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GLP-1 Receptor Agonists in Breast Cancer Survivorship: Current Evidence, Biological Rationale, and Clinical Implications

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Abstract

Breast cancer survivorship has evolved into a multidimensional phase of care that extends well beyond completion of cancer treatment. Obesity, treatment-associated weight gain, metabolic dysfunction, chronic inflammation, fatigue, sleep disturbance, cardiovascular disease, chronic pain, and impaired quality of life contribute substantially to long-term morbidity. As the population of breast cancer survivors continues to grow, optimizing recovery increasingly requires therapeutic strategies that address not only metabolic disease but also the biological, functional, and patient-centered determinants of long-term health.

Glucagon-Like Peptide-1 (GLP-1) receptor agonists are established therapies for obesity, type 2 diabetes, and cardiometabolic disease. Beyond these proven metabolic benefits, accumulating evidence suggests that GLP-1 signaling influences multiple biological processes relevant to survivorship, including inflammatory regulation, immune function, neuroimmune communication, autonomic balance, mitochondrial bioenergetics, and stress physiology. These pleiotropic effects have generated growing interest in the potential role of GLP-1 receptor agonists within comprehensive survivorship care aimed at improving metabolic health, physical function, and physiological resilience.

This narrative review examines the current evidence supporting GLP-1 receptor agonists in breast cancer survivorship. We review major survivorship challenges that intersect with GLP-1 biology including obesity, metabolic dysfunction, chronic inflammation, fatigue, sleep disturbance, and persistent pain while summarizing emerging evidence on the metabolic, neuroimmune, and systemic effects of GLP-1 signaling. Particular emphasis is placed on distinguishing established clinical evidence from evolving mechanistic hypotheses and considering the potential implications of these therapies for long-term health, functional recovery, and quality of life.

Current evidence is strongest for weight management, glycemic control, metabolic health, and cardiovascular risk reduction, whereas survivorship-specific clinical data remain limited. Future research should extend beyond traditional metabolic endpoints to include body composition, preservation of skeletal muscle, physical function, symptom burden, patient-reported outcomes, quality of life, and healthy aging. Such multidimensional investigations will be essential for defining the evidence-based role of GLP-1 receptor agonists within comprehensive, multidisciplinary survivorship care.

Keywords: Breast cancer survivorship; GLP-1 receptor agonists; Cancer survivorship; Obesity; Metabolic health; Quality of life; Weight management; Cardiovascular health

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Introduction

Advances in screening, diagnosis, and treatment have resulted in a steadily growing population of breast cancer survivors worldwide. As survival rates continue to improve, the focus of care has expanded beyond disease control to optimize the long-term health and well-being of individuals living after cancer treatment. Survivorship is now recognized as a distinct phase of care characterized by persistent physical, psychological, and metabolic challenges that may extend for years after

Figure 1: The Survivorship Resilience Wheel: Potential Intersections Between GLP-1 Receptor Agonists and Breast Cancer Survivorship. Conceptual model illustrates the interconnected biological and clinical domains of breast cancer survivorship and the proposed intersections of GLP-1 receptor agonist biology with survivorship health. Intended as a conceptual framework based on current evidence.

therapy. Contemporary survivorship care therefore emphasizes not only prolonging survival but also preserving physical function, promoting healthy aging, maintaining independence, and improving quality of life across the survivorship continuum [1,4].

Among breast cancer survivors, obesity, weight gain, insulin resistance, chronic inflammation, fatigue, sleep disturbance, cardiovascular disease, and persistent pain frequently coexist and interact. These challenges may arise from surgery, chemotherapy, radiation therapy, endocrine therapy, reduced physical activity, psychosocial stress, aging, and preexisting metabolic vulnerability. Rather than occurring independently, they form interconnected biological and clinical networks that influence recovery, functional capacity, and overall survivorship health [13,16].

Obesity and metabolic dysfunction have emerged as central survivorship concerns because their consequences extend far beyond excess body weight. Many survivors experience treatment-associated weight gain accompanied by adverse changes in body composition that persist long after therapy is completed. Increased adiposity has been associated with chronic inflammation, insulin resistance, cardiovascular risk, impaired physical performance, and poorer long-term health outcomes, underscoring the importance of interventions that improve metabolic health while preserving overall physiological function. Accordingly, modern survivorship care increasingly emphasizes health span, preservation of skeletal muscle, physical function, and long-term quality of life alongside longevity [10,16,19].

As understanding of Glucagon-Like Peptide-1 (GLP-1) biology has evolved, attention has expanded beyond its established metabolic effects. GLP-1 receptor agonists have transformed the treatment of obesity and type 2 diabetes through their demonstrated effects on appetite regulation, weight reduction, glycemic control, and cardiometabolic health. Increasing evidence indicates that GLP-1 receptors are widely distributed throughout the central nervous system, immune system, cardiovascular tissues, and peripheral organs, where they participate in inflammatory regulation, neuroimmune communication, autonomic function, mitochondrial biology, and cellular responses to physiological stress. These pleiotropic actions have broadened scientific interest in GLP-1 receptor agonists as therapies capable of influencing multiple determinants of health rather than metabolism alone [5,6].

This expanding understanding of GLP-1 biology is particularly relevant to breast cancer survivorship because many pathways influenced by GLP-1 signaling overlap with mechanisms implicated in persistent symptom burden, physiological resilience, functional recovery, and healthy aging after cancer treatment. Although much of the current evidence derives from obesity, diabetes, cardiovascular medicine, and experimental models, these shared biological mechanisms provide a compelling rationale for examining how established metabolic therapies may contribute to comprehensive survivorship care while maintaining a clear distinction between established clinical evidence and evolving mechanistic hypotheses [7,8,20].

This review examines the evolving role of GLP-1 receptor agonists within breast cancer survivorship by integrating evidence from metabolic medicine, cardiovascular medicine, immunology, neuroscience, rehabilitation, and survivorship research. Rather than focusing solely on weight loss or glycemic control, it considers how the broader biological actions of GLP-1 signaling may influence metabolic health, functional recovery, physiological resilience, and quality of life after breast cancer treatment. Throughout, emphasis is placed on distinguishing established clinical evidence from emerging mechanistic hypotheses while identifying key priorities for future research. By bringing together these diverse areas of investigation,

this review aims to provide a balanced, evidence-based perspective on the potential role of GLP-1 receptor agonists within comprehensive, multidisciplinary survivorship care Figure 1 [1,4,7].

Major challenges in breast cancer survivorship

Breast cancer survivorship is increasingly recognized as a complex biological and clinical state in which recovery is shaped by interconnected metabolic, inflammatory, neurological, cardiovascular, behavioral, and psychosocial processes. Rather than occurring independently, these challenges interact to influence symptom burden, physical function, and quality of life throughout survivorship. This evolving systems-based perspective has expanded survivorship care beyond disease surveillance to include the biological processes that drive recovery, physiological resilience, and healthy aging [1,4,16].

Weight gain, obesity, and metabolic dysfunction

Weight gain, adverse changes in body composition, and metabolic dysfunction are among the most common long-term consequences of breast cancer treatment. Chemotherapy, endocrine therapy, menopause, treatment-related fatigue, reduced physical activity, and altered energy balance all contribute to these changes, which frequently persist long after treatment has ended [3,16,17].

The consequences of obesity extend well beyond excess body weight. Increased adiposity has been associated with chronic low-grade inflammation, insulin resistance, cardiovascular disease, impaired physical function, reduced quality of life, and a greater burden of chronic comorbidities that may complicate recovery [13,16,18].

