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Reconceptualizing obesity and the modern definition of disease

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ABSTRACT

The debate over whether obesity constitutes disease reveals a fundamental limitation in biomedical disease models. We propose a bio-biographical framework recognizing that disease emerges when biological processes and biographical context, including for example lived experience, social position, chronic stressors, trauma, couple together to generate present or potential harm meaningful to the person. Biography is not external to disease but constitutive of it, shaping causation, expression, and trajectory through embodied mechanisms. This reconceptualization applies beyond obesity to cancer, cardiovascular disease, neurodegeneration and more, offering a new foundation for medicine that acknowledges both biological mechanisms and disrupted human lives.

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Introduction

The question of whether obesity constitutes a disease remains contested despite its recognition by major medical organizations. This debate persists because obesity challenges traditional biomedical disease models that privilege purely biological causation and measurable physiological dysfunction. Some critics argue obesity is better understood as a risk factor that increases the probability of future metabolic and cardiovascular disease. Proponents counter with evidence of pathophysiological mechanisms, progressive biological dysfunction, and clinical outcomes justifying intervention.

We argue that this debate reflects fundamental limitations in how disease itself is conceptualized. Traditional biomedical models define disease through biological causation (pathogens, genetic mutations, cellular dysfunction) and biological harm (organ damage, physiological impairment, mortality).[1] This framework proves inadequate for conditions where causation involves complex interactions between biological vulnerability and biographical disruption (lived experience), and where harm manifests across biological, psychological, and social domains simultaneously.

Recently, the debate over whether obesity is a risk factor or disease has sharpened. The Lancet Diabetes & Endocrinology Commission on Clinical Obesity proposed a new obesity definition distinguishing "pre-clinical obesity" from "clinical obesity," while also moving beyond BMI.[2] Yet this reframing from risk to disease remains within an exclusively biological paradigm. A deeper question remains: What counts as a disease in an individual? Epidemiology defines risk as a property of populations; disease is something experienced by an individual. When we label obesity a "risk factor," we invoke statistics; when we label it "disease," we assert something about a person's lived experience and embodiment.

Asking "What counts as a disease in an individual?" forces us to reckon with what medicine knows about persons, bodies, and lives. We argue that the dominant biological model does not adequately address the biographical dimension of disease.[3] Biography, which is the embodied accumulation of social position, environmental exposures, chronic stressors, trauma, and lived experience across the lifespan, exerts powerful influence on disease.[4] Yet it remains invisible in models focused exclusively on

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biological mechanisms. We infer biography's effects from patterns biology cannot explain: social gradients in obesity, persistence of racial disparities after adjusting for known risk factors, resistance of obesity to interventions targeting only biological mechanisms.

Integrating biography with biology suggests the need for a new disease definition of obesity that exemplifies biosocial disease. Obesity emerges from the inseparable entanglement of biological predisposition and lived experience across the lifespan. Its harms operate simultaneously across biological systems and biographical dimensions, with each reinforcing the other through embodied mechanisms.

CLINICAL SIGNIFICANCE

- Our research reframes obesity as a biosocial disease, guiding clinicians beyond BMI and isolated biomarkers;
- Supports individualized diagnosis based on biological—biographical coupling, not population risk alone;
- Explains heterogeneous outcomes among patients with similar metabolic profiles;
- Justifies integrated treatment addressing stress, stigma, function, and meaning alongside biology;
- And extends to other chronic diseases, reshaping definitions of severity, prevention, and personalized care.

Risk as an epistemic failure for medicine

The concept of risk is epidemiology's epistemic triumph by permitting quantification of probabilities, stratification of populations, and allocation of preventive resources.[5] But risk is also medicine's epistemic failure when applied to individual patient care. Risk is fundamentally about what might happen across many people, not what is happening to this person. When a clinician says, "You are at increased risk of diabetes because of your weight," that is statistically true, but knowing that does little to register the unique life, body, and experiences of the patient before her. The abstraction of risk replaces the singularity of the patient with a category of "people like this person." In doing so, risk de-personalizes medical knowledge.[6]

Medicine focuses on care for individuals while risk focuses on populations. This mismatch creates an epistemic gap. What matters for the person, features such as biography, context, and meaning, falls outside risk calculus. The individual becomes a data point in epidemiology rather than a life in clinical time seeking care. Risk as the dominant epistemic mode undermines the human dimensions of clinical care. Risk may guide preventive policy for populations effectively, but when diagnosing disease and caring for an individual, it falls short for the physician and patient. It cannot discern when population risk has become disease in a person. It robs patients of the meaning of their illness.

