An Ecologic Study Investigating the Correlation between Breast Feeding and the Incidence of Leukemia

Victoria María Klyce

Abstract Leukemia is the most common childhood cancer, with 3,000 children diagnosed in the US per year, and the treatment of which costs the federal government $1.4 billion per year. I tested the correlation between breast feeding for at least six months to the incidence of leukemia in an ecologic study where the units of analysis are the nine US Census regions. I did a qualitative analysis through GIS mapping of the data and scatter plot graphing of the data. I used a trendline and a two means analysis to quantitatively interpret the data. The data were best explained by the two means analysis. Once a large enough proportion of the population is breast feeding leukemia incidence significantly drops. None of the high risk populations are confounding the relationship. I predict that higher breast feeding rates will continue to correlate with lower leukemia incidence. Due to this finding and the other positive effects of breast feeding I would recommend all mothers to breast feed their children for at least six months.

Introduction

Childhood leukemia is the most common childhood cancer (Bhatia 2004, Ganyon 2005). Its prevalence in the United States is 3,000 children diagnosed annually (UCSF 2002), with three to five new cases of childhood leukemia per 100,000 children per year in the US (Bhatia 2004, Guise et al. 2005). Leukemia is a cancer of the blood that develops when bone marrow begins to produce immature white bloods cells (leukocytes) which continue to reproduce even when there is insufficient space for them in the bone marrow, eventually crowding out the healthy white blood cells (UCSF 2002). White blood cells are responsible for fighting infection, and since immature cells are nonfunctional, reducing the number of healthy cells deteriorates the body's ability to fight infection, leading to the symptoms of leukemia (UCSF 2002).

The causes of leukemia are largely unknown (Bhatia 2004). Most of the known risk factors affect the baby in the womb. These include maternal or maternal grandmother exposure to carcinogenic or toxic substances which damage oocytes early in life, and the exposure of the mother while pregnant to: ionizing radiation; DNA topoisomerase II inhibitors found in pesticides, cigarette smoke, specific fruits, tea, cocoa, wine, and soy; ELF-EMF radiation (Hunger et al. 2005); use of antihistamines and amphetamines (Ziegler et al. 2005); and smoking marijuana. Either the mother or the father smoking marijuana before conception of the child is also a documented risk factor (Trivers et al. 2006, Ziegler et al. 2005).

Though the causes are unknown, high risk populations are well established in the literature. Individuals particularly at risk for childhood leukemia are children between two and five years of age (Hunger et al. 2005). Children with polymorphisms in gene coding for methylenetetrahydrofolate reductase (an enzyme for metabolizing folate), or with trisomy 21 (Down syndrome), are at particularly high risk, especially in combination with GATA1 mutation, as well as children with leukemia-specific chromosomal translocation or TEL-AML1 fusion gene (Ziegler et al. 2005). African Americans and Hispanics are at significantly higher risk of developing childhood leukemia, while Asians are at low risk compared to Caucasians (Bhatia 2004). Children of low socioeconomic level are also at increased risk of developing leukemia (Bhatia 2004).

Children who suffer from leukemia usually experience anemia, recurrent infections, bone and joint pain, abdominal stress, swollen lymph nodes, and difficulty breathing (UCSF 2002). Currently more than eighty percent of children who develop leukemia survive into adulthood

(Lightfoot 2005). The four available treatments for a child who has the disease are chemotherapy, radiation therapy, bone marrow transplant, and biological therapy (immunotherapy) (UCSF 2002). It is estimated that the United States spends $1.4 billion per year on the treatment of childhood leukemia (Guise et al. 2005).

The available treatments for leukemia are invasive, expensive, and damaging to children. Identifying preventive measures will reduce the need for treatment. Currently only one preventive measure is well established, namely for the mother to have taken folate supplements before becoming pregnant (Hunger et al. 2005, Ziegler et al. 2005), which decreases the risk of the child developing leukemia by sixty percent (Ziegler et al. 2005). This preventive measure is difficult to adhere to, since the folate supplements need to be taken before pregnancy, thus requiring the future mother plan far in advance. A number of studies have suggested breast feeding as an additional measure in preventing childhood leukemia, though this technique has not been sufficiently investigated (Beral et al. 2001, Guise et al. 2005, Hunger et al. 2005, Kwan et al. 2005, Lightfoot 2005, Lightfoot et al. 2004, Martin et al. 2005, Parker 2001, Shu et al. 1999). The studies range from meta analysis review to cross sectional data analysis, and differ greatly in the concerns, problems, and self-identified errors they posses. However, they all coincide in suggesting inconclusively that breast feeding could potentially protect against leukemia, and that further study was needed to determine this.

