Review Articles

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The Associations Between Coffee Consumption and Metabolic Syndrome (MetS) Biomarkers Among Adults: A Systematic Review of Epidemiological Evidence

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ABSTRACT

Objective To synthesize epidemiological evidence for a systematic review on the association between coffee consumption and Metabolic Syndrome (MetS)-related biomarkers, as defined by the used diagnostic framework(s), in human adult populations. This study proposes future directions for MetS-related biomarkers and coffee consumption. **Methods** A comprehensive search was conducted in PubMed, supplemented by manual searching, using predefined inclusion and exclusion criteria (n = 343). 13 observational studies were included in the final review. Extracted eligible studies were analyzed for adjustments, diagnostic frameworks, outcomes, and measurements. All included studies were assessed for bias using the Risk of Bias in Non-randomized Studies – of Interventions, Version 2 (ROBINS-I V2) tool. **Results** Though considerable heterogeneity and modification were observed with the diagnostic framework, a majority implemented the criteria set by the National Cholesterol Education Program's Adult Treatment Panel III (NCEP ATP-III) or the International Diabetes Federation (IDF). Other variations included coffee exposure definitions, country of study, and the stratification of results by binary sex. The given evidence suggests that greater coffee consumption is associated with lower odds of elevated blood pressure (BP), increased waist circumference (WC), reduced high-density lipoprotein cholesterol (HDL-C), and elevated triglycerides (TG). From the adjusted sex-stratified results, increased coffee consumption was frequently associated with lower odds of elevated TG and increased WC in men, and elevated BP and reduced HDL-C in women. **Conclusions** Frequent inverse associations between coffee consumption and specific MetS components – TG and HDL-C – indicate a strong association with lipid-based metabolic outcomes. There were relatively fewer, yet still favorable, statistically significant, lower odds of elevated FBG with higher coffee consumption. Applying broader and additional measurements, such as secondary biomarkers, to assess individual biomarker levels can contribute to the principal standardization of the present heterogeneity. Limitations on additives, coffee preparation methods, and coffee quantity were observed, validating concerns from previous studies.

1. Introduction

Metabolic Syndrome (MetS) constitutes a set of interrelated abnormalities, often characterized by insulin resistance, visceral adiposity/central obesity, hypertension, and dyslipidemia [1], inducing subsequent concerns for cardiovascular diseases (CVD) and diabetes risk. Originally termed Syndrome X to signify the cluster of cardiovascular risk factors [2], MetS has adopted various cut-offs as a formal diagnosis, often shaped by binary sex, ethnicity, and racial demographics [3]. The first formal definition was formulated by the World Health Organization (WHO), which assessed insulin resistance, along with a minimum of two risk factors: central obesity (measured by waist circumference [WC]), low High-Density Lipoprotein-Cholesterol (HDL-C) levels, hypertension, microalbuminuria, and/or high triglyceride levels [4]. In 2001, the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) adjusted the criteria, removing the necessity of insulin resistance assessment. In 2005, conventional meanings were challenged, as neither the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) nor the International Diabetes Federation (IDF) were able to settle upon a true

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measure of abdominal obesity.4 Currently, the commonly employed diagnostic criteria of MetS are the IDF and the NCEP ATP-III [5].

The present established framework for NCEP ATP-III is as follows:

1.Waist circumference >102 cm in men, >88 cm in women

2.Plasma triglycerides ⩾150 mg/dL,

3.HDL-C <40 mg/dL in men, <50 mg/dL in women

4.Blood pressure ⩾130/85 mm Hg

5.Fasting plasma/blood glucose ⩾110 mg/dl

*A minimum requirement of three of the five criteria

*The requirement is also met if an individual is on medication for the treatment of a biomarker level abnormality.

The IDF has the same set of criteria, except that the WC requirement is mandatory when considering the three-criterion minimum.

Mitigation of health disorders, such as metabolic conditions, can often be regulated via dietary behavior, such as coffee consumption. Coffee consumption is often cited as one of the most widely consumed beverages in the world and a contributing factor to a positive metabolic profile, reducing rates of liver cancer, uterine cancers, and cardiometabolic conditions [6]. Observational studies have shown that various coffee consumption diminishes the odds of all-cause mortality, CVD, and cardiometabolic multimorbidity [7]-[9], though coffee exposure and measurement remain varied. Prior studies reviewing coffee consumption and MetS have made operational outcome measurements, employed justifiable modifications to MetS frameworks, and analyzed MetS as one component, yet many studies group coffee with other caffeinated beverages or do not account for additives within the drink.

Due to the aggregation of various metabolic factors, it is plausible to surmise that MetS, nor its clinical relevance, should be considered as a standalone disorder, but an overarching term representing individual physiological biomarkers in unison.

