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# Meta-Analysis: The Relationship of Sodium and Potassium Intake with The Incidence of Hypertension

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***Abstract:*** According to WHO, the highest prevalence of hypertension by region is Africa, which is 27 percent, while Southeast Asia is the third highest, with 25 percent of the total population. High sodium intake and low potassium intake are risk factors that affect blood pressure. This research aims to determine the association between sodium and potassium intake with the incidence of hypertension through a meta-analysis study. The research design uses a systematic review with meta-analysis. The review method uses the PRISMA concept. Search articles with 3 databases, namely Google Scholar, PubMed, and Science Direct, and for statistical tests using the RevMan application. The articles included in the meta-analysis were 15 articles (14 articles on the sodium intake variable and 10 articles on the potassium intake variable). The analysis results showed no association between sodium intake and hypertension in the cohort design ($p$ = 0.14) and case-control design ($p$ = 0.43). Meanwhile, the cross-sectional design showed an association between sodium intake and the incidence of hypertension with a $p$-value = 0.01. The subgroup analysis results also showed no association between potassium intake and the incidence of hypertension in both the cohort ($p$ = 0.32) and cross-sectional ($p$ = 0.06) studies. High sodium intake had a 3.79 risk of incidence of hypertension in a cross-sectional study design.

***Keywords:*** *Blood pressure, sodium intake, potassium intake, hypertension*

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## I. BACKGROUND

Hypertension is when blood pressure increases beyond the normal limit of ≥ 140/90 mmHg. Based on estimates from the World Health Organization (WHO), the global prevalence of hypertension is 22 percent of the total world population. According to WHO, the highest prevalence of hypertension by region is Africa, which is 27 percent, while Southeast Asia is the third highest, with

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25 percent of the total population [1].

According to the 2018 National Basic Health Research (Riskesdas) data, the prevalence of hypertension in Indonesia based on measurement results in the population aged > 18 years is 34.11 percent. The prevalence of hypertension in the Riskesdas data in 2018 has increased compared to the Riskesdas data in 2007 and 2013, where the prevalence of hypertension in 2007 was 25.8 percent, and in 2013 it increased to 31.7 percent. The highest prevalence of hypertension by province based on Riskesdas 2018 data is South Kalimantan Province at 44.13 percent; then the second-highest is West Java Province at 39.60 percent, and the third-highest in East Kalimantan Province [2].

Several factors that influence blood pressure or hypertension increase include social factors (social determinants), including age, income, education, place of residence/housing, urbanization, and globalization. Meanwhile, other factors that affect blood pressure are behavioral risk factors, including an unhealthy diet, namely the consumption of foods high in salt and fat, less consumption of fruits and vegetables that contain lots of potassium, alcohol consumption and tobacco use, lack of physical activity and exercise, and poor stress management [3].

In 2010, it was estimated that the average level of sodium consumption worldwide was 3.95 grams per day, with a range between 2.18-5.51 grams per day. Globally, 99.2 percent of the world's adult population has an average sodium intake exceeding the WHO recommendation (> 2 grams/day) [3].

According to the results of research by [4], the rate of occurrence of hypertension in four years of observation is 58 per 1000 people per year, with a faster incidence rate in the group with high sodium consumption than low sodium consumption; this means high sodium consumption ($\geq$ 2000 mg per days) in adults accelerates the occurrence of hypertension [4]. In addition to sodium intake, which affects blood pressure, [5] showed that the lower the potassium intake, the higher the histolic blood pressure [5, 6].

The study results of [7] showed different results from other studies; the results of this study concluded that sodium and potassium intake were not associated with blood pressure [7]. The results of the [8] also showed that sodium intake was not associated with the incidence of hypertension and research [8]. [9] that there is no significant relationship between sodium intake and hypertension [9]. In addition, the results of [10] research also show no significant relationship between potassium intake and the incidence of hypertension [10, 11].

