smaller CTCs implicated in progressive disease, which requires a different course of therapy. Similarly, isolation based on density is also difficult because very small CTCs might have a similar density to red blood cells and, therefore, be lost with low-density separation media. Technologies based on deformability are hampered because CTCs can be mechanically similar to other blood cells in some cancer types (such as prostate cancer).[9]

At present, the technology used for isolation and enumeration of CTCs depends entirely on the hypothesis investigated. The ideal CTC marker will be expressed on every CTC (including clusters) but is absent from other blood-derived cells and is constitutively expressed throughout disease progression. To establish CTCs as a clinical biomarker, optimised workflows are essential to generate robust, cost-efficient, and reproducible data that can inform clinical decisions. A consensus cutoff regarding the number of CTCs per mL as a clinical biomarker for stratification is undetermined in most advanced cancers, although a recent meta-analysis[10] in metastatic breast cancer has made great progress towards establishing this aim. Overall, analysis of CTCs for prognosis and therapeutic stratification is still not routine in the clinic; however, they are increasingly used in prospective clinical trials for guiding therapy (eg, CTC-STOP [ISRCTN82499869]).

For more on **CANCER-ID** see www.cancer-id.eu

Various multicentre efforts are ongoing to establish the best practice in the field, including CANCER-ID, which aims to provide consensus workflows for sample processing, specimen storage, biobanking, and molecular analysis of ctDNA, CTCs, and microRNAs. Future studies should focus on validating ctDNA assays in compliance with international standards and local legislation, guided by a standardised framework that describes the necessary procedures for validating potential biomarkers. Overall, the liquid biopsy holds promise for patient diagnostics and therapy monitoring. We anticipate that studies reporting over the next few years will help to progress the liquid biopsy from the laboratory to the clinic, to be ready for prime time.

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Cancer hospital advertising and outcomes: trust the messenger?


Lewis Houghton/SPL

Hospitals have made substantial investments in advertising for cancer services in the past two decades, totalling over US$200 million in 2016 alone.[1,2] Advertisements promoting cancer centres are unavoidable in the USA. They hang on highway billboards and on air during prime-time programming. Some advertisements claim superior outcomes, others highlight access to clinical trials, and many present heart-warming patient stories that might be non-representative of actual outcomes.[3] Data suggest that patients are highly aware of advertisements and are likewise influenced by them.[4]

Decades of research have shown wide and consistent variations in cancer care outcomes between US hospitals.[5,6] Although patients might wish to select their cancer care provider based on objective measures of cancer care quality and outcomes,[7,8] few measures are publicly available. Advertising is designed to improve cancer centre recognition and attract patients in an

increasingly competitive environment. It has the potential to provide valuable information about screening and treatment options, and it could benefit patients by attracting them to hospitals with the best outcomes. However, if hospital advertising for cancer services is not correlated with patient outcomes, information shared through advertising might mislead patients and generate inaccurate expectations of treatment benefit.[9]

We did an analysis to evaluate whether advertising spending for a hospital's cancer services was associated with long-term survival outcomes of patients with cancer treated in those centres. For the measures of advertising spending and long-term survival, we applied methods that have been described previously.[9,10] We captured hospital advertising spending for cancer services in 2014 across six different US media outlets (television, magazines, radio, newspapers, billboards, and the Internet), using data from the media-monitoring agency Kantar Media (New York, NY, USA).[9] Medicare fee-for-service 100% research-identifiable files were used to determine hospital risk-adjusted 5-year mortality ratios, including cases from 2011–12.[10] We included the top 50 hospitals (or sets of hospitals) in terms of their advertising spending, accounting for over 89% of the $173 million spent on cancer centre advertising in 2014.

The primary test of association was a linear regression, with advertising spending as the predictor. The outcome was a risk-adjusted mortality ratio that was determined by dividing the observed number of deaths by an expected number. A risk-adjusted mortality ratio below 1 indicates that a hospital performed better than expected, whereas a ratio greater than 1 means a hospital had higher mortality than expected. In total, we used four models to assess the relationship between advertising spending and risk-adjusted mortality. This study was deemed exempt research by the institutional review board of Memorial Sloan Kettering Cancer Center (New York, NY). The Centers for Medicare & Medicaid Services and Kantar Media granted data-use approvals. Additional methodological details can be found in the appendix (pp 1–2).

For the top 50 hospital advertisers, the median number of fee-for-service Medicare patients with cancer treated was 764 (range 93–5945). Spending for advertising that promoted cancer services was unevenly distributed across hospitals (figure). Median spending was $305 900. The 50th hospital spent $106 300, the average hospital spent $3 064 600, and the top advertising spender—Cancer Treatment Centers of America—spent more than the other 49 hospitals combined, totalling $101 740 900. 5-year hospital risk-adjusted mortality ratio for patients with cancer ranged from 0·83 to 1·13, meaning hospitals' mortality ratio ranged from 17% (0·83) below expected to 13% (1·13) higher than expected. Results between the four models were fairly inconsistent. Some of the models found a positive relation between advertising spending and survival outcomes; other models found a negative relation. For two of the four models, this relationship was not significant. None of the models had an R^2 greater than 38%, indicating that hospital advertising did not account for most of the variability in hospital survival outcomes. The figure shows the full explanation of the model results. A list of all hospitals with spending,