Prior systematic reviews have tried to redefine MetS as one definition [10]-[12], discussed limitations of generalizability due to population and coffee consumption characteristics, and have noted the need for more longitudinal studies for this association [13]. Thus, a biomarker-centered focus may result in greater clarity for approaching and understanding the association between MetS and coffee consumption. With attention to the heterogeneity of definitions, outcome measurements, study designs, and population demographics, this systematic review aims to validate the current concerns regarding limitations of the association between MetS and coffee consumption, focusing on the larger framework possibilities that could be inculcated into the framework.

2. Methods

One database, PubMed, was used to identify relevant articles, and was supplemented with manual searching and snowballing. The given search string to PubMed was as follows: ("metabolic syndrome" OR MetS OR "central adiposity" OR "visceral fat" OR "waist circumference" OR "Metabolic Syndrome"[Mesh]) AND (coffee OR "coffee consumption" OR caffeinated OR decaffeinated OR espresso OR latte OR cappuccino OR instant) AND (triglycerides OR "HDL cholesterol" OR "high density lipoprotein" OR lipid* OR "blood pressure" OR hypertension OR "systolic blood pressure" OR "diastolic blood pressure" OR "fasting glucose" OR glucose OR insulin OR "insulin resistance" OR HOMA-IR OR HbA1c OR adiponectin OR leptin). From the results of the search string, eligible articles for screening were published between January 1st, 2000, and January 2026.

Other techniques employed will include forward and backward snowballing, along with manual searches, to identify additional relevant papers. These techniques were performed to include articles involving direct measurements of MetS-related biomarkers - “central obesity,” “waist circumference,” “serum triglycerides,” “blood pressure,” and “fasting glucose.” The other search strategies - involving both manual searching and snowballing - were utilized to ensure a full scope of papers is screened, as they may not appear in the PubMed database search. The objective was to compile a minimum of 10 to 20 articles with snowballing, manual searching, and using the PubMed “Similar articles.” All included articles were uploaded as four zip files onto Rayyan.ai for one screening process. All included articles were screened in the deduplication phase and all successive screening phases.

To avoid redundancy in the references, papers from manual searching, snowballing, and those that were screened as being ineligible for synthesis, were used locate literature for the introduction, future directions, and general context. Secondary research articles, including but not limited to systematic reviews and meta-analyses, that were selected for the introduction, directions, and general context were not part of the screening stage.

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 flow diagram guidelines were followed. In the flow chart, the manual searching and snowballing, under “identification of new studies via other methods”, were grouped with “identification of new studies via databases and registers” as the entirety of all papers was screened together through Rayyan.ai.

The predefined inclusion and exclusion criteria are listed below:

Inclusion:

1.One version of the source must be in English

2.Observational studies and experimental studies

3.The participants, or a subset of the participants, must have coffee (e.g., instant coffee, espresso, black coffee) intake, or be given coffee to consume during the study

4.Coffee intake must be quantified or compared by relative intake

5.The selected paper must include participants or a dataset with a participant pool with reported individual MetS components, as operationally defined by the used diagnostic framework, independent of whether or not the included participants were diagnosed with MetS at baseline. The participant pool, or a subset of the participant pool, may consist of individuals with or without MetS

6.Studies must report findings, categorically or numerically, on one of the core MetS criteria, as defined by the used MetS framework

7.Within the given study, the participant pool, or a subset of the participant pool, may include participants who have normal, borderline, or pathological MetS-related biomarker levels or individual MetS diagnostic criteria, as operationally defined by the used diagnostic framework, at baseline.

Exclusion:

1.Papers and studies published before January 1st, 2000

2.Papers/studies where the primary study outcome is mortality, and no MetS-related biomarkers are reported or discussed

3.Animal studies

4.In-vitro studies

5.Pediatric studies, adolescent studies, and studies that include participants younger than 18 years of age

6.Studies/papers in which coffee intake is not reported independently, nor can it be separated from other combined dietary and lifestyle exposures (e.g., coffee that is grouped in dietary patterns)

7.Studies in which the primary exposure is not coffee, including, but not limited to, caffeine, coffee extracts, tea, and energy drinks

8.Secondary research articles

There were two main stages of screening: the abstract screening phase (ASP) and the full text screening phase (FSP). The first stage of screening, the ASP, was performed after the deduplication stage. In the ASP, any article that meets an exclusion criterion will be removed. However, if additional information was needed to decide the exclusion of an article, the article was moved to the FSP. For example, often, it was unclear if individual MetS-related biomarkers, as defined by the operating diagnostic framework, were discussed, or if MetS was reported in its entirety (e.g., increase or decrease in MetS as opposed to increase or decrease in HDL-C).

