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# A systematic review of financial toxicity among cancer patients in China

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## ARTICLE INFO

ABSTRACT

Financial toxicity (FT) has been used to describe patients' whole economic experience that negatively impacts their well-being. FT's adverse effects on patients' health outcomes have been reported by reviews conducted in Western countries. However, these findings may not apply to patients in China. This review aimed to analyze existing data on the measures, prevalence, risk factors, and health-related consequences of FT in China. We searched 10 databases in May 2021 and again in January 2022 using Medical Subject Headings terms and free text. We also searched the reference lists of included articles. Two reviewers independently screened the studies, extracted the data, and assessed the quality of the included studies using the Joanna Briggs Institute Critical Appraisal Checklist. Thirty-one articles describing 30 studies were included in the analysis. Various FT measures were identified, but the number of validated measures was limited. The prevalence of material, psychological, and behavioral FT was 6%–78%, 61%–84%, and 10%–79%, respectively. We identified common risk factors and health-related consequences associated with FT similar to those reported in previous reviews. We also identified several potential risk factors (eg, increased length of hospital stay and larger household size) and consequences (patients' self-perceived burden) in a limited number of studies. Our findings show an urgent need for more data on the prevalence, risk factors, and health-related consequences associated with FT in Chinese cancer patients, and these data must be generated using validated measures.

## Introduction

The economic burden of cancer is high globally, with oncology drug expenditure increasing from US\$96 billion in 2016 to US\$164 billion in 2020 (a 14% compound annual growth rate)<sup>1</sup> because of the recent surge in innovative treatments, early diagnosis, and treatment access.<sup>1</sup> The society-level economic burden of cancer increases further if productivity losses from disability and premature mortality due to cancer are considered. Cancer patients and their families must bear out-of-pocket (OOP) costs of cancer treatment (ie, medical costs not covered by health insurance) and income loss. Indeed, 15% of previously nonpoor families fall to or below the poverty line because of cancer health care expenses.<sup>2</sup>

The term "financial toxicity (FT)"<sup>3</sup> describes patients' whole economic experience that negatively affects their well-being. It can be used interchangeably with terms such as financial hardship, financial distress, and financial burden.<sup>4–6</sup> The word "toxicity" is used because the financial cost of cancer treatment can cause clinically relevant problems akin to the physical and psychological toxicities of cancer treatment.<sup>6</sup> FT in cancer patients has been studied extensively in both developed and developing countries.<sup>7–17</sup> A systematic review<sup>7</sup> developed a conceptual framework involving 3 domains of FT measures: material condition measures (eg, OOP costs, indirect costs, medical debts, asset depletion, and bankruptcy), psychological response measures (eg, distress and concerns due to cancer care costs and income loss), and coping behavioral measures (eg, taking less medication and/or forgoing care because of costs). Other systematic reviews have reported that 28% to 48% and 16% to 73% of cancer patients experience monetary and subjective forms of FT, respectively,<sup>8</sup> and that the FT prevalence ranges from 15% to 79%.<sup>13</sup> Smith's systematic review<sup>9</sup> of 74 observational studies of FT in the United States showed that 49% of cancer patients reported material or psychological FT, whereas in countries with publicly funded health care systems, the FT prevalence in cancer patients ranged from 22% to 27%.<sup>10</sup>

The experience of cancer care–related FT is affected by multidimensional risk factors.<sup>11,18</sup> At the patient level, certain sociodemographic factors (eg, age, gender, and place of residence), socioeconomic status (eg, income, education, and employment), and disease- or treatment-related

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factors (eg, cancer site, cancer stage, and treatment plan) are associated with FT.<sup>8,9,13,15,16</sup> At the provider and practice levels, detailed patient-provider cost discussions are associated with lower average total OOP spending.<sup>19</sup> Several payer- and policy-level factors, including health insurance and medical assistance programs, also affect cancer patients' FT experiences.<sup>11,18</sup>

FT negatively affects cancer patients' health-related behaviors and outcomes. A meta-analysis showed that compared with cancer patients with a lower financial burden, those with a higher financial burden were approximately twice as likely to show cancer medication nonadherence and have worse overall physical, mental, emotional, and social functioning and well-being.<sup>9</sup> A systematic review<sup>14</sup> identified a positive association between FT and psychological symptoms, such as anxiety, depression, and overall psychological distress, in cancer survivors. Furthermore, studies have identified positive associations of FT with self-perceived burden<sup>20</sup> and mortality rates.<sup>21</sup>

Although systematic reviews have summarized the evidence for the measures used to quantify FT, the risk factors for FT, and the prevalence and health-related consequences of FT in cancer patients,  $^{7-10,13}$  none has focused on China.

As of 2019, more than 95% of Chinese residents, including infants, children, students, and unemployed individuals, were covered under a basic insurance scheme by either Urban Employee Basic Medical Insurance (UEBMI) or Urban and Rural Residents Basic Medical Insurance (URRBMI).<sup>22</sup> However, this scheme does not cover all health care services. The National Medical Security Development Statistical Bulletin<sup>22</sup> reported that the actual hospitalization coverage rates for UEBMI and URRBMI in 2019 were 76% and 60%, respectively. The National Reimbursement Drug List (NRDL) categorizes drugs into 2 types based on how they are covered by insurance: NRDL-A includes widely used, mostly inexpensive, generic drugs, which are fully reimbursed, and NRDL-B includes premium drugs that are only partially reimbursed.<sup>23</sup>

Most targeted anticancer drugs used in personalized therapies are expensive and not covered by the basic medical insurance scheme before 2016.<sup>24</sup> Moreover, the reimbursement rate for cancer treatments (58%) is lower than that for treatments for other chronic diseases (eg, chronic respiratory disease [70%], cardiovascular and cerebrovascular diseases [66%], and diabetes [64%]).<sup>25</sup> After 3 rounds of drug price negotiations by the government in 2017, 2018, and 2019, more than 40 types of targeted anticancer drugs were included in NRDL-B, increasing the reimbursement ratio above 60%.<sup>26</sup> Nevertheless, some cancer patients bear a heavy financial burden, as they generally require long-term treatment<sup>11</sup> and the initial market prices of targeted anticancer drugs are high.<sup>24</sup>

A systematic review<sup>27</sup> of the financial impact of cancer care in China focused on the total cancer care expenditure (ie, the sum of the expenditure covered by medical insurance and that borne by the individual) but did not consider the psychological distress and negative effects of OOP expenses on health-related behaviors and outcomes. To address this knowledge gap, we conducted a systematic review to synthesize the findings from studies of FT in cancer patients in China. This review aimed to determine (1) the tools used to measure cancer care–related FT in China, (2) the FT prevalence in Chinese cancer patients, (3) the FT-associated risk factors in these patients, and (4) the health-related consequences of FT in these patients.

## Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.  $^{\rm 28}$ 

## Literature search strategies

The following English and Chinese literature databases were searched in May 2021 and January 2022: Embase, PubMed, American Psychological Association PsycINFO, Cumulative Index to Nursing and Allied Health Literature, Ovid Emcare, Scopus, China National Knowledge Infrastructure, Wan Fang Database, VIP Chinese Journal Database, and China Biology Medicine Disc. The following Medical Subject Headings were used: "neoplasm," "carcinoma," "financial stress," "cost of illness," "health care costs," "health expenditures," and "China." Free-text terms were also used. The reference lists of included articles were also searched. Appendix A presents the detailed search strategy.

### Inclusion and exclusion criteria

The inclusion criteria were based on the study population, outcomes, design, and language. A study was included if (1) the study population comprised Chinese cancer patients aged  $\geq$  18 years at the time of diagnosis; (2) the main outcomes covered any of the following 4 aspects: risk factors for or measures, prevalence, or health-related consequences of FT (material, psychological, or behavioral FT); (3) it had a quantitative design; and (4) it was written in English or Chinese.

Studies were excluded if cancer treatment-related FT was not the primary focus, for example, studies that (1) primarily compared the costeffectiveness of cancer interventions; (2) evaluated medical costs as an outcome of interventions or policies: (3) evaluated the costs of a specific treatment, procedure, or drug (eg, the economic burden of pain management); and (4) assessed productivity losses or return-to-work problems but not FT. As we aimed to focus on the perspectives of working adult patients and/or their informal carers, studies in which some of the participants were aged < 18 years at the time of cancer diagnosis or that did not report whether all patients were aged > 18 years were also excluded. Moreover, as FT emphasizes the patient-level effect of the OOP expenses of cancer care, studies that analyzed the medical costs of cancer care but did not focus on OOP costs and studies in which all or some of the patients did not receive active cancer treatment (eg, did not receive any treatment or received palliative care) were also excluded. Furthermore, studies that included the potential economic loss due to premature death as an indirect cost of cancer were excluded, as this is classified as a social-level financial burden of cancer. In addition, because Hong Kong Special Administrative Region, Macau Special Administrative Region, and Taiwan Province of China have medical systems and medical insurance policies that are independent from mainland China, studies conducted in these 3 regions were excluded.

## Study selection

Endnote X9 (Clarivate Analytics) was used to manage the articles identified from the databases and manual searches. After discarding duplicates, 2 reviewers (B.B.X. and L.H.) screened and selected the studies independently according to the established inclusion and exclusion criteria. Disagreements were settled through discussion.

## Data extraction

The following data were extracted into Microsoft Word by B.B.X. and L.H.: study characteristics (publication year, first author, study design and aims, setting, time frame, and sample size), patient characteristics (cancer type, cancer stage, age, gender, health insurance status, time since cancer diagnosis, and treatments received), FT measures, key findings, FT-associated risk factors, and health-related behaviors and outcomes associated with FT.

### Quality appraisal

B.B.X. and L.H. independently assessed the quality of the included studies using the Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-Sectional Studies. Discrepancies between their assessments were resolved by a third reviewer (Q.Q.C.). No study was excluded based on the appraisal results.

#### Data synthesis

A narrative synthesis was performed due to the heterogeneous outcomes of individual studies.

## Results

#### Literature search and selection

In total, 10,076 articles were identified from the electronic databases, and 90 additional studies were identified from the reference lists of these articles. After removing duplicates, 7466 studies remained for relevancy screening, and 662 remained for full-text review. Finally, 13 articles published in Chinese and reporting 12 studies<sup>29–41</sup> and 18 articles published in English<sup>42–59</sup> were included in the review. Fig. 1 presents the flowchart of the study selection process.

#### Quality appraisal

Table 1 shows the quality appraisal results of the included studies. Of the 30 included studies, only  $13^{38,41,42,46-49,52,53,56-59}$  clearly defined the inclusion criteria; only  $7^{42,46,48,50,52,53,56}$  described the study subjects and settings in detail; and  $3^{36,39,41}$  were rated as "unclear" for statistical analysis, as they did not describe how the categorical variables were assigned values or how dummy variables were set for polytomous variables, although their selection of statistical analysis method (multiple linear regression) was appropriate. Of the 25 analytical cross-sectional studies,  $2^{9,31,34-41,45-59}$  1 used an exposure measurement tool of unclear validity, <sup>38</sup> and  $5^{35,49,51,54,55}$  did not control for confounding factors.

#### Study characteristics

Twenty-one studies (70%) were published after 2016.<sup>37–39,42–59</sup> All 30 studies used a cross-sectional design,<sup>29-59</sup> of which 26 were survey based, <sup>30–32,34,35,37–42,44–59</sup> 2 were medical or insurance record based, <sup>29,43</sup> and 2 were both survey based and medical record based.<sup>33,36</sup> The sample sizes ranged from 59 to 2746. A variety of cancer types were included, with 20 studies<sup>31–37,39–41,44,47–51,54–56,58,59</sup> focusing on a single cancer type and 10<sup>29,30,38,42,43,45,46,52,53,57</sup> focusing on multiple cancer types. Of the 20 studies focusing on a single cancer type,<sup>31-37,39-41,44,47-51,54-56,58,59</sup> 11 focused on lung cancer<sup>31-37,40,41,44,48,58</sup> (55%), 3 focused on breast cancer<sup>49,50,59</sup> (15%), and 1 each focused on liver cancer<sup>51</sup> (5%), cervical cancer<sup>47</sup> (5%), colorectal cancer<sup>54</sup> (5%), stomach cancer<sup>55</sup> (5%), esophageal cancer<sup>39</sup> (5%), and non-Hodgkin lymphoma<sup>56</sup> (5%). Twenty-eight studies reported in 29 articles focused on material FT.<sup>29-37,39-52,54-59</sup> 9 focused on psychological FT,  $^{38,48-51,53-56}$  and 3 on behavioral FT.  $^{30,50,52}$ Appendix B provides a comprehensive overview of the general characteristics of the studies.

## FT measures

Table 2 shows the frequencies and proportions of various measurements reported in the included studies. In the 29 studies reporting material FT, the most frequently used measures were monetary measures (n = 26, 90%): direct costs such as OOP medical and nonmedical costs (eg, transportation expenses and nutrition expenses); indirect costs (ie, time and income lost due to cancer); health care cost-–income ratios; and the occurrence of catastrophic health expenditure (CHE; refers to a household's medical expenditure exceeding a certain level of capacity to pay) and household impoverishment (ie,



Fig. 1. Flowchart of the study selection process.

Results of the quality appraisal (n = 31).

