Sarcopenia is associated with hypertension in older adults: a systematic review and meta-analysis

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Abstract
Background: Sarcopenia and handgrip strength have been observed and correlated in association with hypertension among the old-age people. However, the results reported in different studies were inconsistent. In the current study, we conducted a systematic review and meta-analysis to reveal the significant association between sarcopenia, handgrip strength, and hypertension in older adults.

Methods: PubMed, MEDLINE, Cochrane Library, and EMBASE databases were searched from inception to 15 November, 2019 to retrieve the original research studies that addressed the association between sarcopenia, handgrip strength, and hypertension. All the relevant data were retrieved, analyzed, and summarized. Results: 19 studies met the inclusion criteria and a total of 21301 participants were included in the meta-analysis. Eight eligible studies have reported the odd ratios (ORs) of hypertension and the ORs ranged from 0.41 to 4.38. When pooled the ORs together, the summarized ORs was 1.29 95% confidence interval (CI) =1.00-1.67. The summarized ORs for the Asian group 1.50 (95% CI=1.35-1.67) was significantly higher than that of Caucasian group 1.08 (95% CI=0.39-2.97). Eleven studies have provided the data on association between handgrip strength and hypertension. The overall ORs and 95% CI was 0.99 (95% CI=0.80-1.23), showing no significant association. Conclusion: Sarcopenia was associated with hypertension, but no correlation was found between handgrip strength and hypertension in older adults.

Background
The number of elderly people among the world population is expected to reach about 30% by the year 2050 [1]. However, the aging process is accompanied with alterations in some physiological systems collaborating to the development of geriatric syndromes and chronic diseases. It was previously reported that hypertension is affecting more than 70% of the older people [2] and predisposing them to an increased risk of stroke (i.e., hemorrhagic and ischemic) and myocardial infarction [2,3]. In the past few years, a large number of studies have indicated that hypertension is predominantly associated with elevated cardiovascular risk [4-6]. Recently, data from population studies have demonstrated that sarcopenia, a neuromuscular disease characterized by a progressive muscular atrophy accompanied by diminished muscle strength and/or
lower muscle limb function, could be a risk factor of hypertension [7-9]. This definition of sarcopenia
consensuses by European geriatric and gerontological societies proposed a mandatory measurement
of the muscle mass with an option to measure either the muscle strength by hand grip or physical
performance by gait speed [10]. Meanwhile, sarcopenia has been demonstrated to have substantial
associations with the aging process and can lead to significant morbidity and disability, including the
loss of independence, poor quality of life, and mortality [11-14]. Sarcopenia had been reported with
several contributing factors, such as primarily advanced age, immobility, inadequate nutrition,
neurodegenerative disease, malignancy, chronic multiple endocrine disorders, and cardiometabolic
disease. Moreover, the rate of sarcopenia in the elderly is expected to increase in the future [15] and
is becoming a major public health problem [16]. Reduced muscle mass has been characterized in
association with other cardiovascular risk factors to induce arterial stiffness [17], and is suggested as
the main additive effects of low muscle mass on blood pressure.
The handgrip strength examination is often applied as a diagnostic approach for sarcopenia in clinical
setting, and such a measure is considered inexpensive, simple, easy, and can be implemented with
portable measuring tool. Up to now, a significant association between sarcopenia and grip strength,
and hypertension in older adults were controversial [7-9,18,19] and has not been systemically
summarized. Therefore, a comprehensive investigation on this topic might allow an early detection of
the key risk factors of hypertension in elderly patients suffering with sarcopenia and may help to
effectively organize prevention or treatment strategies associated with specific vulnerability factors.

Methods

Literature Search

A literature search was conducted using the individual and joint keywords, “handgrip strength”, “grip
strength”, “sarcopenia”, and “hypertension” following the Preferred Reporting Items for Systematic
Reviews and Meta-Analyses (PRISMA) statement [20]. To enhance the retrieval of potential literatures,
we kept the search terms as broadly as possible to identify the relevant publications. A systematic
electronic data search of PubMed, MEDLINE, Cochrane Library, and EMBASE databases were
performed up to 15 November, 2019. Moreover, the bibliographies of all relevant studies and reviews,
and Google Scholar for literatures citing relevant studies were also checked and identified.

