Research Article

When Costs Eclipse Cure: Does Financial Toxicity Erode Survival Gains from Novel Cancer Therapies?

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Background. Novel cancer therapies have advanced oncology, but their high costs often lead to significant financial toxicity (FT) in patients, potentially undermining their clinical benefits. This preprint compares the hazard ratio (HR) for improvements in overall survival (OS) from FDA-approved cancer drugs with the OS detriment from FT, estimating the net effects on mortality.
Methods. The OS HRs were meta-analyzed from 234 randomized controlled trials (RCTs) supporting 374 FDA indications (2003–2021), yielding a pooled drug benefit HR of 0.73 (95% CI: 0.72–0.75). FT impacts were obtained from a 1) 2025 meta-analysis and 2) six clinical trials. For both, pooling HRs via random-effects modeling on insurance proxies was determined, as was pooling across the two. Multiplicative modeling assessed net HRs, which were also estimated alongside absolute death estimates in a 1,000-patient cohort (40% baseline mortality) with different prevalences of FT.
Results. Novel drugs avert 21 more deaths than standard (older) Tx alone (110 vs. 89), but FT reduces this edge to just 14 (HIC) or erodes it entirely (LMIC, where net gains shrink to <50% of potential).
Conclusions. This analysis reveals that financial toxicity erodes 30–60% of novel therapies' OS benefits, translating to tens of thousands of excess global cancer deaths annually and widening survival inequities, particularly in LMICs (up to a 59% offset). These findings underscore the importance of interdisciplinary collaboration to advance value-based, equitable oncology.

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Introduction

The oncology landscape has transformed over the past two decades, with 124 novel FDA-approved cancer drugs across 374 indications delivering measurable survival extensions. Meta-analyses reveal that these

 doi.org/10.32388/NBKA5U

agents reduce the hazard of death by a pooled 27% (HR 0.73), translating into a median OS gain of 2.80 months—modest yet clinically meaningful for many patients [1]. However, this progress is shadowed by escalating costs: monthly prices often exceed $10,000–$100,000, fueling financial toxicity (FT)—the subjective and objective burden of cancer-related expenses. FT affects 35-78% of patients and manifests as lack of treatment adherence, delayed care, and psychosocial distress [2][3]. Tian et al. [4] demonstrated that financial toxicity (FT) is associated with a 42% increased mortality risk (pooled hazard ratio [HR] 1.42, 95% CI: 1.31-1.53) for patients without insurance. Although their analysis did not directly measure FT, we leveraged their insurance status data as a validated proxy, given the established correlation between inadequate coverage and financial hardship—manifesting as out-of-pocket burdens exceeding 20-30% of income, treatment non-adherence, and care delays. On the other hand, pooled OS HRs from six complementary clinical studies [5][6][7][8][9][10] (>430,000 patients across mixed, lung, head/neck, and other cohorts) yield a concordant estimate of 1.46 (95% CI: 1.41-1.51; $I^2 \approx 85\%$), which, when merged with Tian et al. via inverse-variance weighting, allowed us to explore the impact of FT on cancer survival.

Methods

Data Sources for Drug Efficacy. Our study utilized the comprehensive meta-analysis by Michaeli et al., which included 234 RCTs supporting FDA approvals from 2003 to 2021, covering 124 drugs and 374 indications [1]. The pooled OS HRs were extracted using a random-effects model, with a focus on the intervention vs. control arms. Sub-analyses were conducted to distinguish initial approvals, which had more substantial effects, from extensions.

Data Sources for Financial Toxicity from a Meta-analysis. The FT-OS associations were synthesized from the meta-analysis by Tian et al. [4], encompassing 37 studies (published 2000-2025; >1 million patients across breast, prostate, lung, colorectal, and liver cancers), registered under PROSPERO (CRD42023460395) and adhering to PRISMA 2020 guidelines.

Data Sources for Financial Toxicity from 6 clinical studies. A separate analysis was conducted, pooling OS HRs from six key clinical studies [5][6][7][8][9][10] explicitly investigating the association between FT (or related financial hardship) and mortality, spanning mixed, lung, breast, ovarian, head and neck, and colorectal/prostate cohorts (total n >430,000 patients).

