INTRODUCTION
The metabolic syndrome is characterized by abdominal adiposity, dyslipidemia, elevated glucose and blood pressure. The metabolic syndrome is strongly linked to cardiovascular events, cancer and mortality. Given that the metabolic syndrome is becoming a worldwide pandemic, with prevalence rates between 20 and 30% among the adult population, the identification of modifiable risk factors associated with the development of metabolic syndrome is important to public health. Sleep is a basic human need; it takes up more time in a day than any other activity. Too short or too long a duration of habitual sleep are currently thought to be important lifestyle risk factors for such metabolic diseases such as diabetes, obesity and cardiovascular disease, and sleep duration may also be a significant predictor of all-cause mortality in prospective population studies. Several epidemiological studies have been conducted to investigate the association between length of sleep and metabolic syndrome, with inconsistent results. A number of studies in adults have demonstrated an association between short sleep duration and metabolic syndrome. Conversely, some of these studies also showed that long sleep duration was associated with metabolic syndrome. To our knowledge, there has been no published systematic literature review that has characterized the magnitude of these associations. Therefore, we have summarized published data from cross-sectional and prospective cohort studies, and performed a meta-analysis to obtain a quantitative estimate of the risk.

MATERIALS AND METHODS

We planned, conducted and reported this systematic review according to widely accepted standards of quality for reporting meta-analyses of observational studies in epidemiology (Supplementary Table 1). Literature search
A master’s level medical librarian with experience in systematic reviews participated in designing the search strategy. We searched PubMed, Cochrane CENTRAL, PsycINFO and EMBASE via Elsevier from the date of inception until 26 November 2012. A PubMed search for studies on sleep and metabolic syndrome was conducted without restrictions by combining synonymous or related search terms for sleep and metabolic syndrome. The keywords used in the PubMed search were converted to search tags for Cochrane CENTRAL, PsycINFO and EMBASE (Supplementary Table 2). In addition, manual searches of the bibliographies of the relevant articles were performed to identify additional studies.

Study selection
Several criteria were used to identify relevant studies for the meta-analysis. The studies included had an observational design, including cross-sectional studies and cohort studies, and were conducted in human adults. The exposure of interest was sleep duration. The outcome of interest was metabolic syndrome. Finally, the adjusted relative risk estimates (odds ratios [OR] in cross-sectional studies) and their corresponding 95% confidence intervals (CI), or sufficient data to calculate these values, were reported. We selected full-length articles without language

OBJECTIVE: Epidemiological studies have repeatedly investigated the association between sleep duration and metabolic syndrome. However, the results have been inconsistent. This meta-analysis aimed to summarize the current evidence from cross-sectional and prospective cohort studies that evaluated this.

DATA SOURCES: Relevant studies were identified by systematically searching the PubMed, Cochrane CENTRAL, EMBASE and PsycINFO databases through November 2012 without language restriction.

STUDY SELECTION: We identified 12 cross-sectional studies with 76,027 participants including 14,404 cases of metabolic syndrome, and 3 cohort studies with 2055 participants and 283 incident cases of metabolic syndrome.

RESULTS: For short sleep durations (<5 to 6 h), the odds ratios (OR) was 1.27 (95% confidence interval [CI] = 1.10–1.48, \(I^2 = 75.5\%\)) in the 12 cross-sectional studies and 1.62 (95% CI = 0.74–3.55, \(I^2 = 71.4\%\)) in the 3 cohort studies; for long sleep durations (>8 to 10 h), the OR was 1.23 (95% CI = 1.02–1.49, \(I^2 = 75.8\%\)) in the 11 cross-sectional studies and 1.62 (95% CI = 0.86–3.04, \(I^2 = 0.0\%\)) in the 2 cohort studies.

CONCLUSIONS: Short and long sleep durations are risky behaviors for increasing the risk of metabolic syndrome and thus have important public health implications, as sleep habits are amenable to behavioral interventions. The available data are sparse, and further studies, especially longitudinal studies, are needed to facilitate a better understanding of these associations.

