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The financial toxicity of cancer: unveiling global burden and risk factors – a systematic review and meta-analysis

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ABSTRACT

Background Cancer, a major global health challenge. not only threatens lives but also imposes severe financial burdens, known as 'financial toxicity'. This strain extends beyond treatment costs to include indirect expenses like lost income and out-of-pocket payments. Despite its urgency, global insights remain fragmented, often limited to specific regions with inconsistent findings. This systematic review and meta-analysis aims to provide a comprehensive overview of cancer-related financial toxicity and identify key risk factors contributing to this burden. Methods We conducted a systematic review and metaanalysis, searching databases like Medline, Web of Science, PubMed, Scopus, International Scientific Indexing and Google Scholar for peer-reviewed observational studies. Data were extracted into Microsoft Excel 2021, and study quality was assessed using the Joanna Briggs Institute critical appraisal tool. Statistical analysis was performed using STATA V.17, with catastrophic health expenditures (CHEs) pooled via a random-effects model. Heterogeneity was explored to understand variations in study outcomes. Subgroup and sensitivity analyses were conducted to assess individual study impacts, while publication bias was evaluated using Begger and Egger's tests. Univariate meta-regression analysis determined the impact of study-level covariates on CHE estimates. Results This analysis included 35 observational studies, covering 428 373 patients with cancer. The pooled prevalence of CHE was 56.1% (95% CI 48.3% to 63.8%). Key risk factors included large family size, low income, lack of health insurance, longer disease duration, older age and multiple treatments. Higher education levels were associated with reduced CHE risk.

Conclusion Over half of patients with cancer (56.1%) face catastrophic health expenditures, highlighting a severe financial burden. Addressing this issue requires expanding health insurance, providing financial support and ensuring affordable cancer care. Improving education access can also reduce CHE risk among patients with cancer.

INTRODUCTION

Healthcare is a fundamental right for every individual, essential at all stages of life and

WHAT IS ALREADY KNOWN ON THIS TOPIC

- Financial toxicity is a recognised consequence of cancer treatment, significantly affecting patients' quality of life.
- ⇒ Previous studies have highlighted that patients with cancer often face catastrophic health expenditures (CHE), but the data are mostly regional, and there is limited understanding of the global impact.
- ⇒ Known risk factors include low-income, lack of health insurance and extensive treatment requirements, but these findings are fragmented and not consistently analysed on a global scale.

WHAT THIS STUDY ADDS

- ⇒ This study provides a comprehensive global overview of the financial toxicity associated with cancer, using data from 35 observational studies covering 428 373 patients.
- ⇒ It quantifies the global prevalence of CHEs among patients with cancer, revealing that 56.1% of patients experience CHE.
- ⇒ The study identifies critical risk factors, such as large family size, low income, lack of health insurance, older age and extended disease duration, while also highlighting the protective role of higher education.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ This study lays the groundwork for further global and region-specific research into financial toxicity, encouraging more consistent methodologies and comprehensive data collection.
- ⇒ Healthcare providers may use these findings to better identify at-risk populations and tailor financial counselling and support services to mitigate financial toxicity in cancer care.
- ⇒ The findings underscore the need for policies that expand health insurance coverage, provide financial assistance to low-income families and ensure affordable cancer care. Additionally, they suggest that improving educational opportunities could be a strategic factor in reducing the financial burden on patients with cancer.





should not be influenced by one's wealth or income. However, many people still face significant barriers to accessing necessary care due to financial constraints. Households lacking sufficient financial protection are at risk of facing substantial unexpected medical costs. Such unforeseen expenses can result in severe debt, diminished living standards, and, eventually, financial hardship. The situation becomes even more dire when dealing with cancer, as the financial strain can intensify significantly. Each year, around 8.8 million people die from cancer, making it one of the leading causes of death worldwide. Alarmingly, 75% of these cancer-related deaths occur in low-income and middle-income countries (LMICs).

Cancer treatment involves a multifaceted array of costs that extend beyond the price of medical care. Direct costs include expenses for diagnosis, hospitalisation, surgery, chemotherapy, radiation therapy, and supportive care. Indirect costs, on the other hand, involve lost income due to time off work, reduced productivity, and the need for ongoing care and support. For many patients, these costs can be overwhelming, leading to financial strain that can impact their ability to access necessary care and maintain a decent quality of life. In LMICs, the absence of universal health coverage and the high cost of cancer treatments place an even greater strain on patients. In these settings, the lack of financial protection can force individuals to forgo or delay treatment, resulting in poorer outcomes and increased mortality.

Healthcare expenditure is deemed 'catastrophic' when out-of-pocket (OOP) costs significantly surpass a certain percentage of a household's income or financial capacity. Catastrophic health expenditures (CHE) can force households to cut back on essential goods, and in some cases, patients may opt to forgo medical care altogether, leading to worsened health conditions. Catastrophic health spending occurs when the amount a household pays OOP exceeds a predefined share of its capacity to pay for healthcare.

