

## Supplementary Online Content

Mortensen MB, Gaur S, Frimmer A, et al. Association of age with the diagnostic value of coronary artery calcium score for ruling out coronary stenosis in symptomatic patients. *JAMA Cardiol*. Published online October 27, 2021. doi:10.1001/jamacardio.2021.4406

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This supplementary material has been provided by the authors to give readers additional information about their work.

**Table 1.** Number of Events and Event-Rates According to Coronary Artery Calcium Burden and Obstructive Coronary Artery Disease

|                                |                   | Number of events  |  | Event-rates per 1000 person-years |
|--------------------------------|-------------------|-------------------|--|-----------------------------------|
| CAC and obstructive CAD status | Prevalence, n (%) | MI + death, n (%) |  | MI + death (95%CI)                |
| <b>All</b>                     |                   |                   |  |                                   |
| CAC=0, no obstruc. CAD         | 12046 (51)        | 218 (28)          |  | 4.07 (3.56-4.64)                  |
| CAC=0, + obstruc. CAD          | 725 (3)           | 23 (3)            |  | 7.11 (4.72-10.69)                 |
| CAC>0, no obstruc. CAD         | 6670 (28)         | 270 (35)          |  | 9.53 (8.46-10.74)                 |
| CAC>0, + obstruc. CAD          | 4318 (18)         | 263 (34)          |  | 15.00 (13.27-16.90)               |
| <b>Age ≥ 60 years</b>          |                   |                   |  |                                   |
| CAC=0, no obstruc. CAD         | 3130 (32)         | 93 (18)           |  | 6.79 (5.54-8.32)                  |
| CAC=0, + obstruc. CAD          | 226 (2)           | 10 (2)            |  | 9.64 (5.19-17.91)                 |
| CAC>0, no obstruc. CAD         | 3821 (39)         | 210 (41)          |  | 13.17 (11.50-15.07)               |
| CAC>0, + obstruc. CAD          | 2701 (27)         | 199 (39)          |  | 18.27 (15.90-20.99)               |
| <b>Age &lt;60 years</b>        |                   |                   |  |                                   |
| CAC=0, no obstruc. CAD         | 8916 (64)         | 125 (48)          |  | 3.13 (2.63-3.73)                  |
| CAC=0, + obstruc. CAD          | 499 (4)           | 13 (5)            |  | 5.91 (3.43-10.18)                 |
| CAC>0, no obstruc. CAD         | 2849 (21)         | 60 (23)           |  | 4.84 (3.76-6.24)                  |
| CAC>0, + obstruc. CAD          | 1617 (12)         | 64 (24)           |  | 9.60 (7.52-12.27)                 |

CAC= coronary artery calcium; obstruc= obstructive; CAD= coronary artery disease, MI= myocardial infarction

**eTable 2.** Number of MI and MI Event-Rates According to Coronary Artery Calcium Burden and Obstructive Coronary Artery Disease

|                                |                   | Number of events |  | Event-rates per 1000 person-years |
|--------------------------------|-------------------|------------------|--|-----------------------------------|
| CAC and obstructive CAD status | Prevalence, n (%) | MI, n (%)        |  | MI (95%CI)                        |
| <b>All</b>                     |                   |                  |  |                                   |
| CAC=0, no obstruc. CAD         | 12046 (51)        | 60 (27)          |  | 1.12 (0.87-1.44)                  |
| CAC=0, + obstruc. CAD          | 725 (3)           | 11 (5)           |  | 3.41 (1.89-6.16)                  |
| CAC>0, no obstruc. CAD         | 6670 (28)         | 55 (24)          |  | 1.94 (1.49-2.52)                  |
| CAC>0, + obstruc. CAD          | 4318 (18)         | 97 (43)          |  | 5.58 (4.57-6.80)                  |
| <b>Age ≥ 60 years</b>          |                   |                  |  |                                   |
| CAC=0, no obstruc. CAD         | 3130 (32)         | 15 (13)          |  | 1.10 (0.66-1.82)                  |
| CAC=0, + obstruc. CAD          | 226 (2)           | 4 (3)            |  | 3.86 (1.44-10.27)                 |
| CAC>0, no obstruc. CAD         | 3821 (39)         | 38 (32)          |  | 2.38 (1.73-3.28)                  |
| CAC>0, + obstruc. CAD          | 2701 (27)         | 61 (52)          |  | 5.66 (4.40-7.28)                  |
| <b>Age &lt;60 years</b>        |                   |                  |  |                                   |
| CAC=0, no obstruc. CAD         | 8916 (64)         | 45 (43)          |  | 1.12 (0.84-1.51)                  |
| CAC=0, + obstruc. CAD          | 499 (4)           | 7 (7)            |  | 3.20 (1.52-6.71)                  |
| CAC>0, no obstruc. CAD         | 2849 (21)         | 17 (16)          |  | 1.37 (0.85-2.20)                  |
| CAC>0, + obstruc. CAD          | 1617 (12)         | 36 (34)          |  | 5.45 (3.92-7.55)                  |

