Implications of Cure Fractions on Costs of Cancer Care: An Innovative Application to Multi-Cancer Early Detection (MCED) Economic Modeling

MSR4

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Objectives

- Multi-Cancer Early Detection (MCED) tests have an opportunity to detect cancers at earlier stages when survival tends to be higher.[1]
- Economic modeling of MCED tests must consider that some patients diagnosed with cancer will be cured, meaning death will not be due to cancer, while other patients will remain uncured and death will be due to cancer.
- Cured individuals are likely to live longer than uncured individuals, but it is unrealistic to assume that cancer-related costs should be applied uniformly for the remainder of a cured patient's life compared to uncured patients. MCED economic modeling must consider the impact of downstaging on cure fractions and the implications on cancer-attributable costs.
- Mixture cure models are frequently used to determine cure fractions due to cancer pharmacologic therapies; similar methods can be utilized to assess the impact of downstaging on cure fraction.[2]
- The purpose of this analysis is to determine cure fractions by cancer type and stage, and quantify the impact of incorporating these cure fractions into MCED economic modeling.

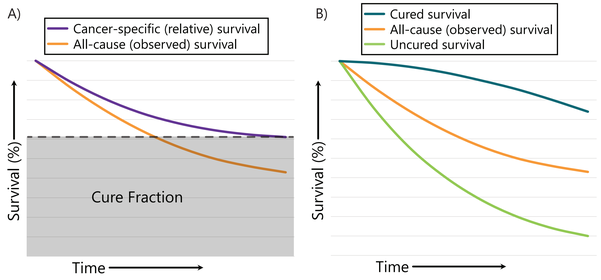

Figure 1. A) Conceptual representation of cure fraction as the asymptotic limit of the relative survival curve over time. B) Mixture cure models combine the calculated cure fraction with all-cause survival to estimate cured and uncured survival.

Methods

Determining Cure Fraction

- Cancer-specific (relative) and all-cause (observed) survival curves were obtained for individuals aged 50-74 by cancer type and summary stage from the Surveillance, Epidemiology, and End Results Program (SEER), and expected survival was obtained from United States Life Tables.[3, 4] A select number of cancer types targeted by typical MCED tests were evaluated.
- The flexsurvcure R package[5] was used to fit a Weibull distribution to each of the relative survival curves to calculate the fraction of patients for each cancer type and stage who experience no excess mortality due to cancer (Figure 1A).
- For the cured population, death is not due to cancer so they experience survival equivalent to U.S. life tables (expected survival). For the uncured population death is due to cancer, and survival is determined using the mixture cure model (Figure 1B).

$$S(t) = S^*(t)\left(\pi + (1-\pi)S_u(t)\right)$$

where $S(t)$ is observed or all-cause survival, $S^*(t)$ is expected survival, π is cure fraction, and $S_u(t)$ is cancer-specific survival function for uncured subjects.

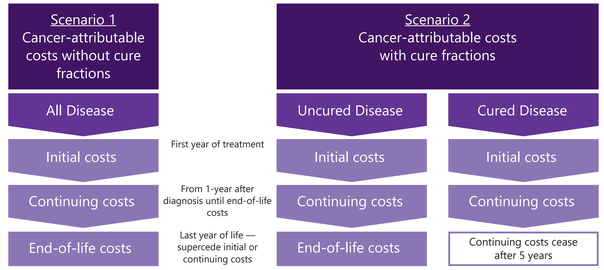

Figure 2. Comparison of two hypothetical scenarios. Scenario 1, where treatment costs for all diagnosed patients are applied the same regardless of whether disease is cured or uncured; and Scenario 2, where a fraction of patients are "cured" with limited continuing and end-of-life treatment costs.

Deriving Economic Impact of Cure Fractions

- 10-year cancer-attributable costs (initial, continuing, and end-of-life) were tabulated across a static diagnosed population of 1,000 individuals for each cancer type and stage.[6]
- Two scenarios were modeled: cancer attributable costs with and without the inclusion of cure fraction:
  - In the no cure fraction scenario, survival was modeled by SEER observed survival, and initial costs were applied to the first year of diagnosis, end-of-life costs for the last year of life (unless death was within one year of diagnosis, in which case end-of-life costs were applied instead of initial), and continuing costs were applied to all remaining years (Figure 2).
  - In the cure fraction implementation scenario, survival was modeled by cured and uncured survival curves determined using the mixture cure model. For the cured population, initial costs were applied to the first year of diagnosis, followed by continuing costs for up to five years, but no end-of-life costs. Costs for the uncured population were applied in the same way as the no cure fraction scenario (Figure 2).