Equally important are treatment-related changes in body composition. Many survivors experience progressive loss of lean muscle mass accompanied by increased fat mass, even when overall body weight changes only modestly. These alterations adversely affect metabolic health, physical performance, and functional recovery, emphasizing that body composition is a more meaningful indicator of survivorship health than body weight alone [10,19,21].

Metabolic dysfunction further compounds this clinical picture. Treatment-related endocrine alterations, impaired energy metabolism, and unfavorable body composition may promote insulin resistance and broader metabolic disturbances that influence cardiovascular risk, fatigue, physical function, symptom burden, and quality of life. These relationships appear bidirectional: persistent symptoms can further impair metabolic health, while metabolic dysfunction may amplify inflammation and delay recovery. Consequently, optimizing metabolic health has become a cornerstone of contemporary survivorship care [1,2,13,18].

Together, these metabolic disturbances may reduce physiological resilience the capacity to maintain or restore biological homeostasis in response to physiological stress. Diminished resilience has emerged as an important concept in survivorship because impaired adaptive capacity may contribute to persistent symptoms, delayed recovery, and accelerated biological aging. This perspective supports therapeutic approaches that target interconnected physiological systems rather than isolated disease processes [3,4,22].

Chronic Inflammation, Immune Dysregulation, and Physiological Resilience

Biological recovery after breast cancer treatment is often incomplete despite successful completion of therapy. Many survivors exhibit persistent low-grade inflammation months or even years later. Surgery, radiation therapy, chemotherapy, endocrine therapy, obesity, psychosocial stress, and metabolic dysfunction may each contribute to sustained inflammatory signaling that persists well beyond active treatment and influences long-term recovery [3,14,16,20].

Persistent inflammation has been associated with fatigue, sleep disturbance, cognitive dysfunction, mood symptoms, impaired physical function, and chronic pain. These inflammatory pathways interact closely with metabolic, immune, neuroendocrine, autonomic, and behavioral regulatory systems, illustrating the integrated physiological networks that shape survivorship health. This growing body of evidence supports a systems-based model in which persistent symptoms arise from coordinated biological dysregulation rather than isolated abnormalities [1,2,5].

Chronic inflammation may also impair physiological resilience by reducing the body's capacity to adapt to ongoing physiological stress. This framework links inflammatory regulation with metabolic health, functional recovery, healthy aging, and quality of life, providing a biological rationale for therapeutic strategies capable of influencing multiple interconnected pathways rather than individual symptoms alone [3,4,22].

Fatigue, Functional Recovery, and Sleep Health

Fatigue, impaired physical function, and sleep disturbance are among the most prevalent and disabling challenges faced by breast cancer survivors. Together, they contribute substantially to impaired recovery, loss of independence, and reduced quality of life[14,16].

Cancer-related fatigue remains one of the most common and persistent symptoms experienced by breast cancer survivors. Unlike normal tiredness, it often persists despite adequate rest and may substantially limit employment, exercise participation, social engagement, and activities of daily living.

The origins of cancer-related fatigue are multifactorial, reflecting interactions among inflammation, metabolic dysfunction, endocrine alterations, sleep disruption, psychological stress, treatment-related toxicities, and physical deconditioning. Fatigue frequently accompanies reductions in strength, endurance, mobility, and exercise tolerance that may persist long after treatment completion. Together, these changes diminish physical reserve and adaptive capacity, reinforcing the importance of preserving functional health throughout survivorship [3,14,22,23].

Sleep disturbance is another common challenge. Difficulties initiating or maintaining sleep, together with poor sleep quality, have been associated with fatigue, cognitive impairment, mood disturbance, and reduced physical performance. Sleep disruption may further amplify inflammatory signaling, impair metabolic regulation, increase pain sensitivity, and contribute to accelerated biological aging, thereby perpetuating symptom burden and slowing recovery [24,27].

Taken together, fatigue, impaired physical function, and sleep disturbance highlight the interconnected nature of survivorship health. These observations reinforce the importance of comprehensive care that integrates exercise, nutritional optimization, rehabilitation, behavioral interventions, and management of metabolic health to preserve function, promote healthy aging, and improve patient-reported outcomes [1,2,28,29].

Figure 2: The Survivorship Journey Map: Evolving Challenges and Potential Points of Influence of GLP-1 Receptor Agonists Across the Breast Cancer Survivorship Continuum. Conceptual model illustrating the evolution of interconnected survivorship challenges from diagnosis through long-term survivorship and healthy aging, together with the potential biological intersections of GLP-1 receptor agonists within the survivorship continuum. Intended as a conceptual framework based on current evidence and not as evidence of therapeutic efficacy for specific cancer-related symptoms.

Stress Regulation, Persistent Pain, and Whole-Person Survivorship

The symptom clusters experienced by many breast cancer survivors are shaped not only by metabolic and inflammatory disturbances but also by dysregulation of stress-responsive physiological systems. Chronic stress associated with cancer diagnosis, treatment, fear of recurrence, and ongoing health concerns may alter neuroendocrine and autonomic function, contributing to inflammation, fatigue, sleep disturbance, impaired recovery, and persistent symptom burden. These interactions underscore the close relationship between psychological and physiological adaptation throughout survivorship [16,22,24,27].

Persistent pain represents another major survivorship challenge. Pain may develop following surgery, radiation therapy, reconstruction, or other treatment-related factors and can substantially impair physical function, sleep quality, emotional well-being, and daily activities. Among the best-recognized pain conditions is post-mastectomy pain syndrome, which is increasingly understood as a multifactorial disorder arising from interactions among peripheral nerve injury, neuroimmune signaling, central sensitization, stress physiology, and psychosocial influences rather than ongoing tissue damage alone [24,30].

Chronic pain rarely occurs in isolation. Instead, it commonly coexists with fatigue, sleep disturbance, mood symptoms, inflammation, metabolic dysfunction, and declining physical function, further illustrating the integrated nature of survivorship health. This supports a whole-person, multidisciplinary approach that addresses biological, behavioral, and functional contributors to recovery rather than individual symptoms in isolation. Viewed through this systems-based perspective, therapies capable of influencing multiple interconnected pathways may offer new opportunities to improve physiological resilience, functional recovery, and overall survivorship health Figure 2 [1,4].

Biological Effects of GLP-1 Signaling Beyond Glycemic Control

Growing recognition that breast cancer survivorship is shaped by interconnected biological systems has expanded interest in therapies capable of influencing multiple physiological pathways rather than isolated disease processes. Persistent symptom burden reflects interactions among metabolic, inflammatory, neuroimmune, autonomic, neuroendocrine, and behavioral mechanisms. Within this framework, Glucagon-Like Peptide-1 (GLP-1) receptor agonists have attracted increasing attention because their effects extend beyond glycemic regulation and intersect with several biological pathways relevant to recovery, functional health, and survivorship [1,2].

Originally developed to treat type 2 diabetes and obesity through appetite regulation, weight reduction, and improved glucose homeostasis, GLP-1 receptor agonists are now recognized to influence a broad range of physiological processes. GLP-1 receptors are expressed throughout the central nervous system, cardiovascular system, gastrointestinal tract, immune cells, and peripheral tissues, where they participate in inflammatory regulation, neuroimmune communication, mitochondrial function, cellular adaptation, and maintenance of physiological homeostasis. These pleiotropic effects have broadened scientific interest in GLP-1 receptor agonists as therapies capable of influencing coordinated biological systems rather than metabolism alone [5,6].

This broader understanding is particularly relevant to breast cancer survivorship because many pathways influenced by GLP-1 signaling, including chronic inflammation, neuroimmune regulation,

metabolic adaptation, autonomic function, oxidative stress, and mitochondrial biology—overlap with mechanisms increasingly implicated in persistent symptom burden and recovery following treatment. Although much of the available evidence derives from obesity, diabetes, cardiovascular medicine, and experimental research, these shared pathways provide a compelling rationale for investigating the potential role of GLP-1 receptor agonists within comprehensive survivorship care while maintaining a clear distinction between established clinical evidence and evolving mechanistic hypotheses [5,7,8,31].

