BLOOD PRESSURE AND AGEING; RESULTS OF A 15–17 YEAR FOLLOW-UP STUDY IN SOUTH WALES

W. E. MIALL AND SUSAN CHINN

M.R.C./D.H.S.S. Epidemiology and Medical Care Unit, and Division of Computing and Statistics, Clinical Research Centre, Northwick Park Hospital, Harrow, Middx.

SUMMARY

1. Several recent studies of the relation between blood pressure and ageing have been re-examined, and it is concluded that none satisfactorily investigates the possibility of separate influences of age and attained pressure in determining the rate of change of pressure with time.

2. If the rate of increase of pressure is proportional to the attained pressure, pressure is an exponential function of age. An attempt has been made to determine the relation of blood pressure with age by fitting curves to individuals' measurements made over periods of 15½ and 17½ years in two epidemiological surveys in South Wales.

3. Three models were used: (1) a linear regression, (2) an exponential function, and (3) a model based on the hypothesis that an individual's pressure fluctuates about a constant mean until a variable age at which it increases at a constant rate. Neither model (2) nor model (3) was significantly better than model (1), but this may have been largely due to the small number of measurements (four) for each subject.

4. A positive slope to the linear regression of pressure on time was obtained for most adults. In middle-aged subjects the distributions of these regression coefficients appear unimodal. The rate of increase was higher in those with initially raised values but increased with age independently of the blood pressure level. In these populations some factor related to ageing appears to play a rôle in causing this increase in pressure in addition to any possible direct influence of the attained pressure.

Key words: blood pressure, age, attained pressure.

If the change of a medical characteristic tends to be predominantly in one direction, and takes time to occur, it is age related, but is not necessarily caused by the degenerative changes of...
ageing. Obesity increases with age, but ageing is not directly involved in its causation. What is the position with respect to hypertension and ageing? In this paper we re-examine some recent analyses which have been carried out to attempt to answer this question and report the results of further analyses of data collected in two longitudinal studies carried out in South Wales between 1954 and 1971.

That arterial pressure appears to increase as a result of ageing is an almost general finding, but in all population studies there is a proportion of old people who have the blood pressures of young adults and total populations exist in the Pacific islands, for example, in which there is little or no tendency for blood pressures to be higher among the elderly (Maddocks, 1961, 1967; Lovell, 1967). In some populations in New Guinea both systolic and diastolic pressures appear, from cross-sectional data, to show a slight but consistent decline with advancing age (Maddocks & Rovin, 1965). Such findings indicate that ageing is not always a cause of raised pressure and pose the question whether ageing, per se, is ever its cause.

TABLE 1. Multiple regression equations for change of pressure on mean pressure and age, South Wales

<table>
<thead>
<tr>
<th>Population</th>
<th>Change in pressure</th>
<th>Constant</th>
<th>Multiple regression coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean pressure</td>
<td>Age</td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rhondda Fach</td>
<td>Systolic</td>
<td>-45.7</td>
<td>+0.358*</td>
</tr>
<tr>
<td></td>
<td>Diastolic</td>
<td>-16.9</td>
<td>+0.256*</td>
</tr>
<tr>
<td>Vale of Glamorgan</td>
<td>Systolic</td>
<td>-28.8</td>
<td>+0.243*</td>
</tr>
<tr>
<td></td>
<td>Diastolic</td>
<td>-14.5</td>
<td>+0.198*</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rhondda Fach</td>
<td>Systolic</td>
<td>-26.7</td>
<td>+0.220*</td>
</tr>
<tr>
<td></td>
<td>Diastolic</td>
<td>-6.7</td>
<td>+0.123†</td>
</tr>
<tr>
<td>Vale of Glamorgan</td>
<td>Systolic</td>
<td>-23.6</td>
<td>+0.235*</td>
</tr>
<tr>
<td></td>
<td>Diastolic</td>
<td>-16.0</td>
<td>+0.243*</td>
</tr>
</tbody>
</table>

* Significant at 0.1% level.
† Significant at 5% level.

Statistical techniques available for the analysis of longitudinal data are less well developed than those for cross-sectional studies. When relating the change between two measurements \((x_2 - x_1)\) to the initial measurement \((x_1)\) we are not dealing with statistically independent variables because \(x_1\) features in each. If the measurements are subject to fluctuation, those with initial readings which are recorded when atypically high will tend to show less positive change, whereas those with atypically low initial readings will show greater positive change, when re-examined later. This manifestation of regression towards the mean can be overcome by relating the change between measurements \((x_2 - x_1)\) to their mean \(\frac{1}{2}(x_2 + x_1)\), as advocated by Oldham (1962, 1968). This was the technique used by Miall & Lovell (1967) in an analysis of the changes in pressure occurring in population samples in the Rhondda Fach and Vale of Glamorgan, in
Blood pressure and ageing

South Wales, between initial measurements made in 1954 and 1956 and those made in 1964, i.e. after intervals of 10 years and 8½ years. Preliminary analyses seemed to suggest that change of pressure was more closely related to the pressure attained than it was to age, and multiple regression analyses of change of pressure on mean pressure and age were carried out which seemed to confirm this. The equations are shown in Table 1.

