Journal of Traditional and Complementary Medicine 7 (2017) 188–194

Contents lists available at ScienceDirect

Journal of Traditional and Complementary Medicine

journal homepage: http://www.elsevier.com/locate/jtcme

Original article

Demographic and medication characteristics of traditional Chinese medicine users among colorectal cancer survivors: A nationwide database study in Taiwan

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ARTICLE INFO

Article history:
Received 27 February 2016
Accepted 11 July 2016
Available online 6 August 2016

Keywords:
Colorectal cancer
Traditional Chinese medicine
National health insurance research database
Chinese herbal product
Costusroot and Amomum Six Gentlemen Decoction

ABSTRACT

Chinese herbal product (CHP) is the major type of traditional Chinese medicine (TCM) and widely used to relief the symptom of colorectal cancer. The aim of the study was to analyze the utilization of CHP for treating patients with colorectal cancer in Taiwan. The usage of CHP, frequency of services, and prescription pattern for colorectal cancer were analyzed from a randomly sampled cohort of 1 million beneficiaries from the National Health Insurance Research Database. The odds ratios for utilization of CHP were estimated with logistic regression model. 2846 patients were newly diagnosed as colorectal cancer during 1998–2008 in the million cohort in Taiwan. 42.7% (n = 1214) of them used CHP. Colorectal cancer was the most common diagnosis coded by TCM doctor, followed by symptoms, signs, and ill-defined conditions. Costusroot and Amomum Six Gentlemen Decoction (香砂六君子湯 xiāng shā liù jūn zǐ tāng) was the most frequently prescribed formula for treating colorectal cancer. Among the top 10 most frequently prescribed CHP for treating colorectal cancer, six containing Ginseng Radix (人參, *Panax ginseng*) and two containing Astragali Radix (黃耆, *Astragalus membranaceus*), which are reported to have potential beneficial synergistic effects on colorectal cancer cells. CHP containing Ginseng Radix or Astragali Radix are the most frequently prescribed for colorectal cancer and their effects should be taken into account by healthcare providers.

1. Introduction

Colorectal cancer (CRC) remains one of the most prevalent cancers and a leading cause of cancer related death world-wide.[1–3] Despite the lack of solid evidence supporting their therapeutic benefits, the reported incidences of use of complementary and alternative medicines (CAM) from the time of initial diagnosis of colorectal cancer until his or her death (colorectal cancer survivors) range from 70 to 86%.[4] Attempting to improve one's physical and emotional health,[5–7] the desire to exert a sense of personal control over one's illness,[8] dissatisfaction with the medical care system or health providers,[9] and doubts concerning the effectiveness of conventional treatment may be the reasons why patients use a wide range of CAM including herbs, vitamins, homeopathic remedies, and CHP.[5,10] The expectations of CAM use varies among individuals. Some just hope to strengthen their immune system, some expect to decrease the treatment-associated toxicity, and some want to alleviate the CRC-derived symptoms.[11–13] However, there is no compelling evidence supporting the effectiveness of CAM use in CRC survivors. In view of such and without further knowledge on how effective CAM is, it is not easy for oncologists or CAM practitioners to provide an appropriate recommendation that can meet the expectations of CRC survivors.

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Peer review under responsibility of The Center for Food and Biomolecules, National Taiwan University.

http://dx.doi.org/10.1016/j.jtcme.2016.07.001

TCM, a long and widely used form of medical care in ethnic Chinese communities and nearby regions, which includes acupuncture, traumatology manipulative therapies and Chinese herbal products, has been growing in popularity and has offered an important alternative or complement to health care in many countries. Previous studies have disclosed that the potential beneficial anticancer effects of the usage of Ginseng Radix[14] or Astragali Radix[15] among CRC survivors. Although a previous randomized clinical trial of a CHP indicated that PHY 906 decrease in CRC survivors' nausea and diarrhea effectively,[16] the utilization of individual CHP has rarely been reported. In Taiwan, CHP have been an important part of health care for hundreds of years and over ten thousands licensed CHPs are reimbursed under the current National Health Insurance (NHI) system.