Based on several research results indicating this gap, it is necessary to conduct a meta-analysis study. A meta-analysis is a form of quantitative research using data from existing studies (secondary data) by analyzing quantitative data from previous research results to accept or reject the hypotheses proposed in these studies. Based on the description above, the researchers hereby conduct research through systematic and quantitative studies with meta-analysis to determine the relationship between sodium and potassium intake with the incidence of hypertension.

## II. METHOD

This study uses a research design with meta-analysis. Meta-analysis is done by integrating, summarizing, combining, and interpreting research results. Meta-analytical research design is a special research method to combine studies whose effect size can be measured [12].

Identification of research questions using Population, Exposure of Interest, and Outcome (PEO) [13]:

TABLE 1
IDENTIFICATION OF RESEARCH QUESTIONS

| | | |
|---|---|---|
| P | Population | Age $\geq$ 18 Years |
| E | Exposure of Interest | Sodium Intake and Potassium Intake |
| O | Outcome | Hypertension |

The research protocol in the meta-analysis uses the concept of Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) with the following stages:

a. Data search (identification) using Google Scholar, Science Direct, and PubMed databases. Research articles were published within a period of 5 years, namely 2016 - 2020.

b. Screening of articles using the Mendeley application. The articles found in the database are entered into the Mendeley desktop by using the Mendeley Importer. Folders in the Mendeley desktop application are created separately for Indonesian and English articles. English articles use 2 databases, namely science direct and PubMed so thatit is necessary to check for duplication in the database using the Mendeley desktop.

c. The next screening stage is done manually by reading the abstract or full text of the article issued based on the inclusion and exclusion criteria.

d. The assessment of the eligibility criteria is used to assess whether the research article is worthy of analysis, namely by conducting a critical appraisal using Joanna Briggs Institute (JBI) critical appraisal tools or tools for a systematic review.

e. The search results of research articles that have met the requirements and criteria will be analyzed using the application.

In the search for articles using sensitive and specific keywords. Each data base has characteristics in keyword search to find articles relevant to keyword research. The article search in this study can be seen in Table 2.

TABLE 2
SEARCH KEYWORDS FOR ARTICLES IN THE DATABASE DATA

| No | Database | Keywords |
|---|---|---|
| 1. | Pub Med | Concept 1: "Sodium, Dietary"[Mesh] OR “sodium intake*”[tw] concept 2: "Potassium, Dietary"[Mesh] OR “potassium intake*”[tw] concept 3: "Hypertension"[Mesh] OR hypertension [tw] OR "high blood pressure*"[tw] |
| 2. | Science Direct | (“Dietary sodium” OR “sodium intake”) AND (“Potassium, Dietary” OR “potassium intake”) AND (“Hypertension” OR hypertension OR “high blood pressure”) |
| 3. | Google Scholar | Sodium AND Potassium AND "Risk factors for hypertension" AND (Hypertension OR "High Blood Pressure") |

The inclusion criteria in this study are as follows:

1. The title and content in the research article are relevant to the research
2. Scopus indexed international journal
3. Accredited national journal (indexed sinta 1 to sinta 4)
4. The latest published research articles within 5 years, namely between 2016 – 2020
5. Research article available full text
6. The population in the research article is age > 18 years
7. Research sites around the world
8. The article contains research variables, namely sodium, potassium, and hypertension
9. Study design in research is observational

The exclusion criteria in this study are as follows:

1. Research articles that cannot be downloaded
2. The research article does not include statistical test results (OR (Odd Ratio) or RR (Risk Ratio) values.
3. Research article with adolescent population

The statistical test in this meta-analysis research uses the statistical application Review Manager (RevMan) version 5.3

## III. RESULTS AND DISCUSSION

The number of articles identified was 617 articles. A total of 4 duplicate articles. so that the number of articles filtered is 614 articles. The next stage is to conduct a review based on the inclusion and exclusion criteria and a total of 592 articles were excluded because the title and content were not relevant to the study, were not indexed by sinta 1-4 and scopus, articles could not be downloaded, did not contain the independent variable, namely hypertension. The number of articles that will be included in the article selection results is as many as 21 articles.