Rayyan.ai offered automated screening, yet this function was not used. Rather, the three phases - deduplication, the ASP, and the FSP - were manually conducted. Figure 1, PRISMA 2020 Flow Diagram, details the systematic process to result in a finalization of 13 studies for data extraction and synthesis. No sensitivity analyses were performed.

The protocol was preregistered on Open Science Framework (OSF) on January 14th, 2026 (DOI: 10.17605/OSF.IO/9GU5Q). No updates or changes have been made to the protocol since the initial submission.

3. Results

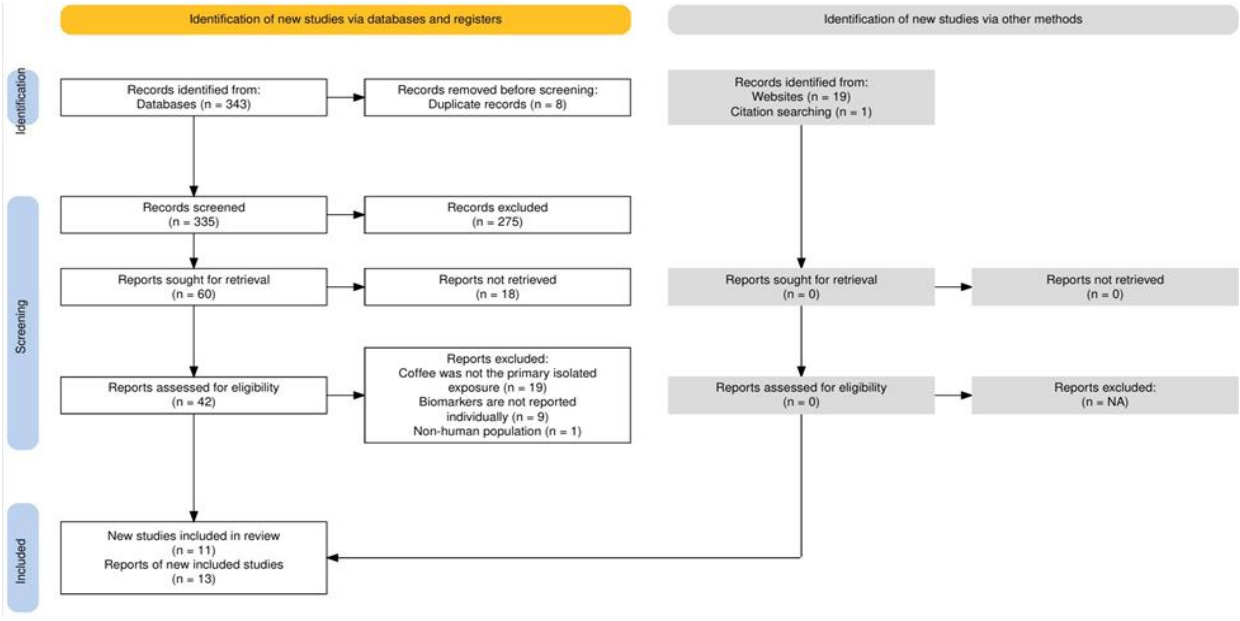

Fig. 1 - PRISMA 2020 flow diagram

With the two screening phases and consistently applying the inclusion/exclusion criteria while determining the eligibility of each publication, 13 studies were included. The full selection process is depicted in Figure 1. Non-significant results were abbreviated as N/S.

Table 1 - Overview of included papers

Paper	Journal	Author	Year	Population	Data Collection of Coffee Consumption	Coffee Consumption	Region of Study	Adjusted Results
The Association between Coffee Consumption Pattern and Prevalence of Metabolic Syndrome in Korean Adults	Nutrients	Kim SA	2019	HEXA	Two-day, 24h recall	No	South Korea	Yes
Relationship Between Coffee Consumption and Prevalence of Metabolic Syndrome Among Japanese Civil Servants	Journal of Epidemiology	Matsuura H	2012	Japanese Civil Servants	Self-administered questionnaire	No	Japan	Yes
The longitudinal association between coffee and tea consumption and the risk of metabolic syndrome and its component conditions in an older adult population	Journal of Nutritional Science	Wong THT	2022	BMES	Semi-quantitative Food Frequency Questionnaire	Yes: 250mL/cup	Australia	No
Factors Associated With Metabolic Syndrome in a Mediterranean Population: Role of Caffeinated Beverages	Journal of Epidemiology	Grosso G	2014	Sicily	Validated administered dietary questionnaire	Yes: 35mL/cup	Italy	No

