



---

# Patient Inclusion

Paolo Ibes & Robert Röhle

Department of Radiology



# Inclusion Criteria

---

- 😊 Indication for ICA
- 😊 Age  $\geq$  30 years
- 😊 Stable chest discomfort
- 😊 Intermediate pretest likelihood of CAD:  
10-70%

→ **Inclusion possible!**

# What We Don't Want

---

## Unstable AP:


- Rest angina
  - >20min
  - New onset <1 week
- New onset angina
  - <2 months
  - At least CCS 3
- Increasing angina:
  - More frequent
  - Longer, lower threshold
  - At least CCS 3

# How to Estimate Pretest Likelihood of CAD?

## Pretest likelihood calculator:

- Individual patient data (n = 6,704)
- *Collaborative Meta-analysis of Cardiac CT (CoMe-CCT)*
- Predictors:
  - Age
  - Gender
  - Angina classification

Schultz et al. *Systematic Reviews* 2013, 2:13  
<http://www.systematicreviewsjournal.com/content/2/1/13>

 SYSTEMATIC REVIEWS


**PROTOCOL** Open Access

Individual patient data meta-analysis for the clinical assessment of coronary computed tomography angiography: protocol of the Collaborative Meta-Analysis of Cardiac CT (CoMe-CCT)

Georg M Schultz<sup>1</sup>, Peter Schlattmann<sup>2</sup>, Stephan Achenbach<sup>3</sup>, Matthew Budoff<sup>4</sup>, Mario J Garcia<sup>5</sup>, Robert Roehle<sup>1</sup>, Gianluca Pontone<sup>6</sup>, Willem Bob Meijboom<sup>7</sup>, Daniele Andrein<sup>8</sup>, Hatem Alkadhi<sup>9</sup>, Lily Honoris<sup>10</sup>, Nuno Bettencourt<sup>9</sup>, Jörg Hausleiter<sup>10</sup>, Sebastian Leschka<sup>11</sup>, Bernhard L Gerber<sup>12</sup>, Matthijs FL Meij<sup>13</sup>, Abbas Arjmand Shabestari<sup>14</sup>, Akira Sato<sup>15</sup>, Elke Zimmernann<sup>1</sup>, Uwe J Schoepf<sup>16</sup>, Axel Diederichsen<sup>17</sup>, David A Halon<sup>18</sup>, Vladimir Mendoza-Rodriguez<sup>19</sup>, Ashraf Hamdan<sup>20,21</sup>, Bjørn E Nørgaard<sup>22</sup>, Harald Brodoefel<sup>23</sup>, Kristian A Øvrehus<sup>24</sup>, Shona MM Jenkins<sup>25</sup>, Bjørn A Halvorsen<sup>26</sup>, Johannes Rixe<sup>27</sup>, Mehraj Sheikh<sup>28</sup>, Christoph Langer<sup>29,30</sup>, Eugenio Martuzelli<sup>31</sup>, Andrea Romagnoli<sup>32</sup>, Arthur JHA Scholte<sup>33</sup>, Roy P Maxcuz<sup>34</sup>, Geir R Ulmer<sup>35</sup>, Koen Nieman<sup>36</sup>, Hans Moolenaar<sup>37</sup>, Konstantin Nikolaou<sup>38</sup>, Jean-Claude Tardif<sup>39</sup>, Thomas RC Johnson<sup>40</sup>, Simone Muraglia<sup>40</sup>, Benjamin JW Chow<sup>40</sup>, David Mainz<sup>20,41</sup>, Michael Lauk<sup>42</sup> and Marc Dewey<sup>17</sup>\*

**Abstract**  
**Background:** Coronary computed tomography angiography has become the foremost noninvasive imaging modality of the coronary arteries and is used as an alternative to the reference standard, conventional coronary angiography, for direct visualization and detection of coronary artery stenoses in patients with suspected coronary artery disease. Nevertheless, there is considerable debate regarding the optimal target population to maximize clinical performance and patient benefit. The most obvious indication for noninvasive coronary computed tomography angiography in patients with suspected coronary artery disease would be to reliably exclude significant stenosis and, thus, avoid unnecessary invasive conventional coronary angiography. To do this, a test should have, at clinically appropriate pretest likelihoods, minimal false-negative outcomes resulting in a high negative predictive value. However, little is known about the influence of patient characteristics on the clinical predictive values of coronary computed tomography angiography. Previous regular systematic reviews and meta-analyses had to rely on limited summary patient cohort data offered by primary studies. Performing an individual patient data meta-analysis will enable a much more detailed and powerful analysis and thus increase representativeness and generalizability of the results. The individual patient data meta-analysis is registered with the PROSPERO database (CoMe-CCT, CRD42012002780).  
(Continued on next page)