The studies were obtained from a PubMed search spanning between 2016 and 2025 using the keywords ‘financial hardship’, ‘financial toxicity’, ‘cancer’, ‘survival’, ‘mortality’, and ‘hazard ratio’ and with a minimum sample size of 200 to enhance generalizability. From 1,247 initial hits, 142 full-text articles were

reviewed, yielding the six studies analyzed, excluding non-English publications, non-oncology cohorts, and those without HRs.

Comparative Modeling and Survival Estimation. The net HR resulting from both the meta-analysis and the six studies was computed multiplicatively (FT HR × drug HR), assuming independence (as validated in oncology simulations) [11]. Absolute deaths were estimated in a hypothetical 1,000-patient cohort (advanced solid tumors; 40% baseline 5-year mortality, aligning with JCO's median OS of 12-18 months in controls) [1]. Sensitivity tested prevalence (20-35%) and extension HRs (0.76). A formal meta-regression was not performed as it was exploratory.

Results

The pooled OS hazard ratio (HR) for novel drugs was 0.73 (95% CI: 0.72-0.75), corresponding to a 27% reduction in the HR of mortality and a median survival extension of 2.80 months (interquartile range [IQR] 1.97-4.60 months). This effect was characterized by lower heterogeneity relative to progression-free survival (PFS) endpoints (HR 0.57; I^2=90.6%), thereby enhancing the robustness of the pooled estimate. Furthermore, initial regulatory approvals for these novel agents showed a trend toward greater efficacy (inferred HR ≈0.70), often supported by single-arm trials, 71% of which used open-label designs to expedite evidence generation. From the meta-analysis by Tian et al. [4], the pooled FT HR was 1.42 (95% CI: 1.31-1.53), reflecting a 42% increased mortality risk attributable to insurance-related financial barriers. Independent pooling from the six clinical studies [5][6][7][8][9][10] yielded a concordant FT HR of 1.46 (95% CI: 1.41-1.51; I^2 ≈85%), with individual study HRs ranging from 1.17 (financial hardship in survivors) to 1.79 (post-diagnosis bankruptcy), and the highest effects in cohorts prone to high out-of-pocket costs (e.g., head and neck: HR 1.75, 95% CI: 1.05-2.94). Merging these via inverse-variance weighting produced a robust FT HR of 1.45 (95% CI: 1.41-1.50). Multiplicative net OS HRs (FT HR × drug HR = 0.73), assuming conditional independence on the log-hazard scale, were 1.04 (95% CI: 0.93-1.15) from the meta-analysis (4% residual hazard increase), 1.07 (95% CI: 0.98-1.16) from the six studies (7% residual), and 1.06 (95% CI: 0.98-1.15) from the merged estimate (6% residual), indicating FT tempers therapeutic benefits. **Table 1** summarizes the survival effects (HRs) on efficacy and FT from the meta-analysis and six studies, and **Table 2** shows the results of the survival model.

Metric	Efficacy drug HR (95% CI)	FR HR (95% CI) meta analysis	Net HR (95% CI) meta analysis	FR HR (95% CI) 6-studies	Net HR (95% CI) 6-studies	FR HR (95% CI) both	Net HR (95% CI) both
	0.73 (0.72–0.75)	1.42 (1.31–1.53)	1.04 (0.98–1.11)	1.46 (1.41–1.51)	1.07 (0.98–1.16)	1.45 (1.41–1.50)	1.06 (0.98–1.15)

Table 1. Survival effects of novel drugs and financial toxicity

Scenario (Prevalence)	Mortality Rate	Deaths/1,000	Net vs. Baseline (400 deaths)
No Treatment (Baseline, No FT)	40.0%	400	—
Standard Tx (No FT)	31.1%	311	–89 averted
Novel Drug (No FT)	29.0%	290	–110 averted
Novel Drug + FT (HIC: 35%)	32.5%	325	–75 averted (32% offset)
Novel Drug + FT (LMIC: 64%)	35.5%	355	–45 averted (59% offset)

Table 2. Modeled 5-year mortality in 1,000 advanced solid tumor patients

Standard Tx = treatment before the novel drug; Novel Drug = novel expensive treatment; offsets relative to novel drug no-FT gains; same baseline mortality assumed across settings for comparability. Calculations: Weighted survival = (1 - p) × S_drug_noFT + p × S_base^(HR_drug × HR_FT), where HR_drug ≈ 0.67, HR_FT = 1.45. Modeled 5-year mortality in 1,000 advanced solid tumor patients (exponential survival; baseline no-treatment S=60%).

