


# Characteristics of Traditional Chinese Medicine Use in Pediatric Cancer Patients: A Nationwide, Retrospective, Taiwanese-Registry, Population-Based Study

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## Abstract

**Background.** Large-scale surveys of complementary traditional Chinese medicine (TCM) use in pediatric cancer patients are lacking. The aim of our study was to investigate the use of TCM in pediatric cancer patients. **Methods.** We analyzed cancer patients younger than 18 years ( $n = 12965$ ) who were registered in the National Health Insurance Research Database in Taiwan between 2001 and 2011. Patients were categorized into TCM or non-TCM users based on their use of TCM. **Results.** In Taiwan, 8086 (62.4%) children with cancer sought TCM treatment at some point. Children in older age groups, including school-aged children and adolescents, were more likely to use TCM. There was no significant difference in the distributions of gender and urbanization. The 3 most common diseases for which TCM users visited the clinic were neoplasm (33.2%), respiratory system disease (32.9%), and infectious disease (8.86%). The most commonly utilized TCM therapy was Chinese herbal remedies. Patients who had comorbid conditions such as allergic rhinitis, dyspepsia, disorders of menstruation, and disease of the musculoskeletal system and connective tissue tended to visit TCM clinics. **Conclusions.** Adjunctive TCM use is not low in Taiwanese children with cancer. Further studies to investigate the efficacy and safety of TCM in children with cancer are warranted.

## Keywords

cancer, epidemiology, National Health Insurance Research Database, pediatrics, traditional Chinese medicine

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## Introduction

Childhood cancer consists of various malignancies and has become the second most frequent cause of child death in the developed world. The most common childhood cancers include leukemia, malignancies of the central nervous system, and lymphoma, accounting for 34%, 23%, and 12% of all childhood cancers, respectively.<sup>1</sup> Despite the improved survival rate of childhood malignancy, several solid cancers remain refractory to treatment. The discomfort that occurs during the treatment course, such as nausea, vomiting, and pain, is difficult to bear for these patients. The long-term toxicity and sequelae of chemotherapy and radiotherapy continue to be concerning. The survivors may develop chronic health conditions and suffer from chronic fatigue, sleep disorders, psychological distress, neurocognitive dysfunction, and a poor health-related quality of life. Another reason for complementary and alternative medicine (CAM)

use in children with cancer is the parents' desire to do everything possible to improve their child's health.

CAM has become popular in the past few decades. The prevalence of CAM varies across different countries, ranging from 6% to 91% in recent studies.<sup>2</sup> CAM therapies used in pediatric cancer are mostly considered to be supportive

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therapies for relieving the symptoms of cancer, reducing pain, or alleviating the side effects of conventional cancer treatment.<sup>3</sup> Some parents hope to boost the immune system of the affected child using CAM therapies.<sup>4</sup> Traditional Chinese medicine (TCM) consists of Chinese herbal remedies, acupuncture, and manipulative therapies and was defined by the United States National Center for Complementary and Integrative Health as a whole medical system of CAM.<sup>5</sup> TCM is one of the most common CAM therapies used in various diseases such as stroke,<sup>6</sup> diabetes mellitus,<sup>7</sup> rheumatoid arthritis,<sup>8</sup> and cancer<sup>9</sup> in Taiwan. Current studies on the use of CAM among pediatric cancer patients are mostly small-scale studies.<sup>10</sup> One large-scale study of the use of CAM in pediatric oncology patients in Germany reported that half of the children with cancer had used CAM but did not report which types of CAM therapy the children had received. A large-scale nationwide survey of TCM use in pediatric cancer patients is yet to be performed in childhood cancer.

The National Health Insurance (NHI) program was instituted in Taiwan in 1995. This program is a single-payer mandatory insurance system and has covered the medical expenditures of approximately 23 million people, accounting for 99.6% of the total population.<sup>11</sup> Although Western medicine is in the mainstream in Taiwan, TCM is also widely used, including in the pediatric population. The NHI program has reimbursed both Western medicine and TCM. This system also provided unbiased economic choices for cancer treatment. All registration files and original claims data for reimbursement were recorded in the National Health Insurance Research Database (NHIRD). Studies have reported the characteristics of TCM use among the general pediatric population<sup>5</sup> and children with allergies<sup>12-14</sup> in Taiwan using the NHIRD.