\* Correspondence: dewey@charite.de  
<sup>1</sup>Department of Radiology, Charité - Universitätsmedizin Berlin Campus Mitte, Humboldt-Universität zu Berlin, Freie Universität Berlin, Charitéplatz 1, Berlin 10117, Germany  
Full list of author information is available at the end of the article

 BioMed Central  
© 2013 Schultz et al.; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

CoMe-CCT Group. *Syst Reviews* 2013; 2:13.

# AP Classification for Pretest Likelihood Calculation

Classification	Criteria	Symptoms <sup>1,2</sup>
Typical Angina Pectoris	3 / 3	<ul style="list-style-type: none"><li>• Retrosternal chest discomfort</li><li>• Precipitated by exertion</li><li>• Prompt relieve (30s – 10 min) by rest or nitroglycerin</li></ul>
Atypical Angina Pectoris	2 / 3	2 out of the 3 criteria for typical AP
Non-anginal chest discomfort	1 / 3	1 out of the 3 criteria for typical AP
Other chest discomfort	0 / 3	None of the 3 criteria for typical AP

<sup>1</sup> Diamond GA & Forrester JS, J Clin Invest, 1980.

<sup>2</sup> Diamond GA, J Am Coll Cardiol, 1983.

# CAD Pretest Likelihood Calculator

---

Software application:

- Excel (only for microcosting & QoL Pilot study)
- eCRF (main phase)

# CAD Pretest Likelihood

## Example 1: <10%

Inclusion: **10-70%** pretest likelihood of CAD

### Probability of Coronary Artery Disease\*

(\* At least one coronary artery with at least one 50% diameter stenosis)

Age in years

32

Age will be rounded to one decimal place if more than one decimal place is given.

Gender

Female

Angina classification<sup>1,2</sup>

Other chest discomfort

Typical Angina Pectoris is defined as 1. retrosternal chest discomfort, 2. precipitated by exertion, 3. promptly relieved (30s - 10 min) by rest or nitroglycerin. Atypical Angina Pectoris = 2 out of the 3 criteria for typical Angina Pectoris. Non-anginal chest discomfort = 1 out of the 3 criteria for typical Angina Pectoris. Other chest discomfort = None of the 3 criteria for typical angina pectoris.

Probability of Coronary Artery Disease (in %)

9.3

<sup>1</sup> Diamond GA & Forrester JS, J Clin Invest, 1980.

<sup>2</sup> Diamond GA, J Am Coll Cardiol, 1983.

# CAD Pretest Likelihood

## Example 2: 10%-70%

Inclusion: **10-70%** pretest likelihood of CAD

Probability of Coronary Artery Disease*		
(* At least one coronary artery with at least one 50% diameter stenosis)		
Age in years	55	Age will be rounded to one decimal place if more than one decimal place is given.
Gender	Female	
Angina classification <sup>1,2</sup>	Atypical Angina Pectoris	Typical Angina Pectoris is defined as 1. retrosternal chest discomfort, 2. precipitated by exertion, 3. promptly relieved (30s - 10 min) by rest or nitroglycerin. Atypical Angina Pectoris = 2 out of the 3 criteria for typical Angina Pectoris. Non-anginal chest discomfort = 1 out of the 3 criteria for typical Angina Pectoris. Other chest discomfort = None of the 3 criteria for typical angina pectoris.
Probability of Coronary Artery Disease (in %)	<b>26.7</b>	

<sup>1</sup> Diamond GA & Forrester JS, J Clin Invest, 1980.

<sup>2</sup> Diamond GA, J Am Coll Cardiol, 1983.



