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Original Article

Symptom improvements and adverse effects with Reishi mushroom use: A Cross-Sectional survey of cancer patients

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ABSTRACT

Background: Reishi, a medicinal mushroom, is increasingly used for symptom control by cancer patients worldwide. However, data around patients' experiences with Reishi in oncology are lacking, limiting safe, effective clinical applications. We thus sought to evaluate patient reported benefits and harms of using Reishi.

Methods: We conducted a cross-sectional survey among Chinese cancer patients using Reishi products, probing for symptom improvements and/or adverse events (AEs) after taking Reishi. Multivariable logistic regression models assessed whether socio-demographic or clinical factors, as well as duration of Reishi use or combination with other TCM herbs, were associated with being a "responder" – reporting "quite a bit" or "very much" symptom improvement.

Results: Among 1374 participants, more than half of participants reported that nausea (55 %), fatigue (52 %), poor appetite (51 %), and depression (50 %) improved quite a bit or very much after taking Reishi. In multivariate analyses, age <65 years (adjusted odds ratios [AOR] = 1.76, p = 0.001), diagnosis ≥ 10 years (AOR = 1.78, p = 0.018), and duration of Reishi use ≥ 1 year (1–3 years: AOR = 1.53, p = 0.045; 3–5 years: AOR = 2.04, p = 0.001; >5 years: AOR = 2.07, p < 0.001) were significantly associated with higher responder rates for symptom improvement. However, 125 (9.1 %) also reported a range of AEs, including dry mouth (5 %), constipation (4 %), insomnia (3 %), pruritus (3 %) and vertigo (3 %).

Conclusion: While majority of cancer patients using Reishi reported symptom improvements, some reported adverse effects. This information can assist clinicians in advising cancer patients on safe and effective use of Reishi and help identify specific outcomes for assessment in future prospective clinical trials.

1. Introduction

Despite significant advances in conventional cancer treatments, patients and survivors still commonly experience persistent side effects and symptoms, such as fatigue, pain, and nausea, that are often poorly controlled.[1,2] To ameliorate these, more than half of cancer patients worldwide use complementary and alternative medicine (CAM) as part of their cancer treatment or recovery, with the highest prevalence among developing countries.[3,4] Herbal medicine in particular is often used by patients with the hopes of preventing cancer metastasis or recurrence, enhancing the immune system, managing comorbid symptoms, improving overall quality of life, and addressing side effects and other needs unmet by conventional care.[5,6] For many patients, herbal medicine also offers a sense of personal autonomy and choice, with locally available, culturally appropriate, and familiar, easy-to follow-regimens.[6,7]

Reishi is one of the most popular herbal medicines among cancer patients worldwide.[8-10] Epidemiological research in China has shown that use among breast cancer survivors increased from 18.9 % in the 1990s to 58.4 % by 2006.[10] Scientifically known as Ganoderma Lucidum (G. Lucidum), Reishi is a type of medical mushroom that has been used in Traditional Chinese Medicine (TCM) for over 2000 years for "promoting vivacity and longevity".[11,12] Beyond China, Reishi is also cultivated in Japan, Korea, Malaysia, North America, and in the tropical and warm temperate regions of India. It has been listed in the American Herbal Pharmacopoeia and Therapeutic Compendium as well as in the Chinese Pharmacopoeia.[13] It typically grows on deciduous trees, especially those

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that are dead or dying, and is commonly found on species such as oak, pyrus, and maple.[14,15] Globally, a variety of Reishi-derived products are available as dietary supplements or other over the counter (OTC) products. However, in many Asian countries such as China, Japan, and Korea, preparations of Reishi may be classified as drugs requiring a physician's prescription.[16]

Research on the therapeutic potential of Reishi indicates that the basidiocarp, mycelia, and spores of Reishi contain around 400 different bioactive compounds,[17] among which triterpenoids and polysaccharides are the two major active anti-cancer constituents.[18] Triterpenoids are recognized for their anti-inflammatory, anti-tumor, and cytotoxic activities, inhibiting tumor invasion and metastasis.[13,19] Polysaccharides, particularly beta-glucans, activate crucial immune cells like macrophages and natural killer cells, supporting immune surveillance and tumor elimination.[20,21] Moreover, these constituents offer symptom relief from cancer and its treatments, impacting various bodily functions including muscle function, antioxidant capacities, cardiovascular and hepatic functions, immunomodulation, hormonal regulation, and blood glucose control.[22]