The aim of our study was to investigate the characteristics of TCM use in pediatric cancer patients. We enrolled every Taiwanese child with cancer who was registered as having catastrophic illness in the NHIRD. The results of this study could offer epidemiological information about TCM applied in pediatric cancer patients.

## Materials and Methods

### Data Source

The NHI program has provided reimbursement for TCM since 1996. Reimbursed TCM services include Chinese herbal remedies, acupuncture/moxibustion, and manipulative therapy in ambulatory clinics. All registry data in the NHIRD consist of demographic characteristics, clinical visits, hospitalizations, diagnostic codes, assessments, procedures, prescriptions, and the medical costs for reimbursement. The registry for catastrophic illnesses patient database (RCIPD) was also established in the NHIRD. Pediatric cancers are

considered to be catastrophic illnesses and are registered by certificate by pathology, image study, laboratory survey, and careful review by pediatric hematologists or oncologists commissioned by the NHI Administration. These cancer patients hold catastrophic illness certificates (CICs) and are eligible for exclusion from copayments. Because the copayments are waived for admission, emergency visits, and outpatient services, this certification is only applied when the patients meet all the criteria by pathology, image, laboratory, and clinical diagnoses. The CIC is canceled if a patient dies. The accuracy of the diagnosis in the cancer population enrolled in this study was high. All the claims data in the study were from the RCIPD of the NHIRD in Taiwan.

### Study Participants

We selected pediatric cancer patients from the RCIPD. First, all beneficiaries who had a diagnosis of cancer (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] codes: 140-208) and were registered in the RCIPD as having had a catastrophic illness between January 2001 and December 2011 were included in this study. Second, individuals ( $n = 12\,965$ ) younger than 18 years of age were selected for this study cohort and included in the study. Those pediatric cancer patients who had at least 1 TCM outpatient clinical record were defined as TCM users ( $n = 8\,086$ ), whereas children who had no TCM outpatient records were defined as non-TCM users ( $n = 4\,879$ ). We divided the study cohort into infants and toddlers (0-2 years old), preschoolers (3-5 years old), school-aged children (6-12 years old), and adolescents (13-18 years old) to analyze the differences among various age groups.

To investigate the differences between urban and rural areas, we used the definition of urbanization of the residence area that was described in a previous study.<sup>15</sup> The residence area of the Taiwan townships was divided into 4 levels of urbanization. Level 1 had the highest degree of urbanization, and level 4 had the lowest degree. These 4 levels were categorized by population density (people/km<sup>2</sup>), by the population ratio of different educational levels, the ratio of elderly people, the ratio of agricultural workers, and the number of physicians per 100 000 people. Urbanization levels 1 and 2 were defined as urban areas, and levels 3 and 4 were defined as rural areas.

### Data Availability Statement

All data are deposited in a properly managed public repository. In this study, we examined and analyzed datasets released from the NHIRD ([http://nhird.nhri.org.tw/en/Data\\_Subsets.html](http://nhird.nhri.org.tw/en/Data_Subsets.html)), which are maintained and managed by National Health Research Institutes (<http://nhird.nhri.org.tw/en>), Taiwan.

## Statistical Analysis

All the data were analyzed by SAS software, version 9.2 (SAS Institute Inc, Cary, NC). Univariate analysis was used to compare the TCM users with the non-TCM users. The  $\chi^2$  test was performed to examine the relationship between the categorical variables and to examine the differences between TCM users and non-TCM users. The incidence rate ratio indicated the extent of the prevalence of disease in the TCM user group relative to the non-TCM users. A *P* value <.05 was defined as statistically significant.

## Ethics Statement

The Research Ethics Committee of China Medical University and Hospital (CMUH104-REC2-115) approved this study. The NHIRD was provided by the NHI Administration and managed by the National Health Research Institutes, Taiwan. All the released datasets of the NHIRD were deidentified and encrypted. Therefore, it was impossible to identify individual patients and care providers at any level.

## Results

A total of 12 965 children who had CICs of cancer between 2001 and 2011 were enrolled in this study. Among them, 8086 (62.4%) children with cancer were TCM users, whereas 4879 (37.6%) children with cancer were non-TCM users.

