# **BMJ Open** Knowledge, attitudes and practices relating to nutritional support and immune-related adverse events among patients undergoing immunotherapy for liver cancer: cross-sectional study

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## ABSTRACT

**Objectives** To examine the knowledge, attitude and practice (KAP) regarding immune-related adverse events (irAEs) and nutritional support among patients with liver cancer (LC).

Design Cross-sectional study.

Setting Recruitment was carried out at Haikou People's Hospital, Haikou, China, from December 2022 to April 2023.

Participants Patients undergoing immunotherapy for LC. Primary and secondary outcome measures Mean knowledge, attitudes, practices, and lifestyle scores were assessed using an investigator-designed questionnaire completed by patients during immunotherapy.

**Results** The study included 402 participants. The mean knowledge, attitudes, practices and lifestyle scores were 6.60±3.51 (/10, 66.00%), 41.26±5.06 (/50, 82.52%), 30.74±4.20 (/40, 76.85%) and 42.37±6.04 (/55, 77.04%), respectively. Attitude scores were associated with practice scores ( $\beta$ =0.381, p<0.001) and lifestyle  $(\beta=1.928, p<0.001)$ . Urban residence was associated with higher attitude scores ( $\beta$ =1.242, p=0.013). Living with someone was associated with a higher attitude score  $(\beta=1.619, p=0.044)$ . More than one immunotherapy line was associated with a higher lifestyle score ( $\beta$ =1.928, p<0.001). Finally, the female gender was associated with a lifestyle score ( $\beta$ =1.431, p=0.023).

Conclusion Patients with LC and undergoing immunotherapy had moderate KAP towards irAEs and nutritional support. They also displayed moderate lifestyle scores. Urban residents, people not living alone, females and those having received two or more immunotherapy treatments were positively associated with attitude, while attitude was positively associated with practice and lifestyle.

# INTRODUCTION

The estimated worldwide incidence of liver cancer (LC) in GLOBOCAN 2022 was 865269 new cases, and mortality was 757 948.<sup>1</sup> Most LCs are hepatocellular carcinoma (HCC).<sup>2 3</sup> The worldwide agestandardised annual mortality rates of LC

# STRENGTHS AND LIMITATIONS OF THIS STUDY

- $\Rightarrow$  While a cross-sectional design is useful for capturing data at a single time point, it limits the ability to establish causality or infer temporal relationships between variables.
- $\Rightarrow$  Conducting the study at a single hospital may introduce selection bias and limit the generalisability of the findings to other settings or populations.
- $\Rightarrow$  The reliance on self-reported measures for assessing knowledge, attitude, practice and lifestyle introduces the potential for response bias and social desirability bias, impacting the accuracy of the results.
- $\Rightarrow$  Although the study identifies certain factors that were associated with attitudes and lifestyle, there may be other unmeasured confounding variables that could affect the outcomes.
- $\Rightarrow$  While the study assessed knowledge, attitude and practices towards immune-related adverse events. nutritional support and lifestyle factors, it may not capture all relevant aspects involved in patient care and outcomes during immunotherapy for lung cancer.

Protected by copyright, including for uses related to text and data mining, AI training, and are 13.9 per 100000 in men and 4.9 per <u>0</u> 100000 in women.<sup>4</sup> The most important risk factors for LC are pre-existing liver cirrhosis and hepatitis B infection (due to both direct oncogenic effect and risk of cirrhosis).<sup>2 3 5 6</sup> Risk factors for liver of cirrhosis (and therefore risk factors for **G** LC) include hepatitis C infection, alcohol **3** use and nonalcoholic steatohepatitis.<sup>2 3 5 6</sup> The incidence of LC is higher in men and

generally follows the geographical distribution of hepatitis B virus and hepatitis C.<sup>256</sup> LC management is multidisciplinary and involves surgery (when possible), chemotherapy, targeted therapy, radiotherapy and immunotherapy.<sup>2 5 6</sup> Despite optimal treatments, the 5 year survival is 22% in the USA<sup>7</sup> and 12.1% in China,<sup>8</sup> with lower survival in rural China (11.2%) compared with urban areas (14.0%).<sup>9</sup>