The following sections examine these biological effects in greater detail, beginning with the central nervous system and neuroimmune signaling before considering mitochondrial function, oxidative stress, immune regulation, autonomic pathways, and broader physiological adaptation.

Central Nervous System and Neuroimmune Effects

One of the most compelling aspects of GLP-1 biology is its influence on the central nervous system, where receptor signaling extends well beyond appetite regulation and metabolic control. GLP-1 receptors are widely distributed throughout brain regions involved in autonomic regulation, stress integration, cognition, emotion, energy homeostasis, and cardiovascular function. Beyond regulating food intake, GLP-1 signaling modulates neuronal excitability, neurotransmitter release, synaptic plasticity, and cellular responses to metabolic stress, supporting broader roles in neural adaptation and physiological homeostasis [32,33].

Evidence increasingly supports an important role for GLP-1 signaling in bidirectional communication between the nervous and immune systems. Microglia, the resident immune cells of the central nervous system, regulate neuroinflammatory responses and neural homeostasis. Experimental studies demonstrate GLP-1 receptor expression on microglia and suggest that receptor activation attenuates pro-inflammatory signaling while promoting more homeostatic cellular phenotypes. Preclinical investigations have likewise demonstrated reductions in inflammatory cytokine production, oxidative stress, and neuroinflammatory activity following GLP-1 receptor activation, supporting an important role for GLP-1 signaling in neuroimmune regulation during physiological stress [5, 34, 35, 36].

Astrocytes represent another key component of this integrated neuroimmune network. In addition to maintaining neurotransmitter homeostasis, they provide metabolic support for neurons, regulate synaptic function, and facilitate communication between neural and immune pathways. Emerging evidence suggests that GLP-1 signaling may influence astrocytic inflammatory responses, glutamate homeostasis, and neuronal metabolic support, although the clinical significance of these observations remains uncertain. Taken together, these findings suggest that GLP-1 signaling contributes to coordinated neuroimmune regulation that supports neural homeostasis, cellular adaptation, and inflammatory control. Although direct evidence in breast cancer survivorship remains limited, these mechanistic observations provide a biologically plausible foundation for future investigation. Similar integrative effects have also been proposed at the level of mitochondrial function and cellular metabolism [6,32,34].

Mitochondrial Function, Metabolic Adaptation, and Oxidative Stress

The biological effects of GLP-1 signaling extend beyond the nervous and immune systems to fundamental mechanisms governing cellular energy metabolism. Mitochondria play a central role in ATP production, redox balance, inflammatory signaling, tissue repair, and adaptation to physiological stress. Disruption of these processes has been implicated in obesity, diabetes, cardiovascular disease, neurodegeneration, fatigue syndromes, sarcopenia, and age-related functional decline, underscoring the importance of mitochondrial health in survivorship and healthy aging [37,38].

Experimental studies indicate that GLP-1 receptor activation enhances mitochondrial efficiency, improves oxidative phosphorylation, reduces reactive oxygen species production, and supports cellular energy homeostasis across neural, cardiovascular, skeletal muscle, and other metabolically active tissues. Additional evidence suggests that GLP-1 signaling promotes cellular adaptation during metabolic stress while modulating inflammatory pathways and oxidative balance. Although these findings derive largely from preclinical and translational studies, they provide important mechanistic insight into the biological actions of GLP-1 receptor agonists beyond glucose regulation [37,39,40].

These findings are particularly relevant because mitochondrial dysfunction and oxidative stress have been linked to fatigue, chronic inflammation, delayed tissue repair, reduced physical performance, and diminished adaptive capacity across multiple chronic conditions. Whether modulation of these pathways translates into clinically meaningful benefits for breast cancer survivors remains uncertain. Nevertheless, the available evidence provides a strong mechanistic foundation for future studies examining how GLP-1 signaling may support metabolic adaptation, cellular resilience, functional recovery, and long-term survivorship outcomes [37,38].

Immune Modulation and Inflammatory Regulation

GLP-1 signaling also influences regulation of the peripheral immune system. Increasing evidence demonstrates GLP-1 receptor expression on macrophages, monocytes, and other immune cell populations involved in inflammatory regulation, supporting coordinated communication between metabolic and immune systems. Experimental and translational studies have shown that GLP-1 receptor activation influences cytokine production, macrophage polarization, innate immune responses, inflammatory signaling pathways, and broader immune-metabolic interactions, highlighting an important role in maintaining immune homeostasis [5,20].

These immunologic effects are particularly relevant because chronic low-grade inflammation is increasingly recognized as a common biological link among obesity, metabolic dysfunction, cardiovascular disease, aging, and many of the persistent health challenges encountered during breast cancer survivorship. Rather than functioning independently, immune regulation and metabolic homeostasis operate through integrated physiological networks that influence tissue adaptation, recovery, and overall health [3,41,42].

Although much of the available evidence derives from experimental models and non-oncology populations, these findings broaden our understanding of the biological actions of GLP-1 receptor agonists. Whether modulation of immune-metabolic

Table 1: Integrated Evidence Framework for GLP-1 Receptor Agonists in Breast Cancer Survivorship.

Survivorship Challenge	Biological Systems Influenced by GLP-1	Established Clinical Evidence	Potential Impact on Survivorship	Highest Research Priority	Representative References
Obesity & metabolic dysfunction	Appetite regulation, insulin sensitivity	Weight loss, glycemic control	Improved metabolic health	Long-term survivorship outcomes	45, 46
Body composition	Skeletal muscle metabolism, mitochondrial adaptation	Limited	Lean muscle preservation	Sarcopenia & frailty	19
Chronic inflammation	Immuno-metabolic regulation	Emerging	Reduced inflammatory burden	Clinical validation	20
Neuroimmune dysfunction	Microglia, astrocytes, CNS signaling	Preclinical	Pain & symptom modulation	PMPS studies	5, 30
Cardiovascular risk	Endothelial & metabolic pathways	Established	Reduced cardiovascular morbidity	Survivorship-specific trials	9
Functional recovery	Multisystem interactions	Emerging	Improved physical function	Patient-reported outcomes	11, 12
Healthy aging	Integrated metabolic resilience	Hypothesis generating	Comprehensive survivorship	Precision survivorship	2, 47

pathways ultimately improves inflammation-related symptoms, adaptive capacity, or functional recovery among breast cancer survivors remains an important question for prospective clinical investigation. These observations also provide a natural transition to another closely integrated regulatory network involving autonomic function, neuroendocrine signaling, and sleep physiology [7,20].

Autonomic, Neuroendocrine, and Sleep-Related Regulation

GLP-1 signaling also influences neural circuits involved in autonomic regulation, neuroendocrine function, and physiological adaptation. GLP-1 receptors are expressed within brain regions that integrate responses to stress, energy balance, cardiovascular regulation, and environmental change. Experimental and translational studies suggest that GLP-1 signaling modulates sympathetic and parasympathetic activity, cardiovascular autonomic regulation, and Hypothalamic-Pituitary-Adrenal (HPA) axis function, supporting coordinated physiological regulation across multiple organ systems [43,44].

Emerging evidence further links GLP-1 signaling with pathways involved in circadian regulation, sleep-wake physiology, and biological recovery. Although these observations remain heterogeneous and derive largely from non-oncology populations, they are particularly relevant because sleep quality influences fatigue, cognition, inflammatory regulation, metabolic homeostasis, and overall quality of life among breast cancer survivors. Together, these findings emphasize the close integration of autonomic, neuroendocrine, metabolic, and immune pathways that support physiological adaptation [6,27,43].

