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Research Article

A 5-Year Systematic Review (01 April 2017 to 31 March 2022) on the Causes of Abdominal Obesity

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Abstract

Abdominal obesity (AO) is a global public health concern with few reviews on the underlying causes. Here, we conduct a systematic review on the causes of AO using publications indexed in PubMed from April 1, 2017, to March 31, 2022. 46 out of 199 (23%) articles were included, revealing 10 themes of causes namely, (a) age, gender, socioeconomic, and genetic/biological determinants, (b) nutritional intake, (c) lifestyle habits, (d) mental and cognitive disorders, (e) smoking, (f) gastrointestinal microbiota, (g) alcohol consumption, (h) rural regions, (i) non-alcoholic fatty liver disease, and (j) noise pollution.

Keywords: *Abdominal Obesity (AO); SARS-CoV-2; Visceral Fat; Metabolic Syndrome (MS); Cardiovascular Diseases (CVDs)*

Introduction

Obesity, specifically abdominal or central obesity, is a silent epidemic affecting millions of people worldwide. According to World Population Review 2022[1], the trends of obesity appear to be more prevalent in persons living in South Pacific countries; namely, Nauru (61.00%), Cook Islands (55.90%), and Palau (55.30%). Obesity rates have more than doubled as a result of the recent SARS-CoV-2 virus pandemic, particularly among the younger population [1].

Abdominal obesity (AO) is commonly referred to as fat around the abdomen area. There are two types of fat: visceral fat and subcutaneous fat. Visceral fat lies in the spaces between the abdominal organs and the omentum whereas subcutaneous fat can be found between the skin and the outer abdominal wall[2]. A study by Sahakyan., *et al*. [2] found that excess visceral fat is associated with an increase in mortality rates when there is less subcutaneous fat, implying that subcutaneous fat may contain some protective factors.

[1]https://worldpopulationreview.com/country-rankings/obesity-rates-by-country

[2]https://www.health.harvard.edu/staying-healthy/taking-aim-at-belly-fat

AO has been reported to be more prevalent in females than in males [3], and it is strongly associated with metabolic syndrome (MS) [4] and cardiovascular diseases (CVDs) [5], eventually increasing mortality rates [6]. MS refers to a cluster of conditions that increases the risk of heart disease, stroke, and type 2 diabetes. According to the NHS[3], MS is especially prevalent in the United Kingdom, affecting one in every three older persons aged 50 and above.

AO can be readily lost by making lifestyle [7] and dietary [8] adjustments, but individuals' motivation remains to be a critical aspect in attaining fat loss [9]. A study by van Germert., *et al*. [10] found that a combination of exercise and dieting is an effective treatment approach to reducing visceral and subcutaneous fat.

AO can be measured with a tape measure, which is a common household tool. Waist circumference (WC) and waist-hip ratio (WHR) are two of the most often utilized methods for assessing body fat proportions since they are simple and inexpensive. WC is considered the gold measurement standard and differs between the different ethnic groups. In this review, we will be following the guidelines for the Chinese Ethnic group. According to International Diabetes Federation[4], the WC guidelines for the Chinese ethnic group are ≥ 90 cm for males and ≥ 80 cm for females as seen in table 1. WHO recommends WHR guidelines of > 0.85 for women and > 0.90 for men[5]. Measurements exceeding the guidelines indicate a risk of AO and its associated health risks. In addition to WC and WHR, BMI is another dependent factor that indicates the individual's health status.

Country/Ethnic group	Male	Female
Europids	≥ 94 cm	≥ 80 cm
South Asians	≥ 90 cm	≥ 80 cm
Chinese		
Japanese		
Ethnic South and Central Americans	Use South Asian recommendations	
Sub-Saharan Africans	Use European recommendations	
Eastern Mediterranean and Middle East (Arab) populations		

Table 1: *WC guidelines for specific country/ethnic group (Adapted from International Diabetes Federation, 2006).*

Although significant research on AO and its associated metabolic concerns had been conducted throughout the years, few reviews have been done on the underlying causes. In this study, we conduct a systematic review on the causes of AO using publications indexed in PubMed from April 1, 2017, to March 31, 2022.

[3]https://www.nhs.uk/conditions/metabolic-syndrome/

[4]IDF Consensus Worldwide Definition of the Metabolic Syndrome.

[5]https://www.hsph.harvard.edu/obesity-prevention-source/obesity-definition/abdominal-obesity/

Methods

Search strategy: A literature search was undertaken on May 14, 2022; to locate studies from the recent 5 years from April 1, 2017, to March 31, 2022, examining the causes of AO. PubMed (https://pubmed.ncbi.nlm.nih.gov/) was one platform used to source for research articles. PubMed was searched using ("cause*[tiab]" AND "abdominal obesity[tiab]") as the search term[6].

Inclusion and exclusion criteria: The following exclusion criteria were applied: (A) articles with no access to the full text were removed; (B) articles that were not written in the English language were removed; (C) secondary research including systematic and narrative reviews, as well as meta-analyses, were excluded; (D) articles with no mentions of abdominal obesity; (E) articles that involve on-going research; (F) articles with no findings on the causes of abdominal obesity. Through the exclusion criteria, the articles remaining were included in this review.