Immunotherapy is a recent paradigm in treating cancers, including LC.<sup>10–12</sup> Cancer cells can escape the immune system through the PD-1/PD-L1 pathway,<sup>13 14</sup> and drugs targeting PD-1 or PD-L1 have been developed to restore the immunosurveillance of cancer cells and their destruction.<sup>10-12</sup> Still, the PD-1/PD-L1 usually plays roles in immune tolerance and preventing autoimmune reactions,<sup>13</sup><sup>14</sup> and inhibiting the PD-1/PD-L1 pathway can lead to immune-related adverse events (irAEs). The pathogenesis of irAEs is still poorly understood, but they involve inflammatory reactions of normal tissues that can be bothersome but also life-threatening.<sup>15–17</sup>

Adequate nutrition is also essential in patients with LC to ensure optimal outcomes, and nutritional support can be necessary in patients with inadequate nutrition due, for example, to gastrointestinal adverse events (AEs) from therapies.<sup>18 19</sup> Still, the palliation of some symptoms of HCC (eg, loss of appetite, weakness, fatigue, etc) using androgens (since most LCs occur in males) can help alleviate the need for nutritional support.<sup>20</sup> The management of irAEs and nutrition involves healthcare providers. It can involve medical interventions (eg, management of irAEs, enteral nutrition and hospitalisation). However, patient selfmanagement is also important to ensure that preventive measures are taken (such as not smoking, not drinking and eating properly) and so that patients know when to consult.<sup>21</sup>

A systematic review showed that the eating habits of Chinese patients with cancer and chemotherapy were poor, but no data are available for immunotherapy specifically.<sup>22</sup> Another study suggested that Chinese patients with cancer had a basic understanding of irAEs,<sup>23</sup> but this study was not specific to LC and did not evaluate attitudes and practices. A knowledge, attitude and practice (KAP) survey is a tool that provides quantitative and qualitative data about gaps, misconceptions and misunderstandings that constitute barriers towards the optimal performance of a given task or set of tasks in a specific group of individuals.<sup>24 25</sup> Compared with other types of cancer, for example, breast cancer, patients with LC have a poorer prognosis, and men are more at risk. In addition, the risk factors for LC are different from other cancers, mainly encompassing chronic liver diseases, alcohol drinking and hepatitis virus infection. Those differences could influence patients' KAP towards irAEs.

Therefore, this study aimed to investigate the KAP lifestyle (KAP-L) of patients with LC and immunotherapy patients regarding nutritional support and irAEs. The results can provide crucial information to design educational interventions to improve patient self-management and outcomes.

# **MATERIALS AND METHODS** Study design and participants

This cross-sectional study was conducted at Haikou People's Hospital from December 2022 to April 2023 and enrolled patients undergoing immunotherapy for LC. This study was approved by the Institutional Review Board of Haikou People's Hospital (2022-Ethical Review-231). All participants signed the informed consent form before completing the survey.

The inclusion criteria were (1) aged 18–90 years, (2) pathologically confirmed locally advanced or unresectable LC and (3) undergoing immunotherapy (any line of treatment). The exclusion criteria were (1) surgical patients; (2) simultaneously suffering from other malignant tumours; (3) before or planned liver transplanta-tion; (4) active autoimmune diseases; (5) ambiguous consciousness, unable to fill out by oneself or with assis-tance: or (6) withdrawal during the filling process tance; or (6) withdrawal during the filling process.

Questionnaire and quality control A self-designed questionnaire consisting of five dimensions was developed based on the relevant literature.<sup>15 18 19 22 23 26</sup> ō After the questionnaire design, modifications were made by incorporating insights from 15 experts in nutrition in oncology and medical oncology, removing similar or redundant questions and refining questions with unclear phrasing. Before the official distribution, a small-scale pilot test (70 participants) was conducted, yielding a Cronbach's  $\alpha$  coefficient of 0.853 (0.879 for knowledge, 0.828 for attitudes and 0.758 for practice), indicating  $\underline{\textbf{9}}$ strong internal consistency.

The final questionnaire was in Chinese and encompassed (1) participants' demographic information (including age, gender, residential area, education level and income level, etc), (2) knowledge dimension (10  $\mathbf{a}$ items, with a score of one assigned for correct answers > and zero for incorrect or uncertain responses), (3) attitude dimension (10 items, scored using a five-point Likert scale, ranging from 'strongly positive' (five points) to 'strongly negative' (one point)), (4) practice dimension (eight items, scored using a five-point Likert scale, ranging from 'always' (five points) to 'never' (one point)) and (5) lifestyle dimension (11 items, also scored using a fivepoint Likert scale, ranging from 'always' (five points) to 'never' (one point)). Higher scores correspond to better knowledge, more positive attitudes and more proactive practices. Scores <60% were considered poor, scores 60%-79% were considered moderate and scores >80\% were considered adequate, based on Bloom's criteria.<sup>27</sup>

An online questionnaire was developed using the WeChat-based Wenjuanxing platform. A QR code was generated for data collection via WeChat. The participants accessed and completed the questionnaire by scanning the QR code received via WeChat. In order to ensure the quality and completeness of the questionnaires, all items were made mandatory. Incomplete questionnaires were excluded during the quality control process. Therefore,

all items were responded to, which would not affect the results.