Despite these promising biochemical findings, rigorous clinical evidence is limited. Promising data suggest Reishi may be a safe, effective complementary therapy alongside conventional cancer treatments,[23,24] although most findings originate from in vitro studies.[23] While several small clinical trials have investigated Reishi use in oncology settings, their outcomes mainly focused on overall quality of life and therefore lack specificity.[25-27] To our knowledge, no studies have specifically evaluated patients' experiences with integrating Reishi into their conventional cancer care. As a result, it is difficult to advise patients on the symptoms for which Reishi may be beneficial, or the potential adverse effects.

To address this critical gap, we conducted a cross-sectional survey of Chinese cancer patients using Reishi products. Our study aimed to identify patients-reported benefits and harms, as well as clinical and demographic factors associated with symptom improvement. Our findings offer novel insights into the effective, safe integration of herbal medicine into oncology care and can also help researchers focus on appropriate, patient-centered outcomes in future trial design, ultimately improving quality of life among patients and survivors.

2. Methods

2.1. Sample and study design

We conducted a cross-sectional survey of cancer patients and survivors using Reishi products in China from October 2022 to December 2022. Participants were recruited from a database of customers purchasing Reishi products from Zhongke Health International LLC. Eligible participants included individuals diagnosed with cancers of all types and stages who were 18 years of age or older, previously or currently using Reishi products, and fluent in both written and spoken Mandarin. Trained research staff contacted potential participants by phone or WeChat (a popular messaging tool in China) to confirm eligibility, explain the study's aims and procedures, and obtain oral or written informed consent. Participants had the option of completing surveys online or by phone, with data was collected by WJX (Changsha Ranxing IT Ltd.), a Chinese platform with functions equivalent to SurveyMonkey. In appreciation for participation, participants received gifts with an approximate value of $2 upon survey completion. This study was approved by Ethics Committee of Xiyuan Hospital, China Academy of Chinese Medical Sciences (2022-XLA129–1).

2.2. Study variables

2.2.1. Outcomes

Symptom improvements: We used items from the Edmonton Symptom Assessment System (ESAS) to evaluate symptom improvements af-

ter taking Reishi. ESAS is a brief instrument widely used to evaluate patient-reported symptoms in cancer care.[28] It measures ten symptoms frequently reported by the cancer population: pain, tiredness, nausea, depression, anxiety, drowsiness, poor appetite, shortness of breath, feeling of not well-being, and distress.[29] It has been validated in Chinese, with a Cronbach's alpha coefficient of 0.72.[30] To focus on Reishi's potential impact on specific symptoms, we excluded "feeling of not well-being". Guided by the current literature and our clinical experience with Reishi,[24,31,32] we included 5 additional relevant symptoms: pruritus, constipation, diarrhea, hot flash, and insomnia. A five-point Likert scale prompted participants to identify and rate any improvements in each symptom after taking Reishi (0 = do not have this symptom, 1 = no improvement, 2 = *a little* improvement, 3 = quite a bit improvement, and 4 = very much improvement).

Adverse events: Our survey also probed participants about a range of potential AEs after using Reishi. Participants were first asked if they had experienced any AEs after using Reishi. If they answered yes, a list of AEs was then presented: poor appetite, dizziness, insomnia, dry month, headache, constipation, facial flushing, diarrhea, and pruritus. These items were chosen based on current literature and our clinical experience with Reishi.[24,31-33] Participants then used a four-point Likert scale to indicate the occurrence and severity (1 = none, 2 = *a little* 3 = quite a bit, and 4 = very much) of each AE experienced after using Reishi. Participants also had the opportunity to specify any other AEs experienced after using Reishi.

