

# NIH Public Access

Author Manuscript

*Cancer Epidemiol Biomarkers Prev.* Author manuscript; available in PMC 2010 September 22

### Published in final edited form as:

Cancer Epidemiol Biomarkers Prev. 2009 June ; 18(6): 1669–1671. doi:10.1158/1055-9965.EPI-09-0318.

# **CANCER SURVEILLANCE RESEARCH (CSR)**

#### William F. Anderson, MD, MPH

Biostatistics Branch (BB), DHHS/NIH/NCI/Division of Cancer Epidemiology and Genetics (DCEG), EPS, Room 8036, 6120 Executive Blvd, Bethesda, MD 20892-7244, Phone: 301 594-9125, Fax: 301 402-0081

William F. Anderson: wanderso@mail.nih.gov

#### Keywords

descriptive epidemiology; age-period-cohort (APC) models; non-identifiability issues

The journal Cancer Epidemiology, Biomarkers, and Prevention (*CEBP*) has launched a new manuscript section entitled Cancer Surveillance Research (CSR). The CSR section will consist of original reports using cancer case and population data to examine, test, and develop hypotheses from patterns for cancer prevalence, incidence, and mortality. The scope of CSR includes descriptive epidemiology, public health statistics for time trends in cancer burden, genetic, behavioral, and environmental risk factors, cancer disparities and geographic variations, screening and diagnostic practice patterns, and, methodological developments for assessing cancer data.

CSR studies are the "eyes and ears" for the monitoring and assessment of cancer burden through the examination of vital health statistics. Evaluation of demographic, temporal, and geographic variations in cancer rates can suggest clues to genetic or environmental exposures, cultural influences, health behaviors, geographic variations, and racial/ethnic variations for subgroups at unexpected risk for certain cancers. Cancer rates may be used to verify the consistency of existing cancer-related hypotheses and/or to generate new ideas for future analytic research. CSR can estimate the external validity of a randomized clinical trial. A well-designed and controlled clinical trial has strong internal validity. However, the generalizability (or external validity) of the randomized study cannot be assumed since subject participation depends upon selection and inclusion criteria, which might not reflect the population at large. Generalizability concerns are further heightened by the fact that clinical trial participants are generally healthier, wealthier, younger, Caucasian and urban dwellers (1,2). The merging of population-based and clinical trial evidence can help to determine if an efficacious clinical trial is effective in the general population (3,4). Additionally, when a disease is rare, cancer surveillance data might be the most reliable source of information. Finally, as the population ages and the cost of cancerrelated services rise (5), CSR can aid health care planners and policy makers manage and direct limited resources.

CSR has been enhanced through advancements in computer hardware and software, bioinformatics, and statistical methodologies, local, national and international databases (6). However, cancer surveillance data are underutilized, largely due to two mistaken impressions (7). First, there is a lack of recognition of the available resources for CSR. Second, descriptive

*Disclaimer*: The author does not have a financial conflict of interest that would have affected this research. This research was supported in part by the Intramural Research Program of the National Institutes of Health, National Cancer Institute. The authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

epidemiology--the core methodology for CSR--is often viewed as simplistic, uncertain, and/ or unreliable.

Contrary to some mistaken views, population-based resources, databases, and statistical tools are readily available from Public-use websites such as the National Cancer Institute's Surveillance, Epidemiology, and End Results program (SEER) (8), Cancer Mortality Maps & Graphs (9), Centers for Disease Control and Prevention (CDC) (10), North American Association of Central Cancer Registries (NAACCR) (11), and the International Agency for Research on Cancer (IARC) (12). SEER provides cancer incidence and survival data from 17 Tumor Registries, covering approximately 26% of the United States. The current SEER database has nearly 5 million cancer cases with more than 1 billion person-years from 1973 through 2005. The Cancer Mortality Maps & Graphs website has interactive charts, text, tables, and figures for more than 40 cancers from 150 through 1994. The CDC's National Program of Cancer Registries (NPCR) supports the maintenance of high quality tumor registries for states in the United States. The CDC's National Center for Health Statistics (NCHS) distributes cancer mortality information for the calendar period 1969-2005. The NAACCR promotes CSR as an umbrella organization for central cancer registries in the United States and Canada, government agencies, and professional organizations. IARC's CANCERMondial website provides information on the occurrence of cancer world-wide through five programs: 1) Cancer Incidence in Five Continents volumes I to IX, 2) ACCIS--incidence and survival data of children and adolescents in Europe, 3) mortality data from the World Health Organization (WHO), 4) GLOBOCAN 2002 for the incidence, prevalence, and mortality from 27 cancers for all countries in the world in 2002 and 5) NORDCAN project from 41 major cancers in Nordic countries.