Annually, over 150 million people worldwide experience financial catastrophe due to healthcare costs, with around 100 million falling into poverty as a result. 13 Additionally, a study conducted across 133 countries revealed that the incidence of CHE rose from 9.7% to 11.7% between 2005 and 2010.¹⁴ Among patients with cancer, the incidence of CHE varies widely, ranging from 14.8% to 78.8%. 15 Research has shown that financial stress and concerns about paying medical bills related to cancer vary widely, with prevalence rates ranging from 22.5% in a nationally representative sample 16 to 64% among working-age cancer survivors.¹⁷ Nearly two-thirds of cancer survivors (63.8%) were deeply concerned about paying large medical bills, while over one-third (33.6%) found themselves in debt, and 3.1% had to resort to filing for bankruptcy. Additionally, 39.7% were forced to make significant financial sacrifices due to the burden of cancer and its treatment.¹⁸

Sociodemographic risk factors significantly impact financial hardship among patients with cancer. Younger

individuals often face higher financial strain due to limited savings and lack of Medicare coverage, making them more vulnerable to financial hardship compared with older patients. ¹⁹ Low-income patients with cancer are also at increased risk, though no specific income threshold is consistently identified. ²⁰ Employment loss exacerbates financial difficulties, as cancer survivors frequently face challenges returning to work. ²¹ ²² Health insurance coverage partially mitigates financial stress but does not eliminate OOP costs, especially for high-cost drugs. ²³

Cancer's financial impact is profound, often leading to CHEs, debt and even bankruptcy, significantly affecting patients' quality of life and treatment outcomes. Despite the growing recognition of this issue, comprehensive data on the global burden and risk factors for financial toxicity in cancer care are limited. This systematic review and meta-analysis aim to fill this gap by examining existing evidence, identifying key risk factors and informing targeted interventions. The study's findings will be crucial for shaping healthcare policies and support systems to alleviate financial distress among patients with cancer globally.

METHODS

Protocol development and registration

The systematic review protocol followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and is registered in the PROSPERO database under the registration number CRD42024574240. (online supplemental appendix 1). The study also adheres to the standard GATHER checklist, ensuring compliance with reporting recommendations for global estimates (online supplemental appendix 2).

Search strategy

We conducted a systematic review and meta-analysis to derive summary estimates. Initial searches were executed on 1 February 2024-5 February 2024 and updated on 8 April 2024. We searched peer-reviewed databases including Medline, Web of Science, PubMed, Scopus, International scientific indexing and Google Scholar databases. Articles were identified using a broad search strategy tailored for peer-reviewed literature. Search terms related to catastrophic health expenditures (eg, "catastrophic health expenditures," "financial burden," "outof-pocket costs") and cancer (eg, "cancer," "oncology," "neoplasm") were used. Grey literature sources were selected based on prior reviews and expert consultations, with the complete list of websites searched provided (online supplemental appendix 3). Since estimates related to health expenditures may be under-represented in peer-reviewed literature, grey literature sources were also searched to ensure comprehensive coverage of relevant reports and estimates. We employed the snowballing technique to identify additional studies by examining the citation lists of the articles included in our initial search.



Eligibility criteria

Observational studies, including those from theses and dissertations, were eligible if they met the following criteria: published in or after 2010 and provided at least one of these elements: (1) an estimate of the prevalence of CHEs among patients with cancer; (2) an analysis of risk factors associated with CHEs in this population or (3) insights into the financial impacts on patients with cancer. Studies in languages other than English were included, with translations performed either by a research team member or using Google Translate. Excluded studies were those that did not present original research, involved non-human subjects, were clinical trials or used case-control or trial methodologies. Additionally, studies with fewer than 40 participants or those with a sample based on a clinical diagnosis unrelated to cancer were excluded. We also reviewed the reference lists of identified reviews to find any additional relevant studies not captured in our initial searches.

Study selection process

Results from the peer-reviewed searches were first de-duplicated in EndNote 20 and then exported to Covidence for screening. Each title and abstract was assessed by two team members (inter-rater agreement=69.1%, Cohen's κ =0.50), and each full-text article was reviewed (inter-rater agreement=86.1%, Cohen's κ =0.54) for inclusion. Discrepancies were resolved by consensus. Grey literature reports were managed in EndNote, with each paper also screened for inclusion by two independent reviewers.

Data extraction process

Studies were extracted into Microsoft Excel 2021 by (TAK and RNH). Extractions were double-checked by a second team member from the same group (AG and BDT), and conflicts were resolved through discussion. Data extracted included authors and study year, location, study design, sex, age, time period at which CHE were measured, outcome measurement criteria, sample size, the number of participants facing CHE, types of cancer and risk factors for CHE (online supplemental appendix 4). Summary estimates were sought, and data were extracted for the entire cohort and specific subgroups (eg, by cancer type, sex or age group). For studies reporting disaggregated estimates, data were extracted separately when possible. A full list of the variables extracted is available in the.

