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Ranking composite Cancer Burden Indices for geographic regions: point and interval estimates

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Abstract

Purpose To develop a composite Cancer Burden Index and produce 95% confidence intervals (CIs) as measures of uncertainties for the index.

Methods The Kentucky Cancer Registry has developed a cancer burden Rank Sum Index (RSI) to guide statewide comprehensive cancer control activities. However, lack of interval estimates for RSI limits its applications. RSI also weights individual measures with little inherent variability equally as ones with large variability. To address these issues, a Modified Sum Index (MSI) was developed to take into account of magnitudes of observed values. A simulation approach was used to generate individual and simultaneous 95% CIs for the rank MSI. An uncertainty measure was also calculated.

Results At the Area Development Districts (ADDs) level, the ranks of the RSI and the MSI were almost identical, while larger variation was found at the county level. The widths of the CIs at the ADD level were considerably shorter than those at the county level.

Conclusion The measures developed for estimating composite cancer burden indices and the simulated CIs provide valuable information to guide cancer prevention and control effort. Caution should be taken when interpreting ranks from small population geographic units where the CIs for the ranks overlap considerably.

Keywords Cancer Burden Index \cdot Rank Sum Index \cdot Uncertainty measures \cdot Small geographic area \cdot Simultaneous confidence interval \cdot Cancer prevention and control

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Introduction

Among all U.S. states, Kentucky has the highest cancer incidence and mortality rates for 2008–2012 [1]. Kentucky also has high poverty rates and low education ascertainment.

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These disparities are especially acute among the state's Appalachian population [2]. To help target limited cancer prevention and control resources toward the areas of the state with the highest cancer burden and to measure the impact of intervention programs, researchers at the Kentucky Cancer Registry have developed a Rank Sum Index (RSI). With 120 counties varying in population size from 2,000 to 750,000, it is not practical to conduct cancer control planning at the county level in Kentucky; for many counties, measures of the cancer burden would be unstable. To implement cancer prevention and control interventions, Cancer Councils have been developed in each of the 15 Kentucky Area Development Districts (ADDs)—clusters of counties that represent regional patterns of commerce and education (Fig. 1).

The term "cancer burden" has different meanings in various settings. It has been used to mean cancer incidence, mortality, or loss of life [3-7]. The RSI has been developed for the major types of cancer for which there are evidence-based interventions (lung, breast, and colorectal). The logic model behind the RSI is that demographic characteristics (poverty or educational attainment) influence risk behavior (smoking or not being screened). In turn, these risk behaviors affect the cancer incidence and ultimately mortality. Instead of using a single outcome measure as the cancer burden, RSI combines factors from population characteristics, risk behavior, and cancer outcome as incidence and mortality to form a composite Cancer Burden Index. This composite index makes it possible for cancer prevention and control planners to develop strategies, allocate resources, and implement interventions for geographic regions in greatest need while accounting for barriers of poverty or literacy and risk behaviors. In RSI, observed values for each selected factor are ranked separately for each ADD, then ranks for each factor in each ADD are summed to create the index. The RSI has been used by Kentucky's statewide comprehensive cancer control coalition to help develop and modify the state cancer control plan and by each ADD Cancer Council to guide the implementation of evidence-based interventions. The RSI has also been used by other U.S. cancer control communities.

RSI calculation can be demonstrated with the following lung cancer example. Four measures were used to define the lung cancer burden in Kentucky: (1) percentages of adult population with less than a high school education based on the 2006–2010 Census data; (2) percentages of current smokers among adult population based on the 2001-2005 Behavioral Risk Factor Surveillance System (BRFSS) data; (3) invasive lung cancer incidence rates; and (4) lung cancer mortality rates for the years 2006-2010 in Kentucky. Instead of using the 2006–2010 smoking prevalence rates, the percentages of current smokers for 2001-2005 were used to acknowledge the time lag from smoking to lung cancer incidence. The four measures captured the main factors in the logic model and all of the factors were weighted equally in the algorithm for the original RSI. All measures were considered equally to emphasize the importance of the aspect of each presented measure. But the weight could be adjusted based on locale focuses of cancer prevention work.

