Excess Stroke Among Hypertensive Men and Women Attributable to Undertreatment of Hypertension

Olaf H. Klungel, PhD; Bruno H.C. Stricker, PhD; Arsenio H.P. Paes, PhD; Jacob C. Seidell, PhD; Albert Bakker, PhD; Zoltán Vokó, MD; Monique M.B. Breteler, PhD; Anthonius de Boer, PhD

Background and Purpose—Most population-based studies indicate that a considerable proportion of hypertensive subjects are undertreated and that undertreatment is more prevalent among hypertensive men than among hypertensive women. The aim of our study was to investigate the consequences of undertreatment of hypertension for women and men in terms of stroke occurrence.

Methods—Approximately 45,000 men and women aged ≥20 years were examined in 2 population-based studies in the Netherlands. A cohort of 2616 hypertensive subjects (pharmacologically treated hypertensives and untreated hypertensives who needed pharmacological treatment according to the severity of their hypertension and the coexistence of additional cardiovascular risk factors) was selected for a follow-up study. Follow-up (mean duration, 4.6 years) was complete for 2369 (91%) of the enrolled hypertensive subjects.

Results—Compared with treated and controlled hypertensives, the relative risks of stroke for treated and uncontrolled hypertensives and for untreated hypertensives who needed treatment were 1.30 (95% CI, 0.70 to 2.44) and 1.76 (95% CI, 1.05 to 2.94), respectively. These relative risks and the prevalence of (undertreated) hypertension in the total population of 45,000 subjects were used to estimate the number of strokes in the Netherlands attributable to undertreatment. Among hypertensive men and women aged ≥20 years in the Netherlands, the proportions of strokes attributable to treated but uncontrolled blood pressure were 3.1% (95% CI, −5.2% to 18.7%) and 4.1% (95% CI, −7.2% to 20.7%), respectively. For untreated hypertensive men and women who should have been treated, these proportions were 22.8% (95% CI, 0.8% to 38.4%) and 25.4% (95% CI, 0.5% to 42.5%), respectively.

Conclusions—Increasing the detection of hypertension and improving adherence to current guidelines might prevent a considerable proportion of the incident strokes among hypertensives. The potential impact of achieving control of blood pressure in patients already being treated on the reduction of strokes requires further investigation. (Stroke. 1999;30:1312-1318.)

Key Words: hypertension ■ population-based studies ■ stroke ■ treatment
or to untreated hypertension.\textsuperscript{13–19} Second, in none of the studies was the coexistence of additional cardiovascular disease risk factors taken into account to assess the need for pharmacological treatment. Finally, in most of these studies, treated hypertensives were compared with the remainder of the population or normotensive controls\textsuperscript{9,13–20} or with untreated hypertensives irrespective of their need for treatment.\textsuperscript{13,14} Thus, the reference groups in these studies were not comparable with the treated hypertensives with respect to risk of cardiovascular disease, and this may have led to confounding by the indication for the treatment of hypertension.\textsuperscript{21}

The aim of our study was to estimate the proportion of incident strokes attributable to undertreatment of hypertension in men and women, taking into account the shortcomings of previous studies.

Subjects and Methods

Data

For the present study we used data from 2 population-based studies in the Netherlands. The first study, the Monitoring Project on Cardiovascular Risk Factors, was started in 1987 as a cross-sectional study in Amsterdam, Maastricht, and Doetinchem. In Doetinchem this study was continued as a prospective follow-up study by reexamining the subjects examined in 1987 again in 1993. The second study, the Rotterdam Study, was started in 1990 in Rotterdam as a population-based prospective follow-up study.

The Monitoring Project on Cardiovascular Risk Factors

This study was conducted from 1987 to 1991. Each year a new random sample of men and women aged 20 to 59 years in Amsterdam, Maastricht, and Doetinchem was selected. The design of this study has been described in detail elsewhere.\textsuperscript{22} The overall response rate in Amsterdam, Maastricht, and Doetinchem was 45%, 58%, and 62%, respectively. Several characteristics such as educational level, smoking, alcohol use, height, and weight of nonrespondents and respondents have been evaluated in previous studies.\textsuperscript{8} The results of these studies suggested that no substantial selection had taken place with respect to these characteristics.

