A Systematic Reviews and Meta-Analysis of Metabolic Risk Factors Prediction for Cardiovascular Diseases: Focused on Community Setting.

Arinrada Ladla RN., PhD *, Kittisak Sawanyawisuth MD., PhD**

*Regional Health Promotion Center 8 Udonthani, Udonthani Thailand

**Department of Community Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

ABSTRACT

It was well estrabish that the incidence of cardiovascular disease in elderly is sharply increase worldwide which would be the cause of morbidities and mortality. There are several risk factors that contribute to cardiovascular disease, but metabolic risk factors are still controversial. **Methods:** A systematic review of research studies, focused on the metabolic risk factors whether affected the cardiovascular disease in elderly. Inclusion criteria's for the article selection were (1) community setting, (2) study designs were analytical cross-sectional study, retrospective – prospective cohort study, prospective cohort study, (3) clinical risk factors focused on metabolic profiles, and (4) outcomes defined as the prediction of cardiovascular disease. Literatures searching was from scientific and medical database; MEDLINE, EMBASE, SCOPUS, Web of Science, Science Direct, Ovid, CINHAL, PsycINFO and the Cochrane Library and unpublished from the conferences proceeding, textbooks. Articles selection was followed the Cochrane Library methods and include the publication between the years 2005-2018. **Results:** There was 11/87 studies met inclusion criteria and 8,678 participants were pooled to determine the metabolic risk factors for the prediction of cardiovascular disease. Metabolic risk factors were the cause to induce the risk of cardiovascular disease 1.77 (95% CI 1.55 – 2.01). **Conclusion:** Abnormal metabolic profiles may play a role as the risk factor to increase the risk of cardiovascular disease in elderly. To prevent the progression of cardiovascular disease should plan to eliminate the risk factors early.

Keywords : Metabolic risk factors; Prediction; Cardiovascular disease.

1. Introduction

The elderly present increasing cardiovascular disease (CVD) worldwide. CVD is the main cause of death and disability.[1-2] In the year 2012, people died from CVD up to 31% of all deaths[3-4], and will be is expected to increase up to 35% of all deaths in the year 2030.[5] Approximately 20% of the world's population will be over 65 years in this age group are CVD by 40%[6]. Consequently, if life will be expanded older than 85 years it will be increased the risk of CVD[7]. As the result, government will spend a huge budget for caring nearly 22% in 2030.[8] Nevertheless, even the cause of CVD is still debate but clinical researches reported that the metabolic syndrome (MS) is the main causes for CVD.[9-10] Not only a single metabolic profile, but also multi risk factors and multi-abnormal metabolic

profiles are associated to increase an evidence of CVD illness.[11] This study was aimed to performed a systematic review and meta-analysis to determine the metabolic syndrome risk factors for the prediction of CVD in elderly. Whether, this prediction might be provided the risk factors that can be devised to eliminate the risk factors for the prevention of CVD in the elderly.

2. Methods

A systematic review and meta-analysis were followed the Cochrane Handbook[12] and included the Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA flow diagram.[13]

2.1 Study Selection

A systematic review of research studies, focused on the metabolic risk factors whether affected the CVD. Inclusion criteria's for the article selection were (1) community setting, (2) study designs were analytical cross-sectional study, retrospective – prospective cohort study, prospective cohort study, case-control study was excluded, (3) clinical risk factors focused on metabolic profiles, and (4) outcomes defined as the prediction of CVD. We will be included the studies that have been published, not published, and were published between the years 2005-2018. The last search date was 19 August 2018, no language restrictions of all studies.

2.2 Search Strategy

We searched the scientific and medical database associated with CVDs. The databases of MEDLINE, EMBASE, SCOPUS Web of Science, Science Direct, Ovid, CINHAL, PsycINFO and the Cochrane Library were search for a combination of relevant words of metabolic syndrome, risk factors, prediction, cardiovascular disease and/or use MESH terms of metabolic risk factors and/or single of metabolic profile such as blood pressure, waist circumference, impaired fasting glucose and increased triglyceride for the prediction of CVDs. Hand searched for relevant journal of the trail registers and published abstract and/or full text proceeding from the conferences will be proceed.