Risk of bias assessment

The Joanna Briggs Institute (JBI) critical appraisal tool was employed to assess the methodological quality of studies. Two independent reviewers evaluated each study using a series of questions with 'yes', 'no' or 'unclear' responses. To ensure objectivity, disagreements were resolved through consensus among the authors and an independent reviewer. Scores were assigned as follows: 1 for 'yes', 0 for 'no' and 'U' for 'unclear'. These scores were converted into percentages to determine the risk

of bias: ≤49% indicated high risk, 50%–69% indicated moderate risk and above 70% indicated low risk. Only studies scoring at least 50% (moderate or low risk of bias) were included. For ongoing disagreements, individual ratings were averaged. Each primary study's quality was recorded in a specific column within the data extraction form to facilitate further analysis.

Definitions

The financial toxicity of cancer was defined by CHE. CHE is measured in three ways: (1) OOP healthcare costs exceed 10% of total household spending, (2) CHE at a threshold above 20% of total household expenditure and (3) households with OOP payments greater than 40% of their capacity to pay for healthcare. CHE refers to OOP medical costs, encompassing both direct and indirect costs. 'Capacity to pay' refers to the financial ability of an individual or household to pay for healthcare expenses without experiencing significant financial hardship. It is typically defined as the proportion of a household's income or resources that can be spent on healthcare while still meeting basic living needs, such as food, housing and education. 'Cost' refers to the total amount incurred for healthcare services, including both direct and indirect costs, while 'expenditure' refers to the actual OOP payments made by individuals or households for healthcare.^{24–26}

Statistical analysis

Once data extraction was completed in Microsoft Excel, the data were imported into STATA V.17 for analysis. Qualitative and narrative methods were employed to summarise the estimates from the included studies. Qualitative methods identified key patterns, focusing on variations in study designs, populations and outcomes. Narrative methods systematically summarised the findings, highlighting similarities, differences and trends. When multiple estimates on the same topic were available, we used either the range of estimates or a pooled estimate. The SE was computed using a binomial distribution formula. CHEs were pooled using a random-effects model, accounting for the high level of heterogeneity observed between studies. To assess heterogeneity among studies, we calculated Cochrane's Q statistics (χ^2), inverse variance (I²) and p values. An I² value of 0 indicated complete homogeneity, while I² values of 25%, 50% and 75% indicated low, moderate and high heterogeneity, respectively. Subgroup analyses were conducted based on study design, age category, country income level, sex, cancer type, outcome measurement, study period and JBI quality score (%). This allowed for examination of variations in prevalence estimates across different contexts and study characteristics. Sensitivity analysis, or leaveone-out meta-analysis, was performed to determine the influence of individual studies on the overall pooled estimates. Additionally, we evaluated publication bias using Begger and Egger's regression tests and constructed a funnel plot to visualise potential asymmetry. A Galbraith



plot was used to explore heterogeneity further and identify potential outliers. Univariate meta-regression analysis was also conducted to determine the impact of study-level covariates on the overall estimates of CHE.

Patient and public involvement

This research did not have patient or public involvement.

RESULTS

Initially, a total of 709 articles were identified: 674 from electronic databases, 27 from registers and 8 from other sources. Among the articles identified from database searches and registers, 398 were excluded as duplicates, and 7 were marked as ineligible by automation tools (using a classifier to eliminate records before screening). Furthermore, a detailed review of titles and abstracts led to the exclusion of 227 records. Of the 69 records sought for retrieval, 5 were not retrieved. From the 64 reports assessed for eligibility, 24 were excluded for not reporting the outcome of interest, 2 had quality issues, 4 had an incorrect population and 1 was available only as an abstract, leaving 33 articles that met the inclusion criteria. Additionally, of the eight articles identified through other methods and sought for retrieval, four were not retrieved. Of the remaining four articles, two were excluded, leaving two eligible articles. Consequently, a total of 35 articles met the inclusion criteria and were included in the systematic review and metaanalysis^{27–60} (figure 1).

Characteristics and quality of the included studies

This systematic review and meta-analysis include studies from diverse continents, with the majority originating from Asia (24 studies) and Africa (7 studies). The predominant study design is cross-sectional (25 studies), followed by cohort studies (10 studies). The sample sizes vary considerably, ranging from 52 to 365 367 participants, aggregating to a total of 428 373 patients with cancer. The methodological quality of the included studies is generally high, as evaluated using the JBI criteria, with 89% of studies achieving scores above 70%. The prevalence of CHE differed significantly. All the studies included in this review are based on nationally representative populations (table 1).

Prevalence of CHE

This meta-analysis identified substantial heterogeneity across the studies (I²=99.96%, p<0.001, H²=2232.51 and T²=0.0541). As a result, we used a random effects model to estimate the pooled prevalence of CHE. The results from 35 studies revealed that the pooled prevalence of CHE among patients with cancer is 56.1% (95% CI 48.3% to 63.8%) (figure 2). In addition, a Galbraith plot indicates a non-zero overall effect, as the regression line deviates from the no-effect line. While most studies fall within the CI, suggesting no significant outliers. The scattered distribution of points confirms heterogeneity among the studies (online supplemental appendix 5).