The Rotterdam Study

This study on the occurrence and determinants of chronic disabling diseases at older ages was started in 1990. All 10 275 residents of a suburb of Rotterdam aged $\geq 55$ years were invited to participate; 7983 (78%) subjects agreed to participate. The design of this study has been described in detail elsewhere.\textsuperscript{23} The baseline measurements took place until 1993.

Baseline Measurements

Information on demographic variables, current health status, medical history, family history of diseases, smoking habits, and current use of medication was obtained during a home interview in the Rotterdam study, whereas self-administered questionnaires were used in the Monitoring Project on Cardiovascular Risk Factors. The self-administered questionnaires were checked at the study center with the participant for completeness. In both studies the physical examinations were performed by either trained technicians or physicians according to a standardized protocol. Blood pressure, weight, and height were measured, and blood was drawn for total cholesterol and HDL cholesterol determination. A random zero sphygmomanometer was used to measure blood pressure twice with the subject in sitting position. Systolic blood pressure (SBP) was recorded at the appearance of sounds (first-phase Korotkoff), and diastolic blood pressure (DBP) was recorded at the disappearance of sounds (fifth-phase Korotkoff). For the analyses, we used the mean of 2 blood pressure measurements.

Follow-Up

For this study, we selected subjects who were treated pharmacologically for hypertension and subjects who were untreated but in need of pharmacological treatment for hypertension (see Definitions) at the baseline measurement in Rotterdam (1990–1993) and Doetinchem (1987–1991). The follow-up period in both studies started at the baseline examination and lasted until April 1, 1996, in Rotterdam, and until January 1, 1996, in Doetinchem. Information on fatal and nonfatal strokes was obtained through patient records of general practitioners (GPs) and the GPs’ archives of specialists’ reports.

Definitions

Hypertension was defined as DBP $\geq 95$ mm Hg and/or SBP $\geq 160$ mm Hg and/or use of antihypertensive drugs for hypertension. Subjects who said that they used blood pressure–lowering drugs and mentioned at least 1 drug with an approved indication for the treatment of hypertension were considered pharmacologically treated for hypertension. With regard to cardiovascular drug use, it was previously demonstrated that concordance between medication use according to patient interview and pharmacy records is very high.\textsuperscript{30,34} Three categories of hypertensives were distinguished according to the Dutch guidelines for the management of hypertension.\textsuperscript{9} First, the reference group was defined as pharmacologically treated hypertensives whose blood pressure was below the treatment goal of the Dutch guidelines (DBP $\leq 90$ mm Hg and SBP $\leq 160$ mm Hg). The second group included pharmacologically treated hypertensives whose blood pressure was above this treatment goal (DBP $> 90$ mm Hg or SBP $> 160$ mm Hg). The third group consisted of untreated hypertensives who need pharmacological treatment when the coexistence of additional cardiovascular risk factors was taken into account. According to the Dutch guidelines, hypertension should be treated pharmacologically when the DBP is between 100 and 105 mm Hg and 1 or more additional cardiovascular risk factors are present, or when the SBP is between 160 and 180 mm Hg and 1 or more cardiovascular risk factors are present, or when DBP or SBP are $>105$ mm Hg or $>180$ mm Hg, respectively. The following additional cardiovascular risk factors should be evaluated according to these guidelines: sex (male), current smoking, hypercholesterolemia (total cholesterol $\geq 6.5$ mmol/L), diabetes, target organ disease, age $\geq 60$ years, and cardiovascular disease among parents or sisters or brothers aged $<60$ years.