Paper	Journal	Author	Year	Population	Data Collection of Coffee Consumption	Coffee Consumption	Region of Study	Adjusted Results
Association between the Prevalence of Metabolic Syndrome and the Level of Coffee Consumption among Korean Women	Public Library of Science One	Kim K	2016	KNHANES	Food Frequency Questionnaire	No	South Korea	No
Association between the prevalence of metabolic syndrome and coffee consumption among Korean adults: results from the Health Examinees study	Applied Physiology Nutrition and Metabolism	S Shin	2019	HEXA	Semi-quantitative Food Frequency Questionnaire	No	South Korea	Yes
Association of Coffee Consumption and Its Types According to Addition of Sugar and Creamer with Metabolic Syndrome Incidence in a Korean Population from the Health Examinees (HEXA) Study	Nutrients	Tan L	2021	HEXA	Semi-quantitative Food Frequency Questionnaire	No	South Korea	Yes
Association of daily coffee and tea consumption and metabolic syndrome: results from the Polish arm of the HAPIEE study	Springer	Grosso G	2014	HAPIEE	Semi-quantitative Food Frequency Questionnaire	Yes: 150mL/cup	Poland	Yes
Coffee consumption is not related to the metabolic syndrome at the age of 36 years: the Amsterdam Growth and Health Longitudinal Study	European Journal of Clinical Nutrition	Driessen MT	2009	AGHL	Coffee consumption questionnaire: self-reported	Yes: 125mL/cup	Netherlands	No
Inverse Correlation Between Coffee Consumption and Prevalence of Metabolic Syndrome: Baseline Survey of the Japan Multi-Institutional Collaborative Cohort (J-MICC) Study in Tokushima, Japan	Journal of Epidemiology	Takami H	2013	J-MICC	Food Frequency Questionnaire	No	Japan	No
Moderate or greater daily coffee consumption is associated with lower incidence of metabolic syndrome in Taiwanese militaries: results from the CHIEF cohort study	Frontiers in Nutrition	K Tsai	2023	CHIEF	Self-reported questionnaire	Yes: ≈ 200mL/cup	China	No
Association Between Coffee Consumption and Metabolic Syndrome Components Among Saudi Adults	Metabolites	W Alzahrani	2025	KAUH	Two-day, 24h recall	Yes:273 mL/cup~ 591mL/cup	Saudi Arabia	No
Association between Coffee Consumption, Caffeine Intake, and Metabolic Syndrome Severity in Patients with Self-Reported Rheumatoid Arthritis: National Health and Nutrition Examination Survey 2003–2018	Nutrients	Wang S	2022	NHANES	24h dietary recall	Yes: 6-ounce/cup	United States	No

3.1. Study Selection and Characteristics

Only adjusted results were incorporated into the current paper. Of the 13 studies, 10 were cross-sectional studies, and three were longitudinal studies (Figure 2), reflecting the predominant observational nature of the current evidence. Sample and population sizes varied, ranging from community cohorts to national datasets. Heterogeneity was particularly present on a geographically representative scale, with datasets from North America, the Middle East, Europe, and Asia (Figure 3). Four studies displayed sex-stratified effects of the association between MetS-related biomarkers and coffee consumption; the remaining studies were a combination of non-adjusted sex-stratified results and no differentiation for sex-based implications.

Plentiful working measurements of the standard volume for a cup of coffee were noted, from 35 mL per cup to 591 mL per cup. Regardless of the discrepancy, there was one consistent alignment across the studies: using cup/day frequency measurements; one study reported results on a volume-based scale. Often, coffee consumption was categorized into “low(er),” “moderate,” and “high(er)” consumption. Difficulty was present in identifying preparation methods and additives, though three studies illustrated adjusted coffee-type stratified results (Table 1).

