

Mapping the Evidence on Interrelationships Between Cancer Stage, Financial Toxicity (FT), and Health-Related Quality of Life (HRQoL)

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INTRODUCTION

- Up to half of cancer patients globally experience financial toxicity (FT)¹ – the distress and hardship resulting from out-of-pocket healthcare costs² – and consequent reduced health-related quality of life (HRQoL).
- Contributors to FT include direct medical expenses, indirect care-related costs, lost income, debt, bankruptcy, and other financial burdens of disease.
- Various tools are available to measure FT, with the COmprehensive Score for financial Toxicity (COST) being a standard tool specifically designed for assessing financial distress in cancer patients³.
- While various aspects of the cancer–FT relationship are well-studied⁴, whether or how cancer type and stage influence FT, and its downstream impact on HRQoL, remains unclear.
- Clarification of these issues could be crucial for informing potential ways to prevent or mitigate FT and its harmful sequelae, such as through adjustments to current diagnostic and management pathways.

OBJECTIVES

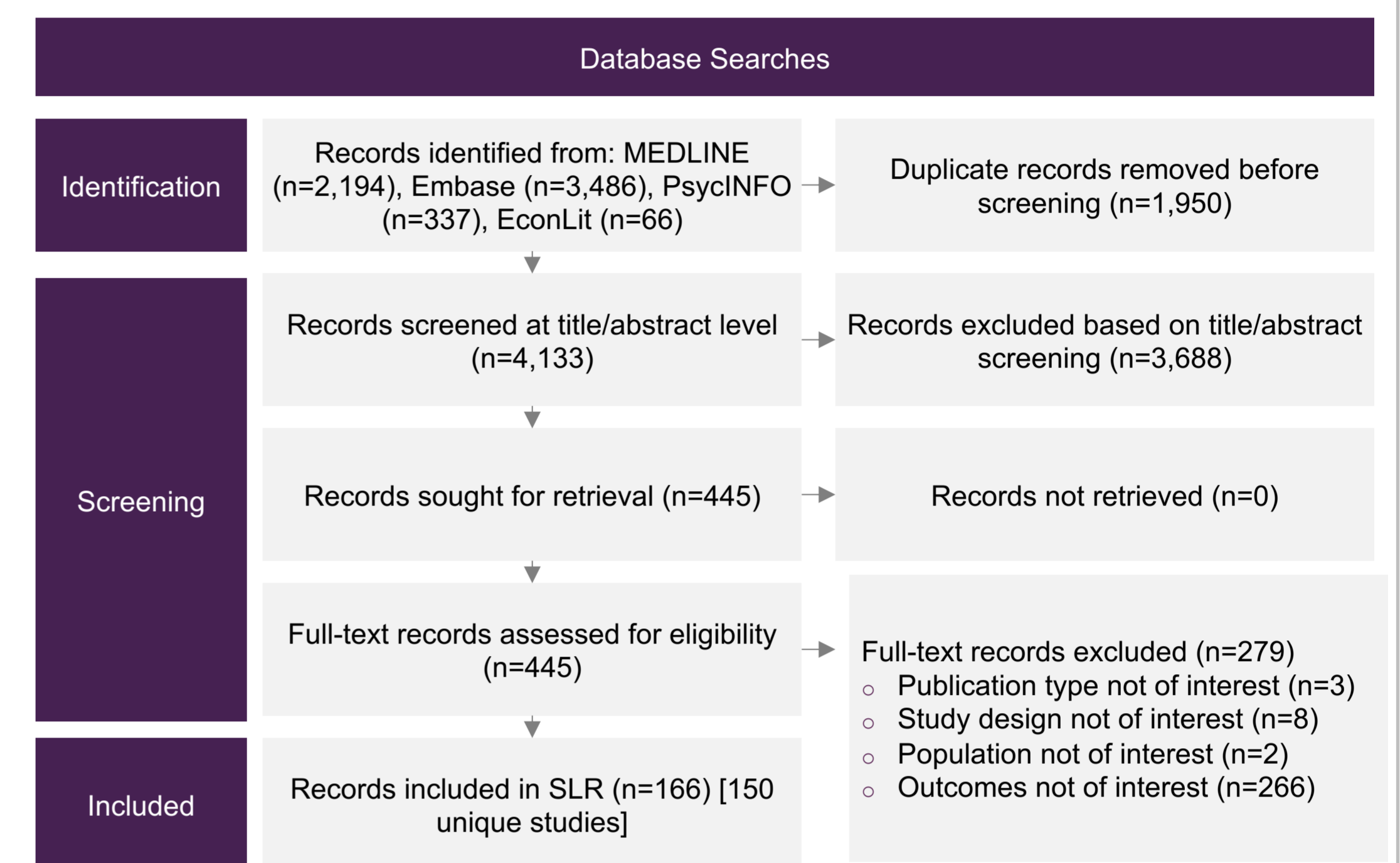
- We conducted a systematic review and evidence-mapping task to collate published research and explore the potential for in-depth analysis of the inter-relationships between cancer-related variables, FT, and HRQoL.
- A targeted review was also conducted to investigate the association between disease stage and FT among selected high-incidence cancers.

