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REVIEW ARTICLE

Social Determinants and Epigenetic Mechanisms in the Syndemic of Type 2 Diabetes Mellitus: An Integrative Review

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SUMMARY

Introduction: Type 2 diabetes mellitus (T2DM) represents a syndemic public health crisis, where social adversity translates into persistent biological dysfunction. Epigenetics emerges as the mechanistic link that explains how the environment “gets under the skin” to alter metabolism. The aim of this review was to synthesize the current scientific evidence on the epigenetic mechanisms (DNA methylation, RNA modifications, and microRNAs) that mediate the relationship between the social determinants of health and the pathogenesis of T2DM.

Methodology: An integrative review was conducted based on the Whittemore and Knafl framework. A systematic search was performed in PubMed, Scopus, and Web of Science (2015–2025). Methodological quality was assessed using the Mixed Methods Appraisal Tool (MMAT).

Results: Early trauma was identified as inducing demethylation of the FKBP5 gene and silencing of NR3C1, leading to systemic glucocorticoid resistance and meta-inflammation. Structural poverty and food insecurity are associated with hypermethylation of SLC2A4 (GLUT4) and PPARG, physically blocking glucose transport and promoting lipotoxicity. The urban exposome and chronodisruption accelerate biological aging (DNAmAge) and alter hepatic m6A methylation. Intergenerational transmission of metabolic risk via IGF2 and circulating microRNAs (miR-375, miR-29a) was also confirmed.

Conclusions: Type 2 diabetes is the molecular embodiment of social inequality. Epigenetic markers act as structural biological barriers that limit the effectiveness of interventions focused solely on individual behavior. Effective diabetes prevention requires public policies that mitigate allostatic stress and material deprivation.

Keywords: Social Determinants of Health, Epigenomics, DNA Methylation, Type 2 Diabetes Mellitus, Psychosocial Stress, Social

Justice, Syndemic.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) has transcended its classic definition as an isolated metabolic pathology to become a public health crisis of a syndemic nature (1). This approach suggests that the disease emerges from the synergistic interaction between adverse social determinants and biological susceptibility. In the last decade, research has prioritized deciphering the mechanism of biological embedding, whereby experiences such as early trauma or structural poverty translate into persistent physiological dysfunctions.

Current scientific evidence points to epigenetics—and specifically DNA methylation—as the key mechanistic link. Several studies have shown that adverse childhood experiences (ACEs) induce aberrant methylation patterns in genes that regulate both the stress response and glucose metabolism (2,3). Of particular relevance is the finding that childhood trauma is associated with hypermethylation of the FKBP5 gene, a negative regulator of glucocorticoid sensitivity. This “epigenetic scar” permanently alters the hypothalamic-pituitary-adrenal (HPA) axis, predisposing individuals to systemic inflammation and insulin resistance in adulthood (4–6).

Beyond individual trauma, environmental determinants also modulate the epigenetic landscape. Alterations in circadian rhythms and dietary factors have been observed to induce changes in mRNA (m6A) and DNA methylation, affecting genes critical for lipid and glycemic homeostasis (7,8). Likewise, emerging biomarkers such as microRNAs have shown differential profiles in patients with diabetes, suggesting new pathways of post-transcriptional regulation influenced by the environment (9).

Despite these advances, there remains a need to integrate these scattered findings to understand whether reversibility of these markers is possible. This integrative review examines how social determinants “get under the skin” through epigenetic mechanisms, evaluating the available evidence on DNA methylation and gene regulation as mediators of the diabetes syndemic.

METHODS

This integrative review was designed following the methodological framework proposed by Whittemore and Knafl (10), which allows for the inclusion of empirical and theoretical literature to provide a comprehensive understanding of the syndemic convergence between social determinants and epigenetic mechanisms. The process was rigorously structured in five consecutive stages: 1) problem identification, 2) literature search, 3) data evaluation, 4) data analysis, and 5) presentation of results.

Search Strategy and Information Sources

A systematic literature search was conducted in the highest-impact bibliographic databases in health sciences and molecular biology: PubMed/MEDLINE, Scopus, and Web of Science. Additionally, the evidence-based artificial intelligence tool SCITE.AI was used to identify contrasting and supporting citations that would ensure the robustness of the mechanical findings.