**Eligibility Criteria**

The inclusion criteria were as follows: (1) The observational studies addressing the association between sarcopenia and hypertension, or handgrip strength and hypertension; (2) studies providing clear diagnostic criteria of sarcopenia and hypertension; (3) necessary data extracted from original studies; (4) studies published in English; and (5) only the study providing more detailed information was included if the population was reported in duplicate.

Reviews, case reports, abstracts or posters for conferences, studies focused on animal experiments or experiments *in vitro*, and studies published in languages other than English were excluded.

**Data extraction**

Two investigators (TTB and FF) have independently extracted the necessary information of included studies using a customized and standardized form, and the consensus were reached on all items by these two authors. For each included study, the following information were extracted: the author and year of publication, country, study design, sample size, patient demographic characteristics (e.g., age, sex, and nation), diagnostic criteria of sarcopenia and hypertension, sample size and characteristics for each group, follow-up period, and outcomes of each group.

**Quality scoring of studies**

Two reviewers (FKL and JMC) have assessed the methodological strength of included studies independently in order to interpret the validity of any findings observed through the Newcastle-Ottawa Scale (NOS), a procedure performed to independently assess the methodological quality of meta-analysis of observational studies [21]. Newcastle-Ottawa Scale included three categories of factors: (1) patient selection (three items); (2) comparability of the two study arms (two items); and (3) assessment of the outcomes (two items). The detailed criteria for the three assessments are: whether the cases were defined adequately, the representativeness of the cases, the process of selection and definition of controls, comparability of cases and controls based on the design or analysis, ascertainment of exposure, the same method of ascertainment for cases and controls, and nonresponse rate.
Studies were awarded one star for each numbered item within the selection and exposure categories, and one or two stars for comparability. Studies were graded on an ordinal scoring scale. The scores ranged from 2 to 9 stars. Therefore, a scale of 0 to 4 stars was considered as poor quality, 5 to 6 stars as moderate quality, and 7 to 9 stars as high quality.

**Statistical analysis**

The inverse variance method with random effects was conducted to summarize the dichotomous outcomes, odd ratios (ORs), and 95% confidence intervals (CIs). Stratified analyses were also performed with respect to the characteristics of the study population and outcome. Heterogeneity between included studies was assessed using the $I^2$ and Q tests. Heterogeneity was defined as low, moderate, and high to $I^2$ values of 25%, 50%, and 75%, respectively [22]. The Begg rank correlation [23] and Egger weighted regression methods [24] were used to assess the publication bias ($P< 0.05$ was considered indicative of a statistically significant publication bias). Review Manager (Version 5.3, The Cochrane Collaboration, Oxford, UK) was used for generation of forest plot and statistical analyses. The Begg and Egger tests were assessed by STATA 15.0 (Stata Corporation, College Station, TX, USA). A $P$ value of $<.05$ was considered significant for all analysis.

**Results**

**Study selection**

In total, 1221 studies were retrieved as potentially relevant literature reports through the initial searches in different databases and after removing the duplicates, 1013 were left. Majority of potentially irrelevant literatures were excluded after reviewing the browsing title or abstract. After retrieving 30 full-length manuscripts, finally, 12 articles [7-9,18,19,25-31] of 19 studies were eligible for data extraction and meta-analysis. The flow chart of the studies enrolled in the current study can be found in **Figure 1**.

**Study characteristics**

19 studies (12 articles) met the inclusion criteria and a total of 21301 participants were included in the study. Four articles [8, 16, 24, 29] were divided into two or four studies as the participants were categorized into several groups according their characteristics. Eight studies [7-9,19,28-30]
addressed the association between sarcopenia and hypertension, and 11 studies [18,25-27,31] focused on the association between handgrip strength and hypertension. The sarcopenia was defined by three methods, the European Working Group on Sarcopenia in Older People (EWGSOP) criteria [32], the Asian Working Group for Sarcopenia (AWGS) criteria, and ASM/weight (kg) less than one standard deviation (SD). The hypertension was defined as systolic blood pressure (SBP) >140 mmHg or diastolic blood pressure (DBP) >90 mmHg. Handgrip strength was diagnosed by dynamometers according to the protocol from the Institute of Medicine [33]. The included studies were published between 2013 and 2019 and the sample size ranged from 72 to 4771. The participants’ demographic characteristics in the included studies can be found in Supplementary Table 1 and Supplementary Table 2.