Results and Discussion

Through the search term, a total of 199 works of literature were returned from PubMed (Figure 1). 185 literatures had full-text articles (Exclusion Criteria A); of which 178 were written in English Language (Exclusion Criteria B). Within the literature written in English, 138 articles consist of primary research (Exclusion Criteria C). Within the articles of primary research, 134 had mentioned "abdominal obesity" in the paper (Exclusion Criteria D); of which 133 articles had completed their research duration (Exclusion Criteria E). Within the articles that have completed the research duration, 46 articles had findings on the causes of abdominal obesity (Exclusion Criteria F), which were used in this review.

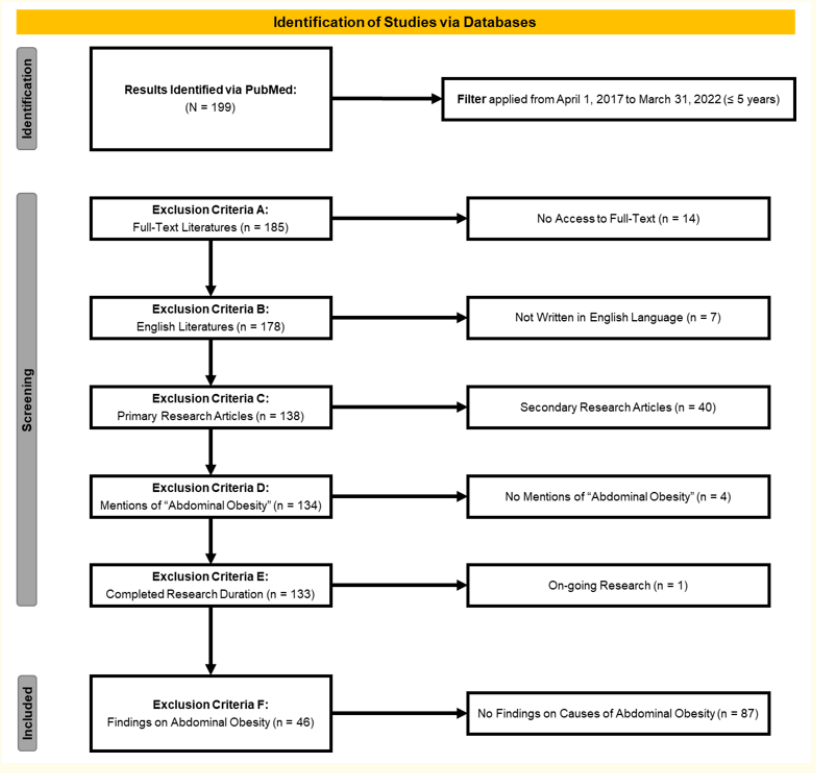

Figure 1: *Flow of process through the 6 exclusion criteria using PRISMA [11-13].*

[6]https://pubmed.ncbi.nlm.nih.gov/?term=cause*[tiab]+AND+"abdominal+obesity"[tiab]&filter=dates.2017/4/1-2022/3/31

Overall workflow and methodologies of causes of AO studies: The primary studies on the causes of AO that were obtained after filtering the literature using the exclusion criteria can be classified into 10 themes, which are listed in table 2. Age, gender, socioeconomic, and genetic/biological determinants top the charts with 32.6% of the studies. However, there are also substantial limitations found in table 3.

Theme	Number of Articles	Percentage of Theme
Age, Gender, Socioeconomic, and Genetic/Biological Determinants	15 [14-28]	32.6%
Nutritional Intake	13 [29-41]	28.3%
Lifestyle Habits	8 [36,38,39,42-46]	17.4%
Mental and Cognitive Disorders	5 [47-51]	10.9%
Smoking	3 [38,45,52]	6.5%
Gastrointestinal Microbiota	2 [53,54]	4.3%
Alcohol Consumption	2 [45,55]	4.3%
Rural Region	2 [24,56]	4.3%
Non-alcoholic Fatty Liver Disease (NAFLD)	2 [41,57]	4.3%
Noise Pollution	1 [58]	2.2%

Table 2: *Thematic classification of studies on the causes of AO.*

Causes	Limitations	Potential Solution(s)
Age, Gender, Socioeconomic, and Genetic/ Biological Determinants [15-17,21,25,27]	Small sample size, selection bias [15,25]	A longitudinal design and a larger sample size are suggested for future studies
	Reduced compliance is reflected in distrust and superstition among individuals living in rural settings [16]	Informing participants of the scope of the study, having transparency
	The study was based on predicted body composition; thus, the results might not be accurate [17]	Standardizing measurement procedures or using the gold standard of measurements such as DEXA
	Recall bias and message bias [21,27]	Choose an appropriate data collection method after the careful selection of research questions
Nutritional Intake [29,31,33]	The 24-hour recall method might not accurately represent the individuals' food consumption [29]	Standardizing measurement procedures to reduce measurement error
	Measurement errors due to the self-reported data [31]	
	Random error and an underestimation from using a single measurement of FFQ [33]	Take repeated measurements with a larger sample size
Lifestyle Habits [36,39,46]	Classified as a prospective cohort study [36,39]	Further studies particularly, randomized controlled trial studies would be needed
	Selection bias [46]	Consecutive sampling, but the lack of representativeness could occur