Table 1 shows how the RSI for the ADDs in Kentucky was developed. The four measures (rates of educational attainment, smoking, lung cancer incidence, and lung cancer mortality) for the fifteen ADDs were sorted in descending order to properly reflect their association with lung cancer burden. These measures are individually ranked based on their sorted order, and the RSI was the final rank based on the sum of individual ranks in an ascending order.

Although RSI is easy to calculate and interpret, there are limitations associated with the measure. First, although often treated as a fixed measure, the RSI has inherent viability. This variability is a function of population size, magnitude of the rates, and the sample size of the survey in each region if a measure is derived from a survey. Interpreting the RSI as a fixed measure limits its applicability by assuming all factors have the same variability and



Fig. 1 Kentucky counties and area development districts

Table 1 Rank Sum Index (RSI) for lung cancer burden in Kentucky, by ADD

ADD	Education ascertainment ^a	Rank for education	Current smoking ^b	Rank for smoking	Lung cancer incidence ^d	Rank for incidence	Lung cancer mortality ^c	Rank for mortality	Sum of ranks	RSI
Kentucky River	34.4	1	35.3	1	128.8	2	99.4	1	5	1
Big Sandy	30.9	3	35.1	2	135.7	1	97.1	2	8	2
Cumberland Valley	32.2	2	34.8	3	117.2	3	86.9	3	11	3
Buffalo Trace	26.7	5	33.5	4	102.8	5	79.1	4	18	4
Lake Cumberland	29.1	4	31.0	9	101.4	7	78.3	5	25	5
Barren River	21.8	7	31.9	7	102.2	6	74.5	8	28	6
Gateway	26.5	6	32.4	6	97.1	13	77.3	6	31	7
Green River	17.1	11	30.5	11	110.7	4	75.8	7	33	8
Pennyrile	20.1	9	31.6	8	99.8	8	73.4	9	34	9
Fivco	21.7	8	32.7	5	99.2	10	67.0	14	37	10
Lincoln Trail	17.4	10	30.8	10	99.3	9	67.2	13	42	11
Purchase	17.1	12	28.9	12	98.8	11	71.0	10	45	12
Northern Kentucky	13.6	15	28.5	13	97.9	12	69.6	11	51	13
Bluegrass	15.4	13	27.5	15	90.8	15	68.7	12	55	14
Kipda	13.6	14	27.9	14	91.6	14	64.0	15	57	15

^aPercentages of population aged 25+ without high school diploma or higher education, 2006–2010

^bPercentages of current smokers among adult population, 2001-2005

^cLung cancer mortality rates (per 100,000), 2006–2010

^dInvasive lung cancer incidence rates (per 100,000), 2006–2010

contribute equally to the overall rank [8]. Second, the RSI does not weight extreme values more heavily than other high or low values which barely differ from one another. For example, three counties A, B, and C had cancer incidence rates 80, 60, and 59 per 100,000 and smoking prevalence rates 28.5, 29.5, and 29%. Intuitively, county A clearly should be the highest because although all three counties have similar smoking prevalence, county A has the highest incidence. However, the RSI will consider that county B has the highest cancer burden as the algorithm for the RSI ranks each measure separately before they are combined and does not take into account the magnitudes of observed values before generating the final rank. Third, in order to understand meaningful differences between the indices for each ADD, a measure of uncertainty, such as confidence intervals (CIs), is needed. For example, the Kentucky ADD Cancer Councils routinely considered the top five ranked ADDs as the focus of cancer control effort. With the availability of CIs, the Cancer Councils will be able to tell the true difference of cancer burden among ADDs and objectively select the ADDs with the highest cancer burden.

In this paper, we modify the original RSI algorithm to take into account the magnitudes of observed values, and use a simulation approach to generate 95% CIs for the modified RSI. We also provide an uncertainty measure to further explain the variations of the index.

Methods

Modified Sum Index (MSI)

The MSI approach altered the RSI approach slightly to take into account the magnitudes of observed values. The MSI approach performed log or logit transformations for rates or proportions to normalize the observed data. The transformed data then were standardized based on means and standard deviations from the transformed observed values in each measure into observed Z scores. Instead of ranking each measure individually as RSI, the MSI is the rank of observed composite Z scores (i.e., sum of the Z scores of the four measures) in a descending order.

CIs for index

Based on the characteristics of each measure, assumptions of distributions for these measures were made and a parametric bootstrap approach was used to obtain CIs for the index via simulation.