The demographic characteristics between TCM users and non-TCM users are shown in Table 1. There were significant differences in the proportional distributions of age between the TCM users and non-TCM users. The percentage of TCM use increased significantly in the older age groups, which included school-aged children and adolescents. The percentage of TCM users in the younger age groups, including infants, toddlers, and preschool children, was significantly lower than that of the non-TCM users. There was no significant difference in the distributions of sex and urbanization. All the pediatric cancer patients were diagnosed as having catastrophic diseases by hematologists or oncologists. Therefore, they all received diagnoses and visited Western medical doctors whether they were TCM users or non-TCM users. The percentage of patients receiving chemotherapy or radiotherapy was similar between these 2 groups. We found that only 4 patients did not visit Western medical clinics after diagnosis—that is, 99.95% of the TCM users still visited Western medicine clinics. Treatment, including chemotherapy and radiotherapy, was similar between these 2 groups. The mean number of visits to the outpatient clinics in the 2 populations was similar, but the proportional distribution was not. The majority (90.3%) of the TCM users visited TCM clinics fewer than 5 times annually.

To determine the frequency distribution of clinical visits between TCM and non-TCM users in the pediatric cancer

population, we analyzed the ICD-9-CM codes from the claims data (Table 2). The 3 leading diseases for which TCM users visited the clinics, including TCM or Western medicine consultations, were neoplasm (33.2%), respiratory system disease (32.9%), and infectious and parasitic diseases (8.86%), whereas non-TCM users visited Western clinics for respiratory system disease (35.2%), neoplasm (28.6%), and digestive system disease (10%). The rankings of these disease categories were identical except the category “certain conditions originating in the perinatal period” (Table 2).

To delineate the distribution of cancer categories between TCM and non-TCM users, we analyzed the ICD-9-CM codes of registry for catastrophic illnesses in these patients. The top 10 cancer types of clinical visits in the TCM and non-TCM groups among different age groups are shown in Table 3. In general, the TCM users had similar distribution (ranking) of cancer types as the non-TCM users. The 3 leading cancer types were leukemia (ICD code: 204-208), malignant neoplasm of the brain (ICD code: 191), and malignant neoplasm of the eye, nervous system, and other specified sites (ICD code: 190, 192-199). There was a higher percentage of children with leukemia (ICD code: 204-208) who chose only Western medicine (48%) rather than TCM (42.3%). Other cancer categories, such as malignant neoplasm of the brain (ICD code: 191; 13.8% to 11.9%), sarcoma (ICD code: 200, 202-203; 9.08% to 7.61%), and malignant neoplasm of the bone (ICD code: 170; 5.74% to 4%), had a higher percentage of TCM users (Table 3).

The number of clinical visits in Table 2 includes both TCM and Western medicine clinical visits for TCM users. To further understand the treatment modalities utilized in TCM clinics, we determined the frequency distribution of various TCM therapies by major disease category (Table 4). Taking as an example musculoskeletal system and connective tissue disorders, 27.79% of visits were for herbal remedies, 34.25% were for manipulative therapy, 26.04% were for acupuncture, 4.47% were for manipulative therapy combined with herbal remedies, 4.26% were for acupuncture combined with herbal remedies, 2.69% were for manipulative therapy combined with acupuncture, and 0.50% were for acupuncture, manipulative therapy, and herbal remedies.

By comparing the prevalence ratio of disease between TCM users and non-TCM users, we found 4 common diseases for which children with cancer tended to seek adjunctive TCM treatment. These diseases included allergic rhinitis, dyspepsia, disorders of menstruation, and diseases of the musculoskeletal system and connective tissue (Table 5).

## Discussion

This study is the first large-scale population-based investigation of adjunctive TCM use in children with cancer. TCM was popular in this population, particularly among school-aged children and adolescents. A total of 62.4% of children

**Table 1.** Demographic Characteristics Between TCM Users and Non-TCM Users Among Children With Cancer From 2001 to 2011 in Taiwan.<sup>a</sup>