This finding accorded with Volhard’s hypothesis of a vicious circle mechanism in which any sustained increase in blood pressure initiates structural or functional changes in the vessels or organs which in turn lead to a further rise in pressure (Volhard, 1948).

However, Feinleib, Halperin & Garrison (1969), in a paper read to the American Public Health Association, pointed out that the sign and magnitude of the correlation between the differences of two measurements and their mean depends on the variances of the measurements at the respective examinations. If the second variance is greater than the first the correlation will be positive; if it is equal to, or less than the first it will be respectively zero or negative. As the variance of the blood pressures of a group of people increases with time, and that of their ages remains constant, the findings of Miall & Lovell (1967), it was pointed out, were predictable in terms of what was to be expected from regression theory.

Feinleib et al. (1969) used measurements from the first seven biennial examinations in the Framingham Heart Study to re-examine the relation between blood pressure and age. As the first two inter-survey intervals in that study had shown a fall in mean pressures, attributed to a stress effect at the earlier examinations, subjects were classified according to their pressures at examination 3 and the trends in pressure from examinations 4 to 7 were noted for each group. By this means they believed they had overcome both the effects of acclimatization to a strange procedure and the phenomenon of regression towards the mean; having done so, Feinleib et al. (1969) claimed that their data showed that the rate of increase of pressure with time was independent of the initial pressure.

However, an examination of the Framingham data used shows that the initial secular trend towards lower pressures was followed by a subsequent secular trend towards higher values. When the mean systolic pressures are plotted for groups according to their age at the third examination it is clear that the rise in pressure from examination 3 to 7 is greater than expected because the separate trends fail to fit where they overlap neighbouring age groups. This second secular trend in either the pressures or their measurement seems to invalidate the authors’ conclusion that pressure rises with the passage of time in all groups independently of the pressure attained.

Few other attempts have been made to examine the relation between change of pressure and ageing. Harlan, Osborne & Graybiel (1962), in an analysis of longitudinal data collected over 18 years in the 1000 Aviator study, concluded that age alone did not appear to have a significant influence on blood pressure after the effects of other variables known to affect pressure had been removed. Oberman, Lane, Harlan, Graybiel & Mitchell (1967), in a subsequent analysis of the same study, concluded that blood pressure does not necessarily rise with age, but their 30 year follow-up will take the cohort to an age at which changes in pressure can be better studied. Mathewson, Corne, Nelson & Hill (1972) reported the results of a similar study of 20 years’ follow-up of 3869 young North American aviators in which they found systolic pressure unaffected by age from 15 to 49, and diastolic pressure unaffected by age from 15 to 44 but beyond these points an apparent effect of age was demonstrated, particularly in those with the higher readings. Evans & Rose (1971) reported the analysis of 5–15 year longitudinal data
from industrial employees which showed that the individual's rate of increase of pressure correlated with his pressure and was independent of age; they commented that 'if rate of increase throughout adult life is an individual characteristic, it is inevitable, other things being equal, that people with higher rates of increase will attain higher levels'. The important question concerning a possible vicious circle phenomenon remains unanswered, and we have been trying another method in an attempt to answer it.

METHODS

Populations and surveys
Details of the populations studied and the technique used in our surveys in South Wales have been described by Miall & Oldham (1958). Casual blood pressure measurements were made by one observer throughout, using an orthodox sphygmomanometer, and with the exception of 10% of the final survey's measurements, making all readings in the subjects' own homes. At each follow-up new measurements were made without reference to previous findings. The first examinations in the Rhondda Fach, a mining valley, were carried out in 1954 and follow-up surveys were undertaken in 1958, 1964 and 1971. In the agricultural Vale of Glamorgan the first survey was carried out in 1956 and repeated in 1960, 1964 and 1971. The intersurvey intervals therefore differ in the two studies whose total durations were 17½ years in the Rhondda and 15½ in the Vale. The extent of the follow-up is shown in Table 2.

