Disparities in the allocation of research funding to gynecologic cancers by Funding to Lethality scores

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HIGHLIGHTS

- There are disparities across cancer sites when NCI funding is measured using the Funding to Lethality score.
- The three major GYN cancers show consistently decreasing Funding to Lethality scores over time.
- Increased funding for GYN cancers is needed to keep pace with laboratory and clinical discoveries of other cancer sites.

ARTICLE INFO

ABSTRACT

Purpose. To analyze National Cancer Institute (NCI) funding distributions to gynecologic cancers compared to other cancers from 2007 to 2014.

Methods. The NCI's Surveillance, Epidemiology and End Results (SEER), Cancer Trends Progress Report, and Funding Statistics were used to analyze 18 cancer sites. Site-specific mortality to incidence ratios (MIR) were normalized per 100 cases and multiplied by person-years of life lost to derive cancer-specific lethality. NCI funding was divided by its lethality to calculate Funding to Lethality scores for gynecologic malignancies and compared to 15 other cancer sites.

Results. Ovarian, cervical, and uterine cancers ranked 10th (score 0.097, SD 0.008), 12th (0.087, SD 0.009), and 14th (0.057, SD 0.006) for average Funding to Lethality scores. The highest average score was for prostate cancer (score 1.182, SD 0.364). In U.S. dollars per 100 incident cases, prostate cancer received an average of $1,821,000 per person-years of life lost, while ovarian cancer received $97,000, cervical cancer $87,000, and uterine cancer $57,000. Ovarian and cervical cancers had lower average Funding to Lethality scores compared to nine other cancers, while uterine cancer was lower than 13 other cancers ($p < 0.01$ for all comparisons). Analyses of eight-, five-, and three-year trends for gynecologic cancers showed nearly universal decreasing Funding to Lethality scores.

Conclusion. Funding to Lethality scores for gynecologic cancers are significantly lower than other cancer sites, indicating a disparity in funding allocation that persists over the most recent eight years of available data. Prompt correction is required to ensure critical discoveries for women with gynecologic cancers.

1. Introduction

On January 12, 2016, the "Cancer Moonshot" was announced—an ambitious research and policy initiative with the goal of expediting a decade's worth of cancer discovery [1]. In December 2016, the 21st Century Cures Act became law and $1.8 billion dollars were appropriated for distribution over the next seven years—specifically focused on accelerating cancer research [2]. Additionally, while the U.S. legislature approved a nearly 9% increase over the initial 2018 Presidential National Institutes of Health (NIH) budget to $37 billion [3], the National Cancer Institute (NCI) budget projections for the 2019 fiscal year are anticipated to decrease [4]. In the current climate where the NIH faces constant pressure to decrease spending, investigators for all cancer sites face significant headwinds. Incorporating increasingly sophisticated genetic and molecular testing into clinical trials means that, although they are encouraged to be smaller and nimbler, the cost of these trials is still significant.

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In previous efforts to understand equitable funding distributions, studies have focused on showing disparities based on differences in cancer incidence, mortality, and years of life lost [5]. However, decision-making about resource allocation based solely on one of these metrics —whether cancer incidence, mortality, or something else—may not maximize the understanding of value, or lack thereof, across cancer sites. To ensure the highest level of equitable funding across cancer sites, the following could be considered: 1) avoid funding cancers based purely on their incidence, as this leaves lower-incidence cancers with much smaller amounts of research funding; 2) take into account the mortality rate of the cancer; and 3) when developing spending strategies, consider the average person-years of life lost [6].

We hypothesized that when evaluated through a lens of an objective measure that incorporates all three points above, gynecologic cancers would be underfunded compared to other cancer sites. The objective was to use the Funding to Lethality metric to determine whether NCI research funding allocations are equitable across cancer sites and to investigate the funding trends over time.