The mortality and morbidity avoided by prevention, as well as money saved, would be extremely beneficial. Little is known about the mechanism of how breast milk could protect a child from developing leukemia, but the more general protective properties are well understood. Breast milk contains a wide range of many biologically active compounds including cytokines, hormones, and enzymes that function in the maturation of a child's immune system (Lightfoot 2005, Lightfoot el al. 2004, Parker 2001). Breast milk also transfers immediate protection against microbes from mother to child through the specific immune response via activation of antibodies and the non-specific immune response via activation of proteins, glycoproteins, and lipids. It is well documented that babies who are breastfed have lower morbidity and mortality rates than babies who are bottle-fed (Parker 2001). Proving an association between breast feeding and lower frequency of leukemia would allow the promotion of breast feeding for the prevention of leukemia. Thus it would lead to the prevention of many cases of the most common childhood cancer, reducing suffering to the children and families, and saving federal money.

I will be exploring the relationship between breast feeding and the development of childhood leukemia. The need for more comprehensive studies stems from two different concerns. While some studies found no statistically significant correlation between breast feeding and reduction in leukemia (Kwan et al. 2005, Martin et al. 2005), Beral et al. 2001 suggests that those studies which have found a correlation may not demonstrate the generalized effect of breast feeding but merely show a consistent systematic bias in those studies. Because the causes of leukemia are poorly understood, and many risk factors are strongly implicated, a study to rule out confounders would be very expensive, work intensive, and time consuming. Before performing a large scale experiment it would be useful to do an ecologic study—which is cheaper and faster—to assess whether a more expensive case-control or cohort study would be worth the time and money.

I predicted there would be an inverse correlation between percent of children breast fed at six months and frequency of leukemia: the higher the percentage of children breast fed for six months or more the lower the frequency of leukemia. Proving this correlation would allow for a second preventative measure of leukemia to be established, and for the promotion of breast feeding to achieve this goal, thus leading to fewer cases of leukemia. It would also encourage money and time to be allocated to the further study of breast feeding and leukemia to prove causation.

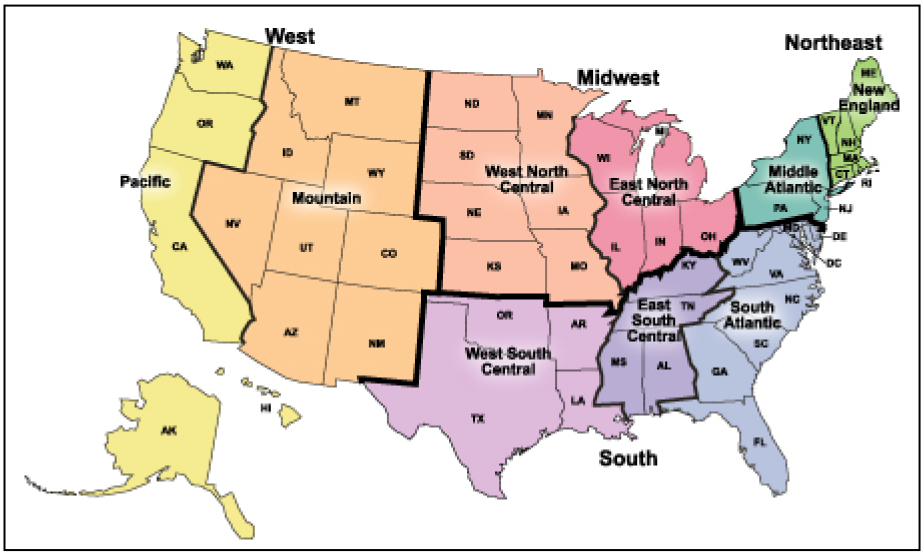
Methods

My objective was to find if a correlation exists between breast feeding for at least six months and the development of childhood leukemia, and if so, to extend the study to the type of correlation that may exist. In order to determine this I conducted a correlational study. Because aggregate data is more accessible for leukemia, and the only data available for breast feeding, I conducted an ecologic study by the nine US Census regions using data that has already been collected. Due to limited time and resources it was not feasible for me to gather enough data on breast feeding and leukemia for my study to have any power and have strong external validity since I cannot do a simple random sample of the United States.

In order to determine this I used breast feeding data from Ross' Mothers Survey, found in *Pediatrics* journal, in the article "The Resurgence of Breastfeeding in the United States", where percent of mothers breast feeding at 6 months is provided by the nine US census regions (Ryan 1997). This was a continuation of the Ross Mother's Survey from 1989. In 1995 approximately 360,000 surveys were completed. In order to get the leukemia incidences I acquired the

Leukemia incidence counts for each state in 2004 from "Cancer Statistics, 2004," published in *Cancer Journal for Clinicians.* To convert from count to rate I divided the Leukemia count of each state in 2004 by the population of that state in 2004. I acquired the population data from the *US Census, Population Bureau.* I then divided the incidence per state by 100,000 to achieve the incidence of leukemia per 100,000 people per state.