Mental and Cognitive Disorders [49-51]	Questions used to assess psychosocial factors are subjective and stress is a personal perception [49]	Further detailed and embedded mechanistic studies in large prospective studies could be conducted in different settings
	Data are derived from an observational longitudinal study and bias due to unmeasured confounding cannot be ruled out [50]	
	Parent Symptom Questionnaire of Conners may have a limited ability to accurately and systematically diagnose ADHD and other related problems [51]	In future research, a more comprehensive and careful scale of participants should be executed
Smoking [38,52]	As behavioral risk factors were self-reported, social desirability bias might occur [38]	Eluding response bias by ensuring anonymity, no leading questions, and the usage of neutrally worded questions
	Study subjects had a short duration of exposure compared with human usage [52]	Warrants further future research and analysis
Gastrointestinal Microbiota [53,54]	Weak instrument bias [53]	Performed sensitivity analyses, including a weighted median method and genetic risk score analysis
	Retrospective and cross-sectional at a single center, which might have resulted in selection bias [54]	Prospective cohort studies are needed to elucidate the relationship between obesity and small intestinal bacterial overgrowth
Alcohol Consumption [45]	Difficulties in obtaining relevant clinical information	More research is required to investigate the real-world implementation of age- and gender-specific intervention and education programs.
	Selection bias	
Rural Region [24]	Misclassification by respondent bias	Perform physical modes of assessments, ensuring that results are accurate
Non-alcoholic Fatty Liver Disease (NAFLD) [41]	Recall bias and measurement error in food intake assessment using the Food Frequency Questionnaire (FFQ)	Standardizing measurement procedures to reduce measurement error
Noise Pollution [58]	Confounding variables and immortal time biases	Multivariate analysis and time-dependent Cox proportional hazards model, and landmark analysis were performed
	Short follow-up period	Long-term and further analysis is needed in the future
	Noise exposure in residential areas was not considered	

Table 3: *Limitations in causes of AO studies and potential solutions for reducing limitations.*

Theme 1: Age, gender, socioeconomic, and genetic/biological determinants

Genetics, behavior, environmental and physical factors, medical care, and social factors are the five main determinants of health[7]. With increasing age, there are increased concerns about psychological and physiological changes. This is commonly referred to as a "midlife crisis," and it affects people between the ages of 40 and 60. Symptoms of midlife crisis vary from person to person, but one notable symptom would involve impulsive and indulgent behaviors[8]. Another explanation for the increase in body fat among the older population is the loss of muscle mass or muscle atrophy (sarcopenia). After the age of 30, the amount of body fat steadily increases, and older people would have nearly one-third more fat than when they were younger[9]. Adipose inflammation causes fat redistribution to the intraabdominal area and fatty infiltrations in skeletal muscles, which results in decreased overall strength and functionality [59]. Liu., *et al*. [17] examined age effect modification on the association between body composition and mortality and indicates that age was a key modifier, with younger participants of less than 60 years old exhibiting a positive correlation of predicted fat mass with mortality.

Several studies suggest that females have a higher prevalence of AO than men [14-16,23,25,26]. There are a few possible reasons. Firstly, being overweight is culturally and idealized in Sub-Saharan African countries as a sign of prosperity, good health, and desirable beauty standards among women [60]. In some cultures, women are not permitted to engage in strenuous physical activity and are encouraged to consume large amounts of food before marriage [16]. Secondly, a decrease in estrogen levels from menopause is associated with changes in body weight and fat distribution. Obesity is a chronic inflammatory state in which estrogen regulates body adiposity and fat distribution via ER alpha (ERα) and beta (ERβ) receptors [61]. Estrogen promotes subcutaneous fat accumulation, and estrogen loss during menopause is associated with an increase in central fat. Lastly, childbearing is associated with preferential accumulation of adipose tissue in the visceral compartment. Gunderson., *et al*. [62] suggest that childbearing is associated with a threefold increase in visceral fat deposition from preconception to postpartum when compared to those who do not bear children. However, Zhou., *et al*. [21] discovered that AO and family history of CVDs were positively associated with males but not with females. The disparities between males and females in age distribution, socioeconomic standing, and levels of education could be a factor in this phenomenon.

There is evidence suggesting that socioeconomic status (SES) is intimately tied to healthy aging [63]. Lower SES is related to greater adverse changes in physical capabilities, sensory function, physiological function, cognitive performance, emotional well-being, and social function [64]. It is probable that people of lower SES are unable to access basic healthcare needs and services; hence, increasing the risk of premature death [65]. For example, low SES households living in less affluent neighborhoods with less access to parks and amenities may not be able to pay for their children to participate in sports and recreational activities [66]. In addition, the lack of education is also a common occurrence among low SES. Being overweight and obese was found to be associated with a lack of education and lower SES [24]. However, Zhao., *et al*. [27] investigated the impact of health insurance on the risk of obesity in rural China and found that the BMI and WC of the female insured group were significantly higher than those of the uninsured group. This may suggest that the insured group had better access to higher calorie, carbohydrate, fat, and protein intakes than the uninsured group.

