Disclosure Statement of Financial Interest

Within the past 12+ months, Nils Johnson has had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship

- Grant/Research Support  
  (to institution)
- Educational organizations  
  (travel support for academic meetings but never honoraria)

Organizations (alphabetical)

- St Jude Medical (for CONTRAST study)
- Volcano/Philips (for DEFINE-FLOW)
- ASNC (travel award, 2007)
- Canadian CPI (Montréal, 2013-15)
- CRF (TCT 2012-14, CPIIS 2014)
- ESC (ETP physiology courses, 2013-15)
- KSIC (annual meeting, 2015)
- SCAI (travel award, 2010)

Nils Johnson has never personally received any money from any commercial company. Specifically, he does not accept commercial consulting, travel, entertainment, or speaking compensation of any kind.
Medical therapy *alone*?

Or *add PCI*?
2013 ESC guidelines on the management of stable coronary artery disease (SCAD)

The traditional understanding of SCAD is that of a disease causing exercise- and stress-related chest symptoms.
55 year-old woman

• new, typical angina
• CCS class II-III severity despite nitrates
• no beta-blocker due to lung disease
2013 ESC guidelines on the management of stable coronary artery disease

The traditional understanding of SCAD is that of a disease causing exercise- and stress-related chest symptoms due to narrowings of \( \geq 50\% \) in the left main coronary artery and \( \geq 70\% \) in one or several of the major coronary arteries.
QCA of lesion

- 58% in LAO, 55% in RAO
- referred for angiography directly without non-invasive testing
symptoms, clinical data, angiogram, treatment decision
symptoms, clinical data, angiogram

predict significance

treatment decision
Anatomic predictions

**ambiguous**
(often unclear if causal)

**imprecise**
(uncertain for an individual)
Cause and effect?

55 year-old woman with new, typical angina

causal?
unrelated?

*Coronary Pathophysiology & Microcirculation*
Cause and effect?

“chest pain unrelated to activity, unrelieved by nitroglycerin and apparently non-cardiac in origin”

1,282 men from 15 US centers

Chaitman BR, Circulation. 1981 Aug, 64(2):360-7 (Figure 3, modified excerpt)
### Cause and effect?

<table>
<thead>
<tr>
<th></th>
<th>Any CAD</th>
<th>Obstructive CAD</th>
<th>Subgroup of obstructive CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1VD</td>
</tr>
<tr>
<td>CACS≤100</td>
<td>1017 (42.5%)</td>
<td>204 (8.5%)</td>
<td>147 (6.1%)</td>
</tr>
<tr>
<td>CACS&gt;100</td>
<td>716 (86.8%)</td>
<td>342 (41.5%)</td>
<td>185 (22.4%)</td>
</tr>
</tbody>
</table>

17% had ≥50%DS
2% with 3VD/LM

CONFIRM registry
3,217 patients asymptomatic from 12 centers in 6 countries

Cho I, *Eur Heart J*. 2015 Feb 21;36(8):501-8 (excerpt from Figure 1)
Cause and effect?

**ECA survey**
13,538 subjects community-based from 5 USA centers

**Lifetime prevalence**
- Chest pain = 25%
- Fatigue = 24%
- Palpitations = 18%
- Dyspnea = 14%

Kroenke K, *Arch Intern Med.* 1993 Nov 8;153(21):2474-80 (data from Table 1)
Cause and effect?

- ≥50%DS
- Symptoms

cause?
"It has been shown that in a randomly selected group of asymptomatic 60-year old men, the prevalence of apparently significant coronary stenoses is 20%. Therefore, one must assume that in a number of such patients, the presence of a lesion may be coincidental and that a direct relation between the angiographic lesion and the chest pain is unclear."

Anatomic predictions

ambiguous
(often unclear if causal)

imprecise
(uncertain for an individual)
Individual imprecision

“Left main” stenosis

4.4mm

50%DS

2.2mm

\[ \Delta P \propto \frac{1}{\text{radius}^4} \]

Poiseuille law: \( \Delta P \propto \frac{1}{\text{radius}^4} \)
“Left main” stenosis

Poiseuille law: $\Delta P \propto \frac{1}{\text{radius}^4}$
(physiology $\propto$ anatomy)
Individual imprecision

“Left main” stenosis

4.4mm

50%DS

2.2mm

ΔP

Relative error $\frac{\Delta P}{P} = 4 \times \frac{\Delta \text{radius}}{\text{radius}}$

(error in physiology $\propto$ error in anatomy)
Individual imprecision

“Left main” stenosis

\[ \Delta P \]

\[ 4.4\text{mm} \]

\[ 50\%\text{DS} \quad 2.2\text{mm} \]

Relative error \( \Delta P/P = 4 \times \Delta \text{radius} / \text{radius} \)

\( \text{(error in physiology } \propto \text{ error in anatomy)} \)

- **Invasive** = \( 4 \times 0.2\text{mm} / 1.1\text{mm} = 73\% \Delta P/P \)
Relative error $\Delta P/P = 4 \times \Delta \text{radius} / \text{radius}$