The simplistic view of descriptive epidemiology partly reflects the reality that descriptive studies are secondary and/or retrospective analyses, dependent upon the observational method. Observational results are cross-sectional, capturing a "snap-shot" in time and are subject to uncontrollable chance, bias, or confounding. All descriptive studies begin with a rate matrix (sometimes referred to as a Lexis diagram (13)), as illustrated in table 1 for female breast cancer from the SEER database (1974–2005). Indeed, it would be imprudent for CSR to ignore the complex interactions associated with the Lexis figure.

For example, the 2-dimensional geometry of the Lexis diagram demonstrates that three fundamental descriptive variables (age, period, and cohort) are in a single plane and are linearly dependent (table 1), i.e., age at diagnosis in rows, year of diagnosis (calendar-period) in columns, and year of birth (birth-cohort) in the diagonals. Given the relationship C = P - A (birth-cohort = calendar-period - age at diagnosis), table 1 has twenty-three birth-cohorts (1893, 1897, ... 1981, referred to by mid-year of birth) that are derived from eighteen 4-year age groups (21–24, 25–28, ... 81–84 years) and eight 4-year time periods (1974–1977, 1978–1981, ... 2002–2005). Birth-cohort reflects time trends that impact all age groups for a given generation. Calendar-period effects reflect secular trends that affect all age groups at a certain point in time, i.e., changing screening or diagnostic practice patterns. Age is a surrogate for age-related biological factors. Because age, period, and cohort are collinear, it is not possible to completely separate calendar-period effects from age effects or the birth-cohort effects from calendar-period effects, giving rise to the so-called "non-identifiability" issue.

Given the uncertainty associated with these non-identifiability issues, CSR requires a close interface between data resources and statistical techniques (14). Age standardization attempts to minimize the impact of different age distributions when comparing rates over time and across populations. Non-linear regression models have been applied to a sophisticated analyses of time trends (15). Careful attention to plotting techniques facilitates temporal comparisons, fairly conveying the data without over emphasizing the results (16). Multivariate analyses

allow for the simultaneous study of two or more dependent variables. Poisson regression can assess cancer-specific hazard rates that are adjusted for any number of covariates such as age at diagnosis, year of diagnosis, stage, grade, etc (17). Age-period-cohort (APC) models estimate a number of identifiable parameters adjusted for age, period, and cohort effects (18).

Two very useful APC parameters for descriptive studies are the "*drifts*" (linear trends) (19, 20) and the "*fitted*" age-specific curves (21). Net drift equals the sum of the linear trends in period and cohort effects for all age groups included during the study period (figure 1A). The net drift quantifies the average annual percentage change in the logarithm of the rates adjusted for period and cohort deviations. It is a summary measure of the overall trend during the study period, and is closely related to the estimated annual percentage change (EAPC) in the age standardized rates (ASR). Figure 1A shows an EAPC of 2.08% per year of calendar time and a net drift of 1.5% per year. In other words, female breast cancer incidence rates rose at a rate of approximately 1.5% to 2% for each yearly increment in the calendar time.

Another type of drift is the longitudinal age trend or LAT (figure 1B). The LAT is the sum of the linear trends in the age and period effects. It provides an estimate of the average annual percentage per year of attained age for the "fitted" age at onset curve (figure 1B). The fitted curve is an extrapolation of the age-specific rates for the mid birth-cohort based upon the age-specific rates for all other cohorts in the study (21). Figure 1B shows a LAT of 9.7% per year (95% CI: 9.4, 10.0). In other words, female breast cancer age-specific rates rose at a rate of nearly 10% for each yearly increment in the age at diagnosis. Note the collinearity (non-identifiability) for the age, period, and cohort effects in table 1 and figure 1. The 1973 birth-cohort in figure 1B corresponds to ages 21–24 to 29–32 years in table 1; the 1961 birth-cohort corresponds to the age-groups 21–24 to 41–44, etc.

In launching the new CSR section, the *journal* hopes to publicize and highlight both the resources and methodology for cancer surveillance; and through CSR, to assess emerging cancer trends and cancer-related hypotheses. CSR manuscripts should be 3000 words or less (not counting abstract, references, or legends), have a total of 6 or fewer tables and/or figures, a structured abstract of 250 words or less (with background, methods, results, and conclusion), and no more than 40 references. Supplemental data can be provided if needed.

