

# Analysis of Interrupted Time Series Mortality Trends: An Example to Evaluate Regionalized Perinatal Care

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**Abstract:** Interrupted time series designs are frequently employed to evaluate program impact. Analysis strategies to determine if shifts have occurred are not well known. The case where statistical fluctuations (errors) may be assumed independent is considered, and a segmented regression methodology presented. The method discussed is applied to the assessment of changes in local and state perinatal postneonatal mortality to identify historical trends and will be used to evaluate the impact of the North Carolina Regionalized Perinatal Care Program when seven years of post-program mortality data become available. The perinatal program region is contrasted with a control re-

gion to provide a basis for interpretation of differences noted.

Relevant segmented regression models provided good fits to the data and highlighted mortality trends over the last 30 years. Considerable racial differences in these trends were identified, particularly for postneonatal mortality. Segmented regression is considered relevant for the analysis of interrupted time series designs in other applications when errors can be taken to be independent. Thus, the methodology may be regarded as a general statistical tool for evaluation purposes. (*Am J Public Health* 1981; 71:38-46.)

## Introduction

Interrupted time series designs occur frequently in evaluation studies since it is then possible to carry out an evaluation by taking advantage of naturally occurring situations or situations in which the evaluator has minimal control. Campbell and Stanley<sup>1</sup> refer to this type of design as a time series design and they proceed to consider a refinement, the multiple time series design, that also employs a control group. Ideally, the intervention is sudden, as otherwise the impact may be dissipated over a period of time, but no other restrictions are necessary. As we shall show, even the requirement of "suddenness" can be dropped because the method of analysis proposed is able to detect a sharp and immediate impact as well as slower changes that occur over time.

It is preferable to employ a control group so that a frame of reference for the interpretation of observed changes is available. The methodologic problem is the possibility that some other event (perhaps unrecognized) is responsible for observed changes rather than the innovation. The decrease in road traffic fatalities during 1956 in Connecticut following

a 1955 speeding crackdown<sup>2,3</sup> illustrates that sounder conclusions can be drawn if an entire time series together with a control is analyzed. There was an immediate reduction in traffic fatalities after the December 1955 crackdown but this reduction followed a substantial increase during 1955 and was of similar magnitude to previous decreases for which there was no particular explanation. In other words, the inherent instability of the time series was such that a drop for just one year was inadequate to justify program impact. However, analysis of an entire series helps the evaluator to assess changes in context and reject one year movements that may be spurious. Further, a control provides a baseline so that changes that could be due to the innovation can be distinguished from those resulting from other naturally occurring phenomena. Unfortunately, regression towards the mean may still provide an alternative, plausible explanation of program impact as it did for the Connecticut data.

The method of analysis proposed here is called segmented regression<sup>4,5</sup> or piecewise regression.<sup>6</sup> Use of the technique as an evaluation tool is illustrated through an application to assess historical trends in perinatal and postneonatal mortality. In connection with this historical review, a proposal to evaluate a Regionalized Perinatal Care (RPC) program in North Carolina using mortality and morbidity as outcomes is discussed. The definitive analysis for this mortality assessment will be undertaken when seven years of post-program data are available at the end of 1981.

A review of perinatal care literature shows the well known decline in perinatal mortality in the United States since 1965, but dramatic racial and geographic differences among mortality rates continue to exist.<sup>7,8</sup> In an effort to decrease these differences and further reduce mortality, RPC programs have become widespread. These programs

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seek to identify high risk pregnancies and newborn infants in order to obtain consultation and referral services from district (level II) and regional (level III) hospitals. Other aspects of RPC include the provision of transportation, continuing education for physicians, nurses, and other health professionals, and nutritional and social counseling during the prenatal period. These services increase costs, making it advisable to evaluate the effectiveness of regionalization. Although evaluations of RPC programs were known to be planned or in progress in at least 26 states as of 1974, there has been little published information to date.<sup>9</sup> Some evidence of a positive association between RPC and declining perinatal mortality was reported by the Perinatal Mortality Committee of the Province of Quebec over the time period 1967 to 1974.<sup>10, 11</sup>

In 1975 an RPC program was started in five rural counties in southeastern North Carolina and, from its inception, a comprehensive program evaluation has been implemented. Key to the evaluation is comparison of the five-county study region in which the program has been implemented with a three-county control region that does not have the direct benefit of regionalization. The control region was chosen on the basis of its similarity to the study region with respect to demographic, socioeconomic, and perinatal statistics as well as availability of health care facilities and local referral patterns. Details of North Carolina's program and the strategy for its evaluation have been described previously.<sup>9, 12</sup> The overall research design includes an evaluation of the following outcomes: perinatal and postneonatal mortality, maternal and newborn morbidity, infant developmental status, and maternal infant attachment at one year.

