Biological clock and the gut: The connection of circadian rhythms, microbiome, and mental Health

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This article was submitted to RAD CASA - Medical Sciences as the original article

Conflict of Interest Statement: 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.

Received: 22 November 2024
Accepted: 2 December 2024
Published: 20 December 2024

Citation:
Vuckovic T, Melvan E. Biological clock and the gut: The connection of circadian rhythms, microbiome, and mental Health
565=68-69 (2024): 64-69
DOI: 10.21857/94kl4c134m

Abstract

Circadian rhythms, the gut microbiome and the brain are closely connected through biochemical and physiological pathways regulating mood, immunity, and metabolism. The circadian system aligns daily gene expression and hormone release with environmental cycles while the gut microbiome exhibits its rhythms that produce key metabolites such as serotonin, SCFAs, and melatonin which are essential for brain function and emotional balance. Disruptions in these rhythms due to irregular sleep, diet, stress or environment can lead to microbial imbalances and circadian misalignment, increasing the risk of mood disorders and anxiety. This review highlights the importance of synchronised rhythms and dietary strategies for supporting mental well-being.

Keywords: Circadian Rhythm, Microbiome, Mental Health, Gut-Brain Axis, Biological Clock

Sažetak:

Biološki sat i crijeva: Povezanost cirkadijalnih ritmova, mikrobioma i mentalnog zdravlja

Cirkadijalni ritam, crijevni mikrobiom i mozak usko su povezani putem biokemijskih i fizioloških putova koji reguliraju raspoloženje, imunitet i metabolizam. Cirkadijalni sustav usklađuje dnevnu ekspresiju gena i oslobađanje hormona s ciklusima iz okoliša, dok mikrobiom crijeva pokazuje svoje ritmove koji proizvode ključne metabolite kao što su serotonin, SCFA i melatonin koji su ključni za rad mozga i emocionalnu ravnotežu. Poremećaji u tim ritmovima zbog neredovitog sna, prehrane, stresa ili okoliša mogu dovesti do mikrobne neravnoteže i cirkadijalnog neusklađenosti, povećavajući rizik od poremećaja raspoloženja i tjeskobe. Ovaj pregled naglašava važnost sinkroniziranih ritmova i prehrambenih strategija za podršku mentalnom blagostanju.

Ključne riječi: Cirkadijalni ritam, mikrobiom, mentalno zdravlje, os crijeva i mozga, biološki sat

Introduction

Mental health disorders, encompassing anxiety, depression, bipolar disorder, autism spectrum disorder (ASD), schizophrenia, and eating disorders present complex challenges with substantial global impact on individuals and healthcare systems (1). Depression and anxiety disorders alone impact an estimated 280 million and 300 million people with depression as one of the leading causes of disability globally (2). The COVID-19 pandemic saw a marked increase in mentioned mental health issues worldwide. This surge is often associated with lifestyle disruptions, including increased stress, irregular eating patterns, and disturbed sleep (3). Increasing evidence underscores the involvement of interconnected physiological systems, notably circadian rhythms and the gut microbiome, in the aetiology of these disorders. Circadian rhythms are intrinsic 24-hour cycles that regulate sleep-wake patterns, metabolic processes, immune function, and emotional regulation, synchronizing internal physiological states with environmental cues such as the light-dark cycle (4). Emerging research suggests that the gut microbiome, a diverse ecosystem of microorganisms within the gastrointestinal tract, also follows circadian oscillations that correspond with the host's biological clock. These microbial rhythms are vital for gut health, influencing digestion, immune modulation, and nutrient absorption (5). Research reveals two-way communication between the microbiota and the central nervous system (CNS). Numerous studies indicate that the microbiota impacts behaviour, and immune challenges linked to anxiety and depression-like behaviours are also associated with changes in the microbiota (6).

This review looks at how circadian rhythms, microbiome balance, and mental health are connected. It covers recent findings, the underlying mechanisms, and how targeting these pathways might help support mental well-being.

Materials and Methods

This review sourced articles from biomedical databases, primarily PubMed and Google Scholar, using terms such as "circadian rhythm," "gut microbiome," "mental health," and "gut-brain axis." Inclusion criteria focused on recent studies, encompassing both human and animal models. Key papers were selected based on their relevance to circadian, microbiome, and mental health relationships.