2.2.2. Co-variables

Sociodemographic factors included age, gender, location, education, and employment status. We also collected data on cancer-related variables, such as cancer type, cancer stage, years since cancer diagnosis, and current cancer treatment status (diagnosis, post-surgery, chemotherapy/radiation, survivorship/endocrine, palliative care, and unknown). Additionally, given that variations in Reishi use may influence its effects, we asked patients to provide information regarding their Reishi utilization, including the types of Reishi used in the past month, the duration of Reishi usage, and whether they combined it with other TCM herbs.

2.3. Statistical analysis

Descriptive statistics were used to assess symptom improvements, AEs, as well as co-variables (e.g., age, gender, and cancer type), using frequencies, proportions and means (standard deviation [SD]). For each symptom, we calculated the proportion of participants who reported improvement, excluding those who reported "do not have this symptom". We categorized those who reported improving "a little", "quite a bit" and "very much" as showing "some" improvement and those who reported "quite a bit" and "very much" as demonstrating "clinically meaningful" improvement. Similarly, the proportion of participants who experienced each AE was calculated. We combined those who reported experiencing each AE "a little", "quite a bit" and "very much" as indicating "some" AEs and those who reported "quite a bit" and "very much" as having "clinical meaningful" AEs.

To explore factors that may influence symptom improvements, we dichotomized participants into "non-responders" and "responders" – those reporting clinically meaningful improvement in at least one symptom. We only included participants who reported having at least one symptom in this analysis (N = 1120, 81.5 %). First, we conducted Chi square tests to assess whether responder status differed by participant characteristics (demographic, clinical, duration of Reishi utilization, and combination with other TCM herbs). Then characteristics with a significance level of $P < 0.2$ were included as independent variables in multivariable logistic regression models, with responder status as the dependent variable. All analyses were two-sided with a p-value of <0.05 for statistical significance. Statistical analyses were conducted using SPSS (version 26; IBM Corp).

Table 1
Characteristics of participants.

Characteristics	Total No.	No.	%
Mean age in years (SD)	1369	68.4 (10.3)	
<65		421	27.1
65–75		598	43.8
>75		350	29.1
Gender	1374		
Male		483	35.2
Female		891	64.8
Education	1374		
Less than college		1122	81.7
College or higher		252	18.3
Employment status	1374		
Working		91	6.6
Unemployed or retired		1283	93.4
Cancer type	1374		
Breast		373	27.1
Lung		276	20.1
Colorectal		197	14.3
Gynecologic		109	7.9
Gastric		104	7.8
Prostate		65	4.7
Other*		250	18.2
Years since cancer diagnosis, mean years (SD)	1373	8.22 (6.3)	
<2		163	11.9
2–5		283	20.6
5–10		452	32.9
≥10		475	34.6
Cancer stage	1374		
l-lll		930	67.7
lV		82	6.0
Unknown		362	26.4
Current cancer treatment status	1374		
Diagnosis		6	0.4
Post-surgery		557	40.5
Chemotherapy/radiation		45	3.3
Survivorship/endocrine		425	30.9
Palliative care		136	9.9
Unknown		205	14.9

Abbreviations: SD, Standard deviation.
* Other cancer types include brain, bone, head and face, esophagus, and other.

Table 2
Factors associated with patient-reported symptom response.

Characteristics	Total No.[†]	Responder (%)	P-value
Mean age in years (SD)			0.056
<65	354	214 (60.5)	
65–75	486	272 (56.0)	
>75	277	141 (50.9)	
Gender			0.49
Male	389	213 (54.8)	
Female	731	416 (56.9)	
Cancer stage			0.31
l-lll	751	434 (57.8)	
lV	68	35 (51.5)	
Cancer type			0.40
Breast	310	179 (57.7)	
Lung	231	119 (51.5)	
Colorectal	164	92 (56.1)	
Gynecologic	93	57 (61.3)	
Gastric	75	36 (48.0)	
Prostate	53	31 (58.5)	
Other*	194	115 (59.3)	
Years since cancer diagnosis			0.000
<2	138	55 (39.9)	
2–5	243	118 (48.6)	
5–10	362	212 (58.6)	
≥10	377	244 (64.7)	
Years since taking Reishi			0.000
<1 year	226	91 (40.3)	
1–3 years	185	94 (50.8)	
3–5 years	167	100 (59.9)	
≥5 years	542	344 (63.5)	
Other TCM herbs			0.70
No	468	266 (56.8)	
Yes	652	363 (55.7)	

* Other cancer types include brain, bone, head and face, esophagus, and other.
† The Total No of each characteristic was calculated excluding participants who reported "do not have this symptom".Characters with p-value < 0.2 were included into multivariate logistic regression.