### Objectives

The major objective of this paper is to present a segmented regression methodology to analyze interrupted time series designs, common in many evaluations today, and illustrate its use through a statistical assessment of perinatal and postneonatal mortality. An essential feature of the analysis will be to identify changes in time trends and test for differences between the study and control regions that were identified for the North Carolina RPC program evaluation. The second objective is to describe concisely perinatal and postneonatal mortality trends in the study and control regions from 1948 to 1974, the period prior to RPC program funding. The purpose of looking at an extended baseline period is to gain insights regarding reasonable expectations of future trends. It is also of interest to examine the past comparability of study and control regions, although differences prior to the late 1960s would not be expected to invalidate the evaluation design.

### Sources of Data

In contrast to other aspects of the overall evaluation of the RPC program, the impact on mortality can be studied without collecting primary data by using vital statistics from

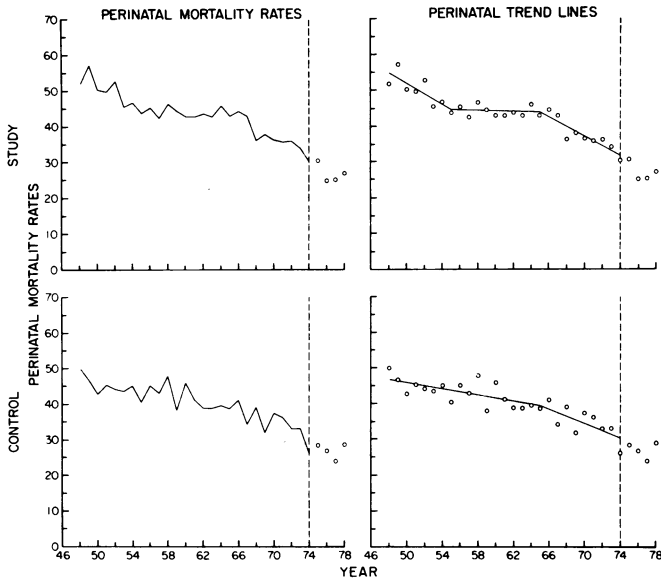
birth and death certificates. Fetal, neonatal, perinatal, postneonatal, and infant mortality rates for study and control regions were calculated by combining data from appropriate counties.\* It is recognized that there could be differences in the quality of reporting vital statistics data between the two regions. No comprehensive assessment of the accuracy of the vital statistics data used has been undertaken although a thorough review of relevant issues was published recently in the *American Journal of Public Health*.<sup>13, 14, 15</sup>

### Methodology

As mentioned in the introduction, the study design for the RPC mortality evaluation may be described as an interrupted time series design with a control group. The interruption is introduction of the perinatal program in the study region. The analytical method needs to be able to detect shifts or changes in trends and then test for differences between study and control changes. A suitable model that adequately describes trends in perinatal mortality from 1948 to 1974 was developed by examining yearly plots of perinatal mortality rates for the study and control regions (Figure 1, left side). The yearly plot for the study region suggests a downward trend in mortality between 1948 and the mid-1950s followed by a leveling off until the mid-1960s, and finally, another decreasing trend from the mid-1960s to 1974. In order to describe these trends in a more exact manner, it was felt desirable to fit a trend line to the yearly perinatal mortality rates. If a reasonable fit to the points was obtained, then trends could be described by a smooth line, eliminating the random variation observed in the jagged plot of Figure 1.

One method of fitting a line to these points is least squares as used in regression analysis. A curve with non-linear terms could be used, but such a model would be difficult to interpret and not appropriate for identifying shifts due to the "interruption" of regionalization. An alternative approach which also uses least squares is segmented or piecewise regression.<sup>4-6</sup> This method is appropriate when the response variable (perinatal mortality) has a linear trend over a certain range of the independent variable (time), followed by another linear trend over a succeeding range. Each time period having a separate linear trend is called a segment, and the years which divide segments are known as join points. When the number of segments and their join points are unknown, they may be estimated using relatively complex methodolo-

\*The definitions of mortality rates conform with those used by the North Carolina vital statistics system: 1) *fetal* (stillbirths of 20 weeks or more gestation per 1000 live births plus fetal deaths); 2) *neonatal* (deaths less than 28 days after birth per 1000 live births); 3) *perinatal* (fetal plus neonatal deaths per 1000 live births plus fetal deaths); 4) *postneonatal* (deaths between 28 days and 364 days after birth per 1000 live births minus neonatal deaths). A 1971 North Carolina law modified the interpretation of a fetal death, since after 1971 therapeutic abortions were no longer considered to be fetal deaths. An example of the law's impact was observed in 1973 when approximately 400 fetal deaths of 20 or more weeks gestation were reported as therapeutic abortions. No information is available regarding whether the impact of the law change was equal in both regions.