For measures, such as proportions of individual with a high school education and percentages of current smokers, we assumed each observation followed binomial distributions:

$$y_i = \text{Binomial}(p_i, n_i),$$

where y_i is the number of subjects with below high school education or being a smoker in regional unit *i*; p_i is the proportion of subjects with a high school education or being a smoker in regional unit *i*; n_i is the corresponding background population in regional unit *i* for education ascertainment or corresponding sample size from the BRFSS in regional unit *i* for smoking; i = 1, 2, ..., 15 for ADD; or i = 1, 2, ... 120for county.

For measures, such as age-adjusted lung cancer incidence and mortality rates, we modeled age-specific rates for 19 age groups separately (age 0, 1–4, 5–9, 10–14, 15–19, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85+), assuming age-specific counts following a Poisson distribution.

 $y_{ii} = \text{Poisson}(p_{ii} \times n_{ii}),$

where y_{ij} is the number of events in regional unit *i*; age group *j*, p_{ij} is the event rate for regional unit *i*; age group *j*, n_{ij} is the background population in regional unit *i*; age group *j*, i = 1, 2, ..., 15 for ADD, or i = 1, 2, ..., 120 for county; j = 1, 2, ..., 19 for age group.

Simulated age-adjusted lung cancer incidence and mortality rates were obtained from the simulated age-specific rates weighted to the 2,000 U.S. population.

For each simulation, Z scores were calculated for each of the four measures. Sum of Z scores of the four measures were then calculated as simulated index values. The simulated index values were ranked to create the composite cancer index. Technically, simulations from the joint distribution of the measures are required. However, in the absence of additional modeling assumptions connecting the parameters across the measures, the measures can be sampled separately and then aligned afterwards to create a joint sample. Two types of CIs were created. One, individual CIs were used to examine one specific geographic region, either county or ADD, compared to other geographic regions in the analysis. Two, simultaneous CIs are used to examine ranks and CIs for all the regional units at the same time.

We let rank^{*k*} be the rank of *i*th geographic unit in the *k*th simulation. For each *i*, the $100(1 - \alpha)$ % individual CIs of the ranks of geographic unit *i* can be obtained by identifying the $100(\alpha/2)$ th percentile and $100(1 - \alpha/2)$ th percentile of rank^{*k*}. Simultaneous CIs were constructed through a Monte Carlo method by searching through the simulated joint rank distribution of rank^{*k*} so that simultaneous CIs [*r*_i, *s*_i]satisfy

 $P(r_1 \le \operatorname{rank}_1 \le s_1, \dots, r_I \le \operatorname{rank}_I \le s_I) = 1 - \alpha,$

where i = 1, 2, ..., I. The detailed algorithms can be found in the paper by Zhang et al. [9] In application, we are generally interested in examining ranking and CIs of all specific geographic units simultaneously. Hence, simultaneous CIs are likely to be used.

Uncertainty measure

To provide a measure of what proportion of geographic units the CIs cover, we computed the average relative width of CIs (upper limit of CIs – lower limit of CIs) divided by total numbers of regional units. For example, if there are 40 counties in a state, and the 95% CIs for a county ranges from a rank of 8–13, then it covers (13-8)/40 = 12.5% of the counties in the state. The proposed uncertainty measure averages this across all of geographic units. If the uncertainty measure is large (i.e., well over 60% for 95% CIs), then the ranks do not really discriminate among the geographic units. Larger regional units lead to smaller uncertainty measures, such as ADD vs. county.

Results

The performance levels of the RSI and the MRI were examined for two types of regional units: ADD and county. There are 15 ADDs and 120 counties in Kentucky with each ADD consisting of 5–17 counties. 10,000 simulations were conducted for this study.

RSI and MSI

The RSI and MSI by ADD are almost exactly the same (Table 2); the only difference was the ranks of Gateway and Barren River that switched places between the two indices. The individual and simultaneous 95% CIs by ADD are almost exactly the same and have very narrow intervals, especially at the top and the bottom of the ranking (Fig. 2). For example, Kentucky River is ranked first in both indices, and the individual and simultaneous 95% CIs for Kentucky River both are (1, 2). Buffalo Trace, the ADD with the smallest population, is ranked fourth with 95% individual and simultaneous CIs (4, 7) and (4, 8), respectively. Gateway, the ADD with the second smallest population, is ranked sixth with one of the widest 95% individual and simultaneous CIs (4, 9) and (4, 10), respectively; while Barren River, the ADD with the fourth large population, is ranked seventh with also one of the widest individual and simultaneous CIs (5, 10). and (4,10), respectively. Overall, the 95% CIs are very narrow for most ADDs.

