LIFE Science Hub
JOURNAL OF SCIENCE
EXPANDING KNOWLEDGE ABOUT NUTRITION AND HEALTH

ORIGINAL RESEARCH

Three glycemic measures and mortality risk: a prospective cohort study

M. Moscati[1]

1 Italy

1. ABSTRACT

The study analyzed compared fasting glycemia, glycated hemoglobin (HbA1c, an indicator of average glucose exposure over the last few months), and plasma glucose two hours after an oral glucose tolerance test (2hPG). In 14,013 US adults not treated with antidiabetic drugs, followed for a median of 9.8 years, elevated values of all three markers were associated with higher total and cardiovascular mortality when evaluated separately.The publication contributes to the narrative of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi, according to which the glucose tolerance test can reveal alterations not fully visible while fasting. Independent studies in European, elderly US, and Chinese cohorts confirm that a higher 2hPG is associated with an increased risk of mortality and cardiovascular events, even when considering other glycemic markers. However, this is observational prognostic evidence: the test identifies a risk profile, but it does not prove that reducing post-load glycemia in isolation reduces mortality.

ONLINE ARTICLE

ARTICLE INFORMATION

Published: November 15, 2026
Updated: November 15, 2026

DOI 10.5281/zenodo.24256176

MISSION

LIFE Science Hub – Journal of Science was founded with the aim of making scientific knowledge accessible without giving up methodological rigour, quality of sources and authoritativeness of content. The journal promotes the dissemination of knowledge in the health, nutrition, medical and longevity sciences, building a bridge between the world of research and society.

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 three tests used to identify diabetes or elevated glycemia—fasting glycemia, HbA1c, and glycemia measured two hours after 75 grams of glucose—provided independent prognostic information on all-cause and cardiovascular mortality. The hypothesis was that each marker might maintain, or lose, its ability to signal risk when considered alongside the other two.The relevance to the book's section is precise. The publication subject to the Evidence Review does not directly measure insulin secretion, muscle sensitivity to insulin, or glucose production by the liver. Instead, it documents the prognostic segment of the narrative: elevated glycemia two hours after a glucose load may contain information about future risk that is not entirely overlapping with that of fasting glycemia and HbA1c.As a prospective cohort study, it can show that a glycemic value precedes and is associated with an outcome over time. It cannot establish that post-load glycemia is the cause of mortality, nor can it demonstrate that the test is necessarily the best examination for every person or in every clinical context.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The authors identified 14,013 U.S. adults from NHANES III and NHANES 2005-2016 who were not taking antidiabetic medication at the time of recruitment. NHANES is a program of health surveys of the U.S. population. The design was a prospective cohort: participants were classified based on initial examinations and then followed over time to track deaths.Elevated glycemia was defined according to the 2023 American Diabetes Association standards: 2hPG equal to or greater than 11.1 mmol/L, fasting glycemia equal to or greater than 7.0 mmol/L, or HbA1c equal to or greater than 6.5%. The authors adopted two strategies. In the first, they included all three glycemic markers simultaneously in the statistical models; in the second, they compared people with an isolated increase in only one of the three markers with people who were normal for all three.Multivariate analyses accounted for the main non-glycemic risk factors. The available material does not report the complete list of adjustment variables, detailed exclusion criteria, methods for ascertaining deaths, the number of participants in each glycemic group, or the technical details of the statistical analyses.

4. RESULTS

During a median follow-up of 9.8 years, 2,869 participants died; 960 deaths were attributed to cardiovascular causes. Considered one at a time, elevated 2hPG, elevated fasting glycemia, and elevated HbA1c were all linked to higher total and cardiovascular mortality. The adjusted hazard ratios—that is, the ratios between the rates at which death occurs in the compared groups—ranged from 1.32 to 1.55. In practical terms, these values correspond to a higher frequency of death in the groups with elevated glycemia compared to the reference groups.The available abstract also reports that the authors evaluated the three tests in the same model and analyzed isolated elevations. However, the provided abstract text cuts off before reporting the complete estimates for these analyses. Therefore, the specific hazard ratios, confidence intervals, P-values, and the exact details of the simultaneous comparison between 2hPG, fasting glycemia, and HbA1c are not reported in the available material.The central data point relevant to the book is therefore that the two-hour post-load glycemia was studied not only as a diagnostic criterion but as a possible prognostic indicator distinct from the other two main glycemic markers. However, the accessible data do not allow for a direct, precise quantification of how much its independent value was greater compared to the other tests.

5. INTERPRETATION

In simple terms, fasting glycemia provides a snapshot of the body in a relatively stable condition, while 2hPG observes how much glucose remains in the blood after a standardized challenge. If the value remains high after two hours, the body has managed the glucose load less effectively.This response depends on several functions simultaneously: the beta cells of the pancreas must release insulin adequately; muscles and adipose tissue must respond to the insulin signal and remove glucose from the blood; the liver must reduce its own glucose production. The test does not measure each of these steps separately, but the final glycemia can reflect the overall result of their interaction.The

transition documented by the analyzed study is therefore prognostic: an elevated 2hPG identifies individuals with higher observed mortality over time. The pathophysiological interpretation proposed in the book is biologically plausible, but it is not directly proven by this cohort because insulin levels, measures of beta-cell function, or direct insulin sensitivity tests were not reported.