**FIGURE 1—Perinatal Mortality Rates and Trend Lines for the Study and Control Regions**

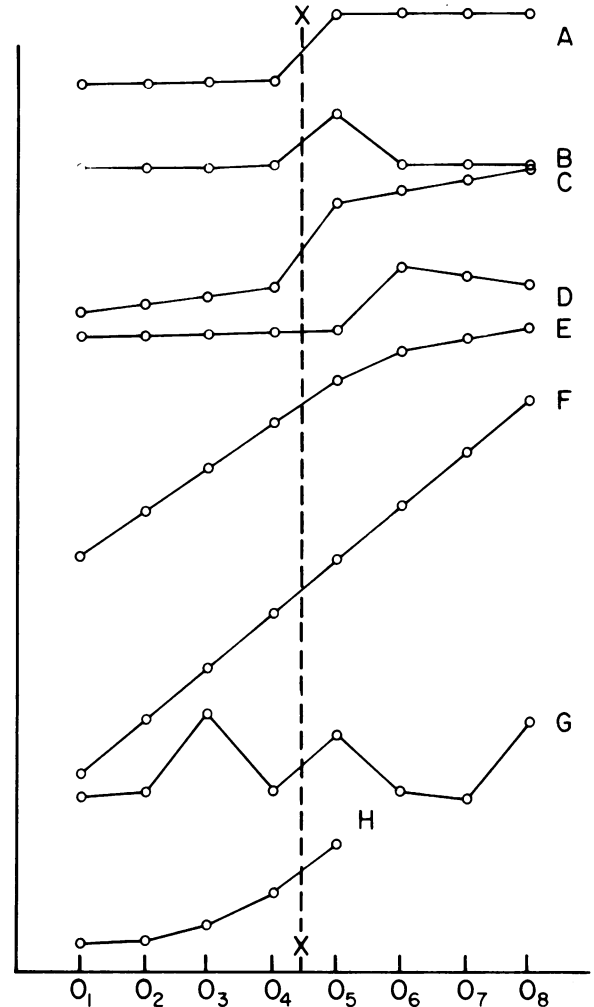
gy.<sup>16, 17</sup> The choice of the join points 1955 and 1965 is subjective but is further supported by sensitivity analyses which indicate that if a preceding or following year was chosen, the trend lines would be unchanged except for shifts in the join points by one year.

Campbell and Stanley<sup>1</sup> identify eight patterns of time series data that may result from a program interruption. These are reproduced in Figure 2. A key consideration is the assumption of independent error terms discussed below. If errors can be considered independent, then segmented regression is appropriate for all cases except B and H. Case B represents a temporary effect and could be detected by fitting a regression line to  $O_1, O_2, O_3, O_4, O_6, O_7,$  and  $O_8$ , i.e., all points except where the temporary impact is supposed to occur. Then a 95 per cent confidence interval for  $O_5$  may be derived from the regression equation and the observed  $O_5$  value compared to this confidence interval. If it is outside the confidence range, then a significant effect can be inferred.

Case H would require a polynomial or other type of regression model, as a linear trend is not appropriate. Usually, situations like H may be identified by inspection or prior knowledge. Further attention to this is given below where a segmented model is compared to polynomial models. The remaining cases (A, C, D, E, F, G) could be handled by segmented regression, although the appropriate join point must be chosen for D if the impact is to be assessed with a powerful statistical procedure.

Details of the proposed segmented regression analysis for perinatal mortality trends are given as Model I in Appendix I. The methodology is identical to ordinary least squares regression, with the response variable perinatal mortality. The following four characteristics or parameters are estimated using this procedure:

$\beta_0$ , the intercept for segment 1 or mean perinatal mortality in 1948;



**FIGURE 2—Some Possible Outcome Patterns from the Introduction of an Experimental Variable at Point X into a Time Series of Measurements,  $O_1$ – $O_8$ . (Except for D the  $O_4$ – $O_5$  gain is the same for all time series, while the legitimacy of inferring an effect varies widely, being strongest in A and B, and totally unjustified in F, G, and H.)**

SOURCE: Campbell DT and Stanley JC: *Experimental and Quasi-Experimental Designs for Research*, Chicago: Rand McNally College Publishing Company, 1966. Copyright 1963 American Educational Research Association, Washington, DC.

$\beta_1$ , the slope for segment 1 or linear trend in perinatal mortality between 1948 and 1955;

$\beta_2$ , the difference in slopes or linear trends in perinatal mortality between segment 1 (1948–1955) and segment 2 (1956–1965); and

$\beta_3$ , the difference in slopes or linear trends in perinatal mortality between segment 2 (1956–1965) and segment 3 (1966–1974).

If the same linear trend continues from the first segment to the second segment, then  $\beta_2 = 0$ . Similarly, if the same linear trend continues from the second to the third segment, then  $\beta_3 = 0$ . If we assume that perinatal mortality rates are normally distributed, then we can test the hypotheses  $\beta_2 = 0$  and  $\beta_3 = 0$  by means of standard procedures in regression.

In addition to changes in slope at the join points, it is also possible for discontinuities in the trend line to occur. This could be due to an event which causes a sudden increase or decrease in mortality with either a continuation of the slope at its previous level or a change in the slope. For example, the introduction of a program designed to decrease perinatal mortality might cause a sudden reduction in mortality rather than a gradual shift through a change in trend. To allow for changes of this sort, the model can contain additional parameters to estimate jumps in the trend line at one or more of the join points. Each additional parameter measures the discontinuity between two adjacent time segments or the difference in mean perinatal mortality for the two estimated trend lines at the join point. As before, we can test whether each of these parameters is significantly different from zero to determine whether a discontinuity at each join point exists.