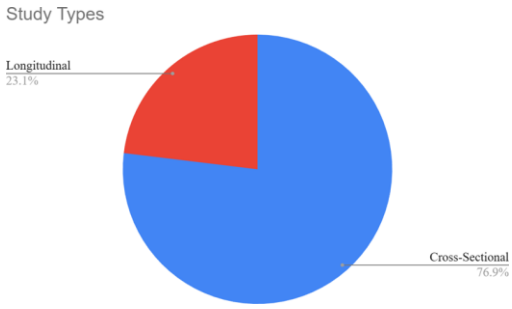

Fig. 2 - Distribution of study designs

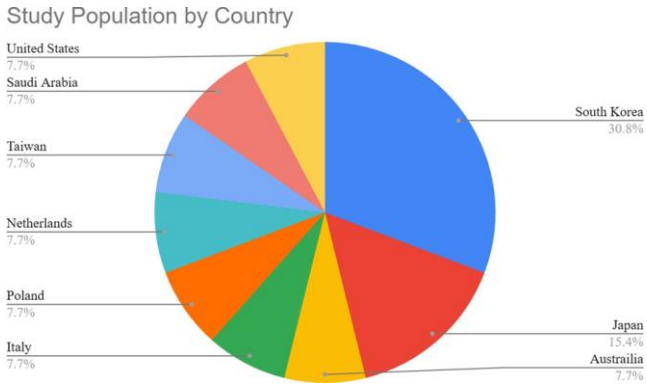

Fig. 3 - Geographic distribution of studies

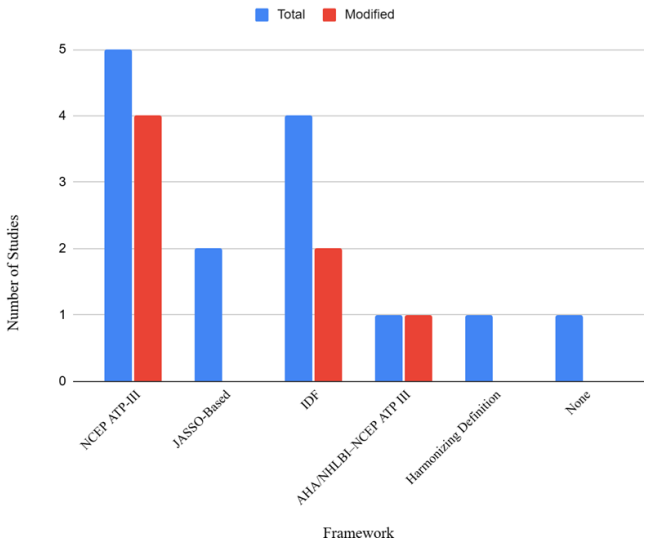

Fig. 4 - Frequency and modification of MetS diagnostic frameworks

3.2. MetS Diagnosis

Not all biomarkers were assessed in every study. However, the diagnostic biomarkers had the least heterogeneity relative to the coffee types and cup-size definitions. From most frequently to least frequently used, the biomarkers were: HDL-C (13 studies), WC (13 studies), TG (13 studies), FBG/FPG (12 studies), BP (10 studies), SBP (3 studies), DBP (1 study), HbA1c (1 study), and BMI (1 study). Additionally, despite the inclusion of medication use as a criterion for MetS, there was only one present study that provided this stratification [13].

Figure 4 demonstrates the functional span of MetS diagnostic frameworks implemented throughout the studies. Despite the definitional diversity, the NCEP ATP-III and IDF definitions tallied to the cumulative majority, contributing to the primary guideline in approximately 69% of all studies, given that the former was used in five and the latter was used in four. All but one study adhered to one guideline. Notably, both NCEP ATP-III and IDF criteria were often modified based on included participant demographics, such as WC cut-offs and glycemic thresholds (Figure 4); approximately 54% of all definitions were modified, two diagnostic frameworks had no modifications (Figure 4), and one study did not use any formal framework [14].

Though heterogeneity was present, it was clear that the most favored uniformities were the description of the frequency of drinking (cup/day), and what the five most applied MetS biomarkers were - HDL-C, WC, TG, FBG/FPG, and BP. The rarity of medication-based stratification offers insight into how MetS is seen as a biomarker-level diagnosis more than the medications used to treat abnormalities in the biomarker levels. The non-uniformity of cup-size and coffee-type stratification creates dissonance between the results of similar MetS and coffee consumption association studies, as even though various sizes and types are used and acknowledged, they are not accounted for in the results, contributing to the generalizability of the effects of coffee.

3.3. Lipid-Based Outcomes (HDL-C, TG)

The majority of studies, through adjusted results, reported that an increase in coffee consumption was associated with lower odds of reduced HDL-C and elevated TG levels. For results separated by sex, the results were similar. Women had more favorable metabolic outcomes with HDL-C with higher coffee intake, often seeing lower odds of reduced HDL-C. Among men, there were favorable metabolic health associations for TG and HDL-C, as relatively higher coffee intake commonly led to lower odds of elevated TG and reduced HDL-C.

3.4. Glycemic Biomarker Outcomes (FBG/FPG, HbA1c)

Four studies found that consuming more coffee was associated with lower odds of elevated FBG, highlighting the inverse association of coffee consumption with glycemic-based outcomes (FBG specifically). However, when a study substituted HbA1c as the glycemic biomarker instead of FBG, the study reported non-significant findings, limiting the nature of glycemic index measurement.

