

1 Date: 22 August 2020

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3 Prof. Dr. Sergio Machado and Dr. Saurabh Chandan,
4 Editor in Chief
5 *World Journal of Meta-analysis*

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7 Dear Prof. and Dr,

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9 RESUBMISSION OF MANUSCRIPT TO *World Journal of Meta-analysis*

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12 We are pleased to enclose herewith a revised manuscript entitled “*Prevalence, awareness and*
13 *control of hypertension in Malaysia in 1980 – 2018: A systematic review and meta- analysis*”
14 by Ching Siew Mooi et al. to the *World Journal of Meta-analysis* for publication.

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16 Revised texts/paragraphs/content in tables are in blue text. We thank you in advance for your
17 attention and we look forward to your reply. It will be our great honoured to publish our
18 manuscript in *World Journal of Meta-analysis*.

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20 Thank you for your kind attention.

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22 “WITH KNOWLEDGE WE SERVE”

23
24 *Ching SM*

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42 **Reviewer #1:**

Scientific Quality: Grade C (Good); Language Quality: Grade B (Minor language polishing); Conclusion: Major revision; Specific Comments to Authors: In this manuscript, a systematic review and meta-analysis is done to determine the trend in prevalence, awareness and control of hypertension in Malaysia. This paper has some significance for clinicians and researchers working. However, there are several issues that need attention.

1. Result---The authors should indicate the results of each meta-analysis by showing figures such as forest plot for the understanding of the readers.

Response: Thank you for your valuable comments. We have now added the result of each meta-analysis by showing their forest plots. As required by editor, we have placed all figures in Microsoft powerpoint (Figure 1-28) to retain its resolution and clarity.

2. Discussion--- The described limitations within the reflection of the results could be worked out more deeply within this part.

Response: Thank you for your comments. We have now revised the limitations (Page 19, line 118-134) to read as following:

Strengths and limitations

The strength of this review was its' large sample size, summarising prevalence of hypertension in Malaysia across four decades. Furthermore, this is interesting to analyze the prevalence of hypertension according to different subgroups especially when Malaysia is known to have different races with corresponding different cultures and lifestyle. The accompanying underlying problems was different from each other and it has been addressed in this systematic review.

However, there are several limitations. First, we found that many studies did not report data of prevalence, awareness and control of hypertension in subgroups of gender, ethnicity and geographical origin, whereby these factors could further help health care policy makers to configure hypertension screening and awareness campaigns according to these subgroups in regards to hypertension prevalence, poor awareness and lack of control. Secondly, we adopted strict inclusion and exclusion criteria and therefore many unpublished data or grey literatures that were not included in the study. However, based on the sensitivity analysis, prevalence of hypertension after removal of these studies with poor quality, non-random sampling and/or extreme sample size were not much changed as compared to overall pooled prevalence of hypertension. Thirdly, the estimates for the earlier time periods were based on fewer studies when compared to that for latter periods, which may have caused a paucity of literature on the topic of interest.

3. Figure -Figure legends should contain a title and a description to figure.

Response: Thank you for your comments. We have now added legend to all figure and their descriptions were indicated in paragraphs.

4. References - References should be uniform. The references are in variable format and need to be consistent and in the format required by the Journal.

Response: Thank you for your comments. We have now re-formatted the references and ensure they are all complied with Journal referencing style.

Reviewer #2:

Scientific Quality: Grade C (Good); Language Quality: Grade A (Priority publishing); Conclusion: Accept (General priority); Specific Comments to Authors: In this manuscript entitled “Prevalence, awareness and control of hypertension in Malaysia in 1980–2017: A systematic review and meta-analysis”, the authors reported the pooled prevalence, awareness and control of hypertension in Malaysia from 1980 to 2017.

1. The manuscript is interesting and suitable for the journal.

Response: Thank you for your support, we thank to all reviewers your generous comments in hope that the revised manuscript is in accordance to high quality of World Journal of Meta-analysis. We had revised this manuscript according to reviewers' comments.

Reviewer #3:

Scientific Quality: Grade D (Fair); Language Quality: Grade C (A great deal of language polishing); Conclusion: Rejection; Specific Comments to Authors: The authors critically evaluated prevalence, awareness and control of hypertension in Malaysia in 1980–2017 using a systematic review and meta-analysis. I have several concerns about publication, at least in its present form.