In applying this methodology to perinatal mortality trends, discontinuity parameters were not included at the join points 1955 and 1965 because there was no reason to expect a sudden shift in mortality at these particular years. However, when extending the model to a fourth time period (1975-1981) to evaluate the impact of regionalization, the addition of a discontinuity parameter between time segments three and four would be appropriate. Model II of Appendix I gives the details of this extension which has two additional parameters, one to estimate discontinuity between trend lines in 1975, and the second to estimate the difference in linear trends between time periods three and four. The program's impact on perinatal mortality will be evaluated by testing whether each of the parameters is equal to zero in the study region, and also testing whether these estimates are equal to corresponding measures for the control region.

It has been suggested that the logarithm of perinatal mortality rates follows a normal distribution more closely than the actual mortality rates.<sup>7</sup> For this reason, the analysis was carried out twice, once using the observed mortality rates and a second time transforming the rates to logarithms. The same parameters were found to be significant in both analyses, and the residual plots were essentially identical. Therefore, to facilitate interpretation, all results will be presented using observed mortality rates rather than logarithms. It should also be noted that the tests of significance used in regression are not invalidated by mild departures from normality.

A critical assumption of the segmented regression methodology is variance homogeneity. Observed mortality may be represented by a binomial distribution, where  $p$  is the true underlying probability of death and  $n$  the number of live births (live births + fetal deaths in the case of fetal or perinatal mortality). Then  $np$  is the expected number of deaths. In practice  $r$ , the observed number of deaths, will not equal  $np$  due to chance fluctuations. These chance fluctuations correspond to the variances of interest when fitting the segmented regression model. It is required that these variances be the same from year to year (homogeneity of variance assumption) in order that the underlying theoretical assumptions be satisfied.

From year to year  $n$  will change by small amounts and  $p$

may change as well. The variance of  $r$  will depend on both  $n$  and  $p$ . Clearly, then, the variances will vary from year to year and so will not be genuinely homogeneous. If there is considerable heterogeneity, weighted least squares procedures should be employed to fit the segmented regression instead of ordinary least squares. Alternatively, some other transformations may be tried such as the square root or arcsin to help stabilize variances. In the present example, plots of residuals showed that variance heterogeneity was only minimal. All of the above alternatives (weighted least squares, square root transformation with ordinary least squares and arcsin transformation with ordinary least squares) were tried but the results changed hardly at all. So the ordinary least squares procedure without a transformation is reported here. In practice this is also the analysis that is most well-known and is a little easier to carry out.

### *Assumption of Independent Error Terms*

It is a moot point whether successive mortality rates are statistically "independent". Clearly, the mortality rates from year to year are linked insofar as they follow a trend and relate to a reasonably constant population in the short term. In this sense the rates from year to year are mathematically dependent. However, regression requires that the "random errors" associated with these rates be independent, not the rates themselves. The random errors are really fluctuations in number of deaths due to instability when small mortality rates are applied to small or moderate numbers of births. By and large, births from one year to the next will be to different mothers, and so there should be little direct carryover of mortality from year to year because of the same mothers giving birth. The Connecticut data concerning the speeding crackdown were analyzed under the assumption of correlated errors of measurement,<sup>3</sup> but those data related to many similar driving patterns by the same drivers in the same cars from one year to the next; so in that case, carryover causing correlated errors of measurement should be substantial, and the method of Box and Tiao<sup>18</sup> should be used. However, the perinatal data show no evidence of violating the assumption of independent error terms,\*\* hence a simple model of segmented regression is appropriate.

### *Perinatal and Postneonatal Mortality Trends*

The segmented regression methodology has been applied separately to all races combined and race specific\*\*\*

\*\*The Durbin-Watson test assumes a first-order autoregressive error model, and tests the null hypothesis that the autocorrelation parameter is zero. For the mortality data being analyzed, this hypothesis was not rejected and, thus, there is no direct evidence that the independence assumption needed for segmented regression is violated.

\*\*\*The term "race specific" throughout this paper is not quite accurate because Blacks and Indians are combined to form one group. This may obscure more detailed race specific differences. However, it was necessary to combine Blacks and Indians in this manner because the numbers of births to Indians were too small in the control region to allow separate analysis.

**TABLE 1—Live Births, Perinatal Deaths, and Perinatal Mortality per 1,000 at Risk**

	1948	1955	1965	1974
Study Region				
Live Births	6,594	6,893	4,639	4,307
Perinatal Deaths	353	308	204	132
Perinatal Mortality per 1000 at Risk	52.0	43.7	43.0	30.1
Control Region				
Live Births	4,344	4,708	3,895	3,310
Perinatal Deaths	223	195	154	88
Perinatal Mortality per 1000 at Risk	50.0	40.5	38.7	26.2
North Carolina				
Live Births	108,834	115,197	97,656	84,246
Perinatal Deaths	5,148	4,608	3,673	2,389
Perinatal Mortality per 1000 at Risk	46.2	39.2	37.0	28.0

perinatal mortality rates in the five-county study region, the three-county control region, and the state of North Carolina. Similarly, trend lines have been fitted to fetal, neonatal, and postneonatal mortality rates. In each case, a parameter indicating a shift in trend was kept in the model if it was significantly different from zero at  $\alpha = .10$ . Otherwise the successive shift parameters were not included, leaving the trend line smooth for the adjacent segments.