2.3 Data collection and analysis

Two reviewers were search the literature and critical appraisal in each article independently, and resolved the unclear of the study by consensus. If article had not 5unidentified the studies through the selection criteria and/or methodology, we consulted an expert opinion. A potential study that met inclusion will be assesses risk of bias for Observational studies follow the guidelines Newcastle Ottawa Scales for cohort study, [14]
and randomized controlled trial assesses risk of bias follow the Cochrane collaborations Risk of bias tool[12]. We recorded data collection in the data extraction form of the included criteria by used the table of information, details in the tables included general information, study characteristics, participant, intervention, outcome and note.

2.4 Analysis

We calculated the results of studies to determine an accuracy by used 95% confidence intervals and considered the results of the information pooling at the study, using random-effects model due to heterogeneity (I^2 >50%).The analysis of the overall results presented by the Forest plot; a graph display to demonstrate the difference between the results of the study, conducted using Review Manager version 5.3 Software (The Cochrane Collaboration, 2000).[15]

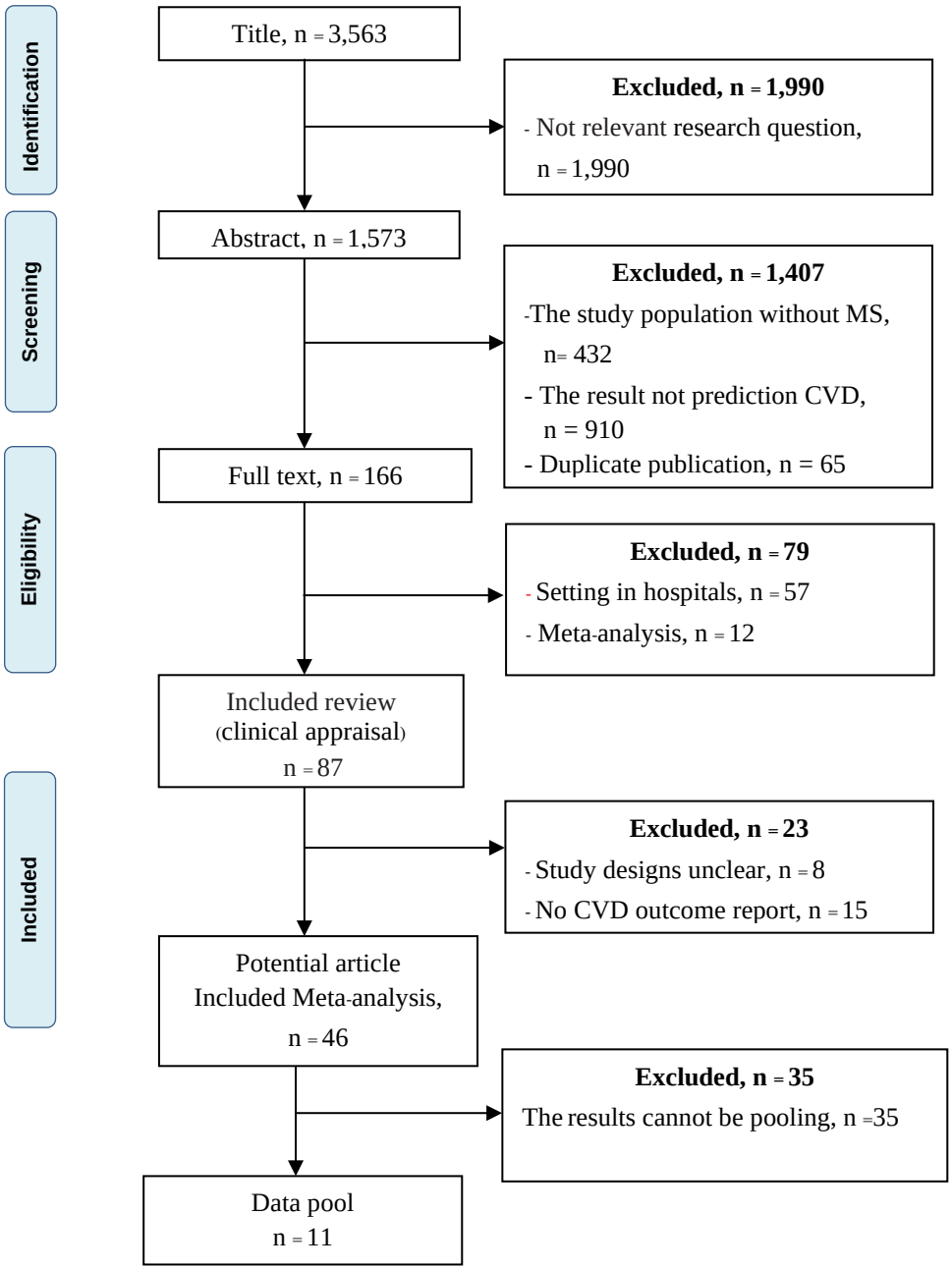


Figure 1: Study flow diagram.

Table 2 Characteristic of pooled articles on the metabolic syndrome associated with the risk of cardiovascular diseases.

Author and Publication Years	Study designs	Population	Sample Size ,n	Age, Years	F/U, Years	Definition of MS	Out come
Boroujeni et al.,2015 (16)	cohort study	Community Population	6,529	≥35	10	NCEP-TPIII WHO IDF AHA EGIR JIS	The MetS using the WHO definition predicted the highest risk for CVD followed by the JIS definition were HR= 2.41,95 % CI(2.05–.83)and HR= 2.14, 95 % CI(1.86–2.46)