3. Results

3.1. Characteristics of participants

Of the 1600 cancer patients and survivors approached, 1374 (85.9 %) agreed to participate and completed the survey. The mean age was 68.4 years (SD, 10.3 years), ranging from 25 to 100 years. The majority were female (891, 64.8 %), had less than college education (81.7 %), and were currently unemployed or retired (93.4 %). Participants were from 24 provincial-level administrative regions (70.6 % of 34 regions total), with the majority from the East (51.4 %) and South (17.3 %) regions.

Participants represented a diverse range of cancer types, with the most common being breast (27.1 %) and lung (20.1 %). The mean time since diagnosis was 8.2 years (SD, 6.3 years). Over two-thirds of participants (67.7 %) were classified as stage I-III, and 40.5 % had completed surgical treatment at the time of the survey (Table 1).

3.2. Reishi utilization

Among the 1374 participants, nearly half (49.1 %) had been taking Reishi for over 5 years, 20.5 % for <1 year, 15.9 % for 1 to 3 years, and 14.5 % for 3 to 5 years. More than half (55.9 %) combined Reishi products with other TCM herbs.

3.3. Patient perceived symptom improvement after using Reishi

Fig. 1 shows symptom improvements reported by participants after using Reishi. Among 1120 (81.5 %) participants who had experienced symptoms, over 80 % reported improvement in at least one symptom. Participants were most likely to report clinically meaningful improvement for nausea (55 %), fatigue (52 %), poor appetite (51 %), depression (50 %), and drowsiness (49 %).

3.4. Factors associated with clinically meaningful response to Reishi

Among participants with survey-specified symptoms ($N = 1120$), 629 (56.2 %) were responders. Chi-square tests (Table 2a) found associations between responder status and age, years since cancer diagnosis, and years taking Reishi (all $p < 0.2$). Compared to participants under 65 years old, those aged 65–75 years and older than 75 years had lower responder rates (60.5% vs. 56.0 % and 50.9 %, respectively, $p = 0.056$). Longer times since diagnosis were associated with higher responder rates (≥10 years, 5–10 years, 2–5 years, and <2 years: 64.7% vs. 58.6% vs. 48.6 %, and 39.9 % respectively, $p = 0.000$). Similarly, longer Reishi usage was related to higher responder rates (≥5 years, 3–5 years, 1–3 years, and <1 year: 63.5% vs. 59.9% vs. 50.8 %, and 40.3 % respectively, $p = 0.000$).

