Tools of the Trade:

EXPLORING RISK RELATIONSHIPS USING THE CHI-SQUARE STATISTIC

Part I: Crude Risk - Significance and Confidence Limits

"The Notion of Risk" discussed the quantification of risk and the difference between risk and causation. We will now examine one of the many statistical methods to quantify risk and determine its statistical significance.

A common method for testing the statistical significance of associations is the Chi-square test. The Chi-square statistic is a robust non-parametric test. Our example will use real data from Pennsylvania birth certificates. We will provide the formulas and calculations used to compute the statistical measures. However, these statistics can be computed using statistical computer software packages such as SAS or the shareware Epi Info that is currently available from the Centers for Disease Control and Prevention (CDC).

The data under examination are birth weight outcomes for singleton Pennsylvania births (1989-1991) in first pregnancies to unmarried black mothers under the age of 21. The analysis has been restricted to this particular group in order to avoid dealing with the risks associated with plural births, parity, prior birth history, marital status, and race. The variables available from birth certificates that might be useful in examining this cohort of births are age, education, smoking, and prenatal care. It must be kept in mind that other variables that are unavailable for our analysis of data from birth certificates might also have a bearing on birth weight outcomes.

We will examine the risk of smoking cigarettes on low birth weight deliveries. In this analysis, the outcome, birth weight, is identified as either less than 2,500 grams or 2,500 grams or more. Smoking is categorized as either smoker or non-smoker.

The crude relative risk (RR_c) provides a measure of the overall relationship (association) between the risk factor and the outcome. This is a straightforward measure and is often very useful in identifying "at risk" groups. However, it has marginal utility in explaining the nature of the disease or condition and usually cannot be used to suggest causation. The crude risk (RR_c) measures the association between the risk factor and the outcome, irrespective of other shared risk factors.

To calculate the crude risk (RR_c) of low birth weight delivery (<2500 grams) for mothers who smoked during pregnancy, a contingency (2x2) table for the disease/exposure relationship is useful. It is shown below:

	Birth Weight <2500	2500+	
Smoker	a 249	b 1,305	n_1 1,554
Non-Smoker	c 1,081	d 8,526	n_0 9,607
	m_1 1,330	m_0 9,831	n 11,161

$$RR_c = \frac{a/n_1}{c/n_0} = \frac{249/1,554}{1,081/9,607} = 1.42$$

A Chi-square test can be used to determine the statistical significance and test based confidence bounds for the relative risk or RR_c.

The following expression calculates the Chi-square value for a disease/ exposure relationship such as depicted in the contingency (2x2) table previously shown. Statistical significance is obtained from the table of a Chi-square (X^2) distribution using the value associated with one degree of freedom X^2 statistic.

$$X^2_1 = \frac{(n-1)(ad-bc)^2}{n_1 \; n_0 \; m_1 \; m_0}$$

Using data from the 2x2 table of smoking risk, we can insert the appropriate numbers according to the above formula to then calculate the Chi-square. In turn, the X^2 statistic will permit us to test the significance of our effect measure of relative risk (RR_c). The resultant equation with all the corresponding numbers imputed from the contingency (2x2) table appears inside the box below.

$$X^2_1 = \frac{(11,161-1)\;((249)(8,526)-(1,305)(1,081))^2}{(1,554)\;(9,607)\;(1,330)\;(9,831)} = 29.004$$

The resulting statistical significance taken from a X^2 distribution with one degree of freedom is P<.001. The probability that the difference in birth weight outcomes between smokers and non-smokers is due to chance is less than 1 in 1,000.

Test-based confidence bounds (using the variance approximation inherent in the Chi-square statistic) can be estimated for RR. The 95% test based confidence bounds for crude risk of smoking in this cohort is determined as follows:

$$RR_c^{(1 \pm 1.96/\sqrt{X^2_1})} = 1.42^{(1 \pm 1.96/5.39)} = 1.42^{(1 \pm 0.364)}$$

$$\text{or } 1.25 \text{ to } 1.62$$

Using the same methodology, the relative risks along with their associated P values and confidence limits can be calculated for all of the available risk factors and are shown below:

Risk Factor	**RR_c**	**P Value**	**95% Test-Based Confidence Bounds**
Age 15 or less	1.09	0.17	0.96 to 1.24
Not High School Graduate	1.07	0.22	0.96 - 1.19
Smoked	1.42	<0.01	1.25 - 1.62
Inadequate Prenatal Care	1.82	<0.01	1.64 - 2.02

Smokers were 1.42 (RR_c) times as likely to deliver a low birth weight infant as non-smokers among this cohort of Pennsylvania mothers. Assuming that the distribution of other risk factors (known and unknown) among this group do not change, we can be 95% confident that smokers (as a group) will deliver between 1.25 to 1.62 times as many low birth weight infants as nonsmokers. It must be kept in mind that this risk could be in whole or in part the result of some other attribute that smokers share.

The association between smoking and lower birth weight is well established by a variety of studies and statistical analyses. The body of evidence suggests a causal relationship between smoking and lower birth weight delivery. However, this analysis of the crude relative risk is insufficient to support the notion that smoking is a causal factor for low birth weight. To suggest that smoking might contribute to lower birth weight delivery, it is necessary to develop a study design that removes the impact of other risk factors that maybe shared by smokers.

Numerous risk factors have already been removed by restriction of the analysis to single deliveries in first pregnancies to black mothers under the age of 21. Had we looked at the crude relative risk of low birth weight for smokers among all singleton births to Pennsylvania mothers, we would have calculated a RR_c of 2.38. In order to remove the impact of the remaining risk factors (those for which we have examined the crude risk) on the relationship between smoking and low birth weight, a statistical method to control for the effect of these variables must be employed.

See Part II to continue this analysis using the Mantel-Haenszel Chi-square statistic in a stratified analysis to control for the other available variables.

NOTE: A more complete explanation of the statistics represented in this analysis can be obtained from the book *Epidemiologic Research, Principles and Quantitative Methods*, Klienbaum, Kupper and Morganstern; 1982, Lifetime Learning Publications of Wadsworth, Ind.; Belmont, California 94002.

*The adequacy of prenatal care was based upon a modified "Kessner Index" which measures the number of prenatal visits relative to the gestational age of the infant.