Strokes that could be confirmed by specialists’ letters to the GPs and strokes that were certain according to the GP were included for the analysis, whereas events that were probable according to the GP were excluded. The end point of interest was a first or recurrent fatal or nonfatal stroke (\textit{International Classification of Diseases, Tenth Revision} codes I60 to I69), excluding transient ischemic attacks (TIA) during follow-up.

History of cardiovascular disease was defined as a self-reported history of any cardiovascular disease or written information from the GPs that indicated presence of any cardiovascular disease, excluding cerebrovascular diseases. History of cerebrovascular disease was defined as a self-reported history of stroke or TIA, confirmed by written information from the GPs.

Analyses

\textbf{Estimation of Risk of Stroke Attributed to Undertreatment of Hypertension}

To study the association between undertreatment and incidence of stroke, the Cox proportional hazards model was used, and multivariately adjusted relative risks (RRs) and their 95% CIs\textsuperscript{26} were calculated. Analyses were initially performed separately for the Doetinchem study and the Rotterdam study to evaluate effect-modification due to differences in study design. The RRs of undertreatment of hypertension for the occurrence of stroke were virtually the same in the Doetinchem study and the Rotterdam study. Therefore, the results from the combined analysis are presented.

In addition to the evaluation of all subjects simultaneously, subgroup analyses were performed after exclusion of patients without a history of cerebrovascular disease and after exclusion of...
patients with any history of cardiovascular disease. Furthermore, men and women and subjects aged <80 and ≥80 years (the efficacy of antihypertensive treatment at ≥80 years is unknown)2 were analyzed separately.

All RR estimates were adjusted for age, history of diabetes, total cholesterol, body mass index, smoking, and history of cardiovascular disease. When men and women were analyzed together, adjustments were also made for sex, and in the analysis of all subjects irrespective of a history of cerebrovascular disease, adjustments were also made for a history of stroke or TIA. For the adjustment of RRs, smoking was categorized into never, former, or current smoking.

**Estimation of Prevalences of Undertreatment of Hypertension**

Age- and sex-specific prevalences of hypertension, treated and controlled hypertension, treated but uncontrolled hypertension, and untreated hypertension that should be treated were estimated among all subjects who were examined in all 4 cities in both population studies. These prevalence estimates were used to compute the number of subjects within these categories of hypertensives in the whole Dutch population.

**Estimation of the Number of Incident Strokes Attributable to Undertreatment of Hypertension**

Age- and sex-specific incidence rates of stroke among all hypertensives, treated and controlled hypertensives, treated but uncontrolled hypertensives, and untreated hypertensives who should be treated were computed (PYRS version 1.2) to estimate the number of incident strokes in these categories of hypertensives in the Netherlands in 1994. This was done by multiplying the age- and sex-specific estimated numbers of subjects within the different categories of hypertensives in the Netherlands in 1994 by the corresponding age- and sex-specific incidence rates. Subsequently, we estimated the proportions of incident strokes attributable to treated but uncontrolled blood pressure and untreated hypertension that should be treated within each of these categories of undertreatment as the ratio (RR−1)/RR. The adjusted RRs of exposed persons (treated but uncontrolled hypertensives or untreated hypertensives who should be treated) compared with unexposed persons (treated and controlled hypertensives) were used for the RR. These proportions were used to estimate the absolute number of incident strokes attributable to both types of undertreatment. Finally, these attributable numbers of incident strokes were expressed as percentages of the total number of incident strokes among all hypertensive subjects. We estimated 95% CIs of the attributable number of incident strokes according to the method of Rothman and Greenland.22

### Results

#### Study Population

A total of 44,571 subjects (12,448 in Doetinchem, 11,488 in Amsterdam, 12,652 in Maastricht, and 7,983 in Rotterdam) were examined in both population studies. After exclusion of pregnant women (n=306) and subjects with missing data (n=1,665), 42,600 subjects remained available for the estimation of prevalences of hypertension and undertreatment of hypertension.