The research team members reviewed the integrity, internal consistency and rationality of all collected questionnaires for quality control. A given IP address could be used to submit a questionnaire only once. Questionnaires that took <110s to complete were excluded. Questionnaires completed using all the same options (eg, the first option) were deemed invalid. Finally, questionnaires containing impossible values (eg, impossible age, height or weight) or logical errors were excluded. The Cronbach's α coefficient for all valid questionnaires was 0.840 (0.913 for knowledge, 0.800 for attitudes and 0.718 for practice).

### **Statistical analysis**

The statistical analysis software was SPSS 26.0 (IBM, Armonk, NY, USA). Quantitative variables were described as means±SD, while group comparisons were conducted using Student's t-test or analysis of variance. Categorical variables were presented as n (%). Pearson's correlation analysis explored the relationships between KAP scores. The study used a structural equation modelling (SEM) analysis to validate various causality hypotheses empirically. These hypotheses encompassed (1) knowledge has direct associations with attitudes, practices and lifestyles, (2) attitudes have direct associations with practices and lifestyles, (3) residential area and status have direct associations with attitudes, (4) gender has direct associations with attitudes and lifestyles and (5) the number of immunotherapy medication usage has a direct association with lifestyles. All statistical tests were two-tailed, and P values <0.05 were considered statistically significant.

# RESULTS

## **Characteristics of the participants**

The study included 419 respondents. After removing the following cases: (1) one respondent with impossible height and weight, (2) nine respondents answered with contradictory answers and (3) seven respondents with a completion time of less than 110s, a total of 402 valid questionnaires were included in the analysis (figure 1).



The participants' ages were 56.84±11.93 years. Most participants were male (71.89%), had a body mass index of  $18.5-23.9 \text{ kg/m}^2$  (60.95%), were living in rural areas (55.97%), were not living alone (89.30%), were married (90.05%), had high school or technical secondary school education (34.08%), had an income of 2000-5000 RBM/ months (48.76%), had health insurance (99.50%), had gastrointestinal symptoms (50.75%), did not experience irAEs (89.80%), received one line of immunotherapy (54.23%) and were not familiar with the name of their Protected by copy immunotherapy (65.17%) (online supplemental table S1).

#### **Knowledge**

The mean knowledge score was  $6.60 \pm 3.51$  (/10, 66.00%) (table 1). No significant differences were observed according to the characteristics of the participants. The knowledge item with the lowest score was K1 (50.75%; "Adverse reactions can occur during immunotherapy, but they are normal occurrences that do not require excessive attention."), while the item with the highest score was K9 (72.39%; "Prompt identification and timely reporting ğ of symptoms of malnutrition and immune-related events uses to healthcare professionals are not only beneficial for immunotherapy and ameliorating immune-related related adverse symptoms and nutritional status but also increase the likelihood of continuing immunotherapy.) (online supplemental table S2).

#### Attitude

<u>a</u> The mean attitude score was  $41.26 \pm 5.06$  (/50, 82.52%) (table 1). Higher attitude scores were observed in urban dwellers (41.99±5.19 vs 40.68±4.89, p=0.010), those not living alone (41.44±5.07 vs 39.72±4.76, p=0.035) and those with higher income (>20000 CNY/month: 43.50±3.46; <2000 CNY/month: 39.66±5.88; p=0.005) (online supple- 2 mental table S1). The attitude item with the lowest ⊳ score was A1 (64.52%; "I consider nutritional support to be highly significant throughout the entire course of immunotherapy."), while the item with the highest score was A10 (93.28%; "I believe that maintaining a positive , and mindset and quality sleep are important during immunotherapy.") (online supplemental table S2).

#### Practice

The mean practice score was  $30.74 \pm 4.20(/40, 76.85\%)$ (table 1). No significant differences were observed according to the characteristics of the participants. The "If required, I am prepared to receive enteral feeding " with the line ") with ") with the line ") with ") with with the line with the highest score was P1 (86.07%; "I am capable of cooperating with medical personnel for comprehensive treatment monitoring and follow-up.") (online supplemental table S2).

