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The Relationship of Blood Lead Levels and Blood Pressure in NHANES II: Additional Calculations

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In performing research for associations and relationships among the data thus far published from the NHANES II survey, only the data for the 64 communities involved may be used. The simple omission of a few essential data makes impossible any valid analysis from the data for the 20,325 individual respondents.

In this research for associations between blood lead levels and blood pressure in NHANES II, the method of forward stepwise regression was used. This avoids the problem of inflated error rates for blood lead, maximizes the number of data analyzed, and minimizes the number of independent variables entered into the regression model, thus avoiding the pitfalls that previous NHANES II research of blood lead and blood pressure has fallen into when using backward stepwise regression.

The results of this research for white male adults, white female adults, and black adults were contradictory and lacked consistency and reliability. In addition, the overall average association between blood lead level and blood pressure was so minute that the only rational conclusion is that there is no evidence for this association to be found in the NHANES II data.

Introduction

The design and operation of the Second National Health and Nutrition Examination Survey, 1976–1980 (NHANES II), has been previously described and commented upon (*1–3*). Essentially, the survey consisted of 64 communities selected at random by a probability sample from among 1924 geographic localities within the 48 states of the contiguous U.S. Within these 64 primary sampling units, districts were selected at random, housing clusters were selected within districts, and households were selected within housing clusters. This design achieved 20,325 sets of responses from a survey of 27,803 noninstitutionalized civilians of ages 6 months to 74 years.

The NHANES II data set includes responses about medical history, dietary recall, health-related behavior, and direct medical examination. Thus, a wealth of data are available for testing hypotheses and computing associations among many health-related indices and measurements. The hierarchical or multistage nature of the survey and the differential weightings of the cases involved preclude the use of simple statistical methods for determining the associations and testing the hypotheses of interest. It is possible (*4,5*) to compute regressions among the 64 communities, among the enumeration districts, among the housing clusters, among the households, or among the 20,325 respondents. This methodology is usually known as analysis of covariance. The particular stage or level of the hierarchy of the design that one chooses to do the regression calculations on depends upon the hypothesis to be investigated. In the case of NHANES II, it also depends upon the information made available by the National Center for Health Statistics (NCHS). In the data published from this survey, only the 64 primary sampling units have been numbered. The other levels of clustering are not identified. Consequently, the only regressions that can be performed currently are the ones using the data for the 64 communities (*1*). Thus, any multiple regression models (*4,5*) must involve fewer than 63 variables, otherwise the problem of fitting regression lines through every one of the 64 data points is inevitably encountered (*6,7*). A more careful regression analysis might be computed using the 20,325 data points, which correspond to the individual respondents in the survey. The resulting inference would then apply to people rather than to communities as at present. However, it will not be possible to do this until NCHS (in addition to numbering the 64 communities) also numbers the other levels of clustering on the data tapes.

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Blood Lead and Blood Pressure

To investigate the possible association of systolic and diastolic blood pressure levels with blood lead transformed to the logarithm in NHANES II, the following regression analyses were performed among the 64 data corresponding to the communities. The dependent variables were the two blood pressure variables, and the independent or explanatory variables were blood lead and demographic, socioeconomic, dietary variables, and other likely confounders that have been listed previously (*2,3*). Analyses were computed separately for white males, white females, and blacks. Data for 20 year age intervals from 21 to 40 through 46 to 65, with consecutive increments of 1 year, were used as described earlier (*2,3*) to provide an assessment of the reliability of the calculations.

Previously, the well-known method of backward stepwise regression analysis has been frequently used with NHANES II data (*2,3,6,7*). However, in this study the alternative method of forward stepwise regression (*8*) was chosen for several reasons. When the initial number of variables in the analysis is large (more than 30) or exceeds 63, then a backward regression will provide unreliable results or even completely erroneous results (*6,7*). Retaining blood lead in the regression model at each backward stage irrespective of its statistical significance will inflate the error rate for this variable far above the 0.05 level and thus negate any possible conclusions about hypotheses of association. Any large survey there will inevitably be missing values throughout the collected data set. Using backward regression, the net number of respondents in the analysis will be smaller and will increase as nonsignificant variables are eliminated. In forward stepwise regression, the number of respondents will be greatest and therefore more reliable. Sometimes two totally different regression models can and have arisen from the same subset of HNANES II data using these two regression methods. Thus, foward stepwise regression is the preferred method here.