Hypertension was prevalent among 2,072 subjects (28.9%) of the Rotterdam study and among 1,096 subjects (9.4%) in Doetinchem. Subjects who did not need antihypertensive drug treatment according to the guidelines (n=552) were excluded from the analysis. Therefore, our study population comprised 2,616 subjects pharmacologically treated for hypertension or untreated for hypertension but in need of pharmacological treatment. Follow-up was complete for 2,369 subjects (90.6%).

The differences in baseline characteristics between those lost to follow-up and those for whom follow-up was complete were negligible (data not shown).

The number of hypertensives who were treated pharmacologically and had DBP <90 mm Hg and SBP <160 mm Hg was 879, whereas 482 subjects were treated pharmacologically but had DBP >90 mm Hg or SBP >160 mm Hg, and 1,008 subjects were inappropriately not treated pharmacologically.

---

**TABLE 1. Baseline Characteristics of Men and Women Aged ≥20 Years by Classification of Undertreatment of Hypertension**

<table>
<thead>
<tr>
<th>Category</th>
<th>Treated, Controlled*</th>
<th>Treated, Uncontrolled†</th>
<th>Untreated but Should Be Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>879</td>
<td>482</td>
<td>1008</td>
</tr>
<tr>
<td>Women</td>
<td>593 (67.5%)</td>
<td>312 (64.7%)</td>
<td>538 (53.4%)</td>
</tr>
<tr>
<td>Age (SD), y</td>
<td>65.8 (10.7)</td>
<td>65.3 (13.0)</td>
<td>66.6 (14.3)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>59 (6.7%)</td>
<td>42 (8.7%)</td>
<td>75 (7.4%)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>360 (42.3%)</td>
<td>216 (45.5%)</td>
<td>395 (40.2%)</td>
</tr>
<tr>
<td>Current</td>
<td>170 (20.1%)</td>
<td>104 (21.9%)</td>
<td>233 (23.7%)</td>
</tr>
<tr>
<td>Former</td>
<td>318 (37.5%)</td>
<td>155 (32.6%)</td>
<td>354 (36.1%)</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>6.6 (1.2)</td>
<td>6.5 (1.2)</td>
<td>6.6 (1.3)</td>
</tr>
<tr>
<td>History of cardiovascular diseases‡</td>
<td>218 (24.8%)</td>
<td>103 (21.4%)</td>
<td>171 (17.0%)</td>
</tr>
<tr>
<td>History of TIA</td>
<td>39 (4.6%)</td>
<td>21 (4.4%)</td>
<td>28 (2.9%)</td>
</tr>
<tr>
<td>History of stroke</td>
<td>30 (3.4%)</td>
<td>23 (4.8%)</td>
<td>27 (2.7%)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.7 (4.0)</td>
<td>28.1 (4.3)</td>
<td>26.8 (3.8)</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>75.6 (8.8)</td>
<td>89.2 (11.9)</td>
<td>88.5 (13.6)</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>135.5 (14.3)</td>
<td>164.1 (19.7)</td>
<td>169.0 (14.9)</td>
</tr>
<tr>
<td>Mean duration of follow-up, y</td>
<td>4.8 (1.7)</td>
<td>4.7 (1.8)</td>
<td>4.3 (1.6)</td>
</tr>
</tbody>
</table>

*Controlled blood pressure, DBP ≤90 mm Hg and SBP ≤160 mm Hg.
†Uncontrolled blood pressure, DBP >90 mm Hg or SBP >160 mm Hg.
‡Excluding TIA and strokes.
ically for hypertension. Baseline characteristics of all 2369 hypertensive men and women stratified by these 3 categories are listed in Table 1. Most risk factors were evenly distributed across these categories. One important difference was a higher prevalence of past cardiovascular disease (excluding cerebrovascular disease) among pharmacologically treated hypertensives compared with untreated hypertensives who should have been treated. This difference was more pronounced for men than for women (data not shown). Prevalence of past cerebrovascular disease was also slightly higher for pharmacologically treated hypertensives.

