS line MERGE (p:Drug{id:line.id,name:line.name,fun:line.fun,number:line.number, fre:line.fre, label:line.label}). The MATCH and WHERE statements are used to query the relationships and nodes; the SET statement is used to set the attributes for the nodes; the ORDER BY and DESC statements are used to descend and sort the frequency of drugs and tongue pulse; the LIMIT statement is used to limit the number of nodes or relationships output; the DELETE statement is used to delete the nodes and relationships; the REMOVE statement is used to delete the attributes of the nodes.

4.2.3 Medication and symptom analysis of Chinese medicine prescription for neocrown pneumonia.

(1) Word frequency statistics of the efficacy of each Chinese medicine,

Through the statistical analysis of the number, efficacy, four qi and five tastes and attribution of 180 flavors of traditional Chinese medicine included in the 75 first prescriptions, the frequency of statistical analysis was carried out. Word frequency statistics were performed by using Python to stop the efficacy of 180 flavored Chinese medicines, remove unrelated efficacy words, jieba participle words, and merge synonyms (for example, thirst and quenching thirst into thirst quenching). Through word frequency statistics, we can more intuitively understand the main overall efficacy of 180 flavors of Chinese medicine. The statistical results of the analysis of word frequency can be seen that the efficacy of the traditional Chinese medicine included this time is to treat "cough", "headache", "clear heat", "phlegm", "dry and wet", and there are fewer drugs for symptoms such as spleen deficiency and wind chill, and most of them are occasional symptoms in the diagnosis and treatment plan, which is lower than the frequency of previous symptoms. This is in line with the main manifestations of the onset of the new coronavirus, and at the same time reflects the characteristics of the "dialectical" treatment of traditional Chinese medicine in the treatment of new crown pneumonia.

(2) Statistical analysis of the four qi, five tastes and the attribution of drugs,

For the 75 prescriptions of Chinese herbal medicines included in the analysis of the four qi, five tastes, and attribution, there were many warming drugs in the prescriptions, such as: almond, Chen Pi, Hou Pu, Cang Zhu, Fa Han Xia, and Wu Wei Zi, with a frequency of 52 times. The main effects of these herbs are to dry dampness and detoxify, relieve pain, dispel wind and cold, and stop cough. In clinical medicine, when symptoms such as dryness and dampness appear, priority can be given to warming drugs. This is followed by cold with a frequency of 36 occurrences. This is consistent with the TCM dialectic of COVID-19. Besides, the prescribed drugs are mainly bitter, sweet and spicy; light, slightly bitter and salty are supplementary. Bitter medicines can stop cough, clear heat and eliminate carbuncles; sweet medicines can stop cough, thirst and swelling; spicy medicines can stop pain, cough and cold. The combined use of bitter, sweet and spicy medicines can treat most of the clinical symptoms of COVID-19. Meanwhile, the drugs are mainly attributed to the lung, stomach and spleen, followed by the liver and heart meridians. The drugs attributed to the lung mainly include raw gypsum, almond, orris, raw licorice, poria and forsythia, which are mostly used to moisten and clear the lung and treat canker sores; the drugs attributed to the stomach mainly include raw gypsum, raw licorice and patchouli. Most of them are drugs to open the stomach, strengthen the stomach, help digestion and treat vomiting; drugs attributed to the spleen mainly include raw licorice, poria and huo xiang zheng qi shui, which are mostly drugs to strengthen the spleen, stop diarrhea and treat spleen deficiency, and the results of this analysis are in accordance with the characteristics of new crown pneumonia in the lung and susceptible to the spleen and stomach [17]. This finding is consistent with the treatment protocol of Professor Yang Zhixu for patients with COVID-19 [17]

(3) Construction-based knowledge graph applications.

In the Neo4j-based knowledge graph, the node-to-node connections show to a certain extent the association between the symptoms of drugs, the four qi, the five tastes, the generalized meridians and the tongue quality, making the invisible knowledge visible.