2. Methods

We used the Funding to Lethality score (see below) to standardize cancer site incidence, mortality, and person-years of life lost across 18 cancer sites in order to analyze the allocation of research funds. The data was derived from NCI's Surveillance, Epidemiology and End Results (SEER) [7], the NCI Cancer Trends Progress Report [8], and NCI Funding Statistics [9]. Cancer sites that had data available for mortality and incidence from the SEER data, average person-years of life lost from the Progress Report, and funding award levels from the Funding Statistics were considered for analysis. Cancers that did not have this data available were excluded in order to eliminate bias from inappropriate comparisons. Data were extracted by two of the authors (CY and RS) to ensure accuracy. The Funding to Lethality score was calculated in three steps.

Step 1 was to calculate the mortality to incidence ratio (MIR). The SEER program was used to obtain age-adjusted cancer incidence rates and age-adjusted mortality rates for the years 2007–2014 (the most recent years available for analysis) [7]. Using the SEER data, we derived site-specific MIRs by dividing the mortality rate by the incidence rate for each cancer in each year of analysis. This was done in order to standardize how the number of deaths per incident cases were measured across the cancer sites. The MIR has been used previously in settings where estimates of incidence need to be derived from mortality rates [10] and shown to be an accurate and appropriate proxy for five-year relative survival across cancer sites [11]. This is specific to population-based assessments of cancer survival in developed countries, including the SEER data in the United States [11–13]. An example of this calculation is as follows: in 2014, the ovarian cancer mortality rate was 7.0191 deaths/100,000 and the incidence rate was 11.3496/100,000. Therefore, the MIR of ovarian cancer in 2014 was 0.618 deaths per new case.

Step 2 was to calculate the Lethality of the cancer by converting to person-years of life lost per incident case. Because person-years of life lost is critically important in understanding cancer burden on populations, we included these cancer site-specific values in our metric [6]. This estimate comes directly from the NCI, which states: "the average years of life lost represents person-years of life lost divided by the number of people who lost their lives" [8]. To adjust for person-years of life lost, we multiplied the MIR of the cancer by the average person-years of life lost per death for each cancer site and referred to it as the Lethality of that cancer. An example of this calculation is as follows: as demonstrated above, the 2014 MIR for ovarian cancer was 0.618 deaths per new case; this value was multiplied by the average of 17.7 person-years of life lost per ovarian cancer death, yielding an anticipated 10.94 person-years of life lost per new ovarian cancer diagnosis. When converted by a factor of 100 for ease of use in the calculation, there were an anticipated 1094 person-years of life lost per 100 new cases of ovarian cancer. This is referred to as the Lethality of the cancer.

Step 3 was to calculate the Funding to Lethality score. In order to make the comparison with NCI funding allocations, we extracted data regarding the total amount of funding reported by the NCI for each cancer site in each year. To continue the example for ovarian cancer: in 2014, $91.5 million USD was awarded by the NCI for ovarian cancer-related research; this figure was divided by the Lethality, which was 1094 (person-years of life lost per 100 new ovarian cancer cases), resulting in a Funding to Lethality score for ovarian cancer in 2014 of 0.083. This score is equivalent to $83,638.00 awarded per the person-years of life lost from each 100 new ovarian cancer cases. We calculated these standardized scores for the 18 cancers for which all data was available from 2007 to 2014.

The Funding to Lethality scores for each year of the eight-year period were tabulated and trend lines were generated (Fig. 1). The scores were compared using the non-parametric Wilcoxon/Mann-Whitney test. Cancer site trends for Funding to Lethality scores were analyzed by linear regression. All statistical tests were conducted with the R statistical package version 3.3.1 and were considered significant at the $p < 0.05$ level.

3. Results

From 2007 to 2011, prostate cancer had the highest Funding to Lethality scores of all the cancers evaluated (range 1.98–2.17), while from 2012 to 2014, breast cancer had the highest scores (range 1.71–1.90). Annual trends demonstrate that cervical, ovarian, and uterine cancers ranked near the bottom of the 18 cancers analyzed year over year (Fig. 1). Aggregated eight-year data showed that prostate cancer had the highest mean Funding to Lethality score at 1.81 and breast cancer followed closely at 1.80 (Fig. 2). Ovarian cancer ranked 10th out of 18 (Score 0.097; SD 0.008), cervical 12th (Score 0.087; SD 0.009), and uterine 14th (Score 0.057; SD 0.006).

