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# PROGNOSIS OF TREATED HYPERTENSION 1951–1981

C.J. BULPITT
Royal Postgraduate Medical School and London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT

**1** The 5 year survival of hypertensive patients in several studies was reviewed to demonstrate the adverse effects of increasing age, being male, having a higher untreated blood pressure or severe retinal changes.

**2** The decrease in survival with increase in diastolic blood pressure was not linear, mortality being relatively constant below 90 mmHg.

**3** The adverse effect of severe retinal changes was independent of the untreated blood pressure.

**4** In patients selected with mild hypertension, 5 year survival can exceed 97% even when untreated.

**5** Owing to the lack of suitable data we cannot conclude that treatment was more effective in prolonging life in the 1970s than in previous decades.

**6** In the United States non-white patients with hypertension fared worse than white patients.

**7** The serum cholesterol was not positively related to mortality in treated hypertensive patients.

**8** Treated hypertensive patients who smoked had at least a two-fold increase in mortality over those who did not.

**9** Treated patients under the age of 50 years had a four-fold increase in mortality compared with the general population. This was greater than any excess mortality observed in the elderly.

The survival of patients treated for hypertension must be the overriding concern of both patient and doctor. Although the quality of life is very important, the length of life will always be the most easily assessed measure of the success of treatment. The 5 year survival has been examined in various studies and calculated either from direct observation or from a life table analysis. This review considers survival in terms of the age of the patients, the severity of their hypertension, the decade in which they were treated, the presence of cardiovascular risk factors and lastly how the survival of treated hypertensive patients compares with untreated patients and the population at large.

## 1. *The age and sex of the patient*

Figure 1 gives the 5 year survival calculated from England and Wales Life Tables by age and for males and females separately (Registrar General, 1975). The strong effect of age is apparent. Also given on this figure are the 5 year survival results for hypertensive patients presenting in New Zealand between 1945 and 1950, the majority of whom did not receive any effective treatment (Smirk *et al.*, 1959). Although survival rates in clinical studies are often presented without details of the age structure of the patients the New Zealand data reveal how important it is to consider the age of the patients. As expected, 5 year survival was greater in women with hypertension than in men with this condition.

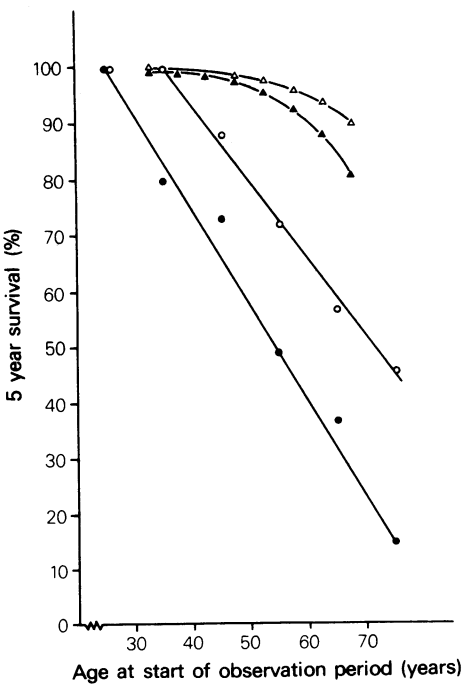


**Figure 1** Five year survival by age for men (▲) and women (△) in the general population of England and Wales and for untreated hypertensive patients (men ●, women ○) in New Zealand.

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**Table 1** Five year survival for men and women in England and Wales, cohort born 1901 (Case *et al.*, 1962) and cross sectional data (Registrar General, 1975). The death ratios are the ratios of male to female deaths.

| | *England and Wales cohort born 1901* | | | *Cross sectional* | | |
|---|---|---|---|---|---|---|
| *Age (years)* | *Male* | *Female* | *Death ratio* | *Male* | *Female* | *Death ratio* |
| 40–45 | 97.6 | 98.2 | 1.3 | 98.6 | — | — |
| 45–50 | 96.9 | 97.9 | 1.5 | 97.3 | 98.3 | 1.6 |
| 50–55 | 95.9 | 97.4 | 1.6 | 95.6 | 97.4 | 1.7 |
| 55–60 | 93.4 | 96.4 | 1.8 | 92.4 | 96.1 | 1.9 |
| 60–65 | 89.6 | 94.7 | 2.0 | 88.2 | 94.0 | 2.0 |