Results

Circadian rhythms

Circadian rhythms are natural 24-hour cycles that are critical for controlling physiological functioning in organisms. They are regulated by cellular "clocks" that align internal biological processes with external cues like light and darkness. When we look at the molecular level, the circadian clock is composed of feedback loops including transcription and translation in which specific genes and proteins collaborate to produce rhythmic gene expression patterns (7). Transcription factors such as *Clock* and *Bmal1* play critical roles in starting rhythmic gene activity, whereas proteins such as *Period* (Per) and *Cryptochrome* (Cry) act as negative feedback controllers. This molecular mechanism is found in almost all cells, providing a coordinated pattern that regulates several vital biological functions required for physiological balance (7).

The primary circadian clock is located in the suprachiasmatic nucleus (SCN) in the brain. It receives environmental signals through the optic nerve, such as light. The SCN then synchronizes other clocks throughout the body by releasing signals to peripheral clocks located in organs and tissues. These peripheral clocks control local processes such as metabolism, immune function, and hormonal secretion. This allows different systems to operate in harmony with the body's needs at specific times of day. For example, metabolic processes and energy usage are timed to align with feeding and activity patterns, ensuring optimized energy intake and expenditure. Disruption of circadian rhythms due to factors such as shift work, irregular eating habits, or sleep disturbances can desynchronize these clocks, impacting overall health and contributing to conditions like metabolic syndrome, immune imbalances, and an increased risk of mental health disorders. Therefore, keeping circadian rhythms aligned is essential for maintaining physiological stability and promoting well-being (8).

Circadian rhythms and gut microbiome

Circadian rhythms and the gut microbiome form a dynamic system that regulates metabolic balance and overall health. The primary circadian clock in SCN sets the pace for peripheral clocks in various tissues, including the gut. The SCN responds primarily to environmental light-dark (LD) cycles, which help synchronize feeding, physical activity, and sleep (5). When the central clock signals optimal times for eating, the gut microbiome responds with rhythmic changes in composition and activity. This synchronization promotes efficient digestion, nutrient absorption, and immune response, all of which are crucial for metabolic stability. Studies show that up to 15% of gut bacteria fluctuate daily in abundance and activity, influenced by feeding cycles and the host's internal clock(9).

These rhythms influence bacterial functions such as amino acid and mucus metabolism, which help maintain gut health and provide nutrients for the host. The gastrointestinal tract also follows a circadian rhythm, with processes like enzyme secretion, motility, and epithelial cell renewal occurring in daily patterns. For example, colonic motility peaks during the host's active hours and slows down during rest, mirroring the daily activity cycles of the gut microbiome.(9).

The microbiome's influence extends beyond the gut. Recent studies indicate that microbial metabolites, such as short-chain fatty acids (SCFAs) and bile acids, vary in concentration throughout the day and affect gene expression in peripheral

organs, including the liver and intestines. These metabolites can even cross into the bloodstream exerting time-dependent effects on host metabolism. Disruptions caused by irregular feeding, abnormal light exposure, or poor sleep can throw off the gut microbiome's natural rhythms, potentially leading to metabolic disorders and increased inflammation (10).

Furthermore, the interaction between the gut microbiota and the host's circadian clock is vital for regulating daily physiological rhythms, including immune and metabolic functions. The circadian system regulates gene expression to align immune responses with times of high pathogen exposure. This includes pattern recognition receptors (PRRs) such as Toll-like receptors (TLRs) and NOD-like receptors, which detect microbial signals known as microbe-associated molecular patterns (MAMPs). In the gut, beneficial bacteria send MAMP signals that sync with circadian cues, creating specific windows for activating immune pathways, such as IKKβ and JNK, to support gut integrity and immunity (5).

Recent studies reveal that the microbiome can further influence circadian gene expression through chromatin modifications, regulating which genes are active at different times. For instance, gut microbes control histone acetylation in intestinal cells, impacting nutrient absorption and metabolic timing. In germ-free animals, the absence of these rhythmic gene patterns underscores the microbiome's essential role in daily cycles. In summary, this interaction between the microbiome and circadian rhythms maintains a time-sensitive balance in immune function, digestion, and metabolism (11).

