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The Association of Foot Hygiene Level with Tinea Pedis Incidence in Military Personnel

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Abstract
Tinea pedis is a condition of fungal infection of the skin on the bottom of the feet which causes disruption to the integrity of the skin in that area. Tinea pedis usually appears in damp environmental conditions, long-term wearing of closed shoes, and poor hygiene. TNI has a potentially high risk of Tinea pedis infection. This study aims to provide an overview members of the Indonesian National Army (TNI) who have a high potential risk of Tinea pedis infection. The study adopts a descriptive analysis employing a cross-sectional design. The research is focused on the military personnel of the Raider Infantry Battalion 328 Kostrad Cilodong. The sample size for this study was determined to be 70 individuals using the Slovin formula. Data collection involved the use of questionnaires and foot skin scrapings. The analysis was conducted using the Chi-square test. The data collection process took place in December 2023. The results showed most soldiers of Infantry Battalion 328 Kostrad Cilodong demonstrate good foot hygiene practices and Tinea Pedis was identified in those 24 soldiers. There was a significant relationship between maintaining foot hygiene and the incidence of Tinea pedis (p=0.026; OR 2.178), despite maintaining good foot hygiene, certain soldiers were still developed by Tinea pedis. Conclusion: The level of personal foot hygiene, in conjunction with extended use of occlusive footwear, predispose individuals—particularly military personnel—to excessive moisture, interdigital occlusion, maceration, and overgrowth of bacterial flora. These changes in the microenvironment of the feet significantly elevate the risk of Tinea pedis infection.

Keywords: Foot Hygiene, Tinea Pedis, Military Personnel

1. Introduction

The skin, as the outermost anatomical element of the human body, serves as the primary organ with an approximate mass of 5 kilograms and a surface area of about two square meters (Gitleman, 2014). The epidermis also functions as a protective shield, playing an essential role in mitigating disturbances and threats that may penetrate through the skin barrier (Indri M. Riwu Djata et al., 2022). Skin health is influenced by the surrounding environmental conditions. In addition to environmental factors, the implementation of clean and healthy lifestyle behaviors

(PHBS) can also act as a potential trigger for the emergence of skin health problems (Indri M. Riwu Djata et al., 2022).

Indonesia, being a tropical country with a hot and humid climate, presents an environment that—when coupled with poor personal hygiene—can increase the risk of fungal skin infections (Hidayat, 2018). Tinea pedis, commonly known as athlete's foot, is a fungal infection of the skin on the lower foot, compromising the integrity of the skin in that area (Yunia Tasya Wanda, 2022). Generally, Tinea pedis most commonly presents between the fourth and fifth toes, and may spread to the undersides of the toes and other interdigital spaces. It is often characterized by maceration, appearing as fragile, white skin (Gitleman, 2014).

Many workers in Indonesia tend to wear closed footwear for extended periods, often accompanied by a lack of proper foot hygiene (Harlim et al., 2023). One notable example includes members of the Indonesian National Armed Forces (TNI), who are at high risk of developing Tinea pedis due to their involvement in activities that require tight footwear and socks worn for long durations. This is supported by findings from a study conducted on Mobile Brigade Corps (Brimob) personnel in Makassar, where Tinea pedis was detected in 24.35% of the participants (Hadi, 2020).

Based on these facts, the researcher intends to conduct a study to examine the correlation between the level of personal hygiene and the incidence of Tinea pedis among TNI soldiers in the Infantry Battalion Para Raider 328 Kostrad, located in Cilodong. This study is based on the observation that their training routines involve prolonged use of occlusive footwear and exposure to damp field conditions, which collectively contribute to increased vulnerability to health issues, including skin infections.

2. Methods

2.1. Subject Characteristics

This study was conducted on 70 TNI Soldiers of Batalyon Infantri Para Raider 328 Kostrad Cilodong, determined by measuring the Slovin formula to ensure adequate representation of the target population. The participants were categorized by established scoring system (questionnaire) based on the level of personal foot hygiene into good and poor groups, and categorized based on the incidence of Tinea Pedis among soldiers of Batalyon Infantri Para Raider 328 Kostrad Cilodong. Skin scrapings were collected from the toe web spaces and plantar surfaces of the soldiers' feet as part of the data collection process. The specimens were subjected to direct microscopic analysis using 10% potassium hydroxide to identify fungal pathogens associated with *Tinea pedis*. The demographic characteristics of the research respondents can be seen in Table 1.

Table 1: Characteristics of Research Respondents

No.	Characteristics	N	%
1.	**Level of Foot Personal Hygiene**		
	Good	32	45,7
	Poor	38	54,3
	Total	70	100,0
2.	**Incidence of Tinea Pedis**		
	Present	24	34,3
	Absent	46	65,7
	Total	70	100,0

Based on Table 1 above, it is known based on the level of foot personal hygiene, the majority of respondents exhibited 54.3% (38 respondents) demonstrated poor foot hygiene maintenance, whereas only 45.7% (32 respondents) maintained adequate hygiene levels. Based on the incidence of Tinea Pedis, Tinea pedis was absent in 46 respondents (65.7%) and present in 24 respondents (34.3%).

2.2. Validity Test

This study assessed the content validity of an eight-item questionnaire administered to a sample of 70 respondents. Several items were adapted from previously validated questionnaires with slight modifications. Item validity was evaluated using Pearson correlation, while reliability was measured using Cronbach's Alpha in SPSS version 27, as shown in Table 2.

Table 2: Questionnaire Validity Analysis Results

The Questionnare	r-value	r-table	Remarks
P1	0,499	0,2352	Valid
P2	0,410	0,2352	Valid
P3	0,767	0,2352	Valid
P4	0,499	0,2352	Valid
P5	0,299	0,2352	Valid
P6	0,366	0,2352	Valid
P7	0,377	0,2352	Valid
P8	0,505	0,2352	Valid

Table 2 shows the analysis revealed that all items related to housing density demonstrated significant correlations ($p = 0.001$; $p < 0.05$). Given a critical r-value of 0.2352 ($n = 70$; $\alpha = 0.05$), all items had correlation coefficients exceeding this threshold. With a sample size of 70 and two variables, the critical r-value at the 5% significance level was 0.2352. An item was deemed valid if its Pearson correlation coefficient (r-calculated) was greater than the critical r-value.

2.3. Reliability Test

The results of the reliability test for this questionnaire can be seen in Table 3 below.

Table 3: Questionnaire Reliability Analysis

Number of Questions	Cronbach's alpha	Remarks
10	0,759	Reliabel

Table 3 shows the reliability test of the foot hygiene maintenance questionnaire resulted in a Cronbach's Alpha value of 0.759, exceeding the acceptable threshold of 0.60. Therefore, the instrument indicates acceptable internal consistency and is thus considered reliable for use in this study.

These findings suggest that the instrument is both valid and reliable for use in the current research context.

2.4. Pearson Correlation Test

This analysis aimed to assess the association between personal hygiene practices and the incidence of Tinea Pedis among Indonesian Army personnel. The outcomes are displayed in the Table 4 below.

Table 4: Correlation Between Foot Hygiene and The Incidence of Tinea Pedis

		Incidence of Tinea Pedis						p *chi-square*	OR (95% CI)
		Present		Absent		Total			
		n	%	n	%	n	%		
Personal Foot Hygiene	Good	14	43,8	18	56,2	32	100,0	0,026	2,178 (0,798-5,947)
	Poor	10	26,3	28	73,7	38	100,0		
	Total	**24**	**34,3**	**46**	**65,7**	**70**	**100,0**		

Table 4 revealed that 14 respondents (43.8%) with good foot hygiene did not develop Tinea pedis, whereas 10 respondents (26.3%) with poor foot hygiene were diagnosed with the condition. Statistical analysis demonstrated a significant association between foot hygiene practices and the incidence of Tinea pedis (p = 0.026; OR = 2.178; 95% CI: 0.798–5.947).

3. Result and Discussion

The primary purpose of the skin is to ensure the survival of the individual. Structurally, Skin was composed of two primary layers—the epidermis and the dermis—the skin plays a central role in protecting the body and maintaining homeostasis. Additionally, the skin includes a subcutaneous layer located beneath the dermis, although it is not considered an integral part of the skin's structure (G. J. Tortora and B. Derrickson, 2017). It has five separate layers: the basal layer, the stratum spinosum (sweat layer), the stratum granulosum, and the stratum corneum (Roy et al., 2018).

Fungal infections of the skin, particularly those affecting the feet—commonly referred to as *Tinea pedis*—tend to have a high prevalence in tropical climates and among individuals who regularly wear closed footwear and pay limited attention to foot hygiene, such as farmers, laundry workers, and military personnel. *Tinea pedis* typically presents around the ankles, between the toes, or on the soles of the feet (Yunia, 2022). According to Zebua (2023), the two most clinically significant variants of this fungal infection are the interdigital and moccasin types (Zebua, 2023). The interdigital type is characterized by macerated, erythematous lesions between the toes, often accompanied by itching, which may lead to secondary complications such as onychomycosis. In contrast, the moccasin variant involves widespread scaling and erythema across the entire plantar surface of the foot (Amalia, 2020).

This study was conducted to determine the effectiveness of using moisturizers with saccharide isomerate content on skin hydration. The moisturizer in this research treatment was given for 7 days and then measured for the difference in skin hydration before and after treatment. A skin hydration examination was carried out using a precision digital skin analyzer.

The study findings revealed that the majority of respondents, including 73.3%, were 19 years old. Additionally, 20.0% of the respondents were 20 years old, while 6.7% were 18 years old. Multiple studies have documented that these skin biophysical characteristics exhibit variations based on age, gender, anatomical area, and season within diverse ethnic communities. The inflection point of this curve becomes apparent at the age of thirty, indicating a more uniform and luminous complexion, enhanced hydration, and a reduced pH level. The skin serves as the primary protective layer, rendering it susceptible to the harmful effects of sunlight, air pollution, and climatic variations. These environmental variables expedite the manifestation of aging in the skin, particularly photoaging induced by ultraviolet (UV) radiation. The advancement of technology has led to the availability of numerous non-invasive instruments for assessing the physiological characteristics of the skin. The commonly utilized parameters include the hydration level of the outermost layer of the skin (stratum corneum), the amount of water lost through the skin (transdermal water loss), the content of sebum (an oily substance produced by the skin), the level of melanin (a pigment responsible for skin color), the level of erythema (redness of the skin), the color system of the skin, and the pH value of the skin surface. Research (Pan et al., 2020) indicates that the cheeks exhibit the highest level of brightness and lightness, with the lowest concentration of sebum. In contrast, the chin has a significantly deeper shade, while the forehead tends to have a yellowish hue. The skin parameters of TEWL, sebum content, and melanin and erythema indices have a direct correlation with age, displaying a linear relationship. On the other hand, the skin hydration value, ITA, and pH demonstrate a non-monotonic relationship with age. Conversely, as age increases, the expression of aquaporin decreases. Aquaporins, also known as AQPs, are a group of water channels that facilitate the movement of water and tiny molecules to maintain fluid balance in the body. Aquaporins (AQPs) are found in a wide range of species, such as bacteria and humans. Thirteen members of the AQP family have been discovered in humans (AQP0-12), and they are found in different organs. Recently, it has been acknowledged that deviations in the levels of AQPs expression can lead to a range of illnesses (Pan et al., 2020; Ikarashi et al., 2017). In this study, the study population and sample were young adults with a small age gap. This can minimize the occurrence of bias and control the age variable as a confounding variable.

The study findings indicated that the majority of respondents were male, specifically 9 respondents (60.0%), whereas 6 respondents were female (40.0%). The variation in population size can be attributed to the factors of hydration, transepidermal water loss, sebum production, microcirculation, pigmentation, and skin thickness. These factors tend to be higher in men, whereas women generally have higher skin pH levels. Understanding the disparities in skin characteristics associated with gender can aid in the strategic design and creation of gender-specific goods, enabling more tailored dermatological treatments and cosmetic interventions. Sex-related disparities exist in the anatomical, physiological, epidemiological, and symptomatic aspects of certain diseases. Regarding skin illnesses, there is a higher incidence of infectious diseases in men, whereas psychological issues, pigmentation abnormalities, specific hair conditions, and autoimmune and allergy diseases are more commonly observed in women. Conversely, women experience a higher prevalence of sex-related skin illnesses, and the occurrence and outcome of some skin cancers are linked to sex-related disparities. The precise mechanisms responsible for the disparities in skin diseases between sexes remain mostly unidentified. These variances may be influenced by sex hormones, behavioral characteristics, ethnicity, and environmental variations (Rahrovan et al., 2018). Circulating hormones have a significant impact on the disparities between male and female facial skin. Oestrogen mostly affects the skin of women, while androgens, such as testosterone and 5α-dihydrotestosterone (DHT), primarily influence the skin of men. Oestrogen has advantageous protective effects on the skin by promoting the synthesis of collagen and the creation of elastic fibers and hyaluronic acid. Oestrogen has been demonstrated to enhance the skin's ability to bind water and regulate local inflammation, granulation, and re-epithelialization processes. As a result, it improves the integrity of the skin barrier and enhances its capacity to heal wounds. Testosterone increases the thickness of the tissue that surrounds the dermal and epidermal layers of the skin, which helps in the creation of collagen. While both males and females generate sebum, the elevated amounts of testosterone in males lead to a more substantial production, resulting in generally consistent sebum production levels as they grow older. Both positive and negative effects are on men's skin. Heightened sebum production aids in the assimilation of oils for skin hydration, but it also exacerbates acne and imparts a sticky or oily sensation to the skin while causing the pores to appear enlarged and more prominent (Sikora et al., 2021; Wang et al., 2017).

The results showed the average skin hydration levels of the right upper arm before treatment was 38.67 ± 6.53% and after treatment was 42.93 ± 11.67%, the left arm before treatment was 37.93 ± 7.32% and after treatment 39.93 ± 12.64%, the right lower limb before treatment was 23.67 ± 10.53% and after treatment 35.73 ± 15.20%, and the left lower limb before treatment was 22.87 ± 10.82% and after treatment was 33.33 ± 16.11%. The results of this study show that the right and left lower limbs have the greatest difference in mean skin hydration before and after treatment, namely 12.07 ± 14.87% and 10.47 ± 18.58%, respectively. The results of this study are in accordance with research (Dewi & Pangkahila, 2022), which shows the mean skin hydration before and after treatment of the upper arm 28.47±4.80 to 71.30±10.79; the forearm 26.63±2.68 to 63.93±9.24; the upper limb 24.20±5.72 to 60.60±14.71; and the lower limb 22.00±2.13 to 41.57±6.95%, respectively (Dewi & Pangkahila, 2022).

The results of this study showed that there was a significant difference in the mean skin hydration of the right lower limb and left lower limb before and after treatment (p values = 0.007 and 0.047), but the level of skin hydration of the right and left upper arms before and after treatment did not have a significant difference. The results of this study are in accordance with research (Vlorensia et al., 2020), which shows that moisturizing creams containing saccharide isomerate and ceramide effectively increase skin hydration. The average skin hydration after treatment was 24.46%, with a standard deviation of 3.83 (Vlorensia et al., 2020). The results of this study are in accordance with research (Gougeon et al., 2023) that showed that, compared to the control area, the application of creams, but especially creams containing saccharide isomerate, significantly improved the hydration and glossy properties of the skin on average after 30 minutes. This significant increase ranged from 1.7-fold in the placebo group to 4.6-fold in the cream containing urea (Gougeon et al., 2023). The results of this study are in accordance with research (Dewi & Pangkahila, 2022) showing that using a moisturizer containing saccharide isomerate led to a significant improvement in skin hydration within a 2-week period ($p<0.05$). Following the discontinuation of the moisturizer, all four sites exhibited notable variations in skin moisture ($p<0.05$). The study findings indicate that incorporating SI 5% into the moisturizer formulation leads to a significant increase in skin hydration. Furthermore, this enhanced hydration is sustained even after discontinuing the use of the moisturizer, surpassing the effects of standard moisturizers (Dewi & Pangkahila, 2022).

Saccharide isomerate is a naturally occurring, biologically active, and environmentally friendly sugar isomerization agent. This product is created by transforming the sugars found in the edible part of maize, which are primarily glucose, into a distinct combination of carbohydrates that closely resemble the skin. These carbohydrates are similar to the natural moisturizing substances present in the outermost layer of human skin, known as the stratum corneum. Saccharide isomerate is a fully plant-derived compound consisting of complex carbohydrates that closely resemble those naturally present in human skin. This vegan hyaluronic acid booster has demonstrated its capacity to deliver sustained skin hydration by effectively adhering to the skin and limiting the loss of water via the epidermis. Clinical evidence supports the efficacy of saccharide isomerate 1% in delivering both immediate and prolonged hydration. It has the ability to attract and retain water and has previously demonstrated positive effects on the skin's protective barrier, moisture levels, and the microorganisms present on the skin (Martin et al., 2023; Hon et al., 2018). Saccharide isomerate has humectant properties that improve skin hydration (Peltier et al., 2022).

Reduced humidity (reduced water content in the outermost layer of the skin) leads to a decrease in the breakdown of desmosomes. The desmosomes present in the SK sheet undergo digestion, resulting in the separation of the sheet into individual cells when placed in a buffer solution. On the other hand, protease inhibitors added to the buffer solution or heating the sheet stops the desmosomes from breaking down and cells from separating. Leupeptin, or chymostatin, exhibited a cell dissociation slowdown that was only around half as efficient as aprotinin. But when the two substances were mixed together, they stopped the breakdown of the stratum corneum layer just as well as aprotinin did alone. he results support the idea that desmosomes are very important for SK cells to stick together, and that these two types of serine proteases break down desmosomes, which leads to SK desquamation. A decline in trypsin-type protease activity associated with aging was seen in individuals without any health conditions. The amount of moisture in the stratum corneum affects the proteases' ability to break down desmosomes there. According to studies, there are two factors that affect desquamation. The water content of the stratum corneum is one factor to consider. Insufficient water levels impede the optimal functioning of enzymes, regardless of their normal enzyme content. Humectant therapy effectively hydrates the stratum corneum by providing it with water. Another contributing element is a reduction in the enzymatic activity of the protease. This phenomenon is observable in skin that is afflicted with illness or undergoing the natural process of aging (Koyama et al., 1999).

Saccaride isomerate (SI) is a complex carbohydrate mucopolysaccharide (glycan) that closely resembles the one present in the outermost layer of human skin, known as the stratum corneum. Therefore, hyaluronan, or hyaluronic acid, will be produced in the epidermis. In the same way that hyaluronan does, SI can raise the water content of the stratum corneum, which keeps the epidermis moist even when the humidity level is low. SI has the ability to adhere to the skin even in extremely acidic environments (Dewi & Pangkahila, 2022).

The difference in significance between hands and feet may be attributed to differences in anatomical location and exposure to environments that can compromise skin hydration. Research (Mayrovitz et al., 2017) skin hydration, as measured by the tissue dielectric constant (TDC) tool, resulted in values in the forearm proving to be greater than in the leg or foot. In the forearm, there was a monotonous decrease in TDC values ($P < 0.001$) as depth increased, with TDC values at 0.5 mm being 38.4 ± 5.5 and 25.8 ± 4.1 at 5.0 mm depth. At the foot site, a similar decrease in TDC values was observed from 0.5 mm to 2.5 mm ($P < 0.001$), but the values at 2.5 and 5.0 mm (34.1 ± 6.3 vs. 33.0 ± 12.1) were not significantly different from each other (Mayrovitz et al., 2017).

4. Conclusions

This study demonstrates that the application of a moisturizer containing saccharide isomerate leads to a substantial enhancement in skin hydration among students enrolled in the Faculty of Medicine and Health Sciences at the Republic of Indonesia Defense University. The findings demonstrated a notable disparity in the average skin moisture levels between the right and left lower limbs following the intervention, therefore confirming the efficacy of the moisturizer in augmenting the water content of the outermost layer of the skin, known as the stratum corneum. Furthermore, the research also discovered that incorporating saccharide isomerate into the moisturizer formulation can significantly enhance skin moisture and sustain it even after the cessation of usage, surpassing the effects of conventional moisturizers. This demonstrates the efficacy of including saccharide isomerate in moisturizer formulations to greatly enhance skin hydration. This can be advantageous in addressing dry skin and prolonging skin moisture retention.

Given the results of this study, it is advisable to extend the observation period to a longer duration beyond the current 7-day timeframe in order to further investigate the topic. Extending the study term is anticipated to yield a more comprehensive understanding of the dynamics or alterations that may transpire over an extended timeframe. To enhance the representativeness of the findings, it is imperative to broaden the pool of respondents by incorporating volunteers who mirror the diversity and variability within the community being examined. Therefore, it is anticipated to generate more precise and pertinent results.

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How AI Can Reshape the Fight Against Medical Misinformation

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Abstract
Artificial Intelligence (AI) has a significant role in propagating and medical misinformation and disinformation. But it can also be used to mitigate this phenomenon. Natural Language Processing and Sentiment Analysis can be used to analyze vast amounts of data to identify and combat misinformation trends in health-related discussions. AI can be used to categorize the severity of misleading claims, while the analysis and identification of framing strategies can flag misleading content through indirect means. Additionally, AI customizes health messaging to specific audiences to improve engagement and effectiveness. There is also need for enhanced information literacy and regulatory measures to prevent AI misuse, highlighting the dual-edge of AI in modern health communication.

Keywords: Generative AI, Misinformation, ChatGPT

1. Introduction

In the current era, so dependent on digital communication, the rapid dissemination of health-related information frequently includes the spread of medical disinformation. This growing phenomenon poses significant challenges to public health outcomes and represents a pressing crisis. Social media is especially susceptible, as the COVID-19 pandemic revealed. (Wakene et al., 2024) It's not limited to COVID, of course. All health topics are subject to both misinformation and disinformation, from vaccine science to the benefits of pasteurization and the causes of diabetes and heart disease. (Suarez-Lledo & Alvarez-Galvez, 2021) Misinformation is damaging enough. But often, disinformation campaigns are weaponized for political ends, such as for fomenting distrust in the lead-up to an election.

Artificial intelligence (AI) has significantly influenced the spread of medical misinformation, especially through its ability to generate convincing but erroneous content rapidly and at scale. Generative AI models are capable of creating highly realistic text, images, audio, and video that can be indistinguishable from content created by humans, leading to an increase in the volume and sophistication of medical falsehoods online. Intentional mimicry of credible sources is one path by which AI deepens the information crisis. (Monteith et al., 2024) The unintentional offering of erroneous information via AI "hallucinations" is another. (Hatem et al., 2023)

It is a certainty that AI will become increasingly embedded into our lives and economies, and will dictate the avenues and qualities by which we engage in information seeking. Its threats in this regard are well documented. But what of its opportunities? This article explores some of the avenues by which AI can contribute to the improvement of health information sharing, and in combatting the spread of both health misinformation and disinformation.

2. Proactively Identifying Trends in Medical Misinformation

Natural Language Processing (NLP), that aspect of AI that allows machines to interpret, manipulate, and comprehend human language, can be used to analyze vast amounts of textual data from social media, news outlets, and forums where health-related discussions occur. By processing the text, AI can identify recurring themes, new emerging terms, and misinformation patterns. For example, AI can detect a sudden increase in discussions around a specific but unproven treatment method during an infectious disease outbreak.

Sentiment Analysis (SA) evaluates the emotional tone expressed in health communications to gauge public perception around certain medical topics. This can indicate potential areas where misinformation may be taking root if there is a high level of fear or skepticism expressed. Pre-trained models like BERT have been modified to assess emotional states from text. (Hossain et al., 2025) Still in its infancy, this approach can be accelerated through the development of more wide-coverage misinformation datasets, "whose data is multilingual and extracted from a variety of different platforms with varying data formats." (Liu et al., 2024)

Initiatives like "Project Heal" seek to address three types of erroneous online claims: misinformation (things that are factually incorrect), disinformation (intentional errors meant to cause harm) and malinformation (things that are correct but expressed out of context in a misleading fashion). Project Heal trains a large language model to categorize likely sources of such incorrect claims, and attempts to rate them by severity and potential impact. (Rama, 2024) A flotilla of tools incorporating Project Heal's ranking approach, NLP, and SA will doubtless prove invaluable in the deepening real-time battle against misinformation.

3. Identifying Framing Strategies

Rather than arbitrating whether a statement is true or false, AI can assess the rhetorical strategies used in a given claim. In other words, AI can identify a statement's "frame." The four identifiable elements of a communication frame in a piece of health text or a snippet of video or audio are its problem definition, causal interpretation, moral evaluation, and treatment recommendation. (Entman, 1993) Savvy communicators know that the choice of frame makes information more noticeable, meaningful, and memorable. (Entman, 1993)

Consider a selection of news articles about the same topic, such as gun violence. One might emphasize gun control, while another might promote gun ownership rights, and a third might emphasize mental health issues. (Liu et al., 2019) In the realm of public health, a given article might emphasize uncertainty in safety around COVID-19 vaccines, or it might try to establish legitimacy by referencing an authority. (Sepulvado & Burke-Garcia, 2024) These are all framing strategies.

The Framed Element-based Model (FEM) proposed by Wang et al (Wang et al., 2024) seeks to use AI to detect likely misinformation in news articles by assessing problem definition, claims of causality, moral positioning, and whether a preferred treatment is recommended. In this way, the AI ascertains falseness by establishing framing patterns that have been observed to be preferred by disinformation and malinformation merchants. By identifying the framing strategy, one does not have to determine the correctness of a claim, but rather only the way that the claim was positioned and communicated.

4. Crafting Health Messaging for Specific Audiences

By personalizing the delivery of health information, AI can help ensure that accurate messages are more engaging and reach a wider audience. In the words of Andrew Beam, "One benefit of [AI models] is they are very good at modulating their voice. They can meet people where they are, delivering high-quality information that's both easy to understand and accessible to folks from a wide variety of demographic and cultural backgrounds." (Beam, 2024) AI can segment audiences based on demographics, health conditions, and online behaviour, among other factors. By identifying subgroups within a larger population, AI can help create messages that are specifically tailored to the characteristics and needs of each group. AI algorithms can analyze past interactions to determine which types of messages and delivery methods have been most effective for different population segments in the past. This information can be used to customize messages by tone, complexity, and format.

Additionally, AI can predict the health information needs of different individuals or groups based on their health trajectories or risk profiles. One can envision an AI model that can continuously learn from how different audiences respond to various health messages. Such a feedback loop would allow for the refinement and optimization of communication, raising the probability that messaging remains effective over time.

5. Final Thoughts

In the digital age, the challenge of medical misinformation has become a significant public health concern, intensified by the capabilities of artificial intelligence to both propagate and combat such misinformation. It is clear that the proactive use of AI will be indispensable and probably unavoidable. But the technology cannot be relied upon to manage this task in isolation. The promotion of both information literacy and transparency in AI training datasets is vital. (Germani et al., 2024) Regrettably, there may eventually be a need to enact laws to prevent the weaponization of AI in the production of medical falsehoods. (Haupt & Marks, 2024).

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The Effect of Chromium Supplements on Insulin Resistance: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Abstract

Background: With diabetes rising as a major health issue in developed nations, insulin resistance is gaining more attention. Understanding insulin's role and treatment options for insulin resistance is critical for preventing chronic diseases. We planned to evaluate the impact of chromium on insulin resistance. Method: A comprehensive search was performed using PubMed, Scopus, Embase, and Web of Science databases to assess the effectiveness of chromium trace element on insulin resistance and glucose profile. This review focused solely on randomized controlled trials that were published in English. Results: Our search yielded 2,363 articles. After removing duplicates and conducting thorough title and abstract screening, 45 articles were chosen for full-text evaluation. Among these, 35 articles were included in our systematic review. Finally, 20 studies with 1147 cases focused on patients with type 2 diabetes mellitus, prediabetic, and individuals with confirmed insulin resistance were selected for meta-analysis. The results demonstrated a significant reduction in the HOMA-IR index (pooled MD= -1.29; 95%CI (-1.84 to -0.73), PV= 0.00, I2= 94.7%). Additionally, a significant reduction in the FBS values (pooled MD= - 13.71; 95%CI (-26.29 to -1.12), PV= 0.03, I2= 97.74%) was observed. Regarding the efficacy of chromium on the HbA1C levels, no significant changes were detected (pooled MD= - 0.17; 95%CI (-0.63 to 0.29), PV= 0.42, I2= 96.03%). Conclusion: According to the available evidence, chromium improves insulin resistance in individuals with diabetes or those experiencing insulin resistance. Nevertheless, Additional well-structured and high-quality clinical trials are needed to thoroughly clarify the impact of chromium supplementation on insulin resistance in other situations, like women with PCOS or prediabetic populations.

Keywords: Chromium, Insulin Resistance, Insulin Sensitivity

1. Introduction

The insulin hormone interacts with receptors on target cells and triggers an anabolic response (Petersen et al., 2017). Primarily, insulin in skeletal muscles and the liver increases glucose consumption through glycogen synthesis while suppressing lipolysis in white adipose tissue. The substance indirectly inhibits hepatic gluconeogenesis by reducing hepatic acetyl-CoA levels and diminishing pyruvate carboxylase activity (Schinner et al., 2005). Insulin resistance (IR) is marked by reduced responses of target cells accompanied by compensatory hyperinsulinemia. Potential contributing factors could include the down-regulation of insulin receptors, or genetic variations affecting tyrosine phosphorylation of these receptors, or may involve abnormalities of GLUT 4 (Glucose transporter proteins) function (Wilcox et al., 2005).