Figure 1. Nine US Census Regions



Census Bureau: Four Geographic Regions and 9 Divisions of the United States
http://www.cdc.gov/nchs/images/nchsdefs/Census-map.jpg

I used scatterplot graphs (Figures 3 and 4) in order to determine if there is a correlation between the percent of children breast fed at six months and the frequency of leukemia. The data points for individual states are shown in blue. Because the leukemia data are by state, and each state has differing population, it would not be accurate to give each point equal weight, since some states make up a more significant portion of the region than others. Therefore, in order to determine the correlation I needed to find the population weighted averages of the incidence of leukemia per 100,000 per region. To do this I multiplied each state's incidence of leukemia by the state's population over the region's population and then summed these products for the region to get the region's weighted average leukemia incidence per 100,000. These points are shown in pink. I then fitted a trendline to the pink population weighted average points to assess the relationship. I calculated the trendline and R^2 for a linear relationship. I then did a two means analysis, on which I did a single factor Anova to determine the statistical significance and R^2.

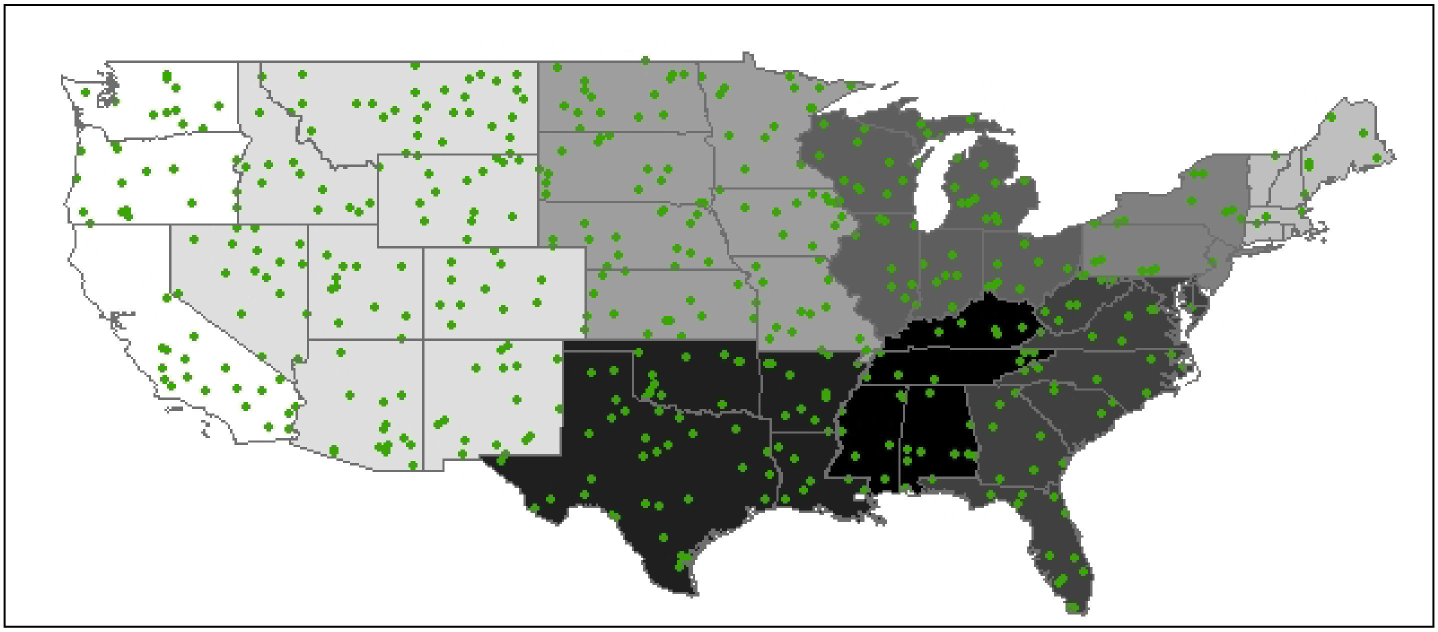
In order to qualitatively analyze the relationship I constructed a Geospatial Imaging Map to show the correlation between percent of mothers breast feeding for at least 6 months and the incidence of leukemia per 100,000. Leukemia incidence is by state and breast feeding is by the nine US Census regions.

Results

For qualitative analysis I created a GIS map to present the data. See Appendix for the data table I used to make the GIS map (Figure 2). Leukemia incidence is represented by dot density, where higher density of dots in each state corresponds to higher incidence of leukemia. Dots are not location specific to cases of leukemia within a state. The shading is as follows:

- ■ 13.0% or fewer of mothers breast feeding at 6 months
- ■ 13.2-17.0% of mothers breast feeding at 6 months
- ■ 17.1-18.6% of mothers breast feeding at 6 months
- ■ 18.7-18.9% of mothers breast feeding at 6 months
- ■ 19.0-19.6% of mothers breast feeding at 6 months
- ■ 19.7-21.4% of mothers breast feeding at 6 months
- ■ 21.5-22.2% of mothers breast feeding at 6 months
- ■ 22.3-30.3% of mothers breast feeding at 6 months
- □ 30.4-30.9% of mothers breast feeding at 6 months

Figure 2. GIS Map



District of Columbia and Alaska are not listed in the data table and are not included in the map or graphs because these two states did not have leukemia data through Census 2004. Because the populations of the two are relatively small, I do not expect this to significantly impact the data.