Gut microbiota and circadian rythms in Mental health

Circadian disruptions are closely associated with mental health disorders, particularly depression and anxiety, as well as ADHD, autism spectrum disorder (ASD), bipolar disorder (BD), schizophrenia, and neurodegenerative conditions like Alzheimer's and Parkinson's disease. Depression and anxiety are often accompanied by disrupted sleep patterns, irregular melatonin and cortisol rhythms, and impaired responses to the light-dark cycle. In depression, symptoms often follow a daily pattern, worsening either in the morning or evening, which points to a potential misalignment of circadian rhythms (12).

A meta-analysis of 36 studies found a notable positive link between evening chronotypes and depression (13). Further analysis supported this, showing a higher risk of depression among evening-oriented individuals compared to those with morning preferences (14).

Chronotherapeutic treatments, including light therapy and social rhythm therapy, have shown efficacy in alleviating symptoms of depression and anxiety by targeting circadian regulation (15).

More recently, a depression-specific bacterial pattern was identified. It was characterised by a higher abundance of pro-inflammatory species, such as Enterobacteriaceae and Desulfovibrio, and lower SCFA producing-bacteria, such as Faecalibacterium, that may have an impact on the regulation of circadian rhythms, as these metabolites regulate the expression of circadian clock genes (16).

In ADHD, circadian misalignment appears as delayed sleep-wake cycles and increased insomnia, with potential effects on core symptoms and an association with obesity risk. In ASD, circadian disruptions often involve sleep disturbances and altered cortisol responses, with certain circadian gene polymorphisms linked to ASD symptoms. Bipolar disorder is highly sensitive to circadian shifts, with mood episodes often triggered by disruptions such as jet lag or irregular social rhythms. In schizophrenia, circadian misalignment appears in altered gene expression and hormone cycles, possibly worsening stress responses through HPA axis dysregulation (17).

Neurodegenerative diseases also exhibit circadian disruptions; Alzheimer's patients often experience "sundowning," where symptoms intensify in the evening, related to reduced melatonin levels. Parkinson's disease is marked by disrupted dopamine regulation, affecting circadian rhythms and increasing neurodegenerative risk. Together, these associations emphasise the importance of circadian-focused interventions, which may help manage depression, anxiety, and other mental health and neurodegenerative conditions by restoring rhythm alignment (18).

The mechanism behind the circadian rhythms and gut in mental health

The interaction between gut microbiota and circadian rhythms is crucial for mental health, involving multiple mechanisms such as producing key hormones and metabolites, including melatonin, serotonin, cortisol, and short-chain fatty acids (SCFAs). These molecules serve a dual purpose, where disruptions in circadian rhythms or microbial balance can influence each other, increasing the risk of mood disorders and cognitive impairments (4).

Melatonin, a hormone typically associated with the sleep-wake cycle, is produced not only in the pineal gland but also in large amounts within the gut by enterochromaffin cells and certain gut microbes. This intestinal melatonin, present at levels much higher than in the pineal gland, acts locally as an antioxidant and anti-inflammatory molecule, helping to preserve the gut barrier and support microbiota balance. Research suggests that melatonin may also influence gut bacterial rhythms, promoting alignment with the host's circadian cycle, which benefits overall gut health. However, exposure to light at night can suppress melatonin production, not only disturbing sleep but also impacting the microbiome by altering gut function, neurotransmitter production, motility, and immune responses, which can ultimately affect mental well-being. Adequate levels of melatonin are linked to feelings of well-being, while imbalances can contribute to mood disorders like depression and anxiety.Research indicates that melatonin supplementation may help reduce symptoms of depression in some cases, though findings are mixed, and more studies are needed (19).