IR is associated with overweight, hypertension (HTN), type 2 diabetes mellitus (T2DM), and hyperlipidemia; however, some mechanisms remain unclear (Rao et al., 2006). Diminished muscle glucose metabolism in response to insulin may cause hepatic steatosis and, along with a reduction in substrate oxidation, may be linked to mitochondrial dysfunction (Petersen et al., 2006). There may be a connection between polycystic ovary syndrome (PCOS) and IR, but the importance of this relationship remains complex and not fully understood (Moghetti et al., 2021). Ongoing research suggests that IR may be a contributing element in the development of cancer by mechanisms that include hyperinsulinemia, which provokes increasing levels of insulin-like growth factor 1 (IGF-1), potentially influencing the initiation and progression of tumors in individuals with IR. Moreover, there is frequently an excessive generation of reactive oxygen species that can be harmful to DNA and potentially contribute to the onset of cancer. (Arcidiacono et al., 2012). Interestingly, brain neurons possess insulin receptors, and insulin is integral to neuronal growth, synaptic development, and mitogenesis. Various preclinical studies have shown impaired insulin signaling to be associated with neurodegenerative diseases of the brain (Cholerton et al., 2011. Hölscher et al., 2020). Insulin resistance exerts a multifaceted influence on the body, potentially leading to long-term complications. Therefore, multiple strategies have been proposed to mitigate insulin resistance. These strategies include using antidiabetic agents, anti-inflammatory medications, and the supplementation of vitamins and minerals, among others (Lebovitz et al., 2004. McDonald et al., 2007. Tong et al., 2022. Zhao et al., 2023). Chromium is one of the medications that has been used for reducing insulin resistance (Nishimura et al., 2021). The exact mechanism by which chromium affects insulin metabolism is not entirely understood. It has been suggested that trivalent chromium improves insulin function in peripheral tissues (Lipko et al., 2018). In vitro research suggests that chromium may enhance insulin sensitivity by stimulating the function of insulin receptors (Sahin et al., 2007). It has been demonstrated that chromium enhances insulin receptor β activity. Additionally, chromium promotes the movement of Glut4, a protein that helps cells take glucose to the cell surface. Chromium reduces the activity of PTP-1B (protein tyrosine phosphatase-1B), which normally slows down insulin signaling. It also helps reduce stress within cells and helps move cholesterol out of cell membranes, which supports the movement of Glut4 and increases glucose uptake (Hua et al., 2011).

Animal studies have shown an increase in chromium losses in diabetic rats (Clodfelder et al., 2017) and have expressed the positive impact of chromium in decreasing insulin resistance in obese mice (Wang et al., 2006. Sreejayan et al., 2008. Król et al., 2010). Clinical trials have examined the effects of chromium, either alone or in combination with other interventions, on glucose metabolism (Lai et al., 2008. Dou et al., 2016. Saiyed et al., 2016. Yao et al., 2021). In addition, some meta-analyses have demonstrated the effects of chromium on reducing insulin resistance in T2DM (Balk et al., 2007. Heshmati et al., 2018.), and some showed a decrease in fasting glucose (Abdollahi et al., 2017. Zhao et al., 2022). While the majority of current research investigates the impact of supplementation on insulin and glucose profiles, in this review, we aimed to explore and compare the impact of chromium on insulin resistance, evaluating its effects across different populations.

2. Method

The protocol for the study has been registered with the International Prospective Register of Systematic Reviews (PROSPERO), and it is assigned the registration number CRD420250655755. The research adhered to the guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Page et al., 2021).

2.1. Search Strategy

An extensive search was performed across PubMed, Web of Science, Scopus, and Embase databases in January 2025. The objective was to identify randomized controlled trials assessing the impact of chromium supplementation on insulin sensitivity and resistance. We included a diverse population rather than narrowing it down to a particular group. The search utilized MeSH terms, synonyms, and related keywords for chromium, insulin resistance, and metabolic syndrome. In addition, a comprehensive manual search was conducted utilizing Google Scholar alongside an exploration of gray literature sources. The full search strategy on different databases is provided in Appendix 1.

Two independent reviewers examined and evaluated all identified articles to determine their eligibility according to the established inclusion and exclusion criteria. To guarantee the correctness of the chosen studies, any conflicts were addressed through discussions with a third reviewer.

2.2. Inclusion and Exclusion Criteria

We employed the PICO framework to assess the population, intervention, comparison, and outcome as a guiding structure to clearly define the eligibility criteria (Table 1). We considered all randomized controlled trials (RCTs) published in English in peer-reviewed journals up to January 2025. These studies focused on the impact of chromium supplementation on insulin and glucose levels.

We excluded non-RCTs, observational studies, case reports, and review articles to ensure a focused analysis. Additionally, we excluded articles that did not report relevant outcomes.

Table 1: The population, intervention, comparison, outcome study design (PICO)

Domain	Criteria selection
Participants	Individuals assessed for insulin resistance (no specific population restriction)
Intervention group	Chromium supplementation
Comparison group	Placebo
Outcomes	Insulin level, Glucose profile, Insulin resistance, Insulin sensitivity

2.3. Data Extraction

Two reviewers were tasked with extracting data, with a clear focus on enhancing the quality of our work. An Excel spreadsheet was used to systematically gather study characteristics, including the lead author's name, year of publication, sample size, and participant demographics. Information related to the intervention, such as the type of supplement, dosage, and treatment duration, was also recorded. The outcome results on fasting blood sugar levels (FBS), glucose tolerance test (GTT), HbA1C, insulin, values for insulin resistance, the methods used to determine insulin resistance, or insulin sensitivity. Furthermore, Additional outcomes, such as body mass index (BMI), blood pressure (BP), and lipid profiles, were recorded when accessible. Any discrepancies in the results were addressed by a third reviewer.

2.4. Quality Assessment

The quality of articles was assessed using the updated Cochrane Risk of Bias (RoB-2) tool. Each research study was categorized as having either a low or high risk of bias or exhibiting concerns in different areas. These key areas included the intriguing dynamics of random sequence generation, the essential practice of allocation concealment, the critical aspect of selective reporting, the various methods of blinding, and the exploration of potential biases (Sterne et al. 2019).

2.5. Data Analysis

The mean change and SD (standard deviation) between the baseline and after intervention HOMA-IR were drawn out. The standardized mean difference (SMD) and 95% confidence interval (CI) were used to compare the effect size. For the studies that provided fasting insulin and glucose values, without stating HOMA-IR, we calculated it by using the following formula:

fasting insulin (mIU/L) ×fasting glucose (mg/dL)/405. For analysis, we included only the studies that were conducted among diabetes, prediabetes, and individuals with documented IR. Our main goal was to assess the efficacy of chromium on the HOMA-IR level. For primary analysis, we excluded the studies among healthy populations and overweight individuals. Then, we assessed the effectiveness of chromium on glycemic variables among women with PCOS as a separate group due to the sufficient included articles to conduct a meta-analysis. Regarding healthy and overweight groups, we did not have enough articles assessing the HOMA-IR index, so we did not include them in the analysis.

We employed a random-effect model using restricted maximum likelihood estimation. The between-study heterogeneity was assessed using Cochrane's Q statistic and Hedges 'g I^2 estimation. I^2 values of 25-50% served as low, values of 50-75% medium, and more than 75% meant substantial heterogeneity. Sensitivity analyses (small study effect) were investigated by the leave-one-out method, and subgroup analysis was conducted by the overall ROB result, age, intervention dose, and duration. Publication bias was studied using standard and contoured funnel plots, Egger's test, and the non-parametric trim-and-fill test. The Grading Quality of Evidence and Strength of Recommendations for diagnostic tests and strategies (GRADE) checklist was used to determine the certainty of evidence. STATA version 17.0.0. Statistical software was used for all analyses.

3. Results

3.1. Study Selection

We initially discovered 2,363 articles, including 351 from PubMed, 484 from Scopus, 792 from the Web of Science, and 736 from Embase. After eliminating duplicate entries, 1,198 articles were screened. The first screening focused on titles, resulting in 155 articles. After reviewing the abstracts, 45 articles were chosen for full-text evaluation, ultimately bringing about the inclusion of 35 articles as shown in Figure 1.

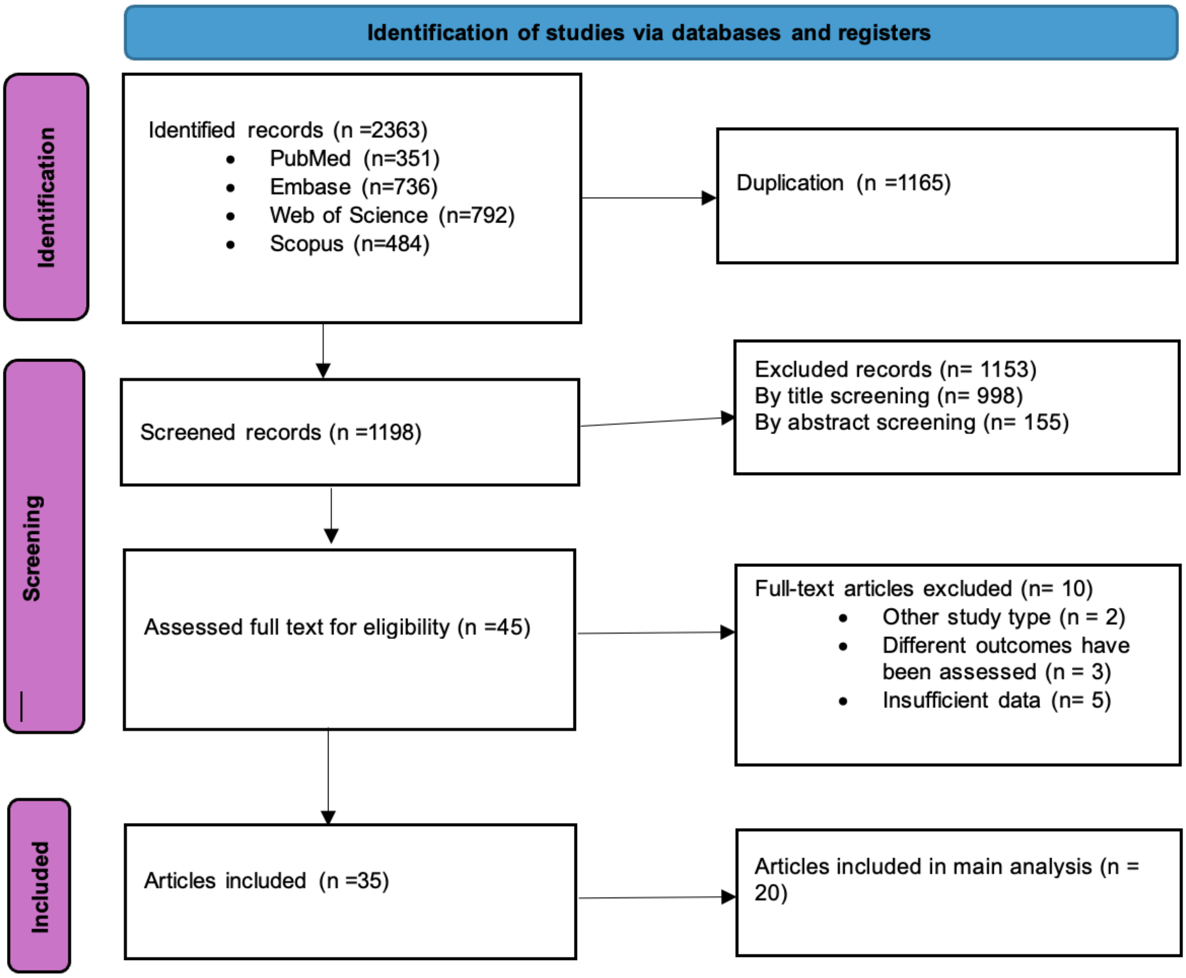

Figure 1: PRISMA diagram for included articles

The RCTs included in our study were published between 1981 and 2024. A total of 35 studies assessing glucose profile and insulin levels were examined. Of these, 14 studies focused on patients with T2DM, three studies on individuals with glucose intolerance, two studies among those with IR, two investigations on HIV-positive cases with IR, and four studies targeted women with PCOS. While four studies involved healthy individuals, five studies involved overweight individuals, and one on non-alcoholic fatty liver patients. Three studies included more than one chromium supplementation arm. These arms were pooled into a single intervention group, as recommended in the Cochrane Handbook, to ensure a single independent comparison with the control group in each study. The interventions lasted 6 to 38 weeks, and the prescribed dosages of chromium supplementation varied from 50µg to 1000µg. The most used form of chromium was chromium picolinate. The trial by Silpa et al. (2024) enrolled 60 participants but did not report group sizes; therefore, an equal allocation of 30 patients in each group was assumed based on the total sample size and comparable baseline variables. Table 2 demonstrates the included studies. Tables 3-5 outline the main findings of these studies based on the population.

Table 2: The characteristics of included studies.

Studies	Population	Sample size(I/P)	Age (I/P)	Male (I/P)	Intervention dose and type	Duration
Silpa et al./ 2024	T2DM	60	50.6+/-4.5 vs 51.9+/-5.5	NS	NS	8w
Talab et al./ 2020	T2DM	52 (26 vs 26)	50.4+/-6.0 vs 51.4+/-6.0	7 / 11	400µg CrP	8w
Farrokhian et al./ 2019	T2DM	64 (32 vs 32)	58.0+/-8.0 vs 60.9+/-7.7	15 / 17	200µg CrP	12w

Imanparast et al./ 2019	T2DM	46 (23 vs 23)	50.4+/-8.5 vs 51.7+/-9.1	10 / 13	500µg CrP	16w
Yanni et al./ 2018	T2DM	30 (15 vs 15)	NS	9 / 9	NS dose CY bread	12w
Chen et al./ 2014	T2DM	66 (38 vs 28)	53.3 ± 10.1 vs 54.2 ± 8.5	22 / 21	400µg CCl (milk)	16w
Guimarães et al./ 2013	T2DM	42	51.35 (200µg) 50.75 (50µg) 50.47 (p)	5 (200µg) 3 (50µg) 4 (p)	(23): 200µg (18): 50µg CrN	12w
Jain et al./ 2012	T2DM	83 28 (CDNC) 28 (CrP) 27 (P)	48.79 (CDNC) 51.12 (CrP) 48.64 (P)	14 (CDNC) 10 (CrP) 4 (P)	400µg	12w
Lai et al./ 2008	T2DM	20 (10 vs 10)	53.2+/-2.0 vs 50.05+/-1.9	4 / 5	1000µg CY	24w
Kleefstra et al. / 2007	T2DM	56 (28 vs 28)	68+/-8.2 vs 66+/-8.6	18 / 17	400µg CY	4w
Pei et al./ 2006	T2DM	60 (30 vs 30)	54.2+/-7.1 vs 55.6/-8.2	16 / 17	200µg Chromium enriched milk	16w
Martin et al./ 2006	T2DM	29 (17 vs 12)	NS	NS	1000µg CrP	12w
Racek et al./ 2005	T2DM	36 (19 vs 17)	61.8 vs 60.8	5 / 4	400µg CrY	12w
Ghosh et al./ 2002	T2DM	100 (50 vs 50)	NS	NS	400µg Trivalent	12w
Nussbaumerova et al./ 2017	prediabetic	70 (35 vs 35)	57+/-10 vs 58+/-9	12 / 13	300µg CY	24w
Ali et al./ 2012	prediabetic	60 (30 vs 30) 58 (29 vs 29)	NS	NS	500µg (15) 1000µg (15) CrP	24w
Gunton et al./ 2005	prediabetic	40 (20 vs 20)	NS	NS	800µg CrP	12w
Zhao et al./ 2024	IR individuals	60 (30 vs 30)	53.87+/-8.73 vs 50.89+/-8.06	18 / 12	160µg CY	12w
Dou et al./ 2016	IR individuals	60 (30 vs 30)	55.3+/-3.3 vs 55.6+/-3.36	NS	160µg CY	12w
Stein/ et al./ 2013	HIV with glucose intolerance	39 (20 vs 19)	47.6+/-1.7 vs 47.3+/-1.7	13 / 13	1000µg CrP	8w
Aghdassi et al./ 2010	HIV with IR	52 (26 vs 26)	46.8+/-1.5 vs 50.2+/-1.4	25 / 25	400µg CrN	16w
Jamilian et al./ 2018	PCOS	40 (20 vs 20)	30.3+/-4.6 vs 32.3+/-3.0	none	200µg CrP	8w
Ashoush et al./ 2016	PCOS	85 (44 vs 41)	24.7+/-3.7 vs 24.6+/-4	none	1000µg CrP	24w
Jamilian et al./ 2015	PCOS	64 (32 vs 32)	24.9+/-5.0 vs 24.4+/-4.4	none	200µg CrP	8w
Lucidi et al./ 2005	PCOS	10 (6 vs 4)	NS	none	200µg CrP	16w

Masharani et al./ 2012	Healthy	31 (16 vs 15)	35.9+/-11.5 vs 38.6+/-10.5	9 / 8	1000µg CrP	16w
Amato et al./ 2000	Healthy	52 (26 vs 26)	69.3+/-1.4	25 / 25	400µg CrP	16w
Riales et al./ 1981	Healthy	23 (12 vs 11)	46+/-9 vs 49+/-9	12 / 11	200µg trivalent	12w
Wilson et al./ 1995	Healthy	26 (15 vs 11)	36.7+/-1.82 vs 35.5+/-1.89	5 / 6	220µg CrP	12w
Sala et al./ 2017	Overweight	24 (8 vs 9 vs 7)	36.6	16.2%	8: 1000µg 9:600µg CrP	12w 24w
Yazaki et al./ 2010	Overweight	80 (40 vs 40)	NS	NS	1000µg CrP	12w 24w
Kim et al./ 2010	Overweight children	25 (12 vs 13)	10.7+/-0.2 vs 10.38+/-0.3	4 / 8	200µg CrCl	6w
Iqbal et al./ 2009	Overweight with Metabolic syndrome	63 (33 vs 30)	47.7+/-10 vs 51.1+/-13	13 / 18	1000µg CrP	16w
Cefalu et al./ 1999	Overweight	29 (15 vs 14)	45+/-3 vs 49+/-4	5 / 6	1000µg CrP	38w
Moradi et al./ 2021	Fatty liver disease	46 (23 vs 23)	38.9+/-7.3 vs 40.3+/-6.7	14 / 12	400µg CrP	12w

T2DM: type 2 diabetes mellitus, IR: insulin resistance, PCOS: polycystic ovary syndrome, HIV: human immunodeficiency virus, NS: non-specified, CrPic: chromium picolinate, CrN: chromium nicotinate, CrCl: chromium chloride, CDNC: chromium dinicocysteinate, CY: chromium-enriched yeast

Table 3: The effects of chromium on the outcomes in those with diabetes, prediabetic conditions, or known insulin resistance

Study	Assessment method	Primary outcome	Other findings
Silpa et al. (2024)	Fasting insulin	-The endpoint means insulin levels in groups differed significantly (P < 0.05). - No significant difference in FBS	- No significant difference in lipid profiles
Zhao et al. (2024)	HOMA-IR	-No significant decreases from the baseline values of FBS and HOMA-IR were observed in both groups.	NS
Talab et al. (2020)	HOMA-IR	- Changes in HOMA-IR between groups were significant (P < 0.001). - No significant changes in FBS and insulin levels were reported.	- Significant improvement in total cholesterol and LDL in the intervention group.
Farrokhian et al. (2019)	HOMA-IR Insulin sensitivity (QUICKI)	- Cr significantly reduced FBS (P = 0.007), insulin, and HOMA-IR (P < 0.001).	- Cr decreased body weight (P = 0.001) and BMI (P = 0.002). - Cr significantly reduced diastolic blood pressure (P = 0.01).
Imanparast et al. (2019)	HOMA-IR	- An increase in the HOMA-IR in the placebo group was reported.	- No changes in the lipid profile were observed.

		- FBS and HbA1c did not change significantly.	
Yanni et al. (2018)	HOMA-IR	- Cr significantly decreased FBS and HbA1C ($P < 0.05$). - Serum insulin and HOMA-IR were lower in the Cr intervention group ($P < 0.05$).	-No difference in lipid profile was observed.
Nussbaumerova et al. (2017)	HOMA-IR	- There were no significant changes in FBS, HbA1C, and HOMA-IR, a slight decrease in insulin levels in the second hour of GTT in the Cr group.	- Fasting lipids, CRP, and oxidative stress markers did not change during the study.
Dou et al. (2016)	HOMA-IR	- No significant decreases from the baseline values were documented in both groups.	NS
Chen et al. (2014)	Insulin sensitivity	-SI was improved in the Cr group notably. - FBS significantly decreases in the Cr group.	-No substantial changes were observed in the TG, total cholesterol, LDL, and HDL. - Waist circumference and ALT decreased significantly in the Cr group.
Stein et al. (2013)	HOMA-IR	- No statistically significant differences were observed in the responses of FBS and HOMA-IR in the Cr group.	- There was a significant improvement in serum HDL in the group supplemented with Cr**.**
Guimarães et al. (2013)	HOMA-IR	- No marked difference between groups in FBS, HbA1C, and HOMA-IR. - HOMA-β increased in the placebo group.	- No marked difference between groups in total cholesterol and LDL. - HDL increased in the placebo group.
Jain et al. (2012)	HOMA-IR	- No differences in glycemic profile after supplementation were observed. - Significant reduction in the insulin level and insulin resistance after supplementation with Cr.	NS
Ali et al. (2012)	HOMA-IR	- The groups had no significant differences in insulin, HOMA-IR, or glucose profile.	- No significant differences on lipid profile or blood pressure were observed.
Aghdassi et al. (2010)	HOMA-IR	- Cr caused a significant drop in HOMA-IR and blood insulin levels. - Baseline IR significantly affected the response to Cr, with a strong link between initial insulin levels and the reduction in	- TG was reduced after Cr supplementation. - There was no change in FBS, Hb A1c, HDL or CD4 cell count between groups.

		blood insulin post-supplementation (p = 0.0001).	
Lai et al. (2008)	HOMA-IR	- In the Cr group, there was a significant reduction in FBS, HbA1c, and the insulin resistance index (p<0.05).	- The glutathione peroxidase activity showed a notable increase (p<0.05).
Kleefstra et al. (2007)	HOMA-IR	- No meaningful differences were found between groups for FBS, HbA1C, and insulin resistance.	- No marked difference in blood pressure, body fat, body weight, or serum lipids was found.
Pei et al. (2006)	HOMA-IR	- The Cr group demonstrated a lower FBS, fasting insulin, and HbA1C, especially in male patients (p<0.05). - A marked improvement in HOMA-IR (p<0.05) was documented.	- No marked changes in lipid profiles were stated.
Martin et al. (2006)	Insulin sensitivity	- Participants given sulfonylurea/Cr showed significantly lower fasting blood sugar, glucose AUC, and improved insulin sensitivity compared to those on sulfonylurea/placebo.	- Those on sulfonylurea/placebo showed notable increases in body weight and body fat percentage.
Racek et al. (2005)	Fasting insulin	- The changes in the FBS in the Cr group were notably different (p < 0.01). - A slight but not statistically significant reduction in insulin levels was found in the intervention group**.**	- No considerable differences in TG, total cholesterol, HDL, and LDL were documented.
Gunton et al. (2005)	HOMA-IR	- The two groups had no significant differences in insulin and HOMA-IR.	- There was a minor deterioration in total cholesterol in the placebo intervention.
Ghosh et al. (2002)	Fasting insulin	-Significant improvement in FBS and HbA1C with Cr supplementation. - Significant reduction in serum insulin was documented in the Cr group.	- No marked changes in lipid profile documented.

Cr: chromium, ISI: insulin sensitivity index, FSIVGTT: frequently sampled intravenous glucose tolerance test, QUICKI: quantitative insulin sensitivity check index, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance, HDL: high-density lipoprotein, LDL: low-density lipoprotein, VLDL: very low-density lipoprotein, TG: triglyceride, FBS: fasting blood sugar, HbA1C: Hemoglobin A1c, AUC: area under the curve, P: P value

Table 4: The effects of chromium on the outcomes in overweight or healthy individuals.

Study	Assessment method	Primary outcome	Other findings
Moradi et al. (2021)	HOMA-IR Insulin sensitivity	- Cr significantly decreased TG, insulin,	- No remarkable differences in total

	(QUICKI)	and HOMA-IR ($p < 0.05$). - There were no major differences in FBS and HbA1C ($P > 0.05$).	cholesterol, HDL, and LDL were noted ($P > 0.05$).
Sala et al. (2017)	Insulin sensitivity (ISI)	- The AUC showed a significant increase in the placebo group ($p < 0.02$), while there was a notable decrease in the group that received 600mg of CrP ($p < 0.03$). -Insulin AUC increased significantly, whereas ISI dropped considerably ($p < 0.03$).	NS
Masharani et al. (2012)	Insulin sensitivity (euglycemic hyperinsulinemic clamp)	- Cr caused no major changes in the IS value ($p=0.83$).	NS
Yazaki et al. (2010)	Fasting insulin	- There was no difference in fasting glucose and insulin levels compared to the baseline.	- No changes in lipid profile observed between groups. - No changes were documented in BMI between groups.
Kim et al. (2010)	HOMA-IR	- Cr significantly dropped HOMA-IR, while placebo rose it. - No considerable changes in FBS were found.	-The decrease in body fat percentage was more significant in the Cr group compared to the placebo group ($P= 0.04$). - No treatment effects were observed for BMI, waist circumference, blood pressure, total cholesterol, TG, and HDL.
Iqbal et al. (2009)	Insulin/ glucose ratio	- After Cr treatment, there were no marked changes in SI and glucose effectiveness index.	- A small, non-significant decrease in LDL levels was noted in the Cr group, while the placebo group experienced an increase.
Amato et al. (2000)	Insulin Sensitivity Assessment (FSIVGTT)	- Insulin sensitivity and glucose effectiveness showed remarkable changes with chromium.	- No significant changes in lipids, or body composition were documented.
Cefalu et al. (1999)	Insulin Sensitivity Assessment (FSIVGTT)	- Those in the Cr group had a significant rise in insulin sensitivity at the midpoint ($P < .05$) and end of the study ($P < .005$). - No changes in glucose effectiveness were noted between groups.	NS
Wilson et al. (1995)	Insulin sensitivity (ISI)	-Participants with high initial insulin resistance showed a significant ($P < 0.03$) decrease after Cr.	NS

		- No significant changes in FBS after Cr was documented.	
Riales et al. (1981)	Insulin/ glucose ratio	- In the Cr group, mean plasma glucose levels were lower at 6 weeks than at baseline, but only the FBS was lower at 12 weeks. - A decrease in the I/G ratio that indicates increased insulin sensitivity.	- A borderline drop in TG was found in the Cr group.

Cr: chromium, ISI: insulin sensitivity index, FSIVGTT: frequently sampled intravenous glucose tolerance test, QUICKI: quantitative insulin sensitivity check index, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance, HDL: high-density lipoprotein, LDL: low-density lipoprotein, VLDL: very low-density lipoprotein, TG: triglyceride, FBS: fasting blood sugar, HbA1C: Hemoglobin A1c, AUC: area under the curve, P: P value

Table 5: The effects of chromium on the outcomes in women with polycystic ovary syndrome.