**Supplementary Table 2.**

Six studies were conducted in China [18,19,28,31], two each in Republic of Korea [8] and Japan [26], and United States [9,25,34,35], one each in Turkey [30], Switzerland [27], Italy [7], and Spain [29]. Most of the studies were cross-sectional studies except two cohort studies [7,9]. The characteristics of the included studies and patients were summarized in Table 1 and Table 2.

**Quality assessment of studies**

Newcastle-Ottawa Scales for the eligible studies were presented in Supplementary Table 3 and all included studies were found to exhibit an acceptable quality. Four studies were evaluated as 6 stars, 6 studies were 7 stars, and 2 studies were 8 stars.

**The association between sarcopenia and hypertension**

All the eight eligible studies have reported the ORs of hypertension, and the ORs ranged from 0.41 to 4.38. When pooled the ORs together, the summarized ORs was 1.29 (95% CI=1.00-1.67, \( P=0.04 \)) with a moderate heterogeneity \( (I^2 = 74\%) \). The detailed information could be found in Figure 2 and Supplementary Figure 1.

To explore the sources of heterogeneity, the subgroup analysis was performed by categorizing the studies according to the ethnicity of the participants and the Newcastle-Ottawa Scales than were equal to or more than 7 stars. The Asian group included 4 studies from China and Korea, the Caucasian group included four studies conducted in United States, Italy, Spain, and Turkey. The
summarized ORs for the Asian group 1.50 (95% CI = 1.35-1.67, \( P = 0.00 \)) was significantly higher than that of Caucasian group 1.08 (95% CI=0.39-2.97, \( P=0.88 \)). The heterogeneities for the two subgroups were significantly decreased to \( I^2 = 34\% \) and \( I^2 =40\% \). When the studies with low quality were removed (Newcastle-Ottawa Scales<6), the overall OR were 1.53 (95%CI = 1.37-1.71, \( P = 0.00 \)) with lower heterogeneity (\( I^2 = 2.62\% \)). More data is presented in Figure 3 and Figure 4.

**The association between handgrip strength and hypertension**

Eleven studies have provided the data on association between handgrip strength and hypertension, and among them ten studies have reported the odds ratios and 95% CI. The overall odds ratios and 95% CI was 0.99 (95% CI=0.80-1.23, \( P=0.93 \)) with a higher heterogeneity (\( I^2 = 76\% \)) and significant publication bias (\( P < 0.01 \)). The detailed data can be found in Figure 5.

As shown in Figure 6 and Figure 7, in order to explore the sources of heterogeneity and publication bias, the included studies were categorized into two groups by the gender of the participants. For the males, the pooled OR was 1.14 (95%CI=0.91-1.43, \( P=0.27 \)) with an acceptable heterogeneity (\( I^2 = 31\% \)) and without publication bias (\( P > 0.05 \)). The female group was not showing any statistically significant difference with an OR as 0.81 (95%CI=0.52-1.26, \( P=0.34, I^2 = 45\% \)) without publication bias (\( P > 0.05 \)).

Seven studies have reported the \( \beta \) value and standard error of the linear regression on hypertension and the pooled \( \beta \) value was -1.57 with an SE equal to 1.03, and the heterogeneity was 99\%. As two studies have provided the data on different body mass indexes, two more subgroup analysis were done, such as underweight or normal body mass index group (OR=1.04, 95%CI=0.81-1.33, \( P=0.77 \)), and overweight or obese body mass index group (OR=1.18, 95%CI=0.94-1.41, \( P=0.16 \)). The data was presented in Supplementary Figure 3 and Supplementary Figure 4.

**Publication bias**

Most of the analysis except one has shown potential publication bias among the included trials according to Begg rank correlation analysis and Egger weighted regression analysis (\( P \) value of the analysis was more than 0.05). The detailed potential publication bias of each analysis can be found in
**Supplementary Table 4**

**Discussion**

To the best of our knowledge, the current meta-analysis is the first systematic review and meta-analysis study summarizing the association between sarcopenia and hypertension, and the association of handgrip strength and hypertension. 19 studies with 21301 participants were included, among which eight studies have addressed the association between sarcopenia and hypertension and indicated that sarcopenia was a risk factor for the hypertension. 11 studies have focused on the association between handgrip strength and hypertension and was found by the pooled results.