Study	1. Were the criteria for inclusion in the sample clearly defined?	2. Were the study subjects and the setting described in detail?	3. Was the exposure measured in a valid and reliable way?	4. Were objective, standard criteria used for measurement of the condition?	5. Were confounding factors identified?	6. Were strategies to deal with confounding factors stated?	7. Were the outcomes measured in a valid and reliable way?	8. Was appropriate statistical analysis used?
Chen, J. E., 2018 <sup>48</sup>	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Jing, J., 2020 <sup>50</sup>	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Huang, H. Y., 2017 <sup>54</sup>	Unclear	Unclear	Yes	Yes	Yes	No	Yes	Yes
Lei, H., 2020 <sup>51</sup>	Unclear	Unclear	Yes	Yes	Yes	No	Yes	Yes
Liao, X. Z., 2018 <sup>49</sup>	Yes	Unclear	Yes	Yes	Yes	No	Yes	Yes
Zhang, K., 2020 <sup>55</sup>	Unclear	Unclear	Yes	Yes	Yes	No	Yes	Yes
Su, M., 2020 <sup>52</sup>	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Yu, H. H., 2021 <sup>53</sup>	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Zhang, X., 2017 <sup>44</sup>	Unclear	Unclear	NA	Yes	NA	NA	Yes	Yes
Wu, Q., 2020 <sup>47</sup>	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Mao, W., 2017 <sup>43</sup>	Unclear	Unclear	NA	Yes	NA	NA	Yes	Yes
Leng, A., 2019 <sup>46</sup>	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Zheng, A., 2018 <sup>45</sup>	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Xu, R. H., 2020 <sup>56</sup>	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Chen, S., 2020 <sup>39</sup>	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear
Xu, H., 2019 <sup>38</sup>	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes
Liu, S., 2017 <sup>37</sup>	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Wang, C., 2016 <sup>36</sup>	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear
Wu, X., 2015 <sup>35</sup>	Unclear	Unclear	Yes	Yes	Yes	No	Yes	Yes
Kang, Y., 2015 <sup>34</sup>	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Peng, H., 2013 <sup>33</sup>	Unclear	Unclear	NA	Yes	NA	NA	Yes	Yes
Huang, H., 2012 <sup>32</sup>	Unclear	Unclear	NA	Yes	NA	NA	Yes	Yes
Huang, H., 2012 <sup>31</sup>	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Zeng, Q., 2011 <sup>30</sup>	Unclear	Unclear	NA	Yes	NA	NA	Yes	Yes
Luo, R., 2006 <sup>29</sup>	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Xiao, S., 2010 <sup>40</sup>	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Shang, M., 2013 <sup>41</sup>	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear
Yao, N., 2019 <sup>42</sup>	Yes	Yes	NA	Yes	NA	NA	Yes	Yes
Sun, C.Y., 2021 <sup>59</sup>	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Sun, C.Y., 2021 <sup>58</sup>	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Fu, W., 2021 <sup>57</sup>	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes

NA, not applicable.

household consumption is below the poverty line). Other measures included the depletion of financial resources because of cancer care, such as medical debt measures (n = 3, 10%). In 9 studies reporting psychological FT, the measures were single questions rated on a 4- or 5-point Likert scale or as yes/no (n = 7, 78%), the Comprehensive Score for Financial Toxicity (COST; n = 2, 22%), or the Family Burden Scale of Diseases score (n = 1, 11%). Three studies evaluated behavioral FT based on reducing or ceasing treatment (n = 3, 10%) or decreasing nonmedical expenses, such as food and daily necessities (n = 1, 33%).

## FT prevalence

The prevalence of material, psychological, and behavioral FT was reported to be 6% to 78%,  $^{42,43,45,48,50,52,56-59}$  61% to 84%,  $^{38,48-51,54-56}$  and 10% to 79%,  $^{30,50,52}$  respectively (Table 3). Although several studies focused on material FT, the majority (n = 20) reported specific cancer-related costs, such as OOP medical costs, nonmedical costs, and working time or income lost due to cancer.<sup>29–37,39–41,44,46–49,51,54,55</sup> These costs cannot be synthesized or compared, as there was high heterogeneity between studies in terms of the period or the disease course during which the costs were incurred, and inflation and exchange rates needed to be considered (Table 4).

## FT-associated risk factors

Eighteen studies<sup>31,37,39–41,45–47,49–55,57–59</sup> evaluated the risk factors associated with material, psychological, and behavioral FT in cancer patients (Appendices C1, C2, and C3).

#### Patient- and family-level risk factors

Seventeen studies reported the patient- and family-level risk factors associated with FT, which may be categorized as socioeconomic, demographic, or clinical factors.

## Socioeconomic factors

A lower patient or household income was associated with more severe psychological FT,<sup>49–51,53–55</sup> a higher ratio of annual OOP medical and nonmedical costs to annual household income,<sup>54</sup> a higher risk of CHE<sup>45,58,59</sup> and household impoverishment,<sup>57</sup> and a higher prevalence of medical debt.<sup>52</sup> Patients' indirect costs differed significantly by their income level;[<sup>31,49,51,55</sup>] one study showed that patients' monthly income was positively associated with their annual indirect costs (B < 0.001, P = 0.04).

Several studies indicated that cancer patients with higher educational levels were less likely to experience CHE<sup>45,59</sup> (odds ratio [OR] < 1.0, *P* < 0.001) and medical debt (OR: 0.4, *P* = 0.002),<sup>52</sup> demonstrating that lower educational level is a risk factor for more severe material FT. The prevalence of psychological FT was significantly different between cancer patients with different educational levels, with a higher prevalence in groups with a low education level than in groups with a high education level.<sup>49,51,54,55</sup>

An association between FT and employment status or occupation was reported in 8 studies. Compared with employed patients, unemployed patients reported more severe psychological FT<sup>53</sup> despite having lower indirect costs.<sup>47</sup> Four other studies<sup>49,51,54,55</sup> reported significant differences in the prevalence of psychological FT between cancer patients with different occupations. Farmers were reported to have lower direct costs

Summary of financial toxicity measu	res ( $n = 31$ ).
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Measures	Articles, n (%)
Material conditions measures ( $n = 29$ )	
Monetary measures	26 (90%)
OOP medical costs	12 (41%)
Income loss due to cancer	12 (41%)
Nonmedical costs	10 (35%)
OOP medical costs + non-medical costs	8 (28%)
Occurrence of CHE <sup>a</sup>	6 (21%)
(Annual OOP medical costs + annual direct non-medical	5 (17%)
costs)/annual household income	
Working time loss due to cancer	4 (14%)
Annual OOP medical costs/annual household income	2 (7%)
(Annual OOP medical costs + annual direct nonmedical	1 (3%)
costs + annual indirect costs)/annual household income	
(Half-year OOP medical costs + half-year direct	1 (3%)
nonmedical costs)/half-year household income	
Occurrence of household impoverishment <sup>b</sup>	1 (3%)
Medical debt	3 (10%)
Psychological response measures $(n = 9)$	
Single question	7 (78%)
Which of the following accurately describes your	3 (33%)
family's financial pressure from your disease?"	
("not at all," "somewhat but manageable," "heavy,"	
and "overwhelmed")	
"Have your disease and treatment caused you and your	1 (11%)
family financial difficulty?" ( $0 = No, 1 = Some$ ,	
2 = Moderate, $3 =$ Quite a bit, $4 =$ Very much)	
Patients' self-concerns of financial stress (Yes/No)	1 (11%)
Self-reported degree of economic pressure ("not at all," "a	1 (11%)
little," "some," and "a great deal")	
An item from the QOL-C30 scale: "Has your physical	1 (11%)
condition or medical treatment caused you financial	
difficulties?" ("not at all," "a little," "quite a bit,"	
and "very much")	
Comprehensive Score for financial Toxicity-Functional	2 (22%)
Assessment of Chronic Illness Therapy	
Family Burden Scale of disease	1 (11%)
Coping behaviors measures $(n = 3)$	
Reduce or quit treatment	3 (100%)
Decrease nonmedical expenses, such as food and	1 (33%)
daily necessaries	

OOP medical costs: out-of-pocket medical costs, which refers to medical costs that are not covered by health insurance.