## References

- Britton A, McKee M, Black N, McPherson K, Sanderson C, Bain C. Threats to applicability of randomised trials: exclusions and selective participation. J Health Serv Res Policy 1999;4:112–21. [PubMed: 10387403]
- Hutchins LF, Unger JM, Crowley JJ, Coltman CA Jr, Albain KS. Underrepresentation of patients 65 years of age or older in cancer-treatment trials. N Engl J Med 1999;341:2061–7. [PubMed: 10615079]
- 3. Cochrane, AL. Effectiveness and Efficiency: Random Reflections on Health Services. London: Nuffield Provincial Hospitals Trust; 1972.
- 4. Berry DA, Ravdin PM. Breast cancer trends: a marriage between clinical trial evidence and epidemiology. J Natl Cancer Inst 2007;99:1139–41. [PubMed: 17652274]
- Meropol NJ, Schulman KA. Cost of cancer care: issues and implications. J Clin Oncol 2007;25:180– 6. [PubMed: 17210937]
- 6. Fraumeni JF Jr, Rimer BK. Cancer surviellance series: inauguration. J Natl Cancer Inst 1999;91:1004.
- Glaser SL, Clarke CA, Gomez SL, O'Malley CD, Purdie DM, West DW. Cancer surveillance research: a vital subdiscipline of cancer epidemiology. Cancer Causes Control 2005;16:1009–19. [PubMed: 16184466]
- 8. SEER. Surveillance Epidemiology and End Results. 2009. [cited 2009; Available from: http://seer.cancer.gov/

Anderson

- 9. Cancer Mortality Maps & Graphs. 2009. [cited 2009; Available from: http://www3.cancer.gov/atlasplus/
- 10. Centers for Disease Control and Prevention (CDC). 2009. [cited; Available from: www.cdc.gov
- 11. North American Association of Central Cancer Registries (NAACCR). 2009. [cited; Available from: www.naaccr.org
- 12. International Agency for Research on Cancer (IARC). 2009. [cited; Available from: www.iarc.fr
- 13. Vandeschrick C. The Lexis diagram, a misnomer. Demographic Research 2001;4:97-124.
- 14. Hankey BF, Ries LA, Edwards BK. The surveillance, epidemiology, and end results program: a national resource. Cancer Epidemiol Biomarkers Prev 1999;8:1117–21. [PubMed: 10613347]
- Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med 2000;19:335–51. [PubMed: 10649300]
- Devesa SS, Donaldson J, Fears T. Graphical presentation of trends in rates. Am J Epidemiol 1995;141:300–4. [PubMed: 7840107]
- 17. Breslow NE, Lubin JH, Marek P, Langholz B. Multiplicative models and cohort analysis. Journal of the American Statistical Association 1983;78:1–12.
- Holford, TR. Age-period-cohort analysis. In: Armitage, P.; Colton, T., editors. Encyclopedia of Biostatistics. 1. Chichester, England: John Wiley & Sons; 1998. p. 82-99.
- Clayton D, Schifflers E. Models for temporal variation in cancer rates. I: Age-period and age-cohort models. Stat Med 1987;6:449–67. [PubMed: 3629047]
- 20. Clayton D, Schifflers E. Models for temporal variation in cancer rates. II: Age-period-cohort models. Stat Med 1987;6:469–81. [PubMed: 3629048]
- Anderson WF, Rosenberg PS, Menashe I, Mitani A, Pfeiffer RM. Age-related crossover in breast cancer incidence rates between Black and White Ethnic Groups. J Natl Cancer Inst 2008;100:1804– 14. [PubMed: 19066264]



#### Figure 1.

(A) Female breast cancer cases (*in situ* and invasive) in SEER's 9+13+17 Registries Databases, diagnosed during the years 1974 through 2005. (A) Age-specific incidence rate trends with the estimated annual percentage change in the age standardized rates (ASR) and the annual percentage change in the net drifts per year of calendar time. (B) Age-period-cohort (APC) "fitted" age-specific curves with the estimated annual percentage change per year of attained age in the longitudinal age trend (LAT).

**NIH-PA Author Manuscript** 

<del>.</del>
ble
Tal

2	
8	
ล	
Ę,	
n	
Ö.	
-hi	
4	
È	
19	
$\mathbf{s}$	
ar	
ýe	
0	
ų,	
50	
.9	
Ē	
Ъ	
Ч	
se	
2	
<u>5</u> 0	
ia	
q	
ંડ	
se	
Зa	
at	
at	
Д	
S	
Ξ·	
st	
.20	
Ş	
<u> </u>	
~	
17	
3+17	
13+17	
+13+17	
s 9+13+17	
C's 9+13+17	
ER's 9+13+17	
EER's 9+13+17	
SEER's 9+13+17	
n SEER's 9+13+17	
) in SEER's 9+13+17	
/e) in SEER's 9+13+17	
sive) in SEER's 9+13+17	
asive) in SEER's 9+13+17	
nvasive) in SEER's 9+13+17	
l invasive) in SEER's 9+13+17	
nd invasive) in SEER's 9+13+17	
and invasive) in SEER's 9+13+17	
tu and invasive) in SEER's 9+13+17	
situ and invasive) in SEER's 9+13+17	
<i>n situ</i> and invasive) in SEER's 9+13+17	
( <i>in situ</i> and invasive) in SEER's 9+13+17	
es (in situ and invasive) in SEER's 9+13+17	
ases (in situ and invasive) in SEER's 9+13+17	
cases (in situ and invasive) in SEER's 9+13+17	
er cases (in situ and invasive) in SEER's 9+13+17	
icer cases (in situ and invasive) in SEER's 9+13+17	
ancer cases (in situ and invasive) in SEER's 9+13+17	
cancer cases (in situ and invasive) in SEER's 9+13+17	
ist cancer cases (in situ and invasive) in SEER's 9+13+17	
east cancer cases (in situ and invasive) in SEER's 9+13+17	
breast cancer cases (in situ and invasive) in SEER's 9+13+17	
e breast cancer cases (in situ and invasive) in SEER's 9+13+17	
ale breast cancer cases (in situ and invasive) in SEER's 9+13+17	
male breast cancer cases (in situ and invasive) in SEER's 9+13+17	
Female breast cancer cases (in situ and invasive) in SEER's 9+13+17	