Funding to Lethality scores, based on cancer site, revealed that ovarian cancer was significantly underfunded compared to eight other cancer sites that ranked above it (Table 1; $p < 0.001$ for all comparisons except for kidney/renal pelvis, $p = 0.004$). Ovarian cancer was funded at a significantly higher rate than five other non-gynecologic cancers (pancreatic, Hodgkin lymphoma, testicular, esophageal, and stomach; $p < 0.001$ for all comparisons). Similar analyses of uterine and cervical cancer revealed significant disparities in funding for these cancers.

Table 1 also highlights the average eight-year monetary value derived from the Funding to Lethality scores. The highest eight-year average was prostate cancer, with $1,812,000 allocated for prostate cancer research per the person-years of life lost from each 100 new cases (SD $364,000). Ovarian cancer received significantly less, with $97,000 of ovarian cancer-related research dollars per the person-years of life lost from each 100 new diagnoses (SD $8000; $p < 0.001$). Cervical and uterine cancers were significantly lower, at $87,000 ($9000; $p < 0.001$) and $57,000 (SD $6000; $p < 0.001$), respectively. Uterine cancer was funded at a significantly lower rate than all 13 cancers that ranked above it ($p < 0.001$ for all comparisons except pancreatic, $p = 0.007$). Esophageal and stomach cancers had the lowest amount of funding, at $17,000 (SD $2000) for both.

The rates of change for Funding to Lethality scores were also analyzed. The 18 cancers were ranked from the highest average annual rate of change in score to the lowest (Table 2). Melanoma had the highest average increase in Funding to Lethality score (0.0274; $p = 0.003$). This corresponds to an average annual funding increase of $27,400 per the person-years of life lost per 100 new melanoma cases. There were 10 cancers that had an average annual increase, while ovarian (-0.0002; $p = 0.876$), uterine (-0.0004; $p = 0.735$), and cervical (-0.0029; $p = 0.024$) cancers all had negative average annual changes in their Funding to Lethality scores. Prostate cancer had the greatest average annual decrease (-0.1338; $p = 0.002$) over the eight-year period.
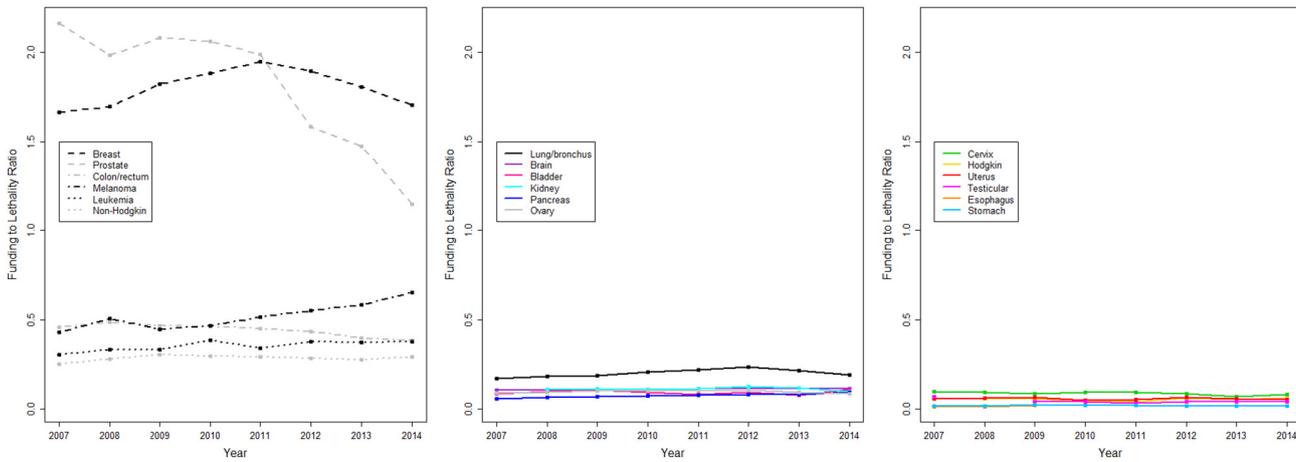
Fig. 1. Funding to Lethality trends 2007–2014. Scales are the same for all three graphs. Cancer sites divided for ease of identification and by 2014 score from highest to lowest.