Based on these Chi square results, three factors with univariate p value of <0.2–age, years since diagnosis, and years taking Reishi–were included in the multivariable logistic regression model (Table 3). This analysis showed participants under 65 years old were 1.76 times more likely to be responders than those over 75 years old (95 % CI 1.26–2.46, $p = 0.001$). Additionally, participants at least 10 years since diagnosis
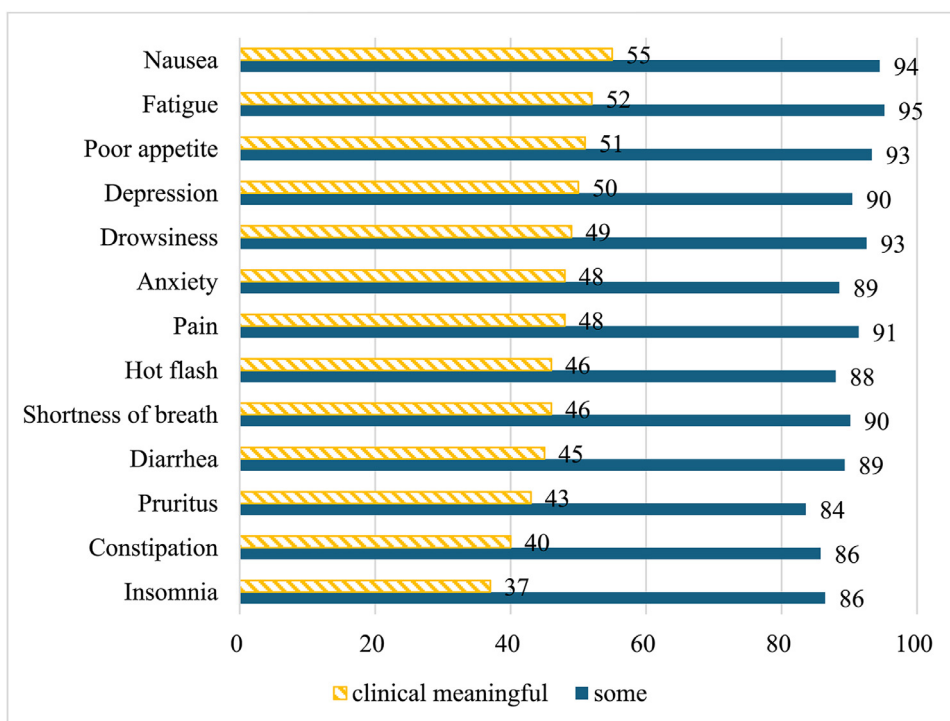
Fig. 1. Proportion (%) of Participants Experienced Symptom Improvement After Reishi Use For each symptom, we calculated the proportion of participants who reported improvement among participants who experienced the symptom (excluding those who reported "do not have this symptom"). We categorized those who reported improving "a little", "quite a bit" and "very much" as showing "some" improvement and those who reported "quite a bit" and "very much" as demonstrating "clinically meaningful" improvement.

Table 3
Multivariate logistic regression: factors associated with patient-perceived symptom response.

	AOR	95 % CI	P-value
Age (years)			
>75	–		
65–75	1.29	0.95–1.75	0.098
<65	1.76	1.26–2.46	0.001
Diagnosis (years)			
<2	–		
2–5	1.09	0.69–1.72	0.72
5–10	1.42	0.90–2.26	0.14
≥10	1.78	1.10–2.89	0.018
Time since taking Reishi (years)			
<1	–		
1–3	1.53	1.01–2.31	0.045
3–5	2.04	1.32–3.17	0.001
>5	2.07	1.39–3.08	0.000

Abbreviations: CI, confidence interval; AOR, adjusted odds ratio.
p-value < 0.05 is statistically significant.

were 1.78 times more likely to be responders than those newly diagnosed (<2 years) (95 % CI 1.10–2.89, $p = 0.018$). Compared to those using Reishi for <1 year, those using it for 1–3 years, 3–5 years, and >5 years were 1.53, 2.04, and 2.07 times more likely to be responders, respectively (1–3 years: 95 % CI 1.01–2.31, $p = 0.045$; 3–5 years: 95 % CI 1.32–3.17, $p = 0.001$; >5 years: 95 % CI 1.39–3.08, $p = 0.000$).

3.5. Adverse events

Among all participants ($N = 1374$), 125 (9.1 %) reported experiencing adverse effects (AEs) after using Reishi. The most common AE was dry month, experienced by 5 % of participants, followed by constipation (4 %), insomnia (3 %), and pruritus (3 %) (Fig. 2). Beyond the survey's

prespecified AEs, 6 participants reported abdominal discomfort (e.g., bloating), and 1 described mild inflammatory reactions.

4. Discussion

To our knowledge, no prior studies have evaluated patients' experiences integrating Reishi into their conventional cancer care. This cross-sectional study of 1374 cancer patients and survivors using Reishi products thus offers novel insights into the population's characteristics, Reishi usage patterns, and patient-reported benefits and risks. We also found that factors such as younger age (<65), longer duration since diagnosis (≥10 years), and extended Reishi usage (≥1 year) were significantly associated with higher responder rates for symptom improvement. These data can inform the design of future clinical trials focusing on patient-reported outcomes. Our findings can also assist clinician-patient communication regarding Reishi use.