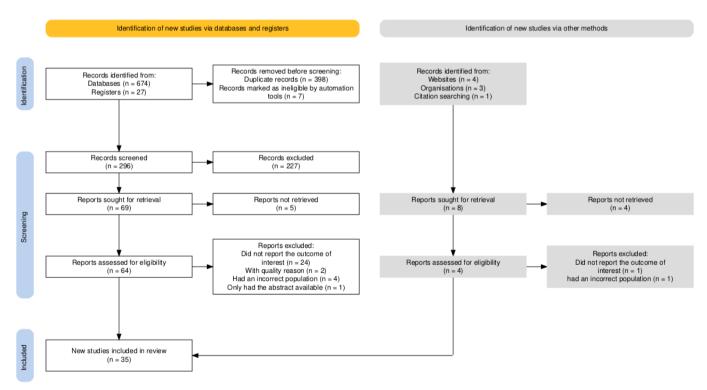


Figure 1 PRISMA flow chart for the selection of studies in a systematic review and meta-analysis of prevalence and risk factors of catastrophic health expenditure among patients with cancer. RISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.



 Table 1
 Basic characteristics and quality of the included studies in a systematic review and meta-analysis of prevalence and risk factors of catastrophic health expenditure among patients with cancer

-	-									
2	Authors name	Study setting	Study design	Sex	Cancer type	<u>명</u> (%)	Outcome measure	Sample size	Outcome	Prevalence
-	Ahmadi et al ²⁷	Iran	Cross-sectional	Female	Breast cancer	72.7	>40% of capacity to pay	138	19	0.138
N	Alinezhad et al ²⁸	Iran	Cross-sectional	Male	prostate cancer	90.9	>40% of capacity to pay	297	92	0.310
က	Zheng et a/ ²⁹	China	Cross-sectional	both	All cancer	90.9	>40% of capacity to pay	1344	575	0.428
4	Azzani et al³0	Malaysia	Cross-sectional	Both	Colorectal cancer	81.8	>40% of capacity to pay	138	99	0.478
C)	Basavaiah et al ³¹	India	Cohort study	Both	Pancreatic cancer	90.9	>10% of total income	86	75	0.765
9	Jane Bates <i>et a/</i> ³²	Malawi	Cohort study	Both	All cancer	63.6	>20% of total income	88	22	0.640
7	Berlin et al ³³	USA	Cross-sectional	Female	Breast cancer	6.06	>10% of total income	1496	476	0.318
œ	Bhoo-Pathy et a/34	Malaysia	Cohort study	Both	All cancer	81.8	>20% of total income	1294	999	0.514
တ	Chauhan e <i>t al³⁵</i>	India	Cohort study	Both	Head and neck cancer	81.8	>40% of capacity to pay	410	141	0.344
10	Choi <i>et al</i> ³⁶	South Korea	Cross-sectional	Both	All cancer	72.7	>10% of total income	212	84	0.396
1	CROCODILE study group	India	Cohort study	Both	Colorectal cancer	81.8	>20% of total income	202	182	0.901
12	Deng et al ³⁷	China	Cross-sectional	Both	All cancer	81.8	>40% of capacity to pay	388	198	0.510
13	Fekri <i>et al</i> ³⁸	Iran	Cross-sectional	Both	All cancer	90.9	>20% of total income	38146	2861	0.075
41	Fu <i>et al</i> ³⁹	China	Cross-sectional	Both	All cancer	90.9	>40% of capacity to pay	2534	1825	0.720
15	Hoang <i>et al⁴²</i>	Vietnam	Cohort study	Both	All cancer	6.06	>40% of capacity to pay	10000	6470	0.647
16	Kasahun e <i>t al⁴³</i>	Ethiopia	Cross-sectional	Both	All cancer	81.8	>40% of capacity to pay	352	262	0.744
17	Kavosi <i>et af</i> ⁴⁴	Iran	Cross-sectional	Both	All cancer	72.7	>40% of capacity to pay	245	163	0.665
18	Leng e <i>t al⁴⁵</i>	China	Cross-sectional	Both	All cancer	81.8	>40% of capacity to pay	792	758	0.957
19	Liew <i>et al</i> ⁴⁶	Malaysia	Cross-sectional	Female	Gynaecological cancer	81.8	>10% of total income	120	77	0.642
										Polinitary.