# Lifestyle

The mean lifestyle score was  $42.37\pm6.04$  (/55, 77.04%) (table 1). Higher lifestyle scores were observed in females

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Table 1 Knowledge, at	itude and practice scores
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	n=402			
Dimension	Range, points	Mean score, mean±SD	Proportion, %	
Knowledge	0~10	6.60±3.51	66.00%	
Attitude	10~50	41.26±5.06	82.52%	
Practice	8~40	30.74±4.20	76.85%	
Lifestyle	11~55	42.37±6.04	77.04%	

(43.43±5.36 vs 41.95±6.24, p=0.027), widows (widows: 45.20±5.55; married: 42.49±5.99; unmarried: 39.09±6.45; p=0.031) and with more than one immunotherapy line (43.46±6.06 vs 41.45±5.88, p=0.001) (online supplemental table S1). The lifestyle item with the lowest score was L11 (30.35%; 'citrus fruits (grapefruit, pomelo, honey pomelo, etc.).)'), while the item with the highest score was L2 (83.84%; 'alcohol consumption') (online supplemental table S2).

# **Correlations**

The knowledge scores were correlated to the attitude scores (r=0.105, p=0.035). The attitude scores were correlated to the practice (r=0.460, p<0.001) and life-style (r=0.486, p<0.001) scores. The practice scores were correlated to the lifestyle scores (r=0.269, p<0.001) (table 2).

# SEM

As shown in table 3 and figure 2, higher attitude scores were associated with higher practice scores ( $\beta$ =0.381, p<0.001) and lifestyle ( $\beta$ =1.928, p<0.001). Urban residence was associated with higher attitude scores ( $\beta$ =1.242, p=0.013). Living with someone was associated with higher attitude scores ( $\beta$ =1.619, p=0.044). More than one line of immunotherapy lines was associated with higher lifestyle scores ( $\beta$ =1.928, p<0.001). The female gender was associated with higher lifestyle scores ( $\beta$ =1.431, p=0.023). (online supplemental table S3) shows that the SEM analysis had a good fit.

### DISCUSSION

Very few data are available in the literature concerning the KAP of patients with LC towards irAEs and lifestyle habits. The present study revealed moderate KAP towards lifestyle habits and irAEs. A previous systematic review has shown that the eating habits of Chinese patients with

Table 3	Structural equation modelling, including lifestyle				
			β	Р	
Attitude	<	Gender	-0.457	0.407	
Attitude	<	Residential area	1.242	0.013	
Attitude	<	Knowledge	0.128	0.069	
Attitude	<	Residential status	1.619	0.044	
Lifestyle	<	Knowledge	-0.048	0.565	
Practice	<	Knowledge	0.011	0.841	
Lifestyle	<	Attitude	0.222	<0.001	
Practice	<	Attitude	0.381	<0.001	
Lifestyle	<	Number of immunotherapy	1.928	<0.001	
Lifestyle	<	Gender	1.431	0.023	

Practice <---</th>Knowledge0.0110.841Lifestyle <---</td>Attitude0.222<0.001</td>Practice <---</td>Attitude0.381<0.001</td>Lifestyle <---</td>Number of<br/>immunotherapy1.928<0.001</td>Lifestyle <---</td>Gender1.4310.023cancer and chemotherapy were poor.22Although no data<br/>were available within this systematic review for immuno-<br/>therapy, its findings are generally in alignment with our<br/>present study. Another study has shown that Chinese<br/>patients with cancer had a basic understanding of irAEs,23or reserve<br/>tuthe study was not specific to LC and did not evaluate<br/>attitudes and practices. Intrinsic differences between<br/>patients with LC and those with other types of cancer<br/>could explain the differences in findings.<br/>Symptoms of advanced HCC affect quality of life, and

Symptoms of advanced HCC affect quality of life, and 6 the treatment of HCC can restore quality of life.<sup>28</sup> Thus, immunotherapy can potentially reverse the HCC-related symptoms and help improve quality of life. Nevertheless, the side effects of immunotherapy need to be factored **a** in, as it can affect empowerment and self-management. Self-management is a critical component of cancer care. Indeed, the patients must remain aware of the signs and symptoms that should prompt consultation. At home, they are also responsible for maintaining lifestyle habits that ⊳ could improve their prognosis or, at least, not worsen it.<sup>21</sup> A previous systematic review revealed poor KAP towards good eating habits among Chinese patients on chemotherapy for various types of cancers.<sup>22</sup> That previous study supports the present one, which also showed poor lifestyle Dd scores for several foods in patients with LC and immuno-S. therapy. Increasing evidence indicates that a healthy diet can improve the outcomes of immunotherapy.<sup>29 30</sup>