The results of two indices by county vary considerably with very few counties having the same RSI and MSI (Table 3). However, this is expected because of the large number of counties involved. In general, the ranking from the two methods are highly correlated with a 98.9% spearman correlation coefficient. Due to the limited space, only 45 out of 120 counties with MSI ranks 1–15, 56–70, and 106–120 are shown in Table 3. A full list of counties with MSI ranks and 95% CIs can be found in Supplementary Table 2Rank Sum Index (RSI),Modified Sum Index (MSI),and 95% confidence intervals(CIs), by ADD for Kentucky2006–2010

ADD	Annual population	RSI	MSI	Individual 95% CIs		Simultane- ous 95% CIs	
Kentucky River	115,395	1	1	1	2	1	2
Big Sandy	155,023	2	2	1	2	1	2
Cumberland Valley	237,269	3	3	3	3	2	3
Buffalo Trace	56,415	4	4	4	7	4	8
Lake Cumberland	205,567	5	5	4	8	4	8
Gateway	81,049	7	6	4	9	4	10
Barren River	279,472	6	7	5	10	4	10
Green River	212,192	8	8	6	10	5	11
Pennyrile	217,650	9	9	6	11	5	11
Fivco	137,459	10	10	6	11	6	12
Lincoln Trail	263,053	11	11	10	13	9	13
Purchase	195,482	12	12	10	13	10	13
Northern Kentucky	431,349	13	13	12	14	11	15
Bluegrass	756,050	14	14	13	15	13	15
Kipda	942,594	15	15	14	15	13	15





Materials (Suppl. Table 1). Several counties with smaller background population differ substantially in ranking. For example, Nicholas County was ranked 35th for the RSI but was 15th for the MSI; Green County was ranked 96th for the RSI but was 111th for MSI. Similar to the CIs by ADD, the widths of simulated CIs by county were much tighter in the top and the bottom of the ranking compared to the ones in the middle. The widest 95% CIs came from Trimble County, a county ranked 60th with a smaller population, with a width 90 for the individual CIs and 115 for the simultaneous CIs, while Fayette County, a county ranked 119th with the second largest population among counties in Kentucky, with a width five for the individual CIs and eight for the simultaneous CIs.

Figure 3 shows individual and simultaneous intervals for the selected counties. The widths of individual CIs are much smaller than the widths of simultaneous CIs for most counties, and individual CIs for some of the topor bottom-ranked counties did not overlap with counties ranked in the middle. However, simultaneous CIs for all top- and bottom-ranked counties overlapped with counties in the middle of ranks. Table 3Rank Sum Index (RSI),Modified Sum Index (MSI), and95% confidence intervals (CIs),by county, for selected counties