# CAD Pretest Likelihood

## Example 3: >70%

Inclusion: **10-70%** pretest likelihood of CAD

Probability of Coronary Artery Disease*		
(* At least one coronary artery with at least one 50% diameter stenosis)		
Age in years	62	Age will be rounded to one decimal place if more than one decimal place is given.
Gender	Male	
Angina classification <sup>1,2</sup>	Typical Angina Pectoris	Typical Angina Pectoris is defined as 1. retrosternal chest discomfort, 2. precipitated by exertion, 3. promptly relieved (30s - 10 min) by rest or nitroglycerin. Atypical Angina Pectoris = 2 out of the 3 criteria for typical Angina Pectoris. Non-anginal chest discomfort = 1 out of the 3 criteria for typical Angina Pectoris. Other chest discomfort = None of the 3 criteria for typical angina pectoris.
Probability of Coronary Artery Disease (in %)	71.9	

<sup>1</sup> Diamond GA & Forrester JS, J Clin Invest, 1980.

<sup>2</sup> Diamond GA, J Am Coll Cardiol, 1983.

# Exclusion Criteria

---

 No sinus rhythm

 Dialysis

 Pregnancy

# Further Checks Before Randomization

---

- Written referral form of indication for ICA?  
(send it to Charité by eCRF)
- Patient informed consent form signed?
- QoL Questionnaires completed?
- Time-Trade-off question answered?
- Patient accepts CTA **and** ICA equally?

→ **Randomization possible!**

# Case 1 – Woman, 74 Years

---

- ✓ Symptoms?
  - Faint feeling of pressure in left chest and retrosternal
  - Dyspnea, Vertigo
  - For 6 years
- ✓ Induction?
  - Sometimes during exertion
  - Sometimes at rest
  - Always during attacks of atrial fibrillation (30-60 min)
- ✗ Relief?
  - Never tried Nitroglycerin
  - After 20 min at rest

→ 2 criteria met: **Atypical Angina Pectoris**

# Case 2 – Man, 36 Years

---

- ✓ Symptoms?
  - Strong pressure on his chest
  - Like a “big hammer“
  - For 5 months

- ✗ Induction?
  - Mostly at rest
  - When having psychic stress

- ✗ Relief?
  - Never tried Nitroglycerin
  - After about 30 min at rest

→ 1 criterion met: **Non-anginal chest discomfort**

# Case 3 – Woman, 70 Years

---

- ✓ Symptoms?
  - Feeling of retrosternal pressure
  - Sticking aches in chest
  - For 11 years
- ✓ Induction?
  - During exertion
  - At rest
- ✓ Relief?
  - Nitroglycerin Spray provides some relief
  - After 5-10 min at rest

→ 3 criteria met: **Typical Angina Pectoris**

# Summary

## Inclusion criteria:

- Indication for ICA
- Age  $\geq$  30 years
- Stable chest discomfort (no unstable angina)
- Intermediate pretest likelihood of CAD: **10-70%**

## Exclusion criteria:

- No sinus rhythm
- Dialysis
- Pregnancy

## Pretest Likelihood calculator:

- Individual patient data (n = 6.704)
- Collaborative Meta-analysis of Cardiac CT (CoMe-CCT, CoMe-CCT Group. Syst Reviews 2013; 2:13.)

Classification	Criteria	Symptoms <sup>1, 2</sup>
Typical Angina Pectoris	3 / 3	<ul style="list-style-type: none"> <li>• Retrosternal chest discomfort</li> <li>• Precipitated by exertion</li> <li>• Prompt relieve (30s – 10 min) by rest or nitroglycerin</li> </ul>
Atypical Angina Pectoris	2 / 3	2 out of the 3 criteria for typical AP
Non-anginal chest discomfort	1 / 3	1 out of the 3 criteria for typical AP
Other chest discomfort	0 / 3	None of the 3 criteria for typical AP

<sup>1</sup> Diamond GA & Forrester JS, J Clin Invest, 1980.

<sup>2</sup> Diamond GA, J Am Coll Cardiol, 1983.

**Probability of Coronary Artery Disease\***  
(\* At least one coronary artery with at least one 50% diameter stenosis)

Age in years	<input style="width: 100%;" type="text"/>
Gender	<input style="width: 100%;" type="text" value="Female"/>
Angina classification <sup>1,2</sup>	<input style="width: 100%;" type="text" value="Atypical Angina Pectoris"/>
Probability of Coronary Artery Disease (in %)	<input style="width: 100%; background-color: #00bfff;" type="text"/>

<sup>1</sup> Diamond GA & Forrester JS, J Clin Invest, 1980.  
<sup>2</sup> Diamond GA, J Am Coll Cardiol, 1983.