<sup>a</sup> CHE: catastrophic health expenditure, refers to a household' medical spending exceeding a certain level of capacity to pay. In 2 included studies, CHE was calculated as patients' annual OOP medical and nonmedical costs exceeding 40% of annual household income; in 2 included studies, CHE was calculated as a household's total OOP medical costs exceeding 40% of nonsubsistence expenditure; and in the other 2 included studies, CHE was calculated as cancer patient's annual OOP medical costs exceeding 40% of nonsubsistence expenditure.

<sup>b</sup> Household impoverishment refers that a household's consumption (ie, the regular and repeated expenses to satisfy the essential needs of household members) is below the poverty line. Both the Chinese Poverty Line and the World Bank Poverty Line in 2015 were used.

(B = -2.1, P < 0.0001) than administrators of organizations, enterprises, or public institutions<sup>40</sup>; however, this association was not reported in another study.<sup>41</sup>

## Demographic factors

Compared with older age, younger age was associated with higher direct costs,<sup>40</sup> higher indirect costs per hospital stay,<sup>47</sup> a greater sum of annual direct costs and indirect costs,<sup>39</sup> a higher risk of medical debt,<sup>52</sup> and more severe psychological FT.<sup>50,53</sup> However, 2 other studies reported inconsistent results, showing that the prevalence of CHE and posttreatment household impoverishment increased with age (both *P* < 0.001).<sup>57,58</sup>

The OOP medical costs incurred by cancer patients varied significantly with the patients' place of residence.<sup>46</sup> Rural residence was associated with more severe material FT in 2 studies.<sup>47,52</sup> A survey of 402

lung cancer patients at Shanghai Jiaotong University Chest Hospital showed that patients living outside of Shanghai tended to have higher annual direct nonmedical costs (B = 1.0, P < 0.001) and annual indirect costs (B = 0.2, P = 0.002) than local patients.<sup>31</sup> Moreover, the OR for households in central China (adjusted OR [AOR]: 2.6, P = 0.01) experiencing posttreatment household impoverishment was more than twice that for households in the most developed eastern region of China.<sup>57</sup>

In 1 study, female cancer survivors were less likely to experience medical debt than male cancer survivors (OR for those aged 30–64 years, 0.6; 95% confidence interval [CI]: 0.4–0.8, P = 0.002; OR for those aged  $\geq 65$  years, 0.5; 95% CI: 0.4–0.7, P < 0.01).<sup>52</sup> Moreover, 1 study showed that a larger household size was associated with a higher risk of CHE (OR: 1.2, P = 0.02), and households without a senior citizen (aged  $\geq 65$  years) were less likely to experience CHE than those with at least 1 senior citizen (OR: 0.6, P < 0.001).<sup>45</sup>

## Clinical factors

FT prevalence in cancer patients differed significantly by cancer stage.  $^{39,47,49-51,54,55}$  Compared with less advanced cancer, more advanced cancer was associated with higher average direct nonmedical costs per hospital stay,  $^{47}$  a greater sum of annual direct and indirect costs,  $^{39}$  and more severe psychological FT.  $^{50}$ 

In a few studies, combination therapy (surgery or radiotherapy combined with chemotherapy) was associated with higher average direct nonmedical costs and indirect costs per hospital stay and a higher risk of CHE than surgery alone, <sup>47,59</sup> and surgery combined with radiotherapy and chemotherapy was associated with higher annual direct nonmedical costs (B = 0.3, P = 0.01) and indirect costs (B = 0.2, P = 0.004)<sup>31</sup> than chemotherapy alone. Moreover, radiotherapy was associated with higher average indirect costs per hospital stay than surgery (coefficient: 3907.3, 95% CI: 1074.9–6739.7, P < 0.01).<sup>47</sup>

A longer hospital stay was associated with a higher risk of material FT,<sup>31,45</sup> manifesting as higher annual direct nonmedical costs (B = 0.01, P = 0.01),<sup>31</sup> higher annual indirect costs (B = 0.01, P = 0.007),<sup>31</sup> and a higher risk of CHE (OR: 1.9, P < 0.001).<sup>45</sup> Two studies identified a longer disease course as a risk factor and showed that cancer patients with a disease course of >1 but <2 years were more likely to experience CHE than patients with a disease course of <1 year (OR: 2.7, P < 0.001; OR: 5.7, P < 0.001).<sup>58,59</sup>

One study reported that breast cancer patients had a lower risk (AOR: 0.5, P = 0.01) of experiencing posttreatment household impoverishment than lung cancer patients.<sup>57</sup> Another study reported that the sum of annual OOP medical, direct nonmedical, and indirect costs in the year before the survey was significantly lower for patients with relapsed esophageal cancer than for patients with new-onset esophageal cancer ( $\beta = -19,921.6,95\%$  CI: -39,002.1–840.9, P = 0.03).<sup>39</sup> Moreover, the time lost and the prevalence of psychological FT in cancer patients varied with pathological type in 4 studies,<sup>49,51,54,55</sup> but there was no evidence identifying which specific cancer type was a risk factor for FT.

#### Provider- and practice-level risk factors

Hospital type was identified as a risk factor for FT in cancer patients in 4 studies.<sup>45,49,51,54</sup> In 1 study, cancer patients in tertiary hospitals were more likely to experience CHE (OR: 2.8, P < 0.001) than those in other types of hospitals.<sup>45</sup> In some studies, the amount of time lost,<sup>49,51,54</sup> the prevalence of psychological FT,<sup>49,51,54</sup> and the ratio of annual OOP medical and direct nonmedical costs to annual household income<sup>54</sup> were higher for patients in specialized hospitals than for those in general hospitals.

## Payer- and policy-level risk factors

Health insurance was associated with FT in 14 studies.  $^{31,37,39-41,45,49,51,52,54,55,57-59}$  In 5 studies, a lack of health insurance was associated with higher direct costs,  $^{40}$  a higher risk of CHE

The prevalence of financial toxicity (n = 16).