S-Y Ju and W-S Choi

S-Y Ju1 and W-S Choi2
Sleep duration and metabolic syndrome in adult populations
S-Y Ju and W-S Choi

RESULTS

Literature searches and study selection

Figure 1 shows a flow diagram of the procedure used to identify the relevant studies. Briefly, we identified 36 potentially relevant articles on sleep duration in relation to metabolic syndrome after an initial screening of titles and abstracts. After we examined the 36 assembled articles, 24 articles were excluded (Supplementary Table 4). Finally, we identified 12 articles including 15 studies that investigated the association between sleep duration and metabolic syndrome risk; 3 articles reported separate results for stratification by gender. No additional studies were identified via cross-referencing.

Study characteristics

Most of studies used multivariate logistic regression to adjust for potential confounders. The 12 cross-sectional studies, with 76,027 participants, including 14,404 metabolic syndrome patients and the three cohort studies, with 2,055 participants, are represented in Table 1. A total of 283 metabolic syndrome cases occurred during follow-up in the three cohort studies.

Three studies defined metabolic syndrome using the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP-III). Four studies assessed metabolic syndrome using the modified NCEP ATP-III. Two studies used the American Heart Association/National Heart Lung and Blood Institute’s criteria. One study used the modified criteria of the AHA/NHLBI and assessed abdominal obesity according to the World Health Organization’s definition. Two studies used the Japanese criteria for metabolic syndrome.

Eight studies used the assessed sleep duration using a questionnaire and four studies used an interview. Of the included studies, five were conducted in men, four in women, and eight in both genders; seven were conducted in Asia, four in the United States and one in Europe. All of the studies were published in the 2000s. The study periods ranged from 1 to 7 years. The patients’ age ranged from 18 to 50 years. The study quality was high in 10 of the 15 included studies (3 cohort and 12 cross-sectional studies).

Short duration of sleep

Short duration of sleep was significantly associated with a greater risk of developing metabolic syndrome in four of the twelve cross-sectional studies and two of the three cohort studies. The pooled OR between short sleep and metabolic syndrome was 1.27 (95% CI = 1.10–1.48, I² = 75.5%) in the 12 cross-sectional studies and 1.62 (95% CI = 0.74–3.55, I² = 71.4%) in the 3 cohort studies (Figure 2). Significant heterogeneity was observed (P < 0.1). No publication bias was detected with Egger’s test (P = 0.17) or Begg’s test (P = 0.92) (Figure 3).

Subgroup analyses of the cross-sectional studies are shown in Table 2. There were significant differences in the mean age, cohort-based group, definition of metabolic syndrome, quality of study and sleeping measure (P for heterogeneity < 0.1). No significant group difference was found for gender or location.

Long duration of sleep

Long duration of sleep was associated with a greater risk of developing metabolic syndrome in five of the eleven cross-sectional studies and none of the two cohort studies. The pooled OR between long sleep and metabolic syndrome was 1.23 (95% CI = 1.02–1.49, I² = 75.8%) in the 11 cross-sectional studies and 1.62 (95% CI = 0.86–3.04, I² = 0.0%) in the 2 cohort studies. Significant heterogeneity was observed between the 11 cross-sectional studies (P < 0.1). No publication bias was detected with Egger’s test (P = 1.33) or Begg’s test (P = 0.95) (Figure 3).

Subgroup analyses of the cross-sectional studies are shown in Table 2. There were significant differences in location, definition of metabolic syndrome, quality of study and sleeping measure (P for heterogeneity < 0.1). No significant group difference was found for gender, age or cohort-based group.

Dose–response relationship

When we assessed the dose–response relationship between sleep duration and metabolic syndrome, we found some evidence of a statistically significant departure from linearity (P < 0.001; Figure 4). Among the shorter and longer sleepers, the risk of metabolic syndrome might increase gradually compared with individuals who report sleeping 7 h per day. Compared with the reference level, the combined odds ratios of metabolic syndrome were 1.33 (95% CI = 1.07–1.65) for ≤5 h per day, 1.21
(95% CI = 1.04–1.41) for 5.5 h per day, 1.11 (95% CI = 1.02–1.21) for 6 h per day, 1.04 (95% CI = 1.00–1.07) for 6.5 h per day, 1.07 (95% CI = 1.00–1.13) for 8 h per day, 1.15 (95% CI = 1.03–1.28) for 8.5 h per day, 1.26 (95% CI = 1.07–1.49) for 9 h per day and 1.38 (95% CI = 1.10–1.74) for ≥9.5 h per day in the eight cross-sectional studies.17,19,22,23,33,35,36 There was significant between-study heterogeneity among study-specific trends defined by the coefficient of the first and second spline transformations of sleep duration (P < 0.1).