In this study, many participants with LC were still regularly smoking, drinking alcohol and had unhealthy dietary habits, all of which are associated with LC development and progression.<sup>31-34</sup> Especially, smoking and

Table 2 Pearson correlation analysis						
	Knowledge	Attitude	Practice	Lifestyle		
Knowledge	1					
Attitude	0.105 (p= <b>0.035</b> )	1				
Practice	0.018 (p=0.253)	0.460 (p< <b>0.001</b> )	1			
Lifestyle	–0.016 (p=0.755)	0.486 (p< <b>0.001</b> )	0.269 (p< <b>0.001</b> )	1		



Figure 2 Structural equation modelling.

alcohol consumption are independent risk factors for confirmed LC<sup>2 3 5 6</sup> because of their impact on inflammation, cancer progression and health in general,<sup>35–37</sup> and they affect liver function and immunotherapy efficacy.<sup>38</sup> Still, the high rates of smoking and drinking could reflect a poor knowledge of the risk factors for poor outcomes in LC but could also reflect patients wishing to maintain activities they associate with pleasure in the face of a disease with poor prognosis. The majority of the participants were not eating citrus fruits. Citrus fruits are rich in vitamins and antioxidants and play roles in maintaining the integrity of immunological barriers and in supporting immune cells.<sup>39-41</sup> On the other hand, citrus fruits are rich in active ingredients, such as furacoumarin, naringin and bergamot, which can inhibit the activity of metabolic enzymes (mainly UGT1A3 or UGT2B7).42 Therefore, in the future, intervention research on the impact of fruits such as grapefruit on medication can be strengthened. Therefore, the lifestyle of the study population was not ideal in terms of LC prognosis.<sup>31-34</sup>

The participants mostly reported not taking probiotics. Recent data also suggests that probiotics should be encouraged to prevent irAEs.<sup>43</sup> Indeed, regulation of the gut microbiome appears crucial in preventing irAEs.<sup>44</sup> The gut microbiota was also shown to modulate the response to immunotherapy, with distinct responses to immunotherapy according to the composition of the microbiome.<sup>45</sup> Gut dysbiosis can even lead to resistance to immunotherapy.<sup>45</sup> Hence, administering specific bacteria could be used to improve the response to immunotherapy and prevent irAEs.<sup>46</sup>

People living in urban areas and not living alone often enjoy a higher socioeconomic status, and it is well-known that higher socioeconomic status is associated with better health literacy.<sup>47</sup> In this study, living in urban areas was associated with higher attitude scores than participants from rural areas.

Women often have a higher healthcare literacy and higher health awareness than men,<sup>48-51</sup> supporting the association observed in the present study between gender and lifestyle. In addition, family support plays an unde- ≥ niable advantage in the management of cancer patients, helping them with daily tasks, cooking for them, caring and for them and remembering instructions and advice that associated with cancer-related events.<sup>52,53</sup> The present associated with cancer-related events. less, efforts should be taken to teach patients with LC the proper lifestyle habits necessary to optimise prognosis. Expanding the scope of the survey and including hospitals in different regions and levels are recommended to validate the results of this study. Clinical intervention research should be performed on the knowledge, attitude, behaviour and lifestyle level of nutrition and irAEs in patients with LC and immunotherapy and evaluate the effectiveness of the intervention. The impact of good sleep and moderate exercise (as good lifestyles) in relation to nutrition and irAEs should also be examined.

In the present study, the knowledge scores were only correlated to the attitude scores, while the attitude scores were correlated to the practice and lifestyle scores. Although knowledge was not associated with attitude in the SEM, improving knowledge could translate into attitude, practice and lifestyle improvements. Healthcare providers are a primary source of information for the patients, but previous studies revealed relatively poor KAP towards cancer nutritional support<sup>26 54</sup> and irAEs<sup>55</sup> among healthcare providers. Patients with LC and immunotherapy should be encouraged to perform physical activity, which is akin to prehabilitation for liver resection to improve tolerance to treatment.<sup>56</sup> It should help reduce the side effects or increase the patient's tolerance to them, hence improving patient outcomes.