Study	Material conditions		Psychological respo	nse	Coping behaviors	
	Measure	Prevalence	Measure	Prevalence	Measure	Prevalence
Chen, J. E., 2018 <sup>48</sup>	CHE <sup>a</sup>	73%	Single question	84%	_	_
Mao, W., 2017 <sup>43</sup>	CHE <sup>b</sup>	9% (Shanghai), 30%	-	-	-	-
		(Beijing), 65% (Fuzhou),				
		and 68% (Chongqing)				
Zheng, A., 2018 <sup>45</sup>	CHE <sup>b</sup>	43%	-	-	-	-
Xu, R. H., 2020 <sup>56</sup>	CHE <sup>a</sup>	58%	Single question	61%	-	-
Sun, C.Y., 2021 <sup>59</sup>	CHE <sup>c</sup>	66%	-	-	_	-
Sun, C.Y., 2021 <sup>58</sup>	CHE <sup>c</sup>	78%	-	-	-	-
Fu, W., 2021 <sup>57</sup>	Household	6% (based on CPL),	-	-	-	-
	impoverishment <sup>d</sup>	13% (based on WBPL)				
Yao, N., 2019 <sup>42</sup>	Borrow money	47%	-	-	-	-
Su, M., 2020 <sup>52</sup>	Borrow money	50%	-	-	Reduce or quit treatment	10%
Jing, J., 2020 <sup>50</sup>	Borrow money	58%	Single question	72%	Decrease nonmedical expense	79%
					Reduce or quit treatment	34%
Zeng, Q., 2011 <sup>30</sup>	-	_	-	-	Reduce or quit treatment	28%
Huang, H. Y., 2017 <sup>54</sup>	-	_	Single question	75%	-	-
Lei, H., 2020 <sup>51</sup>	-	-	Single question	77%	-	-
Liao, X. Z., 2018 <sup>49</sup>	-	-	Single question	77%	-	-
Zhang, K., 2020 <sup>55</sup>	-	-	Single question	79%	-	-
Xu, H., 2019 <sup>38</sup>	-	-	Family Burden	66%	-	-
			Scale of disease			

-, not reported; CPL, Chinese Poverty Line; WBPL, World Bank Poverty Line.

<sup>a</sup> CHE, catastrophic health expenditure, was calculated according to the formula: (patients' annual out-of-pocket medical costs + patients' annual nonmedical costs)/ annual household income >40%.

<sup>b</sup> CHE, catastrophic health expenditure, was calculated according to the formula: annual household's total out-of-pocket health care payments/annual household nonsubsistence expenditure >40%.

<sup>c</sup> CHE, catastrophic health expenditure, was calculated according to the formula: cancer patient's annual out-of-pocket health care payments/annual household nonsubsistence expenditure >40%.

<sup>d</sup> Household impoverishment: impoverished households were identified by assessing household consumption against the poverty line.

(OR: 1.2, P = 0.03)<sup>45</sup> and impoverishment (AOR: 1.9, P = 0.04)<sup>57</sup> in cancer patients' households, lower direct nonmedical costs,<sup>31</sup> and lower indirect costs.<sup>37</sup> Three studies<sup>52,58,59</sup> evaluated the associations of FT with specific insurance types: 1 study showed that UEBMI coverage was associated with lower medical debt than New Rural Cooperative Medical Scheme (NRCMS) coverage for cancer patients aged  $\geq 65$  years (OR: 0.3, 95% CI: 0.2–0.7, P = 0.002)<sup>52</sup>; the other 2 studies found that cancer patients with URRBMI were more likely to experience CHE than those with UEBMI (OR: 1.7, P = 0.02; OR: 2.3, P = 0.01).<sup>58,59</sup> Several studies found significant differences in the prevalence of psychological FT,<sup>49,51,54,55</sup> amount of time lost,<sup>49,51,54</sup> ratio of annual OOP medical and direct nonmedical costs to annual household income,<sup>54</sup> and sum of annual direct medical and indirect costs<sup>39</sup> between cancer patients covered under different health insurance schemes.

## Health-related consequences of FT

Seven studies<sup>30,38,48,50,52,53,56</sup> reported the effect of FT on health-related behaviors and outcomes in cancer patients. The most common effects were reduced health-related quality of life (HRQoL) and treatment nonadherence (Appendix D).

Four studies<sup>38,48,53,56</sup> explored the relationship between FT and HRQoL and consistently showed that both material and psychological FT were associated with a reduced HRQoL in cancer patients, despite differences in the research instruments used. Cancer patients with material FT reported worse overall health status<sup>56</sup> and physical,<sup>56</sup> emotional,<sup>48,56</sup> and social functioning<sup>56</sup> than those without material FT. Cancer patients with psychological FT exhibited poorer overall health status<sup>56</sup>; worse physical,<sup>48,56</sup> social,<sup>48,56</sup> emotional,<sup>48,56</sup> and functional<sup>48,56</sup> well-being; and a greater symptom burden<sup>48</sup> than those without psychological FT.

Treatment nonadherence was associated with FT in 3 studies,  $^{30,50,52}$  with 10% to 34% of patients reporting reducing or ceasing cancer treatment due to financial problems. One of these studies showed that cancer survivors who reported medical debt were more likely to report forgoing cancer treatment (OR: 3.7, 95% CI: 2.1–6.5, P < 0.01 for those

aged 30–64 years; OR: 5.5, 95% CI: 2.7–11.2, P < 0.01 for those aged  $\geq$  65 years) than those without financial problems.<sup>52</sup>

In a study of 440 cancer patients, FT, as measured by the COST, was negatively correlated with the Distress Thermometer (r = -0.2, P < 0.01) and Self-Perceived Burden Scale scores (r = -0.5, P < 0.01), indicating that a higher FT level was associated with a higher distress level and a greater self-perceived burden.<sup>53</sup>

## Discussion

To our knowledge, this systematic review is the first to synthesize findings from studies of material, psychological, and behavioral FT associated with cancer care in China.

This review identified a range of FT measures; monetary measures were most frequently reported. Although cancer care expenses are intuitive indicators of the financial effects of cancer care, it was difficult to compare the results of the included studies because most did not report the disease course or period during which the costs were incurred. One study showed that the average monthly total health care spending per patient increased enormously immediately after cancer diagnosis (from less than US\$2000 to as high as US\$25,000 in the month of cancer diagnosis) and then declined over time but remained higher than the prediagnosis level.<sup>60</sup> Thus, it is inappropriate to compare costs without considering the disease course. Furthermore, the costs reported by older and more recent studies were not comparable because of the effects of inflation. In addition, it is difficult to compare even costs reported simultaneously between countries due to differences in health care cost structures. Economics scholars may be able to perform such comparisons using conversion factors. However, monetary measures should be chosen carefully to best evaluate patients' FT in nursing research and practice.