3.5. Anthropometric Outcomes (WC, BMI)

For anthropometric measurements, WC was the most prominent biomarker. In most studies, WC was reported as its own variable, but two studies provided results through the lens of abdominal obesity. One study, which did not apply any formal diagnostic standard of MetS, used BMI as an anthropometric indicator. Both longitudinal and cross-sectional studies offered a similar insight: lower odds of increased WC as coffee intake increased.

3.6. BP Outcomes (BP, SBP, DBP)

Outcomes reporting BP mainly presented as one variable - BP itself. In sex-stratified analyses, women had a lower incidence of elevated BP with coffee consumption, except in one study where black coffee consumption was associated with increased odds of elevated BP. When studies reported results based on SBP and DBP, the measurements were primarily continuous variables: coffee intake was associated with lower SBP and lower DBP, reflecting a decrease in overall BP.

3.7. Collective Synthesis

Deducing the results across the 13 studies, the associations between MetS-related biomarkers and coffee consumption were dependent upon the biomarker evaluated; however, one pattern emerges: higher coffee consumption led to a favorable metabolic profile. Lipid-based outcomes (HDL-C, TG) demonstrated metabolically favorable improvements. FBG, overall, reported favorable outcomes as well, and was the predominant glycemic biomarker; greater coffee intake demonstrated reduced odds of elevated FBG. However, lipid-based outcomes reported these favorable results more frequently: whereas 10 studies showed significant lipid-based, metabolic improvements, FBG displayed metabolic improvement in four studies. For anthropometric measurements, WC was the main mode of judgement, and BMI was only used once; like HDL-C, TG, and FBG, WC also was seen to have a positive effect with more coffee intake (e.g., reduced odds of increased WC). Coffee consumption resulted in lower odds of BP - both as a continuous and categorical (elevated BP) variable - with one incident of a coffee-type and sex-specific result. These findings indicate that lipid-based outcomes have the most frequent favorable association compared to the other biomarkers. Holistically, all the common biomarkers HDL-C, WC, TG, FBG/FPG, and BP - had metabolic improvements with greater relative coffee consumption per day.

3.8. Overall Risk-of-Bias Assessment

ROBINS-I V2 was performed for all 13 studies to assess the risk of bias. Across the papers for data extraction, the majority were evaluated as a moderate risk of bias. The main sources of this bias were from the data collection process, which was commonly self-reported, giving rise to response bias. Two domains - (bias due to) “Missing data” and “Outcome measurements” - had the highest number of study-level low-risk assessments. One study [15] was marked as having a serious risk of bias due to the population being hospital-specific.

4. Discussion

4.1. Diagnostic Criteria and Biomarker Outcome

This epidemiological systematic review weighs on the current evidence of the association between MetS biomarkers, dependent upon the diagnostic framework used, and coffee consumption. Reviews have already proposed modifications of a singular, standardized MetS definition [10]-[12]. With over half of the included studies having a modified definition (Figure 4), one study comparing and contrasting two frameworks,16 and one study creating its own coffee consumption analysis with the overarching components of MetS [16], this study acknowledges the pluralistic diversity of the heterogeneity of what constitutes the condition - there is not a singular definition that should wholly encompass the entirety of MetS, and it is most effective to continue proceeding with this understanding. For instance, modified definitions catered to the cohort of interest; studies have empirically proven the significant correlation of WC and race/ethnicity [17]. Nine studies implemented either IDF or NCEP ATP-III criteria for MetS diagnosis, and from the seven modified criteria, IDF and NCEP ATP-III were $\approx$ 86% for of the modifications. Even with the high prevalence of these two criteria, overall MetS classification still varies. Modifications of cut-off values and levels based on population demographics may give rise to inequivalent diagnosis classification. In fact, research has shown that the requirement of central obesity as an IDF criterion has resulted in fewer diagnoses of MetS [18]. Though the mandate of certain criteria for MetS indeed enables the severity differentiation, comparability across studies of MetS diagnosis will be hindered regardless, as it may miss the opportunity to conduct patient screening for physiologically similar conditions or premature death. Instead of expanding definitions, this study suggests MetS should be primarily viewed at the biomarker level in future studies - insight that can lead to more effective health management for downstream CVD and diabetes risk, allowing secondary or additional biomarkers to be incorporated into the diagnosis. This study noticed the lipid-based outcome predominance, and thus two suggested biomarkers for a similar glycemic and anthropometric focus, further described in 6.2: HbA1c - used only once throughout 13 studies - and the leptin/adiponectin (L/A) ratio.

