

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Time-saving screening for diabetes in patients with coronary artery disease A report from EUROASPIRE IV
<b>AUTHORS</b>	Gyberg, Viveca; De Bacquer, Dirk; Kotseva, Kornelia; De Backer, Guy; Schnell, Oliver; Tuomilehto, Jakko; Wood, David; Rydén, Lars

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Anne Pernille Ofstad Bærum Hospital Vestre Viken Hospital Trust, Norway  I am employed by Boehringer Ingelheim, but have no competing interests related to this work.
<b>REVIEW RETURNED</b>	17-Sep-2016

<b>GENERAL COMMENTS</b>	<p>The manuscript entitled «A time saving diabetes screening algorithm for coronary artery disease patients. Results from EUROASPIRE IV – a registry from the EuroObservational Research Programme of the European Society of Cardiology” confronts an important and challenging issue; how to improve the detection of type 2 diabetes with CAD. The authors create an algorithm by the use of a combination of fasting blood glucose and OGTT where the new and potentially time saving aspect is the measurement of 1 hour post load glucose value (instead of, or in 29% of the cases in addition to, the 2 hours measurement).</p> <p>The manuscript is clear and well written and the figures are relevant. My main objection to this study is that, in my opinion, in order to significantly improve the detection of T2DM in a cardiology department or out-patient clinic, an algorithm based solely on instant measures, and no OGTT, is needed. The current study provides however important results and may, if confirmed in the upcoming EUROASPIRE V as stated by the authors, be used as a mean to establish better routines in cardiology departments/out-patient clinics for diabetes screening of CAD patients. Of note is also the fact that only 25% of the study participants were women, creating a need for confirmatory studies including more females. Other than that, the limitations of the study are honestly described.</p> <p>Thus, I have only minor comments to the manuscript:</p> <ul style="list-style-type: none"><li>• Page 2 Line 53: the word “disease” is lacking</li><li>• Page 3 line 37: the word “validation” is lacking</li><li>• Please check the manuscript for comma errors (several places a comma is lacking, and some places there seems to be one comma too much).</li></ul>
-------------------------	---

<b>REVIEWER</b>	Dr Sangeet Srivastava The NorthCap University, Gurgaon, Haryana
-----------------	---

	India
<b>REVIEW RETURNED</b>	08-Oct-2016

<b>GENERAL COMMENTS</b>	<p>The research work is indeed important to address the timeline required for the sensitive cases of CAD patients before they go for surgery or other medical help.</p> <p>The paper clearly points out various assimilation of the shorter duration clinical tests to identify DM cases for CAD patients. However, the results, methods and definitions sections are heavily plagiarized (9%) from the earlier publication (ref no. 9). Ethically this is not appropriate and it is suggested to change the flavor of the discussion to remove such high level of plagiarism.</p> <p>Otherwise the work suggests a good alternative for the time consuming test (OGTT).</p> <p>Minor suggestions are</p> <ol style="list-style-type: none"> <li>1. IFG is not defined in the text earlier before introducing it in page 4 at line no. 51.</li> <li>2. The process to identify thresholds in ROC may be discussed a bit to make it more authentic.</li> </ol>
-------------------------	---

### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

We are grateful for the appreciation of our work.

Comment 1

Page 2 Line 53: the word “disease” is lacking

Reply

The text containing this missing word has been deleted in the revised manuscript.

Comment 2

Page 3 line 37: the word “validation” is lacking

Reply

The word validation has been added as suggested.

Comment 3

Please check the manuscript for comma errors (several places a comma is lacking, and some places there seems to be one comma too much).

Reply

The manuscript has been checked and some commas are deleted and some added. This has not been specifically marked.

Reviewer: 2

We are grateful for the appreciation expressed.

Comment 1

However, the results, methods and definitions sections are heavily plagiarized (9%) from the earlier publication (ref no. 9). Ethically this is not appropriate and it is suggested to change the flavour of the discussion to remove such high level of plagiarism.

Reply

The text has been shortened to avoid duplicate information leaving the readers to go the given reference for further details. The new text reads as follows:

### Study population

Details of EUROASPIRE IV, conducted in 24 European countries May 2012 to April 2013, have been presented elsewhere (9). This description relates to details of special interest for the present study. The study population comprises 951 patients (18 – 80 years) with stable CAD and free from diabetes in whom FPG, HbA1c, 1hPG, and 2hPG were determined.

### Methods

Methods for recording and definitions of educational level, current smoking, central obesity and blood pressure have been described elsewhere (9).

A standard OGTT was performed in the morning after  $\geq 10$  hours fasting. Plasma glucose was analysed locally with a point-of-care technique (Glucose 201+, HemoCue®, Ängelholm, Sweden). Values obtained with the HemoCue® instrument were in 69% within 5%, in 91% within 10%, and always within 14.3% of the ID GC-MS method (21). The values were converted from whole venous blood to plasma applying the formula by Carstensen et al (22) : plasma glucose =  $0.558 + 0.119 \times$  whole blood glucose, as used by the Euro Heart Survey on Diabetes and the Heart (23).

Although performing the amendment as asked we do not agree that it is unethical plagiarism to provide the readers with essential details of what was in fact done (patients, methods etc). By necessity such text must be very similar in the reports from EUROASPIRE IV. It would, at least in our minds, be worse to change the text with the risk to deviate from an objective report on material, methods and definitions.

We leave to a editorial decision if the new, abridged version is to be preferred or if we are allowed to be more precise i.e. if the original text can be preserved.

Otherwise the work suggests a good alternative for the time consuming test (OGTT).

### Minor comment 1.

IFG is not defined in the text earlier before introducing it in page 4 at line no. 51.

#### Reply

Impaired fasting glucose is written out with the abbreviation (IFG) put behind the first time it is mentioned (page 4). In the following the text "impaired fasting glucose" is revised to IFG.

### Minor comment 2.

The process to identify thresholds in ROC may be discussed a bit to make it more authentic.

#### Reply

We did already describe this process in the statistical section of the original manuscript. The text has been extended in the revised manuscript to make it clearer how it was done. The new text (last part of the statistics section) reads: The optimal threshold 1hPG was obtained according to the maximum Youden's J statistic (= Sensitivity + Specificity – 1), a measure to find an optimal balance between sensitivity and specificity of a diagnostic test.

It is our hope that the revised manuscript should be in a shape that can receive final approval for publication.