In this large survey study, we identified the most commonly reported symptom improvements and adverse events associated with Reishi use. To our knowledge, only two studies have investigated Reishi's effects on patient-reported outcomes in oncology.[25,33] One pilot randomized clinical trial[33] with 48 breast cancer patients undergoing endocrine therapy showed that 4-week Reishi powder use significantly reduced fatigue, anxiety, depression, and appetite loss compared to the placebo. Similarly, around 50 % participants in our study reported clinically meaningful improvement in these same symptoms. Another study with 82 lung cancer patients undergoing chemotherapy revealed that a Reishi formula led to non-statistically-significant improvements in quality of life, general health, emotional well-being, and fatigue compared to placebo.[25] Additionally, consistent with our study, both studies found Reishi to be safe with mild adverse events. However, the former study[33] reported higher rates of dizziness (16.0 %), dry mouth (12.0 %), diarrhea (8.6 %) compared to our findings, potentially due to its small sample size or the endocrine therapy received by patients.
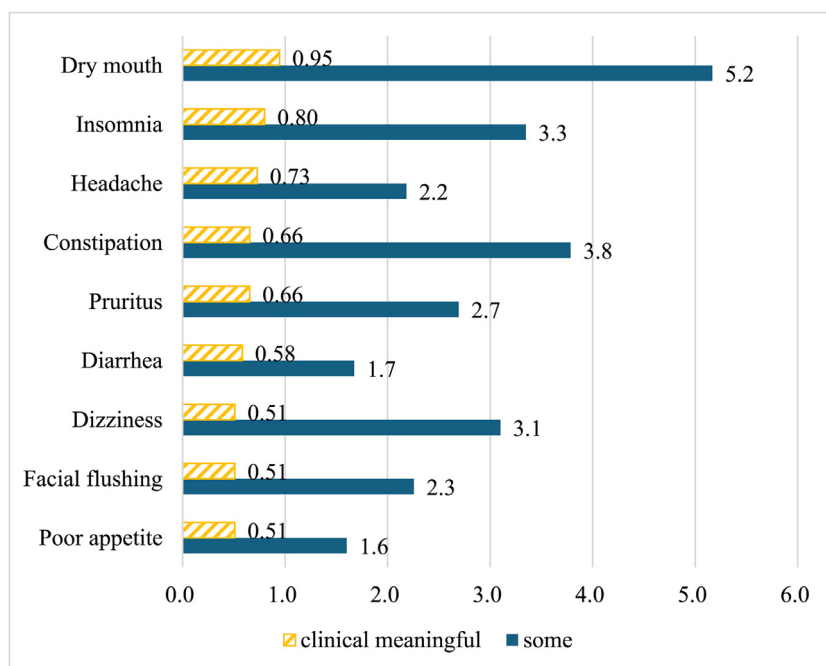
Fig. 2. Proportion (%) of Participants Experienced Adverse Events After Reishi Use (*N* = 1374). For each adverse event, we calculated the proportion of participants who reported experiencing each adverse event among all participants. We combined those who reported experiencing each AE "a little", "quite a bit" and "very much" as indicating "some" AEs and those who reported "quite a bit" and "very much" as having "clinical meaningful" AEs.

Our epidemiological examination of patient-reported benefits can inform future clinical trials to evaluate the specific effects of Reishi. In one large, population-based cohort study of breast cancer survivors. (*n* = 4149), Reishi use was associated with better social but worse physical well-being in breast cancer survivors.[10] However, due to the study's design, it was impossible to determine whether Reishi negatively influenced patients' physical well-being or if individuals with low physical well-being were more likely to use Reishi. In contrast, our study found that the most commonly reported benefits from Reishi were improved fatigue, depression, nausea, and poor appetite. Future prospective clinical trials should aim to target these specific symptoms or symptom clusters. Furthermore, existing literature supports the association between impaired immune function, inflammatory reactions, and the symptoms (e,g. fatigue, depression) highlighted in this study.[34-36] Bioactive components in Reishi, such as fungal immunomodulatory proteins and polysaccharides, may enhance the host's immune response and inhibit pro-inflammatory cytokine expressions in invitro experiments.[37,38] Therefore, future clinical trials should also evaluate immune or inflammation biomarkers, such as natural killer cells, T cells, and B cells[26,37,39] to explore the underlining mechanisms of Reishi's effects on symptom control.

