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ORIGINAL RESEARCH

Glucose fluctuations in subjects with normal glucose tolerance, impaired glucose regulation, and newly diagnosed type 2 diabetes - A review of the evidence

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1. ABSTRACT

The original study compared, through three days of continuous glucose monitoring, 53 people with normal glucose tolerance, 53 with impaired glucose regulation, and 56 with newly diagnosed, untreated type 2 diabetes. The goal was to describe how glucose oscillations change during the transition from normal regulation to prediabetes and diabetes.In section 3.1 of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi, the study contributes to the narrative that glycemic instability appears even before overt diabetes and increases with the deterioration of metabolic control. Independent studies confirm that certain variability metrics are higher in prediabetes and increase in parallel with the reduction of beta-cell function. However, significant limitations remain: the available studies are primarily cross-sectional and short-term, and they do not allow us to establish whether these oscillations are a cause of diabetes or an early signal of its development.

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MISSION

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Through articles, reviews, in-depth analyses and expert contributions, the Journal champions evidence-based medicine and science, fostering a correct interpretation of scientific data and countering misinformation. Every piece of content is developed with the aim of translating the complexity of research into understandable, useful and applicable information, while keeping intact the principles of accuracy, transparency and scientific independence.

Free from political, industrial and commercial influence, the journal stands as an authoritative and independent editorial space, dedicated to promoting scientific culture, professional development and the growth of health awareness among the public.

2. ANALYZED STUDY

The research question was whether the daily glycemic profile becomes progressively less stable as one moves from normal glucose tolerance to impaired glucose regulation and, finally, to newly diagnosed type 2 diabetes. The hypothesis was that individuals in the early stages of metabolic impairment would exhibit wider and less predictable glucose excursions compared to normoglycemic individuals.The research is relevant to section 3.1 of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi because it directly examines the initial segment of the narrative: the emergence of increased glycemic variability before overt diabetes. Glycemic variability refers to fluctuations in glucose levels throughout the day and between different days; it therefore does not coincide solely with average glycemia.As a cross-sectional study, meaning a snapshot of groups evaluated during the same period, it can show differences and associations between stages of glucose metabolism. However, it cannot prove that increased oscillations cause diabetes, nor can it establish the precise temporal order between glycemic instability, insulin resistance, and the loss of pancreatic beta-cell function.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The study adopted a cross-sectional design. It included a total of 162 participants: 53 with normal glucose tolerance, 53 with impaired glucose regulation, and 56 with newly diagnosed, untreated type 2 diabetes. Monitoring was performed using a continuous glucose monitoring system, or CGM (a sensor that repeatedly records glucose in the interstitial fluid), for three consecutive days.The authors calculated the mean glycemia, the standard deviation of mean glycemia, the largest amplitude of glycemic excursions, the MAGE or *Mean Amplitude of Glycemic Excursions* (an index of the amplitude of major oscillations), the MODD or *Mean of Daily Differences* (an index of the differences between consecutive days), and post-meal glycemic excursion. These parameters describe different aspects of the same question: how much glucose deviates from its usual values and how repeatable these variations are.The detailed inclusion and exclusion criteria, the recruitment period, the dietary procedures during monitoring, the complete statistical analyses, and the specific threshold values used are not reported in the available material, which contains only an incomplete abstract.

4. RESULTS

The main result reported in the available material is the presence of glycemic alterations that are measurable even outside of a diagnosed diabetes condition. 22% of participants with normal glucose tolerance and 33.9% of those with impaired glycemic regulation recorded at least one glucose value equal to or greater than 11.1 mmol/L, i.e., 200 mg/dL. Furthermore, episodes detected by the sensor below 3.9 mmol/L, i.e., 70 mg/dL, appeared in 49.1% of the normoglycemic group, 50.9% of the group with impaired glycemic regulation, and 30.8% of the group with newly diagnosed diabetes.These data mean that individual glucose spikes or drops can be observed even in people who have not yet received a diabetes diagnosis. However, this does not mean that such episodes alone equate to a clinical disease: the CGM detects frequent and closely spaced values, whereas a diabetes diagnosis requires standardized criteria based on validated tests.The available abstract states that standard deviation, mean amplitude of glycemic excursions, MAGE, MODD, and postprandial excursions were calculated. However, the complete values of the individual indices in the three groups, the numerical differences between groups, P-values, and correlations between metrics are not reported in the available material. For this reason, it is not possible to attribute further quantitative estimates to the analyzed study beyond those explicitly provided.

5. INTERPRETATION

In simple terms, the study suggests that glucose metabolism may become less stable before diabetes is clinically recognized. The publication subject to the Evidence Review therefore supports the book's assertion that wider and more prolonged fluctuations may appear in the stages preceding overt diabetes.Its contribution is observational and descriptive. The metrics used measure the same general phenomenon from different perspectives: the standard deviation describes the dispersion of values from the mean; MAGE selects the most relevant oscillations; MODD

compares the profile of consecutive days. If these indices increase together, it is plausible that they are capturing correlated components of glycemic variability. However, this consistency does not prove that they are interchangeable, nor that any specific index is the best for predicting diabetes.The segment of the chain actually documented is: normal glucose regulation or impaired glycemic regulation or newly diagnosed diabetes differences in the profile recorded by CGM. The research does not directly demonstrate that reduced beta-cell function causes such oscillations, nor that reducing oscillations prevents diabetes. These links require independent studies and, above all, longitudinal observations.

