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Nano Biosensors for Continuous Monitoring of Metabolic Biomarkers in Obese Diabetic Individuals

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ABSTRACT

Obesity-associated type 2 diabetes is characterized by chronic hyperglycemia, insulin resistance, dyslipidemia and low-grade inflammation, all of which fluctuate markedly in response to meals, physical activity, stress and medication use. Conventional monitoring based on fasting glucose, HbA1c and occasional finger-stick tests provides only sparse snapshots of this dynamic state and is particularly inadequate in individuals with obesity, who often exhibit greater glycemic variability, complex polypharmacy and multiple comorbidities. Nano-biosensors, which integrate biorecognition elements with nanostructured transducers, offer a route to minimally invasive, continuous and potentially multiplex monitoring of key metabolic biomarkers in real time. By exploiting the high surface area, excellent electrical and optical properties and tunable surface chemistry of nanomaterials such as graphene, carbon nanotubes, metal nanoparticles and nanozymes, these systems can reach physiologically relevant detection limits in tiny volumes of interstitial fluid, sweat, saliva or tears. When embedded in skin-interfaced patches, microneedle arrays, textiles or wearable devices, nano-biosensors can track glucose and complementary markers such as lactate, ketones and stress indicators continuously, with the potential to inform precision treatment, improve adherence and enable earlier detection of metabolic decompensation. This review discusses the rationale for continuous metabolic monitoring in obese diabetic individuals, the relevant biomarker landscape, key design principles of nano-biosensors, emerging fluid-specific and wearable platforms, current evidence and translational challenges, and future directions including multiplex devices and AI-assisted analytics.

Keywords: Nano-biosensors; metabolic biomarkers; continuous monitoring; obesity-associated diabetes; wearable sensors

INTRODUCTION

Obesity and type 2 diabetes mellitus frequently coexist as a coupled metabolic disorder, in which excess adiposity, ectopic lipid deposition and chronic low-grade inflammation drive systemic insulin resistance and progressive β-cell dysfunction[1–3]. In these individuals, glycemic control is influenced not only by intrinsic defects in insulin secretion and action but also by variable food intake, sedentary behavior, sleep disruption, stress, use of high-dose insulin or secretagogues, and comorbidities such as nonalcoholic fatty liver disease and obstructive sleep apnea[4–6]. The result is pronounced intra- and inter-day variability in glucose and related metabolites. Traditional monitoring methods fasting plasma glucose, oral glucose tolerance testing, HbA1c and occasional capillary glucose measurements offer essential but limited information. They capture average exposure or isolated time points rather than the full temporal pattern of excursions that damage blood vessels and nerves and complicate therapy titration[7–9].

Continuous glucose monitoring (CGM) has already shown that many patients previously considered well controlled by HbA1c exhibit frequent postprandial spikes, unrecognized nocturnal hypoglycemia and highly variable daily profiles[10]. This is particularly evident in individuals with obesity who require large insulin doses or complex combination therapies. Yet current CGM systems focus almost exclusively on glucose and are typically optimized for general diabetes populations rather than specifically for people with severe obesity, who may have thicker subcutaneous tissue, altered interstitial fluid dynamics and greater device-related discomfort. Moreover, glucose alone only partially reflects the multidimensional metabolic derangements of obesity-associated diabetes[10]. Lactate informs on exercise and tissue oxygenation; ketones indicate shifts toward fat oxidation and risk of ketoacidosis; markers of lipolysis reflect adipose tissue behavior; and inflammatory mediators report on metaflammation. Capturing some of these additional parameters alongside glucose would provide a more holistic, real-time picture of metabolic status.

Nano-biosensors offer several advantages for building such expanded monitoring systems. At their core, biosensors couple a biorecognition interface often an enzyme, antibody, aptamer or molecularly imprinted polymer to a transducer that converts biochemical events into measurable electrical, optical or mechanical signals[11–14]. Incorporating nanomaterials into the transducer greatly enhances performance. Graphene, carbon nanotubes, metal nanoparticles, quantum dots and metal–organic frameworks provide very high effective surface areas for immobilizing recognition elements, facilitate rapid electron transfer, and exhibit unique optical or catalytic properties that amplify signals even when analyte concentrations are low. This is crucial because many biomarkers in sweat, saliva or interstitial fluid are present at lower levels than in blood and must still be detected accurately for clinical use[15, 16].