Butler et al.,2006 (17)	cohort study	Health, Aging, and Body Composition (Health ABC)	3 ,035	70-79	6	NCEP-TPIII	MetS were at a higher risk for coronary events HR= 1.56, 95% CI (1.28 to 1.91) and MI HR =1.51, 95% CI(1.12 to 2.05)
Cho et al., 2013 (18)	prospective cohort study	community	3022	40 - 69	10	NCEP-TPIII	Independent risk factor with MetS (RR=1.838(95%CI 1.23–.74),p=0.003).
Kokubo et al.,2008 (19)	cohort study	General Urban	5,332	30 - 79	2	NCEP-TPIII Japanese critreia	CVD incidence for MetS by the modified NCEP-ATPIII criteria were 1.75 (1.27–2.41) in men and 1.90 (1.31–2.77) in women
Nilsson et al.,2006 (20)	cohort study	non-diabetic	5047	46 - 68	6	NCEP-TPIII WHO IDF EGIR	CVD event associate MetS were HR 1.11 (95% CI: 0.86–1.44), 1.59 (1.25–2.03) and 1.35 (1.05–1.74)

Author and Publication Years	Study designs	Population	Sample Size ,n	Age, Years	F/U, Years	Definition of MS	Out come
Ninomiya et al.,2007 (21)	prospective study	Community Population	2452	≥40	14	NCEP-TPIII	The risk of CVD events HR 1.86(95% CI, 1.32 to 2.62) in men and HR1.70 (95% CI, 1.22 to 2.36) in women.
Niwa et al.,2007 (22)	prospective cohort study	Community Population	2,176	43-68	12.5	Japanese critreia	Cardiovascular mortality was HR= 1.84 (0.68-4.96) in males, and HR= 1.31 (0.17-9.96) in females
Noto et al.,2008 (23)	prospective study	General Population	687	35-75	15	NCEP-TPIII IDF	The MetS increased the risk of CV events with HR 1.9 (95% CI, 1.46–2.46).
Salazar et al.,2013 (24)	prospective cohort study	Community Population	796	15-80	10	IDF	CVD event was increased identified by MetS HR = 3.17, 95% (CI: 1.79–5.60)
Tehrani et al.,2016 (25)	prospective cohort study	Community Population	6,417	45-84	10	ATP III	MetS group was positively associated with CHD events adjusted HR= 1.22, 95% CI (1.01 to 1.48, p <0.05).
Zhang et al., 2012 (26)	prospective cohort study	Shanghai communities	2300	40-94	3.7 3.1	JCDCG	The risk of CVD incidence in the middle-ged group (HR=2.23, P<0.01) and in the elderly group (HR=1.39, P<0.01).