For quantitative analysis I used scatterplot graphs to determine the trendline that best fit the relationship. Below are two graphs of the data. Figure 3 shows the inverse linear relationship that I had predicted. However, the R^2 is only 0.48. so I was not satisfied with this explanation. Because the data appeared to be clumped into two groups—one with low breast feeding and higher leukemia, and the other with higher breast feeding and lower leukemia—I also did a two means analysis, shown in Figure 4. Group 1 is called East because it is made up of the seven eastern census regions: East North Central, East South Central, Middle Atlantic, New England, South Atlantic, West North Central, and West South Central. Group 2 is called West because it is made up of the two western census regions: Pacific and Mountain.

Figure3. Linear relationship

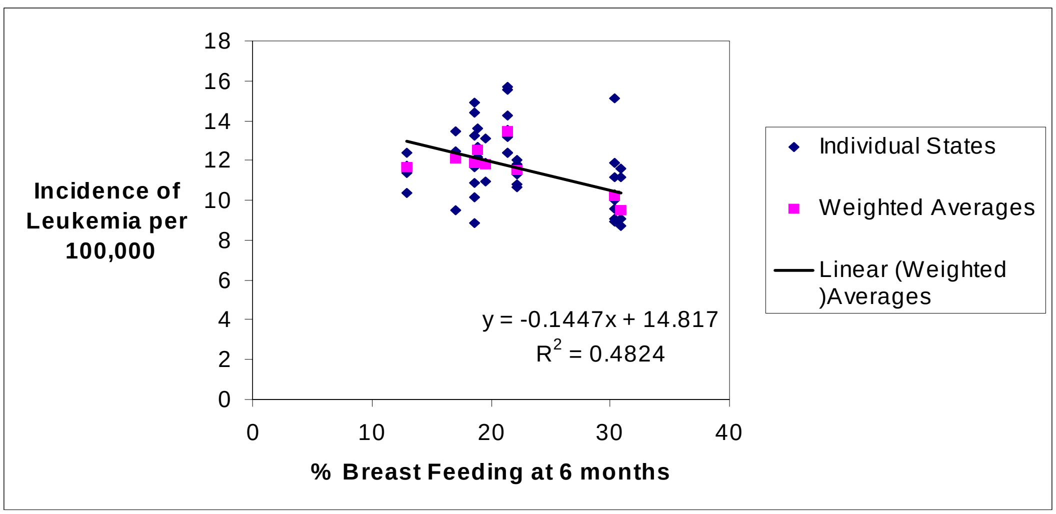
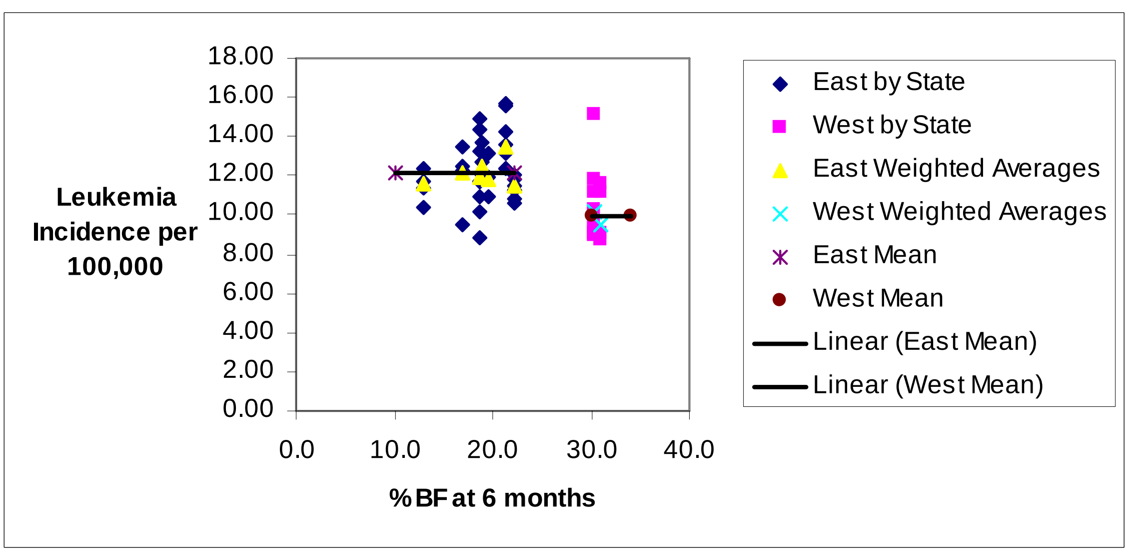