6. INDEPENDENT SUPPORTING EVIDENCE

Particularly relevant confirmation comes from an independent study conducted on 220 people distributed along the spectrum from normal glycemic regulation to type 2 diabetes. All major variability indices measured with CGM increased progressively as one moved from normal regulation to diabetes. For example, MAGE increased from 2.1 to 3.3, 4.3, and 4.8 mmol/L across the four groups of metabolic severity; simultaneously, the oral disposition index, which integrates insulin secretion and insulin sensitivity, decreased. The associations between variability indices and the disposition index were inverse, with correlation coefficients ranging between –0.59 and –0.72. This confirms both the direction described in the book and the link to poorer beta-cell compensation, although it does not demonstrate causality [1].A second study compared 18 people with prediabetes to 18 normoglycemic individuals matched for age, sex, and body mass index, using CGM for one week. The prediabetes group showed greater variability: the median coefficient of variation was 15.2% versus 11.9%, while the median MAGE was 44.3 versus 33.3 mg/dL. Time above 180 mg/dL and mean interstitial glucose were also higher in prediabetes. This result is a direct confirmation, but the sample was small and the design remained cross-sectional [2].In the Maastricht Study, a large population cohort with 851 participants, the standard deviation calculated from CGM was positively correlated with blood glucose at one hour during an oral glucose tolerance test: rho 0.61. The coefficient of variation was positively correlated with both the incremental glucose peak and the one-hour value of the test, rho 0.50 for both. In simple terms, people with higher responses to a glucose load also tended to have wider daily fluctuations. The study also indicated that at least two or three days of CGM are required to measure standard deviation and coefficient of variation with sufficient reliability. This strengthens the interpretation of the metrics but does not prove individual progression toward diabetes [3].Overall, these independent studies build a convergent chain: worsening glucose tolerance is associated with higher variability values; greater variability is also associated with lower beta-cell function as estimated by the oral disposition index. The evidence is stronger for the association than for a causal relationship.

7. CONFLICTING EVIDENCE

Research conducted in real-life conditions among a Spanish population without diabetes shows why the interpretation of CGM traces requires caution. Among individuals classified as normoglycemic based on fasting glycemia and glycated hemoglobin, 73% experienced at least one episode above the threshold for impaired glucose tolerance, and 5% had at least one value above the diabetes threshold. Furthermore, normoglycemic participants with episodes of hyperglycemia showed variability similar to that of people with prediabetes who had episodes of comparable intensity or duration [4].This does not refute the observation that, on average, prediabetes may present greater glycemic instability. However, it indicates that the distributions of values overlap: a single spike or a brief recording does not allow for the certain classification of a person's metabolic status. Differences may depend on diet, physical activity, sleep-wake rhythm, sensor accuracy, duration of monitoring, and the diagnostic criteria used.No directly conflicting evidence sufficiently relevant to the general direction of the association between worsening glucose tolerance and greater glycemic variability has been identified; this does not prove the absence of contrary results.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the study that is the subject of the Evidence Review from the independent publications used to evaluate the same narrative.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Cross-sectional with CGM	162 adults: normal tolerance, impaired glycemic regulation, newly diagnosed type 2 diabetes	Alterations in the glycemic profile detected even before diagnosed diabetes; complete comparative data not reported in available material	biologically consistent evidence	moderate
[1]	Cross-sectional with CGM and oral glucose tolerance test	220 adults across the spectrum from normal regulation to type 2 diabetes	All variability indices increase progressively; the oral disposition index decreases and correlates inversely with these indices	direct confirmation	moderate
[2]	Observational cross-sectional matched with CGM	36 adults, 18 matched prediabetes-normoglycemia pairs	Prediabetes associated with higher coefficient of variation, MAGE, mean glucose, and time above 180 mg/dL	direct confirmation	moderate
[3]	Observational cross-sectional cohort	851 participants from the Maastricht Study, 23% with type 2 diabetes	Standard deviation and coefficient of variation correlate positively with glycemic indices from the tolerance test	indirect confirmation	moderate
[4]	Real-life observational with CGM	Spanish adult population without diabetes, 1,521 complete CGM days	Some normoglycemic individuals show high spikes and variability similar to subjects with prediabetes with comparable episodes	discordant evidence	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The publication analyzed is consistent with how it is used in the book's paragraph: it describes glycemic variability in people with normal glucose tolerance, impaired glucose regulation, and newly diagnosed type 2 diabetes. Independent evidence moderately confirms that various oscillation indices tend to increase as glucose tolerance worsens and that this pattern is associated with reduced compensatory beta-cell function.

The most prudent message is that CGM can make dynamic aspects of metabolism visible that are not expressed by average glycemia alone. However, it is not proven that glycemic variability directly causes diabetes, nor that a single episode of hyperglycemia or hypoglycemia alone identifies a pathological condition. Larger longitudinal studies are needed to define the prognostic value of the different indices in people without diabetes.

Aggiornato al 17/11/2026. Questo contenuto riflette una sintesi divulgativa delle evidenze scientifiche al momento della pubblicazione e non sostituisce il parere medico.

10. TRANSPARENCY AND SCIENTIFIC RESPONSIBILITY

Artificial Intelligence was used solely as a tool for editorial and documentary support. All content, interpretations, bibliographic citations and conclusions have been verified, reviewed and approved by the author, who assumes full scientific responsibility for them.

The manuscript was also subjected to independent peer review prior to publication.

To ensure the greatest transparency, the complete history of the article, including the dates of submission, revision, acceptance and publication, as well as information on the peer review process, is available on the dedicated Article History page.

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