Study	Assessment method	Primary outcome	Other findings
Jamilian et al. (2018)	HOMA-IR Insulin sensitivity (QUICKI)	- Cr resulted in significant reductions in FBS (P = 0.03), serum insulin levels (P = 0.004), HOMA-IR (P = 0.005).	- Cr significantly decreased serum TG (P = 0.004), VLDL (P = 0.004) and total cholesterol values (P = 0.03).
Ashoush et al. (2016)	Glucose/ insulin ratio	- Treatment with Cr did not significantly change FBS in the groups (P = 0.594 and 0.32). - Women in the Cr group had a remarkable decrease in fasting insulin (P = 0.007) along with a major rise in the FGIR (P= 0.047).	- Women in the Cr group had a marked drop in BMI (P< 0.001).
Jamilian et al. (2015)	HOMA-IR, HOMA-B Insulin sensitivity (QUICKI)	- Cr resulted in significant decreases in insulin (p < 0.001), HOMA-IR (p < 0.001), and HOMA-B (p < 0.001) values.	- Cr decreased TG (p = 0.05), VLDL (p = 0.05), and cholesterol concentrations (p = 0.09).
Lucidi et al. (2005)	Insulin sensitivity	- Slight but not significant decrease in insulin sensitivity from baseline in Cr group was observed. - Cr resulted in significant improvement in glucose tolerance tests. -The FBS did not change markedly from baseline after treatment.	NS

Cr: chromium, ISI: insulin sensitivity index, FSIVGTT: frequently sampled intravenous glucose tolerance test, QUICKI: quantitative insulin sensitivity check index, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance, HDL: high-density lipoprotein, LDL: low-density lipoprotein, VLDL: very low-density lipoprotein, TG: triglyceride, FBS: fasting blood sugar, HbA1C: Hemoglobin A1c, AUC: area under the curve, P: P value

3.3. Quality Assessment

Figure 2 illustrates the outcomes of the risk of bias assessment conducted on the selected articles. Out of the total articles reviewed, fifteen were identified as having a high risk of bias. Conversely, eleven articles were classified as having a low risk of bias, suggesting that they adhered to more rigorous research standards and produced reliable results. Additionally, eight articles were identified as having some concerns related to bias, highlighting specific areas where the research may be weakened or questioned.

study	D1	D2	D3	D4	D5	Overall
Aghdassi/2010	+	+	+	+	+	+
Amato/2000	+	+	+	+	+	+
Ashoush/2016	+	+	+	+	!	!
Kim/2010	!	+	+	!	!	-
Lai/2008	!	!	+	+	!	-
Cefalu/1999	!	+	+	!	!	!
Dou/2016	!	+	+	+	+	!
Farrokhian/2019	!	+	+	+	+	+
Lucidi/2005	-	+	+	+	+	-
Guimaraes/2013	+	!	+	!	!	!
Gunton/2005	!	+	+	+	+	!
Iqbal/2009	+	+	+	+	+	+
Jain/2012	+	+	+	+	+	+
Martin/2006	!	-	+	+	+	-
Jamilian/2015	+	+	+	+	+	+
Jamilian/2018	+	+	+	+	+	+
Masharani/2012	-	+	-	+	+	-
Moradi/2021	!	-	+	+	+	-
Kleefstra/2007	+	+	+	+	+	+
Riales/1981	!	-	+	+	-	-
Racek/2005	!	-	+	+	+	-
Nussbaumerova/2017	+	!	+	+	+	!
Pei/2006	!	-	+	+	+	-
Sala/2017	!	-	+	+	+	-
Silpa/2014	!	-	+	+	+	-
Stein/2013	!	!	+	+	+	!
Ghosh/2002	+	+	+	+	+	+
Talab/2020	!	-	+	+	+	-

Wilson/1995	!	-	+	+	+	-
Yani/2018	+	!	+	+	+	!
Yazaki/2010	!	-	+	+	+	-
Chen/2014	+	+	+	+	+	+
Zhao/2024	!	-	+	+	+	-
Ali/2012	+	!	+	+	+	!
Imanparast/2019	!	+	+	+	+	+

Figure 2: Cochrane Risk of Bias (RoB 2 Tool) Summary

+ Low risk ! Some concern - High risk

D1: Randomization process

D2: Intended interventions deviation

D3: Outcome data missing

D4: Outcome measurement

D5: Reported result selection

3.4. Effects of chromium supplementation on HOMA-IR

Twenty studies with 1147 participants compared chromium and placebo on the HOMA-IR index among diabetic and prediabetic individuals. Meta-analysis of these studies demonstrated (Figure 3) that chromium significantly reduced the HOMA-IR index (pooled MD= -1.29; 95%CI (-1.84 to -0.73), P_V= 0.00), but this analysis had a high level of heterogeneity (I^2= 94.7%).

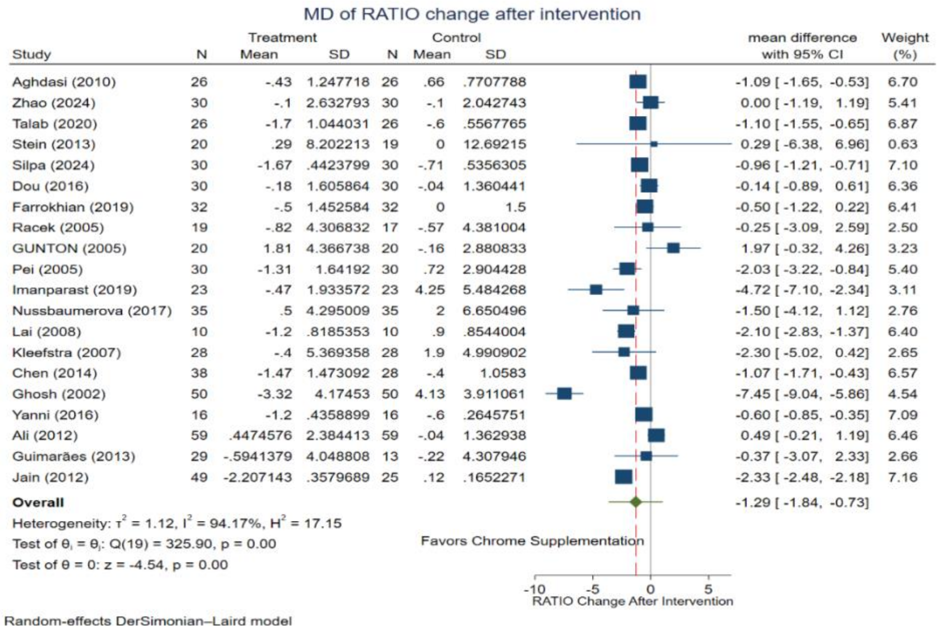

Figure 3: Forest plot for meta-analysis of HOMA-IR mean changes in the chromium group versus the control group

3.5. Effects of chromium supplementation on FBS and HbA1C

Seventeen studies evaluated the efficacy of the intervention on FBS levels and showed (Figure 4) a significant reduction in the FBS values (pooled MD= - 13.71; 95%CI (-26.29 to -1.12), P_V= 0.03, I^2= 97.74%). Regarding the efficacy of chromium on the HbA1C levels, no significant changes were detected (pooled MD= - 0.17; 95%CI (-0.63 to 0.29), P_V= 0.42, I^2= 96.03%) (Figure 5).

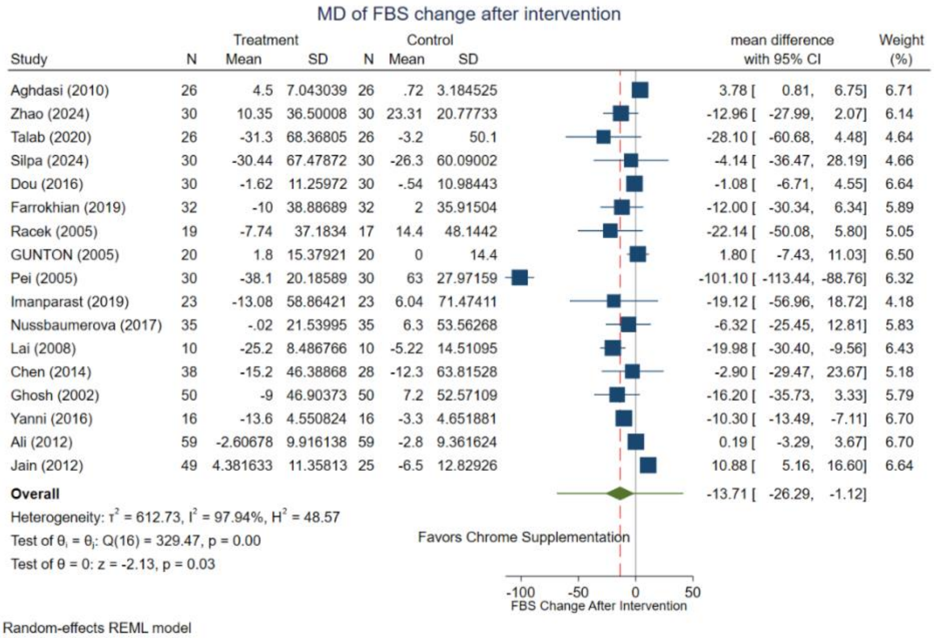

Figure 4: Forest plot for meta-analysis of FBS mean changes in the chromium group versus the control group

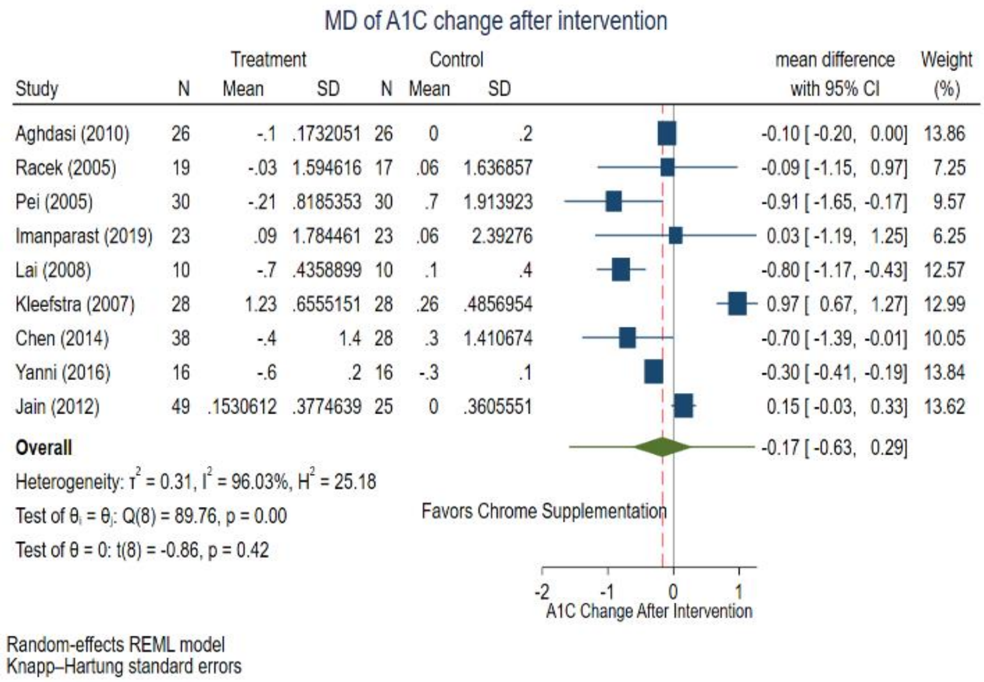

Figure 5: Forest plot for meta-analysis of HbA1C mean changes in the chromium group versus the control group

3.6. Effects of chromium supplementation on HOMA-IR and FBS among PCOS individuals

Four studies with 199 cases assessed the efficacy of chromium on fasting insulin and glucose among women with PCOS. No significant pooled reduction reported (HOMA-IR: (pooled MD= - 0.81; 95%CI (-4.01 to 2.38), P_V= 0.88, I^2= 2.10%), FBS: (pooled MD= - 0.12; 95%CI (-2.46 to 2.22), P_V= 0.48, I^2= 0.00%)) (Figure 6).

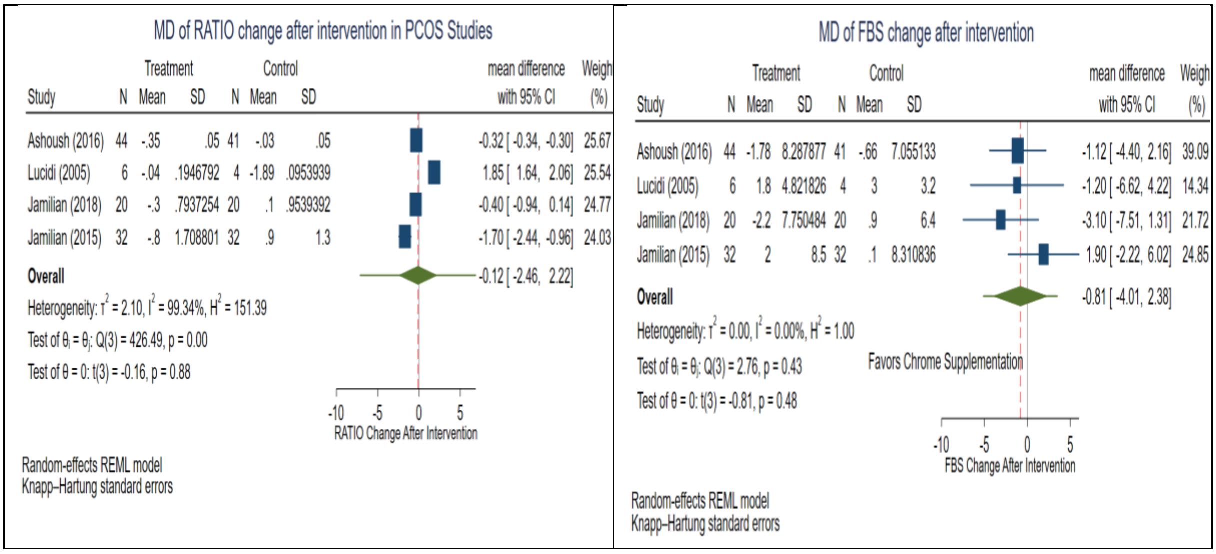

Figure 6: Forest plot for meta-analysis of HOMA-IR and FBS mean changes after intervention in women with PCOS

3.7. Subgroup analysis

Subgroup analysis didn't reveal a significant difference in SMD for HOMA-IR changes based on the patient age, chromium type, chromium dose, or duration of supplementation. The graphs for the subgroup analyses are available in Appendix 2-5. Additionally, the subgroup analysis based on the underlying condition did not show any significant differences in the HOMA-IR SMD (Appendix 6). However, the results of subgroup analysis based on the quality of the included articles partially explained heterogeneity and showed that the quality of the studies is a significant moderator of the effects of chromium on HOMA-IR ratio (Appendix 7).

3.8. Sensitivity analysis

Leve one out sensitivity analyses on HOMA-IR confirmed the robustness of the outcome, as the removal of any study didn't alter the pooled SMD. In contrast, the results for FBS change showed a weaker and less consistent negative effect (Appendix 8,9).

3.9. Publication bias

The standard and counter-enhanced funnel plot inspection demonstrated an asymmetric distribution (Appendix 10). However, several studies were located outside the contour for $p > 10\%$, which suggests that the asymmetry may not be solely due to publication bias, but possibly other factors such as small-study effects. To statistically investigate the asymmetry, Egger's regression test for small-study effects was conducted. The results of the test showed a statistically significant asymmetry (beta1 = -11.43, SE = 1.887, z = -6.06, $p < 0.0001$). A nonparametric trim-and-fill analysis was performed to estimate the impact of publication bias on the overall effect size by imputing missing studies (Appendix 11). The analysis identified no missing studies (observed = 20, imputed = 0). The pooled Hedges's g for both observed studies and the combination of observed and imputed studies was the same (-0.624, 95% CI [-0.748, -0.500]).

3.10. GRADE

The GRADE checklist was applied for three outcomes, including HOMA-IR, FBS, and HbA1C changes. The final level of certainty for these outcomes was moderate, low, and moderate, respectively. The GRADE table is available at https://1drv.ms/x/c/7234bfd3278bfcf9/EaYLYCShZrZMnOqp7S0Hf4kB1TOba-i4QMSzzgcj7B6Kpw?e=HPR00O.

4. Discussion

This meta-analysis demonstrated that chromium supplementation significantly decreased IR in populations with diabetes and those experiencing IR. Furthermore, a significant reduction in FBS was observed. However, the analysis did not detect a significant change in HbA1c levels, suggesting that while chromium may have an acute effect on insulin resistance and fasting glucose, its long-term impact on overall glycemic control, as measured by HbA1c, remains inconclusive. The results of the analysis are consistent with several previous studies and reviews that have supported the beneficial role of chromium in managing insulin resistance (Balk et al., 2007. Abdollahi et al., 2013. Asbaghi et al., 2020). Accordingly, Balk et al. (2007) meta-analysis stated that chromium decreased glycemic indices in diabetics without any effect on glucose metabolism in those with normal blood glucose. Although our results contrast with the Zhao et al. (2022) meta-analysis, which stated that the only glycemic index significantly affected by chromium is HbA1c. This discrepancy may be attributed to differences in the inclusion criteria of the studies, the specific patient populations analyzed, or the high degree of heterogeneity noted in our analysis, which could mask an effect on HbA1c.

While chromium supplementation did not show any significant effect on the HOMA-IR index or FBS in women with PCOS, a non-significant reduction in this population may suggest the benefits of chromium may extend beyond individuals with diabetes and prediabetes, offering a potential therapeutic avenue for improving metabolic health in PCOS patients. Two previous meta-analyses stated the significant effect of chromium on HOMA-IR, with fewer included articles (Tang et al., 2018. Heshmati et al., 2018). Additionally, Fazelian et al. (2017) showed improvement in insulin sensitivity after chromium treatment in women with PCOS. Based on our results, it appears that the statistical significance of this finding diminished as more RCTs were included in the analysis.

A subgroup analysis by intervention duration suggested that the beneficial effects of chromium on IR may be more pronounced at 12 weeks, with no meaningful effects observed at 8 or 24-week durations. These results align with Asbaghi et al. (2020) on the duration of supplementation. Chromium doses up to 500μg were associated with a greater improvement in HOMA-IR levels.

The bioavailability of chromium might be affected by different variables. Certain elements have been demonstrated to affect chromium absorption, as a diet rich in phytate and simple sugars may reduce it (Anderson et al., 2003). Some studies have confirmed that additional trace elements can enhance the beneficial effects of chromium on metabolic health. Zhao et al. (2024) noted that the combined supplementation of chromium and magnesium enhances glucose and lipid levels while decreasing inflammation and oxidative stress markers. Imanparast et al. (2020) showed that co-supplementation of chromium and vitamin D3 significantly decreases HOMA-IR. Lai et al. (2008) demonstrated that combining vitamin C or vitamin E with chromium is as effective as chromium supplementation in improving insulin resistance. Chromium's bioavailability varies by form, with picolinate seeming to be the most stable and bioavailable (Anderson et al., 2008); however, our subgroup analysis did not find any significant differences based on the form of supplementation. Furthermore, given the natural decline in chromium levels with aging, supplementation needs may vary from person to person (Schinner et al., 2005). This is supported by our finding of a non-statistically significant reduction in HOMA-IR in those older than 60, indicating that further research is needed to determine the optimal dosage and duration for this specific population.

5. Limitations

Our results showed that despite a significant pooled reduction in HOMA-IR and FBS with chromium supplementation, the wide 95% prediction interval (PrI) suggests limited generalizability to new populations or settings. Furthermore, there were an insufficient number of studies reporting IR to perform a subgroup analysis in overweight and healthy populations. Further investigation through well-structured RCTs, which modify a range of variables, may be instrumental in accurately assessing chromium's efficacy across diverse populations.

6. Conclusion

Chromium supplementation has been demonstrated to reduce insulin resistance in patients with T2DM and those who already exhibit significant insulin resistance. However, individuals without established insulin resistance may not experience benefits from chromium.

Conflict of interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Ethical Approval: As this article is a review of previously published articles, an ethics approval statement is not applicable.

Declaration of Generative AI and AI-assisted Technologies: This study has not used any generative AI tools or technologies in the preparation of this manuscript.

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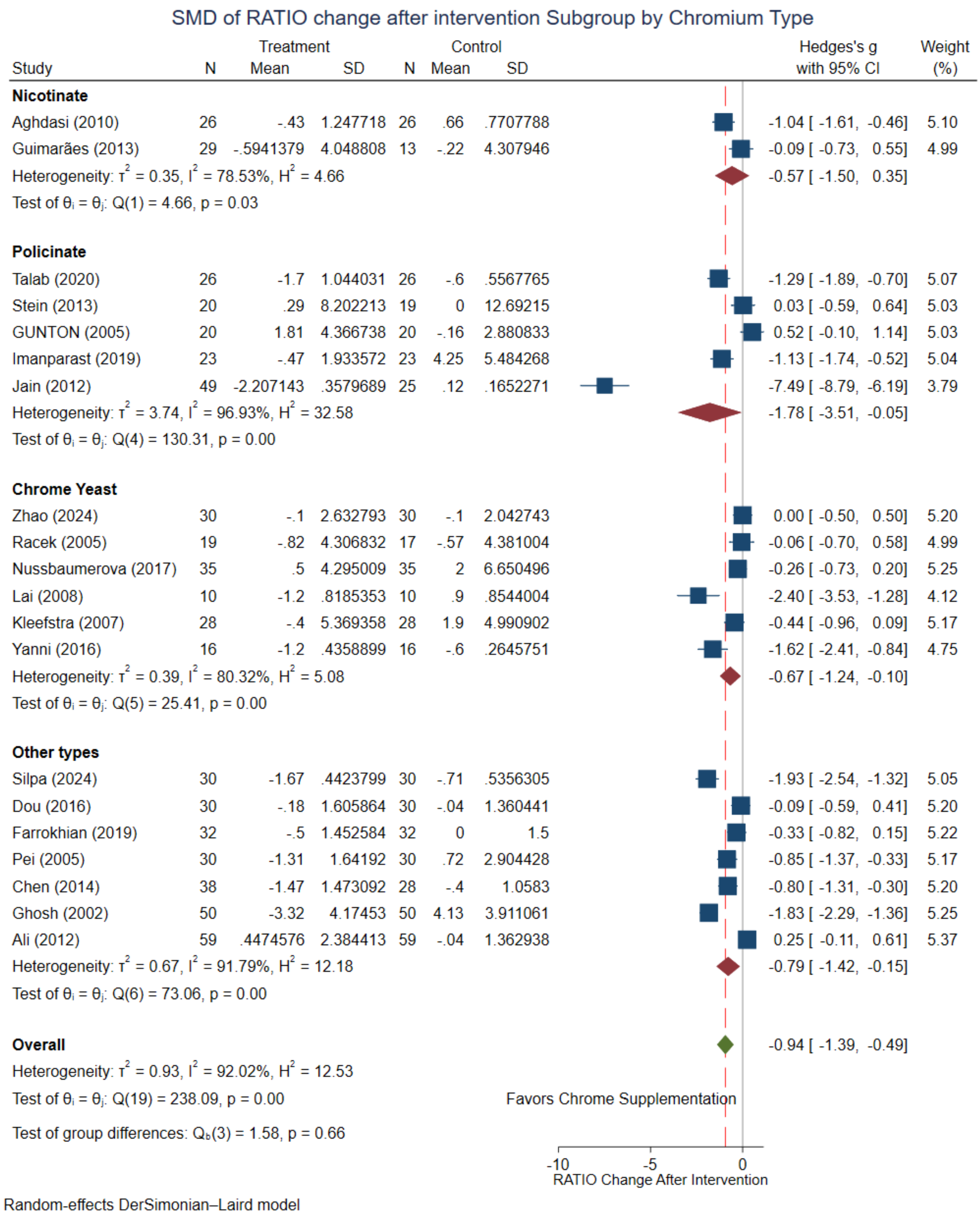
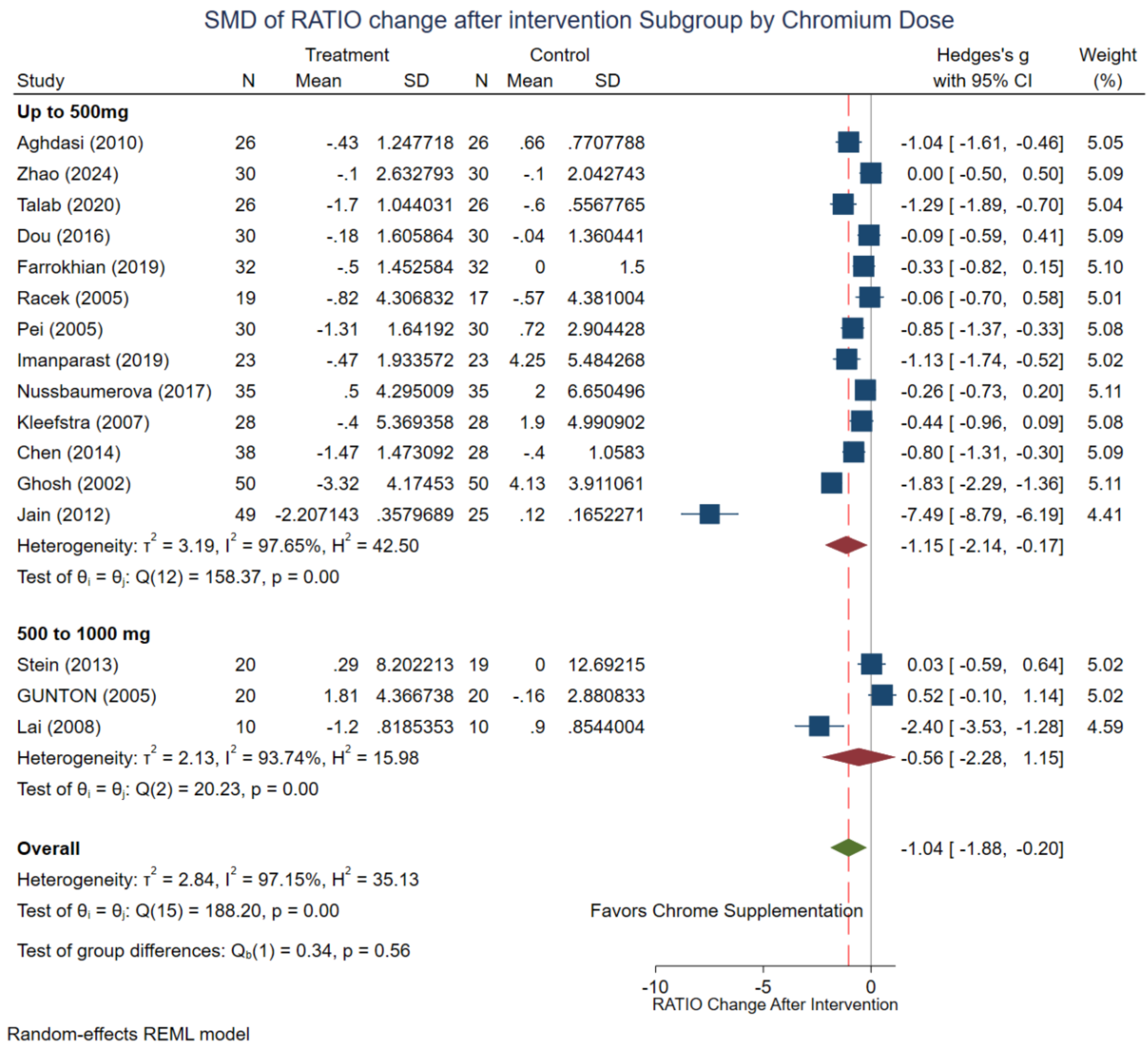
Appendix

PubMed Search Strategy **Results: 351**	("chromium"[mesh] OR chromium[tiab] OR chrome[tiab]) AND ("Insulin resistance"[mesh] OR Metabolic syndrome[mesh] OR Insulin resistance[tiab] OR Metabolic syndrome[tiab] OR Reaven syndrome[tiab] OR Insulin resistance[tiab] OR Metabolic X[tiab])
Embase Search Strategy **Results: 736**	('chromium'/exp OR 'chromium':ti,ab OR 'chrome':ti,ab) AND ('Insulin resistance'/exp OR 'Metabolic syndrome'/exp OR 'Insulin resistance':ti,ab OR 'Metabolic syndrome':ti,ab OR 'Reaven syndrome':ti,ab OR 'Insulin sensitivity':ti,ab OR 'Metabolic X':ti,ab)
SCOPUS Search Strategy **Results: 484**	(TITLE-ABS("Chromium" OR "Chrome")) AND (TITLE-ABS("Insulin resistance" OR "Metabolic syndrome" OR "Reaven syndrome" OR "Insulin sensitivity" OR "Metabolic X"))
Web of Sciences Search Strategy **Results: 792**	(TS= ("chromium" OR "Chrome")) AND (TS= ("Insulin resistance" OR "Metabolic syndrome" OR "Reaven syndrome" OR "Insulin sensitivity" OR "Metabolic X"))