te Rate Birt	2 1981	1	8 1977	8 1977 2 20 1973	8         1977           2         20         1973           9         44         1969	8         1977           2         20         1973           9         44         1969           6         86         1965	8         1977           2         8         1973           2         20         1973           9         44         1969           6         86         1965           55         152         1961	8         1977           2         8         1977           2         20         1973           9         44         1969           6         86         1965           55         152         1961           55         226         1957	8         1977           2         8         1973           2         20         1973           9         44         1969           6         86         1965           55         152         1961           15         226         1957           58         277         1953	8         1977           2         8         1973           2         20         1973           9         44         1969           6         86         1965           55         152         1961           55         226         1957           45         226         1953           8         277         1953           8         273         1949	8         1977           2         8         1977           2         20         1973           9         44         1969           6         86         1965           55         152         1961           55         152         1961           56         226         1957           57         226         1957           58         277         1953           53         323         1949           51         403         1949	8         1977           2         20         1973           2         20         1973           9         44         1969           6         86         1965           5         152         1961           5         152         1961           5         226         1957           6         277         1953           5         323         1949           51         403         1945           51         403         1945	8         1977           2         8         1977           2         20         1973           9         44         1969           6         86         1965           5         152         1961           55         152         1961           55         152         1961           53         226         1953           53         233         1949           51         403         1949           64         451         1941           90         497         1937	8         1977           2         8         1977           2         20         1973           9         44         1969           6         86         1965           5         152         1961           55         152         1961           55         152         1961           55         226         1957           53         2277         1953           53         323         1949           51         451         1945           64         451         1941           69         497         1943           88         513         1943	8         1977           2         8         1977           2         20         1973           9         44         1969           6         86         1965           5         152         1961           5         152         1961           5         226         1961           5         226         1957           8         277         1953           8         277         1953           53         323         1949           64         451         1943           8         513         1945           8         513         1945           64         451         1945           73         323         1949           8         513         1937           8         513         1933           8         513         1933	8         1977           2         8         1977           2         20         1973           9         44         1969           6         86         1965           5         152         1961           55         152         1961           55         152         1961           55         152         1961           55         152         1961           56         152         1961           57         226         1953           53         323         1949           53         323         1949           51         403         1953           54         451         1941           56         457         1953           58         513         1933           55         545         1925           55         545         1925	8         1977           2         20         1973           2         20         1973           6         86         1969           6         86         1965           6         86         1965           6         86         1965           6         86         1965           8         152         1961           8         277         1957           8         277         1953           8         277         1949           9         403         1946           64         451         1947           9         493         1945           8         233         1949           8         513         1943           8         513         1945           9         497         1937           8         513         1933           8         513         1933           8         513         1935           8         513         1935           8         513         1923           8         545         1925           8         545 <th>8         1977           2         8         1973           2         20         1973           6         86         1969           6         86         1965           5         152         1961           55         152         1961           55         152         1961           55         152         1961           55         152         1961           56         152         1961           57         226         1953           53         323         1949           51         403         1949           53         323         1949           54         451         1941           56         533         1949           57         323         1949           58         513         1933           55         545         1925           57         519         1925           519         519         1921           519         519         1921           519         519         1921</th> <th>8         1977           2         20         1973           2         20         1973           9         44         1969           6         86         1965           6         86         1965           6         86         1965           6         86         1965           6         86         1965           15         152         1961           15         226         1957           16         403         1949           11         403         1946           12         403         1946           13         323         1949           14         451         1947           15         447         1953           16         451         1937           16         451         1937           15         536         1929           15         545         1925           17         519         1921           17         519         1917           16         1917         1913</th> <th>8         1977           2         8         1977           2         20         1973           6         86         1969           6         86         