Begum., *et al*. [18] investigated the longitudinal link between C-section (Cesarean birth) and childhood obesity trajectories and discovered that children born via C-section had a higher risk of following accelerated trajectories for both BMI and WC. Furthermore, Chavarro.,

[7]https://www.cdc.gov/nchhstp/socialdeterminants/faq.html

[8]https://neurospatms.com/signs-you-are-experiencing-depression-vs-a-midlife-crisis/

[9]https://medlineplus.gov/ency/article/003998.htm

et al. [67] discovered that those who were born by C-section had an 11% increased risk of adult obesity and a 46% increased risk of developing type 2 diabetes. However, critics have argued that there are no associations between the different modes of delivery and obesity in young adulthood [68,69]. Instead, childhood obesity could be attributed to maternal pre-pregnancy weight status. A review by Heslehurst., *et al*. [70] found that maternal obesity raises the odds of childhood obesity by 264%, and maternal overweight by 89%. Mothers who were exposed to factors that contributed to their obesity development, as well as their children, were potentially exposed to these factors, which exacerbated in utero development and predisposition to obesity. Pitchika., *et al*. [28] discovered that the offspring of mothers with type 1 diabetes had significantly higher WC, BMI, fasting glucose, insulin, and C-peptide levels, as well as insulin resistance and AO later in life. Furthermore, exposure to polycyclic aromatic hydrocarbons was linked to an increased risk of AO, as evidenced by higher levels of monohydroxy-PAH biomarkers namely 2-hydroxynaphthalene, 2-hydroxyphenanthrene, and 2-hydroxyfluorene [22].

Theme 2: Nutritional intake

By adopting a healthy and balanced diet, one would be at a decreased risk of malnutrition and health complications. A healthy diet is defined as the inclusion of 5 different food groups into one's meal namely fruits, vegetables, grains, protein, and dairy. However, dietary guidelines and proportions of food groups may vary among different countries.

Milk is a nutrient-dense white liquid produced by the mammalian mammary glands. Cattles, buffaloes, goats, sheep, and camels are common sources of non-human milk. Milk contains 18 of the 22 essential nutrients [71], several bioactive peptides [72], and fatty acids [73]. Yasar., *et al*. [29] investigated the relationship between dairy consumption and AO in adolescents. The study suggests that a 1-unit increase in milk consumption resulted in a 1.98-, 0.11-, and 0.552-fold reduction in girls' WC, WHR, and BMI, respectively. This demonstrates that insufficient dairy consumption was associated with a rise in WC, which induces the development of AO.

Undernutrition or "malnutrition" in early life can be brought on by a myriad of situations, including poor diet, poor maternal health, socioeconomic level, and foreign conflict. Undernutrition contributed to 45% of mortality among children under the age of 5[10]. Chang., *et al*. [30] studied the effects of undernutrition in early life on overweight, obesity, and AO in those aged 54 to 56. The findings suggest that those born during famine years had a 1.4-fold increased risk of being overweight and a 1.6-fold increased risk of being obese at age of 54 to 56 compared to those born before the famine, suggesting that undernutrition in early life increases the risks of overweight and obesity.

Monosodium glutamate (MSG) is a substance derived from L-glutamic acid, a naturally occurring amino acid found in a variety of food [74] that is widely used as a flavor enhancer. The average daily intake of MSG is thought to be between 0.3 and 1.0g [75]. MSG has been the subject of discussion over its nutritional value and its long-term effects on health. MSG contributes significantly to body weight gain and MS, notably in areas such as higher inguinal and mesenteric fat mass [32,35]. This demonstrates that the consumption of MSG does pose a negative health risk and that it should be taken in moderation. As there is limited research available, more studies are needed to determine the long-term effects of MSG and the risk of AO.

Dieting has seen to become increasingly popular over the years, with people of all ages adhering to it for a multitude of reasons. Diets such as Mediterranean and Dietary Approaches to Stop Hypertension (DASH) has thought to be favorably associated with lowering the frequency of MS and the risk of all-cause and cardiovascular mortality [33,41]. However, some people continue to indulge themselves in negative eating behaviors. The growth in obesity has been associated with a diet high in fat, sugar [40], and processed food [34], and low

[10]https://www.who.int/news-room/fact-sheets/detail/malnutrition

in the consumption of fruits and vegetables [38]. A high inflammatory diet has been linked to a twofold increase in the risk of MS, hypertriglyceridemia, hypertension, and AO [31,37]. This suggests that diet and nutrition play an essential role in determining health outcomes.