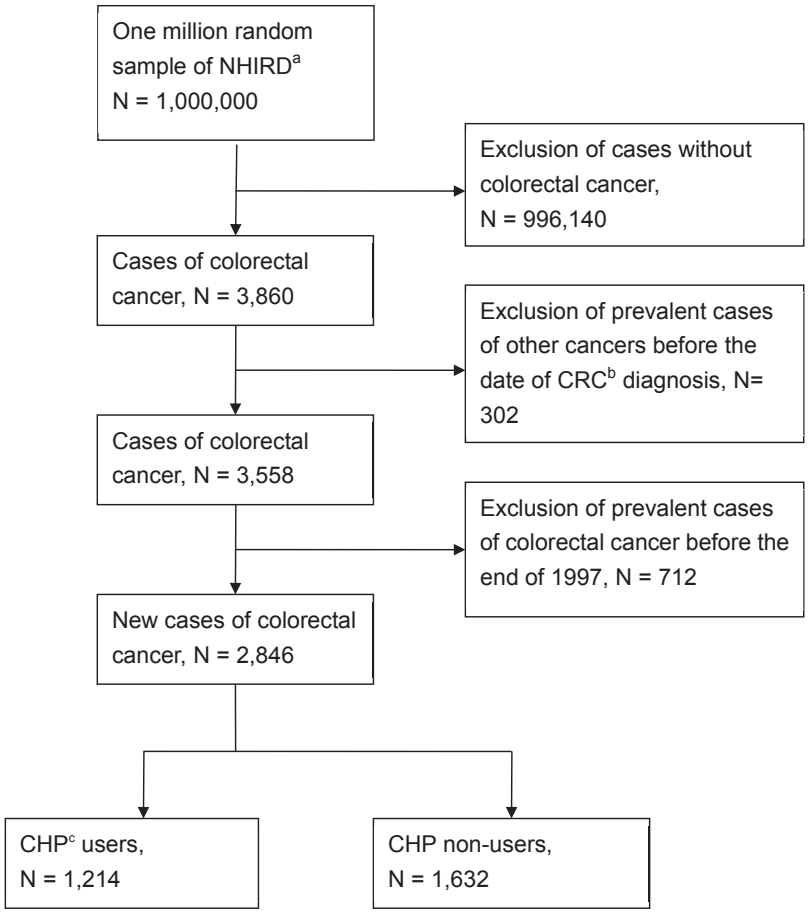
Taiwan launched a single-payer National Health Insurance Program on March 1, 1995. As of 2007, 22.60 million of 22.96 million Taiwan populations were enrolled in this program. The database of this program contains registration files, and original claim data for reimbursement. National Health Insurance Research Database (NHIRD) derived from this system by the Bureau of National Health Insurance, Taiwan (BNHI) and maintained by the National Health Research Institutes, Taiwan (NHRI), is provided to scientists in Taiwan for research purposes. Accordingly, the claims database provides a platform for understanding the utilization of CHP prescribed by licensed TCM doctors. The aim of our study is to analyze a random sample of this comprehensive database and to determine the CHP utilization patterns for CRC survivors in Taiwan. Results of this study may provide valuable information for physicians, enabling them to respond to patients' use of CHP in an informed way and strengthening the patient-physician relationship in CRC care.

2. Materials and methods

2.1. Data resource

Our study protocols were approved by the Institutional Review Board of the Ministry of Health and Welfare (MOHW), Taiwan. Our population-based study retrospectively analyzed the reimbursement records of 1 million NHI beneficiaries in the NHIRD that had been previously selected at random from the 22 million beneficiaries of the NHI to determine the prevalence of prescribed CHP in CRC survivors between January 1, 1998, and December 31, 2008, in Taiwan. The electronic records of the NHIRD use beneficiary identification numbers that are encrypted and maintained by NHRI of Taiwan.[17,18]

The NHIRD records contain demographic information, including age and sex, and clinical data, including all records of clinical visits and hospitalizations and all information regarding prescribed drugs and dosages, including CHPs, and three major diagnoses coded in



[a], NHIRD: National Health Insurance Research Database; [b], CRC: colorectal cancer; [c], CHP: Chinese herbal products.

Fig. 1. Flowchart of recruitment of subjects from the one million random sample of the National Health Insurance Research Database from 1998 to 2008 in Taiwan.

the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) format.[19]

The participant selection from the NHIRD was performed as shown in Figure 1. First, we excluded all beneficiaries without colorectal cancer ($n = 996, 140$). Second, beneficiaries with other cancers ($n = 302$) were excluded. Third, colorectal cancer ($n = 712$) diagnosed before the end of 1997 were also excluded to make sure that all the subjects included were newly diagnosed with invasive colorectal cancer, and the diagnosis was verified by the NHI registry of catastrophic illnesses during 1998–2008. All patients who are registered to have a catastrophic illness are exempted from all co-payments. To be registered as such, patients must have the diagnosis of invasive colorectal cancer (*ICD-9* code 153-154) validated by tissue pathology. Finally, 2846 CRC survivors were included in the study.