(a) Drug recommendation based on clinical symptoms,

During the onset of neocrown pneumonia, TCM practitioners often need to treat patients based on their clinical symptoms. Cough is the main clinical symptom of this new coronary pneumonia. Doctors can use the fuzzy query statement "MATCH (p:Drug) where p.fun =~" in the treatment process. *cough. *" RETURN p "to find out the drugs related to "cough". The query revealed that the drug "almond" plays an important role in the treatment of cough. After querying the relevant results, Neo4j's own "Export CSV" function can be used to export the query results and obtain information on other drugs related to "cough", such as Bei Sha Shen, Ephedra and Radix et Rhizoma. This query can help doctors to select drugs for clinical symptoms to a certain extent.

(b) Drug recommendation based on tongue/pulse.

In the clinical treatment of neo-crown pneumonia, physicians can make TCM prescriptions based on the patient's tongue or pulse. For example, the query statement "MATCH (p:`Tongue`{name: "tongue darkness"})-[r1:`drug with symptom`]->(c:Drug) where r1.confidence ="100" RETURN p,c,r1 " for the query. The query results show that in the clinical treatment of New Coronary Pneumonia, when the tongue symptom is "dark tongue", the prescriptions used must include Wu Wei Zi, Angelica Sinensis, Mai Dong, Almond and Roasted Loquat Leaf, the query results are shown in Figure 2. The yellow path represents the relationship "drug with symptom"; the query path is a directed path (tongue symptom -> required drug); the number on the yellow path represents the probability of a drug appearing when a certain tongue symptom appears. The number on the yellow path represents the probability of a drug appearing when a certain tongue symptom appears. Astragalus membranaceus, Radix Angelicae Sinensis, Radix Paeoniae Alba, Rhizoma Ligustici, Rhizoma Ligustici, Rhizoma Macrocephalae, Fructus Schisandrae, Radix Salviae Miltiorrhizae, Almonds, Roasted Loguat leaf, Radix Bupleurum and Aster. This result is consistent with the query result of this statement.



Fig. 2. Query result chart with "dark tongue" tongue image.

The information obtained by the above query statements shows that the Neo4j graphical database can intuitively and accurately help users to perform the work of querying and presenting information. Based on the above steps, this paper constructs and completes the knowledge mapping of tongue and pulse of novel coronavirus cases, realizes better knowledge representation of novel corona virus, verifies the applicability of knowledge mapping to the treatment work of novel corona virus, and further affirms that knowledge mapping can assist the treatment and decision-making work of TCM.

5 Conclusion and Outlook

The graph database in the semantic knowledge graph can not only visualize the relationships between data, but also handle complex, interconnected and less structured data, and perform complex retrieval of fast-changing data relationships. Taking the graph database Neo4j as an example, this paper extracts knowledge entities from each treatment plan incorporated into the database, establishes the knowledge system construction of information on drugs, tongue and pulse, and uses Neo4j to construct a knowledge graph to describe the TCM-related contents of neocoronavirus prevention and treatment, which realizes the transformation of invisible knowledge to explicit relationships. At the same time, by using Cypher language for retrieval and analysis, a new way was found for knowledge dissemination and learning of diagnosis and treatment protocols, and a certain tool and method reference was found for the optimization of clinical diagnosis and treatment protocols, which proved to a certain extent the feasibility of applying the knowledge map to the adjuvant treatment of novel coronavirus. At the same time, the construction process of this knowledge graph can be extended to other public health events, which lays the foundation for the application of intelligent question and answer system in public health events.

The analytical study in this paper also has many shortcomings, such as the small sample size of the data, the revision and update time of some of the included treatment protocols is not the latest, the tongue shape, tongue texture, moss texture, and moss shape related to the tongue image are not completely split, the symptoms are not included in the knowledge map, and the dosage of drugs are not counted, etc. These problems may cause errors in the data analysis results, so the constructed knowledge map needs to be further optimized in future studies, and we will continue to explore the applicability of the knowledge map to other symptoms in the treatment of novel coronavirus.

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