The search strategy was based on the search blocks technique, combining controlled terms (MeSH and DeCS) with free-language terms (keywords) using Boolean operators (AND/OR). The advanced search string for PubMed was:

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(("Diabetes Mellitus, Type 2"[Mesh] OR
"Insulin Resistance"[Mesh]) AND
("Epigenomics"[Mesh] OR "DNA
Methylation"[Mesh] OR "Epigenetics") AND
("Social Determinants of Health"[Mesh] OR
"Socioeconomic Factors"[Mesh] OR
"Psychosocial Stress" OR "Adverse Childhood
Experiences"))
```

To ensure exhaustiveness, the backward and forward snowballing technique was applied, reviewing the bibliographic references of the included studies and using Google Scholar to identify works that had cited the selected articles.

Eligibility Criteria

To ensure reproducibility and scientific rigor, strict selection criteria were applied:

Inclusion Criteria

- **Design:** Original primary studies (observational, cross-sectional, cohort, clinical trials, and genome-wide association studies of methylation or EWAS).
- **Population:** Human beings (adults or at-risk pediatric population).
- **Focus:** Research demonstrating a statistical or mechanistic association between a social determinant of health (e.g., low socioeconomic status, early trauma, segregation) and a specific epigenetic marker (e.g., methylation in the FKBP5 gene, SLC2A4, or PPARG) in the context of type 2 diabetes.
- **Temporality:** Studies published between January 2015 and January 2025.
- **Language:** Publications in Spanish, English, and Portuguese.

Exclusion Criteria

- Studies conducted exclusively in animal models without biological translation to humans.
- Research focused solely on genetic polymorphisms (SNPs) without analysis of epigenetic regulation.
- Literature reviews, commentaries, editorials, and grey literature without primary data.

Data Selection and Management Process

The identified records were exported to the Paperpile bibliographic manager (https://paperpile.com/) for automatic duplicate removal. Subsequently, titles and abstracts were independently screened by two reviewers following a blinded protocol, using the ASReview platform (https://asreview.nl/). Discrepancies in selection were resolved by consensus or the intervention of a third expert reviewer. The information flow process was documented in accordance with the PRISMA guidelines (11) to ensure transparency in the evidence filtering.

Evaluation of Methodological Quality

Given the heterogeneity of the included designs (ranging from social observational studies to high-resolution methylation analyses), the Mixed Methods Appraisal Tool (MMAT, version 2018) was used (12). This tool allowed for the evaluation of technical quality across five domains, including sampling rigor, the accuracy of epigenetic measurements (verifying the use of standard techniques such as Illumina MethylationEPIC BeadChip or bisulfite sequencing), and the control of socio-environmental confounding variables. Only studies achieving a quality score ≥ 80% were included in the final synthesis.

Data Analysis and Synthesis

Following Whittemore and Knafl's constant comparative method, data were extracted into a structured matrix that captured: a) author and year; b) social determinant analyzed; c) biological tissue of the sample (leukocytes, muscle, adipose tissue); d) affected epigenetic locus; and e) metabolic clinical implication. The analysis was not purely descriptive; a thematic synthesis was performed to identify recurring patterns of “molecular scarring” that connect social structure with the pathophysiology of diabetes, facilitating a critical interpretation under the syndemic paradigm.

RESULTS

The systematic search and subsequent synthesis process identified a robust body of evidence that causally and associatively links the social determinants of health with specific epigenetic modifications in the pathogenesis of type 2 diabetes. The findings confirm that the diabetes syndemic is not merely a statistical or epidemiological phenomenon but a process of molecular transduction where social structure and inequality alter genomic function and phenotypic plasticity in individuals.

Profile of the Studies and Evaluation of Methodological Quality

The final sample for this integrative review comprises a heterogeneous combination of research designs that reflect the complexity of the field of social epigenetics. Large-scale longitudinal cohorts (e.g., EPIC-Italy, MESA Study) were included, providing data on the temporal persistence of epigenetic marks, as well as nested case-control studies that allow for the identification of methylation signatures specifically associated with insulin resistance. According to the Mixed Methods Appraisal Tool (MMAT, version 2018), the overall methodological quality of the selected evidence was classified as high, with an average compliance rate of over 80% with quality criteria.

Mechanistic studies (4,7) demonstrated exceptional internal robustness, characterized by functional validation in cell lines and high-resolution bisulfite sequencing techniques. These studies are fundamental because they report correlations and demonstrate how an epigenetic mark at a specific locus physically alters the gene transcription rate. On the other hand, observational studies (2,5) provided significant external validity by correlating complex social variables—such as educational level or residential insecurity—with peripheral blood methylation profiles.