In contrast with the lipid-based outcomes, glycemic-based outcomes had relatively fewer adjusted and statistically significant findings, giving two possible reasons: 1) Effects of coffee consumption are predominantly lipid-based, or 2) Methodology. There was limited use of HbA1c as a biomarker, restricting the broader interpretation of blood glucose. Sherwani et al. detailed that the American Diabetes Association (ADA) is advancing HbA1c as an equivalent to FBG [19]. Further, denoting HbA1c as a longitudinal marker of glycemic control rather than FBG, this confirms its accurate use in “Association between Coffee Consumption, Caffeine Intake, and Metabolic Syndrome Severity in Patients with Self-Reported Rheumatoid Arthritis: National Health and Nutrition Examination Survey 2003–2018,” given its long-term functionality [14]. If studies on coffee consumption and MetS-related biomarkers are conducted later, HbA1c could serve as a secondary biomarker and an operationalized intra-study reliability measure for FBG.

The findings also presented a WC-heavy diagnostic computation, as all but one anthropometric measurement utilized WC instead of BMI, as WC is considered a stronger indicator of insulin resistance and cardiovascular risk. Recent research has shown that when WC was substituted by BMI as a predictor of diabetes, which hints at insulin resistance, particular characteristics - fat distribution by race/ethnicity, visceral adiposity, and ectopic fat - were masked, validating the need to retain WC-based measures [20]. A meta-analysis further marked the necessity of cut-off points , as replicating the results without consideration of population-based definitions led to no significance of coffee intake on WC. Similarly, however, the meta-analysis discussed the vast non-uniformity in study designs, populations, definitions, and methodologies, as this current systematic review marked as well [21].

4.2. Heterogeneity in Coffee Measurements and Coffee Type

Though seven studies defined how much one cup (mL) of coffee was, each study had a different volume. Even with the summative results showing that higher coffee consumption led to more favorable metabolic health profiles,

the pronounced variability masks the dose-response relationship and creates dependency on categorical, relative comparisons (lower, moderate, higher). The classification of one cup as 125 mL/cup in one study and 250 mL/cup in another study represents differential misclassification, preventing true correlations and comparability across studies [22][23].

The effect of coffee types on MetS-related biomarkers was another element within the expansive variance of definitions. "3-in-1" coffee, consisting of instant coffee, sugar, and non-dairy creamer, demonstrated variable associations, such as resulting in lower odds of reduced HDL-C, elevated BP, decreased TG, and elevated FBG, revealing potentially favorable associations with metabolic profiles. Despite the inclusion of creamer and sugar, information regarding the quantity of cream and sugar was unavailable, hindering the conclusive efficacy of the additives. "3-in-1," espresso, and black coffee consumption all provide favorable associations for TG (lower odds of elevated TG) and/or reduced HDL-C. Coffee consumption in general has a favorable association with lipid-based measurements relative to those who consume no coffee and suggests positive health benefits regardless of the type. Other studies report inconsistencies with the findings of this current article, instead stating that TG levels are seen to be greater than those in non-coffee consumers [24][25].

In a study analyzing cardiac function and coffee consumption, consuming ⩾3 cups/day led to significantly lower SBP and DBP [26]. This review largely encloses the same result, though one study showed increased odds of elevated BP for women who consumed black coffee [27]. More than the type of coffee, caffeine has shown to increase DBP levels in women compared to those in men, but as the study showed, physiological hormones could be a strong intervention for this effect - a working line of assessment not discussed in this paper [28].

4.3. Inconsistencies from Heterogeneity

The identification of steroid intervention and using drinking various types of coffee points to a broader concern [28][29][30]: as these studies consider additives and specific-classifications of coffee, contributing to the distinction in results. Furthermore, studies investigating brewing types, filtration, and production processes have noted that biochemicals, such as diterpenes, can affect the coffee itself, thereby impacting metabolic results and contributing to the inconsistency of significance across studies [31]. Filtered coffee, for instance, has shown to positively favor lipid profiles whereas decaffeinated coffee has been proven to benefit glycemic metabolism as compared to caffeinated coffee [32][33]. The standardization of coffee exposure remains nuanced, but grasping this will help to increase transparency on whether the observed results are confounding variables or metabolic effects. Last, this study's findings are consistent with a collective concern of the 10 cross-sectional studies: the call to conduct more longitudinal studies on the association between coffee consumption and MetS.