2.2. Traditional Chinese medicine

For the purpose of studying the use of CHPs, we downloaded the claims data, which is a sub-file in the data file of ambulatory care expenditures by visits provided by BNHI, for reimbursed CHPs. The corresponding information regarding the CHP was then obtained from the DCMP website (Department of Chinese Medicine and Pharmacy, Ministry of Health and Welfare, Taiwan), including the name of each herb, the proportion of each constituent of the mixture, the date and period of approval for the drug, the DCMP manufacturer code, and the name of the CHP manufacturer. All CHPs with the same DCMP standard formula are classified in the same category, regardless of slight variations in the products among different CHP manufacturers.[20]

2.3. Study variables

To determine the key independent variables for the utilization of CHP among CRC survivors, we selected the demographic factors according to previous studies.[21–24] Patients were classified, based on age, into one of six groups, as follows: ≤39, 40–49, 50–59, 60–69, 70–79, and ≥80 years. The geographic areas of Taiwan in which patients resided were classified as one of the following six regions: Taipei city, Kaohsiung city, Northern (exclude Taipei city), Central, Southern Taiwan (exclude Kaohsiung city), and Eastern Taiwan (include Outlying islands). We also searched the NHIRD database for diagnosis and treatment records related to CRC as independent variables. The locations of CRC were divided into five types: right colon, left colon, sigmoid colon, rectum, and site unspecified. The NHIRD contained all details related to the aforementioned variables and cancer treatment modalities for treating colorectal cancer. Then, for the final analysis, we categorised the types of cancer treatment modalities used as follows: no treatment, surgery only, chemotherapy only, and surgery plus chemotherapy.

2.4. Statistical analysis

Descriptive statistics with chi-square test results are summarized as shown in Table 1. Multiple logistic regression was conducted to evaluate the factors that correlated with CHP use, by

Table 1
Demographic characteristics and results of multiple logistic regression showing the adjusted odds ratio and 95% confidence interval of cases with newly diagnosed colorectal cancer from the one million random sample of the National Health Insurance Research Database from 1998 to 2008 in Taiwan.

Characteristics	CHP[a] non-users	CHP users	aOR[b] (95% CI[c])	*p* of Chi-square
No. of cases	1632	1214		
CHP[d] for colorectal cancer	–	244		
Gender				<0.0001
Male	996 (61.0)	625 (51.5)	1	
Female	636 (39.0)	589 (48.5)	1.51 (1.29–1.76)	
Age at diagnosis (years)	65.9 ± 13.5	62.7 ± 13.0		<0.0001
≤39	71 (4.4)	59 (4.9)	0.89 (0.60–1.31)	
40–49	146 (8.9)	143 (11.8)	1.04 (0.78–1.39)	
50–59	276 (16.9)	259 (21.3)	1	
60–69	393 (24.1)	345 (28.4)	0.94 (0.75–1.18)	
70–79	520 (31.9)	309 (25.5)	0.63 (0.51–0.79)	
≥ 80	226 (13.8)	99 (8.2)	0.46 (0.34–0.62)	
Insured region				0.0137
Taipei city	313 (19.2)	241 (19.9)	1	
Kaohsiung city	107 (6.6)	88 (7.2)	0.99 (0.71–1.38)	
Northern Taiwan (exclude Taipei city)	477 (29.2)	311 (25.6)	0.84 (0.67–1.06)	
Central Taiwan	251 (15.4)	243 (20.0)	1.22 (0.95–1.56)	
Southern Taiwan (exclude Kaohsiung city)	442 (27.1)	298 (24.5)	0.84 (0.67–1.05)	
Eastern Taiwan (include Outlying islands)	42 (2.6)	33 (2.7)	1.00 (0.61–1.65)	
Location of colorectal cancer[e]				0.1554
Right colon	261 (16.0)	164 (13.5)	1	
Left colon	179 (11.0)	115 (9.5)	0.98 (0.72–1.34)	
Sigmoid colon	322 (19.7)	264 (21.7)	1.30 (1.00–1.69)	
Rectum	696 (42.6)	528 (43.5)	1.22 (0.97–1.54)	
Others, unspecified	174 (10.7)	143 (11.8)	1.40 (1.02–1.93)	
Cancer treatment modalities				0.0111
No treatment	157 (9.6)	118 (9.7)	1	
Surgery only	734 (45.0)	539 (44.4)	1.05 (0.79–1.39)	
Chemotherapy only	78 (4.8)	30 (2.5)	0.51 (0.31–0.83)	
Surgery plus chemotherapy	663 (40.6)	527 (43.4)	1.04 (0.78–1.38)	