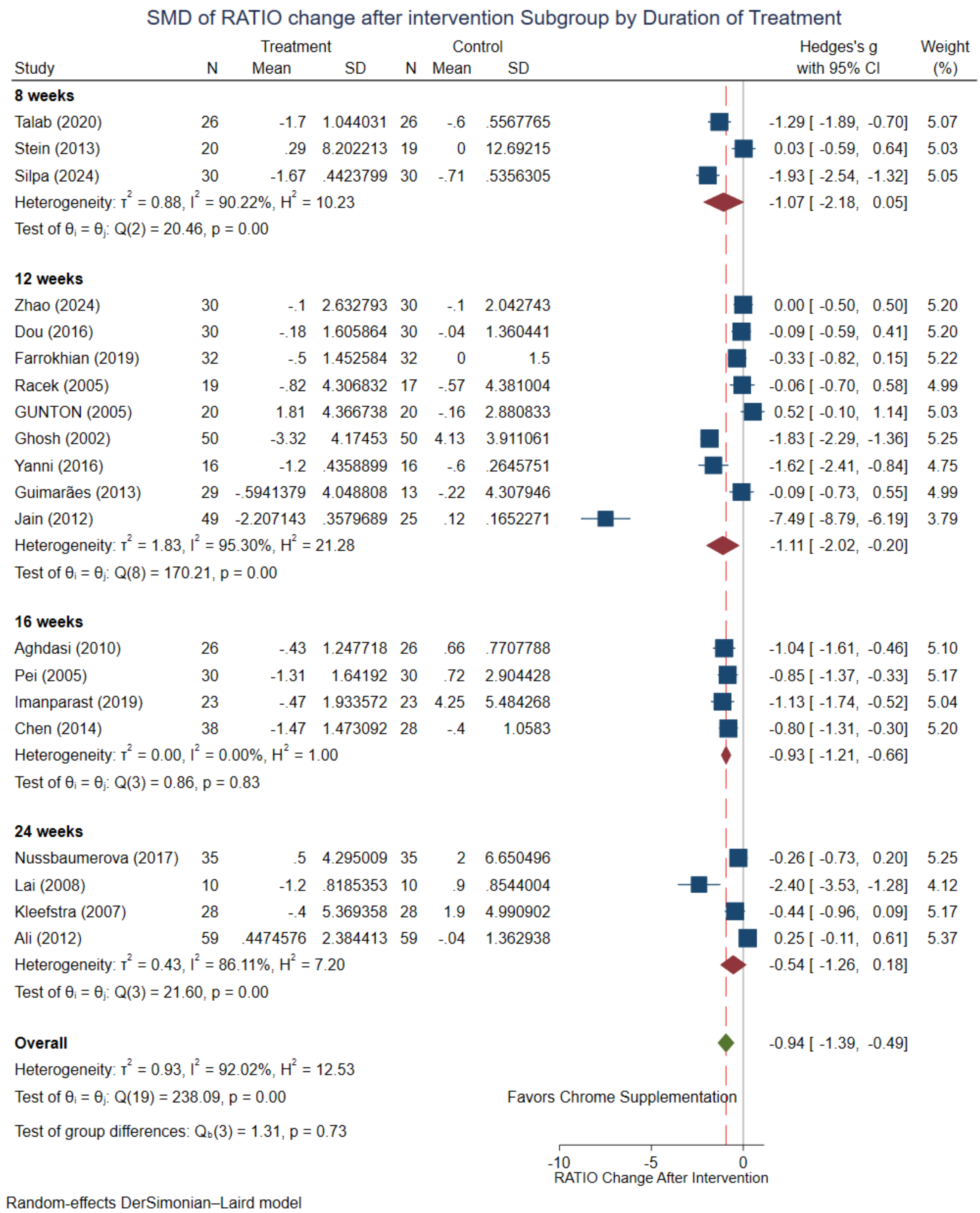
Appendix 2: Search strategy



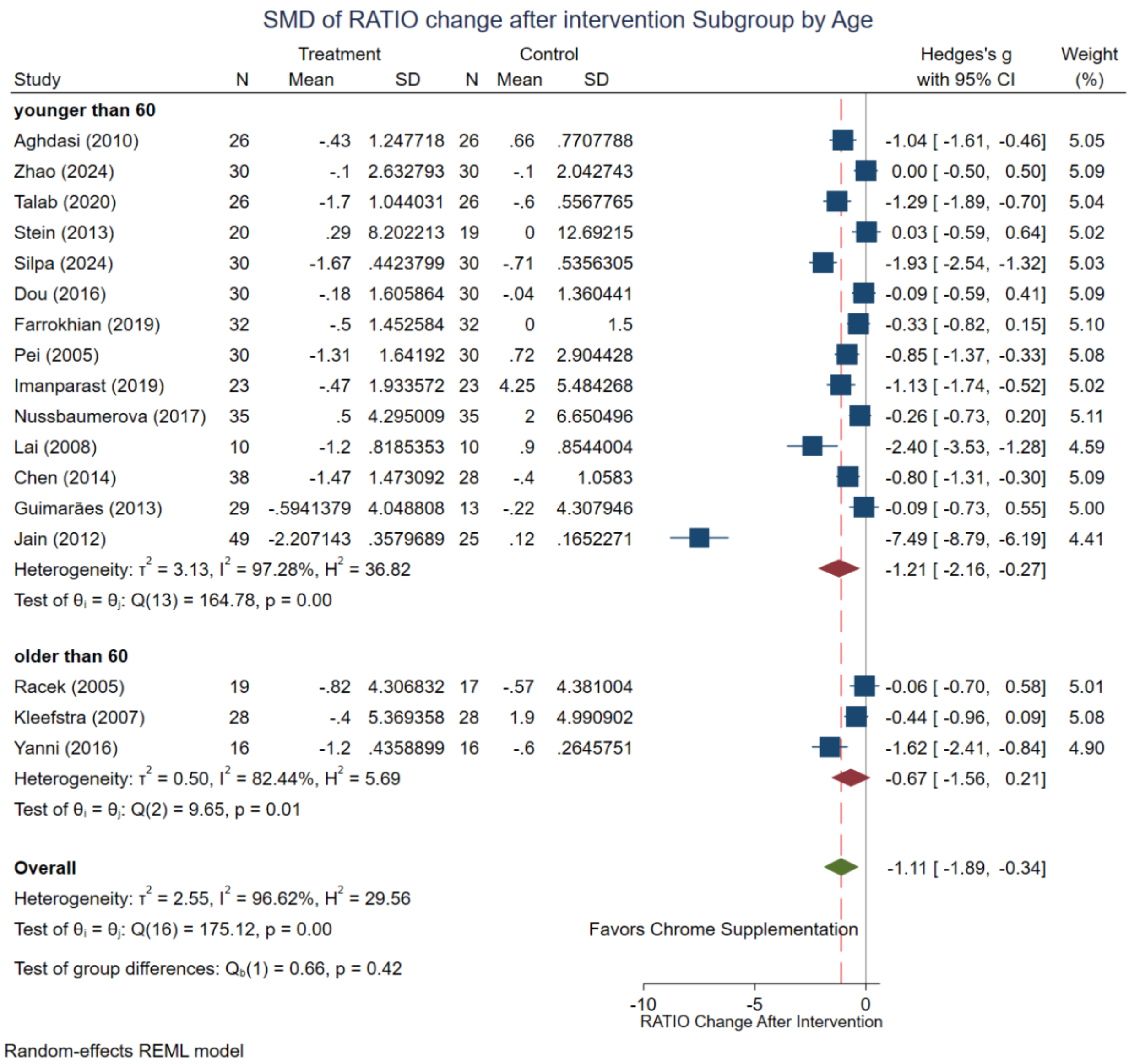
Appendix 2: Forest plot for subgroup analysis on HOMA-IR (Homeostasis Model Assessment for Insulin Resistance) ratio based on the chromium type



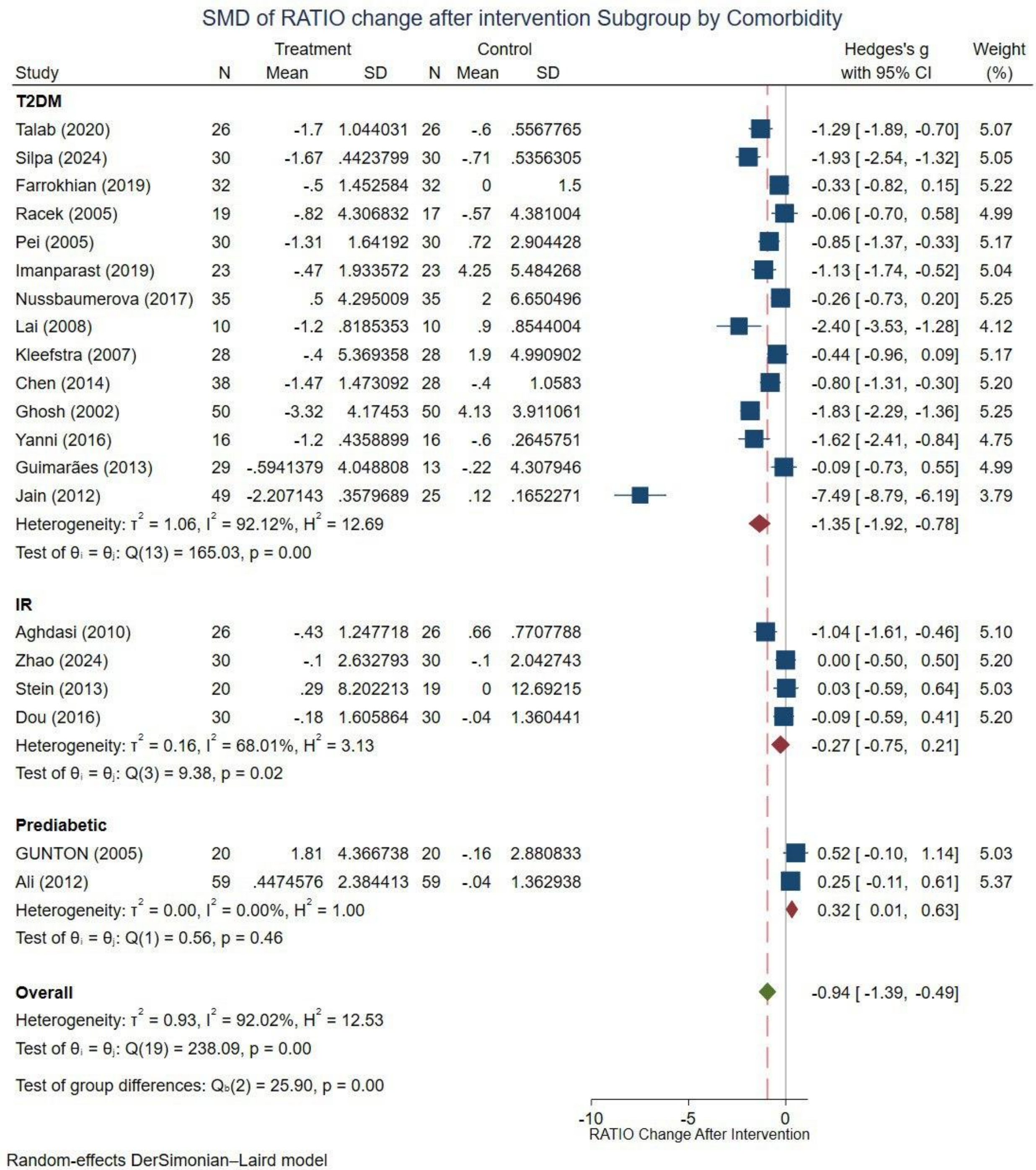
Appendix 3: Forest plot for subgroup analysis on HOMA-IR (Homeostasis Model Assessment for Insulin Resistance) ratio based on the chromium dose



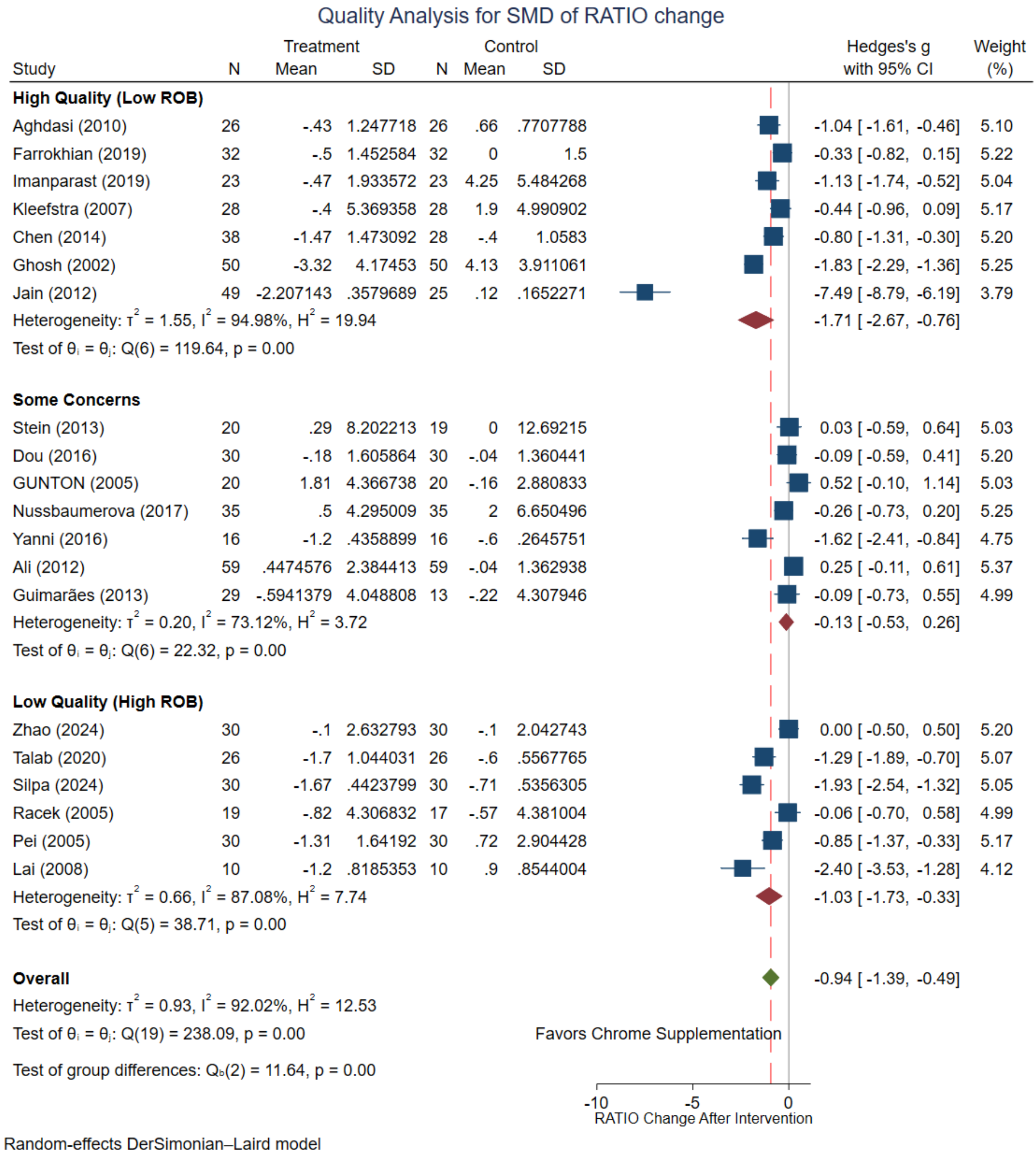
Appendix 4: Forest plot for subgroup analysis on HOMA-IR (Homeostasis Model Assessment for Insulin Resistance) ratio based on the duration of intervention



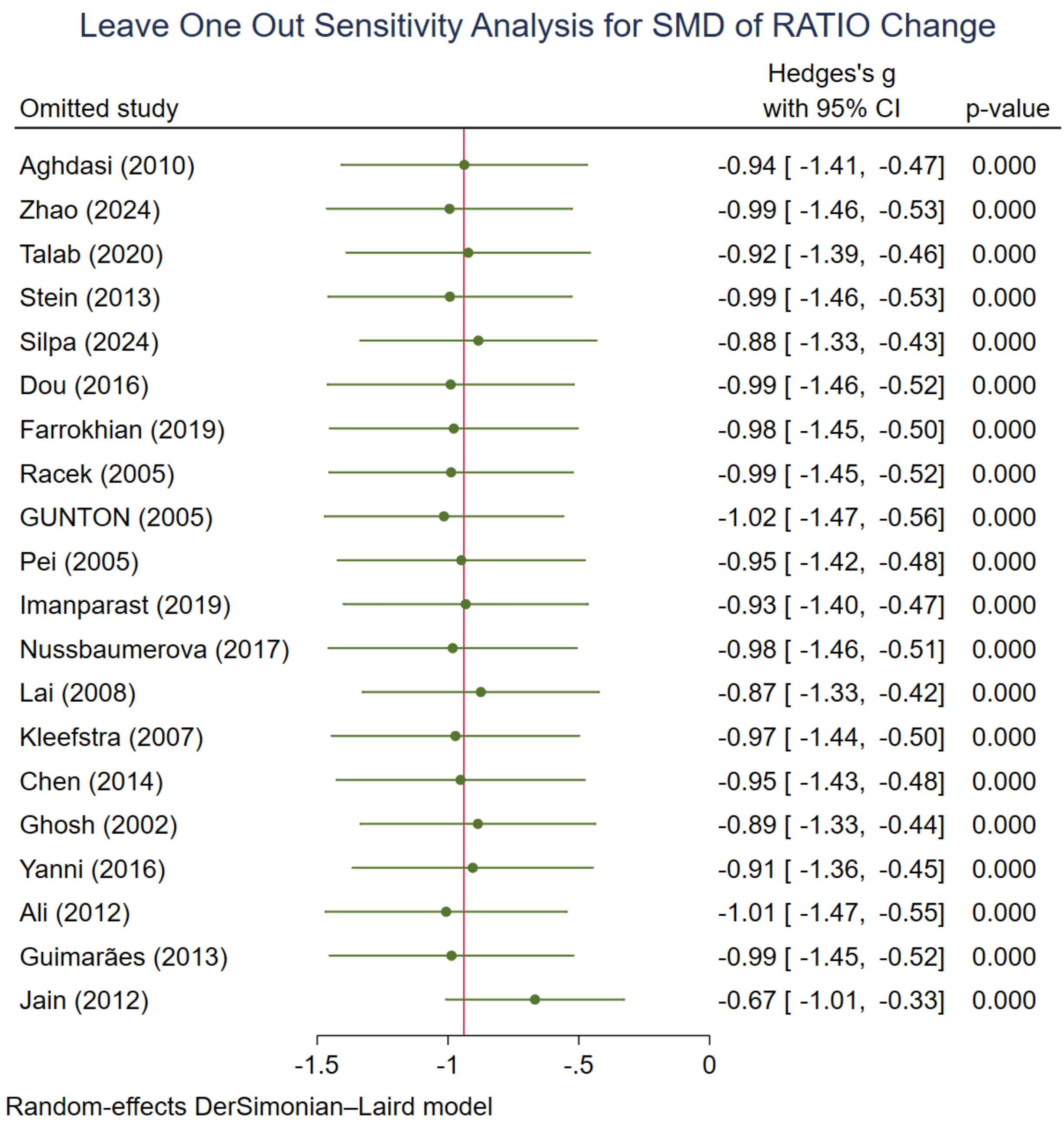
Appendix 5: Forest plot for subgroup analysis on HOMA-IR (Homeostasis Model Assessment for Insulin Resistance) ratio based on the population age



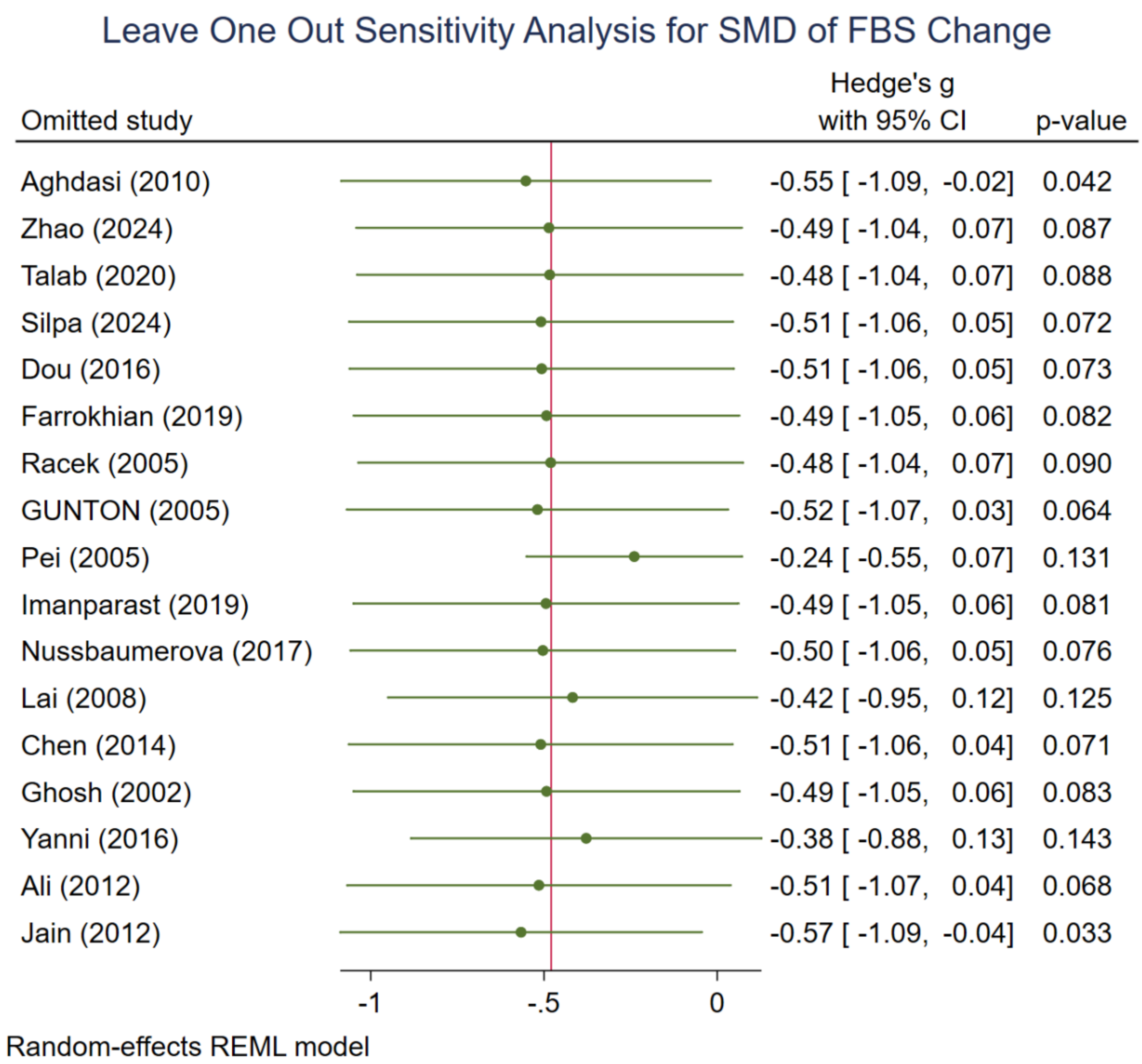
Appendix 6: Forest plot for subgroup analysis on HOMA-IR (Homeostasis Model Assessment for Insulin Resistance) ratio based on the underlying condition



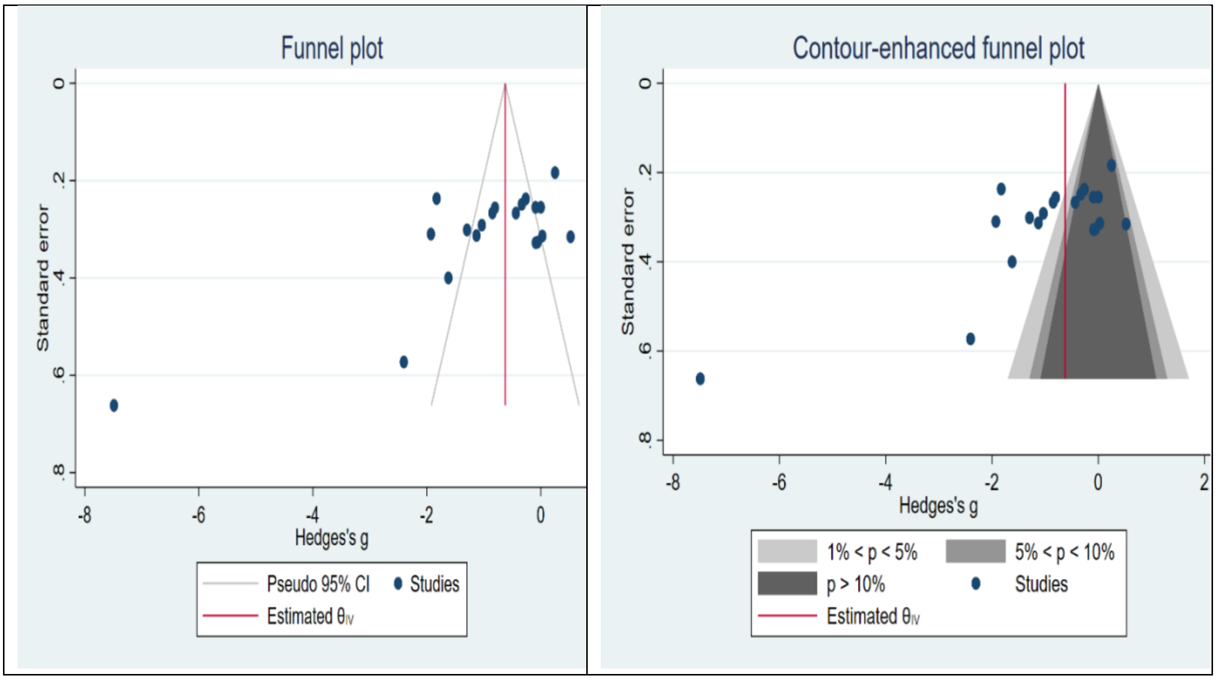
Appendix 7: Forest plot for subgroup analysis on HOMA-IR (Homeostasis Model Assessment for Insulin Resistance) ratio based on the quality of the studies



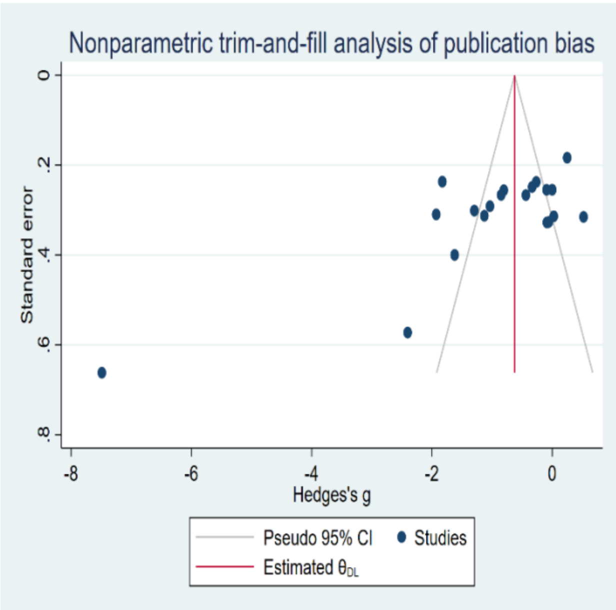
Appendix 8: Forest plot for sensitivity analysis based on the leave-one-out method of HOMA-IR (Homeostasis Model Assessment for Insulin Resistance) ratio



Appendix 9: Forest plot for sensitivity analysis based on the leave-one-out method of FBS (fasting blood sugar)



Appendix 10: Funnel plot for risk of publication bias assessment of the SMD of HOMA-IR (Homeostasis Model Assessment for Insulin Resistance) ratio



Appendix 11: Funnel plot for risk of publication bias assessment based on the trim and fill method of the SMD of HOMA-IR (Homeostasis Model Assessment for Insulin Resistance) ratio

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Differential Effects of Exercise on the Lipid Profile of Normogycemic Offspring of T2DM Patients in Sagamu, South West Nigeria

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Abstract
Background: The primary causes of Type 2 Diabetes Mellitus (T2DM) are largely unknown but abnormal lipid Profile pattern has been reported to be a risk factor for the T2DM Objectives: This study was designed to assess the effect of exercise on lipid profile in offspring of T2DM parents compared with offspring of non-diabetic parents. Design: This study involved purposive selection of 100 offspring of T2DM parents attending Diabetic Clinic of Olabisi Onabanjo University Teaching Hospital, Sagamu and 100 offspring of non-diabetic parents who are undergraduate students aged between 25 and 50 years. Each participant followed a protocol of graded exercise using ‘‘tummy trimmer’’ everyday spending 30-45 minutes daily for 24weeks. Blood samples were obtained after an overnight fasting for determination of lipid profile using standard methods at baseline, six weeks, 12 weeks, 18 weeks and 24 weeks, respectively. Data were analysed using descriptive statistical analysis. Results: In ODP, the mean TC significantly reduced from 150.52mg/dl + 45.56 at baseline to 127.78mg/dl+38.50 after six months of exercise (p=0.001). The mean HDL significantly increased from 44.73mg/dl + 13.01 at baseline to 58.95mgdl+17.25 after six months of exercise(p=0.001). In OCP, the mean TC significantly reduced from 158.35mg/dl + 37.11 at baseline to 148.26mg/dl+34.77 after six months of exercise (p=0.001). The mean HDL significantly increased from 56.57mg/dl + 11.10 at baseline to 65.20mgdl+12.18 after six months of exercise(p=0.001). Conclusions: There is reduction in lipid profiles in all the participants who engaged in exercise. The reduction is more in the study group.

Keywords: Offspring, T2DM, Lipid Profile, HDL, Total Cholesterol

1. Introduction

Diabetes mellitus, commonly known as diabetes, is a disorder of intermediary carbohydrate, protein and lipid metabolism. It is characterized by hyperglycemia, glucosuria, polydipsia, polyuria, polyphagia and weight loss. It is usually accompanied by secondary alterations in glucose, fat and protein metabolism, leading to various biochemical disorders. It is characterized by peripheral insulin resistance, impaired regulation of hepatic glucose production with declining β-cell function and consequently leading to β-cell failure (Bacha et al, 2010). Type 2 Diabetes Mellitus (Type 2DM) is characterized by a combination of peripheral insulin resistance with inadequate insulin secretion by pancreatic beta cells. Insulin resistance has been associated with elevated levels of free fatty acids and pro-inflammatory cytokines in plasma, leading to decreased glucose transport into muscle cells, elevated hepatic glucose production, and pronounced breakdown of fat. Researchers have found that obesity and diabetes are inter-connected. Many people who are obese are at high risk of developing T2DM, particular if a close family member is affected with T2DM. Researchers have not yet discovered a specific gene that causes obesity although, various genes are considered to play a role. There seems to be a connection between abdominal fat and diabetes, hence anything that will decrease abdominal fat will likely reduce diabetes (Taiwo et al 2017). Exercise has been known to ameliorate the effects of diabetes by improving insulin sensitivity and lipid profile. Offspring of T2DM have greater chance of developing diabetes mellitus (Fegan et al, 1998). Insulin resistance is one of the pathophysiologic mechanisms for the development and sustenance of T2DM (Gulli et al, 1992). It is the aim of this work is to study the effect of exercise on lipid profile in normoglycemic offspring of T2DM patients.