Until evidence from well-conducted clinical trials is available, our data can aid patient-centered clinician communication. Despite the widespread use of herbal medicines, there is very limited communication between physicians and patients about such use. A recent survey study revealed that 73 % of oncology professionals lack sufficient knowledge to assist patients with herbs and other CAM treatments,[40] hindering their discussions with patients on appropriate use.[41] Additionally, nearly half of cancer patients avoid disclosing their herbal use to oncologists,[42] increasing the risk of significant side effects due to improper usage. Our study can inform and empower clinicians to raise these issues and communicate evidence-based information about Reishi's reported benefits (e.g. fatigue, depression, nausea, poor appetite) and potential side effects (e.g. dry mouth, insomnia, headaches).

Our study has several limitations. First, it was conducted in a Chinese cancer population, so the attitudes and usage patterns we observed might differ in other contexts. Second, most of our participants were

older, retired, and had relatively low levels of education. Further research should explore Reishi usage among patients in other age, educational, and employment cohorts. Third, the long recall period may give rise to recall bias. Fourth, as the majority of participants in our study were long-term Reishi users, there may be selection bias favoring the benefits of Reishi. Fifth, as this is a cross-sectional survey study, all benefits and AEs were patient-reported and could be due to either placebo/nocebo effects or regression to the mean. Participants may also exaggerate benefits or downplay adverse events due to recall bias or a desire to conform to social expectations. Further research is essential to establish causality and explore the long-term effects of Reishi use. Findings from this study should be tested through rigorous clinical trials. Sixth, the absence of a control group in our study limits the ability to definitively attribute symptom improvements to Reishi, as they could also be influenced by concurrent therapies or the natural progression of the disease. To enable replication and comparison, future research should rigorously document the specifics of Reishi products used, including dosages, preparation methods, and standardization of active compounds. Lastly, our participants were limited to those who took Reishi products from Zhongke Health International LLC; results may not be generalizable to other Reishi products or preparations.

Despite these limitations, the current study is the first with a large sample size to investigate the experiences of people with diverse cancer types using Reishi in their cancer care. The findings identify specific potential benefits and harms, as well as factors related to these effects. Our data provides critical evidence from patients' experiences that can be incorporated in shared decision making about the use of Reishi in cancer settings. Further high-quality clinical trials are needed to develop more robust evidence about Reishi's specific benefits, potential risks, and the underlying clinical mechanisms.

Conflict of interest

Dr. Mao reports grants from Tibet Cheezheng Tibetan Medicine Co Ltd and Zhongke Health International LLC outside the submitted work. Dr. Feng is a co-author of this paper and serves as the president of Zhongke Health Industry Group Corp., Ltd. The author's role in the com-

pany did not influence the design, execution, or interpretation of the study results. All other authors declare no conflicts of interest related to this research.

Funding

Ethics statement

This study was approved by Ethics Committee of Xiyuan Hospital, China Academy of Chinese Medical Sciences (2022-XLA129–1). Informed consent was obtained from all participants.

Data availability

The data of this study will be available from the corresponding author upon reasonable request.

CRediT authorship contribution statement

Xiaotong Li: Conceptualization, Methodology, Formal analysis, Writing – original draft. **Lingyun Sun:** Methodology, Writing – review & editing. **Susan Chimonas:** Writing – review & editing. **Susan Q. Li:** Formal analysis, Writing – review & editing. **Peng Feng:** Writing – review & editing. **Yufei Yang:** Writing – review & editing. **Jun J. Mao:** Conceptualization, Methodology, Writing – review & editing, Supervision, Funding acquisition.

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