Based on the results of critical appraisal as many as 11 articles were issued on the grounds that 4 articles of the population sampled teenagers and 6 articles did not contain the ODS Ratio (OR) and Confident Interval (CI) values. Thus the number of articles that will be included in the meta-analysis is 15 articles (variable sodium intake is 14 articles and variable is potassium intake is 10 articles).

The results of data extraction. The research articles show that the research locations consist of Indonesia as many as 9 articles, Mexico 1 article, China 2 articles, Canada 1 article, German 1 article, and Benin 1 article. For the number of samples at least 45 people and a maximum of 6,788 people. The research design in the meta-analysis was observational with details for the sodium intake variable consisting of a cross sectional design of 7 articles, a cohort of 3 articles, and a case control of 4 articles. As for the potassium variable, the cross-sectional design consisted of 6 articles and the cohort of 3 articles.

After data extraction, the next step is to perform meta-analysis. Statistical tests were carried out using RevMan by performing subgroup analysis according to the research design. Subgroup analysis was carried out on the

study design because there were 3 study designs, namely cross sectional, case control, and cohort. The results of statistical analysis of the relationship between sodium intake and the incidence of hypertension can be seen in Fig. 1. and the variable potassium intake with the incidence of hypertension can be seen in Fig. 4.

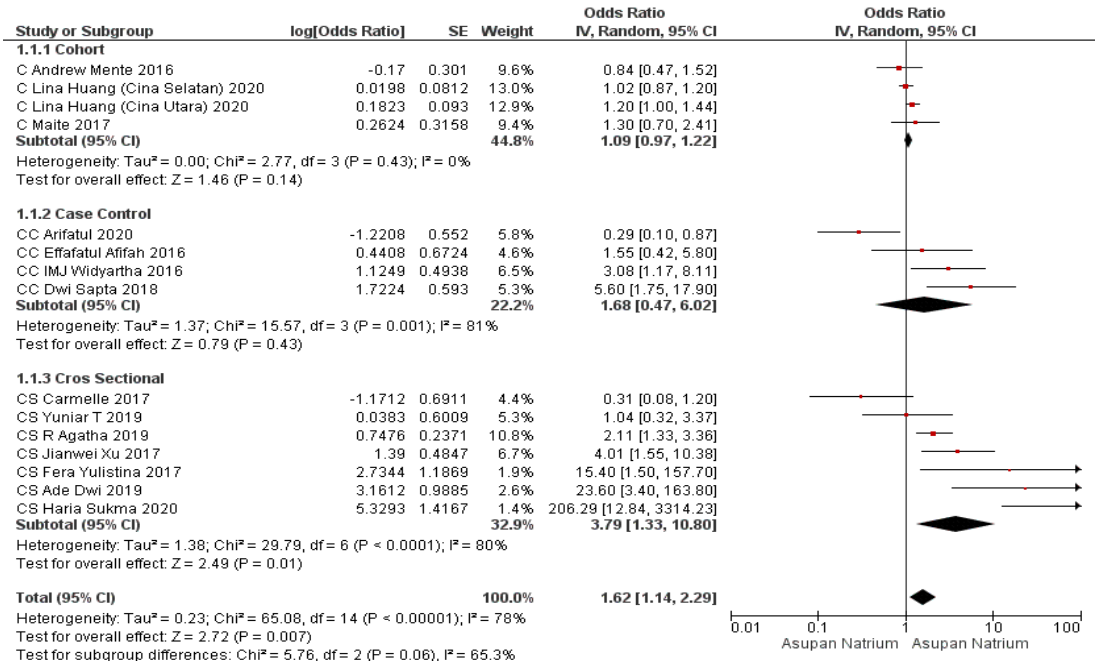


Fig. 1. Forest plot research study of the relationship between age and medication adherence in patients with hypertension