KEY RESULTS: Across the three high-incidence cancers, FT generally worsened with more advanced stages, most consistently when using validated tools like COST

RESULTS

- Of 4,133 citations screened, 166 were deemed to meet the PICOS criteria and 150 unique studies were included (Figure 1).
- These studies represented multiple cancer types (Figure 2), most commonly breast (14%), urological (11%), lung (10%), and GI (9%) cancers.
- Half the studies explored relationships between cancer variables and FT, and the remainder explored FT-HRQoL relationships only (Figure 3).
- 23% of the identified studies simultaneously explored inter-relationships between cancer-related variables, FT, and utilities/HRQoL (Figure 3).
- COST (53%) was the most common FT measure, while FACT-G (33%) was the most common HRQoL measure.
- The targeted review of breast, lung, and GI cancers yielded 19 relevant studies with cancer-specific results (Table 2).
- Among these, 15 conducted univariate analyses, 11 showed an association between more advanced disease and worse FT (8 reached statistical significance), 1 found the inverse relationship and 3 reported no association.
- Of 8 studies reporting multivariate analyses, 5 showed a directional association (4 statistically significant), 1 reported the inverse and 2 found no consistent association.
- All 10 studies examining FT and HRQoL found consistent associations.
- Explored inter-relationship (advanced stage → worse FT → lower HRQoL) was
 - Strong and consistent in breast cancer
 - Mixed in GI/lung but generally evident when FT was measured with validated tools (COST).

Figure 1. PRISMA Flow Diagram



The database searches were designed to capture all relevant conference proceedings (published between 2022 to 2024) indexed in Embase; no manual conference proceeding searches were conducted.

Table 2. Directional association between cancer stage, FT, and HRQoL in high-incidence cancers for studies with FT outcomes across both early and late stages

Cancer Type	Study	Country	Association between Increasing Stage and Increasing FT		Association between Higher FT and Lower HRQoL (HRQoL Measure)
			Univariate/Subgroup Analysis (FT Measure)	Multivariate Analysis (FT Measure)	
Breast	Benedict, C. (2022) ⁵	US	COST		FACT-G
	Chan, R. (2022) ⁶	US	Other		QOL-PV
	Corkum, J. (2022) ⁷	US	COST		
	Storandt, M. H. (2022) ⁸	US	Other	COST	
	Emerson, M. A. (2023) ⁹	US	Other		FACT-G
	Maculaitis, M. C. (2023) ¹⁰	US	COST		FACT-B and FACT-G
Gastrointestinal	Pisu, M. (2015) ¹¹	US		Other	
	Mo, M. (2023) ¹²	China	COST		
	Kircher, S. (2024) ¹³	US	COST		FACT-G7
	Lapen, K. (2024) ¹⁴	US		COST	Not specified
	Muaddi, H. (2024) ¹⁵	US	COST; EORTC QLQ-C30 FT Subdomain		
Lung	Pisu, M. (2015) ¹¹	US		Other	
	Hazell, S. Z. (2020) ¹⁶	US	COST		FACT-L
	Thronicke, A. (2020) ¹⁷	Germany	EORTC QLQ-C30 FT Subdomain		EORTC QLQ-C30
	Deboever, N. (2023) ¹⁸	US		COST	
	Liu, M. (2023) ¹⁹	China	COST		
	Augustovski, F. (2024) ²⁰	Argentina	COST		EQ-5D
	Hsu, M. L. (2024) ²¹	US	COST		EORTC QLQ-C30
All 3 Types	Yap, S. L. (2020) ²²	Malaysia	COST		

Abbreviations: COST= COmprehensive Score for Financial Toxicity; EORTC QLQ-C30= European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EQ-5D= EuroQol-5 Dimensions; FACT-Breast = Functional Assessment of Cancer Therapy-General; FACT-G = Functional Assessment of Cancer Therapy-General; FACT-L = Functional Assessment of Cancer Therapy-Lung; FT= Financial toxicity; NA/NR= Not Available/Not Reported; PROMIS= Patient-Reported Outcomes Measurement Information System; QOL-PV= Quality of Life -Patient Version.