Table 1	1 Continued									
N _o	Authors name	Study setting	Study design	Sex	Cancer type	JBI (%)	Outcome measure	Sample size	Outcome	Prevalence
20	Matebie <i>et af</i> ⁴⁷	Ethiopia	Cross-sectional	Both	All cancer	72.7	>40% of capacity to pay	305	237	0.777
21	Maurya et af ⁴⁸	India	Cross-sectional	Both	All cancer	90.9	>40% of capacity to pay	474	292	0.616
22	Mohanty et af ⁴⁹	India	Cohort study	Women	Breast cancer	100.0	>40% of capacity to pay	429	363	0.846
23	Piroozi et af ⁵⁰	Iran	Cross-sectional	Both	Gastrointestinal cancer	81.8	>40% of capacity to pay	189	117	0.619
24	Prinja e <i>t al⁵¹</i>	India	Cross-sectional	Both	All cancer	81.8	>40% of capacity to pay	12148	8661	0.713
25	Raman et a/ ⁵²	Malaysia	Cross-sectional	Both	Oral cancer	81.8	>10% of total income	52	45	0.865
26	Rezapour et al ⁵³	Iran	Cross-sectional	Both	All cancer	63.6	>40% of capacity to pay	220	154	0.700
27	Rice <i>et al⁵⁴</i>	USA	Cross-sectional	Both	Gastrointestinal cancer	100.0	>40% of capacity to pay	365 367	25956	0.071
28	Sui <i>et al⁵⁵</i>	China	Cross-sectional	Both	Leukaemia	6.06	>40% of capacity to pay	242	105	0.434
29	Sun et al ⁵⁶	China	Cross-sectional	Female	Breast cancer	81.8	>40% of capacity to pay	639	562	0.879
30	Sun et af ⁵⁷	China	Cohort study	Both	Lung cancer	81.8	>40% of capacity to pay	470	367	0.781
31	The ACTION Study Group	Southeast Asia	Cohort study	Female	All cancer	81.8	>20% of total income	6787	3248	0.479
32	Wan Puteh et a/ ⁵⁸	Malaysia	Cross-sectional	Both	All cancer	72.7	>10% of total income	630	343	0.544
33	Zarezadeh <i>et al⁵⁹</i>	Iran	Cross-sectional	Both	All cancer	72.7	>40% of capacity to pay	101	43	0.426
34	Zhao et af ⁶⁰	China	Cross-sectional	Both	All cancer	72.7	>40% of capacity to pay	368	100	0.272
35	Zheng e <i>t al²⁹</i>	China	Cross-sectional	Both	All cancer	90.9	>40% of capacity to pay	1344	575	0.428
JBI, J	JBI, Joanna Briggs Institute.									



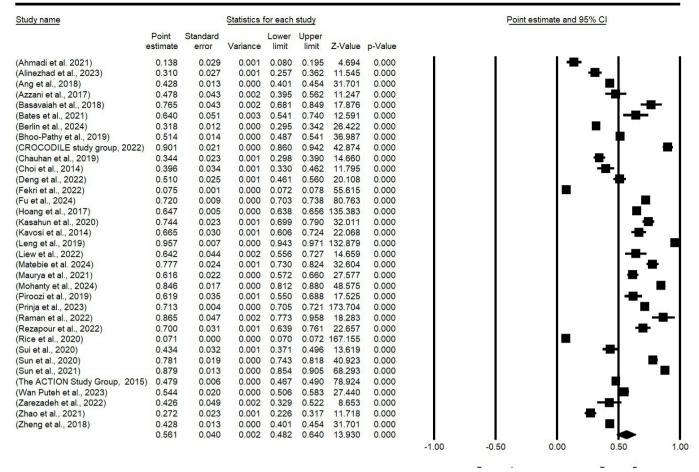


Figure 2 A forest plot on the pooled prevalence of catastrophic health expenditure among patients with cancer.

Publication bias

Publication bias was evaluated using both Begg's and Egger's tests, which provide objective measures of bias. The results from Begg's test (p=0.9101) and Egger's test (p=0.4227) indicated no evidence of publication bias.

Subgroup analysis

Subgroup analysis was done considering study design, age category, countries income level, sex, cancer type, age category, outcome measurement, period and IBI (%). Thus, there is high prevalence of CHE in73.3% (95% CI 66.6% to 80.0%) as compared with middle income (57.6%) and high-income countries (26.0%). Regarding the types of cancer, high polled prevalence of CEH (58.6%) (95% CI 28.9% to 88.3%) is reported among patients with gastrointestinal cancer. Concerning the CHE measurement criteria, the prevalence of CHE is 60.8% as measured by threshold of greater than 10% of annual income, 52.1% at threshold of >20% of annual income and 55.5% as measured by >40% of capacity to pay as recommended measurement of CHE by WHO. The polled prevalence of CHE is also vary as measured in different time interval from diagnosis of cancer. Thus, CHE is found to be high at 24 months after diagnosis (83.0%) and it was 65.2% and 62.8% at 12 and 6 months, respectively (figure 3).

Sensitivity analysis

Leave-one-out analysis was also conducted to explore the influence of a single study on the overall effect size estimate. A leave-one-out meta-analysis omits the corresponding study, and a meta-analysis is performed on the remaining studies (n=1). If the cross-ponding study CI does not include the overall effect size estimate (theta), it is declared that the study significantly influences the overall effect size estimate. In this study, the general effect size estimate (theta) was 0.561 and was included within the confidence intervals of all the studies. Thus, omitting one study did not significantly influence the overall effect size estimate (online supplemental appendix 6).