Equally important, nanomaterials are compatible with flexible, miniaturized and skin-conformal device architectures. Thin films of graphene or networks of metallic nanowires can be patterned onto stretchable substrates, while nanoporous membranes and microfluidic channels can be integrated into soft patches that adhere to the skin[16, 17]. Within these platforms, nano-structured electrodes or plasmonic nanostructures can continuously sense analytes in sweat or interstitial fluid with minimal discomfort. Microneedles incorporating nanostructured electrodes extend this concept beneath the stratum corneum into dermal interstitial fluid, combining the analytical strengths of nano-biosensors with the established physiology of CGM-type measurements.

For obese diabetic individuals, this convergence of nanoscale sensing and wearable formats addresses several unmet needs. First, it reduces reliance on finger-stick testing, which is often painful, stigmatizing and inconvenient, especially for those already struggling with multiple injections or tablets daily[18–20]. Second, it enables richer datasets, allowing clinicians and patients to see how glucose and related biomarkers respond to specific meals, exercise, sleep disruption or changes in medication. This granularity supports individualized titration of insulin, GLP-1 receptor agonists, SGLT2 inhibitors and other agents, with the potential to increase time in target range while reducing hypoglycemia and weight gain. Third, continuous multi-analyte monitoring could improve safety by flagging patterns that precede acute events, such as rising ketones despite near-normal glucose in patients on SGLT2 inhibitors, or sustained elevations in stress markers associated with impending metabolic decompensation.

At the same time, the deployment of nano-biosensor systems in this population faces specific challenges. Obesity is associated with changes in skin structure, microcirculation, sweating patterns and local inflammation, all of which can affect analyte transport to sensors and device comfort[15, 21]. The burden of wearing additional devices must be weighed against potential benefits, particularly in individuals already managing multiple comorbidities and technologies. Data streams must be translated into clear, actionable information to avoid overwhelming users and clinicians. Despite these hurdles, the potential of nano-biosensors to transform metabolic monitoring in obese diabetic individuals is substantial, motivating detailed examination of the relevant biomarkers, sensor architectures, evidence base and translational issues.

2. Metabolic Biomarkers Relevant to Obesity-Associated Diabetes

Continuous monitoring systems for obese diabetic individuals must prioritize biomarkers that both reflect key pathophysiological processes and can be feasibly measured in accessible biofluids. Glucose remains central, as its fluctuations directly inform therapy adjustments and risk of acute complications. In interstitial fluid, glucose tracks blood levels with a short lag, making it appropriate for trend-based management. In sweat and saliva, glucose concentrations are lower and more variable but can still carry useful information when interpreted in context[22, 23].

Lactate is a second important biomarker. It rises with high-intensity exercise, tissue hypoxia and certain drug effects and can indicate whether patients are engaging in sufficient physical activity or developing lactic acidosis in vulnerable settings. In obese individuals with reduced cardiorespiratory fitness, lactate trends may help tailor exercise prescriptions and detect overexertion[24]. Ketone bodies, particularly β-hydroxybutyrate, provide a window into shifts toward fat oxidation during fasting, low-carbohydrate diets or treatment with SGLT2 inhibitors[25]. Continuous or high-frequency ketone monitoring could help prevent ketoacidosis, especially the atypical euglycemic form associated with SGLT2 therapy[24, 26].

Markers linked to lipolysis and lipid metabolism, such as glycerol or non-esterified fatty acids, mirror adipose tissue dynamics and hepatic lipid handling[27]. While continuous lipid monitoring remains technically difficult, even intermittent assessment through minimally invasive biosensors could support risk stratification and evaluation of weight-loss interventions. Inflammatory and oxidative stress markers, including IL-6, TNF-α, C-reactive protein surrogates and reactive oxygen species–related products, reflect metaflammation and vascular risk, though their slower kinetics and lower concentrations pose detection challenges[27].