2. Method

The study involved purposive selection of 100 normoglycemic offspring of T2DM patients attending Diabetic clinic of Olabisi Onabanjo Teaching Hospital, Sagamu. and 100 offspring of normotensive persons living in Sagamu aged between 25 and 50 years. The blood glucose was measured using standard method in order to assert that they are normoglycemic offspring. The subjects had to go through exercise procedure using Tummy trimmer exercise apparatus.

Tummy trimmer, a portable lightweight equipment was selected for the study. It is an in-door anaerobic equipment. It is compact and can fit right in the subject's brief case.

During each phase of exercise the Tummy trimmer, a portable lightweight equipment, is held at the two handles and the soles of the two feet are put inside the pedal rest while the subject assumes different positions. The subject will then pull the tummy trimmer's spring towards himself or herself either while lying flat or sitting up on the floor or carpeted hard surface.

Subject sits up with leg straight, leans his or her body backwards until completely lying back with head on floor. He/she returns to sitting position in harmonic fashion. The subject was advised to start slowly and work up to repetitions as she/he feel comfortable with harmoniously.

The subject was advised to lie flat on floor, extend his/her legs straight up in the air. He will be keeping his/her back on the floor and raises lower legs without bending them. The subject was advised to sit erect with legs straight, he/she raise handle to tummy height using arms only.

Finally, subject was advised to lie flat on the floor while he/she bends knees up to his/her chest. He/She makes a circular motion pushes their feet up and then round towards the floor again. The different positions were observed for exercise period of 30 to 40 minutes (a video clip of the exercise procedure was shown to the subject before the commencement of the exercise). Safety Warnings were given to the subject as follows:(1) He/She should not use the equipment while standing (2) Equipment should be used only with sneakers or bare-foot. (3) He/She should not let the unit slip off his/her feet (4) He/She should not allow the spring to stretch beyond 105centimeters.

Each subject was advised: (1) He/She to undergo the 4 phases of exercise between 30 and 40 minutes daily (either in the mornings or evenings). (2) He/She to contact the researcher on cell phone anytime when he/she has any problems with the unit. (3) There were regular cell phone calls made to each of the subjects by the research assistant to ensure compliance with exercise schedule. (4) The research assistant called them on cell phone and sent s.m.s (Short Message Service) to them to keep return appointments every four weeks. This was done one or two days before appointment schedule.

Determination of Lipid Profile Lipid Profile was determined by following the protocol of Trinder, (1969 as described by Ekor, Osonuga, Odewabi and Oritogun (2010) (Burns et al, 2001). Principle Total cholesterol level was measured spectrophotometrically using standard laboratory supplied by BIOLABO, France. Cholesterol esters in the presence of cholesterol esterase cholesterol and free fatty acids are separated. The cholesterol formed reacts with oxygen in the presence of cholesterol oxidase to form cholesten-4-one-3 and hydrogen peroxide. The hydrogen peroxide formed reacts with phenol and 4-amino-antipyrine in the presence of peroxidase to give aminoneimine (pinkish in colour) and water. The intensity of the pink/red colour formed is proportional to the cholesterol concentration. The procedure employed was as follows: The reagent was prepared by adding 5ml of the buffer (1.75mool/L Amino-2-methyl-2-propanol-1) to 5ml of the Chromogen mixture (76umol/L 0-Cresolphtalein Complexon, 3.36mmol/L/L 8 – Hydroxy-Quinoline, 25mmol/L HCI) and allowed to stand for an hour at room temperature. The reagent solution was prepared by adding equal volumes of the buffer and 5mmol/L Chloro-4-phenol) and the enzyme mixture (100U/L Cholesterol oxidase, 70U/L Cholesterol esterase, 1200U/L peroxidase, 2mmol/L Cholic acid Sodium salt, 0.3mmol Amino antipyrine) and allowed to stand for 5 – 10 minutes while mixing gently at room temperature. To 10µL of each test sample or standard (5.17mmol/L Cholesterol) was added 1ml of the reagent mixture. This was incubated at 37oC for 5 minutes. The absorbance of the mixture was taken against the blank at a wavelength of 500nm. The blank was made up of 10µL of distilled water and 1ml of the reagent mixture. The cholesterol concentration was determined as follows Total cholesterol concentration (mg/dl) = Absorbance sampleX Standard concentration Absorbance standard HDL cholesterol level was measured spectrophotometrically using standard lab kits supplied by BIOLABO, France. Low density lipoproteins (LDL) contained in serum are precipitated by addition of phosphotungstic acid and magnesium chloride. High density lipoproteins (LDL) which remains in the supernatant (obtained after centrifugation) react with the cholesterol reagent and proportionally with the cholesterol standard. The procedure followed was as follows: equal volumes of the serum and reagent mixture (13.9mmol/L phosphotungstic acid and 570mmol/L magnesium chloride) were mixed together and allowed to stand for 10 minutes at room temperature. The reaction mixture was then centrifuged for 10 minutes at 4000rpm to get a clear supernatant. This supernatant was used as sample to get the HDL cholesterol concentration in the serum sample. 1000ul of the Cholesterol reagent was added to test tubes labeled blank, standard and sample containing 50µl water, 50µl of the cholesterol standard and 50µl of the sample respectively. This was well mixed and incubated for 10mins at 37oC. The absorbance of the end sample against the blank was taken at 505nm. HDL cholesterol concentration (mg/dl) = Absorbance sampleX Standard concentration Absorbance standard Triglycerides level was measured spectrophotometrically using standard tab kits supplied BIOLABO, France Triglycerides in the presence of lipase form glycerol free fatty acids. Glycerol formed reacts reversibly with adenosine triphosphate (ATP) in the presence of glycerol lipase to form glycerol – 3 – phosphate and ADP. The glycerol 3 phosphate also reacts reversibly with oxygen in the presence of glycerol - 3- phosphate oxidase to form dihydroxyacetone phosphate and hydrogen peroxide. The hydrogen peroxide then reacts with chlorophenol and amino antipyrine in the presence of peroxidase to form quinoneimine (pink) and water. The intensity of the pink/red colour formed is proportional to the triglyceride concentration. The reagent solution was prepared by adding equal volumes of the buffer (3.5mmol/Lchloro-4-phenol, 6mmol/L Magnesium chloride 100mmol/L PIPES) and the enzyme mixture 500U/I Lipase, 1800U/I peroxidase, 400U/I Glycerol 3-phosphate oxidase, 1000U/I Glycerol (lipase. 0.30mmol 4 Amino antipyrine. 1.72mmol/I Adenosine triphosphate Na) and allowed to stand for 5 – 10minutes. To 10µL of each test sample of standard (Glycerol 200mg/dl) was added 1mI of the reagent mixture. This was incubated at 37oC for 5minutes. The absorbance of the mixture was taken against the blank at a wavelength of 500nm. The blank was made up of 10µL of distilled H20 and 1ml of the reagent mixture. The triglyceride concentration was determined as follows. Triglyceride concentration (mg/dl) = Absorbance sample X Standard concentration Absorbance standard.

Ethical Approval and Informed Consent Ethical clearance for the study was obtained from the Committee on Human Research publication and Ethics of the School of Olabisi Onabanjo University teaching Hospital (OOUTH), Sagamu (with number HREC/OOU/0030/2024). All participants (200) of this study signed an informed consent form, in accordance to the committee regulations, before answering the questionnaire, blood pressure measurement and taking blood samples. Statistical analysis was carried out by using student test. The data obtained was analysed using computer statistical programme package SPSS version 15.0 Probability value of P less than 0.05 was considered statistically significant.

3. Results

Table 1: Variations in the anthropometric parameters, FBS and lipid profile at baseline between the ODP and OCP

Variable	ODP (n=100)	OCP (n=100)	T	P
Age (years)	26.02 ± 5.14	26.11 ± 5.92	0.115	0.909
Gender [n (%)]				
Male	50 (50%)	50 (50%)	0.000	1.000
Female	50 (50%)	50 (50%)		
Height (m)	1.63 ± 0.09	1.65 ± 0.07	1.852	0.066
Weight (kg)	64.10 ±7.77	61.01 ± 6.24	3.108	0.002*
BMI	24.13 ± 3.09	22.34 ± 2.49	4.515	<0.001*
FBS (mg/dl)	91.12 ± 10.27	70.82 ±11.83	12.958	<0.001*
TC (mg/dl)	150.52 ± 45.56	158.35 ± 37.11	1.333	0.184
TG (mg/dl)	100.25 ± 40.11	70.58 ± 21.57	6.515	<0.001*
HDL (mg/dl)	44.73 ±13.01	56.57 ± 11.10	6.921	<0.001*
LDL (mg/dl)	80.93 ± 36.69	87.25 ± 34.86	1.249	<0.001*
SBP (mmHg)	112.33 ± 9.56	108.64 ± 11.53	2.464	0.015*
DBP (mmHg)	72.11 ± 8.53	70.09 ± 8.40	1.687	0.093
Mean arterial BP	58.70 ± 10.10	57.24 ± 8.51	1.108	0.269
Pulse pressure	40.22 ± 8.93	38.55 ± 7.12	1.462	0.145

* Significant at p< 0.05
ODP – Offsprings of diabetic parent
OCP - Offsprings of control parent

There were one hundred participants (100) in each study group and control group. The mean age of ODP and OCP were 26.02 years+5.14 and 26.11years+5.92 respectively. There were 50 males 50 females in each group. The mean height in ODP and OCP were 1.63m+0.09 and1.65m+0.07 respectively (p=0.066). The mean weight in ODP and OCP were 64.10kg+7.77 and 61.01kg+6.24 (p=0.002*). The mean BMI in ODP and OCP were 24.13kgm2+3.09 and 22.34kgm2+2.49(p=0.001*). The mean FBS in ODP and OCP were 91.12mg/dl+10.07 and 70.82mg/dl+11.83 (p=0.001*). The mean TC in ODP and OCP were 150.52mg/dl+45.56 and 158.35mg/dl+37.11 (p=0.184) The mean TG in ODP and OCP were 100.25mg/dl+40.11 and 70.58mg/dl+21.57 (p=0.001*) The mean HDL in ODP and OCP were 44.73mg/dl+13.01 and 56.57mg/dl+11.10 (p=0.001*) The mean LDL in ODP and OCP were 80.93mg/dl+36.69 and 87.25mg/dl+34.86 (p=0.001*). The mean mean arterial BP in ODP and OCP were 58.70mmHg+10.10 and 57.24mmHg+8.51 (p=0.269).

Table 2: Variations in the anthropometric parameters, FBS, lipid profile and hypertensive parameters during 6 months follow-up in ODP

Variable	Baseline	1 month	2 months	3 months	4 months	5 months	6 months
Weight	64.10 ± 7.77	61.44 ± 7.52	59.66 ± 7.29	58.01 ± 7.26	55.41 ± 6.48	53.15 ± 6.50	52.64 ± 6.44
BMI	24.13 ± 3.09	23.13 ± 2.99	22.46 ± 2.90	21.84 ± 2.91	20.88 ± 2.70	20.02 ± 2.64	19.83 ± 2.64
FBS	91.12 ± 10.27	87.48 ± 9.86	84.97 ± 9.53	81.99 ± 9.16	79.14 ± 8.88	77.91 ± 8.75	76.64 ± 8.67
TC	150.52 ± 45.56	144.51 ± 44.05	138.74 ± 42.08	134.58 ± 40.71	129.89 ± 39.24	127.92 ± 38.61	127.78 ± 38.50
TG	100.25 ± 40.11	97.17 ± 38.91	94.41 ± 37.87	90.89 ± 36.45	87.48 ± 35.06	86.19 ± 34.69	84.90 ± 34.13
HDL	44.73 ±13.01	47.90 ± 13.89	51.56 ± 15.16	54.30 ± 15.89	56.47 ± 16.51	57.86 ± 16.88	58.95 ± 17.25
LDL	80.93 ± 36.69	77.79 ± 35.17	75.55 ± 34.29	72.90 ± 33.01	70.37 ± 31.86	69.30 ± 31.31	68.22 ± 30.80
SBP	112.33 ± 9.56	107.72 ± 9.31	104.51 ± 9.11	100.33 ± 8.87	98.83 ± 8.75	97.36 ± 8.66	95.89 ± 8.53

DBP	72.11 ± 8.53	69.17 ± 8.18	67.10 ± 7.96	64.32 ± 7.69	63.37 ± 7.52	62.47 ± 7.44	61.52 ± 7.35
Mean arterial BP	58.70 ± 10.10	56.31 ± 9.72	54.62 ± 9.46	52.32 ± 9.10	51.55 ± 8.88	50.84 ± 8.78	50.06 ± 8.69
Pulse pressure	40.22 ± 8.93	38.56 ± 8.75	37.42 ± 8.58	36.00 ± 8.22	35.46 ± 8.22	34.90 ± 7.99	34.37 ± 7.91

In ODP study group, the mean weight reduced from 64.10kg + 7.77 at baseline to 52.64kg+6.44 after six months of exercise (p=0.001). The mean BMI significantly reduced from 24.13kg/m2 + 3.09 at baseline to 19.83kg/m2+2.64 after six months of exercise (p=0.001). The mean FBS significantly reduced from 91.12mg/dl + 10.27 at baseline to 76.64mg/dl+8.67 after six months of exercise (p=0.001). The mean TC significantly reduced from 150.52mg/dl + 45.56 at baseline to 127.78mg/dl+38.50 after six months of exercise (p=0.001). The mean TG significantly reduced from 100.25mg/dl + 40.11 at baseline to 84.90mg/dl+34.13 after six months of exercise. The mean HDL significantly increased from 44.73mg/dl + 13.01 at baseline to 58.95mgdl+17.25 after six months of exercise(p=0.001). The mean LDL significantly reduced from 80.93mg/dl + 36.69 at baseline to 68.22mg/dl+30.80 after six months of exercise (p=0.001). The mean Mean Arterial Pressure significantly reduced from 58.70mmHg + 10.10 at baseline to 50.06mmHg+8.69 after six months of exercise(p=0.001).

Table 3: Variations in the anthropometric parameters, FBS, lipid profile and hypertensive parameters during 6 months follow-up in OCP

Variable	Baseline	1 month	2 months	3 months	4 months	5 months	6 months
Weight	61.01 ± 6.24	60.01 ± 6.25	59.57 ± 6.09	58.96 ± 6.13	58.04 ± 6.07	57.18 ± 5.84	56.79 ± 6.18
BMI	22.34 ± 2.49	21.97 ± 2.45	21.82 ± 2.43	21.59 ± 2.43	21.25 ± 2.35	20.94 ± 2.34	20.80 ± 2.41
FBS	70.82 ±11.83	69.73 ± 11.76	68.98 ± 11.50	68.21 ± 11.39	67.60 ± 11.20	66.56 ± 11.04	65.58 ± 10.91
TC	158.35 ± 37.11	155.79 ± 36.15	153.79 ± 36.15	152.16 ± 35.81	150.57 ± 35.39	148.42 ± 34.85	148.26 ± 34.77
TG	70.58 ± 21.57	69.97 ± 21.55	69.06 ± 21.09	68.05 ± 20.73	67.58 ± 20.54	66.60 ± 20.28	65.61 ± 19.97
HDL	56.57 ± 11.10	57.71 ± 11.41	59.02 ± 11.59	60.75 ± 11.87	62.38 ± 12.15	63.96 ± 12.53	65.20 ± 12.80
LDL	87.25 ± 34.86	85.92 ± 34.46	85.13 ± 34.19	84.32 ± 33.81	83.51 ± 33.55	82.26 ± 32.95	81.02 ± 32.54
SBP	108.64 ± 11.53	106.88 ± 11.56	105.74 ± 11.50	104.41 ± 11.45	102.92 ± 11.24	101.38 ± 11.03	99.85 ± 10.88
DBP	70.09 ± 8.40	69.05 ± 8.35	68.35 ± 8.31	67.39 ± 8.16	66.39 ± 8.03	65.40 ± 7.90	64.44 ± 7.78
Mean arterial BP	57.24 ± 8.51	56.44 ± 8.47	55.89 ± 8.52	55.05 ± 8.29	54.21 ± 8.19	53.41 ± 8.06	52.63 ± 7.96
Pulse pressure	38.55 ± 7.12	37.83 ± 7.25	37.39 ± 7.45	37.02 ± 7.28	36.53 ± 7.23	35.98 ± 7.07	35.41 ± 7.05

Table 3: Variations in the anthropometric parameters, FBS, lipid profile and hypertensive parameters at baseline and 6 months follow-up in ODP and OCP

Variable	Baseline	6 months	Av % change	T	P
Weight	64.10 ± 7.77	52.64 ± 6.44	-17.86	54.613	<0.001*
BMI	24.13 ± 3.09	19.83 ± 2.64	-17.86	57.075	<0.001*
FBS	91.12 ± 10.27	76.64 ± 8.67	-15.89	68.220	<0.001*
TC	150.52 ± 45.56	127.78 ± 38.50	-15.06	30.897	<0.001*
TG	100.25 ± 40.11	84.90 ± 34.13	-15.38	24.341	<0.001*

HDL	44.73 ±13.01	58.95 ± 17.25	31.80	-31.544	<0.001*
LDL	80.93 ± 36.69	68.22 ± 30.80	-15.71	21.086	<0.001*
SBP	112.33 ± 9.56	95.89 ± 8.53	-14.65	77.278	<0.001*
DBP	72.11 ± 8.53	61.52 ± 7.35	-14.69	66.044	<0.001*
Mean arterial BP	58.70 ± 10.10	50.06 ± 8.69	-14.69	40.648	<0.001*
Pulse pressure	40.22 ± 8.93	34.37 ± 7.91	-14.55	24.176	<0.001*

* Significant at p< 0.05

Variable	Baseline	6 months	Av % change	T	P
Weight	61.01 ± 6.24	56.79 ± 6.18	-6.92	22.675	<0.001*
BMI	22.34 ± 2.49	20.80 ± 2.41	-6.92	22.273	<0.001*
FBS	70.82 ±11.83	65.58 ± 10.91	-7.38	31.748	<0.001*
TC	158.35 ± 37.11	148.26 ± 34.77	-6.33	23.855	<0.001*
TG	70.58 ± 21.57	65.61 ± 19.97	-7.02	22.400	<0.001*
HDL	56.57 ± 11.10	65.20 ± 12.80	15.31	-35.589	<0.001*
LDL	87.25 ± 34.86	81.02 ± 32.54	-7.12	22.081	<0.001*
SBP	108.64 ± 11.53	99.85 ± 10.88	-8.09	39.531	<0.001*
DBP	70.09 ± 8.40	64.44 ± 7.78	-8.06	37.664	<0.001*
Mean arterial BP	57.24 ± 8.51	52.63 ± 7.96	-8.03	22.687	<0.001*
Pulse pressure	38.55 ± 7.12	35.41 ± 7.05	-8.15	12.565	<0.001*

* Significant at p< 0.05

In OCP control group, the mean weight reduced from 61.01kg + 6.24 at baseline to 56.79kg+6.18 after six months of exercise(p=0.001). The mean BMI significantly reduced from 22.34kg/m2 + 2.49 at baseline to 20.80kg/m2+2.41 after six months of exercise (p=0.001). The mean FBS significantly reduced from 70.82mg/dl + 11.83 at baseline to 65.58mg/dl+10.91 after six months of exercise (p=0.001). The mean TC significantly reduced from 158.35mg/dl + 37.11 at baseline to 148.26mg/dl+34.77 after six months of exercise (p=0.001). The mean TG significantly reduced from 70.58mg/dl + 21.57 at baseline to 65.61mg/dl+19.97 after six months of exercise (p=0.001). The mean HDL significantly increased from 56.57mg/dl + 11.10 at baseline to 65.20mgdl+12.18 after six months of exercise(p=0.001). The mean LDL significantly reduced from 87.25mg/dl + 34.86 at baseline to 81.02mg/dl+32.54 after six months of exercise (p=0.001). The mean Mean Arterial Pressure significantly reduced from 57.24mmHg + 8.51 at baseline to 52.63mmHg+7.96 after six months of exercise(p=0.001).

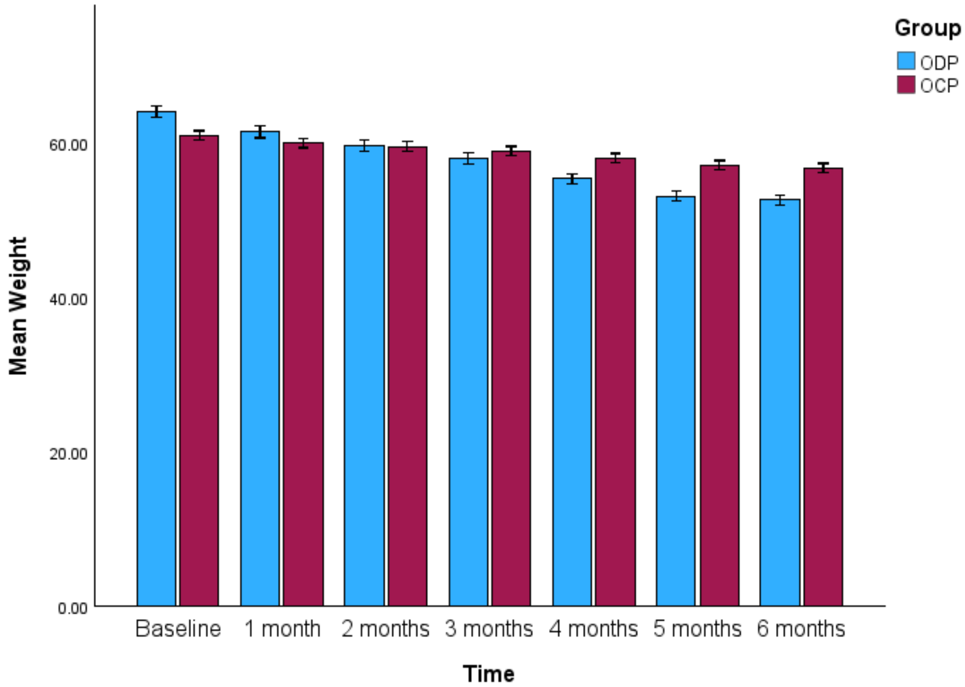

Figure 1: Variation in mean weight in ODP and OCP over the periods of study.

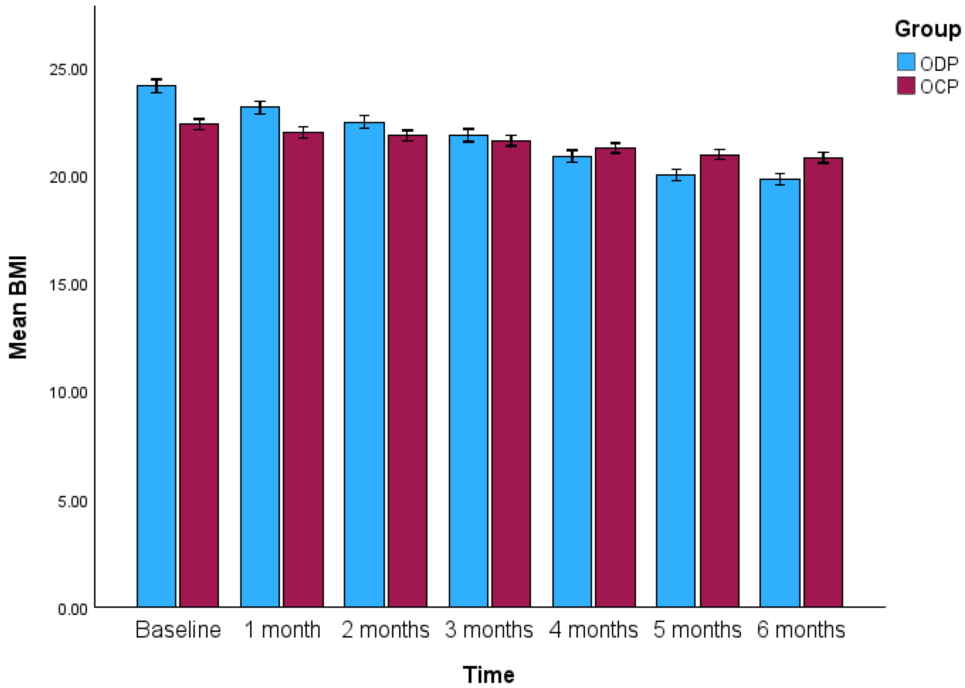

Figure 2: Variation in mean BMI in ODP and OCP over the periods of study.

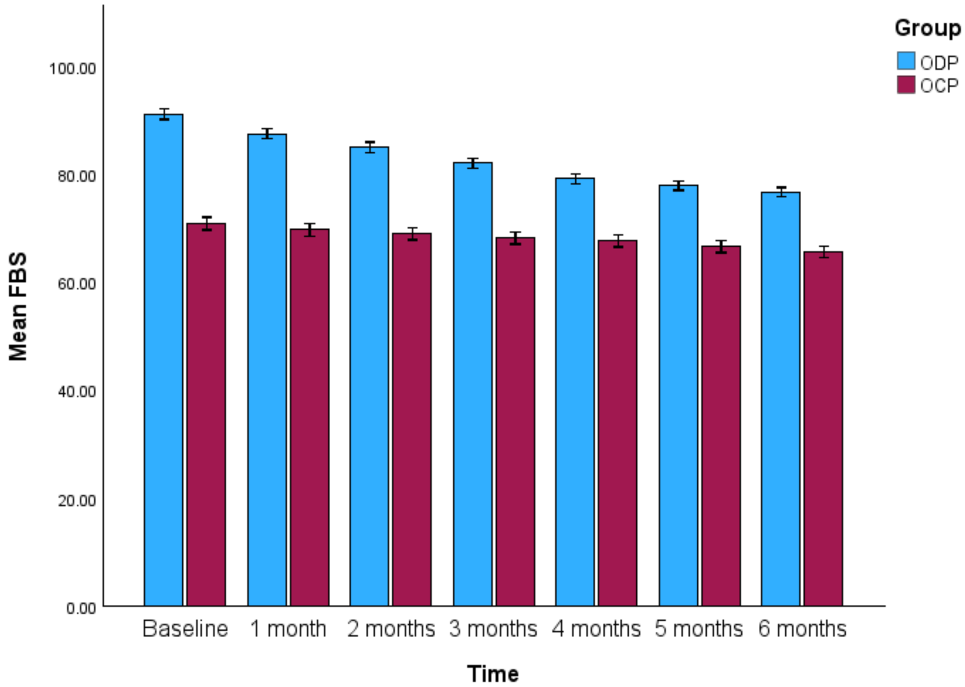

Figure 3: Variation in mean FBSin ODP and OCP over the periods of study.

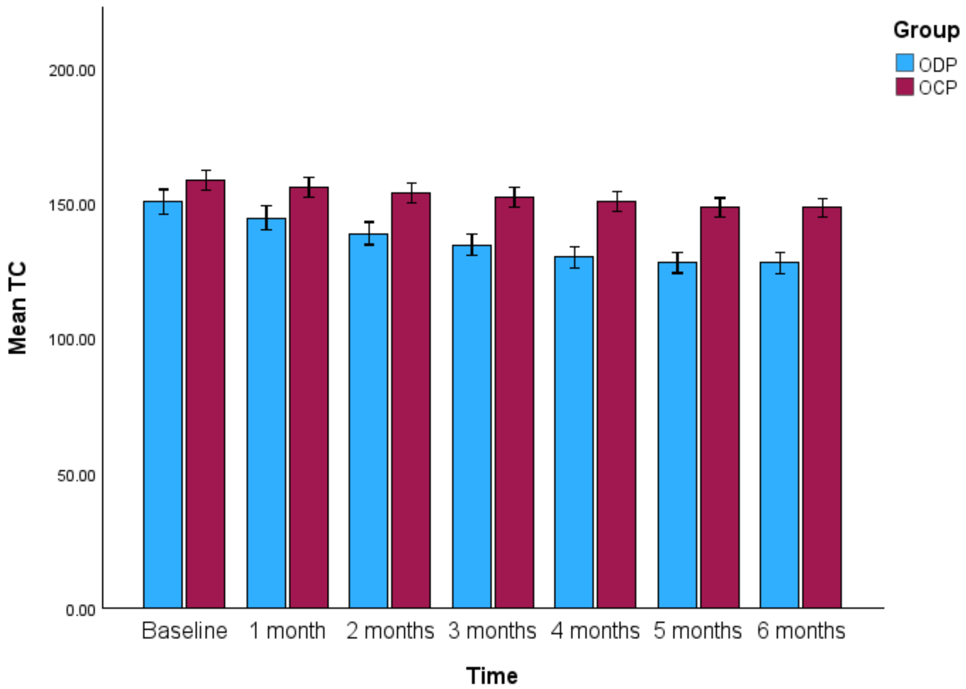

Figure 4: Variation in mean TC in ODP and OCP over the periods of study.