Biography as the dark matter of disease

In cosmology, dark matter constitutes 85% of the universe's matter yet remains invisible to direct observation. Its existence is inferred from gravitational effects on visible matter that visible matter alone cannot explain.[7]

Biography functions as the dark matter of disease. If risk privileges populations and probabilities, biography privileges the person and their lived experience. Traditional biomedical models focus on visible, measurable factors: pathogens, genes, laboratory values, tissue pathology, physiological dysfunction. Yet biological factors alone fail to explain patterns we observe. Why do populations develop disease at different rates, why do identical genetic risks manifest differently as disease, why do treatments effective in trials fail in practice, and why do diseases persist despite addressing known biological mechanisms?

Biography is simply not captured by instruments designed to detect only biological signals. When measured through life course studies, social epidemiology, and assessment of lived experience, biography becomes visible. Its invisibility in traditional models reflects limitations of conceptual frameworks designed to detect only biological phenomena.

Consider two people with identical BMI and metabolic labs who diverge in outcome in which one person remains functionally well while the other rapidly declines. The difference lies not in fat mass alone but in the biographies behind those bodies. Trauma, social stigma, childhood adversity, chronic stress, food insecurity all shape biology. The body remembers what the life has been and the life embodies what the biology becomes.

For obesity, ignoring biography creates systematically incomplete understanding of disease. The biosocial framework makes biography visible and central, recognizing that disease results from biological and biographical forces acting together, inseparably, across time. Biography is not a "social determinant" external to disease but instead a constitutive of disease itself, shaping causation, expression, and trajectory through embodied mechanisms.

Biology and biography are co-constitutive

The Lancet Commission made an important advance by distinguishing preclinical from clinical obesity, recognizing that disease exists when obesity produces actual complications rather than merely statistical risk. However, the Commission's framework remains anchored primarily in biological pathophysiology, defining clinical obesity by metabolic, inflammatory, or other biological dysfunctions. While this represents progress, it perpetuates a conception of disease as fundamentally disrupted biology, with lived experience treated as epiphenomenon. The deeper question of what makes something a disease for a person remains unexamined.

A co-constitutive framework extends the Commission's work by recognizing that biology and biography are not separate domains that occasionally interact, but co-constitutive

elements of disease itself. Obesity becomes disease when excess adiposity and biographical context form a pathological coupling in which biological processes and lived experience create present or potential harm to the person.

This reframing explains why the preclinical/clinical distinction resonates clinically: preclinical obesity represents biological changes that remain uncoupled from biographical disruption, while clinical obesity marks the emergence of a pathological system where biology and lived experience are inseparably interlocked. Crucially, two individuals with identical metabolic profiles may differ in disease status depending on whether their adiposity creates harm through constrained physical capability, threatened or present psychosocial suffering, or the burden of medical management itself.

This formulation recognizes that lived experience leaves biological traces. Chronic psychosocial stress, adverse childhood events, loneliness, and social isolation become biology through neuroendocrine stress response, epigenetic modifications, immune dysregulation, altered fat deposition patterns, and metabolic impairments.[8,9] Over time, the body "remembers" the life. Conversely, bodily states directly influence lived experience. Chronic overweight may lead to fatigue, sleep-disordered breathing, joint pain, and reduced mobility, changing how the person lives in the world, perceives themselves, is treated by others, and what roles they can fulfill.

Most current evidence linking biography to biology emphasizes adversity. But biography is not only a record of harm. Positive lived experiences such as meaning, purpose, supportive relationships, altruism, and spiritual engagement also leave measurable biological signatures that may shape treatment response.