Table 2. Extent of follow-up: Welsh blood pressure surveys, Rhondda Fach, 1954–71; Vale of Glamorgan, 1956–71

<table>
<thead>
<tr>
<th>Population</th>
<th>No. examined initially</th>
<th>Died</th>
<th>%</th>
<th>Left area</th>
<th>No.</th>
<th>%</th>
<th>Re-examined in final survey</th>
<th>% of available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhondda Fach</td>
<td>1216</td>
<td>231</td>
<td>19.0</td>
<td>188</td>
<td>15.4</td>
<td>762</td>
<td>62.6</td>
<td>95.6</td>
</tr>
<tr>
<td>Vale of Glamorgan</td>
<td>1464</td>
<td>268</td>
<td>18.3</td>
<td>242</td>
<td>16.5</td>
<td>899</td>
<td>61.5</td>
<td>94.2</td>
</tr>
</tbody>
</table>

Analysis
Mean systolic and diastolic pressure data were calculated, in 5 year age-groups, for each sex and survey. The resulting curves (illustrated for systolic pressure for Rhondda females, Fig. 1) showed little change in the shape or position of the means from survey to survey indicating that for both systolic and diastolic pressure there exists a relationship with age, whether direct or indirect, which it should be possible to determine. If the shape of the curve were a property of the cohort there would be a shift, between surveys, with the passage of time. A function of age which is non-linear in its parameters, when averaged over a number of subjects, may produce a mean pressure curve in form quite unlike that followed by an individual's pressure. To determine the nature of the relationship of pressure with age it is therefore necessary to fit curves to each person's data.
The mean curves show that over a wide age range systolic pressure does not increase at a constant rate, for then the mean curves would themselves show a linear trend with age. However, over the time-intervals covered by the surveys, a linear regression of pressure on age may adequately describe the data, and this model provides a suitable basis for comparison with other models.

If the rate of increase of pressure is proportional to the attained pressure, then pressure is an exponential function of age. The mean systolic pressure curves suggest that this is a possible relationship for ages above 20 years, and therefore an exponential model was used. A third model was based on the postulate that in adults arterial pressure fluctuates about a constant mean ($\alpha$) until an age ($z$) after which it increases at a constant rate ($\beta$).
The three models considered were:

1. \[ y = \mu + \nu x + \epsilon \] (two parameters, \( \mu, \nu \))
2. \[ y = y_0 e^{\lambda x} + \delta + \epsilon \] (three parameters, \( \lambda, \delta, y_0 \))
3. \[ y = \alpha + \epsilon \text{ where } x < z \]
\[ y = \alpha + \beta (x - z) + \epsilon \text{ where } x \geq z \] (three parameters \( \alpha, \beta, z \))

where \( y \) = arterial pressure in mmHg
\( x \) = age in years
\( \epsilon \) = error term

To be able to fit models with three parameters, subjects who were not seen at all four surveys were omitted. Any person who had been treated for hypertension or had suffered a cardiovascular incident likely to have changed the course taken by his pressure was also excluded. Models (2) and (3) are plausible only for adults. All subjects aged under 20 years at the first survey were therefore excluded for comparison purposes, leaving a total of 996.

For each individual's systolic and diastolic pressures the parameters were estimated by minimizing the residual sums of squares. For the exponential model this was achieved by choosing three initial values of \( \lambda \) and using quadratic interpolation to give an approximate minimum, repeating the process at least twice, each time in the neighbourhood of the last estimate of \( \lambda \). In order to fit the third model, \( z \) was successively constrained to lie in each inter-survey interval. If \( z \) is less than the individual's age at the first survey, then the estimate of \( \beta \) is the same as that of \( \nu \) in model (1); \( z \) and \( \alpha \) cannot be estimated. The parameters were taken as those corresponding to the least of the minima so found. For systolic and diastolic pressure, and for each sex and area, the individual residual sums of squares were pooled to give residual sums of squares for each model.

Analyses were also undertaken to allow an examination of the trends of systolic pressure for groups at different values of pressure and age. Subjects treated for hypertension, and those subsequently dying or suffering cerebrovascular accidents or myocardial infarctions were not

<table>
<thead>
<tr>
<th>Table 3. Total residual sums of squares</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model (1)</td>
</tr>
<tr>
<td>-------------</td>
</tr>
<tr>
<td>Rhondda Fach</td>
</tr>
<tr>
<td>Males Systolic</td>
</tr>
<tr>
<td>Diastolic</td>
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<tr>
<td>Females Systolic</td>
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<tr>
<td>Diastolic</td>
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</tr>
<tr>
<td>Diastolic</td>
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</tbody>
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Blood pressure and ageing

excluded from these analyses. The initial measurements were used to classify the subjects but subsequently discarded.