Tables 1 and 2 give the 5 year survival for the general population of England and Wales and the United States of America respectively. Table 1 gives the results of the usual cross-sectional life table (Registrar General, 1975) and also the results of a life table computation derived from a cohort born in 1901 (Case *et al.*, 1962). The cohort life table is more appropriate when assessing the 5 year survival in observational studies and in Table 2 the results are provided for cohorts born in 1908–12 and 1899–03 in the United States and for whites and non-whites (Moriyama & Gustavus, 1972).

For subjects in England and Wales and for whites in the USA the ratio of male:female deaths over 5 year intervals reaches 2.0 at age 60–65 years. The ratio is in the region of 1.3 to 1.7 at the age of 40–45 years. The sex differential is still present in non-whites in the USA but lower with male:female death ratios varying between 1.2 and 1.5.

In the Hypertension Detection and Follow-up Program (HDFP), (1979), the male:female death ratios were 1.9 for blacks and only 1.3 for whites (average age 51 years). In the Department of Health and Social Security Hypertension Care Computing Project (DHCCP, Bulpitt *et al.*, 1979) the male to female ratio was 1:4 (average age 51 years). Interestingly the excess mortality in these male hypertensives in the United Kingdom was largely removed when other factors such as smoking and plasma urea were taken into account (see section 5.d).

2. *The untreated blood pressure*

Figure 2 gives 5 year survival by age and sex and for three levels of initial diastolic and systolic blood pressure. The rates are those observed after 18 years of follow-up in the Framingham Study (Shurtleff, 1974). There was a dramatic reduction in survival for diastolic pressures of 110–160 mmHg and the effect was true in all three age groups and for both sexes. The non-linear relationship between diastolic blood pressure and cardiovascular events in the Framingham study has been emphasized by Anderson (1978) who concluded 'changes in diastolic blood pressure below about 90 mmHg have little or no prognostic significance'.

Recently, as patients with lower levels of systolic and diastolic blood pressure are being treated, very good survival results are being reported. Thus Trafford and his colleagues (1981) were able to report a 99.5% 5 year survival for patients with an untreated systolic blood pressure of more than 140 mmHg *or* diastolic more than 95 mmHg. These surprising results were due to selecting those who were well

**Table 2** Five year survival as determined from cohort life tables (DHEW, Moriyama & Gustavus, 1972) for white and non-white citizens of the United States and for both sexes. The death ratios are the ratios of male to female deaths and non-white to white deaths.

| | *White* | | *Death* | *Non-white* | | *Death* | *Non-white: white death* | |
|---|---|---|---|---|---|---|---|---|
| | *Male* | *Female* | *ratio* | *Male* | *Female* | *ratio* | *Male* | *Female* |
| *Born 1908–12* | | | | | | | | |
| Age 40–45 | 97.8 | 98.7 | 1.7 | 95.2 | 95.9 | 1.2 | 2.2 | 3.2 |
| (years) 45–50 | 96.5 | 98.2 | 1.9 | 93.7 | 95.1 | 1.3 | 1.8 | 2.7 |
| 50–55 | 94.4 | 97.2 | 2.0 | 90.9 | 93.4 | 1.5 | 1.6 | 2.4 |
| 55–60 | 91.3 | 95.9 | 2.1 | 87.1 | 91.5 | 1.5 | 1.5 | 2.1 |
| *Born 1899–03* | | | | | | | | |
| Age 60–65 (years) | 87.3 | 93.8 | 2.0 | 82.5 | 86.2 | 1.3 | 1.4 | 2.2 |