Taken together, these mechanistic studies show that GLP-1 signaling influences a broad network of physiological systems extending well beyond glucose metabolism. Effects on neuroimmune communication, mitochondrial biology, inflammatory regulation, autonomic balance, neuroendocrine activity, and sleep physiology provide a strong biological framework for understanding the diverse actions of GLP-1 receptor agonists. These mechanistic observations should not be interpreted as evidence of established clinical benefit in breast cancer survivorship. Rather, they establish the scientific basis for determining whether coordinated biological effects translate into meaningful improvements in body composition, metabolic health, physical function, symptom burden, and quality of life. The following section critically examines the clinical evidence supporting these potential applications [7,44].

Current Evidence Relevant to Breast Cancer Survivorship

The mechanistic studies reviewed thus far provide a strong biological foundation for investigating GLP-1 receptor agonists in breast cancer survivorship. The central issue, however, is whether these diverse biological effects translate into clinically meaningful benefits for survivors. Answering that question requires careful interpretation of the available literature while maintaining a clear distinction between established therapeutic outcomes and evolving mechanistic hypotheses.

Most published clinical data come from studies of obesity, type 2 diabetes, and cardiovascular disease rather than breast cancer survivorship. Even so, substantial overlaps exist because many of the challenges encountered during survivorship including obesity, metabolic dysfunction, cardiovascular risk, chronic inflammation, impaired physical function, and reduced quality of life are also established targets of GLP-1 receptor agonist therapy. These shared biological and clinical features provide a compelling rationale for evaluating their potential role within comprehensive survivorship care [2,4,7,8].

At present, the strongest evidence supports the use of GLP-1 receptor agonists for weight reduction, glycemic control, metabolic health, and cardiovascular risk reduction, whereas survivorship-specific data remain comparatively limited. Accordingly, findings established in broader metabolic populations should not be assumed to apply directly to breast cancer survivors. The sections that follow critically evaluate the available evidence across the major domains of survivorship, highlighting both the strengths of the current literature and the key questions that remain unanswered Table 1 [1,7].

Weight Reduction, Body Composition, and Metabolic Health

Weight reduction is among the best-established clinical benefits of GLP-1 receptor agonist therapy. Large, randomized trials involving individuals with obesity and type 2 diabetes have consistently demonstrated substantial and sustained reductions in body weight accompanied by improvements in waist circumference, glycemic control, insulin sensitivity, and multiple cardiometabolic risk factors. Together, these outcomes have established GLP-1 receptor agonists as effective therapies for obesity and metabolic disease [45,46,48].

These established benefits are highly relevant to breast cancer survivorship, where treatment-associated weight gain, obesity, insulin resistance, and metabolic dysfunction commonly develop during or after therapy. Chemotherapy, endocrine therapy,

menopause, treatment-related fatigue, reduced physical activity, and altered energy metabolism all contribute to unfavorable changes in body composition and long-term metabolic health. Consequently, optimizing metabolic health has become an increasingly important component of comprehensive survivorship aimed at preserving physical function, improving overall health, and promoting healthy aging [3,13,16,17].

Despite increasing clinical use of GLP-1 receptor agonists among breast cancer survivors, survivorship-specific outcome data remain limited. Important questions persist regarding their effects on body composition, physical performance, functional independence, and healthy aging. Preservation of lean body mass deserves particular attention because weight loss may include reductions in both adipose tissue and skeletal muscle. Accordingly, nutritional optimization, adequate protein intake, resistance exercise, and longitudinal assessment of body composition should accompany therapy whenever appropriate [10,19,37].

From a survivorship perspective, success should be measured by more than weight loss alone. Preservation of skeletal muscle, favorable changes in body composition, maintenance of physical function, and improvement in metabolic health are likely to be more meaningful indicators of long-term recovery than changes in body weight alone. Future studies should therefore integrate body composition, physical performance, functional status, and patient-reported outcomes alongside traditional metabolic endpoints to better define the role of GLP-1 receptor agonists in comprehensive survivorship care [1,2,12,23].

Inflammation, Immuno-Metabolic Health, and Cardiovascular Outcomes

Beyond weight reduction and glycemic control, accumulating evidence indicates that GLP-1 receptor agonists influence inflammatory and immuno-metabolic pathways that contribute to chronic disease and overall health. Clinical studies have demonstrated reductions in circulating inflammatory biomarkers, while experimental and translational investigations have reported favorable effects on inflammatory cytokine production, oxidative stress, macrophage polarization, immune cell activity, and broader immuno-metabolic signaling networks. Together, these observations suggest that the biological actions of GLP-1 receptor agonists extend well beyond glucose metabolism [20,41].

These effects are particularly relevant to breast cancer survivorship because chronic low-grade inflammation is increasingly recognized as a common biological thread linking obesity, metabolic dysfunction, cardiovascular disease, fatigue, and other persistent health challenges. Rather than functioning independently, inflammatory and metabolic pathways interact through integrated immuno-metabolic networks that influence tissue adaptation, recovery, and physiological resilience. Although direct evidence in breast cancer survivors remains limited, modulation of these pathways represents a biologically plausible mechanism through which GLP-1 receptor agonists may contribute to broader improvements in survivorship health [3,5,42].

The cardiovascular benefits of GLP-1 receptor agonists are supported by particularly robust clinical evidence. Large cardiovascular outcome trials involving individuals with obesity, type 2 diabetes, and established cardiovascular disease have consistently demonstrated reductions in major adverse cardiovascular events together with improvements in multiple cardiometabolic risk factors. These findings have expanded the role of GLP-1 receptor agonists beyond glycemic management and established cardiovascular protection as one of their most clinically validated benefits [9,49,50].

This evidence is especially relevant because cardiovascular disease has become a leading cause of long-term morbidity and mortality among breast cancer survivors. Although existing cardiovascular outcome trials were not designed specifically for oncology populations, they provide a strong rationale for investigating whether similar benefits extend to appropriately selected survivors with obesity, diabetes, or elevated cardiovascular risk. Future survivorship studies should integrate cardiovascular outcomes with assessments of body composition, physical performance, symptom burden, patient-reported outcomes, and quality of life to better define the role of GLP-1 receptor agonists within comprehensive survivorship care [1,2,16].

Quality of Life, Functional Recovery, and Symptom Burden

Improving quality of life has become a defining goal of contemporary breast cancer survivorship care, reflecting the recognition that successful recovery encompasses far more than disease control alone. For many survivors, preservation of physical function, mobility, cognition, emotional well-being, and participation in daily activities are the outcomes that most directly influence everyday life. As a result, patient-reported outcomes and functional assessments have become essential measures of survivorship alongside traditional clinical endpoints [2,12,47].

Studies involving individuals with obesity and metabolic disease have demonstrated improvements in physical functioning, mobility, health-related quality of life, and other patient-reported outcomes following GLP-1 receptor agonist therapy. Although comparable evidence in breast cancer survivors remains limited, these findings are encouraging because many obesity-related impairments including reduced mobility, diminished physical function, fatigue, and impaired quality of life closely resemble the challenges encountered during survivorship [11,16,51,52].

Fatigue, sleep disturbance, cognitive complaints, and chronic pain frequently occur as interconnected symptom clusters rather than isolated conditions. Experimental evidence suggests that GLP-1 signaling influences several biological pathways relevant to these symptoms, including inflammatory regulation, mitochondrial function, neuroimmune communication, and autonomic balance. However, available clinical evidence remains insufficient to conclude that GLP-1 receptor agonists directly improve these survivorship-related symptoms independent of their established metabolic benefits [14,15,25,54].