[a] CHP: Chinese herbal product.
[b] aOR: adjusted odds ratio, also adjusted for comorbidities such as diabetes mellitus, hyperlipidemia, hypertension, crohn's disease and ulcerative colitis.
[c] CI: confidence interval.
[d] CHP: Chinese herbal products.
[e] Right: Appendix vermiformis, Cecum, Ascending colon, Hepatic flexure; Left: Transverse colon, Splenic flexure, Descending colon; Rectum: Rectosigmoid junction, Rectum; Other: Anal canal, Anus, and unspecified site.

using the odds ratio (usually abbreviated "aORs") adjusted for demographic factors, location of colorectal cancer, cancer treatment modalities, and comorbidities as the predicted values of people who is more likely to be a CHP user. Potential predictors (covariates) were risk factors which may increase the chance of using CHP (diabetes mellitus, hypertension, dyslipidemia, crohn's disease, and ulcerative colitis), demographic factors (gender, age at diagnosis, insured salaries, and insured regions), location of colorectal cancer, and cancer treatment modalities. The following 3 models corresponding to three possible underlying biological situations regarding the CHP use across multiple conditions were tested: model 1, adjusted for the demographic factors (age, gender, insured salaries, insured region); model 2, adjusted for the demographic factors, location of colorectal cancer, cancer treatment modalities, and risk factors (diabetes mellitus, hypertension, dyslipidemia, crohn's disease, ulcerative colitis); model 3, adjusted for the demographic factors, location of colorectal cancer, and cancer treatment modalities. CRC survivors aged 50–59 was set as a reference category in the variable "age at diagnosis" because the sharply increasing age-specific incidence of colorectal cancer from around age 50 was reported.[25] "Male" and "Taipei city" were set as reference categories in the other demographic covariates. The value of the model was tested with the likelihood ratio test. It can be assessed by comparing the fit of the two models with and without the independent variables. Overall fit of model 3 shows a strong relationship between most of the independent variables, taken together, and dependent variable. A significance level of $\alpha = 0.05$ was selected. The statistical software SAS 9.2 was used for data management and analysis.

3. Results

Data analysis consisted of descriptive statistics, including the prescription rates of the CHP users stratified by patient's demographic characteristics (Table 1), indications for the prescription of CHP (Table 2), and the most frequently prescribed herbal formulas for treating CRC (Table 3). Primary indications were classified according to their ICD-9 code. The diagnoses were coded according to the ICD-9 and grouped into a series of distinct broad disease categories. For example, ICD-9 codes 460-519 were classified as diseases of the respiratory system; codes 780-799 were grouped as symptoms, signs, and ill-defined conditions, and codes 520-579 were classified as diseases of the digestive system. The potential effects of Chinese herbs Ginseng Radix, Astragali Radix contained in ten most commonly prescribed CHPs were shown in Table 4.[14,15] The database of outpatient claims contained information on 2846 CRC survivors from 1998 to 2008. Prevalence of CRC on the right colon, left colon, sigmoid colon, rectum and site unspecified was 14.9%, 10.3%, 20.6%, 43.0%, and 11.1%, respectively. The male-to-female sex ratio for CRC was 1.32 in Taiwan and rectum was the most common site of involvement, which is in line with previous study.[2] Among them, 1214 (42.7%) CRC survivors took Chinese herbal products. Most CHP users (90.3%) also received cancer treatment. Details on the demographic distribution of CHP users and non-users are provided in Table 1. The mean age of CHP non-users was higher than that of CHP users. There were more CHP users than CHP non-users who were residing in central Taiwan.

Adjusted odds ratios (aORs) and 95% confidence intervals (95% CIs) obtained by multiple logistic regression are also summarized in Table 1. Females were more likely to use CHP. Compared with the age group of 50–59 years (aOR = 1.00), there were no significant differences in ages between CHP users and CHP non-users except those aged 70 years and above who were more likely to be CHP non-users. There was also no significant difference or trend among CRC survivors with multiple chronic conditions, in different income groups, and in use of cancer treatment between CHP users and non-users.

Table 2
Frequency distribution of Chinese herbal product visits by major disease categories according to ICD-9-CM diagnosis codes in cases with colorectal cancer from 1998 to 2008 in Taiwan.