1965           6         86         1965           5         152         1961           5         152         1961           5         152         1961           5         152         1961           5         152         1961           5         152         1961           5         226         1953           6         277         1953           6         277         1953           6         447         1949           9         497         1949           9         497         1937           8         513         1933           55         545         1925           67         519         1925           77         519         1925           77         519         1925           77         519         1917           77         519         1917           7</th> <th>8         1977           2         20         1973           2         20         1973           6         86         1969           6         86         1965           6         86         1965           6         86         1965           6         86         1965           6         86         1965           15         152         1961           15         226         1957           16         403         1949           11         403         1946           12         403         1946           13         323         1949           14         403         1947           15         447         1953           16         447         1937           16         447         1933           15         536         1926           15         545         1926           17         519         1921           16         1921         1917           17         519         1913           18         1913         1913           19</th> <th>8         1977           2         8         1977           2         20         1973           6         86         1969           6         86         1965           6         86         1965           5         152         1961           5         152         1961           5         152         1961           5         152         1961           5         152         1961           5         226         1953           5         226         1953           6         277         1953           6         277         1953           7         403         1949           8         273         1949           8         513         1933           6         447         1933           7         545         1925           8         513         1925           7         545         1925           7         545         1925           8         519         1917           8         519         1917           8         545<th>8         1977           2         20         1973           2         20         1973           6         86         1969           6         86         1965           6         86         1965           5         152         1961           5         226         1957           6         86         1957           15         226         1957           16         403         1953           11         403         1949           12         447         1953           13         451         1941           14         451         1941           15         447         1943           16         447         1943           16         447         1941           16         447         1943           16         447         1943           17         519         1925           18         545         1926           19         1917         1917           19         1914         1914           10         1914         1917           10</th></th>	8         1977           2         8         1973           2         20         1973           6         86         1969           6         86         1965           5         152         1961           55         152         1961           55         152         1961           55         152         1961           55         152         1961           56         152         1961           57         226         1953           53         323         1949           51         403         1949           53         323         1949           54         451         1941           56         533         1949           57         323         1949           58         513         1933           55         545         1925           57         519         1925           519         519         1921           519         519         1921           519         519         1921	8         1977           2         20         1973           2         20         1973           9         44         1969           6         86         1965           6         86         1965           6         86         1965           6         86         1965           6         86         1965           15         152         1961           15         226         1957           16         403         1949           11         403         1946           12         403         1946           13         323         1949           14         451         1947           15         447         1953           16         451         1937           16         451         1937           15         536         1929           15         545         1925           17         519         1921           17         519         1917           16         1917         1913	8         1977           2         8         1977           2         20         1973           6         86         1969           6         86         1965           6         86         1965           5         152         1961           5         152         1961           5         152         1961           5         152         1961           5         152         1961           5         152         1961           5         226         1953           6         277         1953           6         277         1953           6         447         1949           9         497         1949           9         497         1937           8         513         1933           55         545         1925           67         519         1925           77         519         1925           77         519         1925           77         519         1917           77         519         1917           7	8         1977           2         20         1973           2         20         1973           6         86         1969           6         86         1965           6         86         1965           6         86         1965           6         86         1965           6         86         1965           15         152         1961           15         226         1957           16         403         1949           11         403         1946           12         403         1946           13         323         1949           14         403         1947           15         447         1953           16         447         1937           16         447         1933           15         536         1926           15         545         1926           17         519         1921           16         1921         1917           17         519         1913           18         1913         1913           19	8         1977           2         8         1977           2         20         1973           6         86         1969           6         86         1965           6         86         1965           5         152         1961           5         152         1961           5         