Accordingly, GLP-1 receptor agonists should not be prescribed specifically for chronic pain, post-mastectomy pain syndrome, fatigue, sleep disturbance, or cognitive dysfunction outside their approved indications. Their expanding use among breast cancer survivors nevertheless provides an important opportunity to determine whether improvements in metabolic health are accompanied by measurable gains in physical function, symptom burden, body composition, and overall well-being. Future studies should therefore integrate patient-reported outcomes with objective assessments of physical performance and functional status to more fully characterize the multidimensional nature of survivorship recovery [2,4,12,23].

Overall, the strongest clinical evidence supporting GLP-1 receptor agonists remains in weight management, glycemic control, metabolic

health, and cardiovascular risk reduction. Whether these established benefits ultimately translate into greater functional independence, healthy aging, and improved survivorship outcomes remains an important unanswered question. Addressing that question will require studies that extend beyond traditional metabolic endpoints to incorporate body composition, physical performance, symptom burden, patient-reported outcomes, and quality-of-life measures, thereby defining the broader role of GLP-1 receptor agonists in comprehensive breast cancer survivorship care [1,7,9].

Clinical Implications for Breast Cancer Survivorship

The expanding clinical use of GLP-1 receptor agonists has raised important questions for clinicians caring for breast cancer survivors. As these agents have become increasingly integrated into the management of obesity, type 2 diabetes, and cardiovascular disease, attention has naturally expanded beyond their established metabolic indications to their potential role within comprehensive survivorship care. This evolution reflects the broader shift in survivorship medicine toward preserving metabolic health, physical function, cardiovascular well-being, and healthy aging alongside traditional cancer surveillance [1,3].

Current evidence does not support routine survivorship-specific prescribing of GLP-1 receptor agonists or their use as anticancer therapies. Instead, these agents should be regarded as evidence-based metabolic interventions whose established clinical benefits may be particularly relevant for appropriately selected breast cancer survivors who meet approved treatment indications. Within this context, they are best viewed as one component of an individualized, multidisciplinary survivorship strategy rather than a stand-alone therapeutic intervention [7,53].

Clinical decision-making should remain individualized and grounded in careful assessment of potential benefits, risks, and patient preferences. Metabolic status, body composition, cardiovascular risk, treatment history, nutritional health, functional capacity, and personal survivorship goals should all inform therapeutic decisions. This approach aligns closely with contemporary survivorship models that emphasize multidisciplinary care, preservation of function, quality of life, and healthy aging while remaining firmly anchored in evidence-based practice [2,16].

Viewed through this broader perspective, the greatest current value of GLP-1 receptor agonists lies not in expanding their indications beyond the available evidence but thoughtfully integrating proven metabolic therapies into individualized survivorship care. Such an approach offers the opportunity to improve long-term health while acknowledging the important evidence gaps that continue to shape future research.

Potential Benefits and Clinical Opportunities

Breast cancer survivors commonly face overlapping challenges that include obesity, metabolic dysfunction, chronic inflammation, reduced physical function, fatigue, cardiovascular risk, and diminished quality of life. Because GLP-1 receptor agonists have demonstrated meaningful clinical benefits across several of these domains in appropriately selected populations, they may provide important advantages for survivors who meet established treatment indications. Their greatest potential, however, lies not as disease-specific therapies but as evidence-based interventions that support broader survivorship goals through improvements in metabolic and cardiovascular health [9,45,46].

Among survivors with obesity, type 2 diabetes, or elevated cardiometabolic risk, improvements in body weight, glycemic control, and cardiovascular health may facilitate greater mobility, exercise tolerance, and physical function. These established metabolic benefits may also support priorities that matter to survivors, including maintaining independence, participating in daily activities, and promoting healthy aging. Whether these improvements ultimately translate into broader survivorship benefits remains an important question for future clinical investigation [11,16].

Equally important, GLP-1 receptor agonists should not be considered in isolation. Optimizing survivorship requires coordinated attention to nutrition, resistance exercise, physical activity, sleep health, psychosocial well-being, cardiovascular risk reduction, rehabilitation, and management of treatment-related complications. Within this multidisciplinary model, GLP-1 receptor agonists represent one component of a comprehensive survivorship strategy rather than an independent therapeutic solution [1,2].

Instead of replacing established interventions, these agents may complement them by improving metabolic health in ways that enhance participation in rehabilitation, exercise, nutritional optimization, and other evidence-based strategies. Long-term survivorship is most likely to improve through coordinated management of multiple interacting determinants of health rather than any single intervention. This perspective reflects the continuing evolution of survivorship medicine toward preserving function, promoting healthy aging, and improving quality of life across the survivorship continuum [3,16].

To illustrate how these interconnected biological, metabolic, and functional domains collectively shape long-term survivorship health, we developed the Survivorship Resilience Pyramid (Figure 3). This conceptual framework integrates foundational lifestyle factors, physiological regulation, functional capacity, and quality of life into a hierarchical model that identifies potential points at which GLP-1 receptor agonists may contribute to survivorship outcomes while emphasizing that recovery is driven by interactions among multiple biological and clinical processes rather than any single therapeutic intervention.

To illustrate how interconnected biological and functional domains collectively influence long-term survivorship outcomes, we developed the Survivorship Resilience Pyramid (Figure 3).

Body Composition, Functional Health, and Oncologic Considerations

Although weight reduction is often considered a desirable therapeutic outcome, breast cancer survivorship requires a broader focus on body composition and functional health rather than body weight alone. Several studies have raised concerns about loss of lean muscle mass during weight reduction, particularly among older adults and individuals with preexisting sarcopenia. This issue is especially relevant for breast cancer survivors, who may already experience treatment-related muscle loss, endocrine therapy-associated changes, reduced physical activity, and age-related declines in skeletal muscle. Preservation of lean body mass is fundamental to maintaining strength, mobility, metabolic health, physical performance, independence, and healthy aging, making body composition a more clinically meaningful indicator of survivorship health than body

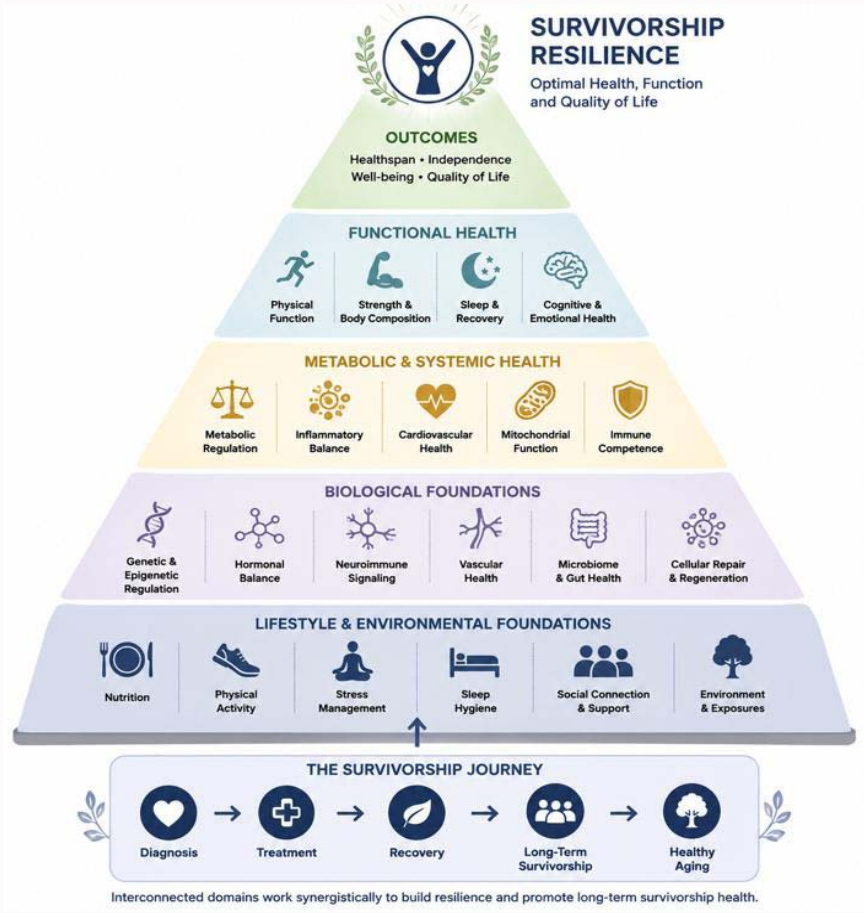

Figure 3: The Survivorship Resilience Pyramid: A Hierarchical Model of Biological and Functional Determinants of Long-Term Survivorship Outcomes. Conceptual framework illustrating how interconnected biological, metabolic, and functional domains collectively support long-term survivorship health.