Sensitivity analyses in the cross-sectional studies
We included five studies of healthy populations and participants not taking antihypertensive medication for our sensitivity analyses.17,20,22,36 The sensitivity meta-analyses yield somewhat weakened summary ORs of 1.22 (95% CI = 0.96–1.54) for short sleep durations and 1.14 (95% CI = 0.98–1.32) for long sleep durations. There was heterogeneity for short sleep (I² = 33%, P = 0.20) and long sleep (I² = 84.6%, P < 0.1). We also excluded two studies from our sensitivity analyses, as they reported the association between sleep duration and metabolic syndrome in police officers. The sensitivity meta-analyses yielded nearly identical summary ORs of 1.25 (95% CI = 1.07–1.46; I² = 78.6%) for short sleep and 1.22 (95% CI = 1.22–1.48; I² = 77.9%) for long sleep.

**DISCUSSION**
To our knowledge, this is the first quantitative systematic review of observational studies investigating the effect of sleep duration on the risk of metabolic syndrome using data from cross-sectional and cohort studies. This study shows a significant increased risk of metabolic syndrome on either end of the distribution of sleep duration in the cross-sectional studies, but not in the cohort studies. Pooled analyses of cross-sectional studies indicate that short sleepers have a greater risk of metabolic syndrome compared with those who sleep 7–8 h per night. Longer sleepers also show an increased risk for metabolic syndrome, confirming the presence of a U-shaped association in the cross-sectional studies. There was some heterogeneity between studies, no publication bias and no differences between men and women. Furthermore, compared with the 7-h sleep duration, U-shaped associations between sleep duration and the risk of metabolic syndrome were observed in a dose–response meta-analysis of eight cross-sectional studies. This complementary investigation may strengthen the plausibility of a causal association, and allow
## Table 1. Characteristics of cross-sectional and cohort studies included in the meta-analysis