	TCM User, n = 8086		Non-TCM User, n = 4879		P Value
	n	Percentage	n	Percentage	
Gender					.02
Girl	3570	44.2	2053	42.1	
Boy	4516	55.8	2826	57.9	
Age, years					<.0001
Infants and toddlers, 0-2 years	1103	13.6	1458	29.9	
Preschoolers, 3-5 years	1230	15.2	899	18.4	
School-aged children, 6-12 years	2576	31.9	1294	26.5	
Adolescents, 13-18 years	3177	39.3	1228	25.2	
Urbanization					.31
Urban	4897	60.6	2911	59.7	
Rural	3189	39.4	1968	40.3	
Treatment					
Chemotherapy	5061	62.6	3150	64.6	.02
Radiotherapy	3533	43.7	2086	42.8	.30
TCM alone	4	0.05	0	0	
Annual Western medicine clinic visit					<.0001
<5	344	4.25	1076	22.1	
5-9	802	9.92	458	9.39	
10-19	2371	29.3	998	20.5	
20+	4569	56.5	2347	48.1	
Mean (SD)	26.5	(16.5)	25.5	(17.4)	.002
Annual TCM clinic visit					
<5	7303	90.3			
5-9	478	5.91			
10-19	221	2.73			
20+	84	1.04			
Mean (SD)	1.84	(4.40)			

Abbreviation: TCM, traditional Chinese medicine.

<sup>a</sup> $\chi^2$  test.

with cancer had received complementary TCM treatment at some point, and the population number was nearly 1.7 times as large as that of non-TCM users. There was no difference between urban and rural populations, probably because TCM is highly accessible and its use is reimbursed by the NHI program.<sup>5</sup> The most common diseases for which children with cancer visited the clinic, be they TCM users or non-TCM users, included respiratory system disease and neoplasm. TCM users visited the clinic less frequently for respiratory system disease and digestive system disease. Children with leukemia tended to seek the use of Western medicine, whereas children with sarcoma or malignant neoplasm of the brain or bone sought adjunctive TCM treatment. This result was consistent with a study conducted in British Columbia that reported that patients with a poor prognosis in childhood cancer were more willing to try CAM therapies. The most common TCM therapy used was Chinese herbal remedies. The pediatric cancer patients who

had comorbidities, including allergic rhinitis, dyspepsia, disorders of menstruation, and disease of the musculoskeletal system and connective tissue, tended to visit the TCM clinic rather than a non-TCM clinic. Overall, this study offers pediatricians or oncologists epidemiological information about how TCM is being applied in pediatric cancer patients.

There were several strengths to this study. First, this is a nationwide, population-based study that enrolled all children with cancer from 2001 to 2011. The population size was larger than that of other studies. Second, the NIH program in Taiwan covers greater than 99% of the total population, and it reimbursed both Western medicine and TCM services. Therefore, none of the claims data in the NHIRD had any selection bias. Third, pediatric cancer patients with CICs were confirmed by pathology, image studies, a series of laboratory surveys, and careful review by hematologists and oncologists commissioned by the NHI Administration.

**Table 2.** Frequency Distribution of Clinical Visits by Major Disease Categories/Diagnoses Among TCM Users and Non-TCM Users.

Disease (ICD-9-CM)	TCM User, Number of Clinical Visits = 756 541		Non-TCM User, Number of Clinical Visits = 2 131 731		P Value
	Visits, n	Percentage	Visits, n	Percentage	
Respiratory system (460-519)	249 007	32.9	749 241	35.2	<.0001
Neoplasms (140-239)	251 118	33.2	609 166	28.6	<.0001
Digestive system (520-579)	60 927	8.05	213 386	10.0	<.0001
Nervous system (320-389)	38 173	5.05	125 449	5.88	<.0001
Infectious and parasitic disease (001-139)	67 050	8.86	86 619	4.06	<.0001
Symptoms, signs, and ill-defined conditions (780-799)	19 770	2.61	76 578	3.59	<.0001
Skin and subcutaneous tissue (680-709)	19 089	2.52	73 008	3.42	<.0001
Injury and poisoning (800-999)	12 317	1.63	65 351	2.98	<.0001
Endocrine, nutritional, and metabolic disease and immunity disorder (240-279)	7 437	0.98	31 260	1.47	<.0001
Genitourinary system (580-629)	6 488	0.86	31 246	1.47	<.0001
Musculoskeletal system and connective tissue (710-739)	5 097	0.67	27 762	1.30	<.0001
Mental disorder (290-319)	7 408	0.98	18 460	0.87	<.0001
Congenital anomalies (740-759)	6 017	0.80	9 746	0.46	<.0001
Blood and blood-forming organs (280-289)	3 855	0.51	7 853	0.37	<.0001
Circulatory system (390-459)	2 053	0.27	6 095	0.29	.04
Complications of pregnancy, childbirth, and the puerperium (630-676)	1 08	0.01	1 586	0.07	<.0001
Certain conditions originating in the perinatal period (760-779)	627	0.08	745	0.03	<.0001

Abbreviation: TCM, traditional Chinese medicine.