weight alone [10,17,19,37].

For this reason, nutritional assessment, adequate protein intake, resistance exercise, and longitudinal monitoring of body composition should accompany GLP-1 receptor agonist therapy whenever appropriate. Clinical management should emphasize preservation of skeletal muscle and functional capacity alongside reductions in adiposity. Future survivorship studies should incorporate standardized assessments of body composition, muscle strength, physical performance, frailty, and patient-reported functional outcomes to better define the long-term impact of these therapies [23,54,55].

Beyond functional health, oncologic safety remains one of the foremost concerns for both patients and clinicians. Current evidence neither supports the use of GLP-1 receptor agonists as anticancer therapies nor demonstrates a role in reducing breast cancer recurrence. Likewise, available data have not identified a consistent increase in recurrence associated with GLP-1 receptor agonist therapy. However, survivorship-specific evidence remains limited, underscoring the need for prospective studies with extended follow-up to better define long-term oncologic outcomes [7,8].

Until additional evidence becomes available, treatment decisions should remain grounded in approved indications, established safety data, individualized assessment of risks and benefits, and shared decision-making. This balanced approach enables clinicians to apply therapies with proven metabolic and cardiovascular benefits while acknowledging the important uncertainties that remain regarding their role in breast cancer survivorship [1,2,7].

Patient-centered Survivorship Care

Symptom burden, multidisciplinary care, and shared decision-making

Many breast cancer survivors seek interventions that improve not only metabolic health but also fatigue, physical function, sleep quality, emotional well-being, and overall quality of life. Although mechanistic studies suggest that GLP-1 signaling influences biological pathways involved in inflammation, neuroimmune communication, mitochondrial function, autonomic regulation, and physiological adaptation, clinical evidence demonstrating improvements in these survivorship-related outcomes remains limited. Consequently, potential benefits beyond established metabolic indications should be interpreted cautiously until confirmed in prospective studies specifically involving breast cancer survivors [5,14,15,24,53].

Current evidence therefore does not support prescribing GLP-1 receptor agonists specifically for fatigue, chronic pain, post-mastectomy pain syndrome, sleep disturbance, cognitive dysfunction, or other survivorship-related symptoms outside their approved indications. Nevertheless, improvements in metabolic health, cardiovascular fitness, body composition, and physical function may indirectly support broader recovery and overall well-being. Future

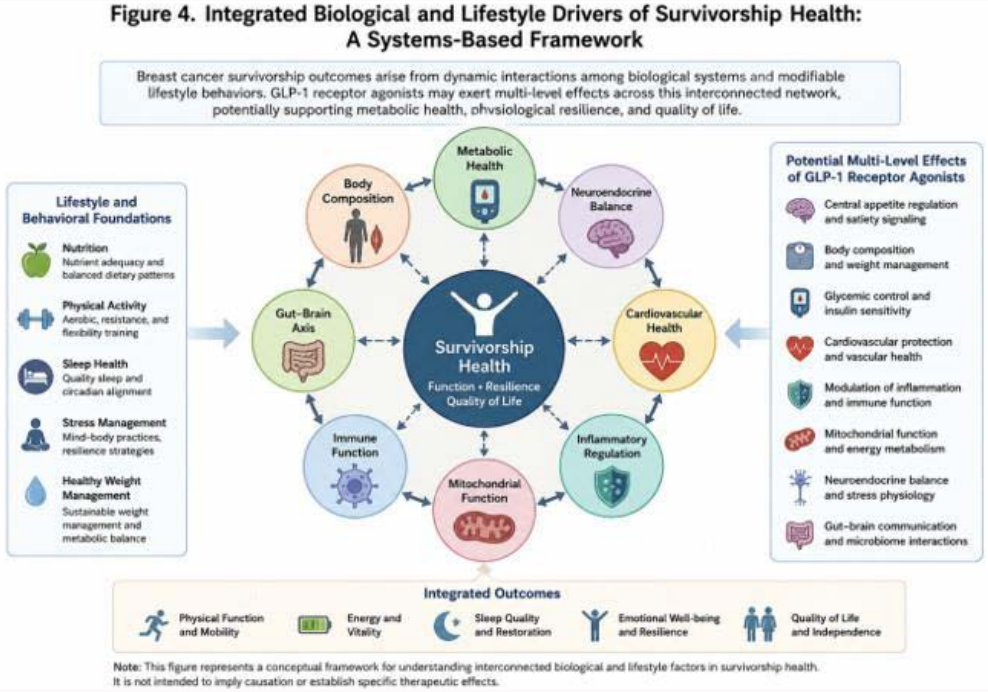

Figure 4: Translational Framework Linking GLP-1 Biology to Breast Cancer Survivorship. Conceptual model illustrating how the biological effects of GLP-1 receptor agonists may translate into interconnected survivorship processes and patient-centered outcomes.

investigations should move beyond traditional metabolic endpoints by incorporating patient-reported outcomes, symptom clusters, functional assessments, and health-related quality-of-life measures to determine whether established metabolic benefits translate into clinically meaningful improvements for breast cancer survivors [7,11,12,47].

These considerations also reinforce the importance of multidisciplinary survivorship care. Optimizing outcomes requires coordinated management involving oncology, primary care, endocrinology, cardiology, rehabilitation, nutrition, physical therapy, behavioral health, and dedicated survivorship specialists. Within this collaborative framework, GLP-1 receptor agonists should be viewed as one component of an individualized treatment strategy rather than a stand-alone therapeutic approach [1,4].

The rapid expansion of public awareness surrounding GLP-1 receptor agonists has understandably increased patient interest and expectations. Clinicians should therefore be prepared to discuss both established benefits and remaining uncertainties in a balanced, evidence-based manner. Shared decision-making is especially important because survivorship priorities frequently extend beyond disease prevention to include preservation of physical function, independence, cardiovascular health, symptom management, and healthy aging. Therapeutic decisions should be individualized according to each survivor's metabolic profile, body composition, comorbidities, nutritional status, treatment history, functional reserve, and personal goals [16,47].

Viewed within this broader framework, GLP-1 receptor agonists are best considered as one component of comprehensive, patient-centered survivorship care. Their greatest current value lies in appropriately selected individuals who meet established treatment indications, while their broader contributions to long-term survivorship continue to be defined through ongoing research. Sustained improvements in survivorship are unlikely to result from any single intervention but instead from coordinated strategies that integrate metabolic optimization, rehabilitation, nutrition, physical activity, cardiovascular risk reduction, psychosocial support, and healthy aging across the survivorship continuum. This system-oriented perspective reflects the continuing evolution of survivorship medicine and provides an important framework for future research and clinical practice [7,8,56].