Major disease category	ICD-9-CM codes	Prescriptions of Chinese herbal product (%)
Infectious and parasitic diseases	001-139	1347 (1.2)
Neoplasms	140-239	34,965 (31.5)
Colorectal cancer	153-154	33,512 (30.2)
Other cancers (remainders of neoplasms)		1453 (1.3)
Endocrine, nutritional and metabolic diseases, and immunity disorders	240-279	1256 (1.1)
Mental disorders	290-319	713 (0.6)
Diseases of the nervous system and sense organs	320-389	2881 (2.6)
Diseases of the circulatory system	390-459	4010 (3.6)
Diseases of the respiratory system	460-519	10,575 (9.5)
Diseases of the digestive system	520-579	16,671 (15.0)
Diseases of the genitourinary system	580-629	3527 (3.2)
Diseases of the skin and subcutaneous tissue	680-709	1988 (1.8)
Diseases of the musculoskeletal system and connective tissue	710-739	9590 (8.6)
Symptoms, signs, and ill-defined conditions	780-799	20,499 (18.5)
Injury and poisoning	800-999	2158 (1.9)
Supplementary classification[b]	V01-V82, E800-E999	153 (0.1)
Others[a]		686 (0.6)
Total		111,019 (100.0)

[a] Others include ICD-9-CM codes 280-289, 630-677, 740-759, 760-779 and missing/error data.
[b] Supplementary classification of factors influencing health status and contact with health service, external causes of injury and poisoning.

Chinese herbal medicines were prescribed in 111,019 of visits made by CRC survivors to TCM doctors. Analysis of the major disease categories for all TCM visits of CRC survivors are summarized in Table 2, which show that "colorectal cancer" was the most common reason for using CHP, followed by "symptoms, signs, and ill-defined conditions" and "diseases of the digestive system". Details on the most frequently prescribed CHP for treating CRC by TCM doctors are provided in Table 3. As can be seen, Costusroot and Amomum Six Gentlemen Decoction is the most frequently prescribed CHP, followed by Ginseng, Poria, and White Atractylodes Powder (參苓白朮散 shēn líng bái zhú sǎn) and Center-Supplementing Qi-Boosting Decoction (補中益氣湯 bǔ zhōng yì qì tāng). Among the top 10 most frequently prescribed CHP, six containing Ginseng Radix (人參, *Panax ginseng*) and two containing Astragali Radix (黃耆, *Astragalus membranaceus*) of various doses were identified.

Although over 1214 (42.7%) CRC survivors had used CHP as the major method of treatment from 1998 to 2008, only about 20.1% (n = 244) of them sought CHP with the intent of either treating their colorectal cancer or relieving the treatment-related side effects. CHP was prescribed in addition to surgery, and/or chemotherapy, and appeared to be used as an adjunct to conventional treatment for cancer, rather than as alternatives.

4. Discussion

Previous studies reported that approximately 75% of CRC survivors used CAM therapies.[4] However, the information of CAM therapies including TCM was collected via self-reported

Table 3
Top 10 herbal formulas prescribed by TCM doctors for treating colorectal cancer among colorectal cancer patients from 1998 to 2008 in Taiwan.

Herbal formula	Pinyin transliteration	Person-day of prescriptions	Average daily dose (g)
Costusroot and Amomum Six Gentlemen Decoction	Xiang-Sha-Liu-Jun-Zi-Tang	3893	4.3
Ginseng, Poria, and White Atractylodes Powder	Shen-Ling-Bai-Zhu-San	2794	4.9
Center-Supplementing Qi-Boosting Decoction	Bu-Zhong-Yi-Qi-Tang	2592	3.2
Pinellia Heart-Draining Decoction	Ban-Xia-Xie-Xin-Tang	2435	3.1
Supplemented Free Wanderer Powder	Jia-Wei-Xiao-Yao-San	2293	4.4
Life Saver Kidney Qi Pill	Ji-Sheng-Shen-Qi-Wan	2280	3.8
Spleen-Returning Decoction	Gui-Pi-Tang	1944	3.4
Honey-Fried Licorice Decoction	Zhi-Gan-Cao-Tang	1760	2.7
Stomach-Calming Powder	Ping-Wei-San	1720	2.5
Lycium Berry, Chrysanthemum, and Rehmannia Pill	Qi-Ju-Di-Huang-Wan	1416	3.1

questionnaire, which represented the patients' own perception and expectation of the prescribed treatment. The strength of the present data is the perspective of TCM doctors concerning the treatment prescribed must be in line with the requirement of the NHI in Taiwan. They had to follow the standard diagnoses using the ICD-9-CM coding system when claiming reimbursement; and CRC survivors are exempted from all copayments once TCM doctors coded their diagnoses as ICD-9 code 153.0–154.1 (malignant neoplasm of colon and rectum) to the NHI bureau. Therefore we can rule out the possibility of recall bias. Although the present findings cannot be generalized to the comprehensive usage of various types of CAM, the present study using a random national-level sample revealed the prevalence in use of CHP prescribed by licensed TCM doctors for treating colorectal cancer.