County	Average annual	RSI	MSI	Individ	ual	Simultaneous 95% CIs	
	population	1		95% CI	s		
Owsley	4,744		1	1	22	1	56
Perry	28,737	9	2	1	10	1	18
Jackson	13,564	2	3	1	18	1	36
Floyd	39,945	5	4	1	11	1	19
Magoffin	13,295	4	5	1	23	1	42
Martin	13,138	12	6	1	24	1	45
Breathitt	14,204	6	7	1	22	1	37
Leslie	11,470	7	8	1	27	1	45
Letcher	24,467	11	9	4	25	1	35
Menifee	6,428	8	10	2	40	1	70
Harlan	29.689	10	11	5	28	2	41
Clay	22,200	16	12	3	31	1	47
Powell	12,789	18	13	2	49	1	83
Ohio	23.843	13	14	6	32	2	45
Nicholas	7,135	35	15	2	66	1	102
Breckinridge	19,896	55	56	33	81	18	97
Laurel	58,166	59	57	38	73	30	86
Meade	28,911	56	58	37	85	24	102
Hopkins	46,885	57	59	40	75	30	86
Trimble	8,871	60	60	19	109	5	120
Carter	27,827	63	61	37	79	26	91
Wayne	20,723	62	62	31	82	20	99
Grant	24,608	65	63	34	90	20	108
Fulton	6,859	61	64	26	103	10	116
Pulaski	62,073	66	65	45	75	33	86
McLean	9,639	53	66	34	93	19	111
Montgomery	25,911	67	67	41	85	30	102
Trigg	14,119	64	68	39	92	23	109
Carlisle	5,126	69	69	28	111	8	120
Todd	12,307	71	70	35	101	16	115
Campbell	89,017	100	106	90	113	81	116
Crittenden	9,317	109	107	68	117	40	120
Christian	72,666	104	108	88	113	73	117
Hickman	4,948	101	109	61	119	36	120
Larue	14,086	111	110	76	117	55	120
Green	11,381	96	111	75	118	51	120
Jefferson	729,453	114	112	103	113	97	115
Scott	44,868	112	113	88	118	70	120
Oldham	58,776	116	114	101	119	86	120
Hancock	8,553	117	115	87	120	49	120
Shelby	40,914	115	116	105	120	85	120
Boone	114,728	118	117	114	120	110	120
Washington	11,593	113	118	101	120	77	120
Fayette	288,050	120	119	115	120	112	120
Woodford	24.520	119	120	111	120	95	120

The top bracket includes 15 counties with the highest MSI rankings 1–15; the middle bracket includes 15 counties with MSI rankings 56–70; the bottom bracket includes 15 counties with the lowest MSI rankings 106–120

Fig. 3 Individual and simultaneous 95% confidence intervals for rank of composite cancer burden, by county, Kentucky 2006–2010



Uncertainty measures

Compared to the ADD level, the relative width of the CIs at the county level is much larger (Table 4). For 95% CIs, the relative widths at the ADD level are 19.5 and 24.8% for individual and simultaneous CIs, respectively. This means, on average, we expect the CIs only cover 2.9 or 3.7 of the 15 ADDs, respectively. At the county level, the values are 35.9 and 56.8% for individual and simultaneous CIs. This means, on average, we expect the CIs will cover 43.1 or 68.2 of the 120 counties, respectively.

Discussions

The cancer burden is often presented as a single measure, such as cancer incidence, cancer prevalence, cancer mortality, loss of life, or a combination of incidence and mortality [3–7, 10–13]. An indicator of the cancer burden by combing incidence and mortality was developed to compare the magnitudes of the cancer burden by regions of the world [13]. Health rankings have also become popular as an effective tool to help local communities improve population health in small geographic areas [14]. However, no Cancer Burden Index has been developed to capture socioeconomics, health behavior, and screening as well as, cancer incidence and mortality to provide a comprehensive view of the cancer burden at community level for the purpose of cancer prevention and control. Thus, the Kentucky Cancer Registry developed the RSI to provide a better measure of the cancer burden for smaller geographic regions in the state.

Easy to calculate and interpret, RSI has been widely used by Kentucky cancer control organizations and the North American Association of Central Cancer Registries. The Kentucky Cancer Consortium has used RSI annually to identify the top five ADDs with the highest cancer burden for lung, colorectal, and breast. The RSI has been used to identify cancer control priorities and coalition efforts at both the state and community levels. It has been proven to be effective in focusing attention on sub-geographic areas of the state where evidence-based interventions are highly needed for the burden of specific cancers. The RSI is also effective for measuring changes once intervention programs have been implemented. However, the RSI method does not take into account variability of the ranks. Determining whether differences between ranks are significant is equally important for assessing the utility of these measures in distinguishing where public health resources should be allocated. Without knowing the variation of the RSI, the utilization of RSI is limited and meaningful differences between ranks are unknown.