Theme 3: Lifestyle habits

A sedentary lifestyle can be defined as a lifestyle with behaviors such as sitting or lying down and very little to no exercise involved. In recent years, the trend of sedentary behaviors has seen to be on a constant rise [76]. According to WHO[11], the top 10 causes of mortality and disability tend to involve physical inactivity, which is responsible for around 2 million premature deaths annually. A few factors suggest that age, gender, income, ethnicity, environment, and education level are related to the likelihood of sedentary behaviors [77,78]. Betancourt., *et al*. [43] investigated the frequency of metabolic components and their associations with sociodemographic variables and physical activity and discovered that AO was the only component that was negatively associated with physical activity (300 to 600 minutes per week). Mamani-Ortiz., *et al*. [38] examined the prevalence of CVDs' avoidable risk factors as well as their ties to socioeconomic and demographic parameters. The findings suggest that a combination of behavioral and socioeconomic risk factors increases the risk of obesity, waist risk or AO, and high blood pressure. This demonstrates that behavioral risk factors such as low physical activity levels increase the risk of AO, ultimately leading to an increase in MS and CVDs.

The increase in adiposity markers is most likely explained by societal and commercial impact, as well as an obesogenic environment [42]. Several factors namely technological advancements, built environment, inactive transportation, occupations, and social networks, have resulted in a decrease in the amount and duration of physical activity in daily life as well as an increase in sedentary activities [79]. The commercial success of the entertainment industry is solely dependent on its ability to hold people's attention for the longest amount of time [80]. Studies have indicated that television viewing for more than two hours per day is linked to a decline in academic success, prosocial behavior, fitness, and self-esteem, as well as an increased risk of obesity [81].

Studies have shown that exercise and strength training reduces weight gain and the associated risk factors for cardiovascular and metabolic disease [44,46]. WHO[12] recommends that adults should engage in 150 - 300 minutes of moderate-intensity exercise or 75 - 150 minutes of vigorous-intensity exercise per week, while children and adolescents should engage in at least 60 minutes of moderate-to-vigorous exercise daily. The adoption of regular exercise habits (> 30 minutes per day) has been widely associated with a decrease in AO and BMI [45]. In addition, health and wellness programs have been seen to be effective in reducing the risk of CVDs [39].

Theme 4: Mental and cognitive disorders

Mental disorders can be defined as a clinically significant disturbance in cognition, emotional regulation, and behavior that impairs areas of functioning, with an estimated one in every eight people worldwide suffers from a mental disorder[13]. Perceived social stigma around the topic of mental disorders, mental health has been a 'silent epidemic' as it poses a barrier for people in need of treatment. The prevalence of mental disorders has been increasing over time [82], and the current COVID-19 epidemic has largely contributed to this trend [83]. Common mental disorders are depression, anxiety, schizophrenia, eating, and bipolar disorder[14]. On the other hand, cognitive disorders are disorders that seriously compromise an individual's ability to think; such as dementia, developmental disorders, motor skill disorders, amnesia, and substance-induced cognitive impairment.

[11]https://www.who.int/news/item/04-04-2002-physical-inactivity-a-leading-cause-of-disease-and-disability-warns-who

[12]https://www.who.int/news-room/fact-sheets/detail/physical-activity

[13]https://www.who.int/news-room/fact-sheets/detail/mental-disorders

[14]https://ourworldindata.org/mental-health

Zavala., *et al*. [47] investigated the association between obesity and depression in the Mexican population and found that women's depression symptom severity was substantially correlated with higher BMI and WC; however, the correlations were weak and might not be clinically significant. Storch Jakobsen., *et al*. [48] investigated the associations between clinical and psychosocial factors and several separate cardiovascular risk factors in persons with schizophrenia and abdominal obesity. At two years of follow-up, negative symptoms were found to predict poorer cardiorespiratory fitness, larger WC, higher hemoglobin A1C, and lower high-density lipoprotein (HDL) levels. Santosa., *et al*. [49] investigated the association of a composite measure of psychosocial stress and the development of CVD events and mortality. The study finds that people who experienced high levels of stress were younger, more likely to be current or past smokers, and more likely to have AO. Similarly, Ploubidis., *et al*. [50] investigated the association between early-life mental health trajectories with biomarkers in midlife and premature mortality. The study finds that high levels of conduct issues and affective symptoms between the ages of 7 to 16 were linked to greater levels of fibrinogen and C-reactive protein, lower levels of HDL, and an elevated risk for AO 28 years later. ADHD is a neurodevelopmental disorder that is frequently identified and diagnosed in childhood and often persists into adulthood[15]. Wei., *et al*. [51] investigated the role of ADHD and abnormal eating and found that emotional overeating brought on by ADHD predicted higher WC when birth weight was lower. The efficacy of both ADHD and eating behavior should be considered when assessing risk for birth weight and childhood obesity-related outcomes. One possible explanation for how ADHD increases the tendency of emotional eating is the experience of feelings such as low social recognition, poor academic achievement, and high association with mood disorders and stress [84]. With the increase in eating behaviors and the lack of physical activity, individuals would be at a higher risk of being obese or overweight.