1. There are some format and grammatical errors in this manuscript. For example, On the section of Abstract, the “while 33.3% of those on treatment had control of hypertension (95% CI: 28.4%, 38.2%).” should be replaced by “while 33.3% (95% CI: 28.4%, 38.2%) of those on treatment had control of hypertension”. On the section of Introduction, the “We not only report..., but also provides” should be replaced by “We not only report..., but also provide”. Therefore, the authors should carefully check their manuscript.

Response: Thank you for your comments. We have revised the abstract (Page 1, line 6-32), to read as:

BACKGROUND: Hypertension is a common public health problem worldwide and is a well-known risk factor for increased risk of cardiovascular diseases, contributing to high morbidity and mortality. However, there has been no systematic review and meta-analysis of a multi-ethnic population such as that of Malaysia.

AIM: This systematic review aims to determine the trend in prevalence, awareness and control rate of hypertension in Malaysia.

METHODS: Systematic searches were conducted in six databases (PubMed, Scopus, Ovid, CINAHL, Malaysian Medical Repository, Malaysia Citation Index) for articles published between 1980 and 2018. Two authors reviewed the studies and performed quality assessment

and data extraction independently. Pooled estimates of hypertension prevalence, awareness and control rate were calculated using the DerSimonian-Laird random-effects model. Subgroup and sensitivity analyses were performed.

RESULTS: We included 56 studies involving a total of 241,796 participants. The overall pooled prevalence of hypertension aged ≥ 18 years was 29.7%. The prevalence of hypertension was the lowest in the 1980s (16.2%, 95% confidence interval (CI): 13.4, 19.0), increasing up to 36.8% (95% CI: 6.1, 67.5) in the 1990s, then decreasing to 28.7% (95% CI: 21.7, 35.8) in the 2000s and 26.8% (95% CI: 21.3, 32.3) in the 2010s. The prevalence of awareness was 51.4% (95% CI: 46.6, 56.3), while 33.3% (95% CI: 28.4, 38.2) of those on treatment had achieved control of their blood pressure.

CONCLUSION: In Malaysia, three in 10 adults aged ≥ 18 years have hypertension, while four in 10 adults aged ≥ 30 years have hypertension. Five out of 10 people are aware of their hypertension status and only one-third of those under treatment achieved control of their hypertension. Concerted efforts by policymakers and healthcare professionals to improve awareness and control of hypertension should be of high priority.

Response: We have revised the introduction session (Page 2 line 57-59) to read as:

We are not only reporting the trend of hypertension prevalence in Malaysia from 1980 to 2018, but are also providing some important insights into the awareness and control of hypertension among Malaysians.

2. An overall risk of bias assessment of each included study is required. Funnel plots have not been undertaken to assess publication bias. The quality assessment of evidence and an overall risk of bias assessment for each included study should be evaluated by GRADEprofiler software and RevMan, respectively.

Response: Thank you for your comments. Actually we have conducted the assessment on risk of bias based on modified critical appraisal as these are cross sectional study. We had added this result in Table 1.

3. On the section of Results, please delete the redundancy sentences and present the results using figures of Meta-analyses.

Response: Thank you for your comments. We had added figure 1-28 to present the finding. We also revised paragraphs in results section (line 5-12, page 152), to read as:

3.RESULTS

Description of included studies

We identified 1493 manuscripts in the initial search (Figure 1). After removal of duplicate records ($n = 251$), 1242 studies were retrieved for further assessment. After careful evaluation of the inclusion/exclusion criteria, 52 studies fulfilled our criteria, and this together with another four studies identified from cross-referencing, a total of 56 studies were included in our meta-analysis.

Characteristics of the included studies

The main characteristics of the included studies are shown in Table 1 and Appendix 3 in encompassing the prevalence, awareness and control of hypertension of the included studies. A total sample size of 241,796 respondents from Malaysia was included in the analysis. Overall, the ethnicity distribution was 56.5% Malay, 24.2% Chinese, 9.7% Indian and 9.5% other ethnicities. Fifty-one studies were conducted in the community setting; four in hospital and one was in a primary care clinic. Quality assessment using a modified critical appraisal checklist showed that the majority of the studies (52/56) were of good quality with only four having poor quality.

Prevalence of hypertension: Overall and subgroup analysis

Table 2 shows the prevalence of hypertension in Malaysia of 29.7% (95% CI: 26.1, 33.3) (Figure 2). The prevalence of hypertension for those aged ≥ 30 years was 40.0% (Figure 3). The pooled prevalence of hypertension increased with age as the prevalence was 8.6% in adults aged 18–29 years as compared to 42.8% in adults aged ≥ 60 years (Figure 4).