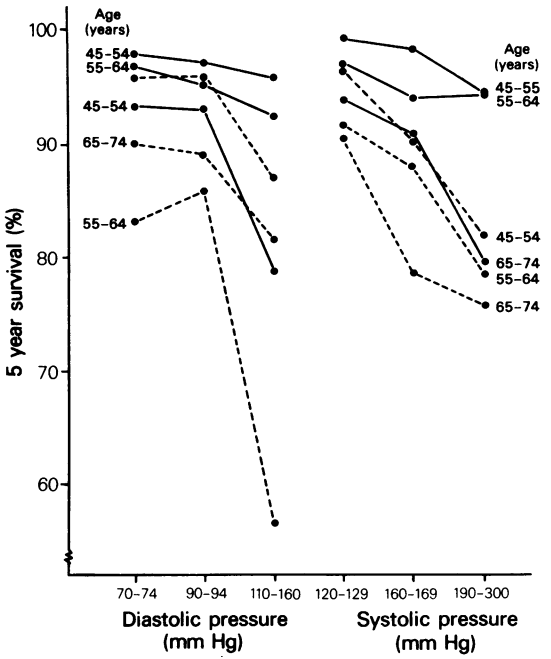


**Figure 2** Five year survival by age and sex (men ---, women ——) and three levels of blood pressure, in the Framingham 18 year follow-up study.

controlled on treatment. Patients with less good blood pressure control had 96.4% 5 year survival and those who were in an untreated (? elderly) group had only a 82.9% survival. The total group of patients was compared with a normotensive control group with a 5 year survival of 97.7%. Similarly excellent results in mild hypertensives have been reported from the Oslo trial (Helgeland, 1980). In this trial men aged 40–49 years were recruited with a systolic pressure between 150 and 179 mm Hg and a diastolic pressure *lower* than 110 mmHg. The men were randomised to two groups either for treatment or as a control group but treatment was given to 17% of the control group when their blood pressure rose. In both groups 5 year survival was greater than 97.5%. With such good survival rates the case for treating all patients with mild hypertension has yet to be proven.

### 3. *Malignant hypertension*

Table 3 reports that 5 year survival of patients with malignant hypertension, this condition being diagnosed when papilloedema results from an elevation in blood pressure. The advent of effective anti-hypertensive treatment in the early 1950s produced a dramatic improvement in 5 year survival from an average of less than 4% to over 30%. Breslin *et al.* (1966) has also shown that retinal appearance predicts survival even after adjusting for the presenting blood pressure. With a diastolic pressure less than 100 mmHg, 10 year survival was reduced from over 80% in patients in his study with grade I retinopathy, to 25% in patients with grade III retinopathy as assessed by the Keith *et al.* (1939) classification.

**Table 3** The 5 year survival for patients with treated malignant hypertension and patients treated when only non-specific measures were available.

| *'Untreated' malignant hypertension* | *5 year survival* |
|---|---|
| Schottstaedt & Sokolow (1953) | 8% |
| Hood (1956) | 3% |
| Kincaid-Smith *et al.* (1958) | 1% |
| Keith *et al.* (1939) | 1% |
| *Treated malignant hypertension* | |
| Smirk (1957) | 40% |
| Newman & Robertson (1959) | 35% |
| Harington *et al.* (1959) | 20% |
| Breckenridge *et al.* 1952–9 (1970) | 25% |
| Breckenridge *et al.* 1960–7 (1970) | 34% |

In the 1950s 32% of the patients seen in the Hammersmith Hypertension clinic had malignant hypertension and this fell to 6% in the 1960s (Breckenridge *et al.*, 1970) and 1% in the 1970s. Although this reduction in incidence may be largely due to changes in referral pattern, the general impression is that malignant hypertension is declining and this reduction can be expected to be associated with an increased survival for hypertensive patients in general. It is not known whether the decline in malignant hypertension is due to prevention by early treatment, dietary changes, the disappearance of nephritis or a reduction in other causes of secondary hypertension.