Analyses of the three-, five- and eight-year Funding to Lethality score trends for cervical, ovarian, and uterine cancer were undertaken separately. Fig. 3 shows that Funding to Lethality scores universally decreased throughout all time periods that were analyzed, with the exception of the five-year uterine cancer trend, which was essentially unchanged. However, the most recent three-year trend for uterine cancer demonstrated a statistically significant downward trend in Funding to Lethality score (slope = −0.0074, p = 0.003). The eight-year cervical cancer trend also decreased at a significant rate (slope − 0.0029, p = 0.035). The five-year (slope = −0.0049, p = 0.089) and three-year (slope = $-p$ = 0.128) trends for cervical cancer had two of the top three greatest decreases, but failed to meet statistical significance.

4. Discussion

When using the Funding to Lethality score—which accounts for differences in the mortality, incidence, and impact on person-years of life lost—for 18 cancers, gynecologic cancers rank in the bottom half of funding allocation from the NCI (ovarian cancer 10/18, cervical cancer 12/18, uterine cancer 14/18). This is a consistent finding when data is analyzed year over year, when aggregated over the eight-year period for which the most recent data is available, and when trends over time are compared. Gynecologic cancers are significantly underfunded compared to many other cancers, the impact of which can be seen in decreased trial enrollment and fewer trials available to patients, as well as in a lower number of high-level treatment recommendations generated. These disproportionately lower levels of funding will make it nearly impossible for gynecologic cancers, with only 17 National Comprehensive Cancer Network (NCCN) "category 1" recommendations combined, to catch up to the great strides being made in melanoma

(33 category 1 recommendations), prostate cancer (38 category 1 recommendations), breast cancer (45 category 1 recommendations), and lung cancer (59 category 1 recommendations), among others [14].

Even though the overall NCI budget varied by only 6% throughout the study period (range $4.789 billion in 2013 to $5.098 billion in 2010), it is estimated that since 2003, the NCI has seen a consistent decrease in its budget when using inflation-adjusted dollars [15]. In a recent position statement, the Society of Gynecologic Oncology and the Foundation for Women's Cancer called the lack of infrastructure for clinical trials in women's cancers a crisis [16]. This same document outlines a five-step action plan, the first step of which is a call to increase NCI funding for clinical trials. This is in harmony with the American Society for Clinical Oncology's message that "increased federal funding is urgently needed to accelerate life-saving research and new cancer breakthroughs" [17]. The ideal outcome would be to increase the level of funding for the NCI and not impose future budget cuts or stagnation. We strongly advocate for using the impact of the incidence of cancers, their lethal potential, and their impact on person-years of life lost to drive allocation of research funding that will offer the most equitable "moonshot" opportunity for all cancers rather than just a few.