Among adults aged ≥ 18 years, the prevalence of hypertension was higher in men compared to women [(31.4%, 95% CI: 26.5, 36.2) versus (27.8%, 95% CI: 20.7, 34.9)] (Figure 5 and 6). The prevalence of hypertension was highest among Malays (37.3%, 95% CI: 32.9, 41.7), followed by Chinese (36.4%, 95% CI: 31.6, 41.2) and the Indians (34.8%, 95% CI: 31.2, 38.4) (Figure 7–10). The prevalence of hypertension was 24.3% in healthcare setting as compared to 30.2% in community setting (Figure 11). The prevalence of hypertension in rural areas was 35.6% as compared to 25.4% in urban areas (Figure 12&13).

The prevalence of hypertension was 16.2% in the first decade (1980–1989), 36.8% in the second decade (1990–1999), 28.7% in the third decade (2000–2009) and 26.8% in the fourth decade (2010–2018) (Figure 14).

The prevalence of hypertension in studies that used mercury sphygmomanometers was 33.2% (95% CI: 26.4, 40.0), as compared to 30.8% (95% CI: 25.5, 36.0) in those studies that used a digital BP device (Figure 15). Sensitivity analysis showed that all studies affected the pooled prevalence of hypertension, causing it to vary from 25.6% to 30.2%. Therefore, we did not eliminate any studies from the analysis.

Prevalence of Awareness towards hypertension

The overall prevalence of awareness towards hypertension in Malaysia was 51.4% (95% CI: 46.6, 56.3) (Table 3 and Figure 16). The prevalence of awareness towards hypertension among male hypertensive patients was 67.8% (Figure 17), whereas it was 62.7% (Figure 18) among female hypertensive patients^[52, 56]. Hypertension awareness among the Malays was 45.4% (Figure 19), while that among non-Malay was 47.9% (Figure 20). The prevalence of awareness towards hypertension among hypertensive patients living in rural areas was 45.3% (Figure 21), as compared to 54.1% in urban areas (Table 3).

Prevalence of Control rate in hypertension

The control rate of hypertension was indicated in Table 3. Among the patients who were aware they were hypertensive, 33.3% (95% CI: 28.4, 38.2) achieved control of their BP (Figure 22). Our analysis found that men had slightly better control than women (37.1% versus 30.4%) (Figure 23 and 24). We also found that 29.3% of Malays had control of their BP (Figure 25), while that of non-Malays was 35.6% (Figure 26). Urbanites had higher hypertension control than those living in rural areas (36.5% versus 34.1%) (Figure 27) (Table 3).

Sensitivity analyses

Visual inspection of the funnel plot of the result of overall prevalence of hypertension showed an asymmetrical plot, suggesting some degree of publication bias (Figure 28). The main analysis for the prevalence of hypertension was re-run by removing one subpopulation at a time. The pooled estimates did not vary much from the original analysis during each removal. The removal of five low-quality

1 studies or smaller subpopulations (size < 100) also did not affect the original estimate of hypertension
2 rates (Table 4).

4. On the section of Discussion, the main findings, limitations, and authors' recommendations should be present more clearly and comprehensively. Please delete the redundancy sentences which have been present in the Introduction or Result sections. Please do not repeat the results again, and focus on the discussion about the meaning and clinical value of results.

Response: Thank you for your pertinent comments. We have made the changes accordingly in discussion (Page 15-19, Line 14-141) to read as:

4.DISCUSSION

To the best of our knowledge, this systematic review is the first in Malaysia to describe the prevalence and its trends over four decades for hypertension awareness and control. In addition, due to the fact that Malaysia [is](#) a multi-ethnic country, its variation in the prevalence, awareness and control of hypertension is crucial for us to examine in order to plan our policy in managing hypertension [on a nationwide scale](#).

Prevalence

The overall pooled prevalence of hypertension in Malaysia was 29.7%. The overall prevalence of hypertension in Malaysia [was](#) within the range of worldwide hypertension prevalence (20–50%), [as](#) described in [a](#) systematic review by Kearney et al., ^[72]. Malaysia has a higher prevalence of hypertension [as](#) compared to Thailand (24.7%), Singapore (23.5%) and China (25.2%) ^[73-75]. A review showed that this prevalence is as high as that in developed countries despite Malaysia being a developing country ^[76]. In fact, the prevalence of hypertension in Malaysia is higher than that of the United States by 0.7% ^[77].