As a standard definition for sarcopenia is lacking, the current study proved that sarcopenia was a risk factor for hypertension. Several prospective and cross-sectional studies have found the correlation between sarcopenia and hypertension [8,19]. The prevalence of sarcopenia can vary dramatically depending on the definition of sarcopenic obesity. In the current study, Asian Working Group for Sarcopenia (AWGS) criteria and the European Working Group on Sarcopenia in Older People (EWGSOP) criteria were used, which showed significantly different odds ratio. This might partly explain that Asian groups had a stronger association with hypertension than that of Caucasian group.

Many potential mechanisms for sarcopenia have been researched, such as chronic inflammation [36], and its relevant catabolic cytokines remain the most widely accepted mechanism of sarcopenia [36]. It was also reported that the chronic inflammation and its relevant catabolic cytokines production is the major risk factor for age-related chronic diseases, such as hypertension [8]. Sarcopenia now needs to be recognized in routine clinical settings. Frailty is the most problematic expression of population ageing. It is a state of vulnerability to poor resolution of homeostasis and is a consequence of cumulative decline in many physiological systems during a lifetime. The adverse outcomes of infirmity might be mediated by sarcopenia, which may be considered the biological substrate for the development of frailty and the related negative health outcomes [37]. Most importantly, it is becoming exceedingly important for us to verify whether preventive strategies focusing on the early detection and treatment of sarcopenia could get better survival in the older people.

In the current study, handgrip strength was significantly associated with hypertension in both men
and women, and these result was controversial in various other studies [26,27]. The specific biological mechanism linking grip strength and sarcopenia with hypertension is largely unknown. However, the regular exercise, which has been shown consistently in plenty of studies to improve the blood pressure, may eventually improve the mitochondrial functions, reduce inflammation, enhance metabolic functions and alleviate sarcopenia symptoms [38].

It is necessary to consider the limitations of the present meta-analysis while interpreting the results. First, the definition of sarcopenia was inconsistent in different studies and the variations in assessment of sarcopenia across studies could have caused methodological limitations and compromised the results. Second, the number of the included studies was limited and majority of them were from Asian countries. As the sarcopenia might be affected by the economic level, medical stage, and genetic factors, the associations between sarcopenia, handgrip strength, and hypertension in different countries could be different. Therefore, the result in the current study can only partly annotate the associations. Third, almost all of the studies addressing the sarcopenia did not provide the specific sarcopenia symptoms by gender and age. Due to the limited sample size and information in each studies, we could not perform more subgroups or sensitivity analyses, especially on the sensitivity analyses based on the age and sex. Moreover, due to the large disparity in the numbers of participants among the included studies, the conclusions related to the association of sarcopenia with hypertension might be overstated. Four, potential language bias might have existed because our literature searches only considered articles published in English.

Conclusions
In conclusion, our meta-analysis provided pooled results based on 19 studies from eight different regions or countries and summarized a large data set of 21301 participants. The current study highlighted that sarcopenia was significantly associated with hypertension. In the future, by stratifying patients, efforts must be made to prevent and treat sarcopenia in the older population, which would also decrease the risk and the comorbidities of hypertension. At the same time, performing larger sample size studies from different countries in future may substantially corroborate the conclusive remarks derived from this study.
List Of Abbreviations

ORs: Odd ratios;

CI: Confidence interval;

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses;

NOS: Newcastle-Ottawa Scale;

AWGS: Asian Working Group for Sarcopenia;

EWGSOP: European Working Group on Sarcopenia in Older People.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Not applicable

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

Study concept: JMC and TTB. Study design: JMC, TTB and FF. Data acquisition: TTB, FF and FKL. Quality control of data and algorithms: JMC and FKL. Data analysis and interpretation: TTB, YR and JAH. Manuscript preparation: TTB and FF. Manuscript editing: TTB and FKL. Manuscript review: JMC and JAH. All authors (TTB, FF, FKL, YR, JAH, JMC) have read and approved the final version of the manuscript.

