

**FHS PUBLIC ACCESS****Author manuscript***J Clin Hypertens (Greenwich)*. Author manuscript; available in PMC 2017 August 01.

Published in final edited form as:

*J Clin Hypertens (Greenwich)*. 2016 August ; 18(8): 784–789. doi:10.1111/jch.12761.

## Examination of Several Physiological and Psychosocial Factors Potentially Associated with Masked Hypertension Among Low-Risk Adults

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### Abstract

We examined the association of factors in addition to prehypertensive office blood pressure (BP) level that might improve detection of masked hypertension (MH, defined as non-elevated office BP with elevated out-of-office BP average) among those otherwise at low-risk. This sample of 340 untreated adults 30 years and older with office BP average <140/90 mmHg all had two sets of paired office BP measurements and 24-hour ambulatory BP monitoring (ABPM) sessions one week apart. Other than BP levels, the only factors that were associated (at  $P < 0.10$ ) with MH at both sets were male sex (75% vs 66%) and working outside the home (72% vs 59% first set; 71% vs 45% second set). Adding these variables to BP level in the model did not appreciably improve detection of MH. We found no demographic, clinical, or psychosocial measures that improved upon prehypertension as a potential predictor of MH in this sample.

### Keywords

masked hypertension; ambulatory blood pressure monitoring; prehypertension

### Introduction

Masked hypertension (MH), defined as non-elevated office blood pressure (BP) with elevated average out-of-office BP, conveys cardiovascular risk approaching that of sustained hypertension (BP elevated in office and out-of-office).<sup>1–5</sup> Studies have demonstrated that MH is a reproducible phenotype and that people with BP in the “high-normal” or upper level prehypertension range are more likely to have MH.<sup>6,7</sup> Detection of MH requires either ambulatory BP monitoring (ABPM) or home BP monitoring to acquire data for calculating

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Conflicts of interest: Dr. Viera has served on the Medical Advisory Board of Suntech Medical, manufacturer of the Oscar 2 ambulatory BP monitor.

out-of-office BP average. Given that either method requires resources including equipment and time, it would be valuable to have a strategy for targeting which patients with a non-elevated office BP ought to have systematically performed out-of-office BP measurements in order to detect MH.

One could posit reasons why BP might be systematically normal inside the office but elevated outside the office. For example, work stress may lead to BP elevations that are actually diminished when one is sitting in a health care provider's office.<sup>8</sup> Home strain, trait-anger, and high stress in general may all act similarly.<sup>9–11</sup> Smoking, which transiently raises BP, may contribute to an elevated out-of-office BP average that is not detected in a clinical setting due to the time refraining from a cigarette.<sup>12,13</sup> In one Israeli study, MH was associated with younger age, male sex, and higher awake pulse rate.<sup>14</sup> Identification of factors consistently associated with MH would help clinicians decide which patients with a non-elevated office BP should be considered for out-of-office BP monitoring.

We previously reported the sensitivity and specificity of prehypertensive office blood pressures for detecting MH.<sup>7</sup> In that study, we noted that while an office BP cutoff of >120/82 mm Hg had the best performance as a screening test for identifying possible MH, it unfortunately had a high false positive rate. A risk assessment that uses variables in addition to office BP level might improve prediction and decrease the proportion of people who would be tested by ABPM but found to have normal ambulatory blood pressure. In this study, we examined the association of several candidate variables with MH and whether any associated variables besides prehypertension improved identification of adults with MH who were not taking BP lowering medications.

## Methods

### Study Recruitment and Setting

We recruited 420 adults via a combination of passive recruitment and active recruitment. For passive recruitment, we posted signs in seven primary care clinics inviting people with a recent office (clinic) BP measurement that was “borderline” or “a little high” to participate. Individuals interested in participating contacted a study coordinator to confirm eligibility and schedule their study visits. For active recruitment, we sent an email about the study to our campus listserv approximately every 3–4 months. Study coordinators also recruited potentially eligible participants via electronic medical records review of vital signs documented during their most recent primary care clinic visit. To be eligible, a person had to be 30 years of age or older, have a primary care clinician, and be on no BP-lowering medications. The participant's most recent clinic visit BP had to be between 120–149 mm Hg systolic or 80–95 mm Hg diastolic with neither greater than 149/95 mm Hg. Exclusion criteria included diabetes, pregnancy, dementia, any condition that would preclude wearing an ambulatory BP monitor, and persistent atrial fibrillation or other arrhythmia. As an incentive, participants were offered \$150 for completion of the study. All study procedures took place in a clinical research center.