RESULTS

Total residual sums of squares obtained from the three models are shown in Table 3. Models (2) and (3), having one more parameter than model (1), produced smaller residuals but these were more than half that obtained by model (1) in all but one case (Rhondda males, systolic pressure, model 3). It can therefore be concluded that neither model (2) nor model (3) was significantly better than model (1).

Fig. 2. Distributions of rate of increase of systolic and diastolic pressures (mmHg/year); Rhondda Fach and Vale of Glamorgan.
Neither model (2) nor model (3) was satisfactory for other reasons. For about a third of subjects there was no unique set of parameters giving a minimum residual sum of squares for model (2), and with model (3) it was not possible to distinguish between the situation in which the individual's pressure had begun to rise at a low rate before the first survey and that in which it did not reach the hypothetical point of change until after the fourth. The estimates of $z$ were found to be equal to the age of the subject at one of the first three surveys in almost every case, including older subjects for whom, if the model is plausible, one would expect $z$ to be less than the age at the first survey.

The slopes of the linear regressions were significantly different from zero (at the 5% level) in about 10% of subjects for systolic pressure and 7% for diastolic pressure, the low values
Blood pressure and ageing

being explained by fluctuations of the individual's pressure and the small number of degrees of freedom. The greatest rates of increase of systolic pressure are found in adolescents and in the middle-aged; for diastolic pressure the rate of increase is greatest in adolescence and diminishes with age. The distributions of the calculated rates of change of systolic and diastolic pressure are shown in Fig. 2 for those whose mid-ages during observation were within the three decades 35–64 years. The slopes of the regressions vary between +6 and −2 mmHg/year for systolic pressure and +3 and −2 mmHg/year for diastolic pressure. In neither sex is there convincing evidence of bimodality.

Fig. 4. Trends of mean systolic pressure for females followed up for 10 years from survey 2, classified according to systolic pressure and age at survey 1. Rhondda Fach and Vale of Glamorgan.

---, Groups with ten or more subjects; ----, groups with less than ten subjects.
Among these untreated survivors in this age range 38% of men and 25% of women showed a rate of increase of systolic pressure of less than 6 mmHg in 15 years. Of men and women of this age 57% and 44% respectively showed little increase in diastolic pressure, using the same criterion. (The inclusion of survivors who had either received treatment for hypertension or suffered a major cardiovascular complication would diminish these proportions.)

The trends in systolic pressure followed by groups classified according to their initial pressures (illustrated for the two surveys pooled in Figs. 3 and 4) show an overall tendency for groups to retain their relative positions, but to follow diverging paths. The rate of increase of pressure is greatest in those with the higher pressures but, in almost all pressure groups, increases with age.

DISCUSSION

Although the evidence points towards a non-linear relationship of systolic pressure with age when considered over a wide age range, it was not possible to demonstrate this for individuals over the 15½ and 17½ years covered by the two surveys. The results are not inconsistent with an exponential function from age 20, nor are they inconsistent with the postulate that systolic pressure in adults fluctuates about a level characteristic for each individual until a variable age at which it starts to increase.

Although the analyses were based on a large number of subjects they were limited by the infrequency of measurements for each individual; for each subject a curve had to be derived from only four measurements and though the measurements themselves related well with the incidence of cardiovascular morbidity and mortality experienced by the whole group, they were subject to the variability characteristic of any series of blood pressure readings. Had the exponential model fitted the data better than the linear model we had hoped to explore the distributions of the parameters to determine whether the rate of increase of pressure depended more on the level of pressure attained than it did on age. This hope was not realized.

The majority of subjects in these two populations had a positive slope to their regressions of pressure on time, but over a third of middle-aged men and a quarter of middle-aged women showed no important increase of systolic pressure (i.e. less than 6 mmHg in 15 years) and more than half the men and almost half the women showed no important increase in diastolic pressure. It has been stated that middle-aged populations can be divided into two classes: those whose pressures rise but little with age and those whose pressures rise steeply (Platt, 1961). The distributions of the rates of change of pressure (Fig. 2) show no natural boundary separating these two classes in South Wales. The rate of increase is higher in those with raised initial values (Figs. 3 and 4) but increases with time at all levels of pressure in these populations. This increase of pressure with the passage of time is not restricted to adults with higher levels, as was suggested previously (Miall & Lovell, 1967). In South Wales it can occur at all levels of pressure. Some factor other than the attained pressure and perhaps causally related to ageing appears to play an important rôle. Whether the level of pressure influences its own rate of increase has yet to be determined and opportunities to investigate this by direct experiment during the course of therapeutic trials may be more rewarding than by the analysis of observational data.
Blood pressure and ageing

REFERENCES