Of particular concern is that trends in the Funding to Lethality scores for cervical, ovarian, and uterine cancers are decreasing in practically meaningful—and statistically significant—ways. One may write these trends off as expected given increasing budgetary constraints, but not all cancers have the same downward-trending Funding to Lethality scores over the time period analyzed. Although breast cancer scores have declined recently, the 2014 score is still higher than the 2007 score. The scores for leukemia (slope = 0.0098, p = 0.015), melanoma (slope = 0.0274, p = 0.0025), and pancreatic cancer (slope = 0.0044, p < 0.001) all significantly increased from 2007 to 2014. The data reveals
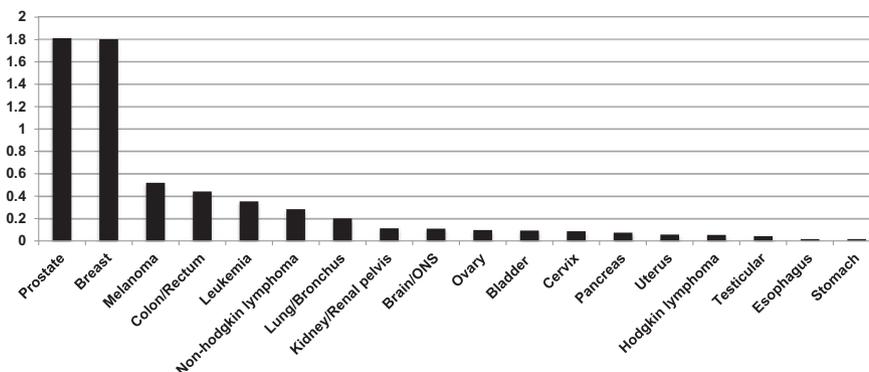

Fig. 2. Eight-year mean Funding to Lethality scores 2007–2014. Score calculated by total amount of annual funding in U.S. dollars reported by the NCI divided by the person-years of life lost per 100 new cases.

Table 1
Analysis of mean eight-year Funding to Lethality scores.

Cancer site	Score[a]	Monetary value[b]	Comparison to ovary p-value	Comparison to cervix p-value	Comparison to uterus p-value
Prostate	1.812 (0.364)	$1,812,000	<0.001	<0.001	<0.001
Breast	1.803 (0.105)	$1,803,000	<0.001	<0.001	<0.001
Melanoma	0.519 (0.075)	$519,000	<0.001	<0.001	<0.001
Colon/rectum	0.442 (0.036)	$442,000	<0.001	<0.001	<0.001
Leukemia	0.353 (0.030)	$353,000	<0.001	<0.001	<0.001
Non-Hodgkin lymphoma	0.284 (0.017)	$284,000	<0.001	<0.001	<0.001
Lung/bronchus	0.201 (0.021)	$201,000	<0.001	<0.001	<0.001
Kidney/renal pelvis	0.112 (0.009)	$112,000	0.004	<0.001	<0.001
Brain/ONS	0.110 (0.005)	$110,000	0.002	<0.001	<0.001
Ovary	0.097 (0.008)	$97,000	Ref.	0.065	<0.001
Bladder	0.092 (0.011)	$92,000	0.44	0.571	<0.001
Cervix	0.087 (0.009)	$87,000	0.065	Ref.	<0.001
Pancreas	0.074 (0.011)	$74,000	0.001	0.021	0.007
Uterus	0.057 (0.006)	$57,000	<0.001	<0.001	Ref.
Hodgkin lymphoma	0.053 (0.008)	$53,000	<0.001	<0.001	0.574
Testicular	0.043 (0.011)	$43,000	<0.001	<0.001	0.021
Esophagus	0.017 (0.002)	$17,000	<0.001	<0.001	<0.001
Stomach	0.017 (0.002)	$17,000	<0.001	<0.001	<0.001

p-Values determined using Wilcoxon-Mann-Whitney test.
ONS = other nervous system.
[a] Score value is the total amount of annual funding in U.S. dollars reported by the NCI divided by the person-years of life lost per 100 new cases; presented as Mean (SD).
[b] Measured per person-years of life lost per 100 new cases.

that the cause of these increases are from increased NCI funding rather than significant shifts in either mortality or incidence.

One powerful example supporting the critical importance of equitable funding is the clinical success that is now being observed in the treatment of melanoma. Melanoma had the third-highest average Funding to Lethality score (0.519) over the eight-year period. There was a statistically significant upward trend in Funding to Lethality score for melanoma, starting at 0.429 in 2008, up to 0.652 in 2014 ($p = 0.0025$). While some of that may be driven by a slight increase in the MIR due to a decrease in incidence, melanoma received 30% more NCI funding in 2014 ($126.2 million) than it did in 2008 ($97.7 million). This increased support has resulted in the development and execution of multiple Phase III clinical trials demonstrating that combination treatment with immunotherapies and molecularly-targeted agents can result in significant

Table 2
Average rates of change for Funding to Lethality scores 2007–2014.