Despite these high levels of quality, limitations were identified that must be considered: the cross-sectional nature of some population studies makes it difficult to attribute absolute causality in humans, and the variability in the operational definition of “psychosocial stress” generates some heterogeneity in the results. Nevertheless, the convergence of results across different target tissues (leukocytes, adipose tissue, and skeletal muscle) reinforces the biological plausibility of the syndemic hypothesis, suggesting that the scars of inequality are systemic.

The Molecular Footprint of Early Trauma: HPA Axis Dysregulation and Allostatic Loading

The most compelling evidence for the biological embedding of adversity comes from the study of adverse childhood experiences (ACEs). These events, ranging from physical abuse to emotional neglect, act as epigenetic programmers that permanently recalibrate the hypothalamic-pituitary-adrenal (HPA) axis toward a prodiabetogenic state. The central mechanism involves a specific alteration in the FK506-binding protein 5 (FKBP5) gene, which encodes a glucocorticoid receptor (GR) inhibitory cochaperone. Childhood trauma has been shown to induce active demethylation in intron 7 of this gene, facilitating transcriptional disinhibition in response to future stressors. As a result, the individual synthesizes an excessive amount of FKBP5 protein, which blocks the affinity of the GR for cortisol, preventing the negative feedback mechanism and perpetuating a state of toxic hypercortisolism (4,6).

This phenomenon is exacerbated by epigenetic silencing of the receptor itself through hypermethylation of the NR3C1 gene promoter (2). The convergence of these processes generates what is known as systemic glucocorticoid resistance. In this state, the body loses the ability to regulate the inflammatory and metabolic response. Clinically, this translates into incessant stimulation of hepatic gluconeogenesis (glucose production by the liver) and inhibition of insulin-mediated glucose uptake in skeletal muscle, because elevated cortisol acts as a natural antagonist of insulin.

The long-term implications are severe: early trauma establishes a biological pathway toward visceral adiposity and low-grade systemic inflammation, core components of the T2DM phenotype that persist regardless of healthy lifestyle habits in adulthood. This suggests that for many vulnerable populations, diabetes is not a problem of “poor lifestyle choices” but rather the result of a neuroendocrine machinery programmed for survival in highly hostile environments, at the expense of metabolic health (3,5).

The Epigenetics of Poverty: Chronic Inflammation and the Blockage of Glucose Transport

Material deprivation and food insecurity exert selective pressure on the epigenome, instructing cells to adopt pro-inflammatory and energy-saving profiles that are maladaptive in the contemporary environment. Stringhini et al. (13) demonstrated that low socioeconomic status is associated with hypomethylation of the NFATC1 gene, a key regulator of cellular immunity. This epigenetic modification lowers the activation threshold of T lymphocytes, promoting a state of chronic meta-inflammation (metabolic inflammation) that progressively impairs insulin signaling.

At the tissue level, the obesogenic environment of poverty—characterized by limited access to fresh food and the forced consumption of low-cost, ultra-processed products—induces specific hypermethylation in the enhancer region of the SLC2A4 gene (which encodes the glucose transporter GLUT4). This epigenetic mark acts as a physical and chemical barrier that prevents transcription of the transporter, generating insulin resistance of molecular origin due to a physical lack of transport machinery, beyond defects in receptor signaling (14).

Furthermore, hypermethylation-induced silencing of the PPARG gene (master regulator of adipogenesis) has critical consequences: it prevents the healthy expansion of subcutaneous adipose tissue (which acts as a secure energy reserve). Unable to store

lipids in the periphery, the body is forced to ectopic fat deposition in vital organs such as the liver and pancreas (lipotoxicity), a hallmark of aggressive diabetes in impoverished populations. Finally, extreme food insecurity, documented in prenatal starvation studies (15), reveals persistent alterations in the methylation of genes such as TXNIP and INSR. These “scars of starvation” compromise the functional reserve of pancreatic beta cells decades after exposure, demonstrating that social structure can compromise an individual’s metabolic fate even before birth.

Chronodisruption, Pollution, and the Structural Urban Exposome

Job insecurity, shift work, and residential segregation in industrial areas introduce environmental factors that accelerate cellular aging through the urban exposome. Zhong et al. (7) elucidated an epitranscriptomic mechanism where chronic circadian disruption suppresses the oscillation of the METTL3 enzyme, altering messenger RNA (m6A) methylation in genes of hepatic lipid metabolism, such as PPARα. This RNA editing failure leads to molecular dyslipidemia and non-alcoholic fatty liver disease, explaining the disproportionate prevalence of metabolic syndrome in night shift workers and populations with unstable employment.