Note. F/U: follow-up; National Cholesterol Education Program–Adult Treatment Panel III (NCEP-ATP III); American Heart Association (AHA) ;National Heart Lung and Blood Institutes (NHLBI) ;The European Group for Study of Insulin Resistance (EGIR) ;International Diabetes Foundation (IDF);Joint Interim Statement (JIS);The Chinese Joint Committee for Developing Chinese Guidelines on Prevention and Treatment of Dyslipidemia in Adults (JCDCG) ; World Health Organization (WHO).

3. Results

There were 3,563 articles related to metabolic syndrome and cardiovascular diseases in the elderly patients. Of those, 87 articles included in the review processes; 23 articles were excluded due to unclear study design (8) and no report on cardiovascular outcomes (15). There were 46 potential articles but only 11 articles were included in the analysis due to unable to pooled data in 35 articles. All eleven articles were shown in Table 1[16-26]

Biases of studies: Two studies had high risk of bias in adequacy of follow-up of cohorts, while other nine studies had questionable biases on five items including selection of the non-exposed cohort, comparability of cohorts on the basis of the design or analysis controlled for confounders, assessment of outcome, not enough follow-up range for outcomes, and adequacy of follow-up of cohorts (Figure 2).

3.1. General Study Characteristics

The 46 included studies were used the characteristic of the metabolic syndromes in associated with the risk of CVD. All studies reported data from prospective cohort study, thirty - five studies from general population, three studies from elderly population and a eight study from non-diabetic, T2DM or impaired glucose tolerance (IGT).

Metabolic syndromes in associated with the risk of CVD were defined by the definition the World Health Organization (WHO) and the National Cholesterol Education Program's Adult Treatment Panel-III (ATP III). The presence of 3 abnormal metabolic profiles or more of those components will be diagnosed as the MetS; include waist circumference, blood pressure, hyper-triglyceride, low high-density lipoprotein cholesterol and blood glucose. All studies reported the MetS that predict the development of CVD were present in Table 1.

3.2. Meta-Analysis

The pooled data from 11/87 studies were reported on metabolic profiles and 8,678 participants were pooled to determine the metabolic risk factors for the prediction of CVD.

Relative risk of metabolic syndrome and cardiovascular diseases: The overall risk ratio of metabolic syndrome on cardiovascular diseases was RR 1.77 (95% CI 1.55 – 2.01) with I^2 of 66% (Figure 2).Two subgroup analyses were performed by study site (Figure 3) and sex (Figure 4 and 5). There were six studies conducted in Asia and metabolic syndrome increases risk cardiovascular diseases by 1.67 (1.43, 1.97) with the I^2 of 66%. For non-Asia studies (Figure 3), the relative risk of metabolic syndrome on cardiovascular diseases was 1.93 (1.51, 2.46) with the I^2 of 72%. Male patients with metabolic syndrome also increases risk of cardiovascular diseases by 1.87 times (1.58, 2.20) with the I^2 of 43% (Figure 4). Similarly to male sex, there were eight studies included in the analysis. The relative risk of female sex for cardiovascular diseases was highest at 1.77 (1.57, 1.99) but the I^2 off 0 % (Figure 5).

Figure 2: forest plot of metabolic syndrome on cardiovascular diseases in eleven studies conducted in hospital setting.