### Office Blood Pressure in the Research Setting

At the 4 study visits (Figure 1), following check-in procedures participants were placed in an exam room within the clinical research center. After at least a 5-minute rest, same arm BP was measured three times by a validated office-type oscillometric device (Welch Allyn Vital Signs<sup>15</sup>) according to recommended timing and positioning and using the appropriate BP cuff size.<sup>16</sup> The three measurements were averaged to determine the participant's office BP measurement for the visit.

For this analysis, we excluded participants (n=80) with initial research office BP average 140/90 mm Hg at the first set of measurements as such participants would either have sustained hypertension or white-coat hypertension as opposed to masked hypertension or sustained normotension.

### Ambulatory Blood Pressure Monitoring

Participants underwent two 24-hour ABPM sessions one week apart using the Oscar 2 oscillometric monitor (Suntech Medical, Morrisville, NC). The Oscar 2 has been validated for use in adults by both the British Hypertension Society protocol and the International Protocol for the validation of blood pressure measuring devices.<sup>17,18</sup> The monitors were programmed to measure BP at 30 minute intervals from 6am to 11pm and at 1 hour intervals from 11pm to 6am. The relaxed intervals were chosen to minimize wearer burden given that we asked participants to wear the BP monitor twice in a short time span. Maximum BP measurement time was limited to less than 140 seconds, and the monitors were set for a maximum pressure of 220 mm Hg. Participants were given verbal instructions on wearing the monitor, including that they should try to leave the cuff on during the entire monitoring period, that they should try to hold their cuffed arm as still as possible during a measurement to ensure that the monitor would get an accurate reading, that cuff inflation would cause a tight feeling around the arm, and that faulty readings would trigger a repeat measurement. The minimum number of readings we accepted as an adequate ABPM session was 14 for daytime and 6 for nighttime.

### Other Variables

Perceived stress was measured using the Perceived Stress Scale.<sup>19</sup> Trait anger, trait anxiety, and state anxiety were measured using the Spielberger inventories.<sup>20,21</sup> Job strain was measured using the Karasek Job<sup>22</sup>, and home life stress was measured using the Home Life Pressure Index.<sup>23</sup> Height and weight were measured at the first study visit and used to calculate body mass index (BMI). Arm circumference at mid-biceps was measured at the first study visit and used to guide BP cuff size. Demographics and medical history items were collected by self-administered questionnaire.

### Analysis

MH was defined as a preceding research office BP average < 140/90 mm Hg with either a mean 24-hour ambulatory systolic BP  $\geq$  130 mm Hg or mean 24-hour diastolic BP  $\geq$  80 mm Hg.<sup>24</sup> Normotension was defined as a preceding research office BP average < 140/90 mm Hg with both a mean 24-hour ambulatory systolic BP < 130 mm Hg and mean 24-hour diastolic BP < 80 mm Hg. We examined bivariate associations of several preselected

candidate “predictor” variables with MH separately for each session of paired office and ambulatory BP measurements. We modeled the MH status at the two time points simultaneously using generalized estimating equations (GEE) method with an exchangeable working matrix to account for dependence between two outcomes. The time factor was not significant in any of the 3 models and hence was dropped from the final models. Using C-statistics with MH based on the first set of measurements as the outcome, we compared a model containing only BP levels to a model containing other variables that were associated with MH at the  $P < 0.10$  level at both sessions.

### Study Approval

This study was approved by the Office of Human Research Ethics at the University of North Carolina at Chapel Hill.

## Results

### Participant Characteristics

The mean  $\pm$  standard deviation ( $\pm$ SD) age of the 340 participants included in the analysis was 48 ( $\pm$ 12) years. Most participants were between 30 and 44 years (44%) or between 45 and 64 years (44%) (Table 1). A small proportion was older than 65 years (12%). Nearly 60% were female. Three-fourth were white, and 22% were Black. Most were college graduates (64%), and the majority (94%) reported good to excellent health. Most (93%) were also nonsmokers and overweight (32%) or obese (39%). The majority were married or living with a partner. Only 3 participants did not have sufficient daytime ambulatory BP monitor readings at the first session, and 5 did not have sufficient daytime ambulatory BP monitor readings at the second session.