CAC= coronary artery calcium; obstruc= obstructive; CAD= coronary artery disease, MI= myocardial infarction

**eTable 3.** Number of Deaths and Mortality-Rates According to Coronary Artery Calcium Burden and Obstructive Coronary Artery Disease

|                                |                   | Number of events | Event-rates per 1000 person-years |
|--------------------------------|-------------------|------------------|-----------------------------------|
| CAC and obstructive CAD status | Prevalence, n (%) | Deaths, n (%)    | Mortality (95%CI)                 |
| <b>All</b>                     |                   |                  |                                   |
| CAC=0, no obstruc. CAD         | 12046 (51)        | 158 (28)         | 2.94 (2.51-3.44)                  |
| CAC=0, + obstruc. CAD          | 725 (3)           | 12 (2)           | 3.68 (2.09-6.49)                  |
| CAC>0, no obstruc. CAD         | 6670 (28)         | 220 (39)         | 7.72 (6.76-8.81)                  |
| CAC>0, + obstruc. CAD          | 4318 (18)         | 172(31)          | 9.65 (8.30-11.20)                 |
| <b>Age ≥ 60 years</b>          |                   |                  |                                   |
| CAC=0, no obstruc. CAD         | 3130 (32)         | 78 (19)          | 5.67 (4.54-7.08)                  |
| CAC=0, + obstruc. CAD          | 226 (2)           | 6 (2)            | 5.77 (2.59-12.85)                 |
| CAC>0, no obstruc. CAD         | 3821 (39)         | 176 (44)         | 10.95 (9.45-12.70)                |
| CAC>0, + obstruc. CAD          | 2701 (27)         | 142 (35)         | 12.84 (10.88-15.13)               |
| <b>Age &lt;60 years</b>        |                   |                  |                                   |
| CAC=0, no obstruc. CAD         | 8916 (64)         | 80 (50)          | 2.00 (1.61-2.49)                  |
| CAC=0, + obstruc. CAD          | 499 (4)           | 6 (4)            | 2.71 (1.21-6.02)                  |
| CAC>0, no obstruc. CAD         | 2849 (21)         | 44 (28)          | 3.54 (2.64-4.75)                  |
| CAC>0, + obstruc. CAD          | 1617 (12)         | 30 (19)          | 4.43 (3.10-6.34)                  |

CAC= coronary artery calcium; obstruc= obstructive; CAD= coronary artery disease, MI= myocardial infarction

**eTable 4.** Post-CTA Statin and Aspirin Use in Those With CAC=0 Stratified by Absence or Presence of Obstructive CAD

| <b>Post-CTA medication</b> | <b>CAC=0 and no obstructive CAD</b> | <b>CAC=0 + obstructive CAD</b> |
|----------------------------|-------------------------------------|--------------------------------|
| <b>Statin use, %</b>       | 26                                  | 65                             |
| <b>Aspirin use, %</b>      | 14                                  | 48                             |

Statin and aspirin use was defined as at least one prescription post-CTA

**eTable 5.** Number of Events and Event-Rates According to Coronary Artery Calcium Burden and Obstructive Coronary Artery Disease (Also Including Events Within the First 90 Days)