Additionally, the microbiota has a significant role in regulating serotonin, a neurotransmitter critical for mood and cognitive function, with about 90% of the body's serotonin synthesized in the gut. Microbial metabolites that are influenced by circadian rhythms help to regulate this serotonin production. When circadian rhythms are disrupted, serotonin production may decrease, leading to challenges in emotional regulation and stability. In contrast, a well-synchronized circadian system allows gut microbes to support consistent serotonin levels, promoting a healthy gut-brain axis and mental well-being (20, 21)
Similarly, certain bacteria produce GABA, a neurotransmitter that calms neural activity, and dopamine, which is associated with reward and pleasure responses. These compounds are produced at different levels throughout the day, coordinated with feeding-fasting cycles and other circadian cues (22).
The vagus nerve serves as a direct communication route between the gut and brain, transmitting signals from the gut to brain regions associated with mood and cognition. Studies show that microbial production of GABA, for example, can stimulate the vagus nerve, reducing anxiety-like behaviour and promoting calm. Beyond vagal signaling, neurotransmitters and their metabolites produced in the gut can enter the bloodstream and cross the blood-brain barrier, affecting mood-regulating centers like the amygdala and prefrontal cortex. These pathways show how gut-derived neurotransmitters, influenced by circadian-regulated microbial activity, play a key role in shaping emotional states and cognitive function (23).
Cortisol, the primary stress hormone governed by the hypothalamic-pituitary-adrenal (HPA) axis, is also subject to circadian rhythms, peaking in the morning and gradually decreasing throughout the day in diurnal animals. The gut microbiota interacts with this axis through bacterial metabolites and strains that can influence stress responses. Dysbiosis, or microbial imbalance, can interfere with cortisol's natural rhythm, leading to irregular release patterns that have been associated with anxiety and depression. Chronic circadian misalignment, such as light exposure at night, may increase cortisol production, or hypercortisolemia, heightening susceptibility to stress-related mental health conditions (24),
Gut microbiota influences HPA axis function through microbial metabolites and gut-derived peptides and hormones. For instance, ghrelin, a hunger-stimulating hormone produced by the gut, is regulated in part by microbial activity and is linked to mood regulation and stress response.Similarly, microbial metabolites like short-chain fatty acids (SCFAs) can affect hormone release, including cortisol, influencing the body's stress response. A properly functioning HPA axis is crucial for handling stress effectively, and disruptions in this system are strongly linked to mental health conditions such as anxiety and depression. Chronic dysregulation of the HPA axis can amplify stress responses, causing prolonged high cortisol levels, which may worsen depressive symptoms and lead to mood instability (25).
SCFAs like butyrate, acetate, and propionate, produced by gut bacteria, follow circadian rhythms in their production. These molecules are vital for neuroprotection and play a key role in reducing inflammation. SCFAs help maintain the integrity of the blood-brain barrier and reduce neuroinflammation, both of which are crucial for supporting mental health. Circadian disruptions can interfere with SCFA production, diminishing their protective benefits. SCFAs also influence the production of melatonin and serotonin, forming a feedback loop that reinforces the circadian system and supports mental health (26, 27).
Experimental models have shown that butyrate has antidepressant-like effects, promoting neurogenesis and enhancing synaptic plasticity, which are essential for learning and memory (28).
Finally, the immune system, modulated by the microbiota in a time-dependent manner, is another link between circadian rhythms, the gut, and mental health. Circadian-regulated immune responses prepare the body for infections during active periods, and gut microbiota play a role in timing immune cell and cytokine production. Circadian disruption can cause dysbiosis, increasing gut permeability and allowing bacterial components like lipopolysaccharides (LPS) to enter the bloodstream. This process triggers chronic low-grade inflammation. This inflammation affects the brain's immune cells, or microglia, and is associated with neuroinflammation which is often linked to depression, anxiety, and other mental health disorders. The gut microbiome's rhythmic activity plays a key role in regulating a balanced immune response, preventing inflammation that could adversely affect mental health (29).

Diet

Diet not only influences the timing of circadian rhythms but also affects the composition and functionality of the gut microbiota, impacting the production of key metabolites like short-chain fatty acids (SCFAs), which are critical for metabolic and immune health. High-quality diets, rich in fiber and complex carbohydrates, enhance the production of SCFAs, including butyrate, acetate, and propionate, which follow circadian patterns and support blood-brain barrier integrity, reduce neuroinflammation, and promote gut health. In contrast, diets high in fats and simple sugars can disrupt the rhythmic production of SCFAs and alter microbial diversity, leading to inflammation and metabolic dysregulation (30).
Furthermore, diet quality impacts how well the gut microbiota aligns with the body's circadian clock. High-fat diets can disrupt the natural rhythms of microbial activity, leading to reduced SCFA production and a loss of their protective benefits. In contrast, time-restricted feeding (TRF), which aligns meal timing with circadian cycles, has been shown to restore diurnal rhythms in SCFA production, improve gut barrier function, and reduce systemic inflammation. This connection underscores how eating

habits and nutrient quality align to maintain circadian-microbiome balance, promoting overall health and lowering the risk of metabolic and immune-related issues (4).

