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

ORIGINAL RESEARCH

The effect of fasting glycemia variation on the risk of myocardial infarction, stroke, and all-cause mortality: a national cohort study - Evidence review

D.ssa M. Mondini[1]

1 Biologist, Italy

1. ABSTRACT

The analyzed study evaluated whether changes in fasting glycemia over a two-year period were associated with myocardial infarction, stroke, and mortality in Korean adults initially free of diabetes and cardiovascular disease. In over 260,000 individuals followed for approximately eight years, the transition from normal values or impaired fasting glycemia to values consistent with diabetes was associated with an increase in specific cardiovascular outcomes and total mortality.In the narrative of “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi, this research contributes to the idea that fasting glycemia has a dynamic significance: it is not just the value measured at a single point in time that matters, but also its evolution. Independent studies support the notion that higher or increasing glycemic trajectories may provide additional prognostic information; however, effects vary across populations and definitions of prediabetes. The evidence is therefore moderately convergent, but observational and does not prove that the increase in glycemia is, by itself, the cause of the events.

ONLINE ARTICLE

ARTICLE INFORMATION

Published: November 12, 2026
Updated: November 12, 2026

DOI 10.5281/zenodo.24159464

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 a change in fasting glycemia, detected in two check-ups spaced about two years apart, was associated with the future risk of myocardial infarction, stroke, and all-cause mortality in people without known diabetes. The hypothesis was that the progression toward higher glycemic values could identify a different risk profile compared to the persistence of stable values.The relevance to section 2.4 of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi is precise: the study does not evaluate a single glycemic measurement as an isolated snapshot, but compares categories of change over time. It therefore documents the segment of the narrative according to which the trend of fasting glycemia can have additional prognostic value.Since this is a retrospective cohort, meaning an analysis of previously collected data without assigning an intervention to the participants, the study can show associations over time. However, it cannot establish that the increase in glycemia directly caused myocardial infarction, stroke, or death, nor can it demonstrate that reducing glycemia necessarily modifies such outcomes.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

Researchers used the Korean National Health Insurance Service-Health Screening Cohort database. They selected 334,377 adults with at least two screening visits, conducted between 2002-2003 and 2004-2005, with fasting glycemia measurements. Individuals with previously diagnosed type 2 diabetes, initial glycemia equal to or greater than 126 mg/dL, previous heart attack or stroke, deaths before the start of follow-up, glycemia levels below 50 mg/dL, and missing gender data were excluded. The final population included 260,487 participants: 149,913 men and 110,574 women.At the first visit, glycemia was classified as normal, below 100 mg/dL, or as impaired fasting glycemia, between 100.0 and 125.9 mg/dL. At the second visit, a third category was added, defined as diabetic fasting glycemia, equal to or greater than 126 mg/dL. Six trajectories were thus created: normal-normal, normal-impaired, normal-diabetic, impaired-normal, impaired-impaired, and impaired-diabetic.From January 1, 2006, to December 31, 2013, hospitalizations of at least two days for myocardial infarction or stroke and deaths from any cause were recorded. The relative risk over time was estimated using Cox models, which produce a hazard ratio or HR, representing the ratio between the rates at which an event occurs in the compared groups. The analyses were adjusted for age, sex, socioeconomic status, body mass index, smoking, alcohol consumption, physical activity, blood pressure, total cholesterol, comorbidities, and initial glycemia. The mean follow-up was eight years; sensitivity analyses excluded events that occurred in the first one or two years.