Table 1 presents the number of live births, perinatal deaths, and perinatal mortality per 1,000 at risk for the study and control regions and North Carolina for years 1948, 1955, 1965, and 1974, selected for illustrative purposes. The perinatal mortality rates reflect the proposed three segment model in that there are relatively large decreases in perinatal mortality from 1948 to 1955 and 1965 to 1974 but virtually no decrease from 1955 to 1965. At each of the selected years, perinatal mortality is slightly higher in the study region than the control, and at each of the first three time points both areas have higher perinatal mortality rates than the state as a whole.

Most critical to the evaluation of the RPC program is a comparison of perinatal mortality trends in the study and control region as shown in the right hand plots of Figure 1. For the study region, there is a significant linear decrease in perinatal mortality between 1948 and 1955 followed by a period of no change in mortality between 1956 and 1965, and finally another significant linear decrease between 1966 and 1974. For the control region, we see a somewhat different picture. The same downward slope continues over the period 1948 to 1965, indicating that there were no significant changes in linear trend between the first two time segments. This is followed by a change in slope between the second and third segments, with perinatal mortality decreasing more sharply than in segments one and two. A comparison of the two types of plots shown in Figure 1 illustrates the clarification to be gained by fitting the segmented trend lines rather than merely plotting the mortality rates.

It was previously mentioned that an alternative to the segmented regression approach would be to fit a nonlinear

curve to the data. A comparison of the proportion of variation explained ( $R^2$ ) by each approach using the perinatal mortality rates for the study and control regions shown in Figure 1 yields the following results:

	$R^2$ for Study Region	$R^2$ for Control Region
Segmented regression	.91	.77
Polynomial regression		
linear	.82	.73
linear + quadratic	.82	.76
linear + quadratic + cubic	.89	.78
best model using backward elimination algorithm	.89	.77 (quadratic + cubic)

For the study region the same number of parameters are used in the segmented model as in the cubic model, and segmented regression explains a greater proportion of variation in the data. For the control region, the same fit to the data is obtained by applying backward elimination to the cubic model. However, the segmented model is much easier to interpret. The meanings of the quadratic and cubic terms are not readily apparent, particularly when it is ambiguous whether a quadratic or cubic model is more appropriate. However, the curves themselves (cubic or quadratic) are quite different as regards shape. In general, there would be no consistency between models fitted to different situations unless one decided arbitrarily that, say, a quadratic was preferred. As regards how well the model fitted, on some occasions it might be a cubic and on others a quadratic model. Then, it would not be clear how to make sensible comparisons between different situations.

The comparability of study and control regions was further investigated using tests of statistical significance as described in Appendix I, Model III. Null hypotheses of no difference in linear trends between the two regions were tested. During the first and second time periods, trends in the study

**TABLE 2—Per Cent Nonwhite Live Births and Perinatal Mortality per 1,000 at Risk by Race**

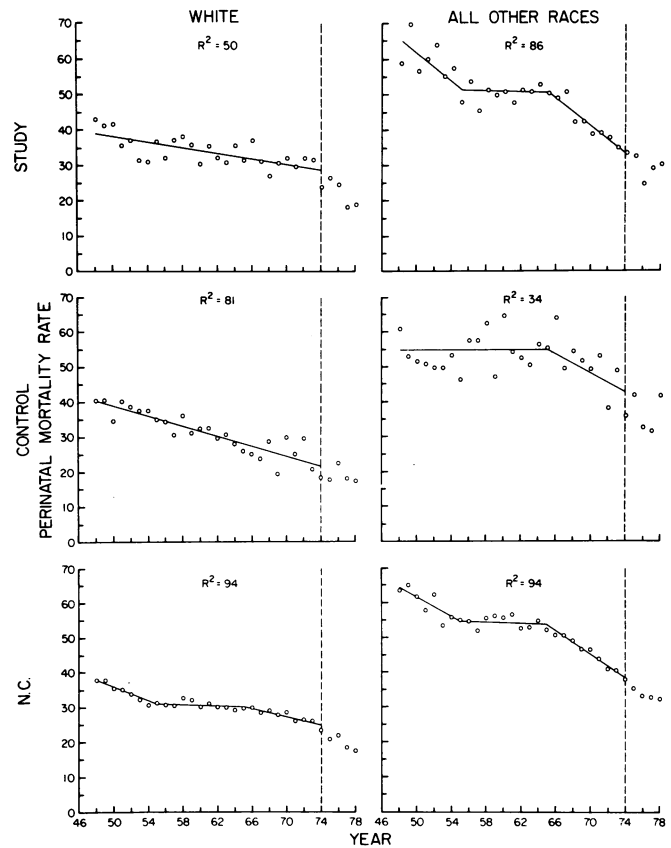
	1948	1955	1965	1974
<b>Study Region</b>				
Per Cent Nonwhite Births	55.3	60.4	59.0	61.8
White Perinatal Mortality	43.1	36.8	31.6	24.1
Nonwhite Perinatal Mortality	59.0	48.2	50.8	33.8
<b>Control Region</b>				
Per Cent Nonwhite Births	46.4	48.1	42.5	44.0
White Perinatal Mortality	40.5	35.0	26.1	18.4
Nonwhite Perinatal Mortality	60.9	46.4	55.4	35.8
<b>North Carolina</b>				
Per Cent Nonwhite Births	31.9	33.3	32.1	31.3
White Perinatal Mortality	37.9	31.2	29.7	23.4
Nonwhite Perinatal Mortality	63.6	55.0	52.2	38.0