Figure 2. Percent of Studies by Cancer Type

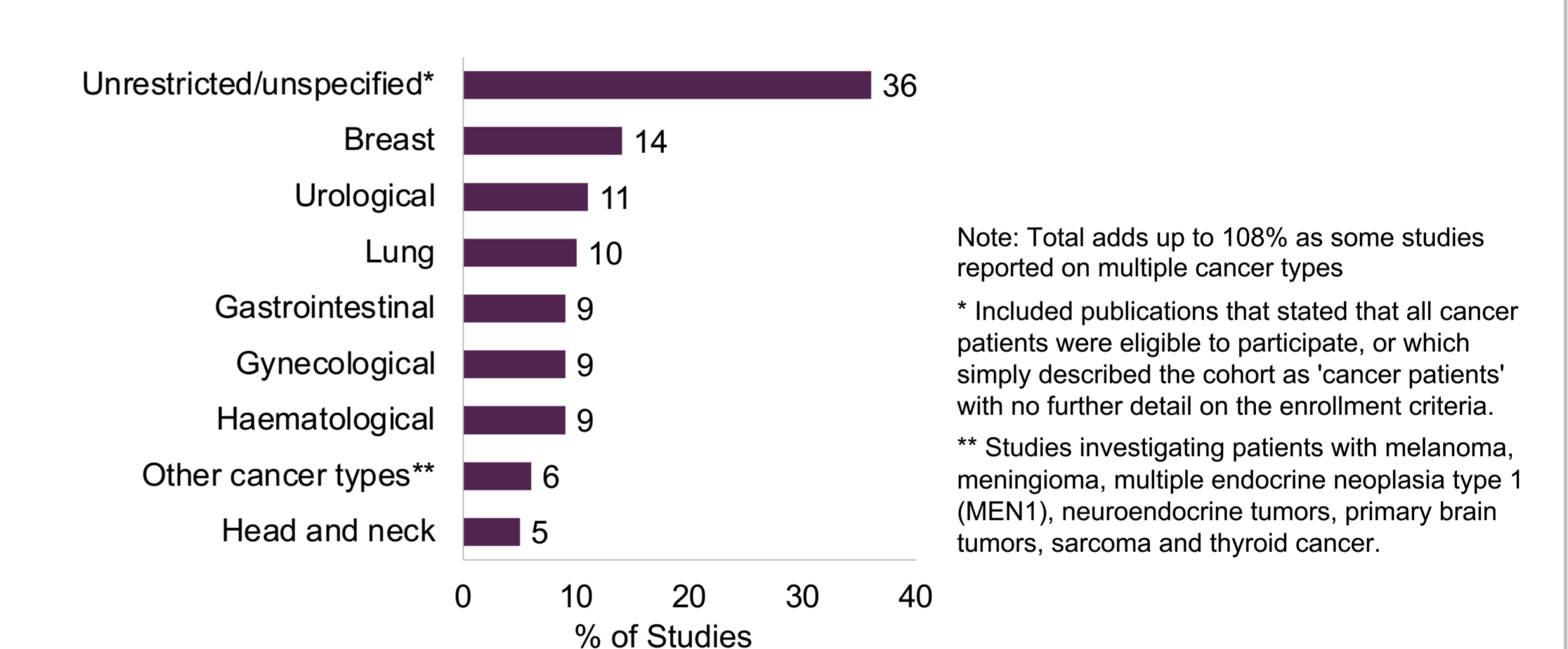
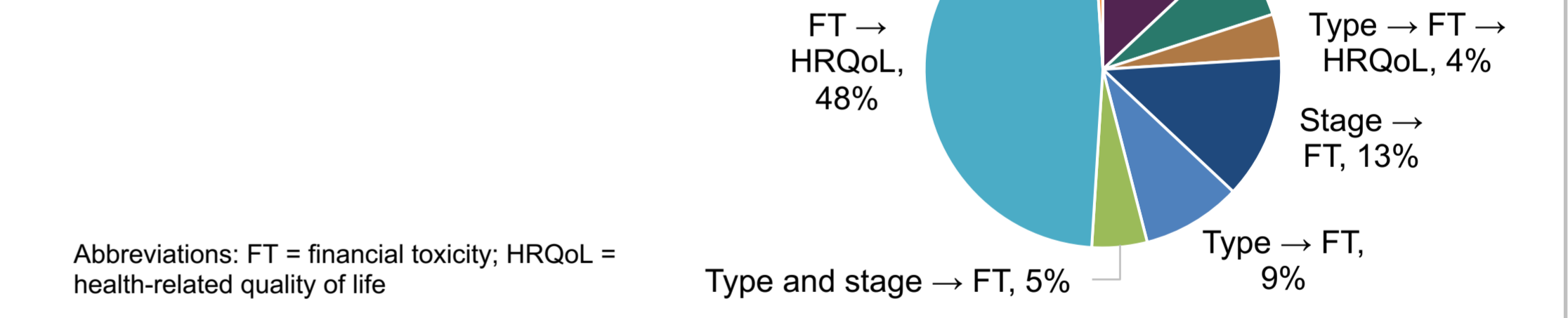


