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Short Communication

Interconnected health: Exploring the bidirectional relationships between cardiovascular disease and comorbid conditions

Yoshiyasu Takefuji

SciencePark Corporation, 3-24-9 Iriya-Nishi, Zama-shi, Kanagawa, 252-0029, Japan

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ABSTRACT

This short survey systematically examines the bidirectional relationships between cardiovascular disease (CVD) and multiple comorbid conditions—including mental health disorders (depression, ADHD, insomnia), cancer, metabolic syndrome, diabetes, obesity, cognitive decline, frailty, gut microbiota, and periodontal health—based on recent peer-reviewed studies indexed in the National Library of Medicine. A systematic Google search restricted to nih.gov identified 299 documents on integrated care and CVD, 298 on CVD and multimorbidity, and 294 on CVD and systemic inflammation published within one year (as of January 14, 2026). Combining all three terms yielded only 30 documents, indicating a significant research gap. Evidence from these studies demonstrates that mental disorders, cancer, metabolic dysfunction, cognitive decline, frailty, gut microbiota dysbiosis, and periodontal disease each share bidirectional pathophysiological links with CVD, primarily mediated by systemic inflammation, immune dysregulation, and metabolic dysfunction. Managing one condition frequently and positively influences others, and emerging fields such as reverse cardio-oncology further illustrate the reciprocal interplay between CVD and cancer. These findings support a holistic, integrated care approach over isolated disease management. Lifestyle modification, gut microbiome-targeted interventions, and personalized medicine represent promising strategies for improving outcomes in patients with CVD-centered multimorbidity. Given the identified research gap at the intersection of integrated care, multimorbidity, and systemic inflammation, future large-scale prospective studies are warranted to establish causal mechanisms and validate multidisciplinary, integrated care models in clinical practice.

1. Introduction

This short survey aims to systematically examine and elucidate the complex bidirectional relationships between cardiovascular disease (CVD) and multiple comorbid conditions, including mental health disorders, cancer, metabolic syndrome, diabetes, cognitive decline, and gut microbiota dysbiosis. By synthesizing recent peer-reviewed evidence, this study seeks to identify shared pathophysiological mechanisms such as inflammation, immune dysregulation, and metabolic dysfunction that link CVD with these interconnected conditions. The research endeavors to demonstrate the clinical implications of these bidirectional relationships, showing how treating one condition may positively impact others through common therapeutic targets. Furthermore, it advocates for integrated, multidisciplinary care approaches that address patients holistically rather than managing diseases in isolation, while exploring emerging therapeutic strategies including lifestyle modifications, microbiome-targeted interventions, and personalized medicine approaches. Ultimately, this review provides evidence-based recommendations for clinicians to implement comprehensive care strategies that improve overall patient outcomes and quality of life in individuals with multiple comorbidities centered around cardiovascular disease.

2. Methods

A systematic Google search analysis reveals the rapidly evolving landscape of cardiovascular disease research at the intersection of multiple health domains. Using the Google search command "integrated care" ("cardiovascular disease" OR CVD) site:nih.gov after:2024– 12– 31, 299 documents published within the last year as of January 14, 2026 were identified, nearly identical to the 298 documents found for cardiovascular diseases and multimorbidity. Notably, 294 documents addressed cardiovascular diseases and systemic inflammation, indicating burgeoning interest in bidirectional relationship mechanisms across these interconnected health domains. However, when combining all three keywords—integrated care, multimorbidity,

E-mail address: takefuji@keio.jp.

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3050-4759/© 2026 Elsevier Ltd. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

and systemic inflammation—with cardiovascular diseases, only 30 documents were retrieved, revealing a significant research gap at this critical intersection. Among these 30 documents, the most highly cited paper (101 citations) was Yang et al.'s comprehensive review on diabetic neuropathy: "Diabetic neuropathy: cutting-edge research and future directions" [1,15]. The second most cited work (46 citations) was Cacciatore et al.'s analysis of urban health disparities: "Urban health inequities and healthy longevity: traditional and emerging risk factors across the cities and policy implications" [16]. This citation pattern underscores the field's emphasis on both mechanistic understanding and population-level health determinants.

3. Results

Drawing from the most recent peer-reviewed publications in the National Library of Medicine, the largest and most trusted biomedical database globally, this 2024 literature review investigated the bidirectional relationship between cardiovascular disease and various other health conditions. It explored how these diseases might influence each other, looking at mental health (depression, ADHD, insomnia), cancer, metabolism, cognitive decline, frailty, gut bacteria, gum disease, metabolic syndrome, diabetes, and obesity. The review highlights the complex interplay between these conditions, suggesting that treating one could improve others. This interconnectedness opens doors for future research, potentially leading to a more holistic understanding of these diseases and better prevention and treatment options. The importance of lifestyle changes and understanding the underlying mechanisms is emphasized. Additionally, personalized medicine and the gut microbiome show promise for more individualized and integrated care in the future.