Hormonal signals such as cortisol and adrenaline, accessible in sweat or saliva, provide context on psychosocial stress and circadian rhythms[28]. Given the strong influence of stress on eating behavior and insulin sensitivity, tracking these signals alongside metabolic biomarkers may clarify why some obese diabetic individuals exhibit pronounced day-to-day variability despite stable medications and diet[29].

In practice, a tiered approach is likely. Glucose would be continuously monitored in most patients; lactate and possibly ketones would be tracked in selected individuals at higher risk of exercise intolerance or ketoacidosis; and inflammatory or stress markers would be measured either intermittently or continuously in research and high-risk settings[28]. Nano-biosensors are particularly suited to this layered strategy because they can be engineered for high sensitivity across diverse analytes and form the basis of multiplex platforms that detect several biomarkers in parallel from the same small sample.

3. Nanomaterials and Transduction Mechanisms in Metabolic Biosensing

The performance of nano-biosensors rests on the interplay between biorecognition elements and nanostructured transducers. For glucose and lactate, enzyme-based recognition remains dominant, typically using glucose oxidase, glucose dehydrogenase or lactate oxidase to catalyze reactions that generate hydrogen peroxide, consume oxygen or produce redox-active species[12, 30]. When these enzymes are immobilized onto nanostructured electrodes graphene sheets, carbon nanotubes, metal nanoparticle decorated surfaces or hybrid composites electron transfer from the enzymatic reaction to the electrode is greatly enhanced, improving sensitivity and lowering detection limits in dilute biofluids.

Non-enzymatic approaches exploit nanomaterials whose surfaces directly catalyze oxidation or reduction of metabolites. Metal and metal-oxide nanoparticles, metal–organic frameworks and doped carbon nanostructures can exhibit intrinsic electrocatalytic activity toward glucose, lactate or other analytes, functioning as "nanozymes[31]." These systems avoid issues of enzyme instability and can operate over wider temperature and pH ranges, which is advantageous for long-term wearables that experience variable ambient conditions.

Optical nano-biosensors rely on localized surface plasmon resonance, fluorescence or surface-enhanced Raman scattering. Metal nanostructures such as gold nanorods, nanoprisms or nanoholes exhibit plasmonic resonances whose spectral position shifts when local refractive index changes due to analyte binding[32]. Functionalizing these structures with glucose-binding moieties, antibodies or aptamers converts biochemical recognition into measurable optical signals that can be read by miniaturized photodetectors embedded in patches or watches. Quantum dots and upconversion nanoparticles provide bright, stable fluorescence labels for multiplexed detection of proteins or nucleic acids when immunoassays or aptasensors are integrated into wearable formats[32].

Magnetic and piezoelectric mechanisms, while less common in metabolic wearables, offer alternative transduction routes. Superparamagnetic nanoparticles can be used as labels in sandwich assays, with binding events detected via changes in magnetic relaxation, enabling measurements in turbid samples without optical interference[33]. Piezoelectric microcantilevers or surface acoustic wave devices detect mass loading and viscoelastic changes upon analyte binding, and their performance can be markedly enhanced by decorating their surfaces with nanostructured materials that increase effective binding area.

Across these strategies, the choice of nanomaterial and transduction mechanism must consider biocompatibility, stability, power requirements and ease of integration with flexible substrates. Carbon-based nanomaterials offer excellent electrical properties, mechanical flexibility and relatively benign biological profiles when properly processed, making them attractive for skin-interfaced devices[33]. Metal nanoparticles and oxides bring powerful optical and catalytic functionalities but raise more complex questions about long-term safety and potential leaching. Hybrid designs that combine multiple nanomaterials often provide the best balance of sensitivity, selectivity and robustness for continuous monitoring.

4. Body-Fluid Specific Nano-Biosensor Platforms

Different biofluids offer distinct opportunities and constraints for nano-biosensor deployment in obese diabetic individuals. Interstitial fluid (ISF) is the most physiologically relevant compartment for glucose monitoring because it closely tracks blood levels. Accessing ISF typically requires minimally invasive approaches such as microneedles or small implanted sensors[34]. Nano-structured electrodes at microneedle tips or on flexible filaments can continuously measure ISF glucose, and in principle additional analytes, while causing minimal discomfort. For individuals with obesity, microneedle length and mechanical strength must be optimized to penetrate the thicker stratum corneum and reach well-perfused dermis without bending or breaking[34].