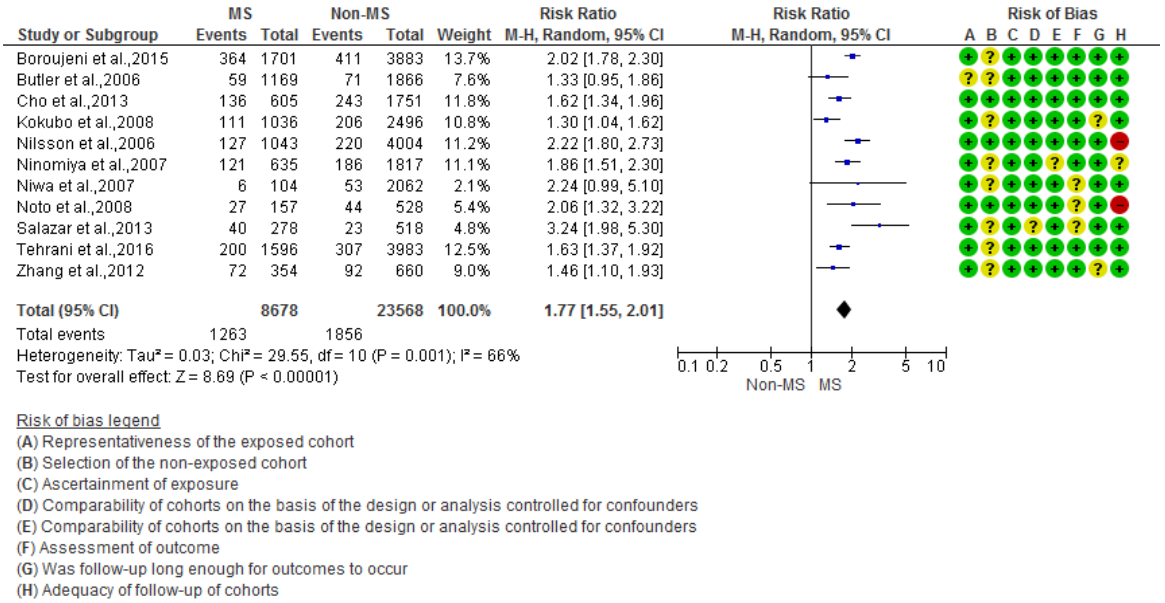


Figure 3 forest plot of metabolic syndrome on cardiovascular diseases in six studies conducted in Asian and five studies in Non-Asian hospital setting