Figure 3. Inter-relationship Mapping Across All Extracted Studies



CONCLUSIONS

- There is a broad evidence base relating cancer type and stage, FT, and HRQoL.
- Evidence suggests advanced-stage cancers are associated with worse FT and detrimental HRQoL impact at least in high-incidence cancer types, despite likely cross-disease heterogeneity in such relationships.
- Further research is needed to confirm the generalizability of these trends.

LIMITATIONS

- The targeted analysis was based only on data relating to selected specific cancer types and therefore it is possible that its findings are biased.

METHODS

- Searches were conducted via Embase, MEDLINE, PsycInfo, and EconLit to identify relevant studies published within the past 10 years, using pre-defined selection criteria for eligibility (Table 1).
- Title/abstract screening used a human–AI hybrid approach via Nested Knowledge[®]; any conflicts between the human reviewer’s decision and the AI decision were adjudicated on by a second human reviewer.
- Full texts were then screened by one human reviewer, with exclusions independently confirmed by a second; any disagreements were adjudicated on by a third human reviewer.
- A GPT-4-based model extracted variables for the evidence map, and all extracted elements were human-validated.
- The population, measures of FT and HRQoL, and reported relationships were extracted from each included study.
- For high-incidence cancers (breast, lung, and gastrointestinal [GI] cancers), a targeted review was conducted of studies reporting FT outcomes across both early and late stages, with extraction of statistical methods, effect estimates, and corresponding significance levels.
- This targeted approach was intended to reduce the potential for confounding factors related to differences in cancer biology, epidemiology, staging systems, treatment pathways, and survival and enhance the clarity and applicability of the findings.

Table 1. Study Selection Criteria

Criteria	Inclusion Criteria	Exclusion Criteria
Population	Patients with cancer of any type or caregivers of patients with any type of cancer	<ul style="list-style-type: none"> Studies not evaluating patients with cancer or caregivers of patients with cancer Studies evaluating only patients with cancer plus specified comorbidities
Interventions/Comparators	Any or none	Not applicable
Outcomes	Measures of financial toxicity (or proxy indicators thereof)* stratified by, or assessed for association with, any of the following: <ul style="list-style-type: none"> Cancer type, Clinical stage, Timing/promptness/delay of diagnosis Utility or other measures of health-related quality of life stratified by, or assessed for association with, financial toxicity (or proxy indicators thereof)*	<ul style="list-style-type: none"> Interventional or observational studies primarily assessing only outcomes of specific treatments, managements strategies, or programs Studies that focus on development, testing, validation, or translation of tools for assessing health-related quality of life or financial toxicity
Study Design	Observational studies	<ul style="list-style-type: none"> In-vitro, ex-vivo, animal studies, genetic studies, economic or other mathematical models, clinical trials Publication types not of interest: editorials, errata, trial protocols, guidelines, case reports, narrative reviews, SLRs (which are to be used only for citation-chasing)
Limits	<ul style="list-style-type: none"> Full-text studies published from 2014 to present Conference proceedings published from January 2022 to present English language only 	<ul style="list-style-type: none"> Full-text studies published prior to 2014 Conference abstracts published prior to 2022 Articles not published in English language

* Studies were considered potentially eligible if they reported on either of the following: i) financial toxicity quantified by the COmprehensive Score for financial Toxicity (COST) tool or other instruments; ii) potential indicators of financial toxicity including, but not limited to, financial distress/worry/concern/crisis/challenge/hardship, job loss/unemployment, financial debt, and bankruptcy.

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