Discussion

The expanding use of GLP-1 receptor agonists among breast cancer survivors reflects the continuing evolution of survivorship medicine. As survival rates improve, the goals of care have expanded beyond disease surveillance to preserving long-term health, maintaining physical function, reducing treatment-related morbidity, and promoting healthy aging. Within this evolving landscape, therapies originally developed for metabolic disease are increasingly being evaluated for their potential contributions to comprehensive, patient-centered survivorship care [1,3].

A consistent theme emerging from the current literature is that survivorship health is shaped by the interplay of biological, clinical, and behavioral processes rather than isolated conditions. Obesity, metabolic dysfunction, chronic inflammation, fatigue, sleep disturbance, cardiovascular disease, chronic pain, psychological well-being, and impaired physical function frequently coexist and influence one another through interconnected metabolic, inflammatory, neuroimmune, neuroendocrine, and behavioral pathways. This systems-based perspective supports viewing survivorship as a dynamic process of physiological adaptation rather than simply the absence of recurrent disease [5,13,47].

Within this framework, GLP-1 receptor agonists are of particular interest because their established clinical benefits extend beyond

glycemic control to include weight reduction, improved metabolic health, and cardiovascular risk reduction. Emerging experimental evidence also suggests broader effects on inflammatory regulation, neuroimmune communication, mitochondrial function, autonomic regulation, and physiological adaptation. Although the clinical significance of many of these biological observations remains uncertain, they provide a strong scientific rationale for continued investigation in breast cancer survivorship [5,9,43,45].

At the same time, the available evidence does not support viewing GLP-1 receptor agonists as comprehensive solutions for the diverse challenges encountered after breast cancer treatment. Long-term recovery is unlikely to depend on any single therapeutic intervention. Instead, optimal outcomes will probably arise from coordinated approaches that integrate evidence-based medical management with nutrition, resistance exercise, rehabilitation, cardiovascular risk reduction, psychosocial support, sleep optimization, and management of treatment-related complications. Within this broader framework, GLP-1 receptor agonists represent one component of individualized survivorship care rather than a stand-alone therapy [7,16].

The expanding use of these therapies also highlights the need to reconsider how survivorship interventions are evaluated. Traditional metabolic endpoints remain important but provide only a partial assessment of recovery after breast cancer. Future studies should therefore incorporate outcomes that directly reflect survivorship health, including body composition, preservation of skeletal muscle, physical performance, functional independence, symptom burden, cognitive function, cardiovascular health, patient-reported outcomes, and quality of life. Such multidimensional measures are likely to provide a clearer assessment of whether the established metabolic benefits of GLP-1 receptor agonists translate into clinically meaningful improvements for breast cancer survivors [10,12,19,23].

More broadly, this evolving field illustrates the growing convergence of metabolic medicine and survivorship science. Rather than focusing primarily on disease-specific outcomes, future research will increasingly emphasize preservation of function, physiological resilience, healthy aging, and long-term well-being. These priorities closely align with the outcomes that matter most to breast cancer survivors and reflect the continuing evolution toward more personalized, multidisciplinary, and patient-centered models of care [3,4,16].

Taken together, the available evidence places GLP-1 receptor agonists at the intersection of metabolic medicine and breast cancer survivorship. Although many questions remain unanswered, their expanding clinical use provides a timely opportunity to determine whether therapies developed for metabolic disease can contribute to broader survivorship goals. This emerging field also encourages a shift beyond traditional metabolic and oncologic endpoints toward more comprehensive measures of recovery that include physical function, body composition, cardiovascular health, patient-reported outcomes, healthy aging, and quality of life. Ultimately, the greatest contribution of GLP-1 receptor agonists may be not only their metabolic effects, but also the opportunity they provide to rethink breast cancer survivorship as an integrated process of preserving health, function, resilience, and quality of life rather than simply preventing disease recurrence Figure 4 [4,7,9,56].

Knowledge Gaps and Future Research Directions

Despite growing scientific and clinical interest in GLP-1 receptor agonists, important questions remain regarding their role in breast cancer survivorship. Although substantial evidence supports their use in obesity, type 2 diabetes, and cardiovascular disease, survivorship-specific data remain limited. As these therapies become increasingly incorporated into the care of breast cancer survivors who meet established treatment indications, robust clinical evidence will be essential to determine whether their established metabolic benefits translate into meaningful improvements in long-term recovery, physical function, and overall health. The following priorities outline the research needed to define the evidence-based role of GLP-1 receptor agonists within multidisciplinary survivorship care [3,7,8].

Survivorship-Specific Clinical Research

Perhaps the greatest limitation of the current literature is the scarcity of prospective studies designed specifically for breast cancer survivors. Although GLP-1 receptor agonists have demonstrated well-established benefits for weight management, metabolic health, and cardiovascular risk reduction in broader populations, it remains uncertain whether these findings apply to survivors with unique treatment exposures, endocrine therapy-associated changes, altered body composition, and distinct long-term health needs. Dedicated survivorship trials are therefore needed before these therapies can be fully integrated into evidence-based clinical practice [7,8].

Future investigations should evaluate outcomes that better reflect the complexity of survivorship rather than relying primarily on conventional metabolic endpoints. In addition to body weight and glycemic control, prospective studies should assess body composition, preservation of skeletal muscle, physical performance, functional independence, cardiovascular health, cognitive function, symptom burden, patient-reported outcomes, and quality of life. These measures would generate evidence that is more directly applicable to patient-centered survivorship care [10,12,13,17,23,47].

Equally important is determining whether improvements in metabolic health are accompanied by sustained gains in physical function, physiological resilience, and healthy aging. Answering these questions will help clarify whether the established metabolic benefits of GLP-1 receptor agonists extend beyond traditional clinical outcomes to improve long-term survivorship [1,2].

Body Composition, Function, and Quality of Life

Body weight alone provides an incomplete measure of survivorship health. Preservation of lean body mass, skeletal muscle function, mobility, physical performance, independence, and quality of life may be equally important determinants of recovery. As survivorship care increasingly emphasizes functional preservation and healthy aging, assessments of body composition should complement conventional measures of body weight to provide a more comprehensive evaluation of treatment effects [17,19,47].

Future studies should incorporate standardized assessments of body composition, skeletal muscle preservation, muscle strength, physical performance, frailty, and functional capacity to distinguish beneficial reductions in adiposity from undesirable loss of lean muscle. Incorporating patient-reported outcomes, fatigue, sleep

quality, symptom burden, physical function, and health-related quality of life will further determine whether improvements in metabolic health translate into meaningful clinical benefits. Together, these outcomes are likely to provide a more complete assessment of recovery than body weight alone while supporting increasingly personalized survivorship care [13,15,24,25].

Mechanistic and Translational Research

Experimental evidence indicates that GLP-1 signaling influences biological pathways extending well beyond glucose regulation, including inflammatory signaling, immune function, neuroimmune communication, mitochondrial bioenergetics, autonomic regulation, and stress physiology. Collectively, these interconnected mechanisms provide a compelling biological rationale for investigating the broader effects of GLP-1 receptor agonists in breast cancer survivorship. However, much of the available evidence derives from preclinical models or non-oncology populations, and the extent to which these biological effects influence recovery after breast cancer treatment remains uncertain [5,41,53].

Future translational research should move beyond studying individual pathways in isolation to investigate how coordinated biological networks influence long-term recovery. Combining biomarkers of inflammation, metabolic health, body composition, autonomic regulation, and neuroimmune function with patient-reported outcomes, physical performance, symptom burden, and quality of life may clarify whether biological changes are accompanied by meaningful clinical improvement. Systems-level approaches that link mechanistic discoveries with clinical outcomes may help bridge the gap between laboratory research and personalized survivorship care while providing a stronger framework for understanding the complex biology of recovery [7,8,57].