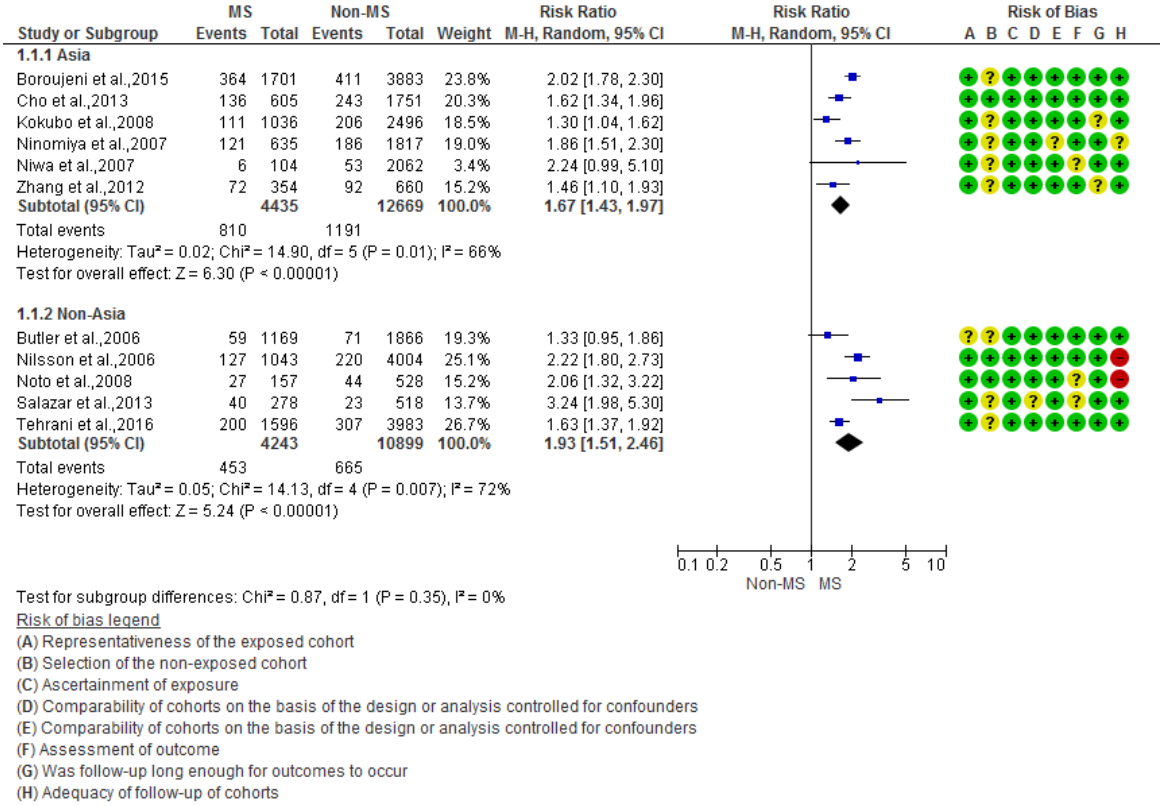


Figure 5: forest plot of metabolic syndrome on cardiovascular diseases in eight studies conducted in hospital setting and male sex.

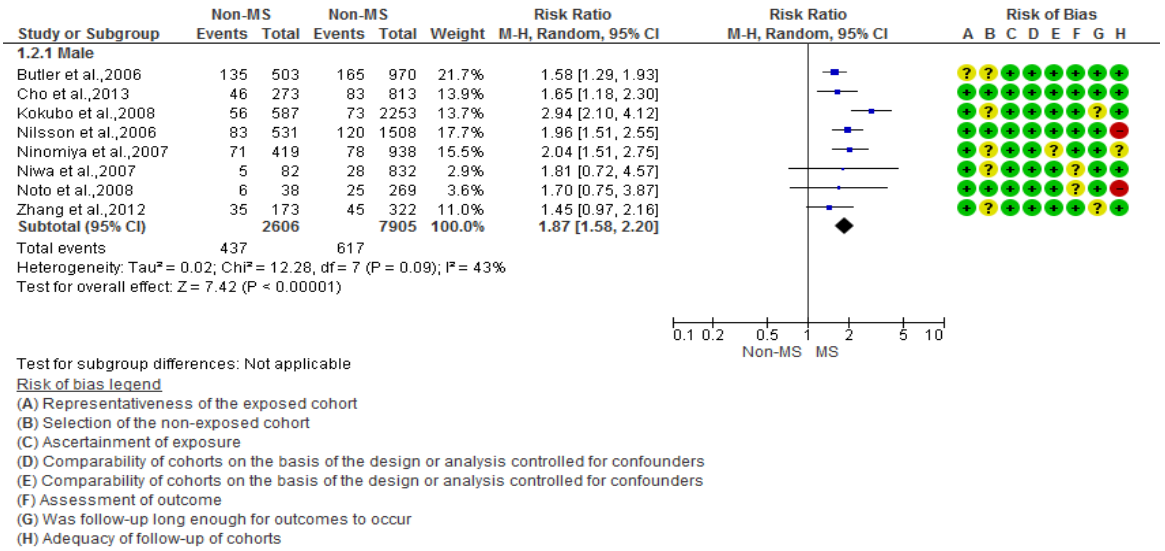
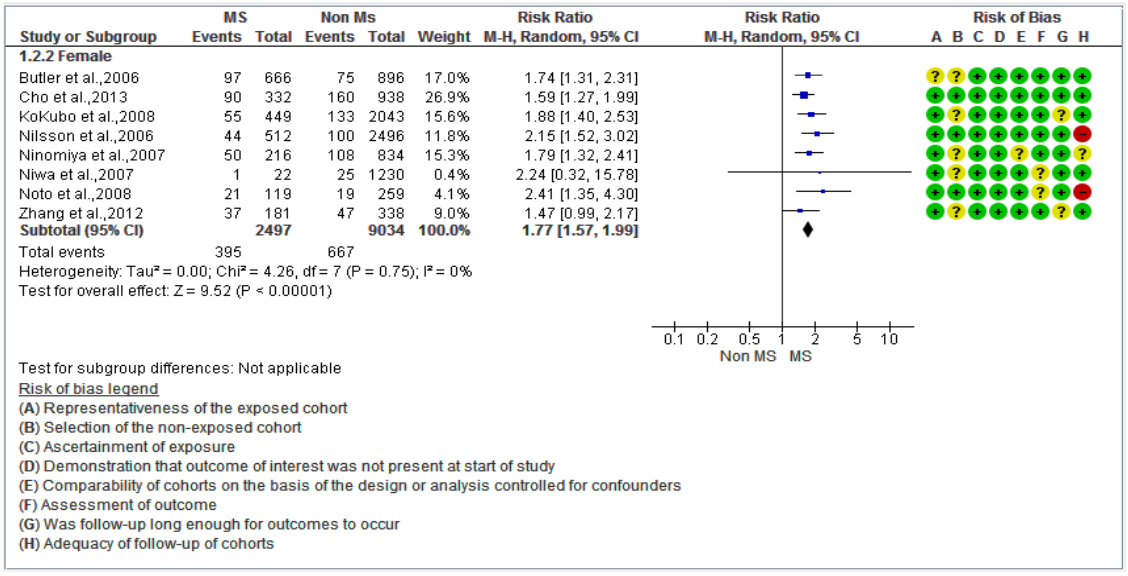