### 4. *The influence of the decade of treatment*

In order to compare survival of patients in the nineteen fifties, with their survival in the sixties and seventies we must be careful to compare similar patients. For example, we should study men who were treated in the same hypertension clinic of a similar age, untreated blood pressure and retinal appearance. Breckenridge and his colleagues (1970) reported the 5 year survival for male and female patients who presented to the Hammersmith Hospital clinic between 1952 and 1959 and 1960 to 1967. The 5 year survival for male patients with 'non-exudative' retinopathy (grade I or II) was 80% in each decade but for women with grade I or II retinopathy, 5 year survival improved by an average of about 9% in the 1960s. This change could have been due to younger patients presenting to the clinic or to lower levels of untreated blood pressure, and we cannot conclude that more modern treatment has a greater effect in increasing survival.

5. *The presence of cardiovascular risk factors*

Certain cardiovascular risk factors are predominantly genetic and little can be done about them, for example being a male, but many other risk factors are part genetic, part environmental, and include (in decreasing order of genetic importance); race, serum cholesterol, blood sugar and cigarette smoking. We shall consider how each factor may affect prognosis in the treated hypertensive patient.

a. *Race* The vital statistics for the USA reported in Table 2 reveal a striking excess mortality in non-whites (mainly negros). The non-white:white death ratio exceeded two for women and ranged from 1.4 to 2.2 for men. In the HDFP trial (1979) the black:white death ratio was 1.3 for women and 1.9 for men.

b. *Serum cholesterol* When discussing the relationship between serum cholesterol and cardiovascular disease in the Seven Countries Study, Keys (1980) stated 'serum cholesterol needs to be 275 mg/100 ml (7.1 mmol/l) or more to have an effect'. In the Framingham Study (Shurtleff, 1974) the general population over the age of 65 years and men over the age of 55 years had a negative relationship between serum cholesterol and all-cause mortality. However, when considering cardiovascular deaths, men and women aged 45–54 years had a positive association between cardiovascular death and serum cholesterol. There is little known concerning the influence of serum cholesterol in treated hypertensive patients but the DHCCP (Bulpitt *et al.*, 1979) found a tendency for a negative relationship between serum cholesterol and both total and cardiovascular mortality. At the present state of our knowledge there appears little point in giving dietary advice to lower serum cholesterol in all hypertensive patients, especially above the age of 55 years. Above the age of sixty the serum cholesterol of treated hypertensives falls year by year without routine dietary advice (Amery *et al.*, 1981).

c. *Blood sugar* An International Collaborative Group (1979) reviewed the association between blood glucose and coronary heart disease (CHD). They concluded 'the results of the several studies considered together do *not* indicate an association between asymptomatic hyperglycaemia and CHD that is consistent, strong and graded'. It remains to be seen whether or not the concentration of glucose in the blood is important in treated hypertensive patients.

d. *Cigarette smoking* In the general population, smoking more than twenty cigarettes a day is associated with a doubling of mortality in both men aged 45–74 years and women aged 40–54 years (Framingham data, Shurtleff, 1974). This association is also observed in treated hypertensive patients. Figure 3 gives the results from the DHCCP study indicating a 2.3 times excess in total mortality for smokers versus non smokers. If is of interest that the adverse effect of smoking on mortality was much greater than the effect of being a male.

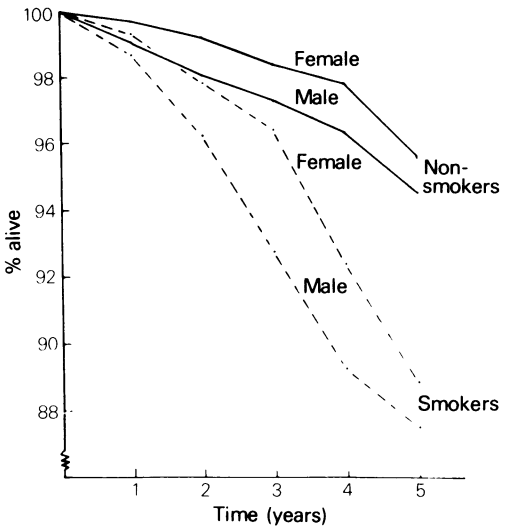


**Figure 3** Life table survival curves for male and female treated hypertensive patients in the DHCCP study. Survival is represented for smokers (------) and non-smokers (——) separately. Reproduced from the *Lancet*, 1979, **ii**, 134–138, with permission.