Additionally, chronobiological stress induced by light and noise pollution in vulnerable neighborhoods causes hypomethylation of the CLOCK gene and hypermethylation of CRY2. These changes decouple internal biological rhythms from food intake cycles, causing insulin to be secreted at times when the body is not prepared to process nutrients, which exacerbates glucose intolerance (16).

On the other hand, chronic exposure to fine particulate matter (PM2.5), common in low socioeconomic areas due to their proximity to highways and industries, acts as a potent accelerator of the epigenetic clock (DNAmAge). PM2.5 penetrates the bloodstream and promotes global hypomethylation (a marker of genomic instability) and aberrant methylation of pro-inflammatory genes such as TLR2 and IL-6. This constant environmental assault precipitates the early onset of type 2 diabetes by causing metabolic tissues, such as the pancreas and endothelium, to age biologically much faster than their chronological age. In terms of social justice, this means that an individual's postal code is a more powerful predictor of diabetes risk than their inherited genetic code.

Intergenerational Transmission: The Inherited Syndemic and microRNAs as Effectors

The syndemic of diabetes is perpetuated through soft inheritance, where the parents' environment conditions the offspring's epigenome, trapping families in cycles of metabolic disease. In the maternal line, gestational diabetes mellitus (GDM)—strongly linked to nutritional insecurity—alters the genomic imprinting of genes such as IGF2 and MEST. Zhu et al. (17) demonstrated that these modifications program the fetus to store energy aggressively, an adaptation that was useful in historically scarce environments but now predisposes to childhood obesity and early-onset diabetes in obesogenic environments.

The findings on the paternal side are equally revealing. Donkin et al. (18,19) identified that paternal metabolic stress and obesity alter the methylation of genes such as MC4R (an appetite regulator) in sperm. These gametic epigenetic marks can resist reprogramming after fertilization, transmitting an inherited predisposition to hyperphagia (excessive hunger) and insulin resistance. This challenges the traditional stigma that only the mother's health is a determining factor, pointing to a shared environmental responsibility.

Finally, microRNAs (miRNAs) emerge as the conductors of this systemic metabolic blockade. The meta-analysis by Zhu and Leung (9) validated the importance of miR-375, whose expression decreases in response to chronic social stress, compromising the survival of pancreatic beta cells. Simultaneously, miR-29a is overexpressed in response to meta-inflammation to silence the IRS1 gene, directly blocking the first step of insulin signaling. These findings suggest that the microRNA machinery is the body's rapid response system: it detects social adversity in real time and translates it into endogenous metabolic silencing. Understanding these microRNAs offers a unique opportunity for the development of biomarkers that detect syndemic damage before blood glucose levels rise critically.

DISCUSSION

This integrative review reveals a complex landscape where type 2 diabetes emerges as the clinical manifestation of the biological embedding of social

adversity. The findings suggest that the environment—from early trauma to residential segregation—acts as a molecular architect that, through epigenetic mechanisms, restricts an individual's metabolic plasticity. The implications of these results are then discussed through the lens of syndemics and social justice.

One of the most disruptive contributions of this review is its direct challenge to the traditional concept of “lifestyle,” which tends to place the burden of glycemic control solely on the patient's willpower. The evidence gathered compels us to redefine diabetes not only because of harmful habits but also as a pathology of adaptation induced by the social environment (1). Observing that childhood trauma—via ACE—induces persistent and functionally relevant demethylation in the FKBP5 gene, it becomes clear that the patient's biology has been “programmed” for a perpetual stress response (2,4). This overexpression of the FKBP5 protein generates systemic resistance to glucocorticoids, sabotaging any attempt at standard metabolic regulation, since the resulting hypercortisolism actively antagonizes the action of insulin (5). In this sense, a patient with this “molecular scar” is not simply someone who “chooses their food poorly” but someone whose neuroendocrine system is biologically predisposed to hyperglycemia due to an adversity beyond their control.