The statistical results of the meta-analysis of the relationship between sodium intake and the incidence of hypertension in the cohort study design were homogeneous and the variation was heterogeneous in the case control and cross-sectional study designs. Meanwhile, in the meta-analysis of the relationship between potassium intake and the incidence of hypertension, both the cohort and cross-sectional designs were heterogeneous. Research with more varied data will have a smaller weight than research with small variation. Weight is the role of a study on the total effect. The weight is directly proportional to the research subject and inversely proportional to the variation of the data, for example a study with 100 subjects will have a greater weight than a study with 50 subjects [14] Based on the data in Fig. 1 it can be seen that the number of subjects or research samples varied at least 45 people and the largest was 6788. Methods in assessing sodium and potassium intake also varied, some assessed intake by calculating food intake and associated with sodium and potassium intake.

The results of the meta-analysis of the relationship between sodium intake and the incidence of hypertension showed that in the cohort study design the variation between studies was homogeneous, where the $p$ value = 0.43 and the $I^2$ value was 0%. Meanwhile, the overall effect value for the cohort study design is $p$ = 0.14 and the pooled odds ratio is 1.09 with a 95% CI value of 0.97-1.22 where the confidence interval in the forest plot diagram touches the vertical line, so it can be concluded that there is no There is a relationship between sodium intake and the incidence of hypertension.

The results of the meta-analysis of the relationship between sodium intake and the incidence of hypertension in the case-control study design showed that the variation between studies was heterogeneous, with $p$ value = 0.001 and $I^2$ value of 81%. For the results of the overall effect value in the case control study design, $p$ = 0.43 and the pooled odds ratio value of 1.68 with a 95% CI value of 0.47-6.02 where the confidence interval in the forest plot diagram touches the vertical line so that it can be concluded that There is no relationship between sodium intake and the incidence of hypertension.

For statistical analysis, meta-analysis of the relationship between sodium intake and the incidence of hypertension in a cross-sectional study design showed that the variation between studies was heterogeneous, with a $p$ value < 0.0001 and an $I^2$ value of 80%. As for the overall effect value $p$ = 0.01 with a pooled odds ratio of 3.79 with a 95% CI value of 1.33-10.80 where the confidence interval in the forest plot diagram does not touch the vertical line so it can be concluded that there is a relationship between intake sodium with hypertension.

According to [15], the incidence of hypertension is influenced by several factors including sodium and potassium intake. Factors that influence the onset of hypertension usually do not stand alone, the occurrence of hypertension is caused by several factors that influence each other [15]. The results of research by [16] showed that high sodium consumption, namely 2000 mg per day in adults, was proven to accelerate the occurrence of hypertension. The speed of hypertension is also influenced by the high consumption of fat and sugar, as well as the lack of consumption of vegetables and fruit. Other factors that can increase a person's tendency to experience hypertension include age, gender, ethnicity, genetic factors and environmental factors including obesity, stress, salt consumption, smoking, and alcohol consumption.

According to [16] sodium intake is not related to the incidence of hypertension, this can be because not everyone has individual sensitivity to sodium intake which can be caused by genetic factors. In addition, the individual's reaction to the amount of sodium in the body depends on the sensitivity that the individual has due to the habit of consuming high-sodium foods such as the use of food seasonings, and eating processed or preserved foods using salt [16]. According to [15] group Certain people with various demographic, physiological, and genetic characteristics, have a tendency to be sensitive to the effect of sodium in food on increasing blood pressure [15].

Furthermore, to see the publication bias in each study, a funnel plot diagram can be used which can be seen in Fig. 2. Based on the funnel plot diagram, the distribution of cohort, case control, and cross-sectional study designs is not symmetrical. The cohort study is only on the left side while the case control and cross-sectional study designs are mostly on the right side. So based on the funnel plot diagram, it can be concluded that the cohort, case control, and cross-sectional study designs indicate publication bias.