The expense–income ratio may be more appropriate than a specific value for medical expenses when measuring cancer patients' FT. However, measurement approaches and definitions were inconsistent in the included studies. For example, studies that used CHE occurrence to measure the prevalence of objective financial burden reported 3 criteria

Study	The duration that costs were incurred	The course of cancer in which the costs were incurred	Direct costs			Indirect costs		Costs adjustment and
			OOP medical costs	Nonmedical costs (eg, transportation expenses, nutrition expenses)	The sum of OOP medical costs and nonmedical costs	Working time loss due to cancer (d)	Income loss due to cancer	exchange rate
Chen, J. E., 2018 <sup>48</sup>	1 mo	NR	US \$2519	_	US \$2883	_	_	Costs adjustment: NR US $$1 = 6.60$ CNY
Huang, H. Y., 2017 <sup>54</sup>	Direct costs: 1 y Indirect costs: NR	Direct costs: From 2 mo before to 10 mo after cancer diagnosis Indirect costs: From cancer diagnosis to the survey	-	_	32,649 CNY	96 in total Patients: 54; Caregivers: 42	6652 CNY	All costs were inflated to the 2014 CNY. 1 CNY = US \$ 0.16
Lei, H., 2020 <sup>51</sup>	Direct costs: 1 y Indirect costs: NR	Direct costs: From 2 mo before to 10 mo after cancer diagnosis Indirect costs: From cancer diagnosis to the survey	-	_	24,953 CNY	73 in total Patients: 42; Caregivers, 31	-	All costs were inflated to the 2014 CNY. Exchange rate: NR
Liao, X. Z., 2018 <sup>49</sup>	Direct costs: 1 y Indirect costs: NR	Direct costs: From 2 mo before to 10 mo after cancer diagnosis Indirect costs: From cancer diagnosis to the survey	-	-	US \$4264	98 in total Patients: 56; Caregivers: 42	US \$1529	All costs were inflated to the 2014 CNY. Exchange rate: NR
Zhang, K., 2020 <sup>55</sup>	Direct costs: 1 y Indirect costs: NR	Direct costs: From 2 mo before to 10 mo after cancer diagnosis Indirect costs: From cancer diagnosis to the survey	-	_	US \$5368	88 in total Patients: 48; Caregivers: 40	US \$996	All costs were inflated to the 2014 CNY. 1 CNY = US \$ 0.16
Zhang, X., 2017 <sup>44</sup>	5 y	Within 5 y of a cancer diagnosis	Insured patients: US \$27,518; uninsured patients: US \$20,529	US \$1890	-	-	US \$795	All costs were inflated to the 2014 US \$. US \$1 = 3.57 CNY (the purchasing power parity values of RMB against the dollar in 2014)
Wu, Q., 2020 <sup>47</sup>	About 1 y	From diagnosis to 1 y after final discharge	-	US \$673, US \$1459, US \$1589, US \$1536, US \$1422, and US \$979 for IA-IV patients.	-	_	US \$814, US \$2325, US \$2080, US \$1559, US \$1933, and US \$2623 for IA-IV patients.	All costs were inflated to the 2018 US . US 1 = 6.62CNY
Leng, A.,2019 <sup>46</sup>	From cancer diagnosis to death Urban: (549 $\pm$ 799) d Rural: (448 $\pm$ 487) d	From cancer diagnosis to death	Urban: US \$ (17,051 ± 23,731) Rural: US \$ (9405 ± 10,625)	-	-	-	-	All costs were inflated to the 2016 US . US  1 = 6.64 CNY
Chen, S., 2020 <sup>39</sup>	1 y	NR	30,257 CNY	4634 CNY	-	-	7322 CNY	Costs adjustment and Exchange rate: NR
Liu, S., 2017 <sup>37</sup>	NR	NR	-	-	-	-	Uninsured patients: (2089 $\pm$ 1964) CNY Insured patients: (3056	All costs were inflated to the 2014 CNY. Exchange rate: NR

Direct and indirect costs of cancer diagnosis/treatment among Chinese cancer patients reported in included articles (n = 20).

(continued on next page)

Table 4 (continued)									
Study	The duration that costs	The course of cancer in which the costs were incurred	Direct costs			Indirect costs		Costs adjustment and	
	were incurred		OOP medical costs	Nonmedical costs (eg, transportation expenses, nutrition expenses)	The sum of OOP medical costs and nonmedical costs	Working time loss due to cancer (d)	Income loss due to cancer	exchange rate	
							$\pm$ 2799) CNY for UEBMI, (2874 $\pm$ 1542) CNY for URBMI, (2509 $\pm$ 1444) CNY for other health insurance.		
Wang, C., 2016 <sup>36</sup>	NR	NR	25,420 CNY	8603 CNY	34,023 CNY	-	-	Costs adjustment and exchange rate: NR	
Wu, X., 2015 <sup>35</sup>	Cost for self-purchasing drugs and outpatients: 6 mo Costs for inpatient: 1 y	NR	2233 CNY per outpatient visit. 7675 CNY per hospitalization. 14,562 CNY for self- purchasing drugs	Outpatient: 160 CNY Inpatient: 2970 CNY	-	-	Outpatient: 86 CNY Inpatient: 33,385 CNY	Costs adjustment and exchange rate: NR	
Kang, Y., 2015 <sup>34</sup>	1 y	NR	-	8425 CNY	-	_	_	Costs adjustment and exchange rate: NR	
Peng, H., 2013 <sup>33</sup>	1 y	In the first year of cancer diagnosis	24,082 CNY	_	-	_	_	Costs adjustment and exchange rate: NR	
Huang, H., 2012 <sup>32</sup>	1 y	NR	37,167 CNY	26,466 CNY	-	_	53,052 CNY	Costs adjustment and exchange rate: NR	
Huang, H., 2012 <sup>31</sup>	1 y	NR	-	Insured patients: 26,897 CNY Uninsured patients: 22,963 CNY	-	-	Insured patients: 53,394 CNY Uninsured patients: 50,090 CNY	Costs adjustment and exchange rate: NR	
Zeng, Q., 2011 <sup>30</sup>	NR	NR	-	_	-	_	10,248 CNY	Costs adjustment and exchange rate: NR	
Luo, R., 2006 <sup>29</sup>	Per hospital stay	NR	16,481 CNY	_	-	-	-	Costs adjustment and exchange rate: NB	
Xiao, S., 2010 <sup>40</sup>	6 mo	Within 6 mo after the discharge of the first hospitalization (including the cost of the first hospitalization)	41,294 CNY	16,344 CNY	57,638 CNY	-	9912 CNY	Costs adjustment and exchange rate: NR	
Shang, M., 2013 <sup>41</sup>	NR	NR	28,460 CNY	7131 CNY	35,591 CNY	-	_	Costs adjustment and exchange rate: NR	

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NR, not reported; –, not reported; UEBMI, Urban Employee Basic Medical Insurance scheme; URBMI, Urban Resident Basic Medical Insurance Scheme; y, year; mo, month; d, days.

to define CHE, a well-established objective tool that measures the household financial burden of health care payments using 2 types of measurement. Expenditure is considered catastrophic<sup>61</sup> if a household spends 10% or more of its annual income on health care services. Another measurement defines CHE as when a household's OOP health care expenditure exceeds 40% of the household's capacity to pay (ie, effective income remaining after basic subsistence needs have been met).<sup>62,63</sup> CHE, thus, evaluates the total health expenditure of a household rather than the health expenditure of a patient. However, 2 of the 3 criteria used to define CHE in the included studies only calculated the OOP costs of cancer patients. Therefore, CHE prevalence in households with cancer patients may be underestimated. Future studies should use this indicator more accurately.