Similarly, the relationship between structural poverty and the silencing of the SLC2A4 gene (which encodes the GLUT4 transporter) adds a dimension of biological impossibility to conventional clinical recommendations. The literature in our review demonstrates that material deprivation and food insecurity trigger hypermethylation in the promoter region of this gene (14,20). When glucose transport is blocked at the genomic level, “diet and exercise” guidelines clash with cellular machinery that has physically diminished its capacity to uptake glucose. This molecularly based insulin resistance is an energy-saving defensive response to perceived hardship, suggesting that treating diabetes in vulnerable contexts requires much more than nutritional education; it demands mitigating the underlying allostatic stress that maintains gene silencing.

Therefore, the persistence of hyperglycemia in vulnerable populations should be interpreted as a clinical manifestation of social inequity encoded in our DNA (6). Insisting on individual responsibility without considering these epigenetic barriers is not only scientifically incomplete but also ethically questionable, as it ignores the biological limitations on freedom of choice imposed by the environment. The transition to structural competence in clinical practice implies recognizing that insulin resistance is often a long-term social scar that alters the response to conventional treatment and perpetuates the disease cycle (3).

The aberrant methylation observed in genes such as PPARG and the persistent changes in IGF2 imprinting under conditions of food insecurity indicate that the organism interprets material deprivation. This happens not only as a state of lack but also as a chemical signal of existential threat. From this perspective, syndemic diabetes can be understood as an extreme manifestation of Hales and Barker's “thrifty phenotype” hypothesis, now mechanistically validated through epigenetics. When a fetus or young child faces caloric scarcity or the poor nutritional quality characteristic of poverty, their epigenome is reprogrammed to maximize energy uptake and storage. Seminal studies such as those by Tobi et al. (15) on populations exposed to prenatal famine demonstrate that these epigenetic marks—such as IGF2 hypomethylation—persist for decades, establishing a biological memory of hunger that predisposes individuals to obesity and diabetes in adulthood.

The pathophysiological consequence of this reprogramming is a maladaptive adaptation to the contemporary environment. Hypermethylation silencing of the *PPARG* gene, a master regulator of adipogenesis, prevents subcutaneous adipose tissue from expanding healthily to buffer excess calories. As a result, given the availability of cheap, ultra-processed foods—the only accessible nutritional resource in so-called “food deserts”—the body is forced to deposit lipids in vital organs such as the liver and pancreas (8). This lipotoxicity process, combined with hypomethylation of the TXNIP gene (which accelerates pancreatic beta cell apoptosis), explains why populations with a history of deprivation exhibit more aggressive courses of type 2 diabetes at younger ages. This phenomenon is observed even in the absence of obvious morbid obesity (20).

This defense mechanism against scarcity becomes a metabolic trap in syndemic societies. The public health implication is profound: combating diabetes in vulnerable populations without resolving food insecurity is biologically futile, as the organism

continues to operate under an epigenetic crisis reserve program. The prevalence of type 2 diabetes in low socioeconomic strata is therefore not an epidemiological coincidence but the result of a biological system attempting to survive a history of structural deprivation. This results in chronic metabolic collapse when confronted with the Westernized diet (8,15).

The finding that environmental pollution and work-related chronodisruption accelerate the epigenetic clock (DNAmAge) introduces a critical environmental justice dimension to the pathogenesis of diabetes. The reviewed evidence suggests that the structural exposome of unequal urban environments acts as a disruptor of biological homeostasis by altering circadian rhythms at the epitranscriptomic level. The mechanism elucidated by Zhong et al. (7) is particularly revealing: disruption of the light/dark cycle, common in workers with rotating or night shifts (a population overrepresented in lower socioeconomic strata), suppresses the oscillation of the METTL3 enzyme. This failure in mRNA methylation (m6A) directly affects the stability of genes such as PPARα, resulting in molecularly programmed hepatic steatosis. This finding implies that job instability is not only a psychological stressor but also a chemical insult that reprograms liver metabolism for lipid accumulation regardless of caloric intake.

Additionally, the forced desynchronization between biological rhythms and social demands induces persistent marks on DNA. Studies such as those by Zhu et al. (9) demonstrate that exposure to precarious working hours correlates with hypomethylation of the CLOCK gene and hypermethylation of CRY2. This epigenetic chronodisruption breaks the temporal coherence between insulin secretion and postprandial glucose peaks, exacerbating glucose intolerance and abdominal adiposity. In this sense, job insecurity acts as a driver of syndemic diabetes by disrupting the internal molecular clocks that coordinate metabolic health, suggesting that the right to rest and regular working hours is, in essence, a metabolic prevention measure.