Figure 4. Two Means



Mean breast feeding:	East=18.7	West=30.6	p=0.001	R^2=0.80
Mean leukemia incidence:	East=12.1	West=9.8	p=0.003	R^2=0.73

For Figure 4 I did a Single Factor Anova to evaluate the R^2 and the significance of the difference between the East's mean and the West's mean. For breast feeding, the West's mean percent of mothers breast feeding was 30.6 and the East's mean was 18.7. The difference between them was statistically significant ($p=0.001$) and $R^2=0.80$. For leukemia incidence, the West mean leukemia incidence per 100,000 people was 9.8 and the East mean was 12.1. This difference was also statistically significant ($p=0.003$) and $R^2=0.73$.

Discussion

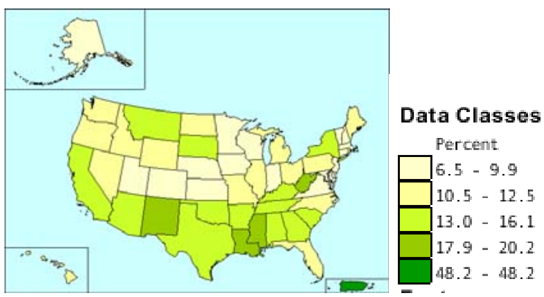
With any ecologic study there are certain realities one has to face. Because populations are the units of analysis, no causation can be proven or even strongly implied. In the case of this study, due to the very large and few units of analysis, no simple correlation is obvious. In the Pacific region, for example, California's incidence of leukemia is much lower than Oregon's or Washington's, but the three share a "common" breast feeding percentage. It would be valuable to see breast feeding percentages by state, instead of by census region. Apart from having 50 data points to find a correlation, it would be possible to distinguish between areas within a region with differing leukemia. In this way the rather arbitrary line drawing of the census regions would no longer influence the data. Another way to improve this ecologic study would be to have stratified breast feeding data and stratified leukemia data by the five high risk populations. In this way we could apply a covariate and prove that the patterns seen in this study are not due to confounding effects.

The obvious question when one looks at the data relates to geography: why is there a significantly lower incidence of leukemia in the western United States? In order for geographic location to be a confounder, it must be correlated to both the X and Y variables. In this case, location could be correlated to breast feeding, though this is far from certain. It is possible that breast feeding could be differently advertised in different regions, and could be dependent on regional culture, practice, or influence. However, there are no data linking leukemia susceptibility to region. Due to the way the regions are drawn, the states in given regions do not consist of overlapping social cleavages. Regions are not homogenous racially, economically, or culturally. Therefore, until proven otherwise, geographic location is not a confounder for breast feeding and leukemia.

There are high risk populations for leukemia that could potentially be the underlying cause of the two mean correlation. The high risk populations were children two to five years old, African Americans, Hispanics, individuals with certain genetic abnormalities, and those of low socioeconomic status. Because the specific genetic abnormalities that are associated with higher risk of leukemia are so rare that they would be unlikely to influence a large-scale ecologic study, I will not address that population in this analysis.

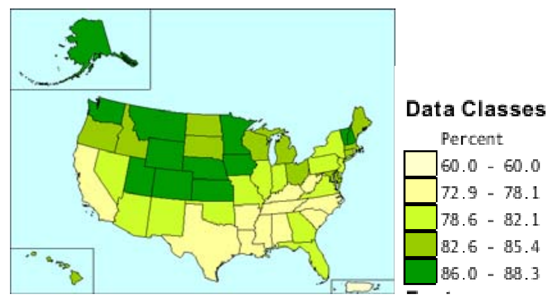
Low socioeconomic status refers to poverty and lack of education. In order to address this possible confounder I present two maps showing the percentage of individuals below the poverty line in each state, and the percent of individuals who graduated from high school in each state (Figures 5 and 6).

Figure 5. Percent Below Poverty Line



US Census Quick Facts
http://quickfacts.census.gov/qfd/states/06000.html

Figure 6. Percent High School Graduates

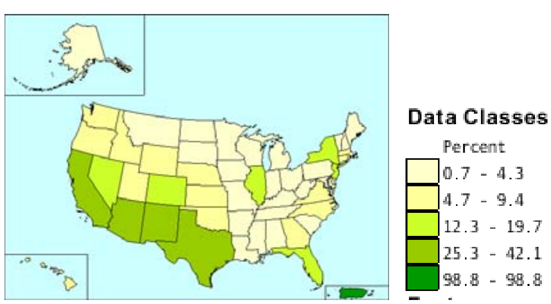


US Census Quick Facts
http://quickfacts.census.gov/qfd/states/06000.html

The West does not have a lower percent of the population below the poverty line or a higher percent of the population with more education than the East, thus socioeconomic status is not a confounder.