**Undertreatment of Hypertension and Risk of Stroke**

During the follow-up period (mean duration, 4.6 years), 40 men and 68 women experienced a first or recurrent stroke. The number of fatal stroke events was 2 for men and 15 for women.

The crude incidence rates of stroke among treated hypertensives with controlled blood pressure levels, treated hypertensives with uncontrolled blood pressure levels, and untreated hypertensives who should have been treated were 6.7, 8.2, and 14.0 per 1000 person-years, respectively (Table 2). Compared with treated hypertensives who had controlled blood pressure and after adjustment for potential confounding factors, treated hypertensives who had uncontrolled blood pressure levels had a 1.30-fold increased risk of stroke (not statistically significant), whereas untreated hypertensives who should have been treated had a 1.76-fold increased risk of stroke (Table 2). These RRs were similar for men and women. Exclusion of subjects with a history of cerebrovascular disease resulted in slightly increased RRs of treated but uncontrolled blood pressure and untreated hypertension that should be treated compared with treated and controlled blood pressure (1.47 [95% CI, 0.73 to 2.95] and 1.86 [95% CI, 1.04 to 3.33], respectively).

Additional analyses of subjects without any history of cardiovascular disease resulted in even higher RRs of treated but uncontrolled blood pressure and untreated hypertension that should be treated compared with treated and controlled blood pressure (2.0 [95% CI, 0.8 to 4.6] and 2.3 [95% CI, 1.1 to 4.8], respectively).

For subjects aged <80 years, the adjusted RRs of stroke of treated but uncontrolled blood pressure and untreated hypertension that should be treated were 1.4 (95% CI, 0.7 to 2.8) and 1.7 (95% CI, 0.9 to 3.0), respectively. For subjects aged ≥80 years, these RRs were 1.2 (95% CI, 0.2 to 5.6) and 2.6 (95% CI, 0.8 to 9.2), respectively. However, because of the small numbers we could not further investigate these associations by age.

**Number of Incident Strokes Attributable to Undertreatment of Hypertension**

The incidence rates of stroke after stratification for age, sex, and categories of hypertension (treated and controlled, treated but uncontrolled, untreated but should be treated) as derived from the 2 population studies are presented in Table 3. In both sexes the incidence rates increased with age. Furthermore, rates were highest in the untreated hypertensives who should be treated. The respective age-adjusted prevalences of hypertension (per 100 population), treated and controlled hypertension (per 100 hypertensives), treated but uncontrolled hypertension (per 100 hypertensives), and untreated hypertension that should be treated (per 100 hypertensives) were 11.2, 28.2, and 14.0 per 1000 person-years, respectively (Table 2). Compared with treated hypertensives who had controlled blood pressure and after adjustment for potential confounding factors, treated hypertensives who had uncontrolled blood pressure levels had a 1.30-fold increased risk of stroke (not statistically significant), whereas untreated hypertensives who should have been treated had a 1.76-fold increased risk of stroke (Table 2). These RRs were similar for men and women. Exclusion of subjects with a history of cerebrovascular disease resulted in slightly increased RRs of treated but uncontrolled blood pressure and untreated hypertension that should be treated compared with treated and controlled blood pressure (1.47 [95% CI, 0.73 to 2.95] and 1.86 [95% CI, 1.04 to 3.33], respectively).
The age-adjusted proportions of strokes among hypertensive men and women attributable to treated but uncontrolled blood pressure were 3.1% (95% CI, 2.5% to 18.7%) and 4.1% (95% CI, 2.7% to 20.7%), respectively (Table 4). For untreated hypertensive men and women who should have been treated, these proportions were 22.8% (95% CI, 0.8 to 38.4%) and 25.4% (95% CI, 0.5 to 42.5%), respectively. Among hypertensive subjects aged ≥20 years in the Netherlands in 1994, 26% (1230) of all incident strokes among hypertensive men and 29% (1975) of all incident strokes among hypertensive women were attributable to undertreatment of hypertension.