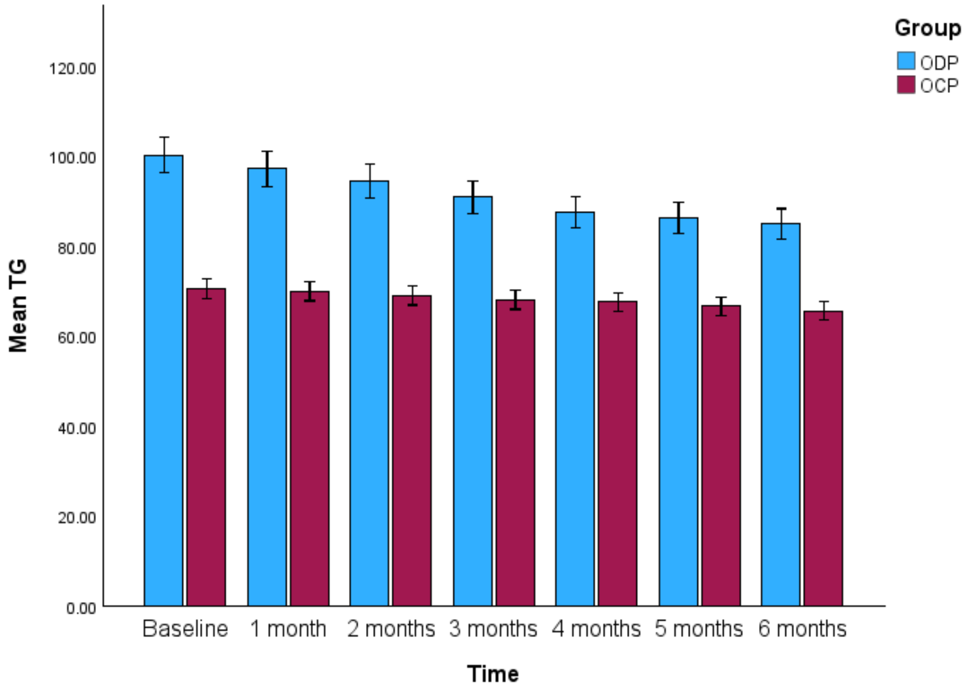

Figure 5: Variation in mean TG in ODP and OCP over the periods of study.

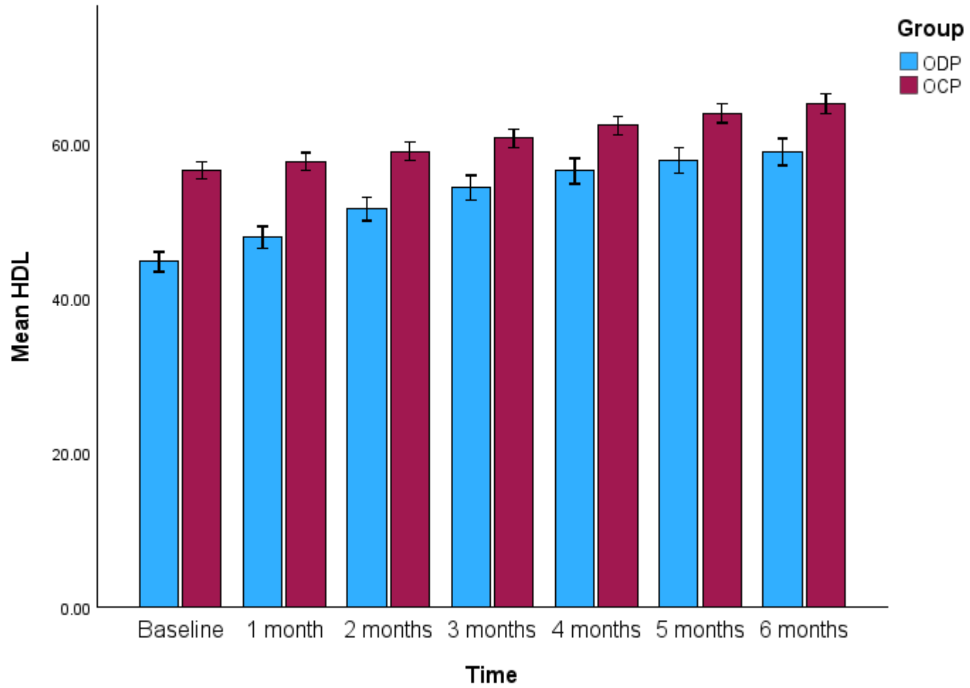

Figure 6: Variation in mean HDL in ODP and OCP over the periods of study.

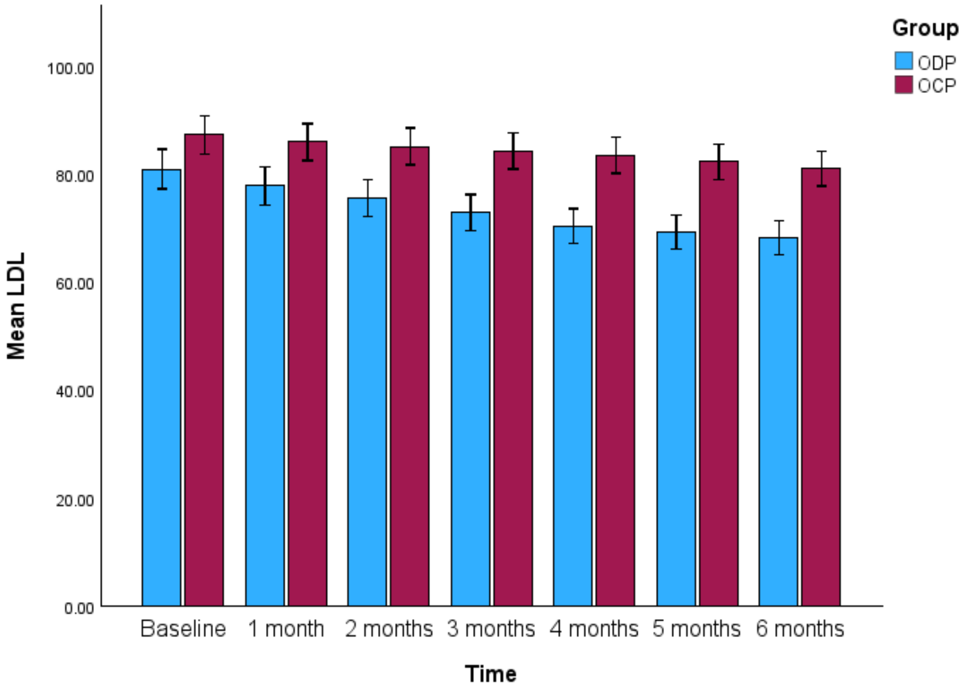

Figure 7: Variation in mean LDL in ODP and OCP over the periods of study.

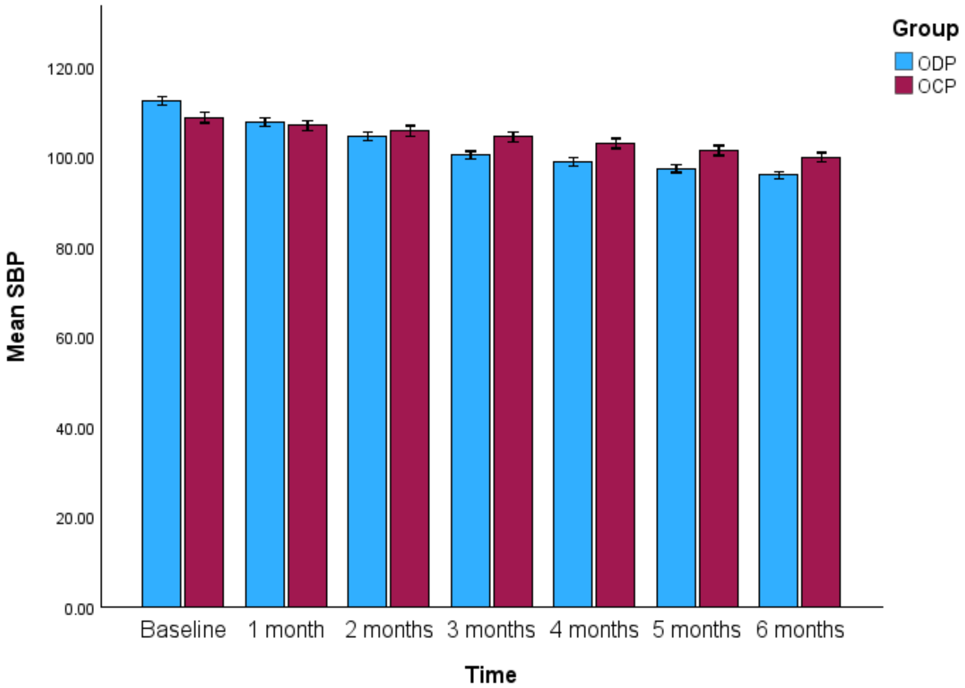

Figure 8:Variation in mean SBP in ODP and OCP over the periods of study.

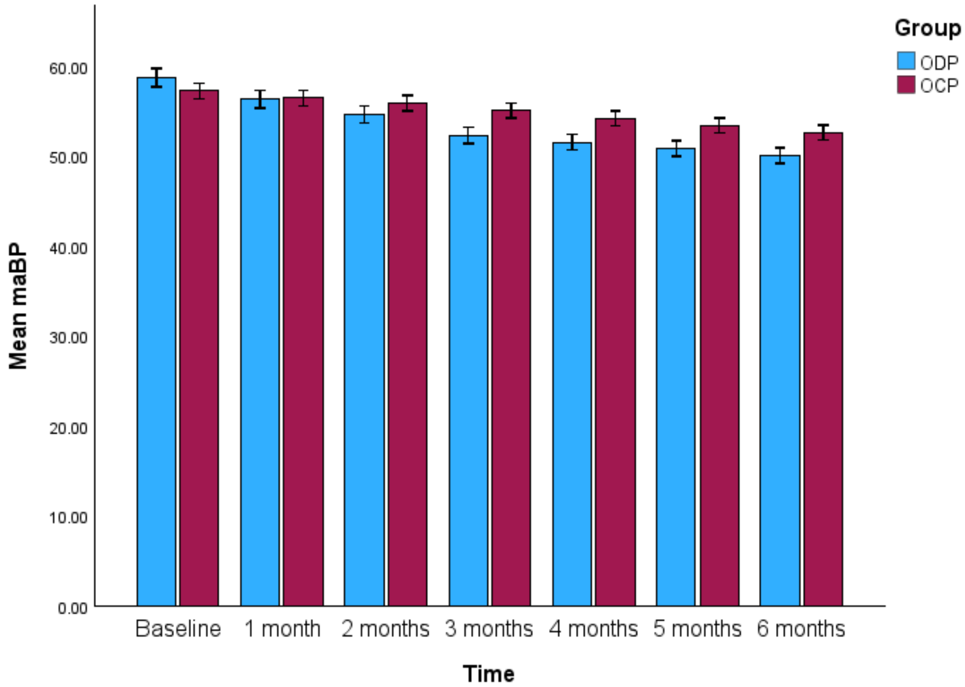

Figure 9: Variation in mean maBP in ODP and OCP over the periods of study.

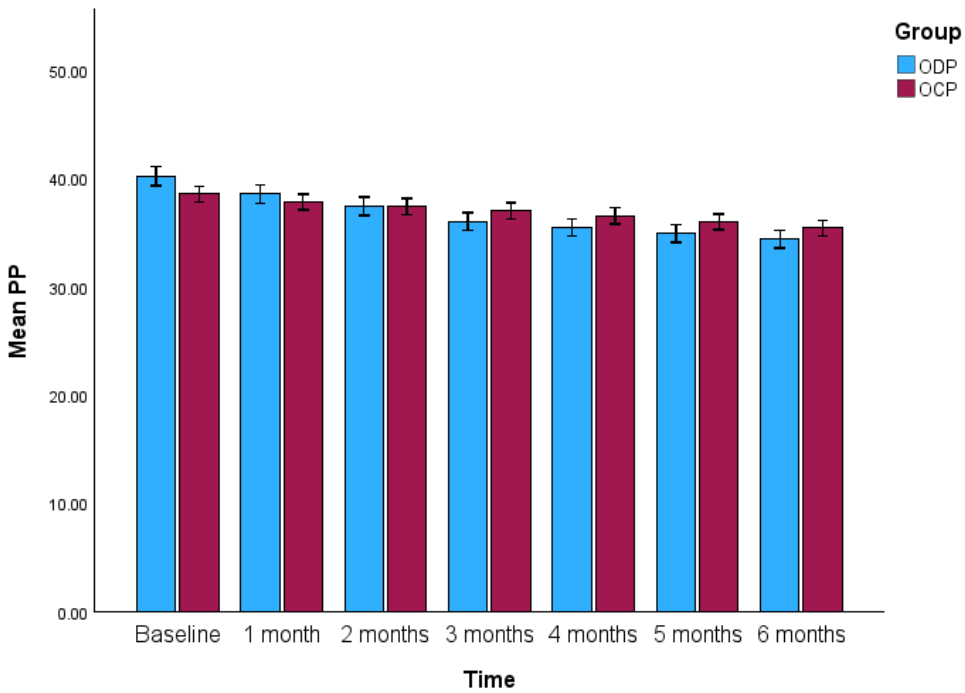

Figure 10: Variation in mean PP in ODP and OCP over the periods of study.

4. Discussion

In this study, lipid profile is the main parameter which was tested in the normoglycemic offspring of type 2 diabetes mellitus patients. Diabetes mellitus is a disorder of intermediary carbohydrate, protein and lipid metabolism associated with high blood glucose level (hyperglycemia) and presence of glucose in the urine (glucosuria). It is associated in many cases by secondary alteration in fat and protein metabolism resulting in an array of biochemical disorders and diabetes mellitus in family members of individuals with type 2 diabetes mellitus (Galbo et al, 1988).

However, it will be instructive to compare these results with the one done by Borghout et. al., 1999 using bicycle ergometer as instrument apparatus to measure lipid profile in normoglycemic offspring of T2DM. Furthermore, regular exercise has been shown to decrease fasting triglyceride concentration in some patients (Fegan et al, 1998). Hannele et al, 1989 studied the effect of body composition and maximal aerobic power on insulin sensitivity. They found that body sensitivity to insulin and lipid profile are directly related to the muscle mass and inversely proportional to adiposity. They also reported that one factor contributing to reduce in insulin sensitivity is obesity which occurred during physical inactivity. Therefore, in this present study, improvement in lipid profile after six months of exercise confirms the importance of physical activity in improving lipid profile in offspring of T2 diabetes patients. Insulin resistance may play a pivotal role in the development and sustanance of diabetic dyslipedemia by influencing several factors such as insulin resistance and type 2 diabetes, promoted efflux of free fatty acids into the liver (Boden et al, 1997, Kelly et al, 1994). Hepatic lipase activity is responsible for hydrolysis of phospholipids in LDL and HDL particles and leads to smaller and denser LDL particles and reduction in HDL (Tan et al, 1995, Zambon et al, 1993) and so leading to rise in serum lipids which is seen in obesity.

Lifestyle interventions such as diet, physical activity, weight loss, and stopping smoking are integral part of any diabetes management plan. Epidemiologic and intervention studies have shown great improvements in the features of diabetic dyslipaedemia such as medical nutrition therapy and physical activity (Kraus et al, 2002, Williams et al, 1990). Exercise is a major therapeutic modality in the management of diabetes mellitus (Laaksonen et, al, 2000). Exercise training has been known to be advantageous in type 2 diabetes mellitus by improving lipid profile (Ibanez et al, 2005), and regular exercise can strengthen antioxidant defenses and may decrease oxidative stress (Kim et al, 1996). Exercises including yoga postures have been shown to play a role in abating type 2 diabetes (Sahay et al, 2002). The yoga postures are slow rhythmic movements which emphasize the stimulation of the organs and glands by easy bending and extensions which do not overstimulates muscles but focus on glandular stimulation (Nayak et al, 2004). A major benefit of non-exhaustive exercise such as yoga is to induce a mild oxidative stress that promote the expression of certain antioxidant enzymes. This is associated with the activation of redox-sensitive signaling pathways (Reid et al, 2001). Obesity, as a result of inactivity in combination with increase food intake, plays a key role in the development of pancreatic beta-cell dysfunction as well as insulin resistance. Various mechanisms mediating this interaction have been identified. It is now well established that a number of circulating hormones, cytokines, and metabolic fuels, such as non-esterified fatty acids (NEFAs), are being released by adipose tissue which can modulate insulin action. An increased mass of stored triglyceride, especially in visceral or deep subcutaneous adipose depots, leads to large adipocytes that are themselves resistant to the ability of insulin to reduce lipolysis. This leads to increased release and circulating NEFA and glycerol levels, both of which aggravate insulin resistance in skeletal muscle (Boden, 1997) and in the liver (Kabir et al, 2005 Peterson, et al, 2005 Ryysy et al, 2000). Ectopic fat storage in hepatocytes, so-called intrahepatic lipids (IHL), has also been associated with the development of hepatic insulin resistance (Ko et al, 2017) and hepatic inflammation, producing non-alcoholic fatty liver disease (Shamizadeh et al, 2016). Our study, however, examines the effect of exercise on the lipid profile of offspring of diabetes using tummy trimmer as exercise apparatus.

However, this study examined the effect of six months of exercise using tummy trimmer on TC, HDL-c, LDL-c, and TGs in normoglycemic offspring of diabetic patients. Findings from the present study showed a significant decrease in TC, LDL-c, and TGs and a significant rise in HDL-c in study group compared to controlled group. The findings of the current study are similar to previous studies that also found significant reduction in TC, LDL-c, and TGs and significant rise in HDL-c (Shaw et al, 2009, Tseng et al, 2009) in EG compared to CG. Various studies conducted in diabetic patients and their reports showed that TC, LDL-c, and TGs were decreased significantly and HDL-c increased significantly in combined aerobic and resistance exercise subjects (Reid, 2001, Kabir et al, 2005). The findings of these studies agreed with the present study. Moreover, the current study is in agreement with the study of Shaw et al Bazzano et al, 2009), in which LDL-c decreases significantly and the study of Tseng et al, 2009 and Tokudome et al, 2004 which showed a pronounced reduction in TGs and a significant rise in HDL-c in combined aerobic and resistance exercise training compared to CG. HDL acts as a remover of bad cholesterol in the reverse transport of cholesterol (Samuel et al, 2007). In our study high adherence to exercise (98%) was found and this may be also the possible reason for the improvement of lipid profiles in the study group, hence, this study has valuable clinical significance for the participants of the study hereby improving their lipid profiles.

Regular exercise can significantly improve lipid profiles in the offspring diabetic patients, decreasing levels of total cholesterol (TC) and LDL cholesterol while potentially causing a rise in HDL cholesterol. These positive changes are linked to a reduced risk of cardiovascular disease. The effectiveness of exercise can be affected by factors like duration, intensity, and age of the individual (Samuel et al, 2007).

Although the mechanism of exercise-induced lipid changes is unclear, exercise itself may be responsible for blood lipid consumption hence to decrease lipid levels (Tseng). Mechanisms may be associated with the increased activity of lipoprotein lipase (LPL) - lipoprotein lipase responsible for chylomicrons and VLDL TAG hydrolysis in granules (*Calabresi et al, 2010*). Most of the catalytically active LPL is situated in the vessel wall and then isolated from the endothelium surface and released in the blood after intravenous injection of heparin (*Kobayashi et al, 2007*). Therefore, the detected LPL is always in the post-heparin LPL. Ferguson et al, 1998 reported that heavy or prolonged aerobic exercise episodes could significantly boost post-heparin plasma LPL activity, thus promoted LPL-mediated TG hydrolysis. Exercise-induced LPL changes were time-related, for example, LPL mRNA peak level occurred at 4 h after exercise (*Kobayashi et al, 2007*). Besides, LPL activation rise could last for 24 h after only a 1 h exercise session in individuals with moderate intensity exercise (*Seip et al, 1997*).

In addition to the traditional mechanisms described above, several other discoveries revealed the mechanisms about exercise changing lipids profile from other aspects. Increased expression of ATP-binding cassette transporter A-1 (ABCA1) in macrophages has a significant effect on RCT, plasma HDL-C formation, and protection against atherosclerosis (*Seip et al, 1997*).

5. Limitation of the Study

Prospective study over years and inability to measure the lipid profile over long period of time and the other underlying health challenges in the subjects which were not identified at the time of study may be cofounding variables. This is an interesting issue for future investigations. However, continuous research is needed to validate our findings.

6. Conclusion

There is reduction in lipid profiles in all the participants who engaged in exercise. The reduction is more in the study group. The disturbances in lipid profile between the control and study subjects will require continuous monitoring of same in study to prevent cardiovascular events. Hence, the study subjects need to be watchful of their lipid profile so that they engaging in regular exercise in order not to cause disturbances of their lipid levels. This can delay the onset of development of T2DM in the future.

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The Accuracy of IJV/CCA CSA Ratio Measurement for Assessing Volume Status and CVP: A Systematic Review

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Abstract
Introduction: Intravenous fluid administration is commonly used in healthcare settings. Yet, there is no gold standard for evaluating the efficacy of fluid therapy. Ultrasound can assess the volume statically and dynamically. One proposed static method involves comparing the cross-sectional diameter of the internal jugular vein to that of the common carotid artery, allowing for normalization of the internal jugular size relative to the common carotid artery size. Here, we planned to assess the value of this method for evaluating volume status. Method: This systematic review followed PRISMA guidelines to examine the value of the internal jugular vein to common carotid artery cross-sectional ratio for assessing volume status. An extensive search was conducted in July 2025 across PubMed, Web of Science, Scopus, and Embase, with additional manual searches of Google Scholar and gray literature. The PICO framework was used to define inclusion criteria for original research studies that directly assessed the diagnostic accuracy of this ratio against a reference standard. Two independent reviewers extracted data and assessed study quality using the QUADAS-2 tool. Due to the limited number of studies, a planned meta-analysis was replaced by a narrative report of the results. Results: Five studies with a total of 183 patients were assessed. The mean age of participants ranged from 7 to 58.86 years. Most studies used CVP as the reference test. Two works reported a correlation between the IJV/CCA CSA ratio and CVP, with cutoff values of 2, while one study suggested a cutoff of 1.66. Another investigation proposed a cutoff of 1.8 when the patient was in a 45-degree position, and one study recommended varying cutoffs based on different physiological conditions influenced by respiratory status. Conclusion: The IJV/CCA CSA ratio demonstrates potential utility in assessing central venous pressure, with an estimated cutoff value near 2. However, the applicability of these findings is constrained by limited study sizes and considerable variability in both populations and research protocols.

Keywords: Internal Jugular Vein, Common Carotid Artery, Volume Status Assessment, Central Venous Pressure, Volume Responsiveness

1. Introduction

Intravenous (IV) fluid administration is one of the most common procedures performed in the healthcare setting. While it can be considered a lifesaving intervention, it could pose harm to the patient if it is inadequate or infused in large amounts (Guest et al., 2020). Experts state that IV fluid therapy should be performed based on the indications and contraindications, and the exact amount of fluid and the type of fluid should be determined precisely (Hilton et al., 2008), therefore, it is necessary to have measurements to assess the adequacy of IV fluid. There is no gold standard for evaluating the efficacy of fluid therapy. Most of the time, it is determined by using various factors: the patient's signs and symptoms, laboratory findings, and some measurements (Nasa et al., 2022). These measures include invasive and non-invasive methods. Commonly invasive techniques are central venous pressure (CVP) determination and pulmonary capillary wedge pressure (PCWP) checked by central venous catheterization. However, they have been shown to be unreliable and have serious complications (Zampieri et al., 2023). Ultrasound examinations are accepted non-invasive methods that can evaluate the heart or vessels statically or dynamically. Fluid status can be measured statically by assessing the diameter of the central veins, heart ventricular size, or function, which measure a single point-in-time value (Millington et al., 2021). Dynamic sonographic assessments involve observing changes in certain parameters in response to a physiological maneuver or a fluid challenge, such as the venous collapsibility index, venous distensibility index, left ventricle outflow tract (LVOT) velocity-time integral (VTI), respiratory variation in VTI, carotid artery flow time, and changes in carotid doppler peak velocity (Evans et al., 2014). Among static sonographic tools, determination of the internal jugular vein (IJV) to common carotid artery (CCA) cross-sectional area (CSA) is one of the suggested methods, which by normalizing the IJV size to the CCA size, may help to account for individual patient anatomy and other confounding factors (Bailey et al., 2012). Various reviews and meta-analyses examined the accuracy of different invasive and non-invasive methods of volume responsiveness (Fatahi et al., 2025, Wang et al., 2022, Orso et al., 2020, Eskesen et al., 2016). Since there was no systematic review evaluating the accuracy of the IJV/CCA CSA ratio, we decided to examine the validity of this non-invasive method for assessing volume status.

2. Methodology

The study protocol was recorded in the International Prospective Register of Systematic Reviews (PROSPERO) with the registration number CRD20251118053. The research followed the PRISMA guidelines set by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Page et al., 2021).

2.1. Literature Search and Search Strategy

An extensive investigation was performed across the PubMed, Web of Science, Scopus, and Embase databases in July 2025. In addition, a comprehensive manual search was conducted utilizing Google Scholar alongside an exploration of gray literature sources. The objective was to identify studies assessing the accuracy of sonographic assessment of the IJV/CCA CSA ratio in predicting CVP. The search utilized MeSH terms, synonyms, and related keywords for IJV, CCA, and volume status. The full search strategy on different databases is provided in Table 1. Two independent reviewers examined and evaluated all identified articles to determine their eligibility.

Table 1: Search strategy on different databases

Search strategy on different datasets
PubMed: (Internal jugular vein*[tiab] AND common carotid artery*[tiab] AND ("central venous pressure"[mesh] OR Central venous pressure[tiab] OR Volume status[tiab] OR Volume responsiveness[tiab] OR CVP[tiab] OR Fluid therap*[tiab] OR Intravenous fluid*[tiab])
Embase: ('internal jugular vein*':ti,ab) AND ('common carotid artery*':ti,ab) AND ('Central venous pressure'/exp OR 'Fluid therapy'/exp OR 'Fluid resuscitation'/exp OR 'Volume status':ti,ab OR 'Volume responsiveness':ti,ab OR 'CVP':ti,ab OR 'Central vein pressure':ti,ab 'Central venous pressure':ti,ab OR 'Blood volume':ti,ab OR 'Fluid resuscitation':ti,ab)
Web of Science: (TS= ("internal jugular vein*")) AND (TS= (common carotid artery*")) AND (TS= ("CVP" OR "Fluid therapy" OR "Fluid resuscitation" OR "Volume status" OR "Volume responsiveness" OR "CVP" OR "Central vein pressure" OR "Central venous pressure" OR "Blood volume" OR "Fluid resuscitation" OR "fluid therap*" OR "Intravenous fluid*"))

Scopus: (TITLE-ABS (“internal jugular vein*”)) AND (TITLE-ABS (“common carotid artery*”)) AND (TITLE-ABS (“CVP” OR “Fluid therapy” OR “Fluid resuscitation” OR “Volume status” OR “Volume responsiveness” OR “CVP” OR “Central vein pressure” OR “Central venous pressure” OR “Blood volume” OR “Fluid resuscitation” OR “fluid therap*” OR “Intravenous fluid*”))

2.2. Study Selection

We employed the PICO framework to assess the population, intervention, comparison, and outcome as a guided structure to clearly define eligibility criteria (Table 2).

Table 2: PICO framework for inclusion criteria

Component	**Description**
Population	Patients in various clinical settings who were assessed for volume status
Intervention	Ultrasound measurement of the internal jugular vein to the common carotid artery cross-sectional area ratio
Comparison	A validated standard for determining volume status
Outcome	Diagnostic accuracy of the method

Original research studies that directly assessed the diagnostic accuracy of the IJV/CCA CSA ratio and were designed to evaluate the ratio against a reference standard for volume status were included. The studies that did not assess the diagnostic accuracy of the IJV/CCA CSA ratio, those that did not calculate the ratio, or did not provide sufficient data were excluded. The detailed inclusion and exclusion criteria are summarized in Table 3.

Table 3: Inclusion and exclusion criteria for the study

Classification	**Category**	**Specific criteria**
Inclusion	Study design	Original research studies that directly assessed the diagnostic accuracy of the IJV/CCA CSA ratio against a reference standard for volume status.
	Population type	Individuals for whom volume status assessment is clinically relevant and conducted in a relevant clinical setting.
	Intervention	Ultrasound measures of the IJV and CCA CSA.
	Data reporting	Reported enough data and a clearly defined reference standard for assessing volume status.
	Language	No restriction on the language of the study.
Exclusion	Publication type	Editorials, letters, case reports, review articles, meta-analyses, and conference abstracts.
	Intervention	Studies that did not assess the diagnostic accuracy of the IJV/CCA CSA ratio.
	Reference standard	Studies that did not use a validated reference to define volume status.
	Data reporting	Studies that did not provide sufficient data for the outcome.

IJV: Internal jugular vein, CCA: Common carotid artery, CSA: Cross-sectional area

2.3. Data Extraction

Two reviewers were tasked with extracting data independently, with a clear focus on enhancing the quality of our work. The extracted data included baseline, IJV/CCA CSA ratio cut-off, sensitivity and specificity with 95% CI, true positive (TP), true negative (TN), false positive (FP), false negative (FN), positive predictive value (PPV), negative predictive value (NPV), and the reference standard for volume assessment. Regarding the articles with insufficient data, emailing the authors was planned.

2.4. Quality Assessment

QUADAS-2 tool (Quality Assessment of Diagnostic Accuracy Studies) was used for examining the quality of studies. Any discrepancies in assessments were resolved through mutual agreement. Each criterion (patient selection, index test, reference standard, flow, and timing) was evaluated for risk of bias, categorized as high, unclear, or low (Schueler et al., 2012).

2.5. Data Analysis

A quantitative meta-analysis was initially planned to calculate the sensitivity and specificity. However, due to the limited number of studies, we decided to report the results narratively.