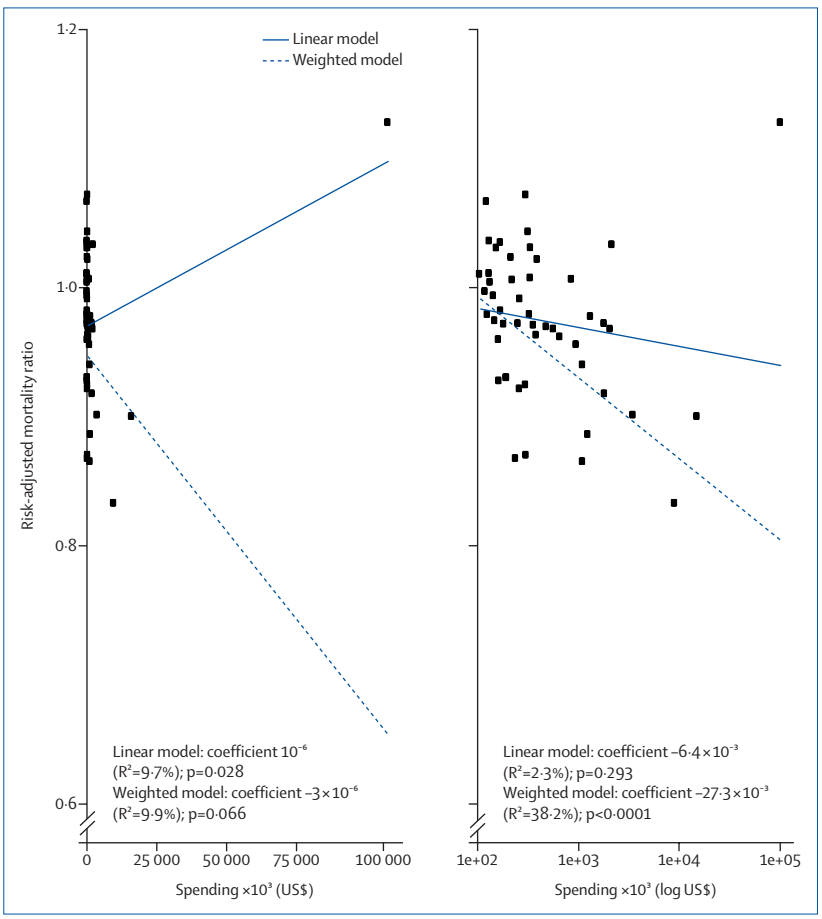

Figure: **Scatterplots of hospitals' advertising spending for cancer services in 2014, compared with risk-adjusted 5-year mortality for fee-for-service Medicare beneficiaries beginning treatment in 2011–12.**
Lower risk-adjusted 5-year mortality ratio means better performance. For detailed methodology see appendix.

See **Online** for appendix

volume, and survival outcomes is available in the appendix (pp 3–4).

We found little evidence that the cancer centres to which people were most likely to be exposed through advertisements were the cancer centres with the best patient outcomes. There was considerable variation in both advertising spending and survival outcomes among the top 50 hospital advertisers. Some hospitals in our sample with excellent outcomes did not have particularly high advertising spending, and the highest-spending set of hospitals—operating as Cancer Treatment Centers of America—had poorer patient outcomes than all other hospitals in our sample. Patients might be inadvertently pursuing treatment choices that do not align with their intentions or preferences by assuming that advertising across national media is indicative of high-quality cancer treatment. Over the past decade, cancer centres have markedly increased the amount of consumer-directed advertising spending. Assuming current trends continue, cancer-centre advertising is likely to constitute a major source of patient information that might influence decisions about where patients with cancer seek treatment. This effect would be good for patients if advertising were predictive of improved patient outcomes. However, our findings suggest that the relation is inconsistent and not particularly strong, with many outliers.

Some limitations should be considered when interpreting our findings. For long-term survival, we only included fee-for-service Medicare beneficiaries, and the generalisability of this outcome to other patients is unknown. Advertising spending totals did not include spending for social media, which has been widely adopted by US hospitals as a means to support hospitals' reputations and attract patients. We also did not have data available on the content of cancer centre advertisements, and we were thus unable to distinguish between advertisements promoting specific cancer therapies and advertisements promoting general cancer centre reputations. Our analysis was limited to cancer centre advertising in the USA, but the USA has the highest health-care spending in the world, and in the past two decades there has been a marked growth in spending for health-care advertising.[1]

Hospital advertising for cancer services continues to increase in the USA, and patients have more options for where to seek cancer care. However, cancer care quality remains uneven. Our findings suggest that cancer care advertising is not reliably valuable for patients as a surrogate of cancer care quality. The absence of correlation underscores the need for publicly available objective data on cancer centres' patient outcomes and other measures of quality that can be easily accessed and interpreted by patients to aid them in decision making. Patients, clinicians, and other stakeholders should view cancer centre advertisements with scrutiny.

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