Sweat is attractive because it can be collected non-invasively at the skin surface. Nano-biosensors integrated into patches, bands or textiles can analyze sweat for glucose, lactate, electrolytes and stress markers. The main challenges are low analyte concentrations, variable sweat rates and the influence of local skin conditions. Nanostructured electrodes and plasmonic surfaces address sensitivity constraints, while microfluidic channels and absorbent layers help manage flow and evaporation[35]. For obese individuals who may sweat more in specific regions and less in others, device placement and sampling area become important design considerations[35].

Saliva offers another non-invasive matrix, with straightforward collection and relatively stable composition. Nano-biosensors embedded in intraoral devices or small test strips could monitor glucose, cortisol or inflammatory markers in saliva. The oral environment, however, is chemically complex and subject to rapid changes with food intake and oral hygiene, requiring robust antifouling coatings and calibration strategies[36].

Tear fluid, accessible via contact lenses, contains glucose and other metabolites at concentrations correlated with blood levels. Smart contact lenses incorporating nanoscale sensors have been proposed for glucose monitoring, though challenges related to comfort, baseline drift and user acceptance remain significant[36]. For many obese diabetic individuals, ocular comorbidities or reduced tolerance may limit this route.

In practice, the most promising near-term platforms are likely those that combine interstitial fluid and sweat sensing via skin patches or microneedle-equipped devices. These can be designed to accommodate variations in body habitus and skin properties common in obesity, while providing multiple analyte channels and redundancy to improve reliability.

5. Wearable Architectures and Data Interpretation in Obesity-Associated Diabetes

Translating nano-biosensors into practical tools for obese diabetic individuals depends on device-level design and data handling as much as on sensing chemistry. Wearable architectures must be thin, flexible and breathable to minimize skin irritation, particularly in skin folds or under clothing where moisture and friction are increased[37]. Stretchable conductors, ultrathin substrates and soft adhesives help maintain stable contact over days of wear. In devices targeting larger body sizes, strap length, patch footprint and mechanical robustness under higher mechanical loads must be considered[37].

Power consumption is critical because continuous sensing and wireless transmission can drain batteries quickly. Low-power nanomaterial transducers, efficient analog front-ends and intermittent sampling strategies reduce energy use. Energy harvesting from body heat or motion is an area of active research but not yet widely adopted in medical devices[37].

From a data perspective, obese diabetic individuals generate complex metabolic patterns influenced by medication schedules, meals, physical activity and sleep. Continuous glucose traces alone can be challenging to interpret; adding lactate, ketone or stress markers further increases complexity[38]. Algorithms must filter noise, correct for lag between biofluid and blood, and fuse biochemical data with contextual information such as accelerometer readings or self-reported meals. For example, a rise in lactate and heart rate during exercise should be interpreted differently from similar lactate changes in a sedentary state[39].

Clinically meaningful summaries such as time in glucose range, frequency and duration of excursions, and associations between behaviors and metabolic responses are essential. For obesity-associated diabetes, additional metrics might include time spent in ketone ranges associated with safe nutritional ketosis versus early ketoacidosis, patterns of lactate response to prescribed exercise, or persistent elevations in stress markers that correlate with poor glycemic control[39]. Presenting these insights in intuitive visual formats to both patients and clinicians is crucial to drive behavior change and therapeutic decisions.

6. Evidence Base for Nano-Biosensor Platforms in Metabolic Monitoring

Most commercial continuous metabolic monitors currently available to diabetic patients are based on established electrochemical technologies rather than explicitly marketed as nano-biosensors, although many incorporate nanoscale features such as nanostructured membranes or electrodes[40]. The clinical benefits of CGM in improving glycemic control, reducing hypoglycemia and enhancing quality of life are well documented across type 1 and type 2 diabetes, including subsets with obesity[41]. These experiences provide a template for how continuous sensing can be integrated into care pathways[40, 42].