and control regions were significantly different ( $p < .05$ ), but there was no statistically significant difference in the more recent time period from 1966 to 1974. This supports the assumption of similarity of study and control regions during the period directly preceding program implementation. The same approach used to test differences in trends between the study and control regions prior to regionalization will also be used for evaluation of program impact during the period 1975 to 1981. The details of this extension of the model and hypotheses of interest are given in Appendix I, Model III.

Trend lines for the two components of perinatal mortality, fetal and neonatal mortality, were also fitted separately for the study and control regions. Since the results were similar to perinatal trends, particularly in the case of fetal mortality, they are not presented here.

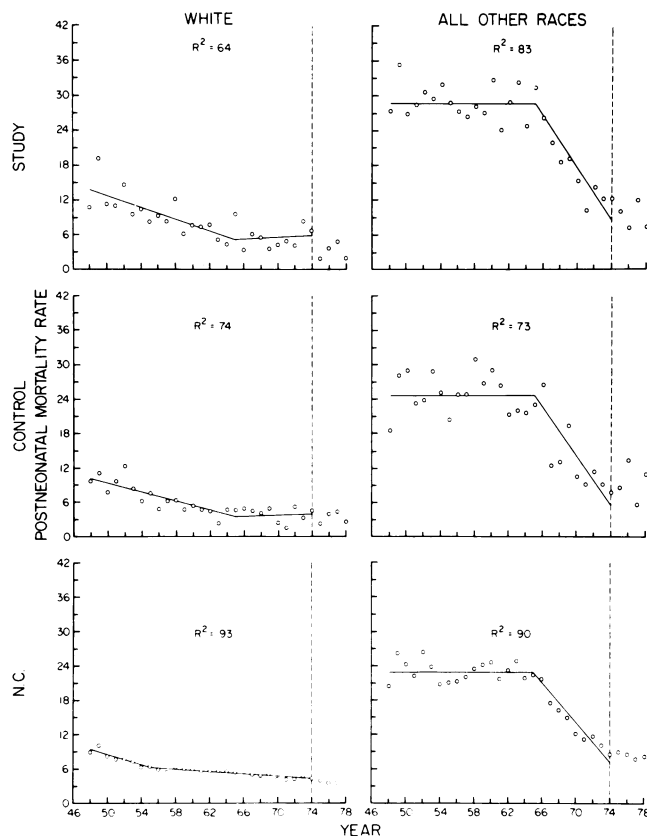
It is well known that perinatal mortality rates differ by race with Blacks having higher mortality than Whites. For this reason, the segmented regression analysis was also carried out separately for Whites and Other Races. The racial composition of live births in the study and control regions and North Carolina is shown in Table 2, along with perinatal mortality by race. The study region has had a lower proportion of White births than the control, primarily due to a large American Indian population. In 1974, the study region had 25 per cent Indian births and 37 per cent Black births. There has been a decrease over time in both White and nonwhite perinatal mortality with the exception of the year 1965 when mortality for Blacks and Indians increased slightly.

Figure 3 presents "race specific" perinatal mortality trend lines. White trends are similar in the study and control regions, and trends for Other Races in the study region are the same shape as overall trends seen in Figure 1. However, the control region's trend line for Blacks and Others indicates that the segmented regression model is not appropriate in this case. Only 34 per cent of variation in mortality rates is explained by the trend line. Although the observed rates follow a smooth line from 1949 to 1953, in general the data points fluctuate too much from year to year for a trend to emerge clearly. This is at least partially due to small numbers since less than one-half of the births in the control region are Black.

**FIGURE 3—Study and Control Region and North Carolina Perinatal Mortality Trends for Whites and All Other Races**

Perinatal mortality rates for the years 1975, 1976, 1977, and 1978 have also been plotted in Figure 3. These are the only data presently available for the time period after the introduction of RPC. It is too early to apply the segmented regression methodology to determine trends for post-1974 data. At present, there is no clear evidence of any shifts in mortality rates.