Risk factors of CHE

Different studies have identified various factors contributing to CHE. These factors include unemployment, ^{36–38} large family size, ^{29 36} low-income level, ^{34 35 40 42 47 50 51 55 58} lack of health insurance, ^{29 34 40 47 50} prolonged disease course (greater than 1 year), ^{29 36 56 57} older age, ^{27 39 42 43 56} higher education level (university and above) ^{27 29 57} and being on multiple treatments. ^{42 56 58}

The odds of experiencing CHE among patients with cancer are significantly influenced by various factors. Patients with cancer with large families have a 1.29 times higher likelihood of incurring CHE (AOR 1.29,



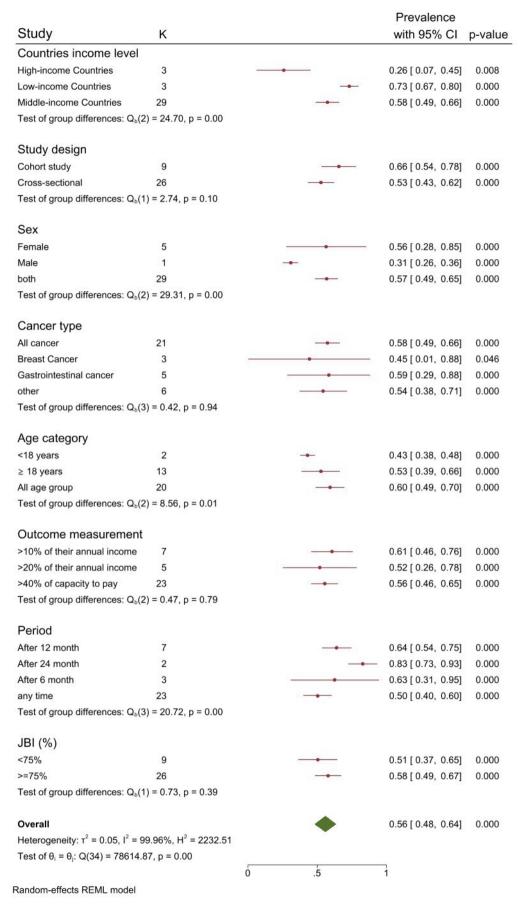


Figure 3 Subgroup analysis of the pooled prevalence of catastrophic health expenditure among patients with cancer. JBI, Joanna Briggs Institute; REML, random-effects model.



95% CI 1.07 to 1.49). Patients in low-income level face a substantially increased risk of CHE (AOR 5.57, 95% CI 3.86 to 7.29). Lack of health insurance increases the odds of CHE by 1.25 times (AOR 1.25, 95% CI 1.10 to 1.41). Additionally, the duration of cancer is associated with CHE risk, with patients having the disease for more than a year facing a 1.89 times higher likelihood (AOR 1.89, 95% CI 1.73 to 1.84). Older age increases the odds of CHE by 1.37 times (AOR 1.37, 95% CI 1.02 to 1.75). Higher education levels are protective, reducing the odds of CHE by 82% (AOR 0.18, 95% CI 0.11 to 0.26). Lastly, undergoing multiple treatments such as chemotherapy, surgery and radiotherapy significantly increases the likelihood of CHE, with these patients being 2.42 times more likely to incur it (AOR 2.42, 95% CI 1.57 to 3.26) (table 2).

Meta-regression analysis

Univariate meta-regression analysis was conducted to determine the impact of study-level covariates on the overall estimates of CHE. We included sample size, year of publication, study design, mean age and the timing of CHE measurement in the univariate meta-regression. The analysis indicated that there was no significant effect of study-level covariates on the overall effect size of CHE (online supplemental appendix 7).

DISCUSSION

This systematic review and meta-analysis aimed to estimate the global burden of CHE and identify key risk factors among patients with cancer. The pooled prevalence of CHE among patients with cancer, based on 35 studies, is 56.1% (95% CI 48.3% to 63.8%). This finding aligns with the range reported by Azzani et al (including 10 studies), which indicated a financial burden between 14.8% and 78.8%. 15 However, our results are higher than those of a previous systematic review by Doshmangir et al (including 19 studies), which found a CHE prevalence of 43.3%, ranging from 36.7% to 50.1%.61 The higher prevalence of CHE among patients with cancer underscores the significant financial burden that cancer treatment imposes. Clinically, this financial strain can affect patient outcomes, as those facing CHE may delay or forgo necessary treatments, leading to poorer health outcomes. It highlights the need for healthcare providers to consider the financial aspects of cancer care and incorporate financial counselling and support services as part of comprehensive cancer care. From a policy perspective, these findings advocate for stronger health policies that protect patients with cancer from financial hardship. Policy-makers should consider expanding health insurance coverage, reducing OOP expenses and providing financial assistance programmes specifically targeted at patients with cancer. Additionally, our findings support the need for international efforts to address the financial barriers to cancer care, especially in low-income countries where patients are disproportionately affected.

Reducing the financial burden of cancer treatment can improve access to care, adherence to treatment, and ultimately, patient outcomes.

The subgroup analysis revealed that patients with cancer from low-income countries experience a significantly higher prevalence of CHE compared with those from middle-income and high-income countries (73% vs 58% and 26%, respectively). These findings align with previous studies. ^{15 61} It is also evident in risk identification analysis, which revealed patients with cancer from low-income countries face more than five and half times increased risk of CHE. This disparity underscores the urgent need for targeted financial support and health policy reforms to alleviate the CHE burden on patients with cancer in low-income countries.