Eudaimonic well-being is associated with lower inflammatory gene expression and more favorable glucocorticoid signaling, independent of hedonic happiness. Higher purpose in life predicts lower all-cause mortality and reduced cardiovascular events. Social integration buffers stress responses, attenuates inflammation, and predicts improved survival. Altruistic behavior and volunteering are linked to lower depression and reduced mortality. Spiritual engagement is associated with healthier neuroendocrine profiles and improved outcomes in cardiovascular disease and cancer.

Obesity causes direct biological harm through interconnected pathophysiological mechanisms including progressive insulin resistance and beta cell dysfunction,[10] ectopic fat deposition leading to organ lipotoxicity,[11] chronic systemic inflammation, and multi-system effects causing sleep apnea, osteoarthritis, kidney disease, liver disease, and increased cancer occurrence.[12] Disease emerges when biology and biography recursively interact. It is not only that excess fat causes metabolic dysfunction. Instead, the interplay among fat, social meaning, mobility, and identity produces a lived condition of illness. Adipose tissue is both a metabolic organ [13] and an experiential one that mediates shame, stigma, fatigue, and altered social roles.[14] Disease is neither purely biological nor purely biographical; it is Biosocial.

Biosocial mechanisms: pathological coupling and obesity

Obesity emerges through distinct yet interconnected pathways where biographical experience becomes biological adiposity and biological changes constrain biographical possibility, forming pathologically coupled systems.

Stress and cortisol pathways represent the most direct coupled mechanism. Chronic biographical adversity including for example poverty, discrimination, job insecurity, and caregiving burden activates the HPA axis, producing sustained cortisol elevation. Cortisol binds directly to adipocyte receptors, promoting visceral fat accumulation while simultaneously stimulating appetite through hypothalamic pathways. A single mother working multiple low-wage jobs experiences chronic activation that is literally adipogenic. Weight gain then produces additional biographical stress through stigma and functional limitations, further elevating cortisol in self-reinforcing cycles.

Sleep disruption creates a critical metabolic junction. Shift work, multiple jobs, and caregiving responsibilities produce chronic partial sleep deprivation that directly alters metabolism. Leptin, for instance, decreases while ghrelin increases. Insulin sensitivity drops, and prefrontal executive function becomes impaired. The warehouse worker on rotating shifts experiences metabolic dysfunction as a biological consequence of biographical circumstance. Weight gain then produces sleep apnea, fragmenting sleep further and deepening the coupling.

Built environment constrains activity patterns that shape metabolism. Neighborhoods without sidewalks or safe spaces, car-dependent living, and sedentary occupations reduce non-exercise activity, decrease muscle mass, and impair insulin sensitivity. The person living where walking is difficult experiences measurable biological changes. Weight gain then further constrains activity through joint pain and diminished respiratory reserve.

Adverse childhood experiences produce lasting biological effects that include epigenetic modifications to stress-regulating genes, inflammatory priming of immune cells, dopaminergic pathway alterations affecting food reward, and impaired emotional regulation capacity. The adult facing obesity carries the biological legacy of childhood adversity inscribed in gene expression patterns and neural circuits decades after the original experiences.

These mechanisms operate simultaneously and synergistically, with each pathway amplifying others. Stress produces sleep disruption; sleep disruption worsens stress reactivity; both promote inflammation; inflammation impairs insulin sensitivity; metabolic dysfunction constrains activity; reduced activity deepens depression; depression intensifies social isolation; isolation elevates inflammatory markers. Disease exists not in any single pathway but in their pathological integration into self-perpetuating systems where biology and biography continuously create one another.

Beyond obesity: biosocial coupling

Yet this principle of biological and biographical coupling applies to diseases beyond obesity. If disease is fundamentally co-constitutive, then nearly all diseases, including those traditionally considered paradigmatically biological, must be understood as resulting from the interplay of biography and biology rather than purely physiological phenomena.