5. Future Directions and Study Limitations

5.1. Study Limitations

Though this systematic review was methodologically conducted, limitations must be addressed. As an independent reviewer of this systematic review project, there was restricted access to other relevant databases, such as Scopus, Web of Science, Cochrane, and Embase. Access constraints arose due to a lack of institutional or organizational affiliation; thus, PubMed was selected for its comprehensive inclusion of all pertinent fields for this study, including epidemiology, nutrition, and MetS. The search, with one database, unintentionally omits journals and papers that could have taken a substantial role in developing the association between coffee and MetS-related biomarkers. Though this paper did include 20 papers via forward and backward snowballing, and hand searching - specifically, hand searching of academic literature - in an effort to mimic the broad extent of literature from various databases, future review recommendations include exploring a larger network of indexed work and include grey literature for a more holistic and contextual understanding of coffee, offering information on coffee production, processing, and consumption trends. Additionally, future searches are expected to include databases prioritizing the aspect of healthcare examined - for instance, this study would have benefited from using databases focusing on metabolic health and nutrition.

Clarity was also limited by the heterogeneity of cup-size measurements, diagnostic definitions, and biomarker use - notably, the effect of medications as a diagnostic tool for the criteria in the MetS definition. Pharmacological treatment for biomarker abnormality is a common diagnostic criterion, but only one study stratified based on medication use. Given that the biochemical processes and molecular interactions differ for individuals with and without medication use, future analytical models and adjustments should analyze how coffee consumption affects MetS-biomarkers here, such as those on anti-diabetic treatments and anti-hypertensive medications.

5.2. Future Directions

Though there have been proposed modified cut-off definitions of MetS, this review does not seek to alter any definitions, but offers a supplementary idea for prospective coffee consumption and MetS-related biomarker studies, inspired by one included study that used HbA1c instead of FBG [22]. Potential directions include continuing to use the modified MetS definitions, but incorporating HbA1c in more correlative studies - especially longitudinal studies. Future observational studies could potentially be given greater depth of glycemic regulation through this additional biomarker. Second, adding a waist-to-hip ratio would provide broader insight into abdominal obesity and WC [34][35]. Alongside anthropometric measurements, a 2015 paper, "What is the best biomarker for metabolic syndrome diagnosis?", reported that high molecular weight (HMW) adiponectin and the leptin-to-adiponectin (L/A) ratio were the best biomarkers for overall MetS diagnosis [36]. "Leptin: Adiponectin ratio discriminated the risk of metabolic syndrome better than adiponectin and leptin in Southwest Nigeria," further affirmed the L/A ratio as the best reporter, and was also a population-specific result [37], paralleling the modifications based on race/ethnicity seen in this current paper.

Regarding coffee exposure and type, each study that reported a measurement had a differing volumetric base of "one cup" of coffee, and this review was unable to curate a singular definition; most studies used a cups/day frequency, but due to the range of one cup, an operationalized definition could not be established, and this introduces variability before data collection. Future meta-analyses that standardize the volume per cup of coffee would be beneficial in providing an equal-quantity comparison. Computing the percent change of biomarker levels from the baseline assessment or standardized mean difference could increase homogeneity across studies, regardless of the original volume. A principal component analysis (PCA) would be advantageous to find the most prominent contributor to variance in the association between MetS-related biomarkers

and coffee consumption, and regression analyses would map how individual additives affect each related biomarker.

6. Conclusions

Synthesis in this systematic review found epidemiological evidence to examine the association between MetS-related biomarkers and coffee consumption, given the diverse interpretability across populations, frameworks, and coffee types. Lipid-based outcomes were most common, as higher coffee consumption was associated with lower odds of reduced HDL-C and elevated TG. Lower odds of elevated FBG were also seen throughout the studies, suggesting improvement in glycemic health as coffee consumption increased, but there were fewer studies demonstrating this than those of lipid-based outcomes.

Evaluating the impact of coffee on MetS-related biomarkers breaks down the singular diagnostic structure, analyzing the condition at a molecular scale. Given the metabolically favorable results, later assessments of this association should consider additional biomarkers while still applying the original MetS framework - modified or not. More longitudinal studies are encouraged, and meta-analyses could attempt to standardize exposure definitions.

A.1. Abbreviations

- Metabolic syndrome: MetS
- Waist circumference: WC
- Triglyceride(s): TG(s)
- Fasting plasma glucose/Fasting blood glucose: FPG/FBG
- High-density lipoprotein cholesterol: HDL-C
- Blood pressure: BP
- Diastolic blood pressure: DBP
- Systolic blood pressure: SBP
- Non-significant: N/S
- Hemoglobin A1C: (HbA1c)
- National Cholesterol Education Program Adult Treatment Panel III: NCEP ATP-III
- International Diabetes Federation: IDF
- American Heart Association/National Heart, Lung, and Blood Institute: AHA/NHLBI
- Japan Society for the Study of Obesity: JASSO
- Homeostatic Model Assessment of Insulin Resistance: HOMA-IR
- Risk Of Bias In Non-randomized Studies – of Interventions, Version 2: ROBINS-I V2

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