Significantly high burden of CHE (59%) was also found in patients with gastrointestinal cancer than other cancer. The significantly high CHE among patients with gastrointestinal cancer can be attributed to several factors. These cancers often require complex and expensive treatments, including surgery, chemotherapy, radiation and targeted therapy. 62 The prolonged duration of care, frequent follow-up visits, high complication rates and hospitalisations further escalate medical expenses. Patients are often diagnosed at advanced stages, necessitating more intensive and costly treatments. ⁶³ Addressing these issues through comprehensive insurance coverage, targeted financial assistance programmes and supportive care interventions is essential to alleviate the financial strain and reduce the prevalence of CHE among patients with gastrointestinal cancers.

CHE increased over time, with rates of 63%, 64% and 83% observed at 6 months, 12 months and 24 months after diagnosis, respectively. This escalation can be attributed to several factors. As treatment duration extends, costs for surgeries, chemotherapy, radiation and other therapies continue to accumulate. Additionally, the risk of complications and recurrences rises over time, resulting in further medical interventions and hospitalisations.⁶⁴

Large family size and lack of health insurance are among the factor that makes the patients with cancer 1.29 and 1.25 at risk to face a CHE. Large family size can lead to CHE for patients with cancer because the financial burden of treatment is compounded by the higher overall living costs. With more dependents, a household's financial flexibility is reduced, making it harder to manage additional medical expenses. Larger families often have limited resources and may struggle to afford comprehensive health insurance, leading to gaps in coverage and increased risk of CHE. Lack of health insurance leads to CHE for patients with cancer because they face high costs for treatments like surgery, chemotherapy and radiation.⁶⁵ Without insurance, patients must cover these expenses OOP, leading to financial strain and potential delays in care. This can worsen health and increase long-term costs. High OOP expenses and accumulating medical debt without insurance further contribute to CHE, making patients more vulnerable to financial



Table 2 Risk factors of catastrop	ohic health expenditure	among patients with	cancer		
Risk factors	OR (95% CI)	Pooled AOR (95% CI)	l ² (p value)	Egger (p value)	Sample size
Unemployment					
Choi et al, 2014 ³⁶	2.63 (2.59 to 2.67)	2.05 (0.93 to 3.16)	99.81 (<0.001)	0.612	38746
Deng et al, 2022 ³⁷	2.68 (1.21 to 4.15)				
Fekri <i>et al</i> , 2022 ³⁸	1.08 (1.01 to 1.15)				
Large family size					
Zheng et al, 2018 ²⁹	1.17 (1.02 to 1.320)	1.29 (1.07 to 1.49)	90.89 (<0.001)	0.097	2900
Choi et al, 2014 ³⁶	1.48 (1.45 to 1.52)				
Zheng et al, 2018 ²⁹	1.17 (1.02 to 1.32)				
Being in low income level					
Bhoo-Pathy et al, 2019 ³⁴	5.78 (3.64 to 7.93)	5.57 (3.86 to 7.29)	61.42 (<0.001)	0.392	32005
Chauhan et al, 2019 ³⁵	5.60 (0.70 to 10.50)				
Hoang et al, 2017 ⁴²	2.89 (1.27 to 4.51)				
Matebie et al 2024 ⁴⁷	9.80 (2.90 to 27.50)				
Piroozi <i>et al</i> , 2019 ⁵⁰	7.10 (2.05 to 20.25)				
Prinja et al, 2023 ⁵¹	10.96 (6.92 to 15.01)				
Sui et al, 2020 ⁵⁵	4.41 (13.46 to 12.28)				
The ACTION Study Group, 2015	5.86 (4.63 to 7.09)				
Wan Puteh et al, 2023 ⁵⁸	4.66 (1.79 to 7.52)				
Health insurance status -Non-insu	ured				
Zheng et al, 2018 ²⁹	1.18 (1.01 to 1.35)	1.25 (1.10 to 1.41)	6.32 (<0.001)	0.117	9919
Bhoo-Pathy et al, 2019 ³⁴	1.90 (1.25 to 2.56)		. ,		
Matebie et al, 2024 ⁴⁷	5.60 (1.65 to 12.85)				
Piroozi <i>et al</i> , 2019 ⁵⁰	3.80 (0.95 to 8.55)				
The ACTION Study Group, 2015	1.27 (1.04 to 1.51)				
Disease course (>1 year)					
Choi et al, 2014 ³⁶	1.78(1.76 to 1.81)	1.89 (1.73 to 1.84)	3.80 (<0.001)	0.074	2665
Sun et al, 2021 ⁵⁶	5.69 (2.11 to 9.28)				
Sun et al, 2021 ⁵⁷	2.74 (1.14 to 4.35)				
Zheng et al, 2018 ²⁹	1.88 (1.67 to 2.09)				
Older patients with cancer					
Ahmadi et al 2021 ²⁷	1.81 (0.80 to 2.82)	1.37 (1.02 to 1.75)	70.02(<0.001)	0.061	13494
Fu et al, 2024 ³⁹	1.34 (1.04 to 1.65)				3465
Hoang et al, 2017 ⁴²	1.75 (0.78 to 2.73)				
Kasahun <i>et al</i> , 2020 ⁴³	1.03 (1.01 to 1.06)				
Sun et al, 2021 ⁵⁶	2.16 (1.01 to 3.38)				
Education level (university and ab	ove)				
Ahmadi et al 2021 ²⁷	0.27(0.210 to 0.33)	0.18 (0.11 to 0.26)	84.65(<0.001)	0.531	13494
Zheng et al, 2018 ²⁹	0.14 (0.10 to 0.18)		64.65(<0.001)	0.001	.0.10.1
Sun <i>et al</i> , 2021 ⁵⁷	0.27 (0.14 to 0.69)				
Zheng et al, 2018 ²⁹	0.14 (0.10 to 0.18)				
Multiple treatment					
Hoang et al, 2017 ⁴²	2.40 (1.01 to 3.79)	2.42 (1.57 to 3.26)	0.00(<0.001)	0.516	11269
Sun <i>et al</i> , 2021 ⁵⁶	2.38 (1.30 to 3.45)				
Wan Puteh et al, 2023 ⁵⁸	4.99 (2.71 to 12.69)				