Discussion

This review highlights the critical interplay between circadian rhythms, the gut microbiome, and mental health. Circadian rhythms, directed by the central clock in the SCN, synchronize with gut microbiota, impacting metabolic, immune, and mental health. Approximately 15% of gut bacteria follow daily rhythms influenced by feeding and fasting, with disruptions leading to dysbiosis—a factor linked to inflammation, metabolic imbalance, and mood disorders such as depression and anxiety.

The gut microbiome's role in producing neuroactive compounds, including SCFAs, serotonin, and melatonin, further supports mental health. SCFAs, produced in a circadian-regulated manner, support brain health by reducing neuroinflammation, while gut-derived melatonin helps maintain microbial balance and gut integrity. Factors like nighttime light exposure disrupt melatonin, impacting both sleep and microbiome stability.

Diet serves as a practical bridge, with high-fibre, time-restricted feeding patterns supporting SCFA production and maintaining microbial rhythms. Conversely, high-fat or irregular diets disrupt these rhythms, contributing to metabolic and mood-related challenges.

In conclusion, the interplay between circadian rhythms, the gut microbiome, and mental health is a multifaceted system that has far-reaching implications for physiological stability and disease prevention. This review supports a holistic approach to health that considers circadian rhythm alignment, diet quality, and gut microbiome balance as central components of mental wellness. Further research into these interactions will continue to clarify mechanisms and open avenues for innovative therapies targeting mental health through circadian and microbiome regulation.

References

1. Lund C, Crick D, et al. Social determinants of mental disorders and the Sustainable Development Goals: a systematic review of reviews. Lancet Psychiatry. 2018;5(4):357-369.
2. Institute of Health Metrics and Evaluation. Global Health Data Exchange (GHDx). Available from: https://vizhub.healthdata.org/gbd-results/. Accessed 4 November 2024.
3. Wang L, Nabi G, Zuo L, Wu Y, Li D. Impacts of the COVID-19 Pandemic on Mental Health and Potential Solutions in Different Members in an Ordinary Family Unit. Front Psychiatry. 2022 Jan 11;12:735653. doi: 10.3389/fpsyt.2021.735653.
4. Codoñer-Franch P, Gombert M, Martínez-Raga J, Cenit MC. Circadian Disruption and Mental Health: The Chronotherapeutic Potential of Microbiome-Based and Dietary Strategies. Int J Mol Sci. 2023 Apr 20;24(8):7579. doi: 10.3390/ijms24087579.
5. Gutierrez Lopez DE, et al. Circadian rhythms and the gut microbiome synchronize the host's metabolic response to diet. Cell Metab. 2021;33(5):873-887.
6. Foster JA, et al. Gut–brain axis: how the microbiome influences anxiety and depression. Trends Neurosci. 2013;36(5):305-312.
7. Takahashi J. Transcriptional architecture of the mammalian circadian clock. Nat Rev Genet. 2017;18:164-179. doi: 10.1038/nrg.2016.150.
8. Jha S. Biology of C Reactive Protein in Health and Disease. 1st ed. Singapore: Springer; 2016. Available from: https://link.springer.com/book/10.1007/978-81-322-3688-7.
9. Liang X, Bushman FD, FitzGerald GA. Time in Motion: The Molecular Clock Meets the Microbiome. Cell. 2014;159(3):469-470.
10. Frazier K, Chang EB. Intersection of the Gut Microbiome and Circadian Rhythms in Metabolism. Trends Endocrinol Metab. 2020 Jan;31(1):25-36. doi: 10.1016/j.tem.2019.08.013.
11. Thaiss CA, et al. Microbiota Diurnal Rhythmicity Programs Host Transcriptome Oscillations. Cell. 2016;167(6):1495-1510.e12.
12. Alachkar A, Lee J, Asthana K, et al. The hidden link between circadian entropy and mental health disorders. Transl Psychiatry. 2022;12:281. doi: 10.1038/s41398-022-02028-3.
13. Paul E, Teng S, Saunders KEA, Goodwin GM. The role of sleep in the prevention and treatment of depression. J Affect Disord. 2017;208:624-635. doi: 10.1016/j.jad.2016.10.011. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0165032716319176.
14. Merikanto I, Kortesoja L, Benedict C, et al. Evening-types show highest increase of sleep and mental health problems during the COVID-19 pandemic-multinational study on 19,267 adults. Sleep. 2022 Feb 14;45(2). doi: 10.1093/sleep/zsab216.
15. Haynes PL, Gengler D, Kelly M. Social Rhythm Therapies for Mood Disorders: an Update. Curr Psychiatry Rep. 2016 Aug;18(8):75. doi: 10.1007/s11920-016-0712-3.
16. Simpson CA, Diaz-Arteche C, Eliby D, et al. The gut microbiota in anxiety and depression - A systematic re-