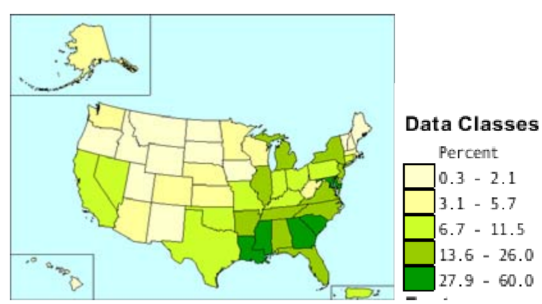
There is much variation when it comes to the racial make up of the United States. To explore if race is a confounder we must investigate if the West has fewer African Americans and Hispanics than the East. For easy comparison, refer to figures 7 and 8.

Figure 7. Percent Hispanic



US Census Quick Facts
http://quickfacts.census.gov/qfd/states/06000.html

Figure 8. Percent African American

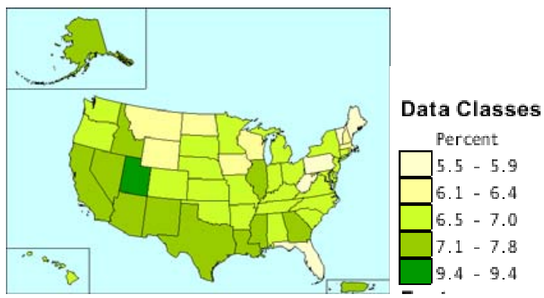


US Census Quick Facts
http://quickfacts.census.gov/qfd/states/06000.html

Again, the Census Regions with the fewest African Americans and Hispanics are not the Pacific and Mountain regions. In fact, the West North Central region appears to have the lowest percent of Hispanics and African Americans, and this is the region with the highest incidence of leukemia. Race is not confounding the relationship.

The last high risk population was children two to five years old. If there are fewer children in this age group in the West than the East this could be causing the lower leukemia incidence. Figure 9 shows percent of population under five years old.

Figure 9. Population under 5 years old



US Census Quick Facts
http://quickfacts.census.gov/qfd/states/06000.html

Here we can see that if anything the West appears to have more children under five years old than the East. This last possible confounder is thus also not applicable. Interesting to note is that Florida has among the lowest percentage of children under 5 years old, and has the fourth highest incidence of leukemia in the country.

So the question remains, why does the West have lower incidence of leukemia than the East? Figure 4 shows that the data can be explained by a two means analysis. The Pacific and Mountain regions of the US (the West) have an average 30.6% of mothers breast feeding for at least six months. The East has a mean 18.7% of mothers breast feeding for at least six months. This difference is statistically significant ($p=0.001$). The two mean scenario for breast feeding corresponds to the two mean leukemia incidence scenario. The West has a mean incidence of 9.8 leukemias per 100,000 people, while the East's mean leukemia incidence is 12.1. This drop in leukemia from 12.1 to 9.8 is also statistically significant ($p=0.003$). Thus, the data can be viewed as two groups: West (Pacific region and Mountain region) and East (the other seven regions).

The East exhibits almost random scattering of leukemia around the mean $y=12.1$ new leukemias per 100,000 people. Because there are so many risk factors and high risk populations associated with leukemia, when a low proportion of the population is breast feeding it is not possible for any relationship between breast feeding and leukemia to shine through. What we see is the "noise" from all the other variables—exposure to risk factors, high risk individuals, and chance. The difference between, for example, 13% of mothers breast feeding (East South Central, leukemia incidence=11.6) and 18.6% of mothers breast feeding (South Atlantic, leukemia incidence=11.9) is not the main influence on each population's leukemia rate—there are simply too many other influential factors.

The two points that make up the West are quite close to each other, (30.9, 9.5) and (30.3, 10.1), with a mean breast feeding of 30.6 and leukemia incidence of 9.8. Once breast feeding rates make this significant ($p=0.001$) jump from the mean of the East to the mean of the West the leukemia incidence significantly ($p=0.003$) drops (East mean=12.1, West mean=9.8). These data show that once a large enough portion of the population is breast feeding an inverse correlation between breast feeding and the incidence of leukemia does occur. Once the percent of mothers breast feeding is high enough to overcome other variables, leukemia incidence begins to drop. In the East, where only two in eleven mothers are breast feeding, the population's exposure to risk factors or membership in high risk populations dominate the population's leukemia risk, and thus we do not see an inverse correlation between breast feeding and leukemia among the regions of the East. Comparing the East to the West, where one in three mothers are breast feeding, we see this difference in breast feeding correlates to a noticeably lower leukemia incidence, and that higher breast feeding rates begin to impact the population's overall leukemia incidence.