To our knowledge, the COST, a patient-reported outcome measure that reflects cancer survivors' experiences that cannot be captured by data or observations made by others, is currently the most commonly used validated instrument to measure FT in cancer patients.<sup>64–66</sup> Both simplified and traditional Chinese versions of the COST have been validated and can be easily accessed.<sup>53,67–69</sup> However, only 2 of the included studies used this instrument. With advances in early cancer detection and treatment technologies, the survival time of cancer patients has been prolonged.<sup>70</sup> It is thus crucial to evaluate the subjective feelings of cancer patients and survivors, for which the COST is potentially an appropriate instrument.

This review suggests that Chinese cancer patients experience material FT, with a prevalence ranging from 6% to 78%. The prevalence varied widely across the studies, probably because of the different indicators used to evaluate FT. FT prevalence was reported to be 9% to 78%, 43,45,48,56,58,59 47% to 58%, 42,50,52 and 6% to 13%<sup>57</sup> when using CHE, medical debt, and household impoverishment, respectively, as indicators. It varied greatly when CHE was used as the measure, with the lowest prevalence of 9% observed in 572 cancer patients with UEBMI in Shanghai,<sup>43</sup> followed by 30% in 561 cancer patients with UEBMI in Beijing<sup>43</sup> and 43% in 1344 cancer patients in 252 medical institutions in Liaoning province.<sup>45</sup> There are 2 possible reasons for this. First, all the participants in Shanghai and Beijing had UEBMI, which offers the best benefits of the 3 social health insurance packages available in China.<sup>4</sup> Second, Shanghai and Beijing are well-developed cities that provide better coverage for outpatient visits than other cities in China.<sup>43</sup> <sup>1</sup> Therefore, patients in these cities tend to use more outpatient services, leading to fewer hospital admissions and consequently lower total annual medical expenditures than in other cities.43 In the remaining 5 studies, the prevalence of material FT in cancer patients was > 50%,  $^{43,45,48,56,58,59}$ much higher than that reported in the general population in 2016 (9%).<sup>71</sup> Only the households in which cancer patients received treatment were considered when using CHE to evaluate material FT.<sup>58,59</sup> If the households that could not afford treatment were included, the prevalence of households with cancer patients experiencing CHE would be higher, indicating that material FT should be regarded as a serious problem in Chinese cancer patients.

The prevalence of psychological FT in the studies included in this review (61%–84%) was higher than that reported in a previous systematic review that summarized cancer diagnosis–associated FT in countries with publicly funded health care (7%–39%).<sup>10</sup> However, we cannot conclude that psychological FT is more prevalent in cancer patients in China than in other countries with publicly funded health care because 7 of the 8 studies reporting the prevalence of psychological FT used a single-question measurement, which decreased the reliability of their findings. Future studies should use standardized and validated measurement tools to facilitate between-country comparisons.

The prevalence of behavioral FT ranged from 10% to 79% in 3 studies using 2 different indicators (reducing or ceasing treatment and decreasing nonmedical expenditure).<sup>30,50,52</sup> These studies reported that 10% to 34% of cancer patients reduced or ceased treatment and 79% decreased nonmedical expenditure.<sup>30,50,52</sup> Two of these studies had small sample sizes (n = 59 and 166), which may have affected the reliability of

their results.<sup>30,50</sup> Thus, more studies of behavioral FT in Chinese cancer patients are warranted.

Regardless of the measurement indicators used, our results illustrate that FT is prevalent in Chinese cancer patients, underscoring the need to assess FT in vulnerable patients early in the treatment and survivorship periods and to develop policy and multidimensional interventions to effectively mitigate FT in this population. Joint efforts are needed from research communities, policymakers, employers, health care providers, nonprofit organizations, and private corporations.<sup>72</sup> Strategies at multiple levels, such as restructuring cost-sharing and insurance design, eliminating low-value prescribing practices, improving cost transparency, and providing financial counseling, may mitigate cancer patients' FT. Immediate solutions should focus on oncologists and patients, as any policy intervention needs a long-term shift and effort.<sup>73</sup> Oncologists should focus on the value of care delivered, prepare for discussions about costs, and initiate conversations about costs with patients to enable them to make a more informed decision.

Only a few studies evaluated the FT-associated risk factors in cancer patients, which included lower income, a lack of health insurance, a lower educational level, unemployment, a younger age, rural residence, advanced cancer stage, and combination therapy.<sup>9,16,18</sup>

Several results from this review conflict with those from previous reviews. For example, 2 reviews identified female sex and cancer recurrence as FT-associated risk factors in cancer patients, 9,16 whereas 1 study reported both variables as protective factors against FT in Chinese cancer patients. In that study, female cancer survivors were reported to be less likely to experience material FT than male cancer survivors.<sup>52</sup> As that study used a survey and relied on patient-reported data, it may have been affected by reporting bias; thus, additional evidence is needed to confirm the association between FT and sex in Chinese cancer patients. Regarding the variable "cancer recurrence," 1 study reported that the sum of annual OOP medical, direct nonmedical, and indirect costs in the year before the survey was significantly lower for relapsed esophageal cancer patients than for new-onset esophageal cancer patients<sup>39</sup>; the authors concluded that the risk of FT was significantly higher in new-onset patients. However, this result must be interpreted with caution because relapsed patients have also experienced the first episode, and their disease course tends to be longer than that of new-onset cancer patients. Although relapsed cancer patients may have had lower expenses in the year before the survey, they may have a longer disease duration. Therefore, future studies need to control for the confounding effects of the disease course when performing such comparisons.

Two studies<sup>31,45</sup> reported several FT-associated risk factors that were not reported in previous reviews. These included a longer hospital stay, a larger household size with at least 1 senior citizen, and treatment in a tertiary hospital. It is unsurprising that a longer hospital stay was associated with FT, and this implies that clinical health care providers should find ways to minimize the length of a patient's hospital stay without affecting their treatment. One study showed that households with a larger size and at least 1 senior citizen were more likely to have CHE than households with a smaller size and without a senior citizen,<sup>45</sup> probably because of the nature of CHE and the unique structure of Chinese families. CHE is a measure of the health care expenditure of the entire family as a percentage of the whole family's income. Generally, Chinese families comprise elderly individuals, a married couple, and children, of whom the married couple are usually the productive members. A larger household contains more elderly individuals and children than a smaller household. In this scenario, family health care expenditure increases, but family income is barely affected, resulting in a higher risk of CHE. Finally, treatment in a tertiary hospital was also associated with FT, probably because of the characteristics of the social health care insurance scheme in China, in which higher-level hospitals have a lower reimbursement ratio than lower-level hospitals. These risk factors may also apply to other countries with similar family structures and medical insurance schemes to China. Thus, additional evidence needs to be generated domestically and internationally.