Theme 5: Smoking

Despite the array of negative health benefits, smoking or the use of tobacco has been indulged by millions of people worldwide. Commonly known health impact would consist of cancer, CVD, respiratory disease, diabetes, reproductive health, and overall health. Some of the less widely known negative impacts would include impaired neuropsychological function [85], newborns with oral clefts [86], and macular degeneration [87]. 8 million deaths are attributed to the tobacco pandemic worldwide, more than 7 million are due to direct contact, and 1.2 million deaths come from second-hand smoke[16]. Tobacco comes in a multitude of forms, including cigarettes, cigars, bidis, kreteks, smoking loose tobacco in a pipe or hookah, and chewed tobacco products such as snuff, dip, and snus[17]. Kikuchi., *et al*. [45] investigated the relative association of BMI and WC with an increased risk of MS by age and gender. The findings suggest that current smoking was associated with a 0.73 cm increase in WC and a 0.41 kg/m^2 increase in BMI. Mamani-Ortiz., *et al*. [38] investigated the prevalence of CVD-related preventable risk factors and the associated demographic and socioeconomic factors. The study suggests that smoking as a behavioral risk factor is one of the contributing causes of AO. Both studies have shown that tobacco smoking on top of other modifiable behavioral risk factors is attributable to the increased risk of AO.

E-cigarettes, also known as 'e-cigs,' are steadily gaining popularity as a result of modern society's developments, with the most common being among young adults aged 18 to 29 who have never engaged in smoking behaviors [88]. E-cigs are the electronic version of a cigarette that primarily consists of a battery, a heating element, and a liquid storage compartment. E-cigs, produce an aerosol by heating a liquid containing nicotine, flavorings, and other chemicals[18]. The smoke from e-cigs is potentially hazardous, containing nicotine, heavy

[15]https://www.cdc.gov/ncbddd/adhd/facts.html

[16]https://www.who.int/news-room/fact-sheets/detail/tobacco

[17]https://nida.nih.gov/publications/drugfacts/cigarettes-other-tobacco-products

[18]https://www.cdc.gov/tobacco/basic_information/e-cigarettes/about-e-cigarettes.html

metals like lead, volatile organic compounds, and cancer-causing elements despite a common misperception that they contain fewer dangerous chemicals than smoke from traditional tobacco cigarettes[19]. Chen., *et al*. [52] conducted an animal study using mice to investigate how e-vapor affects metabolic profiles. E-vapor exposure decreased fat mass in mice fed a high-fat diet or chow, but it had a variable effect on their lipid profiles depending on their diet. A balanced diet had increases in lipid levels in both blood and liver, whereas a diet rich in lipid and simple carbohydrates reduced triglycerides but increased non-esterified fatty acid levels in the blood. Due to the limited amount of research conducted on e-cigs and their risk of AO, it is right to conclude that e-cigs do influence AO but warrant more research in that area with human subjects.

Theme 6: Gastrointestinal microbiota

Gastrointestinal microbiota or gut microbiota (GM) is defined as microorganisms that live in the gastrointestinal tract. They are key aspects of human health that consist of strengthening gut integrity or shaping the intestinal epithelium, providing energy, protecting against pathogens, and regulating host immunity [89]. Small intestinal bacterial overgrowth (SIBO) is characterized by an overabundance of bacteria in the small intestine which remains a poorly understood condition. SIBO is defined as a bacterial population in the small intestine exceeding 10^5 - 10^6 organisms/mL. The upper small intestine normally contains less than 10^3 organisms/mL, most of which are Gram-positive [90]. Some young children and older persons with nonspecific gastrointestinal problems have SIBO. SIBO should be considered one of the causes of abdominal pain in children [91]. Quantitative culture of an aspirate of luminal fluid has been the gold standard for diagnosing bacterial overgrowth; the threshold for a positive culture is more than 10^6 organisms/mL in either aerobic or anaerobic conditions. Positive jejunal cultures (> 10^6 organisms/mL) are indicative of clinically substantial bacterial overgrowth in the upper small intestine in individuals with chronic diarrhea. Various breath tests namely [14C]glycocholate and [14C]xylose have been proposed as non-invasive tests for SIBO [92]. *Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Fusobacteria*, and *Verrucomicrobia* are the dominant phyla of gut bacteria, with *Firmicutes* and *Bacteroidetes* accounting for 90% of the GM [93].

Xu., *et al*. [53] investigated the causal relationship between specific GM and AO and found that *Lachnospiraceae, Bifidobacterium*, and *Prausnitzii* may have causal associations with AO. The primary butyrate producers in the human gut are the *Prausnitzii* and members of the *Lachnospiraceae* family. The amount of butyrate an individual produce in the gut is determined by diet through the addition of fiber to a low-fiber diet and GM [94]. Butyrate has been demonstrated to raise plasma levels of glucagon-like peptide-1 and gastric inhibitory peptide, which increases insulin levels, prevents stomach emptying, and heightens feelings of satiety [95]. An unhealthy GM, on the other hand, can increase inflammatory markers, which leads to weight gain and metabolic diseases [96]. In another study, Jung., *et al*. [54] investigated the association between obesity and SIBO in non-constipation irritable bowel syndrome patients and found that subjects without SIBO showed significantly higher levels of BMI and WC as compared to subjects with SIBO.