This study has limitations. It was a single-centre study. Even though 402 patients with LC and immunotherapy represent a relatively large sample size, it is still too small to derive correlations and recommendations regarding the KAP-L in patients with LC. The questionnaire was designed by the investigators. It was reviewed by 15 experts in LC management, which could introduce bias from the healthcare perspective. In addition, some questions contained medical jargon that could introduce the Hawthorne effect (a type of reactive human behaviour in which people change their behaviour when they feel observed). The question length could be a potential source of bias on the importance ratings. Participants can consider a long and complicated sentence as important and a short sentence as being less important, causing bias. Future surveys should also be reviewed by nursing experts, laypeople and a variety of professionals. The study was cross-sectional in design, preventing us from drawing conclusions around causality. Still, a SEM analvsis was performed to examine the structured associations between variables, but it must be remembered that the associations are purely statistical and remain to be confirmed. In addition, the data represent a single point in time. Still, the results could serve as a historical baseline to evaluate the effect of future interventions. The questionnaire was designed by local investigators based on local practice, policies and reality, limiting generalisability. Finally, all KAP studies are at risk of social desirability bias, in which some participants might be tempted to answer what they know they should do instead of what they are actually doing.<sup>57 58</sup>

In conclusion, patients with LC and immunotherapy had moderate KAP towards irAEs and nutritional support. They also displayed moderate lifestyle scores. Urban residents, people not living alone, females and having received two or more immunotherapy treatments were positively associated with attitude, while attitude was positively associated with practice and lifestyle.

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**Contributors** WW and FG carried out the studies, participated in collecting data and drafted the manuscript. YC and LT performed the statistical analysis and participated in its design. WW and YC participated in the acquisition, analysis or interpretation of data and drafted the manuscript. All authors read and approved the final manuscript. FG acted as guarantor.

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Patient and public involvement Patients with LC were involved as participants. The patients with LC or the public were not involved in the study design or its completion.

Patient consent for publication Consent obtained directly from patients.

Ethics approval This work has been carried out in accordance with the Declaration of Helsinki (2000) of the World Medical Association. This study was approved by the Institutional Review Board of Haikou People's Hospital (2022-Ethical Review-231). All participants signed the informed consent form before completing the survey.

Provenance and peer review Not commissioned; externally peer reviewed.

**Data availability statement** All data relevant to the study are included in the article or uploaded as supplementary information. All data generated or analysed during this study are included in this article and its supplementary materials.

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#### REFERENCES

- 1 Bray F, Laversanne M, Sung H, *et al.* Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2024;74:229–63.
- 2 National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology (NCCN guidelines). Hepatocellular carcinoma. Version 1.2023. Fort Washington, 2023.
- 3 Villanueva A. Hepatocellular Carcinoma. *N Engl J Med* 2019;380:1450–62.
- 4 Sung H, Ferlay J, Siegel RL, *et al.* Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021;71:209–49.
- 5 Marrero JA, Kulik LM, Sirlin CB, et al. Diagnosis, Staging, and Management of Hepatocellular Carcinoma: 2018 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology* 2018;68:723–50.
- 6 Vogel A, Cervantes A, Chau I, et al. Hepatocellular carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2018;29:iv238–55.
- 7 Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. CA Cancer J Clin 2024;74:12–49.
- 8 Qin Y, Tang C, Li J, et al. Liver cancer in China: the analysis of mortality and burden of disease trends from 2008 to 2021. BMC Cancer 2024;24:594.
- 9 Shan T, Ran X, Li H, et al. Disparities in stage at diagnosis for liver cancer in China. J Natl Cancer Cent 2023;3:7–13.
- 10 Mandlik DS, Mandlik SK, Choudhary HB. Immunotherapy for hepatocellular carcinoma: Current status and future perspectives. *World J Gastroenterol* 2023;29:1054–75.