In these analyses, the most significant explanatory variable was entered first into the model. Additional variables were then entered into the model until there were no longer any significant variables remaining. If blood lead had not already been included by the final step, it was added to the model to establish its significance and obtain the value of its slope coefficient.

Results

The results of the regression analyses for white males, white females and blacks are displayed in Table 1. Blacks were not analyzed according to gender because of the amount of data available for them as considerably less than for whites. The rows of the table correspond to 20 year age groups that have consecutive

Table 1. Increase in systolic and diastolic blood pressure for a doubling of blood lead level and significance level for selected age and demographic groups from HNANES II.

	White males				White females				Blacks			
Age group	Systolic increase	Significance	Diastolic increase	Significance	Systolic increase	Significance	Diastolic increase	Significance	Systolic increase	Significance	Diastolic increase	Significance
21–40	1.1	0.371	0.5	0.608	−0.3	0.774	0.8	0.345	5.0	0.051	4.4	0.009
22–41	1.1	0.351	0.6	0.572	−0.3	0.760	0.5	0.568	4.6	0.080	4.8	0.007
23-42	1.5	0.237	0.7	0.500	−0.3	0.734	0.6	0.527	4.7	0.089	5.5	0.004
24–43	1.7	0.178	0.5	0.629	−0.1	0.893	0.5	0.560	4.4	0.109	5.6	0.004
25–44	1.9	0.086	0.6	0.522	−0.3	0.733	0.4	0.655	4.1	0.184	5.4	0.009
26–45	2.1	0.054	0.7	0.444	−0.1	0.903	0.6	0.572	5.7	0.045	4.9	0.006
27–46	2.2	0.058	1.3	0.155	−0.3	0.743	0.6	0.516	5.5	0.055	5.0	0.004
28–47	2.4	0.046	1.6	0.131	−0.2	0.439	0.3	0.751	5.1	0.051	4.9	0.019
29–48	2.5	0.044	1.6	0.146	−0.5	0.641	0.4	0.661	5.3	0.059	5.2	0.019
30–49	3.3	0.018	1.7	0.113	−0.9	0.448	0.2	0.877	4.4	0.147	4.5	0.050
31–50	2.7	0.060	1.6	0.178	−0.8	0.468	0.3	0.750	3.3	0.336	4.1	0.099
32–51	2.4	0.129	1.3	0.308	−0.2	0.893	0.8	0.456	2.9	0.389	3.9	0.129
33–52	2.6	0.093	1.4	0.260	−0.3	0.792	0.6	0.571	1.0	0.746	2.5	0.313
34–53	3.4	0.016	1.6	0.141	−0.2	0.854	0.8	0.372	0.8	0.797	1.6	0.573
35–54	4.4	0.002	2.2	0.059	−0.3	0.832	0.8	0.414	−0.9	0.805	0.9	0.764
36–55	4.3	0.004	2.2	0.068	−0.5	0.714	0.7	0.414	−1.5	0.655	1.5	0.629
37–56	4.1	0.003	1.8	0.141	−0.7	0.589	0.8	0.419	−1.6	0.612	2.2	0.467
38–57	3.9	0.004	1.7	0.115	−0.7	0.611	0.6	0.533	−1.5	0.590	2.1	0.479
39–58	4.2	0.003	1.6	0.165	−0.9	0.528	0.8	0.495	−2.6	0.305	0.9	0.734
40–59	3.9	0.005	1.4	0.194	−0.9	0.534	0.7	0.486	−4.2	0.049	−0.5	0.853
41–60	3.6	0.013	1.2	0.258	−0.4	0.762	1.3	0.152	−2.9	0.221	−1.0	0.740
42–61	3.0	0.040	1.2	0.278	−0.3	0.829	1.0	0.253	−2.3	0.493	−1.4	0.686
43–62	2.9	0.044	1.3	0.225	−0.3	0.815	1.0	0.233	−2.8	0.462	−2.5	0.376
44–63	2.4	0.124	1.3	0.165	−0.1	0.929	0.8	0.304	−3.8	0.324	−3.0	0.686
45–64	2.3	0.151	1.4	0.152	0.5	0.714	1.2	0.111	−4.2	0.321	−3.5	0.270
46–65	2.3	0.155	1.4	0.166	0.7	0.591	1.1	0.119	−4.7	0.226	−3.7	0.215
Mean	2.777		1.323		−0.335		0.700		0.915		2.88	
SD	0.972		0.476		0.374		0.276		3.730		3.088	

increments of 1 year. The columns of the table represent the estimated increase of blood pressure (in millimeters) that corresponds to a doubling of the level of blood lead and the significance level of the coefficient. These are porvided for both systolic and diastolic blood pressure for the three population groups.

