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ORIGINAL RESEARCH

Glucose levels are associated with cardiovascular disease and death in an international cohort of normoglycemic and dysglycemic men and women: The EpiDREAM cohort study - Evidence review

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1. ABSTRACT

The EpiDREAM study evaluated whether different glycemic levels are associated with future cardiovascular events and deaths in an international cohort. It included 18,990 men and women from 21 countries, classified by glycemia and oral glucose tolerance test. During a median follow-up of 3.5 years, the incidence of cardiovascular events or death was found to be progressively higher from normoglycemia to impaired glycemia, up to newly diagnosed type 2 diabetes.In the narrative of “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi, the study contributes to the concept that cardiovascular and prognostic risk increases along a glycemic continuum. A meta-analysis of prospective cohorts confirms an average increase in risk in people with impaired fasting glycemia or impaired glucose tolerance. However, an independent cohort indicates that part of the association may depend on other cardiometabolic factors that tend to cluster together with elevated glycemia. The evidence therefore supports a prognostic association, but does not prove that small increases in glycemia are the sole cause of the events.

ONLINE ARTICLE

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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 blood glucose concentration, measured while fasting and after an oral glucose tolerance test, was associated with the subsequent onset of cardiovascular disease or death. The hypothesis was that the risk does not increase only after a formal diagnosis of diabetes, but grows even in people with impaired fasting glycemia or impaired glucose tolerance.The relevance to the book's section is specific: the research documents an observed increase in the frequency of cardiovascular events or deaths as one moves from normoglycemia to dysglycemia—that is, an alteration in glucose regulation—and subsequently to type 2 diabetes diagnosed during screening. This is the argumentative passage regarding the prognostic continuum of glycemia. The study is prospective and observational: it can detect associations over time, but it cannot establish that the increase in glycemia, by itself, is the cause of the events or death.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The study used an international prospective cohort consisting of 18,990 men and women selected for screening for entry into the DREAM clinical trial across 21 countries. At baseline, clinical and biochemical information was collected, and an oral glucose tolerance test (OGTT)—a test that measures the body's response to a standardized amount of glucose—was performed.After screening, 8,000 participants were classified as normoglycemic, 8,427 as having impaired fasting glucose or impaired glucose tolerance, and 2,563 as individuals with newly identified type 2 diabetes. Participants were followed for a median of 3.5 years, with an interquartile range of 3.0 to 4.0 years. The outcomes considered included coronary heart disease, stroke, hospitalization for congestive heart failure, and death.The available material consists only of the abstract. Detailed inclusion and exclusion criteria, event validation procedures, variables included in the statistical models, sensitivity analyses, and complete results adjusted for potential confounding factors are not reported in the available material.

4. RESULTS

During the follow-up, a total of 491 events occurred: 282 cases of coronary heart disease, 54 strokes, 19 hospitalizations for heart failure, and 164 deaths. In the entire cohort, the annualized rate of cardiovascular events or death was 0.79 per 100 person-years. In simple terms, this corresponds to less than one event for every 100 people followed for one year, but the value was not uniform across the glycemic groups.The rate was 0.51 per 100 person-years in normoglycemic participants, increased to 0.92 in people with impaired fasting glycemia and/or impaired glucose tolerance, and reached 1.27 in participants with newly diagnosed type 2 diabetes. The trend of the result is therefore progressive: as the severity of the glycemic alteration increased, so did the incidence of cardiovascular events or deaths.The section from "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi states that every 1 mmol/L increase in fasting glycemia, equivalent to approximately 18 mg/dL, was associated with a 17% increase in the risk of cardiovascular events or death. This specific value is not reported in the text of the provided abstract; therefore, the corresponding confidence interval, P-value, and degree of statistical adjustment of the model cannot be verified in the available material.

5. INTERPRETATION

The most immediate meaning is that, in this population, individuals with more impaired glycemia levels experienced cardiovascular events or death more frequently during the observed period. The result is consistent with the concept of a gradient: the transition from normoglycemia to conditions of impaired glucose regulation does not necessarily coincide with a sudden jump in risk.The segment directly documented by the study is: progressively more marked glycemic impairment higher observed incidence of cardiovascular event or death. It does not, however, prove that a small increase in fasting glycemia, isolated from other risk factors, directly causes cardiovascular damage. Blood pressure, adiposity, blood lipids, smoking, inflammation, and insulin resistance can both accompany the increase in glycemia and contribute to the same outcomes.This distinction is important for interpreting the reference

in the book. The publication analyzed supports the prognostic claim that risk increases across increasingly impaired glycemic categories. The precise quantification of 17% per 1 mmol/L, however, cannot be critically evaluated in its statistical details because the full text is not available in the provided material.