**Discussion**

In a previous study we showed that during the last decade in the Netherlands, a considerable proportion of hypertensive men and women aged 20 to 59 years were undertreated for hypertension. In the present study we investigated the consequences of undertreatment of hypertension among men and women aged ≥20 years with respect to the occurrence of stroke. We demonstrated that untreated hypertensives who needed treatment according to the severity of their hypertension and the presence of additional cardiovascular risk factors had an increased risk of stroke compared with pharmaceutically treated hypertensives whose blood pressure level was controlled. Among hypertensive men and women aged ≥20 years in the Netherlands, ~1083 and ~1702 incident strokes per year, respectively (23% and 25% of all incident strokes among hypertensive men and women, respectively) might be due to untreated hypertension that should have been treated. According to an average of several general practice registrations in the Netherlands, ~13 026 and ~15 119 incident strokes occurred among men and women, respectively, in the whole Dutch population aged ≥20 years in 1994. On the basis of these figures, ~8.3% and ~11.3% of all incident strokes among men and women aged ≥20 years in the Netherlands were attributable to untreated hypertension that should have been treated. This is probably an underestimation since the definition of stroke was more strict in our study than in these general practice registrations. Because of the imprecise RR estimate of treated but uncontrolled blood pressure, we could not reliably estimate the number of strokes attributable to this type of undertreatment. However, the attributable fraction due to treated but uncontrolled blood pressure appears to be much lower than that due to untreated hypertension that should be treated.

Estimations of the proportion of a disease attributable to exposure are only valid when risk estimates and prevalence
TABLE 4. Number of Strokes Attributable to Undertreatment of Hypertension Among Hypertensives in the Netherlands in 1994

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Treated But Uncontrolled</th>
<th>Untreated but Should Be Treated</th>
<th>Total Undertreated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–29</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>30–39</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>40–49</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>50–59</td>
<td>33 (4.6)</td>
<td>97 (13.7)</td>
<td>129 (18.3)</td>
</tr>
<tr>
<td>60–69</td>
<td>59 (4.7)</td>
<td>274 (21.5)</td>
<td>333 (26.2)</td>
</tr>
<tr>
<td>70–79</td>
<td>55 (3.3)</td>
<td>423 (25.2)</td>
<td>478 (28.5)</td>
</tr>
<tr>
<td>≥80</td>
<td>...</td>
<td>290 (30.1)</td>
<td>290 (30.1)</td>
</tr>
<tr>
<td>≥20†</td>
<td>147 (3.1)</td>
<td>1083 (22.8)</td>
<td>1230 (25.9)</td>
</tr>
<tr>
<td>Women*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–29</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>30–39</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>40–49</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>50–59</td>
<td>39 (8.5)</td>
<td>38 (8.2)</td>
<td>77 (16.7)</td>
</tr>
<tr>
<td>60–69</td>
<td>21 (2.9)</td>
<td>105 (14.4)</td>
<td>127 (17.3)</td>
</tr>
<tr>
<td>70–79</td>
<td>98 (4.8)</td>
<td>413 (20.1)</td>
<td>512 (24.9)</td>
</tr>
<tr>
<td>≥80</td>
<td>114 (3.3)</td>
<td>1145 (33.1)</td>
<td>1259 (36.4)</td>
</tr>
<tr>
<td>≥20†</td>
<td>273 (4.1)</td>
<td>1702 (25.4)</td>
<td>1975 (29.4)</td>
</tr>
<tr>
<td>Total*</td>
<td>421 (3.7)</td>
<td>2785 (24.3)</td>
<td>3205 (27.9)</td>
</tr>
</tbody>
</table>

Values are number (percent) (percentage of all incident strokes among hypertensives). Ellipses indicate that no incident strokes were observed in these age strata.

*Attributable fractions \(AF = (RR - 1)/RR\) of incident strokes were estimated for treated but uncontrolled hypertensive men, women, and all subjects together (adjusted RR of 1.30 was used) and for untreated hypertensive men, women, and all subjects together who should be treated (adjusted RR of 1.76 was used). The number of attributable incident strokes was calculated by multiplying the AFs of both types of undertreatment with the total number of incident strokes within both types of undertreatment.