What we would need to do in order to further examine this conjecture would be to look at populations where breast feeding rates were higher than 30%: 40, 50, ideally up to 100%. These populations where a higher percent of mothers are breast feeding should correspond to lower incidences of leukemia. I would predict that the two means will be the beginning of an inverse linear correlation that would continue as rates of breast feeding increased. This study has shown that when the percent of mothers breast feeding begins to encompass a noteworthy proportion of the population, leukemia incidence drops. Noting this as well as the other benefits of breast feeding stated previously in this paper, I would recommend for all mothers to breast feed their children for at least six months to lower their risk of leukemia and other morbidity.

References

Beral, V., Fear, N.T., Alexander, F. and Appleby, P. 2001. Breastfeeding and childhood cancer. *British Journal of Cancer*. **82**:1073-1102.

Bhatia, S. 2004. Influence of race and socioeconomic status on outcome of children treated for childhood acute lymphoblastic leukemia. *Current Opinion in Pediatrics*. **16**:9-14.

Center for Disease Control. 2002. National Program of Cancer Registries.
http://apps.nccd.cdc.gov/uscs/

Center for Disease Control. 2002. National Program of Cancer Registries Invasive Cancer Incidence.
http://wonder.cdc.gov/

Ganyon, P.S. 2005. Childhood acute lymphoblastic leukaemia and relapse. *British Journal of Haematology*. **131**:579-587.

Guise, J.M., Austin, D. and Morris, C.D. Review of case-control studies related to breastfeeding and reduced risk of childhood leukemia. 2005. *Pediatrics*. **116**:724-731.

Hunger, S.P., Winick, N.J., Sather, H.N. and Carroll, W.L. 2005. Therapy of Low-Risk Subsets of Childhood Acute Lymphoblastic Leukemia: When Do We Say Enough? *Pediatric Blood Cancer*. **45**:876-880.

Kwan, M.L., Buffler, P.A., Wiemels, J.L, Meayer, C., Selvin, S., Ducore, J.M. and Block, G. 2005. Breastfeeding patterns and risk of childhood acute lymphoblastic leukemia. *British Journal of Cancer*. **93**:379-384.

Lightfoot, T.J. 2005. Aetiology of Childhood Leukemia. *Bioelectromag-netics Supplement*.
7:5-11.

Lightfoot, T.J. and Roman, E. 2004. Causes of childhood leukemia and lymphoma. *Toxicology and Applied Pharmacology*. **199**:104-117.

Li, R., Ogden, C., Ballew, C., Gillespie, C. and Grummer-Strawn, L. 2002. Prevalence of Exclusive Breastfeeding Among US Infants: The Third National Health and Nutrition Examination Survey (Phase II, 1991–1994) *American Journal of Public Health*. **92**(7): 1107–1110.

Martin, R.M., Gunnell, D., Owen, C.G. and Smith, G.D. 2005. Breast-feeding and childhood cancer: a systematic review with metaanalysis. *International Union Against Cancer*. **117**:1020-1031.

Parker, L. 2001. Breast-feeding and cancer prevention. *European Journal of Cancer*. **37**:155-158.

Ryan, A.S. 1997. The Resurgence of Breastfeeding in the United States. *Pediatrics*. **99:12-19**

Shu, X.O., Linet, M.S., Steinbuch, M., Wen, Q.W., Buckley, J.D., Neglia, J.P., Potter, J.D., Reaman, G.H and Robinson, L.L. 1999. Breast-feeding and risk of childhood acute leukemia. *Journal of National Cancer Institute*. **9**:1765-1772.

Trivers, K. F., Mertens, J.A., Steinbuch, M., Olshan, A.F. and Robinson, L.L. 2006. Parental marijuana use and risk of childhood acute myeloid leukemia: a report from the Children's Cancer Group (United States and Canada). *Paediatric and Parinatal Epidemiology*. **20**:110-118.
US Census Bureau. Quick Facts Map, 2004. http://quickfacts.census.gov/qfd/states/06000.html

US Census Bureau, Population Division. Annual Estimates of the Population of the United States, Regions, States, and Puerto Rico. 2006.
http://www.census.gov/popest/states/NST-ann-est.html

University of California, San Francisco. 2002. Leukemia.
http://www.UCSFhealth.org/childrens/medical_services/cancer/leukemia/index.html

Ward, E., Feuer, E., Thun, M., Jemal, A., Tiwari, R. C., Murray, T., Ghafoor, A., Samuels, A. 2004. Cancer Statistics, 2004. *CA: A Cancer Journal for Clinicians*. **54**:8-29

Ziegler, D.S., Pozza, L.D., Waters, K.D. and Marshall, G.M. 2005. Advances in childhood leukaemia: successful clinical-trials research leads to individualized therapy. *The Medical Journal of Australia*. **182**(2):78-81.