6. *How does the survival of treated hypertensive patients compare with that of the general population?*

Table 4 reports the cardiovascular-renal death rates in three age groups and both sexes separately for the DHCCP, study, the England and Wales population and the Framingham, USA population. Despite

**Table 4** Cardiovascular-renal death rates in the DHCCP study per thousand per year (Bulpitt *et al.*, 1979), England and Wales General Population and the Framingham study (Shurtleff, 1974).

| | *Age (years)* | | |
|---|---|---|---|
| | *45–54* | *55–64* | *65–74* |
| *Men* | | | |
| Treated hypertensives | 11 | 25 | 23 |
| England & Wales general population | 3 | 9 | 23 |
| Framingham study | 4 | 12 | 19 |
| *Women* | | | |
| Treated hypertensives | 8 | 11 | 17 |
| England & Wales general population | 1 | 3 | 12 |
| Framingham study | 1 | 4 | 12 |

**Table 5** Five year survival in the DHSS Hypertension Care Computing Project (DHCCP) and the general population of England and Wales.

| | *DHCCP* | | *England & Wales* | *AR* | *RR* |
|---|---|---|---|---|---|
| | *Number of subjects* | *5 year survival (1)* | *(2)* | *(2)–(1)* | $\frac{100-(1)}{100-(2)}$ |
| *30–49 years* | | | | | |
| Males | 436 | 94.2 | 98.7 | 4.5 | 4.5 |
| Females | 491 | 97.0 | 99.1 | 2.1 | 3.3 |
| *50–59 years* | | | | | |
| Males | 404 | 94.0 | 94.2 | 0 | 1.0 |
| Females | 356 | 94.0 | 96.8 | 2.8 | 1.9 |
| *60–69 years* | | | | | |
| Males | 247 | 80.5 | 85.8 | 5.3 | 1.4 |
| Females | 305 | 90.5 | 92.5 | 2.0 | 1.3 |

AR = attributable risk. RR = relative risk.