view. Clin Psychol Rev. 2021;83:101943. doi: 10.1016/j.cpr.2020.101943.
17. Lorsung E, Karthikeyan R, Cao R. Biological Timing and Neurodevelopmental Disorders: A Role for Circadian Dysfunction in Autism Spectrum Disorders. Front Neurosci. 2021;15:642745. doi: 10.3389/fnins.2021.642745.
18. Shen Y, Lv Q, Xie W, et al. Circadian disruption and sleep disorders in neurodegeneration. Transl Neurodegener. 2023;12:8. doi: 10.1186/s40035-023-00340-6.
19. Bonmatí-Carrión MÁ, Rol MA. Melatonin as a Mediator of the Gut Microbiota-Host Interaction: Implications for Health and Disease. Antioxidants (Basel). 2023 Dec 23;13(1):34. doi: 10.3390/antiox13010034.
20. Chen Y, Xu J, Chen Y. Regulation of Neurotransmitters by the Gut Microbiota and Effects on Cognition in Neurological Disorders. Nutrients. 2021;13(6):2099. doi: 10.3390/nu13062099.
21. Grau-Del Valle C, Fernández J, Solá E, et al. Association between gut microbiota and psychiatric disorders: a systematic review. Front Psychol. 2023;14:1215674. doi: 10.3389/fpsyg.2023.1215674.
22. Sittipo P, Choi J, Lee S, et al. The function of gut microbiota in immune-related neurological disorders: a review. J Neuroinflammation. 2022;19:154. doi: 10.1186/s12974-022-02510-1.
23. Mhanna AM, Martini NM, Hmaydoosh GM, et al. The correlation between gut microbiota and both neurotransmitters and mental disorders: A narrative review. Medicine (Baltimore). 2024;103(5). doi: 10.1097/MD.0000000000037114.
24. Sudo N. Role of gut microbiota in brain function and stress-related pathology. Biosci Microbiota Food Health. 2019;38(3):75-80. doi: 10.12938/bmfh.19-006.
25. Spencer SJ, Xu L, Clarke MA, et al. Ghrelin regulates the hypothalamic-pituitary-adrenal axis and restricts anxiety after acute stress. Biol Psychiatry. 2012;72(6):457-465. doi: 10.1016/j.biopsych.2012.03.010.
26. O'Riordan KJ, Collins MK, Moloney GM, et al. Short chain fatty acids: Microbial metabolites for gut-brain axis signalling. Mol Cell Endocrinol. 2022;546:111572. doi: 10.1016/j.mce.2022.111572.
27. Kubo M. Diurnal Rhythmicity Programs of Microbiota and Transcriptional Oscillation of Circadian Regulator, NFIL3. Front Immunol. 2020;11:552188. doi: 10.3389/fimmu.2020.552188.
28. Val-Laillet D, Guérin S, Coquery N, et al. Oral sodium butyrate impacts brain metabolism and hippocampal neurogenesis, with limited effects on gut anatomy and function in pigs. FASEB J. 2018;32(4):2160-2171. doi: 10.1096/fj.201700547RR.
29. Fu Y, Gu Z, Cao H, et al. The role of the gut microbiota in neurodegenerative diseases targeting metabolism. Front Neurosci. 2024;18:1432659. doi: 10.3389/fnins.2024.1432659.
30. Lotti S, Dinu M, Colombini B, et al. Circadian rhythms, gut microbiota, and diet: Possible implications for health. Nutr Metab Cardiovasc Dis. 2023;33(8):1490-1500. doi: 10.1016/j.numecd.2023.05.009.