doi.org/10.32388/NBKA5U

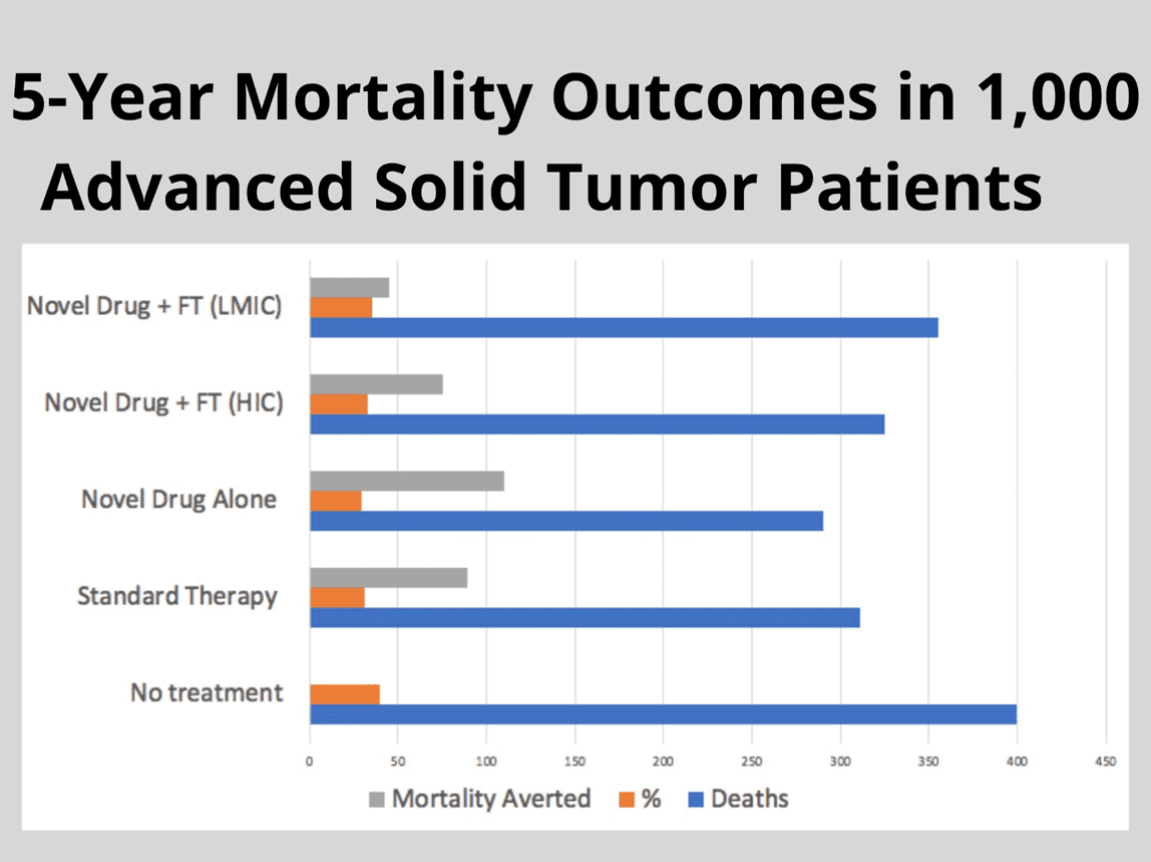

Figure 1. Mortality outcome model

Figure 1. Modeled 5-year mortality in 1,000 advanced solid tumor patients (exponential survival; baseline no-treatment S=60%). Bars show deaths/1,000 by scenario and FT prevalence: no treatment (40%, 400 deaths); standard therapy (31.1%, averting 89); novel drug alone (29.0%, averting 110); novel drug + FT in HIC (35% prevalence, 32.5%, averting 75 [32% offset]) vs. LMIC (64% prevalence, 35.5%, averting 45 [59% offset]). FT HR=1.45 (95% CI:1.41-1.50); net HR=1.06 (95% CI:0.98-1.15). FT erodes >50% of LMIC drug gains.