†Weighted for the age distribution of the Dutch population in 1994.

First, blood pressure was measured only twice on 1 occasion. Because of within-person variability in blood pressure, the group of untreated hypertensives who should be treated will also comprise normotensive subjects.5,29 Misclassification of normotensives as hypertensive has probably caused an underestimation of our RR estimates.

A second limitation of this study could be that the results in part may be caused by confounding by the indication for the treatment of hypertension. However, we compared a high-risk group of untreated hypertensives with additional cardiovascular risk factors with treated and controlled hypertensives, and the differences between untreated hypertensives who should be treated and treated hypertensives were only marginal with respect to the traditional cardiovascular risk factors at baseline. Furthermore, all RR estimates were adjusted for the potential confounding influence of other cardiovascular disease risk factors.

Third, it cannot be excluded that treated hypertensives with controlled blood pressure had lower pretreatment blood pressure levels than treated but uncontrolled hypertensives. We could not adjust for this in the analysis. Nonetheless, the excess risk of treated but uncontrolled blood pressure compared with treated and controlled blood pressure suggests that lowering blood pressure in hypertensives with uncontrolled blood pressure would reduce the risk of stroke among these hypertensive patients.

Fourth, we measured the status of undertreatment only at baseline, whereas during the follow-up period treatment could have been started in untreated hypertensives and control of blood pressure could have been achieved among treated hypertensives who were uncontrolled at the baseline measurements. Assuming that it is more likely that untreated hypertensives are going to be treated during follow-up than that treatment is stopped in treated hypertensives, the RR of untreated hypertension that should be treated was probably underestimated.

Finally, because of the small numbers, some reservation with regard to the precision of the estimated number of attributable strokes must be taken into account. The RR of treated but uncontrolled blood pressure and the number of strokes attributable to this type of undertreatment were not statistically significant. However, several other studies also found an increased risk of stroke among treated hypertensives with uncontrolled blood pressure compared with those with controlled blood pressure.9,10,12,20 Furthermore, the increased risk of treated but uncontrolled blood pressure was consistent across the subgroups that we studied. Nonetheless, the number of strokes attributable to treated but uncontrolled blood pressure should be interpreted with caution.

Although the prevalence of undertreatment of hypertension was higher for hypertensive men than for hypertensive women, the proportion of incident strokes due to undertreatment was slightly smaller for men than for women. The absolute number of incident strokes attributable to undertreatment was also higher for hypertensive women than it was for hypertensive men. This can probably be explained by the higher number of elderly women, in particular at ages >70 years. Above this age the incidence rate of stroke was very high. Another explanation could be that the mortality from coronary heart disease is much higher among men than among women.30–32 This could have resulted in a selective depletion of the pool of men who are at high risk for stroke, resulting in more women than men at high risk for experiencing a stroke event.33

This study provides one of the first estimates of the risk of stroke in the population in relation to the quality of treatment of hypertension. Our findings suggest that improvement of the detection of hypertension and adherence to the current guidelines on the management of hypertension might prevent a considerable proportion of incident strokes among hypertensive men and women. The potential impact of achieving control of blood pressure among those already treated on the reduction of stroke incidence remains uncertain.

Acknowledgment

This study was supported by a grant from the Stichting Maatschappelijke Aandachtsgebieden of the University of Utrecht.
References


Excess Stroke Among Hypertensive Men and Women Attributable to Undertreatment of Hypertension
Olaf H. Klungel, Bruno H. C. Stricker, Arsenio H. P. Paes, Jacob C. Seidell, Albert Bakker, Zoltán Vokó, Monique M. B. Breteler and Anthonius de Boer

*Stroke*. 1999;30:1312-1318
doi: 10.1161/01.STR.30.7.1312

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1999 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/30/7/1312

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Stroke* is online at:
http://stroke.ahajournals.org//subscriptions/