Acknowledgements
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Tables
Table 1. Demographic and clinical characteristics of the subjects included in studies that focused on sarcopenia
| Study included | No. of sarcopenia patients | No. of non-sarcopenia patients | Means±SD (mmHg, non-sarcopenia/sarcopenia) | % of participants taking antihypertensive drugs | Odd ratios (95% CI) |
|----------------|---------------------------|---------------------------------|---------------------------------------------|-----------------------------------------------|-------------------|
|                | HTN (-)/HTN (+)           | HTN (-)/HTN (+)                 | SBP                                         | DBP                                           |                   |
| Landi, et al., 2013 | 154/126                  | 43/28                           | 126.40±0.5/129.30±0.9                      | 74.30±0.30/75.10±0.5                          | 1.50 (1.23-1.84) |
| Han, et al., 2014 a | 2326/1156                 | 894/544                         | 129.30±0.9/129.90±0.8                       | 75.10±0.50/76.90±0.5                          | 1.44 (1.16-1.78) |
| Han, et al., 2014 b | 594/393                   | 1032/771                        | 131.20±0.7/129.90±0.8                       | 77.60±0.40/77.90±0.5                          |                   |
| Koo, et al., 2016   | 239/98                    | 70/41                           | 98.10±14.8/127.9±17.4                       | 77.8±11.0/77.2±11.5                           |                   |
| Can, et al., 2016   | 36/4                      | 36/12                           | NA                                          | NA                                            |                   |
| Han, et al., 2017   | 634/267                   | 77/36                           | NA                                          | NA                                            |                   |
| Montes, et al., 2017 | 148/116                   | 52/33                           | NA                                          | NA                                            |                   |
| Xu, et al., 2019    | 4459/NA                   | 312/NA                          | NA                                          | NA                                            |                   |

Abbreviations: HTN, Hypertension; SD, standard deviation; SBP, systolic blood pressure; DBP, diastolic blood pressure; CI, confidence interval; NA, not available.

a, participants whose BMI was less than 25.00 kg/m².

b, participants whose BMI was equal or more than 25.00 kg/m².

c, Odd ratios stands for hypertension with sarcopenia compared to without sarcopenia.
Table 2. Demographic characteristics of the subjects included in studies that focused on handgrip strength

| Study included          | Sample size | Handgrip strength (means±SD, per kg) |
|-------------------------|-------------|--------------------------------------|
| Mainous, et.al., 2015   | 1469        | 60.8±1.61 a/71.5±0.84 b               |
| Kawamoto, et.al., 2016 a| 742         | 33.40±7.50                           |
| Kawamoto, et.al., 2016 b| 937         | 21.30±4.10                           |
| Gubelmann, et.al., 2017 a| 1891       | NA                                   |
| Gubelmann, et.al., 2017 b| 1577       | NA                                   |
| Ji, et.al., 2018 a      | 2184        | 41.50 ± 8.80                         |
| Ji, et.al., 2018 b      | 2413        | 26.70 ± 5.70                         |
| Ji, et.al., 2018 c      | 563         | NA                                   |
| Ji, et.al., 2018 d      | 1292        | NA                                   |
| Ji, et.al., 2018 d e    | 636         | NA                                   |
| Ji, et.al., 2018 d f    | 1323        | NA                                   |
| Zhang, et.al., 2019 a   | 515         | 35.94±19.72                          |
| Zhang, et.al., 2019 b   | 637         | 14.45±10.41                          |

Abbreviations: CI, confidence interval; SD, Standard deviation; NA, not available.

a, males.
b, females.
c, Underweight or normal body mass index of males.
d, Underweight or normal body mass index of females.
e, Overweight body mass index of males.
f, Overweight or obese body mass index of females.
g, Odd ratios stands for hypertension with sarcopenia compared to without sarcopenia.

Additional Files

Additional file 1(.doc)

Supplementary Figure 1. Funnel plot for the overall odds ratio of hypertension among sarcopenia and non- sarcopenia patients.
Supplementary Figure 2. Funnel plot for the odds ratio of handgrip strength among hypertension and non-hypertension patients.

Supplementary Figure 3. Summarized overall odds ratio of underweight or normal body mass index (BMI) in patients.

Supplementary Figure 4. Summarized overall odds ratio of overweight or obese body mass index in patients.

Additional file 2 (.doc)

Supplementary Table 1. Demographic and clinical characteristics of the subjects included in studies that focused on sarcopenia.

Supplementary Table 2. Demographic and clinical characteristics of the subjects included in studies that focused on handgrip strength.

Supplementary Table 3. Quality assessment of included studies by Newcastle-Ottawa Scale

Supplementary Table 4. Publication bias of summarized outcome.