42.7% of CRC survivors in Taiwan have ever used herbal therapies for relieving their discomfort during the study period. Only 8.6% of all CRC survivors were intending to use CHP for treating their colorectal cancer. Although CHP as a unique traditional therapy for various ailments has been used in Taiwan for over hundreds of years, more than 92% of CHP users received standard colorectal cancer treatment during the 11-year study period. The present study found that, regardless of the sites of involvement in colorectal cancer, the choice of any of the major medical options available to CRC survivors was not associated with the use of CHPs. And, the

Table 4
The composition of the top 10 herbal formulas prescribed by TCM doctors for treating colorectal cancer from 1998 to 2008 in Taiwan.

Herbal formula	Composition
Costusroot and Amomum Six Gentlemen Decoction	Ginseng Radix (*Panax ginseng*)[a], Atractylodis Macrocephalae Rhizoma (*Atractylodis Macrocephalae*), Poria (*Wolfiporia cocos*), Citri Reticulatae Pericarpium (*Citrus reticulata*), Pinelliae Rhizoma (*Pinellia ternate*), Aucklandiae Radix (*Aucklandia lappa*), Amomi Fructus (*Amomum villosum*), Glycyrrhizae Radix (*Glycyrrhiza uralensis*), Zingiberis Rhizoma (*Zingiber officinale*), Jujubae Fructus (*Ziziphus jujuba*)
Ginseng, Poria, and White Atractylodes Powder	Ginseng Radix (Panax ginseng)[a], Atractylodis Macrocephalae Rhizoma (Atractylodis Macrocephalae), Poria (Wolfiporia cocos), Amomi Fructus (Amomum villosum), Lablab Semen (Doiichos iabiab), Dioscoreae Rhizoma (Dioscorea polystachya), Nelumbinis Semen (Nelumbo nucifera), Coicis Semen (Coix lacryma-jobi), Platycodonis Radix (Platycodon grandiflorum), Glycyrrhizae Radix (Glycyrrhiza uralensis), Jujubae Fructus (Ziziphus jujuba)
Center-Supplementing Qi-Boosting Decoction	Ginseng Radix (Panax ginseng)[a], Angelicae Sinensis Radix (Angelica sinensis), Astragali Radix (Astragalus membranaceus)[b], Atractylodis Macrocephalae Rhizoma, Citri Reticulatae Pericarpium (Citrus reticulata), Bupleuri Radix (Bupleurum chinense), Cimicifugae Rhizoma (Cimicifuga heracleifolia), Glycyrrhizae Radix (Glycyrrhiza uralensis)
Pinellia Heart-Draining Decoction	Ginseng Radix (Panax ginseng)[a], Pinelliae Rhizoma (Pinellia ternate), Scutellariae Radix (Scutellaria baicalensis), Coptidis Rhizoma (Coptis chinensis), Glycyrrhizae Radix (Glycyrrhiza uralensis), Zingiberis Rhizoma (Zingiber officinale), Jujubae Fructus (Ziziphus jujuba)
Supplemented Free Wanderer Powder	Angelicae Sinensis Radix (Angelica sinensis), Atractylodis Macrocephalae Rhizoma (Atractylodis Macrocephalae), Poria (Wolfiporia cocos), Gardeniae Fructus (Gardenia jasminoides), Menthae Herba (Mentha haplocaly), Paeoniae Radix (Paeonia lactiflora), Bupleuri Radix (Bupleurum chinense), Moutan Cortex (Paeonia suffruticosa), Glycyrrhizae Radix (Glycyrrhiza uralensis), Zingiberis Rhizoma (Zingiber officinale)
Life Saver Kidney Qi Pill	Rehmanniae Radix (Rehmannia glutinosa), Dioscoreae Rhizoma (Dioscorea polystachya), Corni Fructus (Cornus officinalis), Alismatis Rhizoma (Alisma plantago-aquatica), Poria (Wolfiporia cocos), Moutan Cortex (Paeonia suffruticosa), Cinnamomi Cortex (Cinnamomum cassia), Aconiti Radix Lateralis (Aconitum carmichaelii), Achyranthis Bidentatae Radix (Achyranthes bidentata), Plantaginis Semen (Plantago asiatica)
Spleen-Returning Decoction	Ginseng Radix (Panax ginseng)[a], Angelicae Sinensis Radix (Angelica sinensis), Astragali Radix (Astragalus membranaceus)[b], Atractylodis Macrocephalae Rhizoma (Atractylodis Macrocephalae), Poria (Wolfiporia cocos), Aucklandiae Radix (Aucklandia lappa), Ziziphi Spinosi Semen (Ziziphus jujuba), Polygalae Radix (Polygala tenuifolia), Longan Arillus (Dimocarpus longan), Glycyrrhizae Radix (Glycyrrhiza uralensis), Zingiberis Rhizoma (Zingiber officinale), Jujubae Fructus (Ziziphus jujuba)
Honey-Fried Licorice Decoction	Ginseng Radix (Panax ginseng)[a], Rehmanniae Radix (Rehmannia glutinosa), Cinnamomi Ramulus (Cinnamomum cassia), Asini Corii Colla (Equus africanus asinus), Ophiopogonis Radix (Ophiopogon japonicus), Cannabis Fructus (Cannabis sativa), Glycyrrhizae Radix (Glycyrrhiza uralensis), Zingiberis Rhizoma (Zingiber officinale), Jujubae Fructus (Ziziphus jujuba)
Stomach-Calming Powder	Citri Reticulatae Pericarpium (Citrus reticulata), Magnoliae Officinalis Cortex (Magnolia officinalis), Atractylodis Rhizoma (Atractylodes lancea), Glycyrrhizae Radix (Glycyrrhiza uralensis), Zingiberis Rhizoma (Zingiber officinale), Jujubae Fructus (Ziziphus jujuba)
Lycium Berry, Chrysanthemum, and Rehmannia Pill	Rehmanniae Radix (Rehmannia glutinosa), Dioscoreae Rhizoma (Dioscorea polystachya), Corni Fructus (Cornus officinalis), Alismatis Rhizoma (Alisma plantago-aquatica), Poria, Moutan Cortex (Paeonia suffruticosa), Lycii Fructus (Lycium barbarum), Chrysanthemi Flos (Chrysanthemum morifolium)