Results

Cure fractions are greatest for cancers with higher survival and earlier stage.

- Cure fractions are greatest for local cancers but are also evident for regional and some distant cancers as well (Figure 3A).
- Breast, colorectal, endometrial, and ovarian cancers have the greatest localized cure fractions, while liver, pancreatic, and lung cancers have the lowest localized cure fractions.

Greater curative potential in local stage amplifies cost reduction that results from downstaging to localized cancer.

- The example scenario shows aggregate reductions in cancer-attributable costs after incorporating cure fraction compared to no cure fraction: -26.5%, -9.45%, and -0.5% for local, regional, and distant, respectively.
- All cancers showed cost reductions at the localized stage after implementing cure fractions (Figure 3B), ranging from 39.7% (kidney) to 9.1% (liver).
- Cost reduction for regional and distant stages were generally lower because of lower cure fractions.
- These results suggest that when cure fractions are applied to MCED modeling, downstaging to the localized stage has the greatest opportunity to increase the fraction of cured individuals and reduce cancer-attributable costs.

Conclusions

- We demonstrate the utility of mixture cure models to estimate cure fractions and obtain cured and uncured survival curves that can be used for MCED health-economic modeling.
- Cure fractions are greatest for localized cancers and for cancers with the highest 5-year survival.
- Downstaging through comprehensive cancer screening can increase the opportunity for individuals to reach a cured state.
- Cure fractions can allow for more robust calculation of cancer-attributable costs by isolating end-of-life costs from patients that do not die from cancer.
- Subsequently, the economic cost of managing cancer — and the respective impact due to MCED — can be better represented in health-economic models.

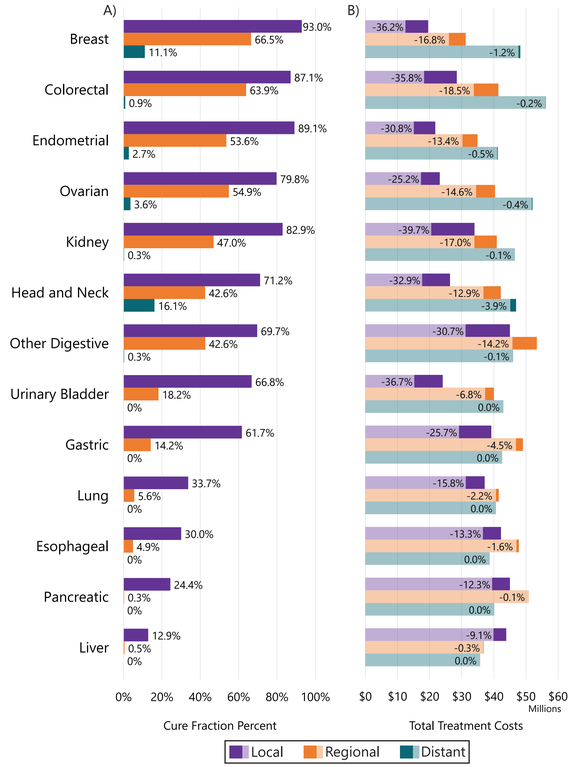

Figure 3. Results of cure fraction analysis and subsequent economic impact. A) For each of the 13 selected cancers in this analysis, the fraction of the population that is "cured" is presented by cancer type and stage. B) The potential economic impact of cure fractions was estimated by comparing the treatment costs over 10 years for a static diagnosed population, first estimated without cure fractions and then estimated with cure fractions. The percent difference between the two approaches is indicated by the data labels, while the absolute difference is represented by the dark color bar segment, in which the upper limit is the cost estimate without cure fractions and the lower limit of the dark color segment is the cost estimate with cure fractions implemented.

References

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