|                                |                   | Number of events  |  | Event-rates per 1000 person-years |
|--------------------------------|-------------------|-------------------|--|-----------------------------------|
| CAC and obstructive CAD status | Prevalence, n (%) | MI + death, n (%) |  | MI + death (95%CI)                |
| <b>All</b>                     |                   |                   |  |                                   |
| CAC=0, no obstruc. CAD         | 12046 (51)        | 228 (28)          |  | 4.24 (3.73-4.83)                  |
| CAC=0, + obstruc. CAD          | 725 (3)           | 25 (3)            |  | 7.67 (5.19-11.36)                 |
| CAC>0, no obstruc. CAD         | 6670 (28)         | 275 (35)          |  | 9.65 (8.57-10.90)                 |
| CAC>0, + obstruc. CAD          | 4318 (18)         | 310 (34)          |  | 17.40 (15.55-19.43)               |
| <b>Age ≥ 60 years</b>          |                   |                   |  |                                   |
| CAC=0, no obstruc. CAD         | 3130 (32)         | 96 (18)           |  | 6.98 (5.72-8.53)                  |
| CAC=0, + obstruc. CAD          | 226 (2)           | 10 (2)            |  | 9.64 (5.19-17.91)                 |
| CAC>0, no obstruc. CAD         | 3821 (39)         | 214 (41)          |  | 13.32 (11.65-15.23)               |
| CAC>0, + obstruc. CAD          | 2701 (27)         | 231 (39)          |  | 20.88 (18.35-23.76)               |
| <b>Age &lt;60 years</b>        |                   |                   |  |                                   |
| CAC=0, no obstruc. CAD         | 8916 (64)         | 132 (48)          |  | 3.30 (2.78-3.92)                  |
| CAC=0, + obstruc. CAD          | 499 (4)           | 15 (5)            |  | 6.76 (4.07-11.21)                 |
| CAC>0, no obstruc. CAD         | 2849 (21)         | 61 (23)           |  | 4.91 (3.82-6.30)                  |
| CAC>0, + obstruc. CAD          | 1617 (12)         | 79 (24)           |  | 11.67 (9.36-14.55)                |

CAC= coronary artery calcium; obstruc= obstructive; CAD= coronary artery disease, MI= myocardial infarction

**eTable 6.** Hazard Ratios for Myocardial Infarction and Death During Follow-up According to the Presence of Obstructive CAD Among Patients With CAC=0 (Also Including Events Within the First 90 Days)

|                          |  | <b>MI and death</b> |                  |
|--------------------------|--|---------------------|------------------|
|                          |  | <b>Model 1</b>      | <b>Model 2</b>   |
| <b>CAC=0, all</b>        |  |                     |                  |
| No or non-obstruc. CAD   |  | Ref                 | Ref              |
| Obstruc. CAD             |  | 1.62 (1.08-2.45)    | 1.62 (1.06-2.44) |
| <b>CAC=0, age ≥60</b>    |  |                     |                  |
| No or non-obstruc. CAD   |  | Ref                 | Ref              |
| Obstruc. CAD             |  | 1.29 (0.67-2.48)    | 1.31 (0.68-2.53) |
| <b>CAC=0, age &lt;60</b> |  |                     |                  |
| No or non-obstruc. CAD   |  | Ref                 | Ref              |
| Obstruc. CAD             |  | 1.97 (1.15-3.38)    | 1.92 (1.12-3.29) |

CAC= coronary artery calcium; Obstruc = obstructive; CAD= Coronary artery disease;