The diagnosis was decidedly accurate, and the database was reliable for epidemiological study in children with cancer.

We found that the high prevalence (62.4%) of TCM use by children with cancer in Taiwan was compatible with a previous small-scale study reporting 73% of CAM use in Taiwan.<sup>16</sup> A previous study found that the prevalence of CAM use in pediatric cancer was 35% in Germany,<sup>17</sup> 47% in the United States,<sup>18</sup> 42% in British Columbia,<sup>19</sup> and 67% in Singapore.<sup>20</sup> Most CAM therapies used in other countries were diet and nutrition, herbal remedies, relaxation, and mind-body therapies.<sup>2,10</sup> In contrast to other countries, TCM constituted a high proportion among CAM therapies in Taiwan because TCM has been used for more than 2000 years and is widely acceptable in Asian countries. TCM also became popular for cancer care in Europe. In a large survey in Europe, acupuncture, herbal medicine, and TCM were the main CAM therapies used to reduce adverse reactions to chemoradiotherapy.<sup>21</sup>

The most common diseases for which TCM or non-TCM users among pediatric cancer patients visited clinics was respiratory system disease and neoplasm. Respiratory system disease was also the most common reason for children visiting outpatient clinics in Taiwan.<sup>5</sup> This is likely because upper- or lower-respiratory tract infection represent the most common acute illness in children, especially in cancer patients with immune compromised status.

Moreover, several chemotherapeutic agents such as methotrexate, cyclophosphamide, and busulfan used in conditioning regimens for bone marrow transplantation may also affect pulmonary function.<sup>22-24</sup> We found that TCM users had lower visiting rates for respiratory system disease. Whether complementary TCM therapy can improve lung function deserves further investigations. Discomforts of the digestive system are also among the top reasons for TCM users to visit TCM clinics. Digestive disorders, including diarrhea, nausea, and vomiting, are the most common symptoms in patients undergoing chemotherapy or radiotherapy. Previous clinical trials have reported that Chinese herbal medicines may be effective in treating these side effects.<sup>25-27</sup> The efficacy and safety in pediatric cancer patients also need further investigations.

In our study, when compared with non-TCM users, pediatric cancer patients with allergic rhinitis, dyspepsia, disorders of menstruation, and musculoskeletal disease tended to use TCM. This result was similar to our previous study in the pediatric population in Taiwan.<sup>5</sup> In contrast to a previous study in an adult population with cancer in Thailand, cancer patients with pain, dyspepsia, abdominal or visceral pain, insomnia, and fatigue tended to use TCM.<sup>28</sup> Allergic rhinitis had a high prevalence rate among children in Taiwan,<sup>29</sup> and some clinical trials had observed that herbal medicines and acupuncture were effective in treating

**Table 3.** Frequency Distribution of the Cancer Types in TCM Users and Non-TCM Users Among Different Age Groups.<sup>a</sup>