| Author study name | Country observation period | No. of participants | No. of cases | Age range mean (s.d.) | Gender population | Metabolic syndrome assessment | Sleeping assessment | Sleep (h) | Odds ratio (95% CI) | Adjusted covariates |
|-------------------|---------------------------|---------------------|--------------|-----------------------|-------------------|----------------------------|-------------------|-----------|----------------------|-------------------|
| **Cross-sectional studies** | | | | | | | | | | |
| Santos et al. | Portugal 1999–2003 | 832 | 96 | 18–92 | Men | NCEP ATP-III | Questionnaire | ≤ 6 | 1.40 (0.76–2.60) | 1, 3, 4, 5 |
| | | 216 | 216 | | | | | 7 | 1.00 (Reference) | |
| | | 247 | 247 | | | | | 8 | 1.10 (0.73–1.70) | 1, 2, 3, 4, 5 |
| | | 1332 | 1332 | | | | | > 9 | 1.50 (0.90–2.60) | |
| | | 270 | 270 | | | | | ≤ 6 | 0.92 (0.55–1.50) | |
| | | 401 | 401 | | | | | 7 | 1.00 (Reference) | |
| | | 388 | 388 | | | | | 8 | 1.46 (0.80–2.60) | |
| | | 216 | 216 | | | | | ≥ 9 | 2.00 (1.30–3.00) | |
| Choi et al. | KNHNS, 2001 Korea 2001 | 633 | 217 | 44.1 (0.4) | Both | Modified NCEP ATP-III | Questionnaire | ≤ 6 | 1.20 (0.87–1.60) | 1, 2, 3, 4, 5, 6, 12 |
| | | 1056 | 293 | | | | | 7 | 1.00 (Reference) | |
| | | 1182 | 274 | | | | | 8 | 1.00 (Reference) | |
| | | 1056 | 293 | | | | | ≥ 9 | 1.70 (1.20–2.50) | |
| Hall et al. | USA 18758 | 30–54 | Both | AHA/NHLBI | Interview | | | 6–6.99 | 1.50 (1.10–2.10) | |
| | | 525 | 100 | | | | | 7–8 | 1.00 (Reference) | |
| | | 100 | 25 | | | | | > 8 | 1.80 (1.00–3.10) | |
| | | 266 | 46 | | | | | < 6 | 0.93 (0.84–1.00) | |
| | | 1069 | 150 | | | | | 7–8 | 1.00 (Reference) | |
| | | 6320 | 101 | | | | | > 8 | 1.80 (1.00–3.00) | |
| | | 1056 | 293 | | | | | ≥ 9 | 1.70 (1.20–2.50) | |
| | | 1332 | 1332 | | | | | ≤ 6 | 0.92 (0.55–1.50) | |
| | | 270 | 270 | | | | | 7 | 1.00 (Reference) | |
| | | 401 | 401 | | | | | 8 | 1.46 (0.80–2.60) | |
| | | 388 | 388 | | | | | ≥ 9 | 2.00 (1.30–3.00) | |
| | | 216 | 216 | | | | | > 9 | 2.00 (1.30–3.00) | |
| Arora et al. | GBCS China 1142 | 329 | 50–96 | Both | Modified NCEP ATP-III | Interview | | 6–7 | 1.00 (Reference) | |
| | | 2020 | 570 | | | | | 7–8 | 1.00 (Reference) | |
| | | 2303 | 603 | | | | | > 8 | 1.10 (1.10–1.20) | |
| | | 1995 | 575 | | | | | ≥ 9 | 1.20 (1.10–1.30) | |
| | | 762 | 226 | | | | | < 6 | 0.93 (0.84–1.00) | |
| | | 100 | 25 | | | | | 7–8 | 1.00 (Reference) | |
| | | 6320 | 101 | | | | | > 8 | 1.80 (1.00–3.00) | |
| | | 1332 | 1332 | | | | | ≥ 9 | 1.70 (1.20–2.50) | |
| | | 270 | 270 | | | | | ≤ 6 | 0.92 (0.55–1.50) | |
| | | 401 | 401 | | | | | 7 | 1.00 (Reference) | |
| | | 388 | 388 | | | | | 8 | 1.46 (0.80–2.60) | |
| | | 216 | 216 | | | | | ≥ 9 | 2.00 (1.30–3.00) | |
| | | 1332 | 1332 | | | | | > 9 | 2.00 (1.30–3.00) | |
| Kobayashi et al. | Japan 2008 | 7295 | 641 | 44.8 (12.8) | Both | JASSO | Questionnaire | | | |
| | | 11335 | 905 | | | | | 6–6.99 | 1.40 (1.20–1.60) | 1, 2, 4, 6, 13 |
| | | 6732 | 592 | | | | | 7–7.99 | 1.00 (Reference) | |
| | | 2410 | 233 | | | | | > 8 | 0.98 (0.83–1.10) | |
| Najafian et al. | Iran 1999–2006 | 1447 | 485 | 38.89 (14.93) | Both | NCEP ATP-III | Interview | < 6 | 1.20 (1.10–1.40) | 1, 2 |
| | | 2336 | 575 | | | | | 7–8 | 1.00 (Reference) | |
| | | 7622 | 1654 | | | | | ≥ 9 | 1.30 (1.20–1.50) | |
| | | 1089 | 223 | | | | | ≤ 6 | 1.20 (1.10–1.30) | |
| | | 5976 | | | | | | 7–8 | 1.00 (Reference) | |
| | | 6320 | | | | | | ≥ 9 | 1.30 (1.20–1.50) | |
| | | 10699 | | | | | | ≤ 6 | 1.20 (1.10–1.30) | |