For white males, the incease in systolic blood pressure for doubling of blood lead ranges from 1.1 mm Hg to 4.4 mm Hg. The largest values occur around the 36 to 55 age group and achieve significance levels of about 0.005. For diastolic blood pressure the increase ranges from 0.5 to 2.2 mm Hg. Again, the largest values occur around the 36 to 55 age group, but do not achieve statistical significance.

For white females, the change in systolic blood pressure for a doubling in blood lead levels ranges from a loss of 0.9 mm Hg to a gain 0.7 mm Hg, while for diastolic blood pressure the range is from a gain of 0.2 mm Hg to a gain of 1.3 mm Hg. None of these changes are statistically significant.

For blacks the change in systolic blood pressure ranges from a loss of 4.7 mm Hg in the older age groups to a gain of 5.7 mm Hg in the younger age groups. Of these, only two age groups achieve statistical significance, the 26 to 45 year age group with a significance of 0.045, and the 40 to 59 year age group with a significance of 0.049. The change in diastolic blood pressure for a doubling of blood lead levels ranges from a gain of 5.6 mm Hg in the younger age groups to a loss of 3.7 mm Hg in the older age groups. Only the changes in the younger age groups are significant, with 0.004 being the best significance level achieved.

In summary, Table 1 shows an overall average increase of 1.1 mm Hg in systolic blood pressure and 1.4 mm Hg increase in diastolic blood pressure for a doubling of blood lead levels. In white males the increase in blood pressure appears to be more in the older age groups, in white females there is no age bias, but a decrease in systolic blood pressure and an increase in diastolic blood pressure. On the other hand, in blacks, the largest increase in blood pressure occurs in the younger age groups and turns into a decrease in the older age groups.

Discussion

The NHANES II survey is a valuable source of date and provides a sound basis for investigating questions about and possible associations with the nation's health. However, although NCHS has achieved a major accomplishment in publishing the results of the survey, an apparent simple oversight prevents researchers from examining relationships among the individual respondents in the survey, even though calculations among the 64 communities can be made. This drawback has led to a modicum of contention and debate about some of the results published thus far from the NHANES II survey (*2,6,7*).

In this particular piece of research, the possible association of blood lead level and blood pressure elevation has been examined. The overall average increase in systolic and diastolic blood pressure for a doubling of blood lead in adults 21 to 65 years of age was 1 mm Hg and 1.5 mm Hg, respectively. While this result does not constitute a starting elevation, the questions of its reliability and possible evidence of causation need to be examined further.

To help answer these questions, several analyses of the data were performed, from the 21 to 40 year age group through the 46 to 65 year age group. This was repeated for white males, white females, and blacks. The increase in blood pressure for the older age groups in white males is missing in white females and is contradicted in older blacks, where instead it decreases. A statistically significant increase in blood pressure occurs in only 24 out of 156 analyses, or 15% of them. The remainder are not statistically significant or present a significant decrease. Thus these results do not provide evidence of any reliability or of any consistency for the hypothesized association.

Even though the increase in blood pressure for a doubling in blood lead is not reliable or consistent, ranging from a decrease of 4.7 mm Hg to a increase of 5.7 mm Hg, the average increase is 1.245 mm Hg, nevertheless. The blood lead level measured in the survey for adults 21 to 65 years of age fell from 15.29 mm Hg to 11.02 mm Hg during the 4 years that NHANES II was being conducted. Therefore, the improvement in reduction of blood pressure from this decrease in blood lead would be expected to be about 0.5 mm Hg. Thus, the strength of the association is only negligible or weak, certainly not strong.

The research carried out here using the NHANES II survey data to look for possible associations between blood lead levels and blood pressure levels was carefully undertaken to aviod the pitfalls and errors found in previous studies (*6,7*). The number of variables used in the regression model was far less than 63 and was, in fact, less than 30, thus avoiding the problem of fitting the regression through all 64 data points. The use of forward stepwise regression allowed the maximum number of data to be used. The use of forward stepwise regression avoided the need to retain blood lead in the model even when not significant and thus avoided inflating the error rate. The results obtained by this careful process lacked consistency, lacked reliability, and were weak or negligible. It is concluded, therefore, that there is no convincing evidence of an association between blood lead and blood pressure in NHANES II.

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