All		0-2 Years		3-5 Years		6-12 Years		13-18 Years	
ICD-9-CM	Percentage	ICD-9-CM	Percentage	ICD-9-CM	Percentage	ICD-9-CM	Percentage	ICD-9-CM	Percentage
TCM user									
204-208	42.3	204-208	46.3	204-208	62.6	204-208	45.1	204-208	25.9
191	13.8	190, 192-199	16.4	191	9.13	191	19.0	191	13.5
190, 192-199	10.8	191	9.46	190, 192-199	8.22	200, 202-203	9.95	190	13.4
200, 202-203	9.08	200, 202-203	7.61	200, 202-203	7.35	190	6.87	170	9.98
170	5.74	184, 187-189	5.81	184, 187-189	3.86	170	6.30	200, 202-203	9.93
171	4.23	155	4.93	171	3.01	171	4.24	140-149	5.98
184, 187-189	2.54	171	3.91	170	1.58	184, 187-189	1.70	171	5.10
140-149	2.43	186	1.96	201	1.18	183	1.67	201	4.38
201	2.20	183	0.97	155	1.10	201	1.60	183	4.00
183	2.07	170	0.67	186	0.34	140-149	1.13	186	1.43
Non-TCM user									
204-208	48.0	204-208	43.4	204-208	65.8	204-208	47.5	204-208	33.7
191	11.9	190, 192-199	17.8	190, 192-199	10.4	191	18.0	191	13.8
190, 192-199	10.9	191	7.92	191	8.09	200, 202-203	9.05	200, 202-203	9.87
200, 202-203	7.61	184	6.52	200, 202-203	5.47	170	7.07	190, 192-199	8.67
171	4.53	200, 202-203	6.41	171	3.01	190, 192-199	6.02	170	8.41
170	4.00	155	5.94	184, 187-189	2.69	171	5.00	140-149	5.54
184, 187-189	3.09	171	5.05	155	1.38	155	1.48	171	5.07
155	2.80	186	3.22	183	0.89	184, 187-189	1.25	201	3.03
140-149	1.42	158	1.14	170	0.65	201	1.20	183	2.25
186	1.28	160-165	0.70	186	0.49	183	1.13	155	2.04

Abbreviation: TCM, traditional Chinese medicine.

<sup>a</sup>140-149: Malignant neoplasm of lip, oral cavity, and pharynx; 155: malignant neoplasm of liver and intrahepatic bile ducts; 160-165: malignant neoplasm of respiratory and intrathoracic organs; 170: malignant neoplasm of bone and articular cartilage; 171: malignant neoplasm of connective and other soft tissue; 183: malignant neoplasm of ovary and other uterine adnexa; 184: malignant neoplasm of other and unspecified female genital organs; 186: malignant neoplasm of testis; 187: malignant neoplasm of penis and other male genital organs; 188: malignant neoplasm of bladder; 189: malignant neoplasm of kidney and other and unspecified urinary organs; 190, 192-199: malignant neoplasm of eye, unspecified parts of nervous system, thyroid gland, other endocrine glands and related structures, ill-defined sites, secondary and unspecified malignant neoplasm; 191: malignant neoplasm of brain; 200: lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue; 201: Hodgkin's disease; 202: other malignant neoplasms of lymphoid and histiocytic tissue; 203: multiple myeloma and immunoproliferative neoplasms; 204-208: leukemia.

allergies of children.<sup>30,31</sup> Some herbal TCM preparations have been shown to have benefit for functional dyspepsia.<sup>32-34</sup> Chinese herbal remedies, such as modified Xiao-yao-san and Modified Liu-Jun-Zi decoction might be effective in the treatment of functional dyspepsia.<sup>35,36</sup> With regard to TCM treatment for disorders of menstruation, there is some evidence supporting Chinese herbal medicine and acupuncture in treating primary dysmenorrhea.<sup>37,38</sup> More than half of primary dysmenorrhea women in Taiwan sought TCM to treat their menstruation-related pain syndrome.<sup>39</sup> Teenage girls with cancer might suffer from irregularities of menstruation as a result of stress, especially during the treatment course. TCM may provide help to regulate menstruation and reduce the side effects of iatrogenic menopause.<sup>21</sup> Our previous study identified that musculoskeletal problems were one of the common reasons for adolescents and school-aged children to visit TCM clinics.<sup>5</sup> Patients with cancer suffered from pain caused by cancer or its treatment such as surgery, chemotherapy, or radiotherapy. Many clinical trials have suggested that TCM may be effective at treating cancer-related pain, and the effects are similar to those of Western analgesics.<sup>40</sup> In contrast to other diseases, TCM doctors

prefer providing acupuncture and manipulative therapies to treat musculoskeletal problems.

There are some limitations of our study. First, some TCM services such as Chinese herbal decoctions and proprietary Chinese medicine purchased directly from TCM herbal pharmacies were not covered by NHI. This may have resulted in an underestimation of the frequency of herb use. Nevertheless, TCM services are fully reimbursed for cancer patients holding a CIC. Hence, we can be certain that the coverage of the TCM services in the study is high. The underestimation would be relatively small and acceptable. Second, all claims data were from RCIPD and collected by ICD-9-CM code numbers of pediatric cancer. We were unable to obtain information on the tumor stage to discriminate differences in TCM use in early and late stages. However, this study still provides the general concept and characteristics of TCM use among children with cancer.