Figures
1221 articles through database searching

1013 articles left after duplicates removed

- Title and abstract excluded: 983
- Review: 56
- Case reports: 6
- Short reports: 52
- Topic no relevant: 786
- Not in English: 83

Full text evaluation: 30

- Excluded: 28
- Cannot extract necessary data: 10
- Did not provide key endpoints: 6
- Posters: 7
- Published duplicate: 5

12 articles included (19 studies)

Figure 1
Flow chart of the study selection.
Figure 2

Summarized overall odds ratio of hypertension

| Study name       | OR   | 95% CI   | Z-value | P-value |
|------------------|------|----------|---------|---------|
| Landi, et.al., 2013 | 0.410 | 0.195 0.860 | -2.359  | 0.018   |
| Han, et.al., 2014 a | 1.570 | 1.340 1.840 | 5.576  | 0.000   |
| Han, et.al., 2014 b | 1.510 | 1.211 1.882 | 3.666  | 0.000   |
| Koo, et.al., 2016  | 2.030 | 1.180 3.491 | 2.559  | 0.010   |
| Can, et.al., 2016  | 4.380 | 1.261 15.213 | 2.325  | 0.020   |
| Han, et.al., 2017  | 1.210 | 0.752 1.946 | 0.786  | 0.432   |
| Montes, et.al., 2017 | 0.480  | 0.241 0.955 | -2.091 | 0.037   |
| Xu, et.al., 2019   | 1.440 | 1.162 1.784 | 3.338  | 0.001   |
| Overall odds ratio | 1.294 | 1.004 1.669 | 1.991  | 0.046   |

Figure 3

a. Summarized overall odds ratio of hypertension of the studies from Asia

| Study name       | OR   | 95% CI   | Z-value | P-value |
|------------------|------|----------|---------|---------|
| Landi, et.al., 2013 | 0.410 | 0.195 0.860 | -2.359  | 0.018   |
| Koo, et.al., 2016  | 2.030 | 1.180 3.491 | 2.559  | 0.010   |
| Can, et.al., 2016  | 4.380 | 1.261 15.213 | 2.325  | 0.020   |
| Montes, et.al., 2017 | 0.480  | 0.241 0.955 | -2.091 | 0.037   |
| Overall odds ratio | 1.079 | 0.392 2.968 | 0.148  | 0.882   |

b. Summarized overall odds ratio of hypertension of the studies from Europe

Summarized overall odds ratio of hypertension of the studies grouped by ethnicity of the participants.

21
Summarized overall odds ratio of hypertension of the studies that with equal to or more than 7 stars of the Newcastle-Ottawa Scales

Summarized overall odds ratio of handgrip strength

Summarized overall odds ratio of handgrip strength based on male participants
Summarized overall odds ratio of handgrip strength based on female participants

| Study name            | OR  | 95% CI | Z-value | P-value | Odds ratio and 95% CI |
|-----------------------|-----|--------|---------|---------|-----------------------|
| Gubelmann, et.al., 2017 b | 1.01| 0.80  | 1.27    | 0.08    | 0.93                  |
| Ji, et.al., 2018 b     | 1.01| 0.80  | 1.27    | 0.08    | 0.93                  |
| Zhang, et.al., 2019 b  | 0.19| 0.07  | 0.53    | -3.16   | 0.00                  |
| **Overall odds ratio** | 0.81| 0.52  | 1.26    | -0.94   | 0.34                  |

Figure 7

Summarized overall $\beta$ for the linear regression and stand error

| Study name            | $\beta$ | SE   | Variance | Z-value | p-value | $\beta$ and 95% CI |
|-----------------------|---------|------|----------|---------|---------|---------------------|
| Ji, et.al., 2018 a    | 0.206   | 0.087| 0.008    | 0.035   | 0.377   | 2.368 0.018          |
| Mainous, et.al., 2015 | -4.930  | 0.030| 0.001    | -4.989  | -4.871  | -164.333 0.000      |
| Ji, et.al., 2018 b    | 0.007   | 0.117| 0.014    | -0.222  | 0.236   | 0.060 0.952          |
| **Overall $\beta$**   | -1.573  | 2.026| 4.105    | -5.544  | 2.398   | -0.777 0.437        |

Figure 8

Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.

Additional file 2.docx
Additional file 1.docx