Trend of hypertension

[We noticed a](#) low prevalence of hypertension in the 1980s. [This could be due to](#) the fact that only one study was conducted to report the prevalence of hypertension in the 1980s. [Furthermore that study](#) involved the Kadazan and Bajau ethnic groups, which are minority groups in a rural part of Sabah ^[32]. Hence, it is not surprising that the prevalence was so low. The possible explanations include [the fact that](#) the study was not only [limited to](#) a rural population, but it was also the era before urbanisation whereby unhealthy lifestyles were [not practiced commonly, reflected strongly by a low prevalence of diabetes of less than 5% in years 1980-1985 in South East Asian](#) ^[78]. Otherwise, we noticed a spike [in hypertension](#) prevalence from 1980s to [the](#) 1990s (36.8%). Then, it decreased to 28.7% in the 2000s and further decreased [to](#) 26.8% in the 2000s. [A possible reason for the stand-out increased prevalence in the 1990s could be due to the fact that among the 30 studies that specified their study period, only two studies were conducted in the 1990s. One study, which reported hypertension prevalence of 21.1%, involved three rural communities in Bagan Datoh, involving a wide variation of citizens from different age groups](#) ^[56], whereas the other study involved three semi-rural areas in Kuala Langat, where the study respondents were from the older age groups (range, 55–95 years; mean age, 65.4 years) ^[29]. This significantly increases the overall pooled prevalence of hypertension if we only take these two studies with their extreme ends of prevalence into account. In comparison to the trend of prevalence of hypertension in other countries, United States was one of the countries with consistent prevalence of hypertension of around 29% according to the United States' National Health and Nutrition Examination Survey (NHANES) ^[77].

Age and hypertension

Epidemiological studies have shown that the prevalence of hypertension increases with age which is consistent with our review. Importantly, we also found that hypertension prevalence was doubled in those aged 40–49 years (27.9%), from those who aged 30–39 years (13.5%). Comparing our results to that of a developed country, we also found a similar doubling phenomenon in hypertension prevalence, but it **only happened** in the older age group, which was 63.1% in those aged ≥ 60 years, rising from 33.2% **from** those aged 40–59 years^[77]. It is expected that aging is closely related to increased rates of hypertension because of the arterial structure alteration and on-going calcification that leads to increased arterial stiffness^[80]. However, **when** focussing on the older population aged ≥ 60 years, the prevalence of hypertension in this age group in Malaysia is the lowest among Asian countries such as Singapore (73.9%), Korea (68.7%), India and Bangladesh (65%), Taiwan (60.4%), Thailand (51.5%) and China (48.8%)^[81-86]. However, this could be due to the fact that studies in Malaysia have defined the elderly as people aged ≥ 60 years old, compared to the other studies above, which defined the elderly as people aged ≥ 65 years^[81, 82, 84, 86]. In Malaysia, the prevalence of hypertension was 8.6% among those aged 18–29 years and 13.5% among those aged 30–39 years. The prevalence rates are fairly similar to China (18–29-year age group, 9.6%; 30–39-year age group, 13.1%)^[87] but lower compared to India (18–29-year age group, 13%; 30–39-year age group, 23%)^[88].

Gender and hypertension

We found that the prevalence of hypertension was higher in men compared to women. This finding is similar to that of the NHANES in the United States^[89], which reported that, regardless of race and ethnicity, men in the 20–40-year age group had higher prevalence of hypertension than women^[89]. The sex differences in hypertension are due to both biological and behavioural factors^[90]. Biologically, the female sex hormone, oestrogen, serves as a protective factor against hypertension and other cardiovascular-related diseases in women^[91, 92]. Unhealthy lifestyle such as smoking was more prevalent among men compared to women^[91-94]. Since smoking is a risk factor of hypertension^[96, 97], it is not surprising that the prevalence of hypertension is higher in men.

Awareness

In our review, 51.4% (95% CI: 46.6, 56.3) of the included sample was aware of their hypertension status. This finding is lower than **the rates reported** in United States (63%)^[95], Singapore (69.7%)^[81] and Korea (91.7%)^[82]. Even though, the awareness of hypertension in Malaysia is higher than that in India (25.1%)^[96] and Indonesia (35.8%)^[73], **this finding** is still worrying as it indicates one out of two adults are remain undetected or untreated for their hypertension. Therefore, various nationwide blood pressure screening campaign is needed urgently. Indeed May Measurement Month was a good move as it was a nationwide blood pressure screening program which was conducted in conjunction with World Hypertension Day under the **tutelage** of International Society of Hypertension in^[97].