**Note:** Some studies included both men and women, but the specific breakdown is not provided in the table. The table includes studies from Portugal, Korea, the USA, China, Japan, and Iran. The assessment of metabolic syndrome and sleep was done using various questionnaires and interviews. The odds ratios and confidence intervals (CI) are provided for different sleep durations and age groups.
| Author study name        | Country observation period | No. of participants | No. of cases | Age range mean (s.d.) | Gender population | Metabolic syndrome assessment | Sleeping assessment | Sleep (h) | Odds ratio (95% CI) | Adjusted covariates |
|-------------------------|---------------------------|---------------------|--------------|-----------------------|-------------------|-----------------------------|---------------------|-----------|---------------------|---------------------|
| Sabanayagam et al.      | USA 2005–2008             | 935                 | 377          | 44.63 (0.46)          | Both              | AHA-NHLBI Questionnaire     | < 5                  | 0.84 (0.70–1.00)    | 1, 2, 3, 4, 5, 8, 10 |
| McCanlies et al.        | USA                       | 28                  | 7            | 39.61                 | Both              | NCEP ATP-III Questionnaire  | < 6                  | 2.30 (0.81–6.50)    | 1, 2, 3, 4          |
| Wu et al.               | Taiwan 2006–2009          | 954                 | 198          | 47.1 (12.0)           | Men               | Modified NCEP ATP-III Questionnaire | < 6           | 1.30 (1.00–1.60)    | 1, 3, 4, 5, 7       |
| Yoo et al.              | USA                       | 32                  | 10           | 22–60                 | Both              | Modified AHA-NHLBI Questionnaire | < 6           | 2.30 (0.71–7.50)    | 1, 2, 4, 8, 17      |
| Choi et al.             | KGRC Korea 2005–2009      | 27                  | 5            | 40–70                 | Men               | Modified NCEP ATP-III Interview | < 6           | 0.62 (0.24–1.60)    | 1, 4, 5, 7, 8       |
| Otsuka et al.           | Japan 2005–2009           | 120                 | 20           | 35–63                 | Men               | The Japanese criteria Questionnaire | < 5           | 3.20 (1.50–6.60)    | 1, 4, 5, 6, 16      |

Abbreviations: AHA-NHLBI, American Heart Association/National Heart Lung and Blood Institute; AHAB, Adult Health and Behavior; CES-D, Center for Epidemiological Studies Depression Scale; CI, confidence interval; GBCS, The Guangzhou Biobank Cohort Study; IHPH, Isfahan Healthy Heart Program; JASSO, Japan Society for the Study of Obesity; KGRC, The Korean Genomic Rural Cohort; KNHNs, Korean National Health and Nutrition Survey; NCEP ATP-III, National Cholesterol Education Adult Treatment Panel III; PSQI, Pittsburgh Sleep Quality Index; PSS, Perceived Stress Scale; 1, age; 2, sex; 3, education; 4, smoke; 5, alcohol; 6, exercise; 7, body mass index; 8, physical activity; 9, race; 10, depression; 11, diagnosed mental illness, insomnia, use of hypnotics, daytime sleepiness, snoring, mean systolic pressure, glucose, total cholesterol and triglycerides; 12, family history of hypertension or diabetes, residential area and monthly income; 13, myocardial infarction and cerebral infarction; 14, low-density lipoprotein cholesterol; 15, menopause; 16, frequency of vegetable intake, frequency of oily food intake and frequency of salty food intake; 17, burnout, Center for Epidemiological Studies Depression Scale and Perceived Stress Scale.
us to draw an overview of the nonlinear relationship between sleep duration and metabolic syndrome risk.

Causal mechanisms relating the short duration of sleep to adverse health outcomes include changes in circulating levels of leptin and ghrelin, which in turn would increase appetite and calorie intake, reduce energy expenditure and impair glycemic control. Increased cortisol secretion and altered growth hormone metabolism have also been implicated. Low-grade inflammation is also activated during short sleep. Conversely, the association between a long duration of sleep and metabolic syndrome may be explained by residual confounding factors and comorbidity. Unrecognized confounders such as sleep fragmentation, fatigue and depression could lead to both metabolic syndrome and an increased need for sleep. Long sleepers have less waking time to undertake physical activity, which may contribute to this association. Lifestyle interventions that aim to reduce weight and physical activity may ameliorate the risk of diabetes in long sleepers. Furthermore, obesity itself is regarded as a chronic inflammatory condition. The elevated levels of proinflammatory cytokines have been considered as factors that contribute to increased sleep durations, which promotes insulin resistance.