Knowledge Gaps and Future Research Directions

Long-term safety and personalized survivorship approaches

Although current evidence has not demonstrated a consistent increase in breast cancer recurrence associated with GLP-1 receptor agonist therapy, long-term survivorship-specific safety data remain limited. Important questions regarding treatment duration, durability of metabolic benefits, body composition, functional outcomes, and oncologic safety require further investigation. Extended follow-up studies incorporating comprehensive oncologic surveillance together with longitudinal assessment of metabolic and functional outcomes will be essential to better define the long-term safety profile of GLP-1 receptor agonists in breast cancer survivorship [7,8].

Breast cancer survivors also represent a highly heterogeneous population with substantial variability in age, treatment history, endocrine therapy exposure, metabolic health, body composition, comorbidities, and survivorship priorities. Consequently, it is unlikely that all survivors will derive comparable benefit from GLP-1 receptor agonist therapy. Identifying the clinical and biological characteristics associated with treatment response including obesity, insulin resistance, cardiovascular risk, body composition, functional reserve, and baseline symptom burden may help determine which patients are most likely to benefit while advancing increasingly individualized survivorship care [13,16,19].

More broadly, these priorities emphasize the need to move beyond a one-size-fits-all approach to survivorship research. Future studies should integrate oncologic safety with assessments of body composition, physical performance, patient-reported outcomes, quality of life, and healthy aging to determine whether the established metabolic benefits of GLP-1 receptor agonists translate into durable improvements in survivorship health. Such multidisciplinary investigations will be essential for defining the appropriate role of these therapies within personalized, evidence-based breast cancer survivorship care [12,47].

Limitations of Current Evidence

Several limitations should be considered when interpreting the evidence presented in this review. Most available data regarding GLP-1 receptor agonists originates from studies of obesity, type 2 diabetes, cardiovascular disease, and metabolic health rather than breast cancer survivorship. Consequently, extrapolation of these findings to breast cancer survivors should be undertaken cautiously, recognizing the unique physiological, therapeutic, and long-term challenges encountered throughout survivorship [3,8].

Similarly, although growing evidence indicates that GLP-1 signaling influences inflammatory, neuroimmune, autonomic, mitochondrial, and metabolic pathways, many of these observations derive from preclinical investigations, translational research, or non-oncology populations. These findings provide an important biological rationale for continued investigation, but their clinical relevance in breast cancer survivorship remains uncertain and requires validation in well-designed survivorship-specific studies [5,20,41,53].

Interpretation of the available literature is further complicated by the marked heterogeneity of breast cancer survivors. Age, menopausal status, tumor biology, treatment exposures, endocrine therapy, body composition, metabolic health, comorbidities, and time since treatment completion may all influence clinical outcomes and therapeutic response. Accordingly, findings observed in one subgroup may not be broadly generalizable, underscoring the importance of individualized clinical assessment and future stratified research [1,13].

Several important questions also remain unanswered. Although robust evidence supports the effectiveness of GLP-1 receptor agonists for weight management, glycemic control, and cardiovascular risk reduction, uncertainties remain regarding optimal treatment duration, nutritional status, body composition, physical function, symptom burden, and quality of life among breast cancer survivors. Addressing these questions will require prospective studies with extended follow-up and multidimensional survivorship outcomes [9,11,45,46].

Attention should be directed toward body composition rather than body weight alone. Weight reduction may not uniformly improve health if accompanied by excessive loss of lean muscle mass, particularly among older survivors or those already experiencing treatment-related sarcopenia, frailty, or functional decline. Future investigations should therefore incorporate comprehensive assessments of skeletal muscle mass, muscle strength, physical performance, and functional independence alongside conventional measures of body weight [10,17,19,23].

Long-term oncologic safety likewise remains an important area for continued investigation. Although available evidence has not demonstrated a consistent increase in breast cancer recurrence

associated with GLP-1 receptor agonist therapy, survivorship-specific safety data remain limited. Continued surveillance and longer-term clinical studies are needed to better characterize oncologic outcomes, treatment duration, and potential interactions with evolving cancer therapies [7,8].

Finally, this review focuses on the biological rationale, emerging evidence, and potential clinical implications of GLP-1 receptor agonists rather than therapeutic recommendations. Discussion of inflammatory, neuroimmune, autonomic, mitochondrial, and metabolic pathways should not be interpreted as evidence that these therapies directly improve chronic pain, fatigue, sleep disturbance, cognitive dysfunction, or other survivorship-related symptoms independent of their established metabolic indications. Although these mechanistic observations provide a compelling foundation for future investigation, their clinical relevance remains to be established through rigorous prospective research [14,25].

Taking together, these limitations provide important context for interpreting the current literature while highlighting the research needed to define the appropriate role of GLP-1 receptor agonists within comprehensive, evidence-based breast cancer survivorship care [2,8].

Conclusion

Breast cancer survivorship extends well beyond completion of cancer treatment and is increasingly recognized as a multidimensional phase of care shaped by complex interactions among metabolic, inflammatory, cardiovascular, neuroendocrine, and functional processes. Obesity, insulin resistance, chronic inflammation, fatigue, sleep disturbance, persistent pain, and impaired quality of life frequently coexist and contribute substantially to long-term morbidity. As the population of breast cancer survivors continues to grow, survivorship care must continue to evolve beyond disease surveillance toward comprehensive strategies that preserve health, maintain function, and promote healthy aging [1,4,47].

GLP-1 receptor agonists have become established therapies for obesity, type 2 diabetes, and cardiovascular risk reduction. Beyond these proven clinical benefits, accumulating evidence suggests that GLP-1 signaling influences a broad range of biological pathways, including inflammatory regulation, immuno-metabolic function, mitochondrial biology, autonomic balance, stress physiology, and central nervous system signaling. Although these emerging biological effects have generated considerable interest within survivorship medicine, their clinical relevance for breast cancer survivors remains to be established through prospective investigation [5,9,53].

Current evidence remains strongest for weight management, glycemic control, metabolic health, and cardiovascular risk reduction. At present, available data do not support the use of GLP-1 receptor agonists specifically for chronic pain, fatigue, sleep disturbance, cognitive dysfunction, or other survivorship-related symptoms independent of established metabolic indications. Determining whether their broader biological effects translate into clinically meaningful improvements in survivorship health therefore remains an important priority for future research [7,8].

Future investigations should move beyond traditional metabolic endpoints to evaluate body composition, preservation of skeletal muscle, physical function, patient-reported outcomes, symptom burden, quality of life, and healthy aging. Collectively, these outcomes provide a more meaningful framework for evaluating survivorship interventions than conventional metabolic measures alone and may help identify the patients most likely to benefit from GLP-1 receptor agonist therapy [10,17].

Ultimately, the future role of GLP-1 receptor agonists in breast cancer survivorship is unlikely to be defined by weight loss alone. Rather, their greatest contribution may lie in advancing a broader vision of survivorship care that values metabolic health, preservation of skeletal muscle, physical function, cardiovascular well-being, patient-reported outcomes, and healthy aging alongside traditional oncologic endpoints. Whether these therapies ultimately fulfill that promise will depend on rigorous survivorship-specific research. Nevertheless, their expanding clinical use provides an opportunity not only to evaluate a promising metabolic therapy but also to reconsider how recovery after breast cancer is defined and measured. This broader systems perspective recognizes survivorship as the coordinated function of interacting biological networks that collectively influence physiological resilience, functional recovery, and long-term health [3,7,58].

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