[a] Ginseng Radix.
[b] Astragali Radix.

healthcare-seeking behavior of CRC survivors who experienced receiving different types of colorectal cancer treatments was not associated with deciding whether to visit TCM doctors. Possibly a fear of the side effects of cancer treatment, together with the stress of recurrent local and metastatic diseases following initial "curative" therapy,[26,27] is a motivation for CRC survivors to use CHPs in Taiwan. Hence, we inferred that CHP for CRC survivors in Taiwan was generally used as adjuncts to cancer treatment, rather than as replacements for it.

The present findings show that, among CRC survivors, females and those aged 40–49 years were more likely to be CHP users than males and other age groups as shown in Table 1. As shown in Table 2, "colorectal cancer" was the most common reason for using CHP (33,512). Further analysis found that TCM doctors tended to use Chinese herbal remedies targeting symptom relief as well as gastrointestinal disorders that might be the uncomfortable side effects of cancer treatment. The results indicate that, besides colorectal cancer care, health care providers should pay more attention to the general health conditions of patients suffering from either cancer-derived or cancer treatment induced symptoms and provide proactive recommendations for these medical needs.

Costusroot and Amomum Six Gentlemen Decoction and Ginseng, Poria, and White Atractyodest Powder were the two most frequently prescribed formulas for treating colorectal cancer among CRC survivors, which are all derivatives of Four Gentlemen Decoction (四君子湯 sì jūn zǐ tāng), are prescribed to alleviate various common symptoms of gastrointestinal disorders, namely vomit, lump-like feeling in the abdomen, poor appetite, abdominal distention and pain, emaciation, fatigue, or turgidity. Four Gentlemen Decoction has a long history of use as part of the traditional Chinese pharmacopoeia and was first documented in the classical Chinese text Tai-Ping Imperial Grace Pharmacy Formulas (太平惠民和劑局方 tài píng huì mín hé jì jú fāng) approximately 1107 A.D. In the classical literature Costusroot and Amomum Six Gentlemen Decoction is mainly used for treatments of phlegm and retained fluid due to Qi deficiency, incoordination between the spleen and the stomach, and other derivative symptoms and signs, while, Ginseng, Poria, and White Atractyodest Powder is said to invigorate spleen, replenish Qi, and eliminate dampness to relieve indigestion, distention and fullness in chest, borborygmus, diarrhea, myasthenia of limbs, sallow complexion, and emaciation. Other commonly prescribed formulas are associated with relieving the focal distention or fullness in the stomach along with vomiting, nausea, loose stool or poor appetite (Pinellia Heart-Draining Decoction (半夏瀉心湯 bàn xià xiè xīn tāng); Supplemented Free Wanderer Powder (加味逍遙散 jiā wèi xiāo yáo sǎn)), with a distention in the abdomen along with belching, a desire to sleep, and fatigue (Stomach-Calming Powder (平胃散 píng wèi sǎn); Center-Supplementing Qi-Boosting Decoction) or with flaccidity, with a distention in the abdomen along with low leg edema Life Saver Kidney Qi Pill (濟生腎氣丸 jì shēng shèn qì wán), with insomnia, forgetfulness due to Qi deficiency (Spleen-Returning Decoction (歸脾湯 guī pí tāng)), or with anemia, palpitation, and short of breath (Honey-fried Licorice Combination (炙甘草湯 zhì gān cǎo tāng)), or with blurred vision (Lycium Berry, Chrysanthemum, and Rehmannia Pill (杞菊地黃丸 qǐ jú dì huáng wán)). Among the top 10 most frequently prescribed CHP for treating colorectal cancer, seven have been documented to have potential beneficial effects on gastrointestinal-related symptoms. It is apparent from this study that TCM doctors in Taiwan prescribed herbal therapies mainly to