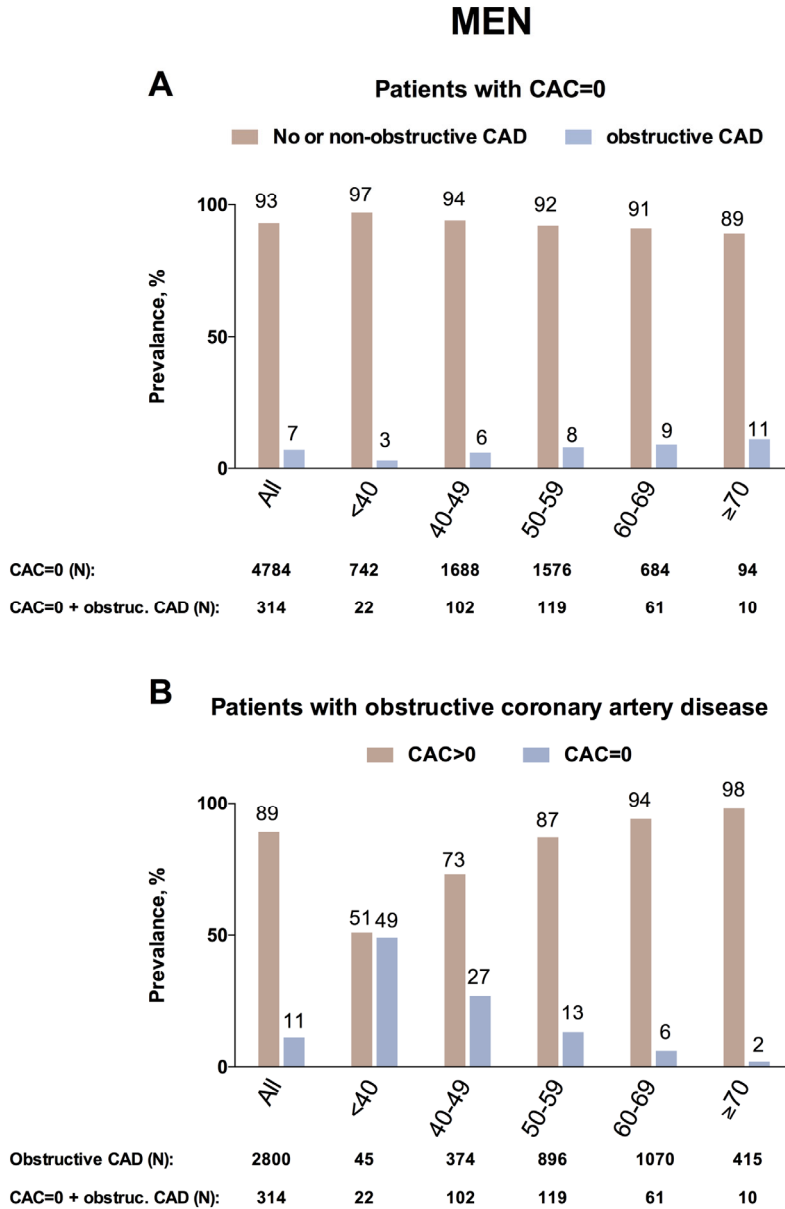
MI= myocardial infarction; Ref = reference

Model 1: Adjusted for age and sex

Model 2: Adjusted for age, sex, smoking status, diabetes and symptom characteristics

**eFigure 1.** Absence of Coronary Artery Calcification and Obstructive Coronary Artery Disease in Men

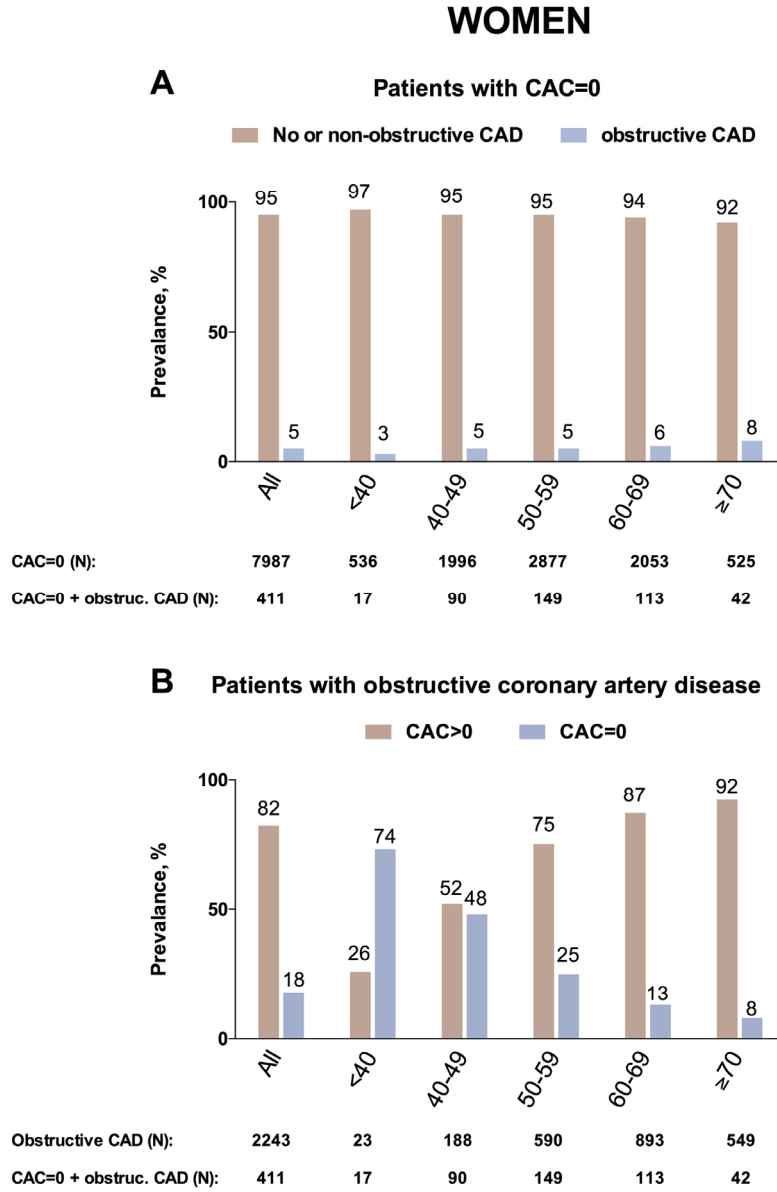
A: Prevalence of obstructive coronary artery disease among male patients with CAC=0. B: Prevalence of CAC=0 among male patients with obstructive CAD.