There are several possible reasons for the risk of metabolic syndrome according to sleep duration. Hypothalamic–pituitary–adrenal hyperactivity has a role in the pathogenesis of the metabolic syndrome, and activation of the hypothalamic–pituitary–adrenal axis can lead to sleeplessness. Sleep fragmentation or restriction leads to insulin resistance, which appears to have a key role in the pathophysiology of metabolic syndrome. In addition, longer sleep could be associated with circadian and hormonal alternations. A previous report suggested that the nocturnal intervals of high plasma melatonin levels, increasing cortisol levels, low body temperature and increasing sleepiness are longer in long sleepers than short sleepers. However, the mechanisms that underlie these associations are not fully understood. An investigation reporting an association between variants of the human CLOCK gene and sleep duration may prove fruitful in this regard. Some evidence has suggested that the covariation among sleep parameters and clusters of metabolic syndrome may be partially related to genetic influences. For example, disruptions of the core CLOCK genes that regulate endogenous circadian rhythmicity are linked to perturbations in glucose metabolism, adipocyte and vascular function, obesity and metabolic syndrome. Thus, it is possible that short and long sleep are linked to metabolic syndrome risk through different pathways.

There were significant differences in the relationship between sleep duration and metabolic syndrome risk in different groups based on age, location, type of cross-sectional study (community based or hospital based), sleep measure, quality of study and definition of metabolic syndrome. However, due to the limited number of studies within several groups, these results should be interpreted cautiously. For short duration of sleep, a significant 33% increase in metabolic syndrome was observed in hospital-based studies. Not surprisingly, hospital-based samples of patients suffering from disease are at a higher risk of developing metabolic syndrome.

Figure 2. Forest plots of the risk of metabolic syndrome associated with (a) short duration of sleep compared with the reference group, and (b) long duration of sleep compared with the reference group. The results are expressed as odds ratio (relative risk in cohort studies) and 95% confidence intervals.

Figure 3. Inverse funnel plot with 95% CIs of the odds ratio of metabolic syndrome according to (a) short duration of sleep compared with the reference group (Egger's test, $P = 0.17$; Begg's test, $P = 0.92$), and (b) long duration of sleep compared with the reference group (Egger's test, $P = 1.33$; Begg's test, $P = 0.95$).
levels of sleep categories were used in a restricted cubic spline
ratios. The eight cross-sectional studies (out of 12) with at least four
reference duration of 7 h per day was used to estimate all odds
the risk of metabolic syndrome in the cross-sectional studies. The
line) for the dose–response relationship between sleep duration and
Figure 4.
The odds ratio (filled circle) with 95% CI (solid longitudinal
Abbreviations: AHA-NHLBI, American Heart Association/National Heart
Lung and Blood Institute; CI, confidence interval; JASSO, Japan Society
for the Study of Obesity; NCEP ATP-III, National Cholesterol Education
Adult Treatment Panel III; OR, odds ratios. *Middle, <60 or ≤61. **Elderly,
>60 or ≥61.

Table 2. Subgroup meta-analyses of cross-sectional studies to explore
sources of heterogeneity