reduce gastrointestinal-related symptomatic discomfort. Although clinical studies on various herbs have shown promising effects and herbal medicine has been prescribed safely by professionals in Taiwan for many years, there is as yet insufficient evidence to allow a conclusion to be reached regarding the cost-effectiveness of the aforementioned formulas in relation to the anticancer effects and the provision of symptomatic relief among CRC survivors. Further studies are warranted to assess the formulas found to be generally used by TCM doctors in this study and to determine whether they should be used as an add-on treatment for CRC survivors receiving conventional anticancer treatment.[28]

The present study has four limitations. Firstly, because the identities of the patients were encrypted and thus not available in the NHI reimbursement database, we were unable to obtain any histopathology reports to verify the diagnoses. However, because the registration of colorectal cancer as a catastrophic illness is approved on the basis of pathology and/or cytology evidence and is followed by a full waiver of copayment, such a diagnosis is made only after very serious review and is generally accurate. We have included all patients who were newly diagnosed with colorectal cancer between 1998 and 2008 from a simple random sample of one million subjects among the insured general population and the rate of insured individuals has been consistently above 96% since 1997. Therefore we can rule out the possibility of selection bias. Secondly, this study did not include Chinese herbal remedies purchased directly from TCM herbal pharmacies, nor did we include health foods containing herbs. Thus, the frequency of CHP utilization might have been underestimated. However, because the NHI system has a comprehensive coverage for TCM prescriptions, which is generally less costly than the cost of herbs sold in Taiwan's markets, the likelihood is that subjects purchased large quantities of other herbs outside the NHI database is not high. Thirdly, we are unable to draw any conclusion about the relationship between the severity of the CRC-related symptoms and CHP utilization for lack of actual clinical data. Lastly, our study is its retrospective nature or lack of a randomized placebo group. Thus, great caution is necessary in interpreting results of the most commonly prescribed Chinese formulas obtained in present study due to the high likelihood of a placebo effect. And, further research is needed to determine the safety and efficacy of these CHPs.

5. Conclusions

It is apparent that our findings may have implications for physicians attending to CRC survivors. Our results suggest that, under the co-existence of the conventional medical treatments and TCM, most CRC survivors consumed herbal therapies with the intention of relieving their gastrointestinal disorders, rather than rejecting standard cancer treatments. Recognizing the use of CHP, exploring potential interactions and adverse effects, and integrating both approaches might be more beneficial to the overall health, or survival and quality of life, of CRC survivors. Thus, health care providers had better proactively explore a personalized optimal treatment for CRC survivors, as well as attend to the patients' cancer-related or cancer treatment-induced gastrointestinal disorders.

Acknowledgments

This research was conducted at the Institute of Traditional Medicine at the School of Medicine, National Yang-Ming University. We would like to express our sincere gratitude for the support provided for this project in the form of grants from the Ministry of Health and Welfare (CCMP100–RD-033) and the National Science Council (NSC99-2320-B-010 -011 -MY2), Taiwan.

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