hardship. To mitigate this burden, expanding affordable health insurance schemes that include comprehensive cancer care is crucial. Targeted financial support for large families, such as subsidies or cash transfers, can alleviate their heightened vulnerability. Additionally, community-based initiatives like pooled health funds and integration of financial counselling into oncology care can provide immediate relief. Promoting family planning and health education may also help reduce long-term financial strain, emphasising the importance of holistic, targeted interventions.

Older patients with cancer also suffer from CHE 1.37 times than other population group. This finding is in agreement with previous study.²⁴ Older patients with cancer typically have higher healthcare needs, often managing multiple comorbidities that necessitate frequent and extensive medical interventions, which significantly raise overall healthcare costs. Additionally, many older individuals depend on fixed incomes, such as pensions or savings, which may be insufficient to cover the high costs of cancer treatment.^{66 67} This highlights the need for targeted financial support and better insurance coverage for this demographic.

As the duration of the cancer is beyond 1 year, the likelihood of suffering from CHE is increased by 1.89 times. Prolonged treatment often involves continuous medical appointments, procedures and therapies, leading to significant costs accumulating over time. Additionally, the financial strain can be compounded by the loss of income if patients or their caregivers are unable to work due to the demands of ongoing treatment and care. This underscores the necessity for long-term financial planning, comprehensive insurance coverage and supportive policies to mitigate the financial burden on these patients and their families.

Being on multiple treatments simultaneously, such as chemotherapy and surgery, increases the risk of CHE by 2.42 times. The combined cost of different treatments can be exorbitant, as each treatment involves separate fees for medications, medical professionals and hospital stays. Additionally, multiple treatments often require extra supportive care and follow-up appointments, further increasing the financial burden. ⁶⁹ Higher educational levels are found to be protective against CHE by 82%. Individuals with higher education often have better access to well-paying jobs, which translates to higher incomes and greater financial stability. This economic advantage allows them to better absorb the costs associated with severe illnesses, such as cancer. Additionally, higher education is often linked to better health literacy, enabling individuals to make informed decisions about their healthcare and navigate insurance options more effectively. 70 Policies that integrate education with health awareness, particularly in communities with low literacy levels, could serve as a long-term strategy to reduce financial toxicity among patients with cancer.

The study's reliance on observational data means that the relationships between CHE and its risk factors may not be causal. While subgroup analyses provide detailed insights into the prevalence of CHE using various measurements and definitions, the overall pooled prevalence may not accurately capture the true burden. Additionally, the concentration of studies in specific regions limits the global generalisability of the findings. Moreover, the high level of heterogeneity across studies is another limitation.

CONCLUSION

This systematic review and meta-analysis highlights the alarmingly high prevalence of CHE among patients with cancer, illustrating the substantial financial burden they endure. The analysis identified several critical risk factors associated with CHE. Patients with large families are at an elevated risk, indicating the need for tailored financial support programmes to ease the burden on these households. Low-income patients also face a significantly higher risk, underscoring the necessity for increasing direct financial assistance and broadening social safety nets. The lack of health insurance significantly contributes to the risk of CHE, emphasising the need for reforms aimed at expanding insurance coverage and making it more affordable. Additionally, the likelihood of CHE rises with prolonged illness, suggesting a need for developing financial support structures specifically designed for long-term cancer care. Older patients face heightened risks, which indicates a need for targeted financial support services that address the unique challenges of this demographic. For patients undergoing multiple treatments, there is a clear need for integrated financial support mechanisms that can accommodate the cumulative costs of various treatment modalities. Furthermore, education is a protective factor against CHE. Investing in educational programmes that improve financial literacy and planning could help mitigate the economic impact of cancer care. Developing community-based support systems that offer financial counselling and assistance can also play a critical role in addressing the financial challenges faced by patients with cancer.

By diversifying approaches-such as enhancing insurance options, expanding direct financial aid, creating targeted support services for older patients and investing in financial education—policy-makers can more effectively alleviate the financial strain on patients with cancer and improve their overall quality of life.

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