One noteworthy result regarding FT-associated risk factors was that in 1 study, farmers had lower direct costs than administrators of organizations, enterprises, and public institutions.<sup>40</sup> In China, farmers are a relatively disadvantaged group with low incomes: according to the 2020 National Statistical Yearbook,<sup>74</sup> the per capita disposable income of Chinese urban residents in 2019 was 42,359 yuan, whereas that of rural residents was only 16,021 yuan. Moreover, farmers are covered by URRBMI (known as the NRCMS before 2016), which has a lower reimbursement ratio than UEBMI. Thus, cancer-related FT prevalence is expected to be higher in farmers than in administrators of organizations, enterprises, and public institutions. The lower direct costs for farmers reported in that study<sup>40</sup> may be because they had insufficient income and thus had to forgo some treatments. Furthermore, the study was conducted in 2010, so it may be outdated and not applicable in the present context. Further investigation is required to determine whether farmers are indeed more vulnerable to cancer-related FT than nonfarmers. Considering that the low cost of cancer treatment does not necessarily indicate that FT is not severe, as it may be because of patients forgoing some treatments, future research should focus more on the health-related behaviors and outcomes of cancer patients due to OOP costs and their subjective feelings, rather than relying solely on cost-related data.

In this review, some results related to FT-associated risk factors need to be interpreted carefully, as they were based on univariate analyses and thus might be affected by confounding factors, including the associations between indirect costs and income level, <sup>49,51,54,55</sup> between psychological FT and educational level (or occupation), <sup>49,51,54,55</sup> and between FT (psychological or material FT based on medical costs or time loss) and health insurance <sup>49,51,54,55</sup> Furthermore, no modifiable risk factors were identified. Several modifiable factors, including provider–patient discussions about costs, social support, and perceived stress, may affect FT in cancer patients.<sup>18,75,76</sup> Well-designed studies are warranted to examine the association between these factors and FT in cancer patients.

Finally, our review demonstrates that FT adversely affects cancer patients' treatment adherence, and HRQoL, consistent with the results reported in previous reviews.<sup>9,13,16</sup> This underscores the need to design interventions to effectively mitigate FT to improve treatment adherence and HRQoL in Chinese cancer patients. Additional studies on the effect of FT on patients' perceived burden are required, given that only 1 study provided evidence for an association between psychological FT and patients' self-perceived burden.<sup>53</sup>

### Limitations

The included studies had several limitations. Most studies did not clearly define their inclusion criteria<sup>29–37,39,40,43–45,50,51,54,55</sup> or describe their study subjects or settings in detail.<sup>29–41,43–45,47,49,51,54,55,57–59</sup> Some studies did not control for confounding factors<sup>35,49,51,54,55</sup>; others did not describe their statistical analyses in detail.<sup>36,39,41</sup> These methodological weaknesses may have led to biased results in the individual studies and this review and should be considered when interpreting the findings.

Several review-level limitations have also been identified. First, our synthesis of the findings was narrative rather than quantitative because of the high heterogeneity in the measures used in the included studies. Second, we did not synthesize or compare specific cancer-related costs (including OOP medical costs, nonmedical costs, and lost working time or income) across the 21 studies because of the high heterogeneity in the period or disease course during which the costs were incurred, inflation, and exchange rates.

#### Implications for practice

Assessing FT is not typically a part of routine clinical assessment.<sup>16</sup> This review found that FT is prevalent in Chinese cancer patients and has adverse consequences for cancer patients and their families. Therefore, more attention should be paid to FT in cancer patients in clinical practice. The assessment, recognition, and discussion of FT are important steps. As nurses have the closest contact with cancer patients and their caregivers, they could cooperate with doctors in assessing patients' FT and provide information support for patients. Accordingly, strategies such as education and training programs to increase nurses' knowledge about FT assessment and patient assistance programs should be developed by the government, cancer foundations, and other organizations.

## Implications for research

As some studies had methodological weaknesses, future studies must be rigorously designed: they must have clear definitions of the inclusion criteria, provide detailed descriptions of study subjects and settings, use strategies to control for confounding factors, and use appropriate methods of statistical analysis. Most of the included studies focused on material FT; thus, more research is needed on psychological and behavioral FT in Chinese cancer patients. Moreover, the FT measures were mainly monetary, which makes it difficult to compare research results horizontally and vertically. Future studies should use standardized and validated measurement tools. A few studies evaluated the FT-associated risk factors: several factors with conflicting results were found, and no modifiable factors were identified. Future studies should explore the association of FT with factors yielding conflicting results and potentially modifiable factors reported in studies of cancer patients in other countries. Finally, only a few studies explored the association between FT and health-related consequences; more research is needed on this topic.

## Conclusions

This review identified various measures used to quantify FT in Chinese cancer patients; however, few of these measures have been validated. The prevalence of material and behavioral FT in cancer patients varied widely between studies, but that of psychological FT was relatively high in all studies. Lower income, a lack of health insurance, a lower educational level, unemployment, a younger age, rural residence, advanced cancer stage, and combination therapy were risk factors associated with material, psychological, or behavioral FT. There was limited evidence that female sex, a longer hospital stay, a longer disease course, a larger household size with at least 1 senior citizen, and treatment in a tertiary hospital may be associated with a higher risk of FT. Furthermore, FT was associated with treatment nonadherence and decreased HRQoL. One study suggested that FT was associated with patients' self-perceived burden. Future studies should use standardized, validated measurement tools, such as the COST, to evaluate FT in cancer patients so that the results can be compared horizontally and vertically across studies. Additional research is needed to confirm the association between FT and potential risk factors, especially modifiable factors, such as social support, perceived stress, and provider-patient discussions about costs. Overall, there is an urgent need for new studies to provide more data on the health-related consequences of FT in Chinese cancer patients.

## Declaration of competing interest

The corresponding author, Prof. Winnie K. W. So, is the Editor-in-Chief of the journal. The article was subject to the journal's standard procedures, with peer review handled independently of Prof. So and their research groups.

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## Authors' contribution

Winnie K.W So conceived the aim and design of the review. Binbin Xu and Li Hu performed the literature search, study screening, data

extraction, and quality appraisal of the included studies. Qinqin Cheng solved the discrepancies between two 2 reviewers regarding data extraction and quality appraisal. Binbin Xu drafted the review article. Winnie K.W. So critically revised the article. All authors have read and approved the final version of the article.

#### Appendix A. Supplementary data

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