Tools of the Trade:

EXPLORING RISK RELATIONSHIPS USING THE CHI-SQUARE STATISTIC

Part II: Statistical Control of Risk Factors Using Stratification

In Part I, we examined birth weight outcomes for singleton Pennsylvania births (1989-1991) in first pregnancies to unmarried black mothers under age 21. The analysis was restricted to this particular group in order to avoid accounting for the risk associated with plural births, parity, prior birth history, marital status, and race. The variables available from birth certificates that are being examined in this cohort of Pennsylvania births are age, education, smoking, and prenatal care. It must be kept in mind that other variables that are unavailable to us in our analysis of data from birth certificates might also have a bearing on birth weight outcomes. The prior analysis of this data set revealed that the important factors exhibiting high crude risk for this group were prenatal care and smoking. Neither age nor education exhibited a statistically significant crude risk. Therefore, in order to simplify our example, we will concentrate on the risks of prenatal care and smoking.

Stratified analysis using Mantel-Haenszel one degree of freedom Chi-square statistic requires that the outcome and the risk factor under analysis must be posed as dichotomous variables (divided into two mutually exclusive groups). Remaining risk factors requiring control must be defined for analysis as categorical (or classified) variables. In this analysis, the outcome (low birth weight) is dichotomized as less than 2,500 grams and 2,500 grams or more. The factor being examined (smoking) is dichotomized as smoker and non-smoker. The control variable (stratifier) of prenatal care is grouped into three categories-- adequate, intermediate, and inadequate, using a modified Kessner index*.

The stratified analysis will permit the calculation of a measure of the adjusted relative risk (RR_{MH}) which identifies the risk attributable to the risk factor of interest when risk from the other factor(s) is statistically removed. The statistical significance of this risk can also be calculated.

The adjusted relative risk (RR_{MH}) is calculated as follows:

$$RR_{MH} = \frac{\sum_{g=1}^{G} \frac{a_g m_{0g}}{n_g}}{\sum_{g=1}^{G} \frac{b_g m_{1g}}{n_g}}$$

The Mantel-Haenszel one-degree-of-freedom Chi-square statistic (X^2_{MHS}) is calculated as follows:

$$X^2_{MHS} = \frac{\left(\sum_{g=1}^{G} \frac{a_g d_g - b_g c_g}{n_g} \right)^2}{\sum_{g=1}^{G} \frac{n_{1g} n_{0g} m_{1g} m_{0g}}{(n_g - 1) n_g^2}}$$

The first steps in this analysis are to calculate the crude risks (RR_c) and p values (see Part I) for each category or stratum (g) of prenatal care (adequate, intermediate, and inadequate). Then, stratum-specific data (g=3) can be used to generate the overall (G) adjusted relative risk.

The 2x2 data table of mothers by smoking status and birth weight and the crude risk and p values for each stratum of care follow:

Inadequate Care:

	Birth Weight <2500	2500+	
Smoker	a_1 91	b_1 386	n_{11} 477
Non-Smoker	c_1 392	d_1 2,200	n_{01} 2,592
	m_{11} 483	m_{01} 2,586	n_1 3,069

$$RR_c = \frac{91/477}{392/2,592} = 1.26$$

$$p = 0.029$$

Intermediate Care:

	Birth <2500	Weight 2500+	
Smoker	a_2 71	b_2 267	n_{12} 338
Non-Smoker	c_2 267	d_2 1,612	n_{02} 1,879
	m_{12} 338	m_{02} 1,879	n_2 2,217

$$RR_e = \frac{71/338}{267/1,879} = 1.48$$

$$p = 0.001$$

Adequate Care:

	Birth <2500	Weight 2500+	
Smoker	a_3 85	b_3 652	n_{13} 737
Non-Smoker	c_3 416	d_3 4,714	n_{03} 5,130
	m_{13} 501	m_{03} 5,366	n_3 5,867

$$RR_e = \frac{85/737}{416/5,130} = 1.42$$

$$p = 0.002$$

The values for each stratum or category of prenatal care (g=3) within the formulas appear below:

Inadequate Care (g=1):

$$\frac{a_1 m_{01}}{n_1} = \frac{(91)(2,586)}{3,069} = 76.68$$

$$\frac{b_1 m_{11}}{n_1} = \frac{(386)(483)}{3,069} = 60.75$$

$$\frac{a_1 d_1 - b_1 c_1}{n_1} = \frac{(91)(2,200) - (386)(392)}{3,069} = 15.93$$

$$\frac{n_{11} n_{01} m_{11} m_{01}}{(n_1 - 1) n_1^2} = \frac{(477)(2,592)(483)(2,586)}{(3,069-1)\ 3,069^2} = 53.44$$