Theme 7: Alcohol consumption

The trend of alcohol intake can be seen growing over the years and would continue to rise in the future [97]. Alcohol has been linked to an array of negative short- and long-term health consequences. To name a few, short-term risks from binge drinking would include immediate effects namely physical injuries [98], risky behaviors [99], and alcohol poisoning [100]; whereas long-term effects could lead to the development of chronic diseases namely cardiovascular heart diseases [101], cancer [102], and cognitive impairments [103]. Åberg., *et al*. [55] investigated the association between alcohol and metabolic disorders in chronic liver disease patients, and suggests an increase

[19]https://www.cancerresearchuk.org/about-cancer/causes-of-cancer/smoking-and-cancer/whats-in-a-cigarette-0

in concomitant MS (waist circumference or WC, serum triglyceride, HDL cholesterol, hyperglycemia, and elevated blood pressure) for the group of risk and moderate drinkers over the course of 10 years. Kikuchi., *et al*. [45] investigated the relative association of BMI and AC with an increased risk of MS by age and gender, and suggests that alcohol is a contributing factor to an increase in WC among different drinking habits. Probable causes of the increase in WC include alcohol's impact on the body's ability to burn fat, high-calorie content, and an increase in hunger that leads to poor dietary choices. Firstly, alcohol impairs the body's ability to burn fat because ethanol alters the composition of fat by interfering with ethanol metabolism in adipose tissues [104], which may result in increased WC. Secondly, alcohol is a caloric dense with an estimated 29 kJ or 7.11 kcal per gram. Hence, current and lifetime alcohol consumption were positively associated with overall and central obesity, in both women and men [105]. Thirdly, an increase in hunger might be due to the activation of neurons namely Agouti-related peptide (AgRP) which can be found in the hypothalamus [106]. This potentially leads to an increase in poor food choices such as fast food. Fast foods are easily accessible as most chains are open 24 hours a day and could provide one with a quick alternative if they are craving some on-the-go meal. However, there are also purported benefits of alcohol drinking. Low to moderate drinking has been shown to help improve psychological well-being [107], cognitive functioning [108], CVDs [109], and mortality rates [110]. Alcohol consumption of 1-150 g/week was found to have a lower risk of CVDs, cancer, and mortality when compared to non-drinkers and heavy drinkers [111].

Theme 8: Rural regions

A rural area is an open swath of land with few homes or other buildings, with a low population density. On the other hand, urban regions or "metropolitan areas" are more developed and heavily populated. In these areas, there is a high density of human-made structures, including residences, office buildings, roads, bridges, and railways. Ma., *et al*. [42] examined the secular trends in the prevalence of overweight, obesity, and AO among Chinese adults at the national level from 1993 to 2015; and found an increase in WC risk for persons living in rural regions compared to urban regions. Additionally, Brenner., *et al*. [24] discovered that both rural men and women had higher probabilities of having a WC in the heightened risk category. It has been suggested that the prevalence of a higher risk of WC in people living in rural regions might be due to a series of reasons such as a lack of healthy eating knowledge, fewer means to adopt healthy diets and lifestyles, limited access to weight management programs, and a decreased in physical activity levels [112]. Contrary to the belief that people who live in rural regions have a healthier body composition compared to their counterparts as they often engage in labor such as farming or manual work, studies have proven otherwise. Pickett., *et al*. [112] found that a large proportion of farmers who engage in mechanized farm work were overweight or obese. Mechanized farm work typically involves the use of agricultural machinery such as tractors, trucks, and combine harvesters which provides various benefits such as an increase in work productivity, improvement in labor shortages, and an increase in economic returns[20]. As such machinery is being utilized, there would be a decrease in physical activity levels; thus, accounting for the increased risk of being overweight or obese.

Theme 9: Non-alcoholic fatty liver disease (NAFLD)

NAFLD is a silent liver disease characterized as a series of liver conditions affecting persons who consume little or no alcohol. As the name implies, the etiology is an accumulation of fat cells in the liver[21]. The global prevalence of NAFLD is on the rise [113], mostly affecting people in the Middle East and South America [114]. NAFLD develops in four main stages differing in severity levels: (a) simple fatty liver (steatosis), (b) non-alcoholic steatohepatitis (NASH), (c) fibrosis, and (d) cirrhosis[22]. Some risk factors of NAFLD would include age,

[20]https://www.fao.org/sustainability/news/detail/en/c/460221/

[21]https://www.nhs.uk/conditions/non-alcoholic-fatty-liver-disease/

[22]https://www.nhs.uk/conditions/non-alcoholic-fatty-liver-disease/

gender, ethnicity and genetics, diabetes mellitus, overweight/obesity, central obesity, and MS [115]. NAFLD is a common disease among children with a likely prevalence rate of between 5% and 10% in the general population [116]. NAFLD is seen to be especially prevalent among children and adolescents aged 10 to 19 years, affecting more boys than girls. Among the different races/ethnicity, the Asian and Hispanic groups have a higher prevalence compared to their counterparts [117]. Song., *et al*. [57] examined prevalence and correlates of suspected NAFLD in Chinese children at the national level, with findings suggesting that 9.03% (75 out of 831) of Chinese children had suspected NAFLD. Childhood suspected NAFLD was associated with overweight and obesity, AO, hyperuricemia (uric acid > 327 mol/L), and elevated total cholesterol. In another study, Clemente., *et al*. [118] investigated the relationship between the degree of WC and NAFLD in obese adolescents. The findings suggest that 72.4% of girls and 71.9% of boys with NAFLD, were classified in the highest quartile of WC (WC > 107.5 cm). Among obese teenagers, a rise in WC can accurately predict the risk of NAFLD, and WC measurement is a low-cost technique that could aid in identifying those who may have NAFLD.