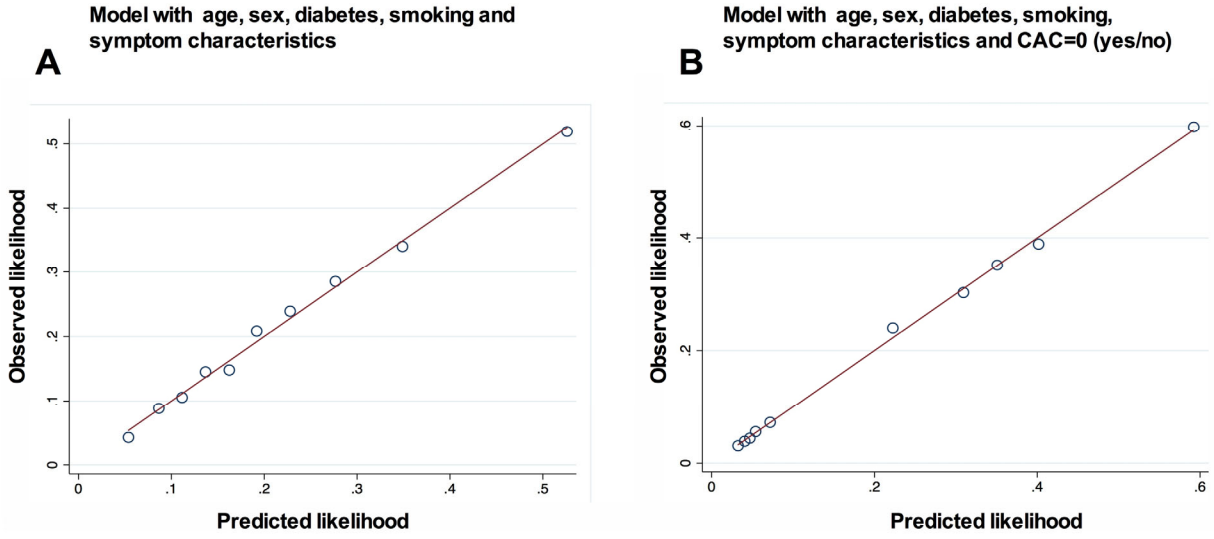
**eFigure 2.** Absence of Coronary Artery Calcification and Obstructive Coronary Artery Disease in Women

A: Prevalence of obstructive coronary artery disease among female patients with CAC=0. B: Prevalence of CAC=0 among female patients with obstructive CAD.



**eFigure 3. Calibration of Logistic Risk Prediction Models**

A: Model based on age, sex, smoking status, diabetes and symptom characteristics. B: Model based on the variables in A as well as information on presence or absence of CAC=0.



**eFigure 4.** Diagnostic Likelihood Ratio of a Coronary Artery Calcium Score of Zero for the Likelihood of Obstructive Coronary Artery Disease

The diagnostic likelihood ratio of CAC=0 shows how posttest risk changes when CAC=0 is considered together with a clinical model containing age, sex, smoking status, diabetes and symptom characteristics. The DLR of CAC=0 is not the same for all patients at a given age, but also depends on his/her distribution of risk factors. Each dot therefore represents the DLR of individual patients in the Western Denmark Heart Registry.