## Conclusion

In this large-scale, nationwide, population-based study, we found that complementary TCM use among children with

**Table 4.** Frequency Distribution of Various TCM Therapies by Major Disease Categories/Diagnosis.

Disease Categories (ICD-9-CM)	Herbal Remedies	Manipulative Therapy	Acupuncture	Manipulative Therapy Combined With Herbal Remedies	Acupuncture Combined With Herbal Remedies	Manipulative Therapy Combined With Acupuncture	Acupuncture, Manipulative Therapy and Herbal Remedies
Respiratory system (460-519)	99.61	0.01	0.27	0.02	0.09	0.00	0.00
Neoplasms (140-239)	92.84	0.30	5.52	0.02	1.31	0.00	0.01
Symptoms, signs, and ill-defined conditions (780-799).	99.15	0.11	0.55	0.04	0.14	0.005	0.005
Injury and poisoning (800-999)	11.50	54.40	19.47	6.84	3.39	3.57	0.83
Digestive system (520-579)	99.74	0.01	0.19	0.02	0.04	0.00	0.00
Musculoskeletal system and connective tissue (710-739)	27.79	34.25	26.04	4.47	4.26	2.69	0.50
Skin and subcutaneous tissue (680-709)	99.53	0.02	0.21	0.06	0.18	0.00	0.00
Genitourinary system (580-629)	99.64	0.00	0.10	0.06	0.2	0.00	0.00
Nervous system (320-389)	62.00	3.60	30.24	0.36	3.15	0.55	0.10
Blood and blood-forming organs (280-289)	98.29	0.00	0.66	0.00	1.05	0.00	0.00
Infectious and parasitic disease (001-139)	98.01	0.50	1.00	0.33	0.00	0.16	0.00
Circulatory system (390-459)	88.69	0.00	9.25	0.24	1.82	0.00	0.00
Endocrine, nutritional and metabolic disease, and immunity disorder (240-279)	99.30	0.12	0.35	0.00	0.23	0.00	0.00
Mental disorder (290-319)	53.04	1.09	39.00	0.16	6.71	0.00	0.00
Congenital anomalies (740-759)	64.67	5.33	30.00	0.00	0.00	0.00	0.00
Complications of pregnancy, childbirth, and the puerperium (630-676)	100.00	0.00	0.00	0.00	0.00	0.00	0.00

Abbreviation: TCM, traditional Chinese medicine.

**Table 5.** Incidence Rate Ratio for 4 Common Diseases Between TCM Users and Non-TCM Users.<sup>a</sup>

Disease (ICD-9-CM)	TCM User		Non-TCM User		IRR (95% CI)
	n	Percentage	n	Percentage	
Allergic rhinitis cause unspecified (477.9)					
All	4424	54.7	1527	31.3	1.85 (1.74-1.96)
Dyspepsia and other specified disorders of function of stomach (536.8)					
All	2120	26.2	596	12.2	2.26 (2.06-2.48)
Disorders of menstruation and other abnormal bleeding from female genital tract (626)					
All	1542	19.1	194	3.98	3.51 (3.05-4.09)
Disease of the musculoskeletal system and connective tissue (710-739)					
All	5414	67.0	1570	32.2	1.91 (1.80-2.02)

Abbreviations: IRR, incidence rate ratio in Poisson regression; TCM, traditional Chinese medicine.

<sup>a</sup>IRR, adjusted for age, gender, urbanization, and number of clinical visits. All *P* values <.0001.

cancer is high. This study provides valuable information for those concerned about health care in pediatric cancer patients. Further pharmacological investigation and clinical trials of TCM used in children with cancer are warranted.

### Authors' Note

Hung-Rong Yen and Wan-Yu Lai contributed equally as co-first authors. This study was based in part on data from the National Health Insurance Research Database, provided by the National Health Insurance Administration and Ministry of Health and Welfare, and managed by National Health Research Institutes. The interpretation and conclusions contained herein do not represent those of National Health Insurance Administration, Ministry of Health and Welfare, or National Health Research Institutes.

### Declaration of Conflicting Interests

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