4. RESULTS

Over 2,042,960 person-years of observation, there were 1,318 myocardial infarctions, equal to 0.5% of the cohort, 8,144 strokes, equal to 3.13%, and 10,065 deaths from all causes, equal to 3.86%. People with impaired glycemia at the first check-up tended to be older on average, more frequently men, and had higher body mass index, blood pressure, and cholesterol compared to those with normal glycemia.Among participants who were initially normoglycemic, the transition to diabetic levels within two years was associated with an increased risk of stroke compared to remaining in the normal range: HR 1.19, 95% confidence interval from 1.02 to 1.38. In practical terms, after statistical adjustments, the stroke incidence rate was estimated to be 19% higher in that group. The transition from normal to impaired glycemia was associated with higher all-cause mortality, with an HR of 1.08 and a confidence interval from 1.02 to 1.14. The direct transition from normal to diabetic values was associated with a larger increase in total mortality, with a confidence interval from 1.39 to 1.75.Among those who already had impaired fasting glycemia, the progression to diabetic values was associated with an increased risk of myocardial infarction, with a confidence interval from 1.20 to 2.27, and total mortality, with a confidence interval from 1.02 to 1.33, compared to the persistence of impaired glycemia. Not all transitions were associated with all outcomes: for example, the return from impaired glycemia to normal values did not show a statistically significant reduction in cardiovascular events in the available data.In the subgroups, the association between the progression from impaired glycemia to diabetic values and

myocardial infarction was more evident in adults aged 65 or older, in men, and in participants with a body mass index of less than 25 kg/m². For total mortality, the associations tended to be more marked in those over 50, in men, and in subjects with a body mass index equal to or greater than 25 kg/m² according to Asian criteria. These analyses describe differences between groups but do not prove that sex, age, or weight are the cause of the observed differences.

5. INTERPRETATION

The main takeaway is that two people with similar glycemia at a single point in time may not have the same prognostic profile if one remains stable while the other increases rapidly. In the analyzed sample, the transition toward the diabetic range was associated with the clearest and most significant increases in risk. This supports the common understanding that fasting glycemia should be viewed as a trend, not just as an isolated number.The specific segment documented by the publication is: increase in fasting glycemia over time higher subsequent frequency of certain cardiovascular events and/or death. It does not demonstrate the entire biological chain linking hyperglycemia to vascular damage. The authors point to possible mechanisms, such as endothelial dysfunction—that is, impairment of the inner lining of blood vessels—oxidative stress, and increased arterial stiffness. These mechanisms are biologically plausible but were not measured directly in the study.It is also necessary to distinguish between prognosis and prediction. The variation in glycemia showed prognostic value, meaning an association with the likely future course within the cohort. It was not verified whether it predicts the response to a specific treatment. The presence of concomitant factors, such as obesity, high blood pressure, smoking, diet, therapies, and diabetes developed during the follow-up, may explain the residual associations at least in part.

6. INDEPENDENT SUPPORTING EVIDENCE

Confirmation that aligns closely with the book's narrative comes from a Chinese prospective cohort of 68,297 adults without diabetes, heart attack, stroke, or cancer at baseline. After three fasting glycemia measurements over four years, different trajectories were identified. Compared to a moderate and stable glycemia, a high and stable trajectory was associated with an increased risk of myocardial infarction, with a confidence interval of 1.04 to 2.26. Conversely, an initially high but decreasing trajectory was associated with a lower risk of heart attack, with a confidence interval of 0.38 to 0.98. The authors also report that the mean glycemia over time and the rate of increase, rather than the baseline value alone, predicted future risk of heart attack [1]. This is direct confirmation of the concept that the temporal profile adds information compared to a single measurement, although it remains an observational study.A meta-analysis of 53 prospective cohorts, totaling 1,611,339 participants, broadens the picture regarding the prognostic significance of impaired glycemia. Compared to normoglycemia, impaired fasting glycemia according to American Diabetes Association criteria was associated with a 13% increased risk of composite cardiovascular events, a 6% increased risk of stroke, and a 13% increased risk of all-cause mortality. Using the higher World Health Organization threshold, the estimated increases were 26%, 17%, and 13%, respectively [2]. This synthesis does not study the rate of increase in glycemia, but it confirms the intermediate step of the narrative: fasting glycemia values outside the normal range are associated, on average, with a less favorable cardiovascular and general prognosis.A further independent analysis pooled 14,378 adults from three population cohorts—ARIC, MESA, and the Tehran Lipid and Glucose Study—without diabetes at baseline. After approximately three years, fasting glycemia transitions were linked to total, cardiovascular, and cancer mortality over a median follow-up of 18 years. In women, progression from impaired glycemia to diabetes was associated with higher cardiovascular mortality, with a confidence interval of 1.42 to 3.44; in men, the significant increase in total mortality emerged primarily with the conversion to diabetes [3]. The result confirms the general direction observed in the original study, but also shows that the association is not uniform: sex, diagnostic thresholds, and type of outcome modify the picture.