3. Results

3.1. Study selection

The search yielded a total of 60 records from various databases: PubMed (11), Embase (20), Web of Science (14), and Scopus (15). After removing 21 duplicates, 39 studies remained, which were then screened based on their titles and abstracts. During this screening process, 26 records were excluded, leaving 13 studies. Additionally, 8 studies were found manually through a Google search, resulting in a total of 21 studies selected for full-text screening. This process ultimately identified 5 studies, as illustrated in the PRISMA flow diagram in Figure 1.

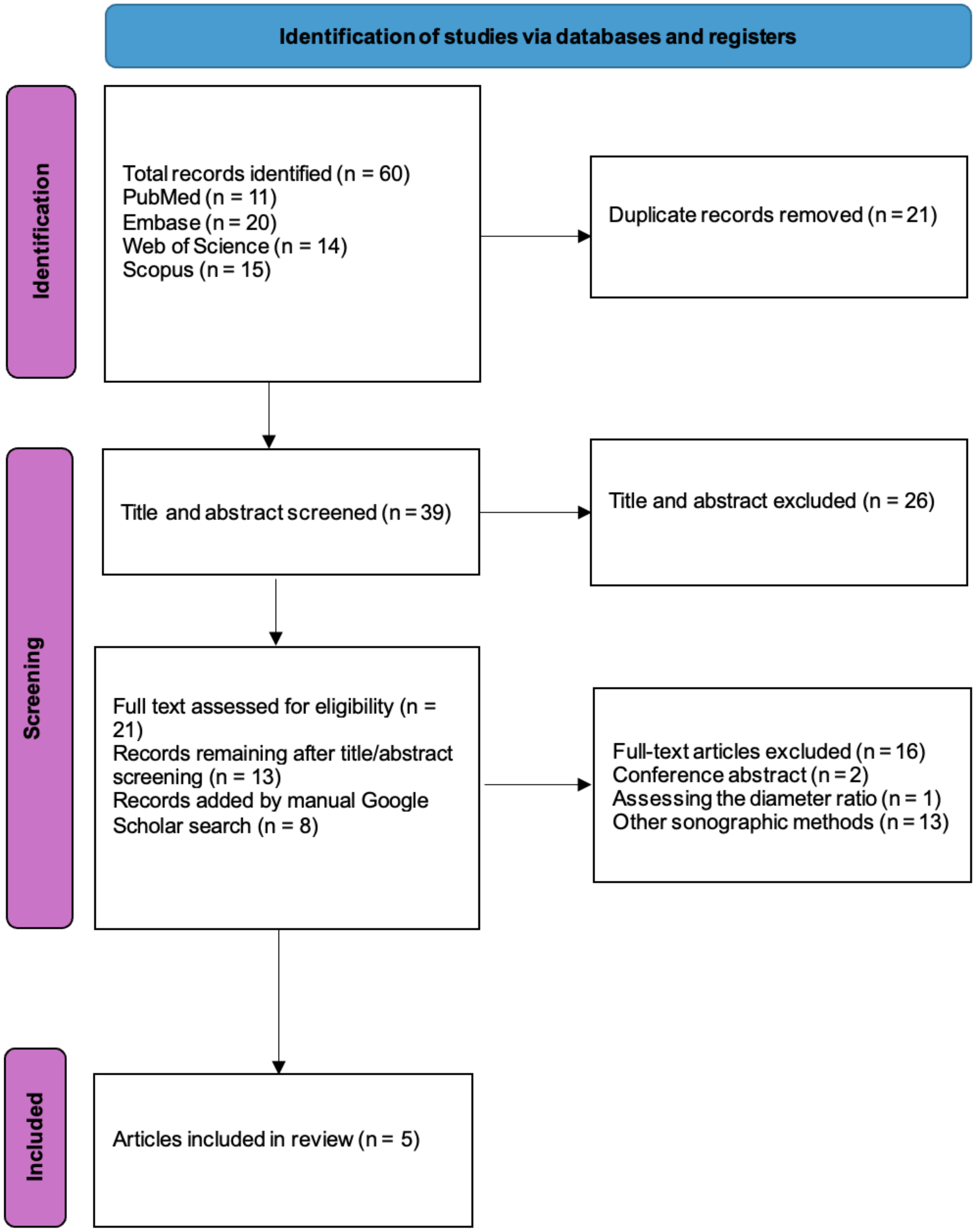

Figure 1: PRISMA flow diagram for the included articles

3.2. Study characteristics

Five studies involving 183 patients were evaluated in the included articles. The mean age of participants was between 7 to 58.86 years. Most studies considered the CVP as a reference test for assessing volume status. The characteristics of the included articles are provided in Table 4.

Table 4: Cardinal characteristics of studies

Author	**Country**	**Study design**	**Number**	**Mean age**	**Setting**	**IJV/CCA CSA cutoff**	**Reference test and cutoff**	**Main findings**
Kasem et al., 2021	Egypt	prospective	35	42.23 ± 9.27	Ill patients, spontaneous breathing	NS	CVP= 8-12	The IJV/CCA CSA ratio can be used for the evaluation of intravascular volume status.
Min et al., 2019	China	Cross-sectional	50	NS	Ill patients	1.66	CO= 15%	The IJV/ CCA CSA ratio is a reliable method to evaluate the volume responsiveness in critical patients.
Azapoglu et al., 2017	Turkey	Prospective	40	NS	ICU patients, mechanically ventilated	< 1.8	CVP< 10	The IJV/CCA CSA ratio at a 45-degree position was significantly correlated with a low CVP.
Hossein Nejad et al., 2016	Iran	Prospective	52	58.86 ±10.7	Ill patients, spontaneous breathing	2	CVP= 10	A cutoff of 2cm for IJV/CCA CSA ratio has the highest sensitivity and specificity for CVP.
Bailey et al., 2012	USA	Cross-sectional	6	7± 3.5	Children with thermal injury, mechanically ventilated	2	CVP= 8	The cross-sectional area of the vein at least twice that of the artery, may suggest the CVP> 8 mmHg.

CVP: Central venous pressure, CO: Cardiac output, IJV/CCA CSA: Internal jugular vein to common carotid artery cross-sectional area

3.3. Risk of bias assessment

In the patient selection area, two studies showed a significant risk of bias, while three others had an uncertain risk of bias. The risk of bias in other areas was low. Concerning applicability, in the patient selection domain, two articles indicated a high risk, one article showed a low risk, and two articles had unclear risk assessments (Figures 2, 3).

	Risk of bias				Applicability		
Study	Patient selection	Index test	Reference standard	Flow & timing	Patient selection	Index test	Reference standard
Kasem et al., 2021	?	☺	☺	☺	☺	☺	☺
Min et al., 2019	☹	☺	☺	☺	☹	☺	☺
Azapoglu et al., 2017	☹	☺	☺	☺	☹	☺	☺
Hossein Nejad et al., 2016	?	☺	☺	☺	?	☺	☺

Bailey et al., 2012	?	☺	☺	☺	?	☺	☺

Figure 2: Risk of bias assessment based on the QUADAS-2 tool

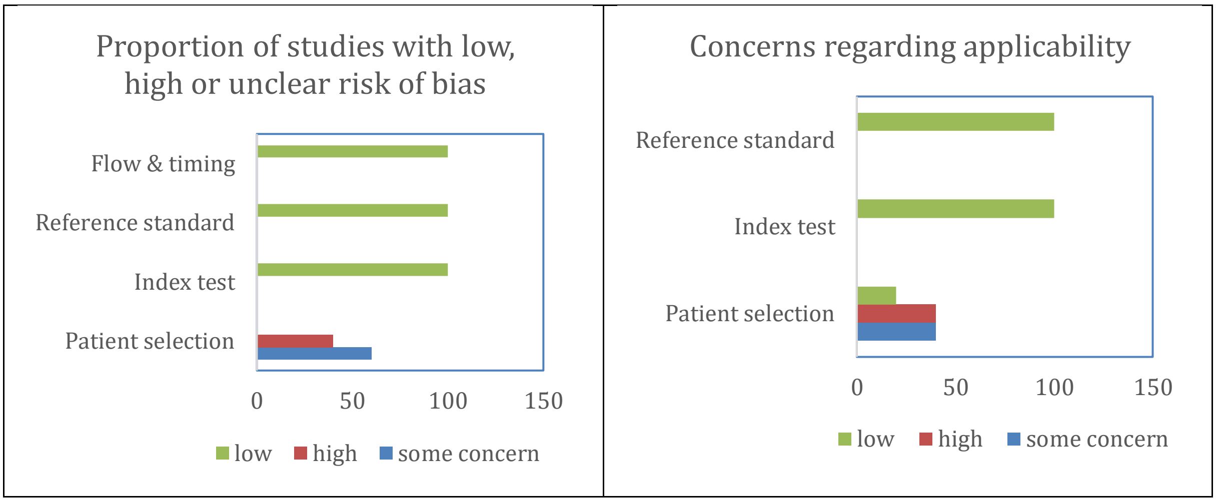

Figure 3: Risk of bias assessment

3.4. Narrative analysis

In 2012, Bailey et al. conducted a pilot study to investigate the relationship between the diameter and cross-sectional area ratio of the IJV and CCA, and its correlation with CVP. Their study found a poor relationship between the diameter ratio and the CVP. A notable connection was identified between the ratio of the cross-sectional area (CSA) and central venous pressure (CVP). Specifically, a ratio of 2 or higher showed a significant association with a CVP of 8 mm Hg or more (P< 0.001) (Bailey et al., 2012). Subsequently, a study by Hossein-Nejad et al. (2016) involved 52 participants. Their results indicated that the average IJV/CCA CSA ratio was 1.89±0.83 during inhalation and 1.90±0.83 during exhalation. A significant relationship was found between the IJV/CCA CSA ratio and CVP for both inhalation and exhalation, with optimal accuracy noted at a cutoff ratio of 2. They stated the correlation is not statistically affected by respiration. In their research on patients receiving mechanical ventilation, Azapoglu et al. (2017) found no significant differences between the IJV/CCA ratio and different CVP values when patients were in supine position. However, in the 45° position, a notable correlation was observed between a lower CVP and the ratio.

Min et al. (2020) examined how accurately this ratio can assess volume responsiveness, using a reference of at least a 15% increase in cardiac output (CO) to define volume status. Their findings indicated a negative correlation between the ratio of the IJV to CCA cross-sectional area and the change in ΔCO value, with a significance level of P < 0.01. Finally, Kasem et al. (2021) examined various cutoffs for the ratio of inspiration to expiration. Additionally, they reported a strong positive correlation of this ratio and the maximum diameter of the IVC before and after fluid infusion (r = 0.923, P < 0.001, and r = 0.390, P = 0.021, respectively). The main results of the included studies are provided in Table 5.

Table 5: Summarized results of the included articles

Study	Narrative analysis
Kasem et al., 2021	The IJV/CCA CSA ratio cutoff of 2.58 had a sensitivity and specificity of 65.2% and 75% for CVP=8-12 after fluid administration during inspiration. The ratio of 2.65 showed 52.2% sensitivity and 67% specificity during expiration. They also discovered a positive link between the inspiratory IJV/CCA CSA ratio and the minimum diameter of the inferior vena cava, both before and following fluid infusion, with correlations of r = 0.605 (P < 0.001) and r = 0.496 (P = 0.002), respectively.

Min et al., 2019	At the IJV/CCA CSA ratio of 1.66, the sensitivity, specificity, and the areas under the ROC curve were 87. 1%, 79. 6%, and 0.836(95%CI:0.710-0.952) for identifying volume responsiveness with a negative correlation between the ratio and the ΔCO value after PLR.
Azapoglu et al., 2017	A significant correlation in 45-degree position was documented between IJV/CCA CSA ratio less than 1.8 and CVP< 10mm Hg.
Hossein Nejad et al., 2016	There was a significant correlation between the IJV/CCA ratio and CVP during both inspiration (r=0.728, p<0.0001) and expiration (r=0.736, p<0.0001). Sensitivity, specificity, PPV, and NPV were 90%, 86.36%, 90%, and 86.36% for the prediction of CVP <10cm H2O.
Bailey et al., 2012	A pilot study assessing the relationship of the IJV/CCA CSA ratio to the CVP, suggesting that a ratio of at least 2 states the CVP higher than 8 (p< 0.001).

CVP: Central venous pressure, CO: Cardiac output, IJV/CCA CSA: Internal jugular vein to common carotid artery cross-sectional area, PPV: Positive predictive value, NPV: Negative predictive value, PRL: Passive leg raising

4. Discussion

There have been limited studies exploring the connection between ultrasound measurements of the IJV/CCA cross-sectional area ratio and CVP. In this systematic review, two studies reported a correlation between the IJV/CCA CSA ratio and CVP (Hossen-Nejad et al., 2016, Bailey et al., 2012), whereas Azapoğlu Kaymak et al., 2017 found significance only in the 45-degree position. Kasem et al., 2017 evaluated different CSA ratio cutoffs at expiration and inspiration and described a positive correlation between the ratio and the IVC maximum diameter before and after fluid infusion.

The relationship between the IJV/CCA CSA ratio and CVP may not reliably translate into predicting fluid responsiveness. Meta-analytic data in related domains have shown a relatively weak relationship between static venous indices and the hemodynamic gains after fluid challenges (Eskesen et al., 2016, Marik et al., 2013). Consistent with this, Min et al. reported a negative correlation between the IJV/CCA CSA ratio and ΔCO following fluid administration, arguing against a simple linear relationship between the CSA ratio and volume responsiveness (Min et al., 2020).

Bano et al. (2018) found a notable relationship between the ratio of the IJV to CCA diameters and central venous pressure, specifically during the expiration phase. Their research indicated that the average IJV/CCA diameter ratio was 1.60 ± 0.55 at expiration compared to 1.41 ± 0.56 at inspiration. They observed a significant correlation between this diameter ratio and CVP at expiration ($r = 0.401$, $P = 0.004$). This correlation was also significant in patients who were not mechanically ventilated ($r = 0.439$, $P = 0.032$).

A notable strength of the current evidence is the demonstration of a statistically significant association between the IJV/CCA CSA ratio and CVP in some cohorts, with a frequently observed cutoff near a ratio of 2 associated with higher CVP. However, substantial heterogeneity across studies (regarding populations, imaging protocols, and measurement planes) constitutes a major limitation to generalizability. The IJV ultrasound assessment has shown a value in estimating CVP (Parenti et al., 2018); however, IJV diameter is affected by respiratory phase (Danahue et al., 2009), and by mechanical ventilation setting, particularly the level of end expiratory pressure (An et al., 2019). Overall, while CSA-based metrics may offer a more consistent reflection of venous filling status than diameter-based measures, their utility for predicting fluid responsiveness remains uncertain. The findings across studies are not uniformly concordant, and this limits their immediate clinical applicability. Standardized measurement techniques, breath-hold or respiratory phase, reporting both inspiration and expiration values, distinguishing spontaneous breathing from mechanically ventilated patients, and documenting patient positioning are necessary steps for conducting studies to evaluate this method. Additionally, the indices should be linked to a meaningful output such as ΔCO over CVP, with recognizing the limitations of each reference since introduction implies they could be unreliable. Finally, larger prospective studies are needed to validate a cutoff across diverse populations and settings to clarify its implications for predicting volume status.

5. Conclusion

The results indicate that the IJV/CCA CSA ratio may offer a more consistent association with CVP than diameter ratios, with a suggested approximate cutoff near 2 in several datasets. However, these associations are influenced by respiratory status, patient positioning, and ventilation mode; furthermore, the relationship with fluid responsiveness is not universally robust and remains unclear.

Contributions: Mansoureh Fatahi: conceptualization, search and screening, data extraction, quality assessment, writing original draft, revision. Marziyeh Rashidi: data extraction, quality assessment, writing original draft, editing

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How to Assess a Country's Preparedness to Face a Public Health Emergency? A Scoping Review

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Abstract
Disasters and emergencies significantly affect public health, making preparedness assessments essential to demonstrate progress and identify gaps for decision-makers. However, knowledge of how countries assess their preparedness is limited. Tools created by national authorities often cater to specific evaluation needs and may not apply to others due to unique health system characteristics. This checklist evaluates parameters used to measure a region's preparedness for emergencies based on data collected from article searches. We searched various databases online using keywords related to public health, tools, and preparedness. The databases used included Proquest, Pubmed, Sage, ScienceDirect, and Scopus. The data were analyzed using thematic analysis to identify parameters used to assess preparedness and epidemic vulnerability. 13 articles were used in this analysis, most of which were assessed on the African continent. The most widely used instruments in the articles were JEE and GHSI. Preparedness parameters that almost appeared in most of the instruments included surveillance preparedness, financing, physical infrastructure, emergency response operations, coordination, and health workforce. Regularly assessing a country's health preparedness is crucial for effective responses to health emergencies. Evaluations identify strengths and weaknesses in the health system and highlight needed improvements. Tools like the Joint External Evaluation (JEE) and WHO Toolkit focus on key areas, including surveillance, funding, infrastructure, collaboration, workforce, and emergency preparedness. These assessments enhance a nation's ability to tackle future health challenges and strengthen the global health system.

Keywords: Preparedness, Emergency, Public Health, Country, Health Crisis

1. Introduction

A health crisis can impact a country's morbidity and mortality and can even spread quickly to other countries. This situation requires every country to be prepared to deal with emergencies caused by health crises. Assessing a country's emergency preparedness involves technical aspects or resources and diverse social, cultural, and political dynamics. It is, therefore, challenging for a country to assess its preparedness because emergencies are often unpredictable (Khan et al., 2018). Various health system preparedness assessment concepts are used to measure the preparedness of health system actors, such as health facilities, to be prepared for infectious disease outbreaks and other health emergencies.(Nuzzo et al., 2019). Preparedness assessments illustrate progress, identify gaps, inform decision-makers, and indicate where investment in preparedness is needed. (Institute, 2018).

The International Health Regulations (IHR), revised in 2005 due to the global health crisis, are designed as a key health security instrument to prevent and address significant health threats internationally. Preparedness assessments serve several important purposes. They help demonstrate progress, identify gaps, inform decision-makers, and indicate areas where investment in preparedness is necessary.(Kluge et al., 2018). More than 100 countries have adopted the Joint External Evaluation (JEE) process, and WHO assessments are now used to measure global preparedness for infectious disease outbreaks and other public health emergencies. However, the JEE only assesses a few capacities and capabilities required for health system preparedness and response. Health systems play a direct role in supporting countries' ability to respond quickly and efficiently to infectious disease outbreaks, so it is important to consider health system preparedness for these events as countries assess their overall preparedness. A framework or tool that comprehensively identifies the health system capacities and capabilities required for effective outbreak preparedness and response is needed. (Nuzzo et al., 2019). The COVID-19 pandemic at the global level shows the importance of evaluating the Government's preparedness in responding to emergencies (Meyer et al., 2020). Until 3 years have passed globally, 676,609,955 people have been confirmed infected with COVID-19, and 6,881,955 people have died (University, 2023). The emergence of these pandemics highlights new threats related to public health. Emerging disease events like this have challenges to handle because the Government must meet the high demand for resources in the community. However, this fulfillment cannot be achieved in the short term because virus transmission is unpredictable, and the virus's situation cannot be known due to its effects and weaknesses (Hossain, Akter, Rashid, Khair, & Alam, 2022). A country's emergency response capacity requires improvement to control the threat effectively (Haider et al., 2020).

Various parameters are used to evaluate and assess a country's preparedness for health emergencies. Various instruments have been developed to evaluate national and subnational (regional/local) country-specific preparedness that may only apply to some countries, given the specific characteristics of a country's health and public health emergency response system (Haeberer et al., 2021). Using data from the article search, this checklist analyzes the parameters used to assess the Government's preparedness for health crisis emergencies.

2. Method

A team of pharmacists and public health officials conducted the scoping review. Four authors (ESS, DA, PJ, SS) were responsible for data extraction and analysis.

2.1. Search strategy

Article search strategy through online search on electronic databases conducted in February - March 2024. The databases used were Proquest, Pubmed, Sage, ScienceDirect, and Scopus. The stages carried out include (a) identifying research questions, (b) identifying relevant research in predetermined databases, (c) selecting studies that match the predetermined criteria, (d) extracting and charting data, and (e) summarising and reporting results. The search used specific and uniform keywords, as in Table 1.

Table 1: Searches strings

No	Databased and Keywords
1	Proquest (n = 1.516)
	Abstract (("public health" OR "health system") AND (emergency OR disaster OR pandemic) AND (planning OR preparedness OR response) AND (evaluation OR assessment OR measurement OR tool OR toolkit OR checklist OR standard))
2	Pubmed (n = 37)
	("public health" OR "health system") AND (emergency OR disaster OR pandemic) AND (planning OR preparedness OR response) AND (evaluation OR assessment OR measurement OR tool OR toolkit OR checklist OR standard)

3	Sage (n = 1.315)
	assessment OR Evaluation OR Measurement OR tool OR Toolkit OR Checklist OR Standard AND emergency OR Emergencies OR Disasters OR Disaster OR Pandemic OR Pandemics AND preparedness OR Response AND public health OR Health System AND country OR subnational OR Regional OR government
4	ScienceDirect (n = 205)
	("public health") AND (emergency OR pandemic) AND (planning OR preparedness) AND (evaluation OR assessment OR toolkit)
5	Scopus (n = 786)
	assessment OR evaluation OR measurement OR tool OR toolkit OR checklist OR standard AND emergency OR emergencies OR disasters OR disaster OR pandemic OR pandemics AND preparedness OR response AND public AND health OR health AND system AND country OR subnational OR regional OR government

2.2. Inclusion criteria

The article search results were processed and analyzed using the Endnote X9 application. The article search criteria used included: (1) all articles related to the assessment or evaluation of government preparedness for health emergencies; (2) original research full-text written in English; (3) all design studies; (4) articles published from 1 January 2018 to 31 December 2023.

2.3. Exclusion criteria

Exclusion criteria used were (1) articles that did not contain parameters or assessments of state preparedness in facing health emergencies; (2) articles in the form of review articles, study protocols, conference paper commentaries, series, letters to the editor, news, books, guidance or other types of articles not based on primary data collection; (3) publications in non-English journals; (4) abstract only.

The total number of articles obtained from 5 databases is 3,919. After screening using the PRISMA flow diagram, selected articles were reduced due to duplication, incompatibility of titles and abstracts with themes, and screening of full text needed an instrument or component of measuring preparedness, so 13 suitable articles were obtained. (Aceng et al., 2020; Bakiika et al., 2023; Coccia, 2022; Guyo et al., 2022; Huang & Yu, 2023; Neogi & Preetha, 2020; Oppenheim et al., 2019; Sajjad, Raza, & Shah, 2022; Talisuna et al., 2019; Kyeng Mercy Tetuh et al., 2023; Ul-Haq et al., 2019; Van Hoang, Tran, Vu, & Duong, 2021; Zhao et al., 2023). The results of the article screening can be seen in Figure 1.

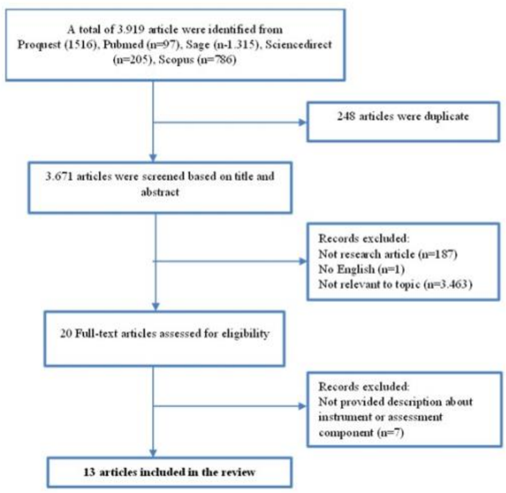

Figure 1: PRISMA flow diagram showing screening and selection of published articles

3. Results

A comprehensive search was conducted on five sources: Proquest, Pubmed, Sage, ScienceDirect, and Scopus. The results of the articles obtained were 3,919 relevant articles according to the keywords that have been determined. After screening this scoping review, 13 articles met the predetermined inclusion and exclusion criteria. The data for each study was mapped using the following headings: first author, year of publication, title, country, research objectives, research design, tools/instruments, and research results. The results of the data extraction can be seen in Table 2.

Based on the screening results, all articles (n=13) discussed government preparedness in dealing with emergencies in infectious disease hazard situations. Most of the infectious disease hazards in this article are exposure to infectious diseases such as the Ebola virus, MERS, SARS, and COVID-19. Most articles discussing indicators of a region's preparedness in facing health emergencies were published in 2023 (n=4), and the rest were divided into 2019-2022. There has been an increase in research in these years because, at that time, the global situation had just faced the COVID-19 pandemic, so an evaluation was carried out on the preparedness and preparation of a country and government to deal with emerging diseases. This pandemic event is a starting point for governments globally to evaluate how prepared their countries are in the face of disasters. The study design in this research mainly uses a quantitative approach (n=9), and the rest uses a mixed methods approach. The search results showed that 11 instruments/assessments are used to assess preparedness for health emergencies. The characteristics and explanations of each article can be seen in Table 2.

Each instrument used has parameters that become a reference for assessing the preparedness of an area in the face of a disaster or emergency. The parameters used, although different instruments and limitations and strengths of each instrument, can be seen in Table 3. In table 3 it describes the use of instruments from the reviewed articles, objectives, usage topics, scope, strength, limitation, and validity. A total of 12 articles used instruments, and one other article was analyzed without instruments. The instruments used can measure various regional, national, and global levels. Most of the instruments used in the above articles are Joint External Evaluation and WHO's toolkit for assessing health system capacity for crisis management. The indicators or parameters used in each instrument have a different number of domain items or indicators, which can be seen in Table 4.

There are 11 instruments used to assess the preparedness of an area for emergencies, especially health crises. Overall, there are no parameters that cover all instruments. Based on this data, factors commonly found as indicators in assessing the preparedness of an area in the face of a disaster can be extracted. The most common indicators include surveillance, financing, physical infrastructure preparedness, emergency response operations, coordination, and the health workforce. The different indicator domains for each instrument can be seen in Table 5.

Table 2: Characteristics of the included studies

No	Authors (year)	Title	Study design	Country	Tools	Results of the study
1.	Talisuna, *et.al* (2019)	Joint external evaluation of the International Health Regulation (2005) capacities: current status and lessons learned in the WHO African region	Quantitative	WHO African Region (47 countries)	Joint External Evaluation (JEE)	1. JEE findings are a red flag' about the inadequate public health emergency preparedness and response capacities in the WHO African region. 2. Most countries (>80%) had an IHR capacity level at score 1 (no capacity) or 2 (limited capacity) 3. There is a need to build a more robust national public health capacity and infrastructure to protect against epidemics and health emergencies
2.	Ul-Haq, *et.al* (2019)	Health system preparedness in Pakistan for crisis management: a	Quantitative	Evaluated 12 districts in Khyber Pakhtunkhwa and six	Six Core Functions of the WHO Health	1. 72% of indicators in vulnerable districts must be more prepared for crisis management. 2. None of the 16 Key Components scored at an acceptable level of preparedness

		cross-sectional evaluation study		districts in Punjab, Pakistan	Systems Framework	3. The study detected, in addition to the overall poor preparedness of the health system for crisis management, a consistent pattern of poorer performance in process, coordination, and operational aspects compared to structural elements
3.	Oppenheim, *et al.* (2019)	Assessing global preparedness for the next pandemic: development and application of an Epidemic Preparedness Index	Quantitative	188 countries	Epidemic Preparedness Index (EPI)	1. The analysis found that the most prepared countries are concentrated in Europe and North America 2. the least prepared are in Central and West Africa and Southeast Asia - regions known to have a high risk for the emergence of pathogens with pandemic potential. The capacity to detect and respond to epidemics and pandemics is weak in West and Central Africa and Southeast Asia, regions known to have a high risk for the emergence of pathogens with pandemic potential. 3. There were 36 countries with EPI cluster 1 score (most prepared) and 18 countries with EPI cluster 5 score (least prepared) out of 188 analyzed.
4.	Neogi, *et.al* (2020)	Assessing health systems responsiveness in tackling COVID-19 pandemic	Quantitative	Europe (Italy and Spain) Western Pacific (Australia, China, and Singapore), South East Asia (South Korea and India), Eastern Mediterranean (Saudi Arabia and Egypt), Americas (the USA and Brazil), and Africa (Nigeria and South Africa).	1. Global Health Security Index 2. WHO Health System Framework	1. The health systems of high-income countries are more potent than their counterparts from low- and middle-income countries. 2. As per the GHS Index 2019, the analysis indicated that no country was fully prepared for global emergencies such as pandemics. 3. The responsiveness of the countries is different from the results emerging from the assessment as per the health systems framework. 4. Analyzing the health systems shows that public health systems are much stronger in higher economies. However, that only sometimes translates into health systems' responsiveness when dealing with global health emergencies.
5.	Jane, *et.al*, (2020)	Uganda's experience in Ebola virus disease outbreak preparedness, 2018–2019	Mixed Methods	Uganda	The eleven key WHO Ebola Virus Disease Preparedness component	1. The results of the initial risk assessment show that 20 districts are at high risk and 10 districts are at medium risk for Ebola Virus Disease. 2. The preparedness assessment found that all 30 high- and moderate-risk Ugandan districts scored less than 50% for EVD preparedness at baseline.
6.	Van Hoang, *et.al* (2021)	Covid-19 Preparedness and Response Capability: A Case Study of the Primary Healthcare System	Mixed Methods	Four districts of Hanoi, Vietnam	Public Health Emergency Preparedness and Response Capabilities Framework	1. COVID-19 preparedness and response at the primary healthcare level must be consistently fully implemented or sometimes not. The results of this study revealed that in the first wave of COVID-19, primary healthcare facilities needed to prepare for prevention and control. 2. With the existing health workforce, coping with the future disease burden is impossible. 3. The role of the police and military is crucial in terms of cross-sector collaboration.