- **CTA** = $4 \times 0.6 / 1.1 = 218\%$ error in $\Delta P/P$
- **Invasive** = $4 \times 0.2 / 1.1 = 73\%$
- **IVUS** = $4 \times 0.1 / 1.1 = 36\%$
- **OCT** = $4 \times 0.02 / 1.1 = 7\%$

**“Left main” stenosis**

- 4.4mm
- 50%DS
- $\Delta P$
- 2.2mm
CT-modeled FFR

Johnson NP, *Circ Cardiovasc Imaging* 6(5):817, 2013, Figure 4A
CT-modeled FFR

Johnson NP, *Circ Cardiovasc Imaging* 6(5):817, 2013, Figure 4A

Koo BK, *JACC* 58(19):1989, 2011, Figure 4
CT-modeled FFR

Johnson NP, *Circ Cardiovasc Imaging* 6(5):817, 2013, Figure 5A
Anatomy *versus* physiology

SFR (angiography) = Bartůnek J, *JACC*. 1995 Aug;26(2):328-34 (Figure 3, bottom)

FFR\textsubscript{CT} (CT angiography) = Koo BK, *JACC*. 2011 Nov 1;58(19):1989-97 (Figure 4)

MLA (IVUS) = Waksman R, *JACC*. 2013 Mar 5;61(9):917-23 (Figure 1A)

%DS (angiography) = White CW, *NEJM*. 1984 Mar 29;310(13):819-24 (Figure 2)
Anatomy *versus* physiology

“anatomy”
(QCA)

“physiology”

Toth G, *Eur Heart J* 2014 Oct 21;35(40):2831-8 (Figure 1A)
Anatomy *versus* physiology

*Mild* anatomy, *severe* physiology  
→ How to treat?

Aalst = Toth G, *Eur Heart J*. 2014 Oct 21;35(40):2831-8 (part of Figure 1A)
RIPCORD = Cruzen N, *Circ Cardiovasc Interv*. 2014 Apr;7(2):248-55 (part of Figure 2)
Anatomy *versus* physiology

FFR = 0.2 to 1.0

ToFth G, *Eur Heart J* 2014 Oct 21;35(40):2831-8 (Figure 1A)
NONOPERATIVE DILATATION OF CORONARY-ARTERY STENOSIS
Percutaneous Transluminal Coronary Angioplasty

Andreas R. Grünzig, M.D., Åke Senning, M.D., and Walter E. Siegenthaler, M.D.
First scatter plot

Anatomy (%DS) versus physiology (mmHg)
58 ± 14 mmHg (before)

\[ \frac{Pd}{Pa} \approx \frac{(100-58)}{100} \]

<<0.75 (even at rest!)

Grüntzig AR, NEJM 1979 Jul 12;301(2):61-8 (modified Figure 3)
58 ± 14 mmHg (before)

19 ± 13 mmHg (after)

n = 34

Grüntzig AR, NEJM 1979 Jul 12;301(2):61-8 (modified Figure 3)
Anatomy versus physiology

Fractional Flow Reserve versus

Angiography for MultivesSEL Evaluation
Anatomy *versus* physiology

**anatomy**

Survival Free of Death from Any Cause and Myocardial Infarction

Hazard ratio, 1.05; 95% CI (0.87–1.27); P=0.62

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Medical therapy</th>
<th>PCI</th>
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<tbody>
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<tr>
<td>30</td>
<td>35</td>
<td>35</td>
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</tbody>
</table>

**physiology**

Survival Free from Major Adverse Cardiac Events (%)

Relative risk, 0.72; 95% CI (0.54-0.96); P=0.02

<table>
<thead>
<tr>
<th>Days since Randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
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<tr>
<td>240</td>
</tr>
<tr>
<td>300</td>
</tr>
<tr>
<td>360</td>
</tr>
</tbody>
</table>

**COURAGE**

**FAME**

Johnson NP, *Circ Cardiovasc Imaging*. 2013 Sep;6(5):817-32 (Figure 6)
symptoms, clinical data, angiogram predict significance treatment decision
symptoms, clinical data, angiogram

guess significance

treatment decision
“Participants were asked to make their decisions assuming ideal world conditions, without considering any financial restrictions or local regulations, but only after the best clinical practice achievable in this virtual catheterization laboratory.”
Do we **guess**?

Almost a 50%/50% split vs FFR (coin toss!)
symptoms, clinical data, angiogram

measure significance

treatment decision
symptoms, clinical data, angiogram
treatment decision
Coronary Pressure
From a Physiological Index to a Clinical Tool

Thesis by
Bernard de Bruyne, MD
From the Cardiovascular Center, Aalst, Belgium

To be submitted in partial fulfillment of the requirements for the degree of
“Agrégé de l’Enseignement Supérieur”

Co-Promoters:
Jacques A. Melin, MD
William Wijns, MD

1995
“Albeit often statistically significant, the correlations between angiographic and functional indices … are too weak to be clinically relevant”