Association of glycated haemoglobin A1c levels with cardiovascular outcomes in the general population: results from the BiomarCaRE consortium

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Background: Glycated haemoglobin A1c (HbA1c) is used to monitor the quality of diabetes treatment; however, its role in predicting cardiovascular outcomes in the general population remains uncertain.

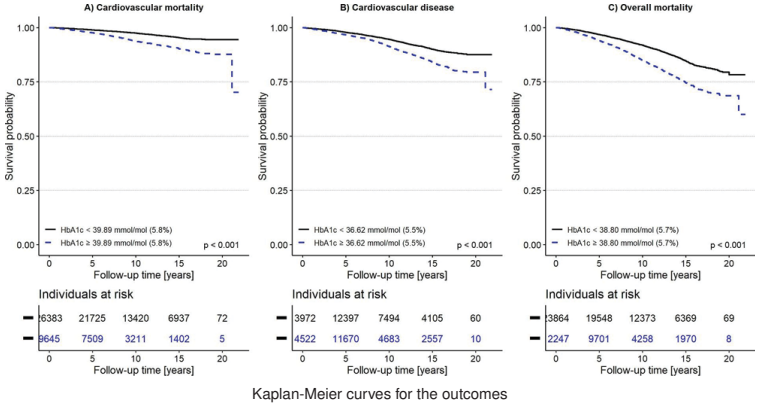
Purpose: The additional use of glycated haemoglobin A1c (HbA1c) as a biomarker might highlight subjects of the general population with an increased risk for cardiovascular outcomes with cardiovascular disease, cardiovascular mortality or overall-mortality.

Methods: Data from six prospective population-based cohort studies across Europe comprising 36,180 participants were analysed. HbA1c was evaluated in conjunction with classical cardiovascular risk factors (CVRFs) for association with cardiovascular mortality, cardiovascular diseases (CVD), and overall mortality in the study population, in non-diabetic (N=32,477), and diabetic participants (N=3,703).

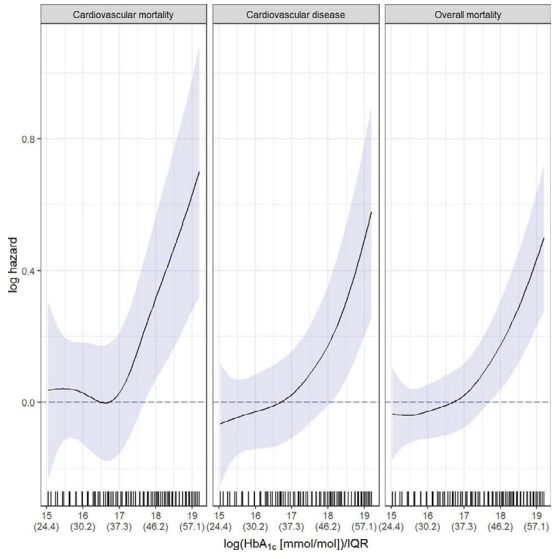
Results: Kaplan-Meier curves showed higher event rates with increasing continuous log-transformed HbA1c levels. Cox regression analysis revealed significant associations between HbA1c (in mmol/mol) log-transformed divided by interquartile range and the examined outcomes, with a hazard ratio (HR) of 1.12 (95% confidence interval (CI): 1.04–1.20, p=0.0019) for cardiovascular mortality, 1.10 (95% CI: 1.04–1.16, p<0.001) for CVD, and 1.09 (95% CI: 1.05–1.14, p<0.001) for overall mortality per one unit increase.

An increased risk of CVD was observed in subjects without diabetes with increased HbA1c levels (HR 1.09; 95% CI: 1.01–1.16, p=0.021). An HbA1c cut-off value of 39.89 mmol/mol (5.8%), 36.62 mmol/mol (5.5%), and 38.80 mmol/mol (5.7%) for cardiovascular mortality, CVD, and overall mortality, respectively, was determined for selecting individuals at an increased risk.

Conclusion: HbA1c was demonstrated to be an independent prognostic biomarker for all investigated outcomes in the general European population. An approximately linear relationship was observed between an increase of HbA1c levels and the outcomes. Elevated HbA1c levels were also associated with the outcomes in participants without diabetes (i.e. HbA1c levels <6.5% (<48mmol/mol) which underlines the importance of HbA1c levels in the overall population.



Kaplan-Meier curves for the outcomes



Penalised cubic splines HbA1c/time event