Given the widespread adoption of AI analytical tools, rigorous evaluation of data quality and detection of AI misapplications have become essential, yet existing studies frequently fail to validate their results adequately. A fundamental gap persists: many researchers lack understanding of core supervised learning principles, particularly the critical distinction that supervised models generate two fundamentally different types of accuracy: target prediction accuracy and feature importance accuracy. While target prediction accuracy can be validated against ground truth labels, feature importance measures inherently lack ground truth for validation, creating a methodological blind spot that frequently leads to erroneous causal interpretations. This problem is compounded when researchers apply linear methods to nonlinear data or employ parametric/semiparametric approaches on nonparametric data, producing systematically distorted outcomes and flawed conclusions. To establish true associations rather than mere statistical artifacts, two essential criteria must be rigorously validated: consistency across multiple analytical approaches and dose-response relationships. Unfortunately, existing studies routinely overlook these validation requirements, perpetuating a cycle of unreliable findings in AI-driven research.

A reciprocal relationship exists between mental disorders and cardiovascular disease (CVD). This study explored how they influence each other [1]. They found that depression, attention deficit disorder and insomnia raise the risk of CVD, and using antidepressants is also linked to higher CVD risk. Interestingly, depression itself wasn't directly linked to CVD. The study suggests that antidepressants might be a reason behind the connection between depression and CVD [1].

Atherosclerosis and cancer were linked in a complex, two-way relationship [2]. Both diseases were underpinned by shared risk factors and analogous biological processes. This interplay influenced how they develop and progress. Cancer and its treatments can worsen atherosclerosis, and vice versa. Understanding this connection was crucial for improved prevention and treatment of both conditions [2].

A new field in medicine, reverse cardio-oncology, explored the bidirectional link between CVD and cancer [3]. While traditionally focused on cancer treatment harming hearts, their approach examined how pre-existing CVD raises cancer risk. Shared unhealthy habits and underlying inflammation were potential culprits. Their review explored this connection, including risk factors, mechanisms, and future directions for collaborative care and research [3].

A bidirectional Mendelian randomization (MR) analysis was performed to investigate the causal relationship between basal metabolic rate (BMR) and CVDs [4]. Results indicated a genetically predicted higher BMR is causally associated with an increased risk of Heart Failure, Atrial Fibrillation, Aortic Aneurysm [4].

Park et al. explored the two-way link between cognitive function and CVD in older adults [5]. Researchers compared cognitive performance in older adults with and without CVD. Those with CVD showed lower scores on various cognitive tests. Notably, congestive heart failure and being older than 80 years with CVD were associated with a steeper decline in cognitive function. Overall, their study suggested CVD can worsen cognitive performance, particularly among those with certain CVD subtypes or older age [5].

Frailty, a state of increased vulnerability, was a major concern in cardiac intensive care units (CICU) for both young and old patients [6]. It created a two-way street with cardiovascular disease, worsening outcomes and making treatment trickier. CICU stays can worsen frailty, creating a cycle of decline. Their review examined how to assess frailty in CICU patients and how best to care for them during and after their stay [6].

Previous studies linked gut microbiota to cardiovascular disease, but the link to endocarditis remained unclear [7]. A bidirectional MR study was performed to investigate the relationship between gut microbiota and endocarditis. Their results suggested specific gut bacteria like Victivallaceae and Eubacterium fissicatena group might protect against endocarditis, while Blautia and Ruminococcus2 might increase the risk. Interestingly, endocarditis was also found to have a negative effect on Eubacterium fissicatena group. Overall, their study highlighted the potential role of gut microbiota in endocarditis [7].

Qu et al. investigated the bidirectional relationship between cardiovascular health (CVH) and gum disease (periodontitis) [8]. Analyzing data from a large national survey, researchers found that better CVH (higher LE8 score) corresponded with a lower chance of having periodontitis. This association held even after accounting for factors like age and socioeconomic status. Interestingly, socioeconomic status seemed to influence this connection, suggesting a need for tailored approaches to improve both oral and heart health in vulnerable populations [8].