### Prevalence of Masked Hypertension in the Study Sample

As previously described, the prevalence of MH in the overall study sample was high.<sup>25</sup> This high prevalence may have been the result of our method of recruiting people who had a recent “borderline” office BP measurement. When the sample was restricted to only those with prehypertensive research office visit BP average, the prevalence was especially high. Using the office BP average paired with the immediately following ABPM average, the prevalence of MH based on the first sets of measurements was 69.4% (95% CI 64.1%–74.7%), and the prevalence based on the second sets of measurements was 65.9% (95% CI 60.5%–71.3%).

### Associations with Masked Hypertension

Other than the BP levels, the only factors that were associated (at  $P < 0.10$ ) with MH at both time periods were male sex and working outside the home (Table 2). Using the first set of measurements, 75% of men vs 66% of women had MH, and using the second set, 73% of men vs 61% of women had MH. Among those who worked outside the home, 72% and 71% had MH by first and second set of measurements vs 59% and 45% among those who did not work outside the home. None of the candidate psychosocial measures we examined appeared to be associated with MH (Table 3). Adding variables to BP level in the model did not appreciably improve detection of MH (Table 4).

## Discussion

In this study, we sought to identify factors consistently associated with MH. Identification of such factors would help clinicians decide which patients with a prehypertensive office BP should be considered for out-of-office BP monitoring in order to detect masked hypertension. We examined several candidate demographic, clinical, and psychosocial variables, but none was strongly associated with MH. The best “predictor” of MH is prehypertensive office BP level.

Other investigators have identified some factors associated with MH. Male sex, high pulse rate and smoking were associated with MH in one Israeli study.<sup>14</sup> We did not note high pulse rate or smoking to be associated with MH, but our study had a low prevalence of smokers, and our participants also differed in that they were not actually being seen for a clinical visit. We did observe male sex to be associated, but it was not helpful in improving detection of MH. A different study, conducted in Finland, found older age, higher BMI, smoking, and excessive alcohol consumption to be associated with MH.<sup>26</sup> Our study did not replicate these findings, but we note that the Finnish study was of a much larger sample size (N=1459), which increased its power to find statistically significant associations. A prior study, also with a much larger sample size, also found job strain (high demand and high decision latitude) to be associated with MH in a sample of male white-collar workers, but not among female white-collar workers.<sup>27</sup>

In our study, we noted that simply working outside the home was associated with MH. It is important to acknowledge that guidelines recommend that ABPM be performed on a workday. In previous work, we pointed out that home BP monitoring and ABPM are not interchangeable for detecting MH. The obvious limitation is that home BP measurements are typically only made in the morning and in the evening, periods that may miss times when BP is prone to elevation. It is possible that a home BP monitor taken to work and used in the workplace, or used mid-day at home, might be able to identify MH. Such a protocol could be tested in further studies.

Prehypertension increases cardiovascular risk compared to optimal BP, but not enough to justify antihypertensive therapy for most patients. It is possible that much of the risk attributable to office prehypertension is actually a reflection of a population in which a large proportion of people have masked hypertension. We know from multiple studies that the cardiovascular risk of MH approaches that of sustained hypertension. Thus, ambulatory BP monitoring may be useful to risk stratify patients who have prehypertensive office BPs, for whom treatment beyond lifestyle modifications might be considered. It was our hope that additional variables could be used to guide such a strategy, but the BP level itself may indeed be the best clinical harbinger of potential MH. Further studies are still needed to determine whether treatment of MH, guided by out-of-office BP measurements, leads to reduced CVD events. The answer may also depend on the natural history of MH, or the time it takes for such patients to “transition” to sustained hypertension. Patients’ acceptance of treatment of MH—when their office BP is “normal” —also needs to be examined.

Streamlining use of ABPM to identify MH is desired because of the costs and the potential discomfort involved. For patients whose office BP is elevated (i.e. 140/90 mmHg), ambulatory BP monitoring has been shown to be cost-effective compared to reliance of office BP measurements alone because of its ability to identify white-coat hypertension, which most evidence suggests need not be treated.<sup>28</sup> Future analyses could also examine the cost of using ambulatory BP monitoring among patients whose BP is prehypertensive. Assuming treatment of MH reduces the risk of CVD events, such a strategy might be cost-effective compared to relying only on office BP measurements and not treating patients with MH.