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- Sangro B, Sarobe P, Hervás-Stubbs S, et al. Advances in 11 immunotherapy for hepatocellular carcinoma. Nat Rev Gastroenterol Hepatol 2021;18:525-43.
- 12 Li J, Xuan S, Dong P, et al. Immunotherapy of hepatocellular carcinoma: recent progress and new strategy. Front Immunol 2023:14:1192506
- 13 Han Y, Liu D, Li L. PD-1/PD-L1 pathway: current researches in cancer. Am J Cancer Res 2020;10:727-42.
- 14 Ghosh C, Luong G, Sun Y. A snapshot of the PD-1/PD-L1 pathway. J Cancer 2021.12.2735-46
- National Comprehensive Cancer Network. NCCN clinical practice 15 guidelines in oncology (NCCN guidelines). Management of immunotherapy-related toxicities. Version 2.2023. Fort Washington, 2023
- Conroy M, Naidoo J. Immune-related adverse events and the 16 balancing act of immunotherapy. Nat Commun 2022;13:392.
- 17 Choi J, Lee SY. Clinical Characteristics and Treatment of Immune-Related Adverse Events of Immune Checkpoint Inhibitors. Immune Netw 2020:20:e9.
- van Dijk AM, Coppens BJP, van Beers MA, et al. Nutritional status 18 in patients with hepatocellular carcinoma: Potential relevance for clinical outcome. Eur J Intern Med 2022;104:80-8.
- Elsebaie EM, Abdel-Fattah AN, Bakr NA, et al. Principles of 19 Nutritional Management in Patients with Liver Dysfunction-A Narrative Review. Livers 2023;3:190-218.
- 20 Teng TZJ, Shelat VG. Testosterone gel improves appetite and reduces tiredness in males with advanced cancer. BMJ Support Palliat Care 2021;11:145.
- 21 van Dongen SI, de Nooijer K, Cramm JM, et al. Self-management of patients with advanced cancer: A systematic review of experiences and attitudes. Palliat Med 2020;34:160-78.
- Tang H, Zhang Y, Cao B, et al. Knowledge, attitudes and behaviors 22 toward healthy eating among Chinese cancer patients treated with chemotherapy: A systematic review. Asia Pac J Oncol Nurs 2023;10:100163.
- Zhang L, Wang J, Zhang B, et al. Attitudes and Practices of Immune 23 Checkpoint Inhibitors in Chinese Patients With Cancer: A National Cross-Sectional Survey. Front Pharmacol 2021;12:583126.
- 24 Andrade C, Menon V, Ameen S, et al. Designing and Conducting Knowledge, Attitude, and Practice Surveys in Psychiatry: Practical Guidance. Indian J Psychol Med 2020;42:478-81.
- World Health Organization. Advocacy, communication and social mobilization for TB control: a guide to developing knowledge, attitude and practice surveys. Available: http://whqlibdoc.who. int/publications/2008/9789241596176\_eng.pdf [Accessed 22 Nov 20221.
- 26 Zhang XW, Li W, Chen GY, et al. Knowledge, Attitude and Practice (K-A-P) of Cancer Nutrition in Chinese Medical Staff. J Nutr Oncol 2017:2:83-90.
- 27 Bloom BS. Learning for Mastery. Instruction and Curriculum. Regional Education Laboratory for the Carolinas and Virginia, Topical Papers and Reprints, Number 1. Evaluation Comment 1968;1.
- 28 Ahmed S, de Souza NN, Qiao W, et al. Quality of Life in Hepatocellular Carcinoma Patients Treated with Transarterial Chemoembolization. HPB Surg 2016;2016:6120143.
- 29 Spencer CN, McQuade JL, Gopalakrishnan V, et al. Dietary fiber and probiotics influence the gut microbiome and melanoma immunotherapy response. Science 2021;374:1632-40.
- 30 Soldati L, Di Renzo L, Jirillo E, et al. The influence of diet on anticancer immune responsiveness. J Transl Med 2018;16:75.
- 31 Jain D, Chaudhary P, Varshney N, et al. Tobacco Smoking and Liver Cancer Risk: Potential Avenues for Carcinogenesis. J Oncol 2021;2021:5905357.
- 32 Zelber-Sagi S, Noureddin M, Shibolet O. Lifestyle and Hepatocellular Carcinoma What Is the Evidence and Prevention Recommendations. Cancers (Basel) 2021;14:103.
- Pelucchi C, Gallus S, Garavello W, et al. Cancer risk associated with 33 alcohol and tobacco use: focus on upper aero-digestive tract and liver. Alcohol Res Health 2006;29:193-8.
- Luu HN, Behari J, Goh GB-B, et al. Composite Score of Healthy Lifestyle Factors and Risk of Hepatocellular Carcinoma: Findings from a Prospective Cohort Study. Cancer Epidemiol Biomarkers Prev 2021;30:380-7.