Cardiovascular Disease (CVD) has complex bidirectional relationships with other conditions like cancer, diabetes, and depression, meaning each can worsen the other through shared pathways like inflammation, immune responses, and common risk factors (smoking, poor diet), creating a vicious cycle where heart disease increases cancer risk (and vice versa), diabetes accelerates vascular damage, and depression heightens heart attack risk, emphasizing the need for integrated care [9–11].

4. Discussion

This literature review highlights the intricate bidirectional relationships between cardiovascular disease (CVD) and various health conditions, emphasizing the complexity of these connections. A particularly significant link exists between liver and heart health in individuals with metabolic syndrome or type 2 diabetes. These conditions raise the risk of fatty liver disease and cardiovascular issues, creating a cycle driven by insulin resistance, which deteriorates both liver and heart function. Furthermore, obesity serves as a bidirectional risk factor for multiple cardiovascular diseases, including atrial fibrillation, heart failure, and diabetes, exacerbating these conditions while also being exacerbated by them.

Recent advancements in obesity management were explored, with researchers focusing on medications, gut microbiome research, and

personalized medicine. Although surgical interventions like liposuction and bariatric surgery exist, a strong emphasis remains on lifestyle changes and understanding the underlying mechanisms of obesity. The role of the gut microbiome is particularly promising, and ongoing research into personalized dietary interventions offers new avenues for treatment and prevention.

The findings of this review also indicate that mental health disorders—such as depression and insomnia—not only heighten the risk of developing CVD but can also be influenced by cardiovascular issues themselves. This reciprocal relationship highlights the need for integrated treatment approaches, where addressing mental health may simultaneously improve cardiovascular outcomes.

Moreover, the interplay between atherosclerosis and cancer further illustrates the complexities of these conditions, as both share risk factors like inflammation and unhealthy lifestyle habits. This connection suggests that efforts to manage one condition could positively affect the other, reinforcing the need for a multidisciplinary approach in clinical practice. The emergence of reverse cardio-oncology, which explores the interplay of cardiovascular and cancer care, emphasizes the importance of a more integrated understanding of these two vital health domains.

Research has also examined cognitive function in relation to CVD, identifying that older adults with heart disease often experience cognitive decline, necessitating early intervention and monitoring strategies for these populations to address associated impairments.

The recognition of frailty as a complicating factor in cardiac intensive care units (CICUs) reveals multifaceted challenges for healthcare providers. By assessing frailty alongside cardiac conditions, clinicians may tailor interventions more effectively to improve patient outcomes and disrupt the deterioration often seen in these settings.

Additionally, emerging research on gut microbiota indicates that these microorganisms may play a protective role against conditions like endocarditis while also being susceptible to its effects. This emerging field may promote innovative probiotic or dietary strategies to enhance cardiovascular health.

The review also emphasizes the bidirectional connections between cardiovascular health and periodontal disease, illustrating the interconnectedness of overall health. By considering socioeconomic factors in these relationships, healthcare providers can develop targeted strategies to address disparities and improve both oral and heart health in vulnerable populations.

In summary, the findings call for a holistic approach to health, advocating for the simultaneous treatment of interconnected conditions rather than isolating them. Such an approach could lead to enhanced preventative strategies, optimized treatment plans, and improved health outcomes for patients with complex health challenges. Continued research in this area holds significant promise for advancing integrated care models that improve both quality of life and longevity.

Future research should prioritize the development and validation of integrated care models that simultaneously address cardiovascular disease and its interconnected comorbidities through multidisciplinary team approaches, as comprehensive care models have demonstrated synergistic impacts on both mental health and cardiovascular wellness [12]. Large-scale prospective studies are needed to establish causal relationships between CVD and conditions like depression, cancer, and metabolic syndrome, moving beyond observational data. Investment in precision medicine technologies, including artificial intelligence and machine learning algorithms, can enable personalized risk stratification and treatment optimization based on individual genetic, metabolic, and lifestyle profiles. The gut microbiome represents a promising therapeutic target requiring rigorous clinical trials to assess microbiome-modulating interventions for cardiovascular protection. Implementation science research should focus on translating evidence-based integrated care protocols into routine clinical practice, particularly in resource-limited settings where policy frameworks for integrated cardiovascular and mental health management in primary care are urgently needed [13]. Furthermore, investigating novel anti-inflammatory therapies targeting shared pathophysiological pathways across multiple conditions may yield breakthrough treatments. Finally, longitudinal studies examining the bidirectional temporal relationships between CVD and comorbidities will enhance understanding of disease progression and inform early intervention strategies that maximize patient outcomes, particularly in managing the diabetes-cardiovascular disease continuum through integrated care approaches [14].

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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