152         1961           5         152         1961           5         152         1961           5         226         1953           5         226         1953           6         277         1953           6         277         1953           7         403         1949           8         273         1949           8         513         1933           6         447         1933           7         545         1925           8         513         1925           7         545         1925           7         545         1925           8         519         1917           8         519         1917           8         545 <th>8         1977           2         20         1973           2         20         1973           6         86         1969           6         86         1965           6         86         1965           5         152         1961           5         226         1957           6         86         1957           15         226         1957           16         403         1953           11         403         1949           12         447         1953           13         451         1941           14         451         1941           15         447         1943           16         447         1943           16         447         1941           16         447         1943           16         447         1943           17         519         1925           18         545         1926           19         1917         1917           19         1914         1914           10         1914         1917           10</th>	8         1977           2         20         1973           2         20         1973           6         86         1969           6         86         1965           6         86         1965           5         152         1961           5         226         1957           6         86         1957           15         226         1957           16         403         1953           11         403         1949           12         447         1953           13         451         1941           14         451         1941           15         447         1943           16         447         1943           16         447         1941           16         447         1943           16         447         1943           17         519         1925           18         545         1926           19         1917         1917           19         1914         1914           10         1914         1917           10
	2 2	∞		22 20	22 20 49 44	22 20 49 44 96 86	22     20       49     44       96     86       165     152	22     20       22     20       49     44       96     86       165     152       245     226	22     20       22     20       49     44       96     86       165     152       245     226       308     277	22     20       22     20       49     44       96     86       165     152       245     226       308     277       363     323	22     20       22     20       49     44       96     86       165     152       165     152       245     226       308     277       363     323       421     403	22     20       22     20       49     44       96     86       165     85       165     152       245     226       308     277       363     323       363     323       421     403       464     451	22     20       22     20       49     44       96     86       165     152       165     152       245     226       308     277       308     277       363     323       421     403       464     451       509     497	22     20       22     20       49     44       96     86       165     85       165     152       245     226       308     277       308     277       363     323       363     323       421     403       464     451       509     497       538     513	22     20       49     44       96     86       165     152       245     226       308     277       308     277       308     277       308     277       308     277       363     323       421     403       464     451       509     497       538     513       575     536	22     20       49     44       96     86       165     152       245     226       308     277       308     277       363     323       421     403       421     403       421     403       569     497       509     497       538     513       575     536	22     20       49     44       96     86       165     152       165     152       245     226       308     277       308     277       363     323       421     403       464     451       509     497       538     513       538     513       572     536       575     545       547     519	22     20       49     44       96     86       165     152       245     226       308     277       363     323       364     451       363     323       421     403       421     403       421     403       569     497       509     497       513     536       575     545       547     519	22     20       49     44       96     86       165     152       165     152       245     226       308     277       308     277       363     323       421     403       464     451       509     497       538     513       538     513       572     545       572     545       547     519       547     519	22     20       49     44       96     86       165     152       245     226       308     277       308     277       363     323       421     403       421     403       509     497       509     497       513     536       575     536       572     545       547     519       547     519       547     519	22     20       49     44       96     86       165     152       165     152       245     226       308     277       308     277       363     323       363     323       364     497       509     497       509     497       538     513       572     545       572     545       574     519       575     545       547     519       547     519       547     519       547     519	22     20       49     44       96     86       165     152       165     152       245     226       308     277       363     323       421     403       421     403       569     497       509     497       513     536       575     536       574     519       575     545       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519	22     20       49     44       96     86       165     152       165     152       245     226       308     277       308     277       363     323       421     403       421     403       421     403       509     497       509     497       513     536       575     545       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       547     519       548     519       549     519