The focus of the program evaluation is on the perinatal period, but it is also important to examine postneonatal trends to ensure that a decrease in perinatal mortality has not been accompanied by an increase in postneonatal mortality. Such an increase could indicate a postponement of death rather than its prevention. Figure 4 presents "race specific" postneonatal mortality trends for the study and control regions. The most striking aspect of these trends is the tremendous difference between Whites and Other Races. An adequate fit to the data is obtained in all four cases. The study and control regions have had similar trends in postneonatal mortality for Whites and Others with the study region having somewhat higher mortality rates. Prior to 1965, White postneonatal mortality decreased at a constant slope and then plateaued with a slight tendency to increase. However, this upward slope appears to have leveled off for the years 1975–1978. Prior to 1965, postneonatal mortality for Blacks and Others was strikingly higher than White mortality and fluctuated.



**FIGURE 4—Study and Control Region and North Carolina Postneonatal Mortality Trends for Whites and All Other Races**

tuated from year to year with no consistent trend. From 1966 to 1974, there was a sharp downward slope in mortality for Blacks and Others so that racial differences have narrowed considerably in recent years.

Figures 3 and 4 also present “race specific” perinatal and postneonatal trend lines for North Carolina. The North Carolina perinatal mortality trends closely resemble those for the study region as do the postneonatal trends for Blacks and Others. One difference that is observed for White postneonatal mortality is that the North Carolina rates do not show the slight tendency to increase after 1965 that was seen in the study and control regions.

*Discussion*

The analysis of time series designs can be awkward as it is not straightforward to distinguish discontinuities in trend lines from yearly fluctuations that typically occur. However, segmented regression seems to be a natural approach to this methodological problem in the case where the error terms for successive years may be assumed to be independent, since it is designed specifically to deal with situations that involve discontinuities or sharp changes. Segmented regression, as applied here, assumes a linear trend for each successive section. Whereas the assumption of linearity may be un-

warranted over a long interval, usually for the short haul it will serve as a good approximation to most real life situations. A comforting bonus is that linear approximations are easy to understand and the appropriate methodology relatively trivial to apply when modern computer packages are employed.<sup>19</sup> No statistical theory other than regression is required. The North Carolina perinatal and postneonatal data had only a small amount of variance heterogeneity and so ordinary least squares was applied. If variances are definitely heterogeneous, weighted least squares should be employed, where the weights are the inverse of the variances at each time point.

In the present example, the fitting of linear segments to data extending back to 1948 provides an historical review of the nature of previous shifts in trends. This has important implications to the ongoing RPC evaluation in North Carolina. The interpretation of, say, a significantly superior improvement regarding the reduction of perinatal mortality in the study region may be a less than convincing demonstration of the impact of regionalization if there were previous situations, without compelling explanations, where changes, in either direction and of similar magnitude, had taken place. Further, an historical comparison of study with control provides a thorough summary of the degree of similarity of perinatal and postneonatal mortality rates between the two regions. It is important for the control to be judged similar since then there is a valid basis for the assessment of program impact via a comparative analysis. North Carolina as a whole serves as an indirect control in that it identifies broader trends that have been taking place. Note that both pilot and control regional trends are contributing, albeit a small amount, to the overall state trends.

The study region was chosen partly because it had relatively high perinatal mortality, and so it is possible that regression toward the mean might operate to confuse the interpretation of results. However, the indicators of program impact used here are changes in trend as well as sudden shifts. It is unlikely that regression toward the mean will change trends to any large extent although such effects could influence the presence or size of sudden shifts. In any event, regression towards the mean would be as likely to occur in the control as the study region, and so this phenomenon is not regarded as a problem of any consequence for the analysis presented here.

It is well known that birthweight is the most powerful predictor of neonatal and perinatal mortality with the highest rates observed for low birthweight infants ( $\leq 2500$  grams).<sup>20, 21</sup> A decrease in perinatal mortality should be accompanied by changes in birthweight distribution and/or weight-specific mortality rates. Evidence to date suggests that reductions in perinatal mortality have been primarily due to mortality decreases among low birthweight infants, rather than shifts in birthweight distributions, and that this decline is at least partially explained by advances in perinatal medicine such as neonatal intensive care units.<sup>22</sup> Future work on the evaluation of RPC in North Carolina will examine birthweight specific changes in perinatal mortality and changes in birthweight distributions using vital statistics data.