### Strengths and Limitations

Strengths of our study included its repeated sets of measurements of office and ambulatory BP as well as its measurement of several candidate factors. We also acknowledge several limitations. Our sample may not be representative of a general clinic population, and we did not include diabetics. The sample also had a high prevalence of MH, which may have diminished our ability to identify associated factors. Our sample also had relatively low prevalence of risk factors, such as smoking, that have been found in other studies to be associated with MH. Finally, there may be factors that are associated with MH that we simply did not measure.

### Conclusion

Prehypertensive BP levels are associated with MH. The additional factors examined in this study did not significantly improve ability to discriminate between people more vs less likely to have MH. For now, clinicians and researchers interested in using ambulatory BP monitoring to detect MH could consider offering it to patients 30 years and older whose BP is in the prehypertensive range.

### Acknowledgments

This study was supported by grant R01 HL098604 from the National Heart Lung and Blood Institute.

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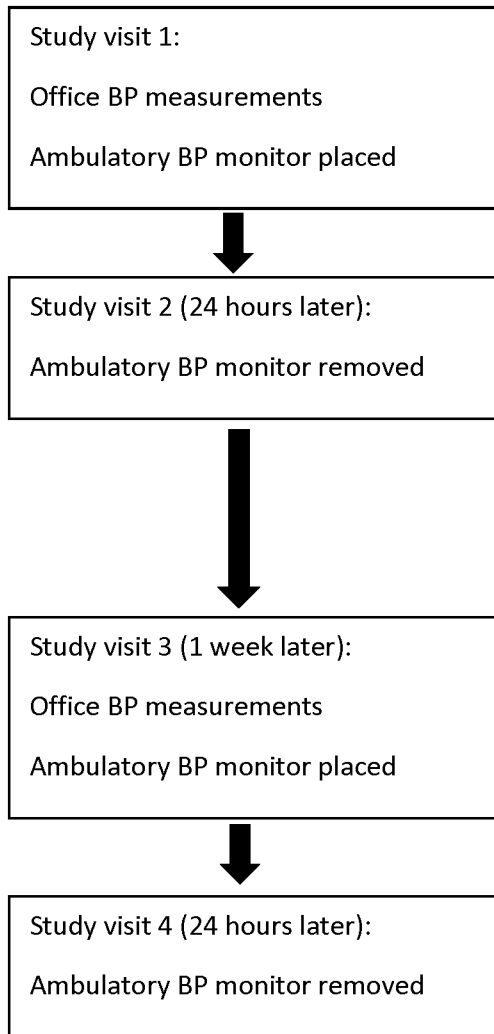
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**Figure 1.**  
Participant Study Flow

**Table 1**

## Participant Characteristics (N=340)

| Characteristic                             | n   | Percent |
|--|-----|---------|
| Age group (years)                          |     |         |
| 30–44                                      | 151 | 44      |
| 45–64                                      | 149 | 44      |
| >65  | 40  | 12      |
| Female sex                                 | 199 | 59      |
| Race                                       |     |         |
| Black                                      | 74  | 22      |
| White                                      | 254 | 75      |
| Other                                      | 12  | 3       |
| Education level                            |     |         |
| Some high school                           | 5   | 1       |
| High school graduate                       | 16  | 5       |
| Some college                               | 64  | 19      |
| College graduate                           | 255 | 75      |
| Work outside home                          | 263 | 77      |
| Total household income (annual)            |     |         |
| <\$25,000                                  | 42  | 13      |
| \$25,000–50,000                            | 68  | 20      |
| >\$50,000                                  | 226 | 67      |
| Insurance status                           |     |         |
| Private                                    | 239 | 71      |
| Public                                     | 45  | 13      |
| Both                                       | 33  | 10      |
| Uninsured                                  | 21  | 6       |
| Self-reported health                       |     |         |
| Excellent/very good                        | 231 | 68      |
| Good                                       | 90  | 26      |
| Fair or poor                               | 19  | 6       |
| Nonsmoker                                  | 315 | 93      |
| Drink alcohol                              | 125 | 56      |
| Caffeine intake > 75 <sup>th</sup> percent | 81  | 24      |
| Married or living with partner             | 217 | 64      |
| BMI  |     |         |
| Normal (<25 kg/m <sup>2</sup> )            | 99  | 29      |
| Overweight (25–29 kg/m <sup>2</sup> )      | 109 | 32      |
| Obese (≥ 30 kg/m <sup>2</sup> )            | 132 | 39      |
| Resting pulse <75 bpm                      | 233 | 69      |
| Microalbuminuria                           | 76  | 23      |
| Office systolic BP at visit 1              |     |         |

| Characteristic                 | n   | Percent |
|--------------------------------|-----|---------|
| < 120 mmHg                     | 94  | 31      |
| 120–130 mm Hg                  | 125 | 41      |
| 131–139 mm Hg                  | 87  | 28      |
| Office diastolic BP at visit 1 |     |         |
| <80 mmHg                       | 178 | 56      |
| 80–84 mm Hg                    | 62  | 20      |
| 85–89 mm Hg                    | 77  | 24      |