2 2		8 8	22 20		49 44	49         44           96         86	<ul> <li>49 44</li> <li>96 86</li> <li>165 152</li> </ul>	49     44       96     86       165     152       245     226	49     44       96     86       165     152       245     226       308     277	49     44       96     86       165     152       245     226       308     277       363     323	49     44       96     86       165     152       245     226       308     277       363     323       421     403	49     44       96     86       165     152       165     226       245     226       308     277       363     323       421     403       464     451	49     44       96     86       96     86       165     152       245     226       245     226       308     277       363     323       363     323       421     403       464     451       509     497	49     44       96     86       165     152       245     226       308     277       308     277       308     277       363     323       421     403       464     451       509     497       538     513	49     44       96     86       165     152       245     226       245     226       308     277       308     277       363     323       363     323       421     403       421     403       464     451       509     497       538     513       575     536	49     44       96     86       165     152       165     226       245     226       308     277       308     277       363     323       363     323       421     403       421     403       464     451       509     497       538     513       575     536       572     545	49     44       96     86       96     86       165     152       245     226       245     226       308     277       363     323       363     323       364     451       421     403       421     403       454     451       509     497       538     513       575     536       575     545       577     519	49     44       96     86       165     152       165     226       245     226       308     277       363     323       363     323       363     323       363     323       363     323       364     451       421     403       464     451       509     497       538     513       575     536       575     545       547     519	49     44       96     86       96     86       165     152       245     226       245     226       308     277       363     323       363     323       364     451       421     403       421     403       421     403       569     497       578     513       575     545       577     545       547     519	49     44       96     86       96     86       165     152       245     226       308     277       308     277       363     323       464     451       464     451       509     497       509     497       575     536       575     536       575     547       547     519       547     519	49     49     44       96     86     86       165     152     85       245     226     226       308     277     233       363     323     323       364     451     403       421     403     497       509     497     513       538     513     536       572     545     545       572     545     545       573     545     545       574     519     545       575     545     545       571     519     545       572     545     545       573     545     545       574     519     545       574     519     545       575     545     545       574     519     545       574     519     545       574     519     545       574     519     545       574     519     545	49     44       96     86       95     86       165     152       245     226       308     277       308     277       363     323       421     403       421     403       421     403       536     536       575     536       575     547       575     546       577     519       578     519       574     519       575     546       574     519       575     547       574     519	49     44       96     86       95     86       165     152       245     226       245     226       308     277       363     323       363     323       364     451       464     451       464     451       509     497       538     513       572     545       572     545       573     545       574     519       575     545       574     519       575     545       574     519       575     545       574     519       575     545       574     519       575     545       574     519       575     545       574     519       575     545       574     519       574     519       575     545       574     519       575     545
5 ∞ 12	∞ {		77	49		96	96 165	96 165 245	96 165 245 308	96 165 245 308 363	96 165 245 308 363 421	96 165 245 308 363 421 464	96 165 245 308 308 421 421 464 509	96 165 245 308 363 421 421 464 509 538	96 165 245 308 308 363 421 421 464 509 538 538	96 165 245 308 308 308 308 421 421 421 464 509 509 538 538 575	96 165 245 308 308 308 308 421 421 464 538 509 538 538 572 547	96 165 245 308 308 308 363 421 421 464 509 509 538 538 575 575 547	96 165 245 308 363 464 464 509 538 538 538 538 538 538 538 538	96 165 245 308 308 308 363 421 421 464 509 509 538 538 575 575 575 575 547	96 165 245 308 363 421 464 539 538 538 538 538 538 538 538	96       165       165       308       308       308       308       308       308       308       308       308       308       308       308       308       308       308       308       308       308       509       575       575       575       575       575       575       575       575       575       575       575       575       575       575       575       575       575       575	96       165       165       308
2 7 21	7 21	21		48	92		158	158 241	158 241 306	158 241 306 335	158         158           241         306         335           335         383         383	158 241 306 335 333 333 419	158           241           241           306           335           335           419           472	158       241       241       306       335       335       333       333       3419       419       510	158       241       241       306       335       335       335       335       335       379       3710       510	158       241       241       306       335       335       335       335       335       335       335       333       334       533	158       241       241       306       335       335       333       419       510       533       533       533	158       241       241       306       335       335       335       335       335       335       335       335       335       336       337       419       510       534       533       533       498	158       241       241       306       335       336       337       338       338       339       3310       3310       3310       3310       3310       3310       3310       3310       3410       3510       3510       3510       3510       3510       3510       3510       3510       3510       3510       3510       3510       3510       3510 <tr< td=""><td>158       241       241       306       335       335       335       335       335       335       335       335       335       335       335       335       335       335       335       335       335       336       337       338       339       331       332       333       349       498       498</td><td>158       241       241       306       335       336       337       338       338       339       3310       3310       332       333       340       353       353       360       370       3710       3710       3710       3710       3710       3710       3710       3710       3710       3710       3710       3710       3710       3710       3710</td><td>158       241       241       306       335       335       335       335       335       335       335       335       335       336       337       333       333       333       335       335       333       333       333       333       333       333       333       333       333       333       333       333       333       333       334       335       333       333       334       335       333       344       353       353       353       364       375       376       376       376       376       377       378       379       379       370       371       371       371       371       371       371       371       371   <!