Intermediate Care (g=2):

$$\frac{a_2 m_{02}}{n_2} = \frac{(71)(1,879)}{2,217} = 60.18$$

$$\frac{b_2 m_{12}}{n_2} = \frac{(267)(338)}{2,217} = 40.71$$

$$\frac{a_2 d_2 - b_2 c_2}{n_2} = \frac{(71)(1,612) - (267)(267)}{2,217} = 19.47$$

$$\frac{n_{12} n_{02} m_{12} m_{02}}{(n_2 - 1) n_2^2} = \frac{(338)(1,879)(338)(1,879)}{(2,217-1)\ 2,217^2} = 37.03$$

Adequate Care (g=3):

$$\frac{a_3 m_{03}}{n_3} = \frac{(85)(5,366)}{5,867} = 77.74$$

$$\frac{b_3 m_{13}}{n_3} = \frac{(652)(501)}{5,867} = 55.68$$

$$\frac{a_3 d_3 - b_3 c_3}{n_3} = \frac{(85)(4,714) - (652)(416)}{5,867} = 22.07$$

$$\frac{n_{13} n_{03} m_{13} m_{03}}{(n_3 - 1) n_3^2} = \frac{(737)(5,130)(501)(5,336)}{(5,867-1)\ 5,867^2} = 50.05$$

As previously mentioned, the summation of the stratum-specific data (g=3) yields the total of all strata (G), permitting the calculation of the overall adjusted relative risk(RR_{MH}) and its probability, using a one degree of freedom Chi-square (X^2_{MHS}). This calculation follows:

$$RR_{MH}(G) = \frac{76.68 + 60.18 + 77.74}{60.75 + 40.71 + 55.68} = \frac{214.60}{157.14} = 1.37$$

$$X^2_{MHS}(G) = \frac{(15.93 + 19.47 + 22.07)^2}{53.44 + 37.03 + 50.05} = \frac{(57.47)^2}{140.52} = 23.50$$

one degree of freedom Chi-square, $p < 0.001$.

The 95% test-based confidence bounds are estimated for the Mantel-Haenszel Adjusted Relative Risk (RR_{MH}) as follows:

$$RR_{MH}^{(1 \pm z_{1-\alpha/2}/\sqrt{X^2_{MHS}})} = 1.37^{(1 \pm 1.96/4.85)} = 1.37^{(1 \pm 0.404)}$$

$$or\ (1.21,\ 1.56)$$

Had all of the available strata (age, education, smoking and prenatal care) been used to control the analysis, the adjusted relative risks, their associated p values and confidence limits for all of the available risk factors would have resulted in the statistics as shown in the table below.

Risk Factor	RR_{MH}	P Value	Confidence Limits
Age 15 or less	1.01	0.94	0.86 - 1.18
Not High School Graduate	0.99	0.93	0.86 - 1.15
Smoked	1.35	<0.01	1.19 - 1.55
Inadequate Prenatal Care	1.80	<0.01	1.62 - 1.99

After controlling those risk factors available from Pennsylvania birth certificates for this cohort of singleton first pregnancies to black unmarried Pennsylvania mothers under the age of 21, smokers were 1.35 times more likely to deliver a low birth weight infant than non-smokers. Not being sample data, this cohort of mothers for live births during the years of 1989 through 1991 exhibited these risks without regard to sampling error. Nevertheless, the p values and confidence bounds are very useful in the practical matter of assessing future risk or generalizing risk to a broader population.

The use of a stratified analysis and the Mantel-Haenszel statistics provide an effective methodology for analysis of health risks when statistical control of a few variables is required. This approach is also very useful in exploring much more complex relationships and can sometimes be used to effectively quantify risk when there are numerous variables to control.

The use of this technique to identify complex relationships among numerous variables requires a more complete understanding of its statistical properties and limitations than can be covered here. If you are interested in learning more about the Mantel-Haenszel statistics, *Epidemiologic Research* by Kleinbaum, Kupper and Morganstern (Lifetime Learning Publications, Wadsworth, Inc; Belmont California; 1982) can provide a more complete understanding of its use. You are also likely to find information on this procedure in other biostatistics and epidemiology references. Computer software such as SAS or Epi Info that is available from the Centers for Disease Control can also be used to generate these statistics.

*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.