- 35 Liu Y, Lu L, Yang H, et al. Dysregulation of immunity by cigarette smoking promotes inflammation and cancer: A review. Environ Pollut 2023;339:122730.
- 36 Elisia I, Lam V, Cho B, et al. The effect of smoking on chronic inflammation, immune function and blood cell composition. Sci Rep 2020.10.19480
- Meadows GG, Zhang H. Effects of Alcohol on Tumor Growth, 37 Metastasis, Immune Response, and Host Survival. Alcohol Res 2015:37:311-22.
- 38 Deshpande RP. Sharma S. Watabe K. The Confounders of Cancer Immunotherapy: Roles of Lifestyle, Metabolic Disorders and Sociological Factors. Cancers (Basel) 2020;12:2983.
- Miles EA, Calder PC. Effects of Citrus Fruit Juices and Their 39 Bioactive Components on Inflammation and Immunity: A Narrative Review. Front Immunol 2021;12:712608.
- 40 Wang J, Gao J, Xu H, et al. Citrus fruit intake and lung cancer risk: A meta-analysis of observational studies. Pharmacol Res 2021;166:105430.
- 41 Song JK, Bae JM. Citrus fruit intake and breast cancer risk: a quantitative systematic review. J Breast Cancer 2013;16:72-6.
- 42 Liu D, Wu J, Xie H, et al. Inhibitory Effect of Hesperetin and Naringenin on Human UDP-Glucuronosyltransferase Enzymes: Implications for Herb–Drug Interactions. Biol Pharm Bull 2016;39:2052-9.
- 43 Yoshikawa S, Taniguchi K, Sawamura H, et al. Encouraging probiotics for the prevention and treatment of immune-related adverse events in novel immunotherapies against malignant glioma. Explor Target Antitumor Ther 2022;3:817-27.
- 44 Zhang Y, Cheng S, Zou H, et al. Correlation of the gut microbiome and immune-related adverse events in gastrointestinal cancer patients treated with immune checkpoint inhibitors. Front Cell Infect Microbiol 2023;13:1099063.
- Yu Z-K, Xie R-L, You R, et al. The role of the bacterial microbiome in the treatment of cancer. BMC Cancer 2021:21:934.
- Fernandes MR, Aggarwal P, Costa RGF, et al. Targeting the gut 46 microbiota for cancer therapy. Nat Rev Cancer 2022;22:703-22.
- Svendsen MT, Bak CK, Sørensen K, et al. Associations of health 47 literacy with socioeconomic position, health risk behavior, and health status: a large national population-based survey among Danish adults. BMC Public Health 2020;20:565.
- 48 Chakraverty D, Baumeister A, Aldin A, et al. Gender differences of health literacy in persons with a migration background: a systematic review and meta-analysis. BMJ Open 2022;12:e056090.
- Clouston SAP, Manganello JA, Richards M. A life course approach to 49 health literacy: the role of gender, educational attainment and lifetime cognitive capability. Age Ageing 2017;46:493-9.
- Bärebring L, Palmgvist M, Winkvist A, et al. Gender differences in perceived food healthiness and food avoidance in a Swedish population-based survey: a cross sectional study. Nutr J 2020;19:140.
- 51 Vlassoff C. Gender differences in determinants and consequences of health and illness. J Health Popul Nutr 2007;25:47-61.
- Molassiotis A, Wang M. Understanding and Supporting Informal 52 Cancer Caregivers. Curr Treat Options Oncol 2022;23:494-513.
- 53 Laryionava K, Pfeil TA, Dietrich M, et al. The second patient? Family members of cancer patients and their role in end-of-life decision making. BMC Palliat Care 2018;17:29.
- Mubin N, Bin Abdul Baten R, Jahan S, et al. Cancer related 54 knowledge, attitude, and practice among community health care providers and health assistants in rural Bangladesh. BMC Health Serv Res 2021;21:191.
- 55 da Silva GFM, Landim JIVD, Dos Santos Brasil LT, et al. Knowledge gap about immune checkpoint inhibitors among rheumatologists and medical students: a survey. Rheumatol Int 2021;41:939-42.
- Toh EQ, Wong HPN, Wang JDJ, et al. Prehabilitation programs in liver resection: a narrative review. Chin Clin Oncol 2024;13:9.
- Bergen N, Labonté R. Everything Is Perfect, and We Have No 57 Problems: Detecting and Limiting Social Desirability Bias in Qualitative Research. Qual Health Res 2020;30:783-92.
- Latkin CA, Edwards C, Davey-Rothwell MA, et al. The relationship between social desirability bias and self-reports of health, substance use, and social network factors among urban substance users in Baltimore, Maryland. Addict Behav 2017;73:133-6.

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