--</td--><td>158       241       306       335       335       335       333       419       419       419       533       510       533       498       498       1498</td></td></tr<>	158       241       241       306       335       335       335       335       335       335       335       335       335       335       335       335       335       335       335       335       335       336       337       338       339       331       332       333       349       498       498	158       241       241       306       335       336       337       338       338       339       3310       3310       332       333       340       353       353       360       370       3710       3710       3710       3710       3710       3710       3710       3710       3710       3710       3710       3710       3710       3710       3710	158       241       241       306       335       335       335       335       335       335       335       335       335       336       337       333       333       333       335       335       333       333       333       333       333       333       333       333       333       333       333       333       333       333       334       335       333       333       334       335       333       344       353       353       353       364       375       376       376       376       376       377       378       379       379       370       371       371       371       371       371       371       371       371 </td <td>158       241       306       335       335       335       333       419       419       419       533       510       533       498       498       1498</td>	158       241       306       335       335       335       333       419       419       419       533       510       533       498       498       1498
2 7 7 21	21	21	18	10	92		158	241	158 241 306	158 241 306 335	158 241 306 335 333	158 241 306 335 335 335 335 415	158 241 306 335 383 383 415 415 477	155 241 306 335 335 335 332 383 383 383 383 383 383 383 383 383	158 241 306 335 335 335 415 415 477 510 534	155 241 306 305 335 383 383 383 415 415 417 510 510 510 513	158       241       243       335       335       3419       472       534       534       534       534       534       534	155 241 305 335 335 382 383 383 415 415 415 516 516 516 516 534 496	158       241       243       335       3419       534       534       534	155       241       243       335       335       335       335       553       516       517       518       517       518       5198       498	155 241 306 335 335 332 415 415 415 510 510 510 510 513 51 510 510 510 510 510 510 510 510 510	155       241       243       335       335       335       335       335       335       335       335       335       335       335       335       335       335       335       335       335       335       336       337       337       337       337       337       337       337       337       337       337       337       337       337       338       338       338       338       338       338       338       338       338       338       338       338       338       338       338       338       338       338       338       349       340       340       340       340       340       340       340       340       340 </td <td>155 241 306 335 335 332 415 415 510 510 510 510 510 510 510 510 510 5</td>	155 241 306 335 335 332 415 415 510 510 510 510 510 510 510 510 510 5
2 7 22 47	7 22 47	22 47	47		91	160		246	246 290	246 290 312	246 290 312 356	246 290 312 356 399	246 290 312 356 399 459	246 290 312 356 399 459 486	246 290 312 356 399 459 486 510	246 290 312 356 399 459 486 510 510	246 290 312 356 399 459 486 510 489 499	246 290 312 356 356 359 459 486 510 499 492	246 290 312 356 399 459 486 510 499 482	246 290 312 356 356 399 459 486 510 499 499	246 290 312 356 399 459 486 510 499 482	246 290 312 356 356 399 459 486 510 499 482	246 290 312 356 356 459 486 499 482 482
2 8 22 48	8 22 48	22 48	48		94	166		238	238 277	238 277 296	238 277 296 345	238 277 296 345 396	238 277 296 345 396 446	238 277 296 345 396 474	238 277 296 296 345 396 446 474 487	238 277 296 345 396 474 474 487 493	238 277 296 296 345 396 446 487 487 493 464	238 277 296 345 396 474 474 487 493 464	238 277 296 296 345 396 446 487 487 487 493 464	238 296 345 396 474 474 493 493 464	238 277 296 296 345 396 474 487 487 493 493 464	238 277 296 296 345 346 446 487 487 493 464	238 277 296 296 345 396 474 487 487 493 493 464
2 7 7 42 83	7 19 83	19 42 83	42 83	83		137	193		223	223 245	223 245 292	223 245 292 328	223 245 292 328 371	223 245 245 292 328 371 386	223 245 245 292 371 371 386 410	223 245 245 292 328 371 371 386 410 405	223 245 245 292 371 371 386 410 410 405 381	223 245 245 292 328 371 338 410 410 405 381	223 245 245 292 371 371 386 410 410 405 381 381	223 245 245 292 371 371 386 410 410 410 381 381 381	223 245 245 292 371 371 386 410 410 405 381 381 381	223 245 245 292 371 371 386 410 410 405 381 381 381	223 245 245 292 371 371 410 405 381 381 381
1 6 17	6 17	17		39	72	117		164	164	164 194 217	164 194 217 254	164 194 217 254 286	164 194 217 254 286 317	164 194 217 254 286 317 341	164 194 217 254 254 286 317 341 353	164 194 217 254 286 317 341 348 348	164 194 217 254 254 256 317 317 341 348 348	164 194 217 254 286 317 341 341 348 348 348	164 194 217 254 254 286 317 341 341 353 353 348 348 348	164 194 217 254 286 317 341 341 348 348 348 348 348	164 194 217 254 286 317 341 341 353 353 348 348 348 348	164 194 217 254 254 317 341 3353 341 348 348 348 348 348	164 194 217 254 286 317 341 341 348 348 348 348 348 348
1 4	v	0	19	39	72	116		167	167 202	167 202 222	167 202 222 260	167 202 222 222 260 287	167 202 222 260 287 328	167 202 222 260 287 328 344	167           202           202           202           202           222           233           3357	167           202           202           202           222           233           344           357	167           202           202           222           222           232           233           344           357           352	167       202       202       202       232       338       344       357       352	167       202       202       202       232       260       287       287       387       344       357       352	167       202       202       202       232       334       357       352	167       202       202       222       232       260       287       287       387       374       374       352	167       202       202       202       232       344       357       352	167       202       202       222       232       2360       287       387       374       352
		8	32	36	40	44		48	48 52	48 52 56	48 52 56 60	48 55 60 64	48 52 56 60 64 68	48 55 66 64 68 68 72	48 55 56 60 64 68 68 72 77 77	48 55 55 66 66 64 77 77 77 72 80	48 55 55 60 64 68 88 76 88 88 88 88 88 88 88 88 88 88 88 88 88	48 55 56 66 66 68 88 88 88 88 88 88 88 88 88 88	48 55 55 66 64 68 88 88 88 88 88 88 88 88 88 88 88 88	48           55           56           66           67           68           88           88           88           84	48           55           55           56           66           67           68           88           88           88           88           88           88	48           60           63           84           88	48           55         55           56         64           66         64           76         72           88         88           88         88           88         88

Cancer Epidemiol Biomarkers Prev. Author manuscript; available in PMC 2010 September 22.