Theme 10: Noise pollution

Any unwanted or disturbing sound that has an impact on the health and well-being of people and other organisms is referred to as noise pollution. Sound can be measured using a decibel meter, with its units in decibels (dB). As a general guideline, a whisper is approximately 30 dB, a typical conversation is approximately 60 dB, and a running motorcycle engine is approximately 95 dB. Long-term noise exposure more than 70 dB can compromise hearing, while sudden loud noise of more than 120 dB can injure the ears[23]. There are 2 main categories of noise, namely from natural and artificial sources. Examples of natural sources of noise can include sounds from natural disasters, flowing water bodies, and animal sounds ranging up to 140 dB, whereas artificial sources would include sounds created by manmade activities such as construction work, transportation, industries, and machinery ranging from 30 to 140 dB[24].

Occupational noise (ON) is referred to as noise-exposed in workplaces. High levels of ON could potentially lead to noise-induced hearing loss (NIHL). Exposure to workplace noise for more than 10 years increased the odds of having any hearing loss and moderate-to-severe hearing loss in older adults [119]. In addition to NIHL, other health concerns, such as MS, might be associated with ON. Kim., *et al*. [58] investigated the relationship between ON and MS and discovered a negative relationship between these two variables. However, no statistical significance was found for the component of abdominal obesity. Similarly, to ON, traffic noise (TN) can be referred to as the unwanted sound created by motor vehicles. TN is especially common in cities where motor vehicles are extensively used as a means of transportation and delivery. Pyko., *et al*. [120] investigated the associations between exposure to noise from road traffic, railways, and aircraft and the development of obesity markers. The findings suggested that road TN was significantly associated with WC with a 0.21 cm increase per 5 dB. The combination of exposure to various sources of TN may pose an elevated WC risk. Other studies [121,122] that delve deeper into the research on the relationship between noise pollution and WC, with results indicating a correlation between both factors.

A possible explanation for the increase in WC with the mitigating factor of noise pollution would be the increase in stress levels [123]. Prolonged or repeated periods of exposure to everyday noise found in table 3. would potentially cause an increase in stress hormone levels leading to autonomic imbalance, oxidative stress, inflammation, and endothelial dysfunction, which accelerates the development of cerebrocardiovascular risk factors and disease [124]. In response to stress, individuals tend to engage in maladaptive coping mechanisms such as an increase in eating behaviors [125].

[23]https://www.cdc.gov/nceh/hearing_loss/what_noises_cause_hearing_loss.html

[24]https://www.medicinenet.com/what_is_noise_or_what_is_noise_pollution/article.htm

Principal findings of this review

Through this review, it can be determined that the most heavily weighted theme would be age, gender, socioeconomic, and genetic/ biological determinants (32.6%). It is believed that determinants of health are the fundamental attributes of establishing health equity. Amongst the different health determinants, the only modifiable component that would increase or decrease the risk of AO would be socioeconomic factors namely income, wealth, and education. As such, nutritional intake (28.3%) is also another heavily weighted theme in this review. It has been demonstrated that the lack of dairy products such as milk and undernutrition in the early years would increase the risk of AO. However, the consumption of MSG and the association between AO might need to be investigated and studied further. Lastly, lifestyle habits (17.4%) are also another heavily weighted theme in this review. It has been shown that physical inactivity would lead to an increased risk of MS and AO. However, there are substantial constraints found among the studies as listed in table 3, with the most critical being biasness in the participant's responses and the mode of selection. In addition, there was a lack of standardizing protocols and procedures which could have led to measurement inaccuracies. The WC guidelines would be evaluated differently since the studies were conducted in different regions with diverse groups of people.

Main strengths and weaknesses of this review

There are a few strengths and weaknesses found in this review. Firstly, this review adopted pre-specified eligibility criteria and a systematic search strategy using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [11-13]. We also included a thematic classification and weightage of the individual themes, which allowed us to determine which theme was the most significant. Another strength that this review had was the inclusion of limitations and potential suggestions for the individual themes. This approach could help future researchers understand the common gaps identified in previous studies, allowing them to direct their research in a different direction. The main limitation of this review would be the limited usage of databases as sources for studies. PubMed was the only scientific database used; thus, might not have sufficient coverage for this systematic review [126-128]. In addition, another limitation of this study would be the variation in the age of the study participants. It was difficult to determine which age group is most susceptible to the risk of AO since the studies were performed among various age groups.

Conclusion

46 out of 199 (23%) articles were reviewed on the causes of AO, revealing 10 themes of causes, namely, (a) age, gender, socioeconomic, and genetic / biological determinants, (b) nutritional intake, (c) lifestyle habits, (d) mental and cognitive disorders, (e) smoking, (f) gastrointestinal microbiota, (g) alcohol consumption, (h) rural regions, (i) non-alcoholic fatty liver disease, and (j) noise pollution.

Supplementary Materials

Data files for this study can be downloaded at https://bit.ly/AO_SSR.

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