Cancer illustrates how biography shapes even conditions defined by cellular pathology. The same genetic mutation produces different disease trajectories depending on chronic stress exposure, nutritional status, social support systems, and environmental carcinogens.[15] Conversely, cancer's biology immediately restructures biography. A cancer diagnosis reorders life priorities, relationships, and possible futures before any symptom appears.[16] The person with slow-growing prostate cancer and the person with fast-growing pancreatic cancer face different disease systems not only because tumor biology differs, but because the coupling of biology with biographical time, treatability, and life stage creates fundamentally different lived circumstances and therapeutic decisions.

Cardiovascular disease demonstrates co-constitution across the lifespan. Atherosclerosis develops through decades of interaction between genetic predisposition, systemic inflammation, dietary patterns shaped by food access and cultural practices, chronic stress from discrimination or economic adversity, and physical activity constrained by built environments.[17]

Biology and biography are inseparable at every stage. A myocardial infarction represents an acute biological crisis, yet its meaning and impact depend also on biographical context. Consider that the same cardiac event may end a construction worker's livelihood while minimally affecting a knowledge worker's valued activities. Disease encompasses both the damaged myocardium and the disrupted life it inhabits.

Neurodegenerative disorders perhaps most clearly reveal co-constitution because they directly attack the biological substrate of biography itself. Alzheimer's disease progressively destroys the neural networks that encode memory, personality, and relational capacity which are the very stuff of biographical existence.[18] Yet the rate and features of decline are shaped by cognitive reserve (itself accumulated through education, occupation, and lifelong learning), social engagement, and caregiving relationships.[19] Two individuals with identical amyloid burden and tau pathology experience different diseases because their biographical resources interact differently with the biological process.

These examples reveal that disease is neither purely biological fact nor purely biographical construction. Instead, disease emerges when biological processes and biographical context mutually constitute one another. We propose this Biosocial disease definition:

> "Disease exists when biological processes and biographical context are coupled together to generate present or potential harm meaningful to the person."

This understanding carries implications for how we define, diagnose, and treat disease. First, disease severity cannot be determined by biological measures alone since it emerges from the coupled system. The person with significant radiographic arthritis who remains physically active and socially engaged has less disease than the person with moderate changes who has become isolated and immobile. This difference exists not because we are privileging quality of life over objective findings, but because disease itself exists in the coupling of biology and biography, not merely in the joint.

Second, prevention and treatment must address the coupling of biology and biography. Intervening only on biology through pharmaceuticals or surgery without addressing biographical factors leaves half the pathological system intact. The diabetes medication that controls glucose but does nothing for chronic stress cannot fully disrupt the disease system. Conversely, addressing only social or psychological factors while ignoring biological mechanisms fails when physiology drives progressive harm. Treatment must target the biology-biography coupling itself.

Third, disease boundaries become necessarily individual and contextual. The threshold at which biological variation becomes disease depends on knowledge of a particular life. The same hemoglobin A1c, coronary calcium score, or degree of adiposity represents disease or not depending on the system it inhabits. This is not medical relativism. The biological processes are real and measurable, even as we realize that disease exists in the space between physiology and biography, between cellular dysfunction and disrupted human flourishing.

Toward a modern architecture for disease

If biography is the dark matter of disease, then medicine's next paradigm must be Biosocial. Biosocial medicine begins with the recognition that disease is not located solely within the body, but at the intersection of biological process and lived experience. [20] In this view, disease is not an object sitting in tissue but a condition of disruption between body and person, between physical function and the person's role in the world. [21]

Epistemically, biosocial medicine challenges the dominance of risk-based reasoning or a solely biological concept of disease. Recognizing this mutual constitution calls for a modern architecture of disease that restores the whole person as the central unit of analysis. The individual is neither a collection of organs nor a node in a dataset but a living system in which cells, meanings, and experiences continuously interact. Etiology, pathogenesis, and treatment response must therefore be understood as biosocial.[22] By integrating the lived experience of our patients into our models of disease, we move from treating biological anomalies to caring for intact lives. This is the true promise of personalized medicine: not genomically personalized but personally understood.

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