| Subgroups | Short sleep | Long sleep |
|-----------|-------------|------------|
|           | No. of studies | OR (95% CI) | P for heterogeneity | No. of studies | OR (95% CI) | P for heterogeneity |
| Gender    |              |            |                       |              |            |                       |
| Men       | 3            | 1.27 (1.08, 1.49) | 0.156 | 3 | 1.03 (0.80, 1.33) | 0.588 |
| Women     | 3            | 1.49 (1.29, 1.72) | 0.94 (0.80, 1.12) | 3 | 1.06 (0.86, 1.31) | 0.210 |
| Mean age (years) |              |            |                       |              |            |                       |
| *Middle   | 5            | 1.34 (1.21, 1.48) | 1.15 (1.04, 1.28) | 4 | 1.03 (0.90, 1.18) | 0.100 |
| **Elderly| 2            | 0.96 (0.86, 1.06) | 1.00 (0.90, 1.18) | 2 | 0.93 (0.80, 1.07) | 0.100 |
| Location  |              |            |                       |              |            |                       |
| Asia      | 6            | 1.18 (1.11, 1.26) | 1.08 (1.01, 1.16) | 6 | 1.12 (1.03, 1.21) | 0.263 |
| Europe    | 2            | 1.09 (0.74, 1.61) | 1.81 (1.30, 2.52) | 2 | 1.01 (0.86, 1.18) | 0.210 |
| USA       | 4            | 1.40 (1.15, 1.72) | 1.18 (0.89, 1.56) | 3 | 1.01 (0.86, 1.18) | 0.210 |
| Cohorts-based |           |            |                       |              |            |                       |
| Community | 6            | 1.15 (1.07, 1.23) | 1.12 (1.03, 1.21) | 6 | 1.12 (1.03, 1.21) | 0.210 |
| Hospital  | 3            | 1.33 (1.18, 1.49) | 1.01 (0.86, 1.18) | 3 | 1.01 (0.86, 1.18) | 0.210 |
| Measure of sleeping |    |            |                       |              |            |                       |
| Interview | 3            | 1.14 (1.06, 1.23) | 1.09 (1.00, 1.19) | 6 | 1.12 (1.03, 1.21) | 0.263 |
| Questionnaire | 9        | 1.29 (1.18, 1.42) | 1.16 (1.03, 1.31) | 8 | 1.16 (1.03, 1.31) | 0.100 |
| Metabolic syndrome |              |            |                       |              |            |                       |
| NCEP ATP-III | 4            | 1.48 (1.30, 1.68) | 0.93 (0.80, 1.07) | 4 | 1.07 (0.94, 1.11) | 0.100 |
| Modified NCEP | 4          | 1.02 (0.94, 1.11) | 1.24 (1.13, 1.36) | 4 | 1.12 (1.04, 1.20) | 0.100 |
| ATP-III   | 2            | 1.36 (1.10, 1.67) | 1.15 (0.86, 1.54) | 1 | 1.30 (0.71, 2.00) | 0.100 |
| AHA-NHLBI | 1            | 2.30 (0.71, 5.50) | 1.89 (0.51, 0.70) | 1 | 1.39 (1.21, 1.60) | 0.100 |
| JASSO     | 1            | 1.39 (1.21, 1.60) | 0.96 (0.63, 1.46) | 1 | 1.39 (1.21, 1.60) | 0.100 |
| Quality of study |       |            |                       |              |            |                       |
| High      | 7            | 1.06 (0.99, 1.15) | 1.23 (1.13, 1.34) | 6 | 1.23 (1.13, 1.34) | 0.100 |
| Low       | 5            | 1.44 (1.31, 1.58) | 0.96 (0.86, 1.07) | 5 | 1.06 (0.99, 1.15) | 0.210 |

Figure 4. The odds ratio (filled circle) with 95% CI (solid longitudinal
line) for the dose–response relationship between sleep duration and
the risk of metabolic syndrome in the cross-sectional studies. The
reference duration of 7 h per day was used to estimate all odds
ratios. The eight cross-sectional studies (out of 12) with at least four
levels of sleep categories were used in a restricted cubic spline
random-effects meta-analysis.
syndrome risk. Further studies could also shed light on possible sources of heterogeneity across the studies included in this meta-analysis.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

ACKNOWLEDGEMENTS
We thank Jeong So-Na for reviewing and editing this manuscript. This work was supported by research grants from the Catholic Medical Center Research Foundation in the 2012 program year.

AUTHOR CONTRIBUTIONS
Study concept and design: Ju, Choi. Acquisition of the data: Ju, Choi. Analysis and interpretation of the data: Ju. Drafting the manuscript: Ju. Critical revision of the manuscript for important intellectual content: Choi. Statistical analyses: Ju. Obtaining of funds: Choi. Providing of administrative, technical, or material support: Ju and Choi. Supervision of the study: Choi.

DISCLAIMER
The funding sources had no role in the design or execution of the study; the collection, management, analysis or interpretation of the data; or the preparation, review or approval of the manuscript.