Table 4Uncertainty measuresfor confidence intervals (CIs)of simulated rank of compositecancer burden for Kentucky2006–2010

Region	Relative wid	dth for individua	al CIs	Relative width for simultaneous CIs			
	80% CIs	90% CIs	95% CIs	80% CIs	90% CIs	95% CIs	
County level	23.6%	30.0%	35.9%	51.5%	53.9%	56.8%	
ADD level	7.6%	9.3%	19.5%	8.9%	10.7%	24.8%	

The MSI improves upon the RSI by taking into account magnitudes of observed values. As shown in Table 2, the Gateway's rank changed from seventh in RSI to sixth in MSI, and vice versa for Barren River. Compared to Barren River, Gateway had higher ranking for each individual measure except the lung cancer incidence for which Gateway was ranked 13th and Barren River sixth (Table 1). Although the difference of individual ranks for lung cancer incidence was large between the two counties, the absolute difference of the incidence rates was small compared to the overall variation of lung cancer incidence. Hence, MSI provides a more accurate ranking than RSI.

More importantly, adding the individual and simultaneous 95% CIs provides critical information to objectively assess the cancer burden ranking. As shown in Table 2, the top three ranked ADDs (Kentucky River, Big Sandy, and Cumberland Valley) clearly had significantly higher lung cancer burden than other ranked ADDs based on both individual and simultaneous CIs, and the cancer burdens were not statistically different among ADDs ranked 4–10. Instead of subjectively focusing on the top five ranked ADDs, Kentucky's statewide comprehensive cancer control coalition will be able to develop cancer planning appropriately targeting the top three ADDs and allocate their resource and effort accordingly.

Many factors impact the variation of the indices and their CIs, such as variation of individual measures, population size, number of geographic units, number of measures, and similarity of geographic units. The shorter range of the CIs at the ADD level and the wider range of the CIs at the county level demonstrate that the background population size has a significant impact on the indices stability. The uncertainty measures further qualify the variations. This presents challenges when producing meaningful CIs for geographic units such as counties since some counties in Kentucky can have a population larger than 750,000 persons while some can be less than 3,000 persons. However, because cancer is a relatively rare event and data from small populations would be unstable, most state cancer control programs are organized around larger populations found among clusters on counties, such as the Kentucky's ADDs or Health Districts in other states. The simulated CIs could be very useful for cancer control program planners and provide the tools to distinguish significant differences between the cancer burden ranks within each state.

Because simultaneous CIs at the county level are quite wide, one needs to be very cautious when utilizing either the RSI or the MSI indices for small geographic units. To reduce widths of CIs, one can either use larger geographic unit such as ADDs or Health Districts, or combine data across a number of years. However, in some cases, it would be better to combine smaller geographic units to units with larger population across multiple years for stable estimates. It is also worth mentioning that cancer prevention and control activities usually target either the top- or the bottom-ranked geographic units which tend to have much smaller CIs than those ranked in the middle. Although the uncertainty measure is high for small geographic units such as county, MRI and CIs still provide valuable information, particularly if the top or the bottom geographic units separate from the rest.

There are situations when using larger geographic units or combining several years data together is not ideal, for example, when counties have to be the targeted unit of analysis because of the available resource and infrastructures; or only 1 or 2 years of data are available. To improve the precision of MSI and the simulated CIs for a small geographic unit, a modeling approach could be examined. Another example would be to utilize Bayesian hierarchical modeling controlling for demographic covariates or fitting multiple related outcomes in one single hierarchical model [15–17]. Compared to the direct approach as RSI or MSI, the modeling approaches may provide better results depending on the validity of the assumptions. However, the resources needed to perform such complex analysis may not be readily available at the state and regional level.

The National Cancer Institute (NCI) Surveillance Research Program has developed CI*Rank, a web-based tool to rank incidence and mortality rates by state, county, and special regions and also to provide ranking data and composite Cancer Burden Index for policy evaluation and program planning at the state and local levels [18]. The results based on the MSI approach by ADD and simulated CIs are also available in the CI*Rank website (https:// surveillance.cancer.gov/cirank/index.html). The website allows users to input data using their own predefined geographic regions. Availability of this functionality will make it convenient for state and local organizations to produce their own composite Cancer Burden Index and utilize it for their cancer prevention and control efforts.

In summary, we strongly believe all cancer control programs should use meaningful data to focus their limited cancer control resources on the areas with the greatest need and to measure the impact of their intervention programs. The MSI method and the simulated CIs provide the tools to make these critical measurements. The available CI*Rank web program makes it easier to create these measures tailored by the needs of cancer prevention and control planner in individual states or communities.

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Compliance with ethical standards

Conflict of interest The authors declare that they do not have any potential financial conflict of interest in the subject matter or materials discussed.

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