						4. A robust health information system (HIS) that is adequately funded and developed before future outbreaks can cyclically strengthen health systems, pandemic preparedness, and response capacity. 5. Enabling factors at the health system level include adequate infrastructure and equipment to respond rapidly to the COVID-19 pandemic, strong leadership from higher to lower levels, and good collaboration across public sectors (police and military engagement).
7.	Coccia, *el.al* (2022)	Preparedness of countries to face COVID-19 pandemic crisis: strategic positioning and factors supporting effective strategies of prevention of pandemic threats	Quantitative	Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland and the United Kingdom.	Robustness Index (r) Readiness Index/prevention (p)	1. No country is highly prepared for a significant outbreak/pandemic. 2. The best-performing countries tend to have smaller populations and better public governance associated with high health expenditure.
8.	Shahid, *et al.* (2022)	Joint external evaluation of the international health regulations (2005) capacity in South Sudan: assessing the country´s capacity for health security	Quantitative	Sudan Selatan	JEE	South Sudan's overall mean score across 48 indicators was 1.5 (with a maximum score of 4), indicating a weak health system. This could be due to the civil conflicts experienced, which have negatively impacted the health system.
9.	Sajjad, *et.al* (2022)	Assessing Response Readiness to Health Emergencies: A Spatial Evaluation of Health and Socio-Economic Justice in Pakistan	Quantitative	Province Punjab, Pakistan	Response Readiness Index (RRI)	1. There is a difference in preparedness between the southern and northern regions of Punjab, with the southern region being more vulnerable. 2. As many as 45% of indicators scored below average, including shortages of health facilities, hospital beds, health insurance coverage, and low communication and literacy levels.

10.	Tetuh, *et.al* (2023)	Evaluating event-based surveillance capacity in Africa: Use of the Africa CDC scorecard	Quantitative	African Union (AU)	Event-Based Surveillance (EBS)	1. The score results show that EBS capacity in most member countries is at a minimal (score <60%) to the average level (score 60-80%), 2. There is a need to strengthen EBS capacity in Africa to ensure preparedness for future public health threats.
11.	Huang, *et.al* (2023)	Assessment of Regional Health Resource Carrying Capacity and Security in Public Health Emergencies Based on the COVID-19 Outbreak	Quantitative	31 provinces in China 150 Country	COVID-19 Safety Index	1. The results of the two indicators reveal the weaknesses of epidemic prevention in mainland China, which will provide a strong basis for formulating epidemic prevention policies and deploying medical resources in the next round of outbreaks caused by the omicron variant. 2. There are significant differences in the financial and demographic distributions of the countries worldwide when responding to public health emergencies. 3. The physical control of the epidemic, vaccination rates, and adequate medical supplies are the most important measures to prevent and control the current epidemic. 4. The carrying capacity of healthcare resources is generally high in eastern Asia, northern Europe, and most North American and Australian regions. 5. The carrying capacity of healthcare resources could be higher in regions such as Africa, South America, and Southeast Asia, with African countries generally having low carrying capacity for healthcare resources. 6. Countries with higher HRCCs tend to be safer.
12.	Zhao, *et.al* (2023)	Evaluation of health system resilience in 60 countries based on their responses to COVID-19	Mixed Methods	1. Twenty countries with the highest number of COVID-19 deaths per million citizens. 2. Twenty countries with the lowest number of deaths. 3. Twenty countries from different regions have intermediate tolls, large populations, and very different health systems.	Health System Resilience Evaluation	1. Government governance, coordination, and prevention are essential for any country and are the most important first-level indicators. 2. Switzerland, Japan, Germany, Australia, South Korea, Canada, New Zealand, Finland, the United States, and the United Kingdom were the ten countries with the highest health system resilience. 3. The ten countries with the lowest health system resilience were (from best to worst) Liberia, Tanzania, Burundi, Mozambique, Nigeria, Benin, Côte d'Ivoire, Guinea, South Sudan, and Burkina Faso. 4. Moderate resilience levels dominated South America, South Asia, and Eastern Europe. 5. Based on data from 60 countries worldwide, the evaluation showed that increasing health system resilience will improve responses to future public health emergencies. 6. All four first-level indicators contributed to resilience and success in achieving resilience required high scores for all indicators. 7. Each indicator was needed to compensate for low scores in other indicators.

13.	Bakiika , *et.al* (2023)	Contribution of the one health approach to strengthening health security in Uganda: a case study	Mixed Methods	Uganda	Not available	1. The study demonstrated that a One Health framework was used to implement multiple activities in the National Action Plan for Health Security. 2. The National One Health Platform approach strengthened Uganda's outbreak detection, preparedness, and response for prioritized zoonotic diseases through effective multisectoral coordination and synergies decentralized to sub-national levels.

Table 3: Instruments that can be used to assess government preparedness for health crisis emergencies

No	Instrument	Objectives	Topics of usage	Scope	Strengths	Limitation
1	Global Health Security Index (GHSI) Score	Evaluate health security and capacities across 195 countries using a broad framework that includes six categories and 37 indicators.	Analysis of each country's Preparedness and response risk of pandemics or epidemics such as infectious disease outbreaks.	Count ry	1) Somewhat valid measure of health security; 2) Covers a wide range of countries 3) Comprehensive assessment; 4) Large number of indicators; 5) High availability of indicators that improve the comparability across nations; 6) The index is based on publicity available data ensuring transparency and objectivity 7) Assess additional variables that may influence preparedness; 8) Enabling countries to compare their health security capabilities against others	1) Some countries may be underestimated due to unavailable data; 2) Depending on public and published information, some information may not published 3) The quantitative and qualitative results are different when calculated as the arithmetic-geometric (GM) and harmonic (HM) are used 4) Have little correlation with the experience in various countries; 5) Inadequate in assessing the unique history of structuring public health responses
2.	Joint External Evaluation (JEE)	Measure a country´s status in building the necessary capacities to prevent, detect, and respond to infectious disease threats and establish a baseline measurement of capacities and capabilities.	Preparedness and Response in pandemic and other hazards	Count ry	1) External validation and objective measurement 2) IHR-based assessment; 3) It is accepted among WHO member states and agencies; 4) It promotes transparency, openness, and data sharing, and it serves as an objective basis for formulating National Action Plans for Health Security (NAPHS) 5) Provide various aspects of emergency response 6) Specific indicators in accurately assessing response capacity 7) Multisectoral approach 8) Evidence-based recommendations 9) Support for policy development	1) Only 90 countries have undergone joint external evaluation 2) Inadequate human resources for self-assessment in some countries. 3) Self-assessment bias 4) ERCT scores were often lower than transformed JEE scores, indicating discrepancies in the assessment of response capacity. 5) Inadequate coverage of emerging threats
3.	Index Preparedness & Index Resilience	Measuring the performance of countries to cope with	Preparedness of countries and ranking of their performance	Count ry	1) Simple indicators to assess the performance of countries; 2) Compare different units;	Potential bias between countries in detecting and reporting due to different approaches for counting

		pandemic threat			3) Its ability to provide comprehensive information; 4) Supporting effective vaccination plans	deaths and variations in data quality and healthcare system
4.	WHO's toolkit for assessing health-system capacity for crisis management	Assessing health-system capacity for crisis management includes evaluating and implementing to enhance health-system resilience during emergencies	Preparedness in disaster for crisis management	Country, regional	1) Include its comprehensive coverage of the six core functions; 2) Standardized assessment 3) Cover essential attributes and indicators; 4) The ability to assess readiness levels through a structured evaluation process conducted by trained personnel 5) User-friendly design 6) Support for multisectoral collaboration	1) Cannot be generalized to the entire country as the evaluation was limited to high-risk districts 2) Implementing the toolkit may require significant time and resources 3) Potential for subjectivity 4) Limited scope for emerging threat 5) Need for training
5.	Epidemic Preparedness Index (EPI)	Measure national preparedness capacity to detect and respond to future disease outbreaks	Preparedness to respond to the epidemic	Country	1) Includes non-health system factors; 2) Developed from JEE and covers 188 countries; 3) Able to update quickly the change of countries	1) Not cover disease-specific elements
6.	Response Readiness Index (RRI)	The measure of competency/incompetency of different regions in health crises based on their health system and socio-economic vulnerability	Emergency response readiness in bio-hazard and pandemic	Regional	1) The indicator data are collected from several resources; 2) Development indicators; 3) Compare indicators on the same scale; 4) Include cross-regional health and socio-economic vulnerability aspect	1) Some regions may be unavailability of the data on several health system indicators; 2) Not cover the indicator of IHR
7.	Event-based surveillance (EBS) scorecard	Monitoring, assessment, and interpretation of primarily unstructured ad hoc information regarding health-related events or risks that may represent an acute risk to human, animal, plant, or environment health	Detection and reporting of capacity needed for outbreak	Country	1) Addressed several gaps such as early capturing, tracking, analysis, and reporting of public health events 2) Used a multisectoral approach 3) Integrating several sources at different levels of the system. 4) Comprehensive evaluation framework	1) Potential biases in self-reporting 2) Lack of comprehensive support components for Early Warning Systems (EBS) implementation 3) Focus on national levels 4) Gaps in sensitivity
8.	COVID-19 Safety Index	Evaluate and analyze various aspects of decision-making, economic evaluation, water	Preparedness for epidemic risk and guide future epidemic prevention	Country Regional	1) shown significant correlation results with the performance of resistance to epidemics 2) Reliable and objective approach for assessing epidemic safety indexes	1) Inconsistency in the statistical caliber of medical resources in each country

		resources management, human resources evaluation, and disease forecasting models.				
9.	Public Health Emergency Preparedness and Response (PHEPR) Capabilities Framework	to assess and enhance the prepared ness public health systems' readiness to effectively respond to emergencies.	Preparedness to respond to emergencies	Country Sub-regional/local	1) Comprehensive evaluation framework 2) Evidence-based practices 3) Multisectoral collaboration 4) Support for policy development 5) Easily adjustable system to different contexts and types of emergencies	1) Complexity of the system 2) Fragmented research and funding 3) Insufficient evidence base 4) Communication challenges 5) Limited access to data
10.	The eleven key WHO Ebola Virus Disease Preparedness Component	To enhance the readiness of countries to effectively respond to potential Ebola outbreaks.	Preparedness to respond to Ebola outbreaks	Country	1) Objective Evaluation 2) Multisectoral coordination 3) International Collaboration: collaboration between WHO teams and Ministries of Health in at-risk countries	1) Key reference documents such as guidelines, training manuals, and guidance notes to support the implementation of key activities for each component. 2) Snapshots of dynamic situations 3) Reliance on previous experience 4) Limited risk assessment 5) Lack of adequate data and analyses
11.	Health System Resilience Assessment Analysis	To assess health system resilience the world with a quantitative evaluation system	to assess differences in health system resilience in response to COVID-19 across countries.	Country	1) It is easier because the assessment only consists of 4 domains. 2) Developed from WHO indicators of six building blocks. 3) A resilient health system can respond effectively to epidemics. 4) Provide strong national protection and reduce the negative impact of the epidemic. 5) Our results show that all four first-level indicators contribute to resilience and that success in achieving resilience requires high scores for all indicators; more than one indicator is required to compensate for low scores on the others.	1). The indicators are limited, so other factors are not analyzed despite contributing to a country's resilience. 2) The study focuses only on quantitative analysis, not including qualitative analysis, which could provide additional insight into the contextual factors influencing each country's response.

Table 4: Indicators used in each of the Health Crisis Emergency Preparedness Assessment Instrument

Global Health Security Index (GHSI) Score	Joint External Evaluation (JEE)	Epidemic Preparedness Index (EPI)	Response Readiness Index (RRI)	Health System Resilience Assessment Analysis	Health System Resilience Assessment Analysis
1. Prevention	1. Prevent		1. Health System		1. Government

a. Antimicrobial resistance b. Zoonotic disease c. Biosecurity d. Biosafety e. Dual-use research and the culture-responsible science f. Immunization 2. Detection and Reporting a. Laboratory systems strength and quality b. Laboratory supply chains c. Real-time surveillance and reporting d. Surveillance data accessibility and transparency e. Case-based investigation f. Epidemiology workforce 3. Rapid Response a. Emergency preparedness and response planning b. Exercising response plans c. Emergency response operation d. Linking public health and security authorities e. Risk communication f. Access to communications infrastructure g. Trade and travel restrictions 4. Health System a. Health capacity in clinics, hospital, and community care centers b. Supply chain or health system and healthcare workers c. Medical countermeasures and personnel deployment d. Healthcare access e. Communication with healthcare workers during a public health emergency	a. National, legislation, policy and financing b. IHR coordination, communication and advocacy c. Antimicrobial resistance d. Zoonotic disease e. Food safety f. Biosafety and biosecurity g. Immunization 2. Detect a. National laboratory systems b. Real time surveillance c. Reporting d. Work force development 3. Respond a. Emergency preparedness b. Emergency response operations c. Linking public health with security authorities d. Medical countermeasures and personnel deployment e. Risk communication 1. Other IHR Hazards and points of entry a. Points of entry b. Chemical events c. Radiation emergencies	1. public health infrastructure a. surveillance b. immunization c. medical workforce d. hospital capacity e. coordination 2. physical infrastructure a. water and sanitation b. roads c. phones d. internet e. logistics 3. institutional Capacity a. political stability b. corruption c. bureaucratic effectiveness d. armed conflict e. homicide f. vital registration 4. economic resources a. government revenue generation b. per capita income c. gross domestic product d. health spending e. resource dependency 5. public health comunications a. public education b. risk communication	a. Health facilities b. Number of beds c. Immunization d. Access to improved sanitation e. Sustainable access to improved water f. Health insurance g. Mortality rate per 100 h. Hygiene behavior 2. Societal Conditions a. Total population b. Population density c. Literacy rate d. Access to internet e. Ownership of assets f. Access to mobile phone g. Poverty h. Acess to electricity i. Registered as permanent resident j. Average household size k. Household dependency ratio	1. Community resilience a. Community preparedness b. Community recovery 2. Incident management a. Emergency operations coordination 3. Information management a. Emergency public information and warning b. Information sharing 4. Countermeasures and mitigation a. Medical material management and distribution b. Medical countermeasure dispensing and administration c. Nonpharmaceutical interventions d. Responder safety health 5. Surge management a. Fatality management b. Mass care c. Medical surge d. Volunteer management 6. Biosurveillance a. Public health laboratory testing b. Public health surveillance and epidemiological investigation	Governance and Prevention a. Government effectiveness b. E-government c. Statistical capacity d. Information technology e. Emergency preparedness f. Stringency index g. Monitoring and testing 2. Health financing a. National health expenditure b. Population health expenditure c. Insurance coverage 3. Health service provision a. Health institution b. Hospital bed c. Medical access d. Health coverage e. Health care f. Health service supply pressure 4. Health workforce a. Surgeon b. Physician c. Nurse d. Pharmacist e. Biomedical technicians

f. Infection control practices g. Capacity to test and approve new countermeasures 5. Compliance with international norms a. IHR reporting compliance and disaster risk reduction b. Cross-border agreement on public health emergency response c. International commitments d. Completion and publication of WHO JEE and the OIE PVS e. Financing f. commitment to sharing genetic and biological data and specimens. 6) Risk environment a. Political and security risk b. Socioeconomic resilience c. Infrastructure adequacy d. Environmental risks e. Public health vulnerabilities				
Index Preparedness & Index Resilience	**WHO's toolkit for assessing health-system capacity for crisis management**	**Event-based surveillance (EBS) scorecard**	**COVID-19 Safety Index**	**The eleven key WHO Ebola Virus Disease Preparedness Component**
1. Average mortality rate 2. Hospital occupancy rate per 100,000 people 3. Intensive care unit occupancy rate per 100,000 people 4. COVID-19 vaccination vaccine dose 5. Number of vaccines administered per 100,000 people	1. Health service delivery 2. Health Workforce 3. Health information system 4. Essensial medicines 5. Health financing 6. Governance	1. Surveillance and digital intelligence 2. Information system 3. National laboratory systems and Networks 4. Preparedness and response 5. Public health research and institutes 6. Legislation 7. Finance 8. Workforce 9. Strategic plan 10. Structure	1. Density of medical technicians 2. Density of nursing and midwifery personnel 3. Density of medical doctors 4. Healthcare access and quality index 5. Vaccination rate 6. Average of 13 international health regulations core capacity scores	1. Coordination and leadership 2. Surveillance and Laboratory 3. Case management, Infection Prevention and Control 4. Risk Communication, social mobilization, and community engagement 5. Vaccination and operational research 6. Logistics

7. Domestic general government health expenditure (GGHE-D) as a percentage of general government expenditure (GGE) 8. General government receipts 9. General government expenditure (GGE) 10. Population density 11. Ageing rate	7. Strategic Information, Research and Innovation 8. Ecological/anthropological studies/investigations 9. Mental Health and Psychosocial support 10. Budget 11. Monitoring and evaluation

Table 5: Differences in each indicator on each preparedness assessment instrument

No	Parameter/indicators	Index Preparedness Index Resilience	Global Health Security Index (GHSI) Score	Joint External Evaluation (JEE)	WHO's toolkit for assessing health-system capacity for crisis management	Epidemic Preparedness Index (EPI)	Response Readiness Index (RRI	Event-based surveillance (EBS) Scorecard	COVID-19 safety index	Public Health Emergency Preparedness and Response Capabilities Framework	WHO Ebola Virus Disease (EBV) Preparedness	Health System Resilience Assessment
1	mortality rate per 100	✓					✓					
2	Hospital occupancy rate	✓										
3	Intensive care unit occupancy rate	✓										
4	Immunization/vaccination rate	✓	✓	✓		✓	✓		✓		✓	
5	The number of vaccine doses administered	✓										
6	physical infrastructure	✓	✓			✓	✓				✓	
7	social condition	✓	✓				✓		✓	✓		
8	Health insurance	✓					✓					✓
9	Antimicrobial resistance	✓	✓	✓								
10	Zoonotic disease	✓	✓	✓								
11	Biosecurity	✓	✓	✓								
12	Biosafety	✓	✓	✓								
13	Food safety	✓		✓								
14	chemical events	✓		✓								
15	radiation emergencies	✓		✓								
16	Research/public health research and institute	✓	✓					✓			✓	
17	Governance and leadership	✓		✓	✓							✓

18	Legislation	✓		✓				✓				
19	Policy	✓		✓								
20	Institutional Capacity/political stability	✓	✓			✓						
21	Economic resources	✓	✓			✓			✓			✓
22	Financing/budget	✓	✓	✓	✓			✓			✓	✓
23	Coordination	✓		✓		✓					✓	
24	Communication	✓	✓	✓								
25	Advocacy	✓		✓								
26	Laboratory	✓	✓	✓				✓		✓	✓	
27	Surveillance	✓	✓	✓		✓		✓		✓	✓	
28	Reporting	✓		✓								
29	Emergency Preparedness	✓	✓	✓				✓				✓
30	Emergency strategic/planning	✓	✓					✓			✓	✓
31	Emergency response operations	✓	✓	✓				✓		✓	✓	
32	Linking public health with security authorities	✓	✓	✓								
33	Information management	✓								✓		
34	Public awareness and community engagement	✓				✓					✓	
35	Risk communication	✓	✓	✓		✓					✓	
36	Public education	✓				✓						
37	Trade and travel restrictions	✓	✓									
38	Medical countermeasures and personnel deployment	✓	✓	✓						✓		
39	Surge management	✓								✓		
40	Health capacity in clinics, hospitals, and community care centers	✓	✓			✓						✓
41	Health facilities	✓					✓					✓
42	number of beds	✓					✓					✓
43	Supply chain/ Essential Medicine/logistics	✓	✓		✓						✓	✓
44	Health service delivery	✓			✓							
45	Healthcare access	✓	✓						✓			✓
46	Infection control	✓	✓								✓	✓

47	Capacity to test and approve new countermeasures	✓	✓									✓
48	Health workforce	✓			✓	✓		✓	✓			✓
49	Health information system	✓			✓			✓			✓	✓
50	Compliance with international norms and IHR Score	✓	✓						✓			
51	Environmental risks	✓	✓								✓	
52	Public health vulnerabilities	✓	✓									
53	point of entry	✓		✓							✓	
54	Mental health and psychosocial support										✓	
55	Monitoring and Evaluation										✓	✓
56	Stringency index											✓

4. Discussion

Monitoring the risks and vulnerabilities of a region, whether a country or a city/district, needs to be done regularly. This monitoring is necessary to ensure that each region, government, and community is prepared for emergencies such as health crises. Monitoring in the face of emergencies is necessary to identify weaknesses and strengths of the health and disaster preparedness system. The assessment results are helpful to illustrate and become a reference for decision-making in formulating strategies to improve a region's response to emergencies in the future. The results of this literature search indicate that 11 assessments or measurement tools can be used to assess preparedness at both the country and regional levels for emergencies. This study summarizes the various instruments or assessments to evaluate preparedness and looks at what indicators or factors are the parameters of preparedness. This can determine what factors make up the majority of emergency preparedness assessments, especially in emerging disease situations.

The most common instruments or assessments in the literature search above are the JEE and WHO's toolkit for assessing health-system capacity management. The JEE covers 19 technical areas: national policy, coordination, risk communication, epidemiological surveillance, and emergency response (Kentikelenis & Seabrooke, 2021). The JEE assesses a country's ability to fulfill International Health Regulations (IHR) and preparedness for global threats. The assessment can be done by a country's self-assessment, which conducts a comprehensive evaluation of the country's Health system in its capacity for prevention, detection, and response to epidemics and pandemics, as well as an external assessment from a team that will conduct an in-depth evaluation and provide recommendations. (Nguyen et al., 2021). WHO is Six Building Blocks, an important tool to assess and strengthen a country's health system. Although it has the same purpose, this system analyses the health system as a whole. It is divided into six main components: health service delivery preparedness, health workforce, health information system, essential medicines, health financing, and governance. The assessment is conducted in more depth for each block and evaluated based on specific indicators to see the strengths and weaknesses of the health system. (Organization, 2010). The difference between the two assessments can be seen if the JEE provides recommendations to provide a country's health preparedness capacity so that it can develop action plans against global threats, while the Six Building Blocks model is to develop health policies and improve the efficiency and effectiveness of health services because it assesses the whole health service. (Fall et al., 2023; Organization, 2023). Therefore, if a country evaluates with both, it can complement each other in preparing the country for a health crisis and strengthening the health system to increase global health security.

The most significant number of assessment parameters is found in the GHSI, which assesses preparedness and ability to deal with global health threats, including pandemics and epidemics. This indicator consists of 6 categories and 37 indicators developed to encourage the acceleration of improving national health security and international capabilities in addressing the most dangerous health risks, namely infectious disease outbreaks that can cause international epidemics and pandemics (Nuclear Threat Initiative, 2021). The results of the assessment using the GHSI index in 2019 in 195 countries show that no country is ready to face the threat of future epidemics and pandemics. Each country's national Health security needs to be stronger, and no country is fully prepared for an epidemic or pandemic. However, some studies show the GHSI has poor predictability and does not meet the needs of policymakers in society (Kaiser, Chen, & Gluckman, 2021).

The indicators or factors in each measurement become parameters that need to be prepared in each country in the face of emergencies. In general, the preparedness parameters most valued as factors that need to be prepared in an emergency are surveillance and financing preparedness. Instruments that include these two indicators as aspects of preparedness in dealing with emergencies are the assessment instruments using the Preparedness Index and Resilience Index, GHSI, JEE, EBS, and WHO EBV. In addition, parameters that often appear include physical infrastructure preparedness, emergency response operations, coordination, and the health workforce.

Surveillance is important in early detection, rapid response, and resource management. This aspect needs to be guaranteed to provide information related to emergencies and impacts, allowing a country to intervene more quickly before the disaster becomes more severe (Sukardi, Kataren, Rohana, Dachi, & Tarigan, 2022). Data obtained from the surveillance process helps in planning and decision-making, such as allocating resources more efficiently, designing health programs, and developing responsive policies. A robust surveillance system will enhance a country's ability to respond quickly and effectively to emerging health challenges. (Khatri et al., 2023). Then, the financing aspect plays an important role too because it is a source of preparing health resources (McMahon, Peters, Ivers, & Freeman, 2020). Financial resources are a necessary indicator in the event of a disaster because they can fulfill the pandemic preparedness needs. The government should have a long-term vision of financial resources, as the ongoing impact of the pandemic affects the country's budget collection sources. (Boyd, Wilson, & Nelson, 2020). Governance is only effective if there is money to pay for health workers, medicines, and hospitals; all factors can help access them (Ajisegiri, Chughtai, & MacIntyre, 2018).

Health infrastructure also plays an important role in preparing to reduce the impact of the health crisis. Any development in an area must also consider the potential risk of future disasters. Careful planning can make facilities available and ready to deal with emergencies more effectively (Hassan et al., 2023; Radford et al., 2024). Emergency response operations also play an important role in a country's preparedness for a health crisis. This is because preparing for the next epidemic or pandemic is important, as well as knowing the risk factors so that public health and medical emergency plans can be coordinated and activated effectively and timely. In an emergency such as this, it is seen that Rapid Response, Detection, and Reporting have the most impact (Chang & McAleer, 2020; Hassan et al., 2023). One of its greatest strengths in health service delivery is immediate notification following early detection and confirmation of a case. Improving health system resilience is the most fundamental approach to infectious disease prevention and control. In Indonesia, the government delayed the public health emergency response to avoid a sizeable economic impact, and as a result, had the highest number of confirmed cases in March 2020 in Southeast Asia. This exacerbated a significant imbalance in access to health services. (Olivia, Gibson, & Nasrudin, 2020). In managing a country's emergency preparedness, effective cross-sector coordination is essential. The synergy of various agencies can respond quickly to emergencies. The coordination that is formed can equalize perceptions and strategies in dealing with disasters, thereby reducing the risk of overlapping responsibilities (Arslan, Golgeci, Khan, Al-Tabbaa, & Hurmelinna-Laukkanen, 2021). The role of the government and laws and regulations related to outbreak control is very important, including cross-sector cooperation, and serves to sanction violations in pandemic control. (Van Hoang et al., 2021). Good coordination across sectors can ensure that the country is ready to face future health challenges.

Another factor widely valued as a parameter of preparedness is related to the preparedness of health workers. Health workers are a fundamental part of the health system; they perform duties that include carrying out medical research to improve disease prevention, diagnosis and treatment, clinical consultation, and provision of care to safeguard each patient. In practice, health workers are closely related to communication because they act as allies in dealing with the pandemic, especially in raising awareness among the public and fighting the stigma associated with the disease. (Aceng et al., 2020). Health workers face a more significant and stressful workload than usual during an epidemic, so they must be more resilient and adapt quickly to the changing situation (Chen et al, 2020). When faced with a public health crisis, health workers are often the first to respond. Adequate mobilization and coordination of health workers and medical supplies can significantly reduce mortality (Hanefeld et al, 2018).

Evaluating pandemic preparedness and control globally is important because each country has very different policies and practices depending on country-specific conditions. Adapting, validating, and routinely improving the validity of tools in health systems is an important process in disease control and prevention (Tran et al., 2022). Few preparedness assessment tools are available electronically and are user-friendly in facilitating participant and stakeholder data collection, analysis, dissemination, and discussion of results. This should be one of the drivers for developers to produce assessment tools in a more user-friendly manner (Haeberer et al., 2021). The findings in this study also illustrate a need to improve the current tools, such as proposing new fields to develop new tools with parameters customized to country-specific conditions, especially for infectious disease control. Further research is needed to develop specific domains for each country's priorities, given that most current tools may be broad. For example, some important variables for epidemic preparedness, such as community variables (e.g., population density, community interaction, or coverage of different protective measures) and individual factors (e.g., knowledge-attitude-practice, social networks, or trust in government), should be included and measured (Kundu et al., 2021).

5. Conclusion

Regularly monitoring the preparedness of a country and its respective regions is vital to ensure a swift and effective response to health crisis emergencies. This comprehensive assessment not only sheds light on the existing strengths and weaknesses of the health system but also identifies specific strategies that need to be implemented for improvement. Various measurement tools, such as the Joint External Evaluation (JEE) and the World Health Organization's (WHO) Toolkit, can be used to conduct a thorough evaluation. These tools are critical in gauging a country's capacity to prevent and respond to epidemic and pandemic situations. Several key factors are assessed as parameters of preparedness for health crises, including the preparedness of surveillance systems to detect and monitor outbreaks, the availability of sufficient financing to support health initiatives, the robustness of healthcare infrastructure, the effectiveness of cross-sector coordination, the adequacy of the health workforce, and the overall emergency response preparedness capabilities. A preparedness evaluation enhances a nation's ability to tackle future health challenges. Such evaluations bolster individual countries' health systems and strengthen the global health infrastructure, ensuring a more resilient response to upcoming health threats.

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