6. INDEPENDENT SUPPORTING EVIDENCE

A meta-analysis of 53 prospective studies, involving 1,611,339 participants and a median follow-up of 9.5 years, examined the risk associated with prediabetes—that is, glycemic values higher than the diagnostic norm but below the threshold for diabetes. Compared to normoglycemia, impaired fasting glucose according to the American Diabetes Association threshold of 5.6–6.9 mmol/L was associated with a 13% increased risk of composite cardiovascular disease and a 13% increase in all-cause mortality. With the higher World Health Organization threshold of 6.1–6.9 mmol/L, the increases were 26% and 13%, respectively. Impaired glucose tolerance showed even stronger associations. This summary independently confirms the passage in the book stating that intermediate glycemic alterations are associated with less favorable cardiovascular and prognostic outcomes [1].The European DECODE collaboration followed 29,714 adults from 22 cohorts for 11 years and evaluated the trend of glycemia in relation to mortality. For cardiovascular mortality, glucose measured two hours after an oral load showed a gradually increasing relationship; for fasting glycemia, however, the authors observed a J-shaped trend, with higher risk at both very low values and in diabetes. This study confirms the part of the chain regarding the fact that the relationship between glucose and prognosis is not necessarily governed by a single diagnostic threshold, and reinforces the utility of the post-load test in identifying part of the risk [2].Overall, this evidence is independent of the EpiDREAM cohort because it derives from other populations and different combinations of studies. However, it remains largely observational evidence: it shows that exposure and outcome occur together over time, not that intervening on glycemia alone automatically reduces cardiovascular risk.

7. CONFLICTING EVIDENCE

An independent cohort, Whitehall II, followed 5,427 people without diabetes, aged between 50 and 79, for a median of 11.5 years. Individuals with prediabetes, defined by fasting glycemia or glycated hemoglobin, initially showed higher rates of cardiovascular events or death compared to normoglycemic individuals. However, after adjusting for previous cardiovascular disease, smoking, cholesterol, blood pressure, and antihypertensive therapy, the excess risk was no longer statistically significant. For fasting glycemia alone of 6.1-6.9 mmol/L, the fully adjusted hazard ratio was 1.00, with a confidence interval of 0.79-1.26 [3].This result does not invalidate the association observed in the original study or that of the meta-analysis, but it defines its interpretive limit. Part of the risk attributed to elevated glycemic values may reflect the simultaneous presence of other cardiometabolic factors. Furthermore, the strength of the association may vary according to age, the population studied, the method used to define prediabetes, and whether fasting glycemia, post-load glycemia, or glycated hemoglobin is measured. No directly conflicting evidence sufficiently relevant to the increase in incidence observed across glycemic categories in the original study has been identified; this does not prove the absence of contrary results.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the publication under review from independent research that confirms or defines the book's narrative.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	International prospective cohort	18,990 men and women in 21 countries; median follow-up 3.5 years	The rate of cardiovascular events or death increased from 0.51 to 0.92 and 1.27 per 100 person-years from normoglycemia to newly diagnosed diabetes.	biologically consistent evidence	moderate
[1]	Systematic review and meta-analysis of prospective cohorts	53 studies; 1,611,339 participants from the general population	Prediabetes associated with increased cardiovascular disease and mortality compared to normoglycemia.	direct confirmation	high
[2]	Multicenter prospective cohort	29,714 adults from 22 European cohorts; 11-year follow-up	Post-load glycemia showed a gradual increase in cardiovascular mortality risk; fasting glycemia showed a J-shaped trend.	indirect confirmation	moderate
[3]	Prospective cohort	5,427 adults without diabetes from the Whitehall II cohort; median follow-up 11.5 years	The excess of events or death in prediabetes became non-significant after adjustment for cardiometabolic factors.	discordant evidence	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The EpiDREAM study documents that, in the observed cohort, the rate of cardiovascular events or death increases when moving from normoglycemia to glycemic alterations and newly diagnosed diabetes. This association is moderately supported by meta-analysis and independent cohorts. The overall picture indicates an increasing prognostic risk in conditions of dysglycemia, but requires caution: it does not prove that small increases in glycemia are an independent cause of cardiovascular events, nor that glycemic control alone eliminates the risk.

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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