BMI, body mass index

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**Table 2**

**Bivariate Associations of Participant Characteristics with Masked Hypertension**

| Characteristic                  | Category                         | Percent with MH at visit 1 | P-value | Percent with MH at visit 2 | P-value |
|---------------------------------|----------------------------------|----------------------------|---------|----------------------------|---------|
| Age group (years)               | 30-44                            | 71                         | 0.64    | 74                         | 0.029   |
|                                 | 45-64                            | 69                         |         | 61                         |         |
|                                 | >65                              | 63                         |         | 54                         |         |
| Sex                             | Male                             | 75                         | 0.09    | 73                         | 0.03    |
|                                 | Female                           | 66                         |         | 61                         |         |
| Race                            | Black                            | 70                         | 0.95    | 62                         | 0.40    |
|                                 | White/other                      | 69                         |         | 67                         |         |
| Education level                 | <College grad                    | 69                         | 0.90    | 63                         | 0.61    |
|                                 | College graduate                 | 70                         |         | 67                         |         |
| Work outside home               | Yes                              | 72                         | 0.04    | 71                         | 0.0001  |
|                                 | No                               | 59                         |         | 45                         |         |
| Total household income (annual) | <\$25,000                        | 75                         | 0.45    | 68                         | 0.91    |
|                                 | \$25,000-50,000                  | 63                         |         | 64                         |         |
|                                 | >\$50,000                        | 69                         |         | 67                         |         |
| Insurance status                | Insured (any)                    | 69                         | 0.41    | 66                         | 0.64    |
|                                 | Uninsured                        | 78                         |         | 60                         |         |
| Self-reported health            | Excellent/very good              | 70                         | 0.61    | 66                         | 0.91    |
|                                 | Good                             | 66                         |         | 64                         |         |
| Current smoker                  | Fair or poor                     | 78                         |         | 69                         |         |
|                                 | Yes                              | 87                         | 0.06    | 81                         | 0.18    |
| Drink alcohol                   | No                               | 68                         |         | 65                         |         |
|                                 | Yes                              | 74                         | 0.78    | 65                         | 0.78    |
| Caffeine intake                 | No                               | 72                         |         | 63                         |         |
|                                 | High                             | 75                         | 0.20    | 73                         | 0.13    |
| Relationship                    | Low/moderate                     | 67                         |         | 64                         |         |
|                                 | Married / living with partner    | 69                         | 0.80    | 65                         | 0.58    |
|                                 | Single / not living with partner | 70                         |         | 68                         |         |
| BMI                             | Normal (<25 kg/m <sup>2</sup> )  | 70                         | 0.94    | 64                         | 0.45    |

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| Characteristic      | Category                              | Percent with MH at visit 1 | P-value | Percent with MH at visit 2 | P-value |
|---------------------|---------------------------------------|----------------------------|---------|----------------------------|---------|
| Resting pulse       | Overweight (25–29 kg/m <sup>2</sup> ) | 70                         |         | 71                         |         |
|                     | Obese (≥30 kg/m <sup>2</sup> )        | 68                         |         | 63                         |         |
|                     | <75 bpm                               | 66                         | 0.055   | 66                         | 0.87    |
| Microalbuminuria    | 75 bpm                                | 77                         |         | 65                         |         |
|                     | Yes                                   | 79                         | 0.055   | 73                         | 0.14    |
| Office systolic BP  | No                                    | 66                         |         | 63                         |         |
|                     | <120 mm Hg                            | 47                         | <0.0001 | 48                         | <0.0001 |
|                     | 120–130 mm Hg                         | 82                         |         | 70                         |         |
|                     | 131–139 mm Hg                         | 77                         |         | 83                         |         |
| Office diastolic BP | <80 mm Hg                             | 60                         | 0.0001  | 55                         | <0.0001 |
|                     | 80–84 mm Hg                           | 82                         |         | 73                         |         |
|                     | 85–89 mm Hg                           | 83                         |         | 89                         |         |