REFERENCES
1 Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA 2001; 285: 2486–2497.
2 Mottillo S, Filion KB, Genest J, Joseph L, Pilote L, Poirier P et al. The metabolic syndrome and cardiovascular risk: a systematic review and meta-analysis. J Am Coll Cardiol 2010; 56: 1113–1132.
3 Esposito K, Chiodini P, Colao A, Lenzi A, Giugliano D. Metabolic syndrome and type 2 diabetes: a systematic review and meta-analysis. Diabetes Care 2012; 35: 2402–2411.
4 Wu SH, Liu Z, Ho SC. Metabolic syndrome and mortality: a meta-analysis of prospective cohort studies. Eur J Epidemiol 2010; 25: 375–384.
5 Grundy SM. Metabolic syndrome pandemic. Arterioscler Thromb Vasc Biol 2008; 28: 629–636.
6 Chaput JP, Despres JP, Tremblay A. Association of sleep duration with type 2 diabetes and impaired glucose tolerance. Diabetologia 2007; 50: 2298–2304.
7 Gottlieb DJ, Punjabi NM, Newman AB, Resnick HE, Redline S, Baldwin CM et al. Association of sleep time with diabetes mellitus and impaired glucose tolerance. Arch Intern Med 2005; 165: 863–867.
8 Kim J, Kim HM, Kim KM. Kim DJ. The association of sleep duration and type 2 diabetes in Korean male adults with abdominal obesity: the Korean National Health and Nutrition Examination Survey 2005. Diabetes Res Clin Pract 2009; 86: e34–e36.
9 Hitze B, Bosy-Westphal A, Biefieldt F, Settler U, Plachta-Danielzik S, Pfeuffer M et al. Determinants and impact of sleep duration in children and adolescents: data of the Kieler Obesity Prevention Study. Eur J Clin Nutr 2009; 63: 739–746.
10 Park SE, Kim HM, Kim DH, Kim J, Cha BS, Kim DJ. The association between sleep duration and general and abdominal obesity in Koreans: data from the Korean National Health and Nutrition Examination Survey, 2001 and 2005. Obesity (Silver Spring) 2009; 17: 767–771.
11 Cappuccio FP, Stranges S, Kandala NB, Miller MA, Taggart FM, Kumari M et al. Gender-specific associations of short sleep duration with prevalent and incident hypertension: the Whitehall II Study. Hypertension 2007; 50: 693–700.
12 Lombardi C, Hedner J, Parati G. Sex and age differences in the relationship between sleep duration and hypertension. J Hypertens 2010; 28: 883–886.
13 Cappuccio FP, D’Elia L, Strazzullo P, Miller MA. Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies. Sleep 2010; 33: 585–592.
elevated ghrelin levels, and increased hunger and appetite. Ann Intern Med 2004; 141: 846–850.
40 Vgontzas AN, Chrousos GP. Sleep, the hypothalamic-pituitary-adrenal axis, and cytokines: multiple interactions and disturbances in sleep disorders. Endocrinol Metab Clin North Am 2002; 31: 15–36.
41 Miller MA, Cappuccio FP. Inflammation, sleep, obesity and cardiovascular disease. Curr Vasc Pharmacol 2007; 5: 93–102.
42 Pan A, Keum N, Okereke Ol, Sun Q, Kvamki M, Rubin RR et al. Bidirectional association between depression and metabolic syndrome: a systematic review and meta-analysis of epidemiological studies. Diabetes Care 2012; 35: 1171–1180.
43 Grandner MA, Drummond SP. Who are the long sleepers? Towards an understanding of the mortality relationship. Sleep Med Rev 2007; 11: 341–360.
44 Stranges S, Dorn JM, Shipley MJ, Kandala NB, Trevisan M, Miller MA et al. Correlates of short and long sleep duration: a cross-cultural comparison between the United Kingdom and the United States: the Whitehall II Study and the Western New York Health Study. Am J Epidemiol 2008; 168: 1353–1364.
45 Tuomilehto H, Pettonen M, Partinen M, Lavigne G, Eriksson JG, Herder C et al. Sleep duration, lifestyle intervention, and incidence of type 2 diabetes in impaired glucose tolerance: The Finnish Diabetes Prevention Study. Diabetes Care 2009; 32: 1965–1971.
46 Williams CJ, Hu FB, Patel SR, Mantzoros CS. Sleep duration and snoring in relation to biomarkers of cardiovascular disease risk among women with type 2 diabetes. Diabetes Care 2007; 30: 1233–1240.
47 Cagampang FR, Poore KR, Hanson MA. Developmental origins of the metabolic syndrome: body clocks and stress responses. Brain Behav Immun 2011; 25: 214–220.

This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivs 3.0 Unported License. To view a copy of this license, visit http://creativecommons.org/licenses/by-nc-nd/3.0/

Supplementary Information accompanies this paper on the Nutrition & Diabetes website (http://www.nature.com/nutd)