Appendix

State	Region	Leukemia Incidence per 100,000	% BF at 6 months	State Population	Region Population	Weighted incidence	Sum
Illinois	East North Central	12.19	18.9	12,713,548	45,990,429	3.370	12.503
Indiana	East North Central	12.69	18.9	6,223,329	45,990,429	1.718	12.503
Michigan	East North Central	11.99	18.9	10,093,398	45,990,429	2.631	12.503
Ohio	East North Central	12.65	18.9	11,461,347	45,990,429	3.153	12.503
Wisconsin	East North Central	13.64	18.9	5,498,807	45,990,429	1.631	12.503
Alabama	East South Central	11.73	13.0	4,517,442	17,436,134	3.040	11.642
Kentucky	East South Central	11.35	13.0	4,140,427	17,436,134	2.696	11.642
Mississippi	East South Central	10.37	13.0	2,892,668	17,436,134	1.721	11.642
Tennessee	East South Central	12.40	13.0	5,885,597	17,436,134	4.187	11.642
New Jersey	Middle Atlantic	11.87	19.6	8,675,879	40,344,786	2.553	11.798
New York	Middle Atlantic	10.94	19.6	19,291,526	40,344,786	5.230	11.798
Pennsylvania	Middle Atlantic	13.09	19.6	12,377,381	40,344,786	4.015	11.798
Arizona	Mountain	10.27	30.3	5,745,674	19,825,188	2.976	10.189
Colorado	Mountain	9.57	30.3	4,598,507	19,825,188	2.219	10.189
Idaho	Mountain	10.04	30.3	1,394,524	19,825,188	0.706	10.189
Montana	Mountain	15.11	30.3	926,345	19,825,188	0.706	10.189
Nevada	Mountain	11.15	30.3	2,332,484	19,825,188	1.311	10.189
New Mexico	Mountain	8.94	30.3	1,900,620	19,825,188	0.857	10.189
Utah	Mountain	9.09	30.3	2,421,500	19,825,188	1.110	10.189
Wyoming	Mountain	11.87	30.3	505,534	19,825,188	0.303	10.189
Connecticut	New England	11.45	22.2	3,493,893	14,241,495	2.809	11.516
Maine	New England	10.66	22.2	1,313,921	14,241,495	0.983	11.516
Massachusetts	New England	11.81	22.2	6,435,995	14,241,495	5.337	11.516
New Hampshire	New England	10.79	22.2	1,297,961	14,241,495	0.983	11.516
Rhode Island	New England	12.05	22.2	1,078,930	14,241,495	0.913	11.516
Vermont	New England	11.28	22.2	620,795	14,241,495	0.492	11.516
California	Pacific	9.04	30.9	35,841,254	46,895,256	6.909	9.532
Hawaii	Pacific	8.74	30.9	1,259,299	46,895,256	0.235	9.532
Oregon	Pacific	11.14	30.9	3,589,168	46,895,256	0.853	9.532
Washington	Pacific	11.60	30.9	6,205,535	46,895,256	1.535	9.532
Delaware	South Atlantic	13.27	18.6	828,762	54,692,843	0.201	11.885
Florida	South Atlantic	14.40	18.6	17,366,593	54,692,843	4.571	11.885
Georgia	South Atlantic	8.84	18.6	8,935,151	54,692,843	1.444	11.885
Maryland	South Atlantic	11.70	18.6	5,553,249	54,692,843	1.188	11.885
North Carolina	South Atlantic	10.90	18.6	8,531,040	54,692,843	1.700	11.885
South Carolina	South Atlantic	11.68	18.6	4,194,694	54,692,843	0.896	11.885
Virginia	South Atlantic	10.17	18.6	7,472,448	54,692,843	1.390	11.885
West Virginia	South Atlantic	14.91	18.6	1,810,906	54,692,843	0.494	11.885
Iowa	West North Central	15.57	21.4	2,953,679	19,692,216	2.336	13.457
Kansas	West North Central	12.42	21.4	2,738,356	19,692,216	1.727	13.457
Minnesota	West North Central	12.37	21.4	5,094,304	19,692,216	3.199	13.457
Missouri	West North Central	13.56	21.4	5,752,861	19,692,216	3.961	13.457
Nebraska	West North Central	13.17	21.4	1,746,980	19,692,216	1.168	13.457
North Dakota	West North Central	15.73	21.4	635,848	19,692,216	0.508	13.457
South Dakota	West North Central	14.28	21.4	770,188	19,692,216	0.559	13.457
Arkansas	West South Central	13.47	17.0	2,746,823	19,692,216	1.879	12.129
Louisiana	West South Central	12.23	17.0	4,495,706	30,536,434	1.801	12.129
Oklahoma	West South Central	12.49	17.0	3,522,827	30,536,434	1.441	12.129
Texas	West South Central	9.50	17.0	22,517,901	30,536,434	7.008	12.129