**Table 3**  
 Bivariate Associations of Psychosocial Measures with Masked Hypertension

| Characteristic     | Quartile | Percent with MH at visit 1 | P-value | Percent with MH at visit 2 | P-value |
|--------------------|----------|----------------------------|---------|----------------------------|---------|
| State anxiety      | 1        | 71                         | 0.83    | 70                         | 0.55    |
|                    | 2        | 68                         |         | 63                         |         |
|                    | 3        | 65                         |         | 61                         |         |
|                    | 4        | 72                         |         | 70                         |         |
| Trait anxiety      | 1        | 68                         | 0.97    | 64                         | 0.95    |
|                    | 2        | 71                         |         | 69                         |         |
|                    | 3        | 68                         |         | 66                         |         |
|                    | 4        | 70                         |         | 65                         |         |
| Job strain         | 1        | 71                         | 0.77    | 73                         | 0.29    |
|                    | 2        | 67                         |         | 68                         |         |
|                    | 3        | 76                         |         | 64                         |         |
|                    | 4        | 74                         |         | 79                         |         |
| Home life pressure | 1        | 70                         | 0.98    | 69                         | 0.79    |
|                    | 2        | 71                         |         | 66                         |         |
|                    | 3        | 68                         |         | 68                         |         |
|                    | 4        | 68                         |         | 61                         |         |
| Perceived stress   | 1        | 62                         | 0.18    | 67                         | 0.36    |
|                    | 2        | 75                         |         | 73                         |         |
|                    | 3        | 62                         |         | 60                         |         |
|                    | 4        | 72                         |         | 62                         |         |
| Trait anger        | 1        | 68                         | 0.037   | 58                         | 0.35    |
|                    | 2        | 80                         |         | 72                         |         |
|                    | 3        | 67                         |         | 64                         |         |
|                    | 4        | 59                         |         | 68                         |         |

**Table 4**

Models with Sex and Work Outside the Home Added to Blood Pressure Levels

|                            | Model 1 |          |         | Model 2 |          |         | Model 3 |          |                   |
|----------------------------|---------|----------|---------|---------|----------|---------|---------|----------|-------------------|
|                            | OR      | 95% CI   | p-value | OR      | 95% CI   | p-value | OR      | 95% CI   | p-value           |
| <b>Office systolic BP</b>  |         |          |         |         |          |         |         |          |                   |
| <120 mm Hg                 | 1.0     |          |         | 1.0     |          |         | 1.0     |          |                   |
| 120–130 mm Hg              | 2.2     | 1.4, 3.4 | <0.001  | 2.2     | 1.4, 3.3 | <0.001  | 2.3     | 1.5, 3.6 | <0.001            |
| 131–139 mm Hg              | 2.3     | 1.4, 3.7 | <0.001  | 2.2     | 1.4, 3.5 | <0.001  | 2.4     | 1.5, 3.8 | <0.001            |
| <b>Office diastolic BP</b> |         |          |         |         |          |         |         |          |                   |
| < 80 mm Hg                 | 1.0     |          |         | 1.0     |          |         | 1.0     |          |                   |
| 80–84 mm Hg                | 1.8     | 1.1, 3.0 | 0.029   | 1.7     | 1.0, 2.9 | 0.036   | 1.7     | 1.0, 2.9 | 0.049             |
| 85–89 mm Hg                | 2.5     | 1.4, 4.3 | 0.001   | 2.4     | 1.4, 4.2 | 0.001   | 2.4     | 1.4, 4.2 | 0.001             |
| <b>Sex</b>                 |         |          |         |         |          |         |         |          |                   |
| Male                       |         |          |         | 1.0     |          |         | 1.0     |          |                   |
| Female                     |         |          |         | 0.7     | 0.5, 1.1 | 0.16    | 0.8     | 0.5, 1.2 | 0.26              |
| <b>Work outside home</b>   |         |          |         |         |          |         |         |          |                   |
| No                         |         |          |         |         |          |         | 1.0     |          |                   |
| Yes                        |         |          |         |         |          |         | 2.4     | 1.5, 3.8 | <0.001            |
| C-statistic                | 0.709   |          |         | 0.714   |          | 0.78*   | 0.736   |          | 0.26 <sup>†</sup> |

\* p-value for model 1 and model 2 comparison;

<sup>†</sup> p-value for model 2 and model 3 comparison