Regarding **the** higher prevalence of awareness towards hypertension in Malaysia **as** compared to India^[96] and Indonesia^[73], the possible explanation **could be due to the fact that** one of the **study was conducted in a residential home with a higher care-giver to resident ratio and frequent supervision**. This explain why **the residents' awareness of hypertension** was high^[58]. On the other

hand, another study involved university staff with high education levels, and therefore the awareness of hypertension will certainly be high ^[61]. In terms of ethnicity, only one study examined the ethnic differences of hypertension awareness¹⁶, while the two other studies involved only Malay ethnicity as the study population ^[62] and Malay villagers in rural communities, respectively ^[70]. Comparison of geographical origin yielded similar results, where only one study examined the difference in awareness ^[16] while the three other studies all focussed on awareness among the rural communities rather than examining the geographical difference of hypertensive awareness ^[46, 52, 62]. With this in mind, it will be right to assume that there will be much bias and higher heterogeneity, and therefore pooled analyses were not done for these subgroups.

Control

Hypertension control in Malaysia was 33.3%, which is much lower than that of developed countries such as the United States (53%) ^[17]. Conversely, it is higher than that of nearby countries such as China (13.8%) ^[73, 85], Hong Kong (25.8%) ^[99] and the Philippines (27.0%) ^[100]. This could be due to the fact that Malaysia has been improving its quality of healthcare facilities, building more clinics and hospitals and more of the latest drugs are available in these healthcare facilities ^[101]. We found that men achieved better BP control than women. Despite being consistent with a large-scale local nationwide study, this is surprising, as women are more likely to have better health-seeking behaviour, including the fact that being a female is not a risk factor of hypertension ^[94]. Urban dwellers had better BP control, which correlates with a study in Southern China that reported similar results ^[102]. This may be due to limited access to healthcare facilities persisting in rural areas despite the number of rural clinics increasing throughout the past four decades in Malaysia ^[101]. It seems very likely that a poorer health awareness among those living in rural areas or with lower socioeconomic profiles remains as an important barrier to visiting healthcare facilities and thereby, receiving proper treatment.

Strengths and limitations

The strength of this review was its' large sample size, summarising prevalence of hypertension in Malaysia across four decades. Furthermore, this is interesting to analyze the prevalence of hypertension according to different subgroups especially when Malaysia is known to have different races with corresponding different cultures and lifestyle. The accompanying underlying problems was different from each other and it has been addressed in this systematic review. However, there are several limitations. First, we found that many studies did not report data of prevalence, awareness and control of hypertension in subgroups of gender, ethnicity and geographical origin, whereby these factors could further help health care policy makers to configure hypertension screening and awareness campaigns according to these subgroups in regards to hypertension prevalence, poor awareness and lack of control. Secondly, we adopted strict inclusion and exclusion criteria and therefore many unpublished data or grey literatures that were not included in the study. However, based on the sensitivity analysis, prevalence of hypertension after removal of these studies with poor quality, non-random sampling and/or extreme sample size were not much changed as compared to overall pooled prevalence of hypertension. Thirdly, the estimates for the earlier time periods were based on fewer studies when compared to that for latter periods, which may have caused a paucity of literature on the topic of interest.

Suggestion for future research

Future studies on the prevalence of hypertension can address some of issues noted in this research. The prevalence of hypertension according to gender, ethnicity and geographical origin should be studied in more detail. Non-random sampling method should be avoided, as it would lead to bias in the conducted study. Besides that, future studies should also emphasize on adequate or larger sample size, which is more representative of a population.

5. On the section of reference, the format and grammatical errors should be corrected.

Response: Thank you for your comments. We have now re-formatted the references and ensure they are all complied with Journal referencing style.

6. The manuscript does need to be reviewed by a statistician who is familiar with meta-analysis.

Response: Thank you for your comments. This manuscript and revised manuscript were reviewed and approved by statistician whom is familiar with meta-analysis.

Science Editor:

(1) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Response: Thank you for your comments. We have placed figure 1-28 in powerpoint.

(2) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

Response: Thank you for your comments. We have revised the reference according to journal references style.

(3) The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text; and

Response: Thank you for your comments. We have added Article highlights (Page 21, line 187-190) to read as:

Article Highlights

1. The overall pooled prevalence of hypertension in Malaysia was 29.7%.
2. The overall prevalence of awareness was 51.4%.
3. 33.3% of those on treatment had achieved control of their blood pressure.

(4) As shown in the CrossCheck report, the similarity of the manuscript is a little high. Some parts of the manuscript should be revised according to the CrossCheck report.

Response: Thank you for your comments. We have revised this manuscript accordingly.

(5) Re-Review: Not required.

(6) Recommendation: Conditional acceptance.