6. INDEPENDENT CONFIRMING EVIDENCE

Historical confirmation comes from the European DECODE project, which brought together 13 prospective cohorts with 25,364 adults aged 30 or older and a mean follow-up of 7.3 years. Within the same fasting glycemia categories, mortality increased as the two-hour glycemia rose. Conversely, in the categories of impaired glucose tolerance or diabetes defined by 2hPG, no similar gradual increase in mortality emerged with increasing fasting glycemia. For impaired glucose tolerance, the hazard ratio for mortality was 1.51 in men and 1.60 in women compared to their respective groups with normal values. This directly supports the book's assertion that the OGTT can add prognostic information compared to the baseline value alone [1].A second confirmation comes from the Cardiovascular Health Study, a prospective cohort of 2,394 elderly Americans without treated diabetes, with a mean age of 78 and a median follow-up of 11.2 years. After adjustment for clinical factors and fasting glycemia, each one-standard-deviation increase in 2hPG remained associated with a 12% increase in all-cause mortality; hazard ratio 1.12, 95% confidence interval from 1.04 to 1.19. In the same model, the association of fasting glycemia with mortality did not remain statistically significant. The study confirms the direction of the association, but it primarily concerns elderly individuals and does not demonstrate a causal effect of post-load glycemia [2].In a large Chinese cohort of 193,846 adults aged at least 40, followed for up to five years, untreated diabetes defined by a 2hPG of 200 mg/dL or higher was associated with higher all-cause mortality, with a hazard ratio of 1.57 and a 95% confidence interval from 1.41 to 1.76. The corresponding associations with diabetes defined by fasting glycemia and HbA1c were 1.37 and 1.33, respectively. Furthermore, 2hPG remained associated with outcomes in models that also included the other two markers and statistically improved the model's predictive capacity. This extends the confirmation to a population very different from the American one, while maintaining the inherent limitations of an observational study [3].

7. CONFLICTING EVIDENCE

No directly conflicting evidence of sufficient relevance has been identified; this does not prove the absence of contrary results.However, there are limitations that reduce the possibility of considering 2hPG universally superior. The three markers do not represent exactly the same biological phenomenon, and their utility may vary with age, population origin, prevalence of undiagnosed diabetes, pre-analytical conditions, and clinical objective. Even when 2hPG is more strongly associated with mortality, the increase in absolute predictive capacity compared to already available clinical models may be modest. Furthermore, a prognostic association does not prove that selectively intervening on post-load glycemia changes cardiovascular outcomes or survival.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the publication subject to the review from independent research that confirms the specific narrative of the book's paragraph.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Prospective cohort	14,013 US adults not on antidiabetic medication	Elevated 2hPG, fasting glycemia, and HbA1c were associated with higher mortality when assessed separately; complete estimates from simultaneous models are not available in the provided abstract.	biologically consistent evidence	moderate
[1]	Joint analysis of prospective cohorts	25,364 European adults, 13 cohorts	Mortality increased with 2hPG within fasting glycemia categories; fasting alone did not fully identify risk.	direct confirmation	high
[2]	Prospective cohort	2,394 US elderly without treated diabetes	Higher 2hPG remained associated with increased mortality and cardiovascular disease after adjustment for fasting glycemia.	direct confirmation	moderate
[3]	Prospective cohort	193,846 Chinese adults aged 40 or older	Diabetes defined by 2hPG was associated with higher mortality; 2hPG added information to models with fasting glycemia and HbA1c.	direct confirmation	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The analyzed publication pertinently supports the use of 2hPG in the book's section as a prognostic indicator of the body's response to a glucose load. Independent evidence confirms quite well that higher post-load glycemia is associated with increased mortality and higher cardiovascular risk, often beyond the information provided by fasting glycemia alone.It is, however, necessary to distinguish this data from a complete explanation of the mechanism. 2hPG is consistent with integrated alterations in insulin secretion, insulin sensitivity, and hepatic glucose regulation, but the studies evaluated here do not directly measure all these processes. The prognostic value is well-supported; the causal implication and the choice of the most appropriate test for the individual patient require clinical evaluation and further interventional confirmation.

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.

11. RIFERIMENTI BIBLIOGRAFICI

[1] **Glucose tolerance and mortality: comparison of WHO and American Diabetic Association diagnostic criteria**
1999
The Lancet
DOI: https://doi.org/10.1016/S0140-6736(98)12131-1

[2] **Relations of Postload and Fasting Glucose With Incident Cardiovascular Disease and Mortality Late in Life: The Cardiovascular Health Study**
Brutsaert et al., 2016
The Journals of Gerontology Series A: Biological Sciences and Medical Sciences
DOI: https://doi.org/10.1093/gerona/glv106

[3] **Predictive Value of Fasting Glucose, Postload Glucose, and Hemoglobin A1c on Risk of Diabetes and Complications in Chinese Adults**
Lu et al., 2019
Diabetes Care
DOI: https://doi.org/10.2337/dc18-1390