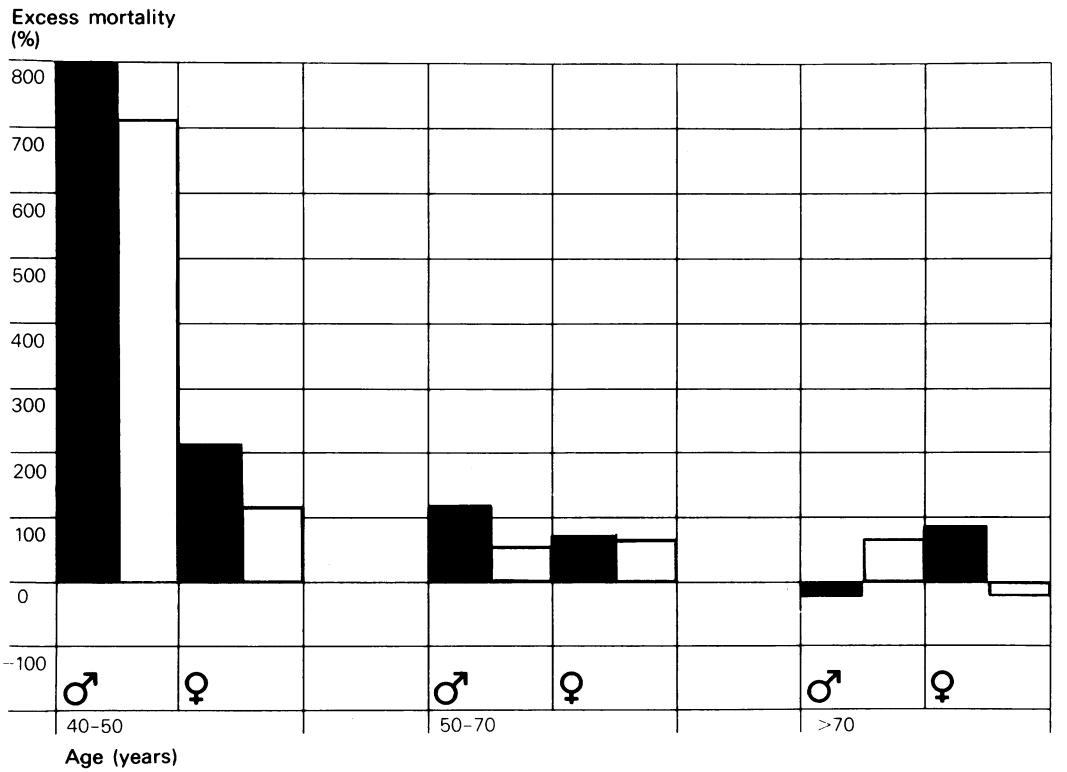


**Figure 4** Excess mortality for male and female hypertensive patients according to age at diagnosis. Dark bars represent data from Bechgaard (1946) and lighter bars from Frant & Groen (1950). Reproduced with permission from *Hypertension* by E.J. Dorhort Mees, published by Boehringer Ingleheim 1978, p. 35.

treatment the patients in the DHCCP study had a three-fold and eight-fold excess mortality for male and female patients respectively aged 45–54 years. However, for the older patients the excess mortality disappeared for men but there was still a 1.5 fold excess in women. Table 5 reports the 5 year survival in the DHCCP study and for the general population in abridged cross-sectional life tables for the United Kingdom (Registrar General, 1975). The death rates in the hypertensive patients were calculated for ages 30–49, 50–59, 60–69 years and divided by the rates for the corresponding general population to give a measure of the relative risk (RR) from dying when having treated hypertension. In the table the hypertensive and general population death rates are also differenced to give the number of deaths/100/5 years attributed to having treated hypertension (attributable risk (AR)). Although the AR did not differ conclusively between the age groups, the relative risk was much higher in patients under the age of 50 years.

The relative risk calculation suggests that younger patients fare worse than the general population and that the older patients have a death rate more similar to that of older people in general. However owing to the larger number of deaths in the elderly, the attributable risk indicated that a small proportional improvement in the relative death for the older hypertensive would save a similar number of lives. The finding of a low relative risk in the elderly is in agreement with the findings of Holme & Waaler (1976), Bechgaard (1967), Frant & Groen (1950) and Fry (1974). The results of two of these studies are illustrated in Figure 4, a relative risk of unity being found after the age of 70 years. Of special note is that elderly hypertensive patients were not treated in these studies.

On the basis of these observations two suggestions may be made:

1. As there is often a long period of elevated blood pressure prior to commencing treatment in middle age we cannot expect to reduce the subsequent risk of death to normal. This may explain the poor results observed for patients less than 50 years of age.
2. The majority of patients who survive hypertension until the age of seventy do not require treatment.

The latter suggestion may explain the lack of excess mortality in elderly hypertensives whether untreated or treated but we must remember that within elderly populations there is still a positive association between blood pressure (especially systolic) and both total mortality (Miall & Chinn, 1974; Shurtleff, 1974), and stroke (Shurtleff, 1974; Holme & Waaler, 1976). It appears that the latter observations are in direct contrast with the suggestion of a normal expectation of life in the elderly hypertensive. Whatever the truth it is difficult to be certain that there is a causal relationship between hypertension and death in the elderly. Systolic blood pressure may be associated with existing cardiovascular disease and thus predict death in the same way as the presence of an old myocardial infarction on an electrocardiograph tracing. Those found to be hypertensive in old age may also have developed the condition recently or have survived the condition for a considerable number of years. In either case their hypertensive state may not be similar to that observed in middle age. We must prove whether or not any risk associated with blood pressure in the elderly can be reversed, i.e., whether antihypertensive treatment in the elderly is of benefit. Fortunately there is one large multicentre, placebo-controlled randomised trial in progress which could throw some light on the problem (Amery *et al.*, 1978).

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