Figure 6 forest plot of metabolic syndrome on cardiovascular diseases in eight studies conducted in hospital setting and female sex.



4. Discussion

This meta-analysis demonstrates that metabolic syndromes associated with the risk of CVD. All risks; the waist circumference, blood pressure, hyper-triglyceride, low high-density lipoprotein cholesterol and blood glucose, were associated to increase the risk of CVD.

Therefore abnormal metabolic profiles may play a role as the risk factor to increase the risk of CVD in elderly; it is very important for early planning to prevent the progression of the CVD by eliminate the risk factors.

REFERENCES

1. Sahin, Ergün, et al. "Telomere dysfunction induces metabolic and mitochondrial compromise." Nature 470.7334 (2011): 359-365.
2. Go, A.S., et al., 2014. Executive summary: heart disease and stroke statistics – 2014 update: a report from the American Heart Association. Circulation 129, 399–410
3. World Health Organization. Cardiovascular diseases (CVDs) [Online]. Available from URL:http://www.who.int/mediacentre/ factsheets/fs317/en/ Accessed on July 28, 2015
4. Mendis, Shanthi, Pekka Puska, and Bo Norrving. Global atlas on cardiovascular disease prevention and control. World Health Organization, 2011.
5. Ohira, Tetsuya, and Hiroyasu Iso. "Cardiovascular disease epidemiology in Asia." Circulation Journal 77.7 (2013): 1646-1652.
6. Lozano, R., et al., 2012. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 380, 2095–212
7. Shanmugasundaram M, Rough SJ, Alpert JS. Dyslipidemia in the elderly:should it be treated? Clin. Cardiol. 2010;33:4e9.
8. Bloom, David E., et al. The global economic burden of noncommunicable diseases. No. 8712. Program on the Global Demography of Aging, 2012.
9. Simmons, R. K., et al. "The metabolic syndrome: useful concept or clinical tool? Report of a WHO Expert Consultation." Diabetologia 53.4 (2010): 600-605.
10. Corella,D. ,et al. ,2013. Mediterranean diet reduces the adverse effect of the TCF7L2rs7903146 polymorphism on cardiovascular risk factors and stroke incidence: a randomized controlled trial in a high-cardiovascular-risk population. Diabetes Care 36, 3803–3811
11. Tanmay Nag , Arnab Ghosh,2013 Cardiovascular disease risk factors in Asian Indian population: A systematic review. Journal of Cardiovascular Disease Research Volume 4, Issue 4, 209-260
12. Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.
13. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009; 62:1006–12.
14. Wells, G. A., Shea, B., O'connell, D., Peterson, J., Welch, V., Losos, M., & Tugwell, P. (2015). The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa Hospital Research Institute, 2014.
15. The Cochrane Collaboration. Review Manager (RevMan) [Computer program] Version 5.3. Copenhagen:The Nordic Cochrane Centre; 2014.
16. Khosravi-Boroujeni, H., Ahmed, F., Sadeghi, M., Roohafza, H., Talaei, M., Dianatkhah, M., ... & Sarrafzadegan, N. (2015). Does the impact of metabolic