In contrast, many nano-biosensor platforms remain at the preclinical or early clinical prototype stage. Laboratory studies have shown that graphene-based and carbon-nanotube-based electrodes can detect glucose, lactate and other metabolites in buffer solutions and artificial sweat at physiologically relevant concentrations, with response times compatible with real-time monitoring[42]. Flexible patches integrating nanostructured electrodes and microfluidics have been demonstrated on human volunteers for sweat glucose and lactate sensing during exercise, though often in small numbers of healthy individuals.

Microneedle devices with nano-enhanced electrodes have measured interstitial glucose in animal models and in limited human experiments, showing reasonable correlation with reference methods over short wear periods[43]. Similarly, optical nano-biosensors using plasmonic structures or quantum dots have been tested for non-invasive or minimally invasive glucose monitoring in small feasibility studies. However, long-term stability, calibration procedures, and performance in real-world settings with movement, temperature changes and variable skin conditions require further evaluation[43].

For obese diabetic individuals specifically, data are sparse. Most prototypes have been tested in lean volunteers or general diabetes cohorts without stratified analysis by BMI or adiposity distribution[44]. Nevertheless, there is no fundamental reason why nano-biosensors could not perform in individuals with obesity if device geometry, insertion depth (for microneedles), and placement are carefully optimized. Future studies must explicitly include obese diabetic participants, as subcutaneous tissue thickness, sweating patterns and skin integrity can influence sensor performance and user experience.

7. Challenges and Future Directions

Several barriers must be addressed before nano-biosensors for continuous metabolic monitoring become routine in the management of obesity-associated diabetes. Analytical validation is a priority[45]. Devices must demonstrate accuracy and precision across a wide range of conditions, compared with laboratory standards and established CGMs, and maintain performance over days to weeks without frequent recalibration. Interference from other sweat or ISF components, biofouling and drift in nanomaterial properties over time must be systematically characterized[45].

Safety and biocompatibility are equally important. Even though diagnostic devices typically use small amounts of nanomaterials, chronic skin contact and repeated application raise concerns about local irritation, sensitization or nanoparticle leaching[46, 47]. Selecting inert or biodegradable materials, encapsulating nanostructures within stable polymer matrices, and rigorously assessing long-term effects are essential, particularly in people with obesity who may have compromised microcirculation and wound healing.

Cost, manufacturing scalability and access pose additional challenges. Sophisticated nano-biosensor wearables may initially be expensive and concentrated in high-resource settings, while obesity and diabetes disproportionately affect lower-income populations[48]. Designing platforms that use low-cost fabrication methods and widely available materials, and that integrate with commodity smartphones rather than proprietary readers, can support broader dissemination.

Looking forward, the most impactful developments are likely to involve multiplexed nano-biosensor arrays embedded in comfortable wearables that continuously monitor glucose and a small set of additional biomarkers such as lactate and ketones. Integration with adaptive algorithms and, where appropriate, closed-loop therapeutic systems like insulin pumps, smart injectors or drug-releasing patches could enable therapy that responds to a richer metabolic picture than glucose alone. For obese diabetic individuals, such systems might guide not only insulin dosing but also timing and intensity of exercise, nutritional choices and stress management strategies. As evidence accumulates, nano-biosensors may evolve from experimental tools into integral components of personalized, proactive care models for obesity-associated diabetes.

CONCLUSION

Nano-biosensors hold considerable promise for continuous monitoring of metabolic biomarkers in obese diabetic individuals, a population characterized by complex, dynamic physiology and high cardiometabolic risk. By combining highly sensitive nanostructured transducers with flexible, skin-interfaced device architectures, these systems can track glucose and complementary analytes such as lactate and ketones in minimally invasive ways, generating rich datasets that capture day-to-day metabolic patterns. Early work demonstrates technical feasibility and suggests potential benefits for therapy personalization and safety, although most platforms remain in preclinical or early clinical stages and data specific to people with obesity are limited. Realizing the full potential of nano-biosensors will require rigorous validation, attention to safety and equity, and thoughtful integration with existing clinical workflows and digital health ecosystems. If these challenges can be overcome, nano-enabled continuous metabolic monitoring could become a key tool in the precision management of obesity-associated diabetes.

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