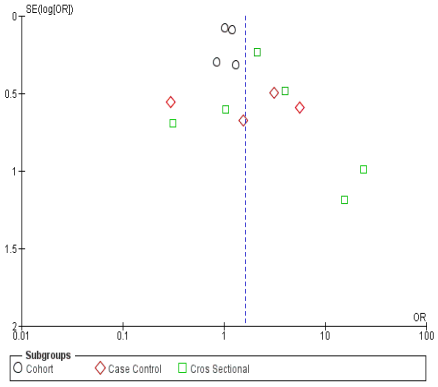


Fig. 2. Funnel plot relationship between sodium intake and the incidence of hypertension

The results of the meta-analysis of the relationship between potassium intake and hypertension can be seen in Fig. 3. The results of the study with a cohort design show that the variation between studies is heterogeneous, this can be seen from the $p$ value of less than 0.02 and the $I^2$ value of 71%. As for the overall effect value of the cohort study design $p = 0.31$ and the pooled odds ratio value of 0.85 with a 95% CI value of 0.61-1.18 and in the forest plot the confidence interval of the combined effect touches the vertical line so that it can be concluded that there is no There is a relationship between potassium intake and the incidence of hypertension. The cross-sectional study design shows that the variation between studies is heterogeneous, with a $p$ value $< 0.00001$ and an $I^2$ value of 86%. Meanwhile, the overall effect value is $p = 0.06$ with a pooled odds ratio of 0.

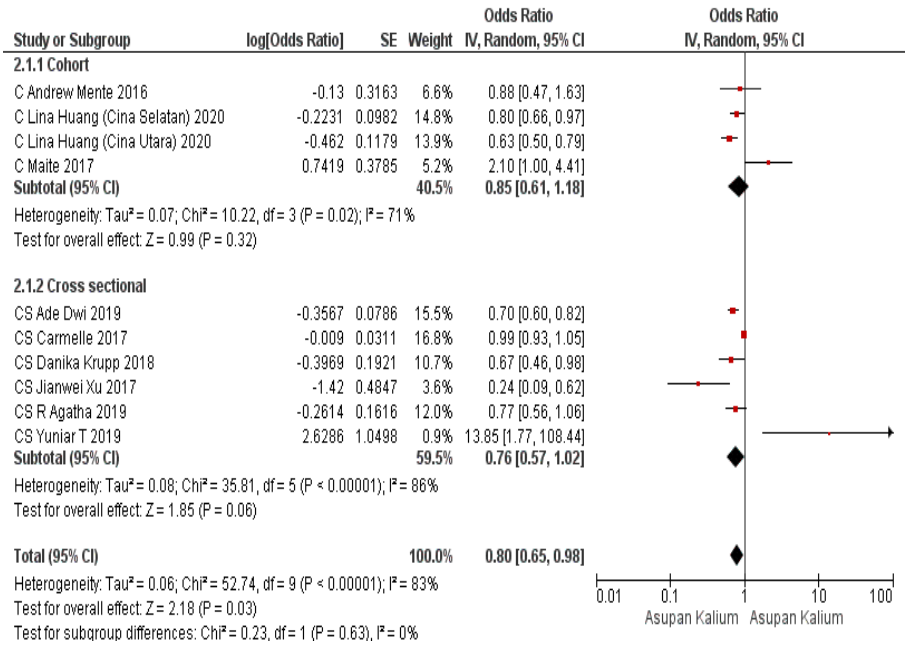


Fig. 3. The results of statistical analysis of meta-analysis of the relationship between potassium intake and the incidence of hypertension