7. CONFLICTING EVIDENCE

An important note of caution comes from the British Whitehall II cohort, which followed 5,427 people without diabetes, aged between 50 and 79, for a

median of 11.5 years. Before statistical adjustment, prediabetes defined by fasting glycemia was associated with a higher frequency of cardiovascular events or death. After adjusting for blood pressure, lipids, smoking, cardiovascular history, and other factors, prediabetes defined by fasting glycemia alone was not associated with a statistically significant excess of events; the authors concluded that most of the excess risk was explained by the accumulation of other cardiometabolic factors [4].This evidence does not directly contradict the result regarding glycemic variations in the original study, as it primarily evaluates definitions of prediabetes rather than a rapid transition toward diabetic values. However, it is directly relevant to the message of this paragraph: impaired fasting glycemia, or an increase in it, should not be interpreted as an isolated and invariable cause of cardiovascular events. Its prognostic significance depends on the clinical context, the measures used, and the overall set of risk factors.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the original study from independent publications. The directions of the evidence describe the relationship with the specific narrative of the book's chapter, not proof of causality.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	National retrospective cohort	260,487 Korean adults without diabetes or cardiovascular disease at baseline	Progression to diabetic glycemia was associated with an increase in stroke, heart attack, or mortality, depending on the initial category	biologically consistent evidence	moderate
[1]	Prospective cohort	68,297 Chinese adults without diabetes, with three glycemic measurements	Stable high trajectories increased the risk of heart attack; decreasing trajectories reduced it compared to a stable moderate trajectory	direct confirmation	moderate
[2]	Systematic review and meta-analysis	53 prospective cohorts, 1,611,339 participants	Prediabetes defined by impaired fasting glycemia was associated with higher cardiovascular and mortality risks	indirect confirmation	high
[3]	Pooled analysis of prospective cohorts	14,378 adults from three population cohorts	Progression from impaired glycemia to diabetes was associated with higher mortality, especially cardiovascular in women	direct confirmation	moderate

[4]	Prospective cohort	5,427 British adults without diabetes, 50-79 years old	After adjustment, prediabetes defined by fasting glycemia did not show a significant excess of events or death	discordant evidence	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The study analyzed pertinently supports the book's claim that fasting glycemia should also be interpreted over time. In the large Korean cohort, the worsening toward diabetic values was associated with a selective increase in heart attack, stroke, and mortality, while the transition from normoglycemia to impaired glycemia was associated with higher all-cause mortality.

Independent evidence makes this narrative moderately supported: persistent or increasing glycemic trajectories have been associated with unfavorable cardiovascular outcomes, and prediabetes is associated on average with a higher cardiovascular risk. However, important limitations remain: association does not mean causality, effects differ between populations and sex, and elevated fasting glycemia often coexists with other risk factors that contribute to the prognosis.

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] **Longitudinal Change in Fasting Blood Glucose and Myocardial Infarction Risk in a Population Without Diabetes**
Jin et al., 2017
Diabetes Care
DOI: https://doi.org/10.2337/dc17-0610

[2] **Association between prediabetes and risk of cardiovascular disease and all cause mortality: systematic review and meta-analysis**
Huang et al., 2016
BMJ
DOI: https://doi.org/10.1136/bmj.i5953

[3] **Changes in Fasting plasma glucose status and risk of mortality events in individuals without diabetes over two decades of Follow-up: a pooled cohort analysis**
Kohansal et al., 2022
Cardiovascular Diabetology
DOI: https://doi.org/10.1186/s12933-022-01709-z

[4] **Risk of Cardiovascular Disease and Death in Individuals With Prediabetes Defined by Different Criteria: The Whitehall II Study**
Vistisen et al., 2018
Diabetes Care
DOI: https://doi.org/10.2337/dc17-2530