Rank	Cancer site	Average change in score[a]	Dollar value average rate of change per year[b]	p-Value[c]
1	Melanoma	0.0274	$27,400	**0.003**
2	Breast	0.0136	$13,600	0.444
3	Leukemia	0.0098	$9800	**0.015**
4	Lung/bronchus	0.0052	$5200	0.115
5	Pancreas	0.0044	$4400	**<0.001**
6	Non-Hodgkin lymphoma	0.0023	$2300	0.421
7	Brain/ONS	0.0017	$1700	**0.006**
8	Hodgkin lymphoma	0.0004	$400	0.772
9	Esophagus	0.0004	$400	0.520
10	Bladder	0.0003	$300	0.320
11	Ovary	−0.0002	($200)	0.876
12	Stomach	−0.0003	($300)	0.512
13	Uterus	−0.0004	($400)	0.735
14	Kidney/renal pelvis	−0.0005	($500)	0.789
15	Cervix	−0.0029	($2900)	**0.024**
16	Testicular	−0.0030	($3000)	0.106
17	Colon/rectum	−0.0129	($12,900)	**0.004**
18	Prostate	−0.1338	($133,800)	**0.002**

p-Values determined using Wilcoxon-Mann-Whitney test.
ONS = other nervous system.
[a] Funding to Lethality score calculated by total amount of annual funding in U.S. dollars reported by the NCI divided by the person-years of life lost per 100 new cases.
[b] Parentheses indicate a decrease.
[c] Bold indicates significance at the $p < 0.05$ level.

improvements to overall survival [18–20]. In one of these trials, five-year overall survival more than doubled, from 8.8% to 18.2% [21]. While there is important work to be done to overcome resistance mechanisms and treatment side effects, the investments in preclinical and clinical studies for melanoma are bearing fruit and demonstrating the positive impact that prioritizing funds for a cancer site can have for patients. We applaud the work of the NCI and investigators to bring melanoma research to its present position.

Strengths of this study include that the data is taken from reliable sources, with little reason to suspect selection or information bias. The study represents the dollar amounts awarded from the largest and most important funding source for cancer research. Additionally, the data lends itself to reliably studying and understanding trends in cancer funding, incidence, and mortality over time.

There are several potential weaknesses to consider. First is that the funding data includes awards that are both directly and indirectly related to each cancer and may not represent funds given specifically for that cancer. For example, cervical cancer funding includes all of the funding awarded for HPV-related research and pre-invasive diseases of the cervix as well. Although this may be a source of bias in the data, it represents a bias that may not necessarily affect one cancer site more than another. Secondly, the Funding to Lethality score is not a widely-used metric. However, the authors are transparent regarding how the calculations are derived and offer the metric for consideration of how to best understand the equitability of research funding.

It is important to note that NCI funding for pre-clinical and clinical research is a shifting landscape. Budgets and the allocation of funds are part of complex processes that involve many considerations year over year. Contemporary trends are the most meaningful and the metrics that are the most impactful are challenging to elucidate. This project can be used as a critical baseline in the years to come for both policy and advocacy, as well as to monitor the direction of funding trends after the important changes to the NCI's National Clinical Trial Network and the Cancer Moonshot. Future research will continue to monitor these trends over time, funding allocations to specific research areas such as biomarkers and genomics, and work toward correlating changes in funding levels to survival.