Potassium is one of the nutrients needed by the body that plays a role in the balance of water and minerals in the body. Potassium works with sodium to maintain normal blood pressure in the body. The results of the [8] showed that rarely consuming foods containing potassium had a 13,854 risk of developing hypertension [8]. High potassium intake was associated with a decrease in blood pressure. The results showed that potassium lowered blood pressure more in black people than white people. In a meta-analysis, an increase in urinary potassium excretion of 2 g/day (50 mmol/day) was associated with a mean reduction in systolic and diastolic blood pressure of 4.4 mm Hg and 2.5 mm Hg in people with hypertension and 1.8 mm Hg in those with hypertension. mm Hg and 1.0 mm Hg in nonhypertensive individuals. Increasing potassium has a beneficial effect on lowering blood pressure by regulating potassium intake [17]

Potassium and sodium interact in such a way that the effect of potassium on blood pressure depends on concomitant sodium intake and vice versa. Specifically, increased potassium intake had a greater blood pressure-lowering effect when sodium intake was higher and had a lower blood pressure effect when sodium intake was low. In contrast, the reduction in blood pressure from a low sodium intake is best when potassium intake is also low [17].

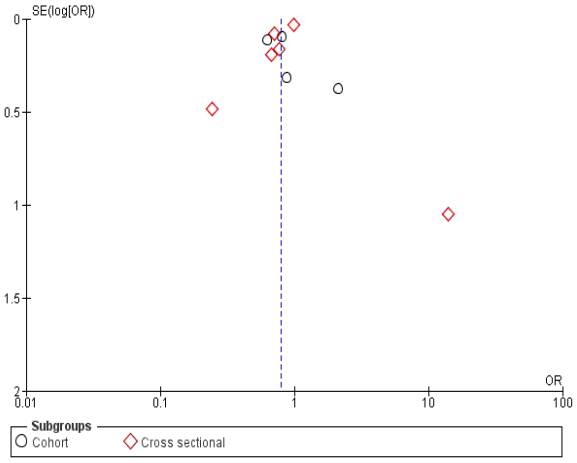


Fig. 4. Funnel plot of the relationship between potassium intake and the incidence of hypertension

Furthermore, to see the publication bias of each study design in the meta-analysis of the relationship between potassium intake and the incidence of hypertension, a funnel plot diagram can be used which can be seen in Fig. 4. In the funnel plot diagram, the cohort study design is represented by black circles and red cross sectional rhombuses. Based on the funnel plot, the distribution of the cohort study design is symmetrical, indicating that there is no publication bias. Meanwhile, in the cross-sectional study, the asymmetric distribution was more on the left side, indicating a publication bias.

The limitation in this study is that the search for research articles only uses three databases, namely Google Scholar, PubMed, and Science Direct. Some articles do not include OR and CI values so that meta-analysis cannot be carried out. There are 3 study designs in this article related to the relationship between sodium and potassium intake, but the number of articles for the cohort and case control designs is less than the cross-sectional study design articles. In addition, in this meta-analysis, there is no limitation on the number of research subjects in the article. while it is known that the weight is directly proportional to the research subject and inversely proportional to the variation.

The results of this meta-analysis indicate a publication bias. Publication bias is caused because the primary study data used tend to be published data which usually shows significant data, while insignificant data tends not to be published. Another factor that can cause the bias to be high in the effect size is language bias, where the articles selected are only in Indonesian and English according to those mastered by the researcher. In addition, there is an availability bias in which researchers choose research articles that are more accessible [12].

## IV. CONCLUSION AND ACKNOWLEDGMENT

The results of the meta-analysis of the relationship between sodium intake and the incidence of hypertension in the cohort design and case control design concluded that there was no relationship between sodium intake and hypertension. Meanwhile, in the cross-sectional design, the value showed that there was a relationship between sodium intake and the incidence of hypertension where high sodium intake had a risk of 3.79 more have high hypertension.

For the results of the meta-analysis of the relationship between potassium intake and the incidence of hypertension, both studies with cohort and cross-sectional designs showed that there was no relationship between potassium intake and the incidence of hypertension.

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## ETHICAL CLEARANCE

There is no ethical test because it uses the general analysis method.

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