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## APPENDIX

## Segmented Regression Models

## Model I

The segmented regression model for mortality trends between 1948 and 1974 with join points at 1955 and 1965 can be specified as follows:

$$E(y) = \beta_0 + \beta_1 x_1 + \beta_2 (x_1 - 7)x_2 + \beta_3 (x_1 - 17)x_3$$

where  $y$  is the dependent variable, and  $x_1$ ,  $(x_1 - 7)x_2$ , and  $(x_1 - 17)x_3$  are the three independent variables of interest. In particular,

$y$  = yearly perinatal mortality rate

$x_1$  = year - 48

$$x_2 = \begin{cases} 1 & \text{if year} > 55 \\ 0 & \text{if year} \leq 55 \end{cases}$$

$$x_3 = \begin{cases} 1 & \text{if year} > 65 \\ 0 & \text{if year} \leq 65 \end{cases}$$

$\beta_0$ ,  $\beta_1$ ,  $\beta_2$ ,  $\beta_3$  are parameters to be estimated and represent respectively the intercept term and coefficients for the

independent variables. The model is fitted in the normal manner for multiple regression where there are several independent variables. The fact that two of the independent variables are composites of other variables, i.e.,  $(x_1 - 7)x_2$  and  $(x_1 - 17)x_3$  presents no problem. The composite variables are computed and handled like any other single variable. Once the variables have been defined, the model is fitted easily using PROC GLM in SAS.<sup>19</sup>

## Model II

The evaluation of RPC requires the extension of Model I to a fourth time segment, 1975-1981. Two additional parameters are needed, one to estimate discontinuity in trend between segments three and four, and a second to estimate change in slope between segments three and four. The model is specified as follows:

$$E(y) = \beta_0 + \beta_1 x_1 + \beta_2 (x_1 - 7)x_2 + \beta_3 (x_1 - 17)x_3 + \beta_4 (x_1 - 26)x_4 + \beta_5 x_4$$



where the definitions for Model I still apply and

$$x_4 = \begin{cases} 1 & \text{if year} > 74 \\ 0 & \text{if year} \leq 74 \end{cases}$$

$\beta_4$  and  $\beta_5$  are additional parameters to be estimated.

**Model III**

Model II has been used to estimate trends for each region separately. An extension of this model allows tests of significance regarding the equality of trends in the study and control regions as follows:

$$E(y) = z_1\{\beta_{01} + \beta_{11}x_1 + \beta_{21}(x_1 - 7)x_2 + \beta_{31}(x_1 - 17)x_3 + \beta_{41}(x_1 - 26)x_4 + \beta_{51}x_4\} + z_2\{\beta_{02} + \beta_{12}x_1 + \beta_{22}(x_1 - 7)x_2 + \beta_{32}(x_1 - 17)x_3 + \beta_{42}(x_1 - 26)x_4 + \beta_{52}x_4\}$$

where

y = yearly perinatal mortality rate for the study and control regions

$$z_1 = \begin{cases} 1 & \text{for study region} \\ 0 & \text{for control region} \end{cases}$$

$$z_2 = \begin{cases} 1 & \text{for control region} \\ 0 & \text{for study region} \end{cases}$$

$x_1, x_2, x_3, x_4$  are defined as before

$\beta_{01}, \beta_{11}, \dots, \beta_{52}$  are parameters to be estimated.

The following hypotheses can be tested:

$H_0$	Interpretation
$\beta_{01} = \beta_{02}$	The study and control regions are equal with respect to: perinatal mortality in 1948
$\beta_{11} = \beta_{12}$	linear trend between 1948 and 1955
$(\beta_{11} + \beta_{21}) = (\beta_{12} + \beta_{22})$	linear trend between 1956 and 1965
$(\beta_{11} + \beta_{21} + \beta_{31}) = (\beta_{12} + \beta_{22} + \beta_{32})$	linear trend between 1966 and 1974
$\beta_{21} = \beta_{22}$	change in linear trend between time periods one and two
$\beta_{31} = \beta_{32}$	change in linear trend between time periods two and three.

Hypotheses of interest for the program evaluation are:

$H_0$	Interpretation
$(\beta_{11} + \beta_{21} + \beta_{31} + \beta_{41}) = (\beta_{12} + \beta_{22} + \beta_{32} + \beta_{42})$	The study and control regions have equal linear trend between 1975 and 1980.
$\beta_{41} = \beta_{42}$	Change in linear trend between time periods three and four are equal for study and control regions.
$\beta_{51} = \beta_{52}$	There are equal discontinuities in the trend lines for the study and control regions in 1975.

### Early Philosophy on Population Control

*Plato and Aristotle both recommended abortion as a means of controlling the growth of the population. In his inquiry about the ideal state Plato suggested that women after the age of forty should be allowed to have intercourse, but should not give birth to children; in other words should have abortions. And Aristotle thought that abortion should be practiced before the embryo had "sensation and life". Now we know that the Hippocratic Oath forbids physicians to "give to a woman an abortive pessary." How can we reconcile this prohibition with the fact that abortion was generally practiced not only by midwives but also by Hippocratic and other physicians; that it was accepted by society and even recommended by the greatest philosophers of the period?*

*There were, however, religious groups in Greek society, notably the Orphics and Pythagoreans, who perhaps under Indian influence, had profound respect for life. We shall see later that the so-called Hippocratic Oath actually was a Pythagorean document, which, therefore, did not represent the general view of the period but was rather a reform program, a manifesto of a relatively small religious group.*

*Sigerist H: A History of Medicine, Volume II: Early Greek, Hindu and Persian Medicine. New York: Oxford University Press, 1961.*