In summary, gynecologic cancers have been relatively underfunded and will continue to lag in identifying and subsequently exploiting targeted therapies—an explicit goal of the new NCI cooperative group system. This is demonstrated in the small number of NCCN category 1 recommendations for gynecologic cancers compared to other cancer
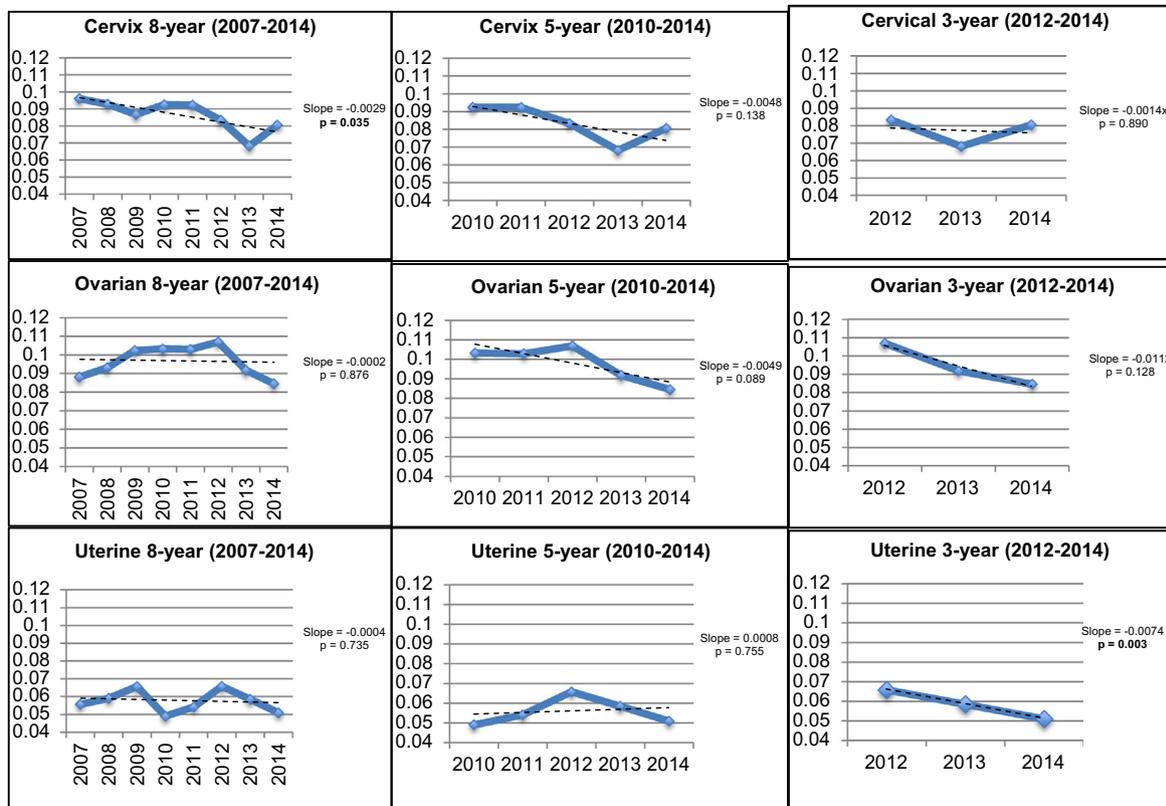
Fig. 3. Funding to Lethality score trends for gynecologic cancers.

sites under investigation. If the current funding trends continue, gynecologic cancers will fall behind in all facets of care including bench science, translational correlates, prevention, options for molecular targeted therapies, and beyond. Organizations for all cancer disease sites have developed talented clinical and laboratory researchers and will continue to do so, but without appropriate funding, certain fields will not be able to push beyond the current prevention strategies and survival rates. All cancers need access to appropriately allocated funding levels in order to find their 21st century cures.

Conflict of interest statement
The authors declare that there are no conflicts of interest.

Author contribution

Ryan J Spencer: Study conception and design, analysis and interpretation of results, writing and editing manuscript.

Laurel W Rice: Study design, analysis of results, and editing manuscript.

Clara Ye: Study design, data acquisition, and editing manuscript.

Kaitlin M Woo: Statistical analysis and editing manuscript.

Shitanshu Uppal: Study conception and design, analysis and interpretation of results, writing and editing manuscript.

Author disclosures

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IRB approval and informed consent

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Presentations

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