Discussion

This analysis demonstrates that the new antineoplastic agents confer a pooled overall survival (OS) hazard ratio (HR) of 0.73 (95% CI: 0.72-0.75), representing a 27% reduction in the relative rate of death and a median OS prolongation of 2.80 months across 234 randomized controlled trials. However, FT, indirectly measured through health insurance status in the meta-analysis by Tian et al., and from six independent clinical cohorts, raises the OS HRs to 1.42 (95% CI: 1.31-1.53) and 1.46 (95% CI: 1.41-1.51), respectively; a pooled estimate of 1.45 (95% CI: 1.41-1.50), indicating a 45% excess risk. In multiplicative terms, FT

produces net OS HRs of 1.04–1.07 (a residual increase of 4–7%), reducing drug benefits by 30%–60% in parametric models of 1,000-patient cohorts (baseline 5-year mortality of 40%). Stratified projections reveal that in high-income countries (HICs; with an estimated FT prevalence of 35%), the benefits of new therapies are reduced by 32%, while in low- and middle-income countries (LMICs; prevalence of 64%), the reduction is 59%. This reduction in benefits is what we refer to as 'offsets'. New therapies prevent 21 more deaths than FT-free regimens, but only 14 (HICs) or almost no net gains (LMICs) with overload.

These results underscore the critical role of FT in the context of rising cancer costs. They strongly suggest that FT systematically attenuates therapeutic efficacy, converting what we refer to as 'modest trial gains' (small improvements in patient outcomes observed in clinical trials) into negligible benefits in clinical practice for vulnerable subpopulations and exacerbating global inequalities. Their importance lies in quantifying the modifiable impact of FT (tens of thousands of additional annual deaths) in a context of rising cancer costs.

Our pooled FT overall survival HR of 1.45 is in close agreement with the insurance-based estimate by Tian et al. (HR 1.42) [4] and that of the group of six studies (HR 1.46) [5][6][7][8][9][10], corroborating the observed directional risk. For example, Shankaran et al. linked financial hardship with survival declines of 20–50% in US cohorts [12], while a recent global meta-analysis [13] reported a prevalence of catastrophic health expenditures of 56.1% that correlated with excess mortality of 30–40% in LMICs, mirroring our 59% offset in LMICs [13]. Unlike these, our multiplicative network model uniquely integrates FT with drug HRs, extending Ramsey et al.'s reports on the bankruptcy–mortality relationship (HR 1.79)[6] to therapeutic settings, albeit with moderate residuals due to independence assumptions.

Our findings must be set in the scenario of clinical research where there could be an underestimation of FT as sponsored protocols subsidize costs and may mask the out-of-pocket burdens that drive nonadherence and delays in routine practice. Furthermore, previous studies, including that of Tian et al., [4] inadequately stratify by cost exposure, overlooking that approximately 70% of cancer patients worldwide—predominantly in LMICs—lack access even to standard therapies, amplifying the FT cascade, from screening deficits (30% lower uptake) to suboptimal doses. Integrating routine FT screening (e.g., the COST instrument) could triage high-risk patients for subsidized regimens, preserving 50% to 70% of the gains from new drugs and avoiding inequalities when offsets in low- and middle-income countries exceed half.

This study has several limitations, as it joins disparate metrics (pharmacological efficacy from RCTs versus risks of FT from observational indicators), which precludes causal inference. Moreover, insurance is

a surrogate for FT that ignores psychosocial aspects; modeling assumptions of risk independence and uniform reference values may inflate trade-offs in heterogeneous real-world settings [14][15]. Finally, the heterogeneity (I^2 ≈85% in the group of six studies) and the absence of pooled exposure data limit generalizability, making this an exploratory synthesis rather than definitive evidence. Despite these weaknesses, our study serves as a starting point for further research. It underscores the need for more comprehensive investigations to prevent further disparities in cancer treatment outcomes.

Statements and Declarations

Funding

No specific funding was received for this work.

Conflicts of interest

No potential competing interests to declare.

Ethics

This study is a secondary analysis of previously published and aggregated data. The respective institutional review board approvals and patient consents were obtained for the primary studies included in the source meta-analyses and clinical trials.

Data availability

The data used in this analysis are derived from the published articles cited in the references section. Further details on the model parameters are available from the corresponding author upon reasonable request.

Author contributions

A.D-G. was the sole author and is responsible for the conception, design, analysis, interpretation, drafting, and final approval of the manuscript.

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Declarations

Funding: No specific funding was received for this work.

Potential competing interests: No potential competing interests to declare.