syndrome on cardiovascular events vary by using different definitions?. BMC public health, 15(1), 1313.
17. Butler, J., Rodondi, N., Zhu, Y., Figaro, K., Fazio, S., Vaughan, D. E., ... & Holvoet, P. (2006). Metabolic syndrome and the risk of cardiovascular disease in older adults. Journal of the American College of Cardiology, 47(8), 1595-1602.
18. Cho, Nam H., et al. "The relationship of metabolic syndrome and constitutional medicine for the prediction of cardiovascular disease." Diabetes & Metabolic Syndrome: Clinical Research & Reviews 7.4 (2013): 226-232.
19. Kokubo, Yoshihiro, et al. "Impact of metabolic syndrome components on the incidence of cardiovascular disease in a general urban Japanese population: the suita study." Hypertension Research 31.11 (2008): 2027.
20. Nilsson, P. M., Gunnar Engström, and Bo Hedblad. "The metabolic syndrome and incidence of cardiovascular disease in non-diabetic subjects—a population-based study comparing three different definitions." Diabetic Medicine 24.5 (2007): 464-472.
21. Ninomiya, Toshiharu, et al. "Impact of metabolic syndrome on the development of cardiovascular disease in a general Japanese population the Hisayama study." Stroke 38.7 (2007): 2063-2069.
22. Niwa, Y., Ishikawa, S., Gotoh, T., Kayaba, K., Nakamura, Y., & Kajii, E. (2007). Metabolic syndrome mortality in a population-based cohort study: Jichi Medical School (JMS) Cohort Study. Journal of epidemiology, 17(6), 203-209.
23. Noto, Davide, et al. "The metabolic syndrome predicts cardiovascular events in subjects with normal fasting glucose: results of a 15 years follow-up in a Mediterranean population." Atherosclerosis 197.1 (2008): 147-153
24. Salazar, M. R., Carbajal, H. A., Espeche, W. G., Aizpurua, M., Leiva Sisnieguez, C. E., March, C. E., ... & Reaven, G. M. (2013). Identifying cardiovascular disease risk and outcome: use of the plasma triglyceride/high-density lipoprotein cholesterol concentration ratio versus metabolic syndrome criteria. Journal of internal medicine, 273(6), 595-601.
25. ZHANG, Ming Liang, et al. "Metabolic disorders increase the risk to incident cardiovascular disease in middle-aged and elderly Chinese." Biomedical and Environmental Sciences 25.1 (2012): 38-45.
26. Tehrani, D. M., Zhao, Y., Blaha, M. J., Mora, S., Mackey, R. H., Michos, E. D., ... & Wong, N. D. (2016). Discordance of low-density lipoprotein and high-density lipoprotein cholesterol particle versus cholesterol concentration for the prediction of cardiovascular disease in patients with metabolic syndrome and diabetes mellitus (from the Multi-Ethnic Study of Atherosclerosis [MESA]). The American journal of cardiology, 117(12), 1921-1927.