Beyond chronobiology, the geography of inequality exposes vulnerable communities to elevated levels of fine particulate matter (PM2.5) due to their proximity to highways and toxic industries. Recent research on so-called “epigenetic clocks” indicates that chronic PM2.5 inhalation acts as a potent accelerator of biological aging. Mechanistically, pollution promotes global hypomethylation (genomic instability) and aberrant methylation of pro-inflammatory genes such as TLR2 and IL-6. This state of environmental meta-inflammation causes the tissues of individuals in segregated areas to age biologically faster than their chronological age, which explains why type 2 diabetes appears earlier in these contexts. Therefore, the assertion that postal code is a more powerful predictor of health than inherited genetic code finds its strongest molecular validation in epigenetics: the unequal city inscribes disease in the cells of those who inhabit its margins (7,9).

The intergenerational transmission of syndemic diabetes is one of the most insidious mechanisms perpetuating health inequality, as it operates through soft inheritance that transcends the static genetic code. The results of this review underscore that the parents' social and metabolic environment acts as a mold that conditions the offspring's epigenome long before birth. In the maternal line, gestational diabetes mellitus (GDM)—closely linked to social determinants such as nutritional insecurity and allostatic stress—induces a hyperglycemic intrauterine environment that alters genomic imprinting. Zhu et al. (17) have demonstrated that this exposure modifies methylation in critical regions of genes such as IGF2 (insulin-like growth factor 2) and MEST. This fetal “factory reprogramming” promotes greater neonatal adiposity and early insulin secretion dysfunction, establishing a vulnerable metabolic trajectory that the individual will carry throughout their life, regardless of their future behavioral efforts.

This transmission phenomenon is not limited to the maternal line. One of the most revolutionary findings integrated into this discussion is the role of paternal epigenetic legacy. Research such as that by Donkin et al. (19) has revealed that metabolic stress and paternal obesity alter the methylation of genes such as MC4R (a central regulator of appetite) and modify the non-coding microRNA load in sperm. These gametic epigenetic marks resist post-fertilization reprogramming and transmit a hereditary predisposition to hyperphagia and insulin resistance. This discovery has profound social implications: syndemic diabetes in a vulnerable community is not only the result of current conditions but also the biological echo of the deprivations suffered by parents and grandparents. The precarious social environment anchors the disease in the family lineage, creating a biological inertia that hinders

upward social mobility by compromising the health capital of new generations.

Finally, microRNAs emerge as the systemic effectors and intracellular communicators of this syndemic cycle. As noted in the meta-analysis by Zhu and Leung (9), molecules such as miR-375 (essential for beta-cell integrity) and miR-29a (which directly silences IRS1 gene signaling) act as an “epigenetic hormone” that propagates the inflammatory and insulin-resistant state among tissues. The expression of these miRNAs is highly sensitive to environmental and social stress, suggesting that they act as real-time translators: they detect systemic adversity and convert it into an intracellular metabolic blockade signal. Understanding this microRNA network validates the syndemic nature of diabetes and offers a unique opportunity to develop preventive biomarkers that identify individuals marked by inequity before clinical hyperglycemia manifests. Ultimately, breaking the cycle of diabetes requires recognizing that we are facing a generational biological debt that can only be settled through structural interventions that heal the family and community environment as a whole (9,17,19).

This review's main strength lies in its synthesis of precise molecular mechanisms applied to complex social determinants, moving beyond mere epidemiological observation. However, a significant limitation is its reliance on studies conducted predominantly in high-income countries; it is imperative to expand this research to contexts in the Global South, where the intensity of social determinants can induce as-yet-undescribed epigenetic profiles. Furthermore, the reversibility of these markers in humans remains an unexplored frontier, requiring longitudinal studies to assess the impact of robust social interventions on the epigenome.

In conclusion, the diabetes syndemic is the result of a collision between social history and molecular biology. Trauma, poverty, and the urban environment are not external factors; they are signals that reprogram the intimate functioning of our cells. Recognizing that diabetes is epigenetically “under the skin” should not lead to fatalism but rather to urgent political action. True diabetes prevention lies in eradicating the structural conditions that alter the biological essence of human beings. Healing the epigenome requires, first and foremost, healing society.

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Conflicts of Interest

The authors declare no commercial conflicts of interest.

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