

Institute for Health Economics and Clinical Epidemiology | University Hospital of Cologne

# Sex differences in guideline adherence for coronary angiography in patients with suspected chronic coronary artery disease in Germany: Insights from the ENLIGHT-KHK trial

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## Background

- Invasive coronary angiography (CA), a well-established procedure for diagnosing coronary artery disease (CAD)<sup>1</sup>, is only restrictively recommended by evidence-based guidelines for patients with suspected chronic CAD<sup>2</sup>.
- Although the diagnostic algorithm applies equally to female and male patients, evidence suggests that less CA is performed in women with suspected CAD than men<sup>3,4</sup>.
- It is unclear whether this variation in the use of CA reflects differences in providers' adherence to evidence-based guidelines, as suspected in the management of acute coronary syndrome (ACS)<sup>5,6</sup>.

## Research questions

- ① Is providers' **guideline adherence** for the use of CA **lower in female patients than in male patients** with suspected CAD?
- ② Is providers' guideline adherence in female patients **determined by different predictors than in male patients**?

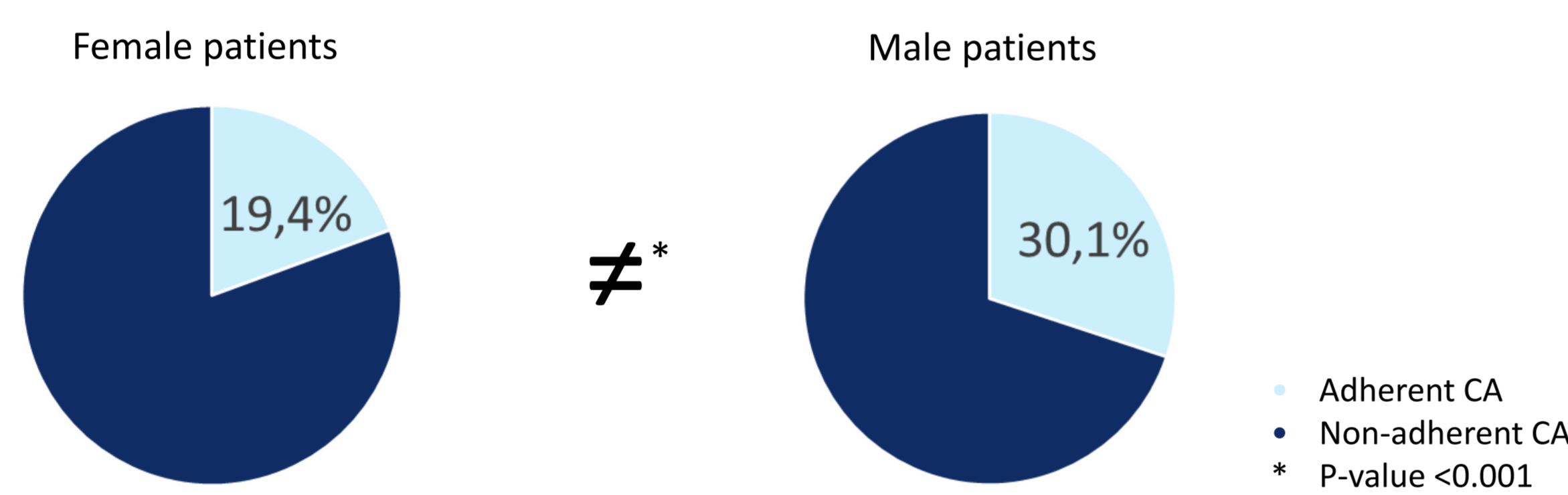
## Methods

- Population and data: Adults with suspected obstructive CAD<sup>7</sup>; **German ENLIGHT-KHK trial** (prospective, observational study that investigated the nature and extent of guideline adherence for CA<sup>7</sup>).
- Primary outcome: **Difference in providers' adherence** to the German national disease management guideline (GNDMG) "Chronic CAD" 2019 for CA between female and male patients.
- Secondary outcome: **Patient-related sex difference in predictors** of guideline adherence for CA.
- Analysis method: **Binary logistic regression model**. Covariates included age, type of anginal symptoms, angina severity, risk factors, comorbidities, non-invasive testing, and the test result (model 1). A second regression model included all covariates except non-invasive testing and its results (model 2).
- Model performance was assessed by Nagelkerke's R<sup>2</sup>. A p-value <0.05 indicated statistical significance.

## Results

- 659 patients were included (41% female, 59% male).
- Patients were on average 67 ± 10 years old and 34% of them had a typical angina.

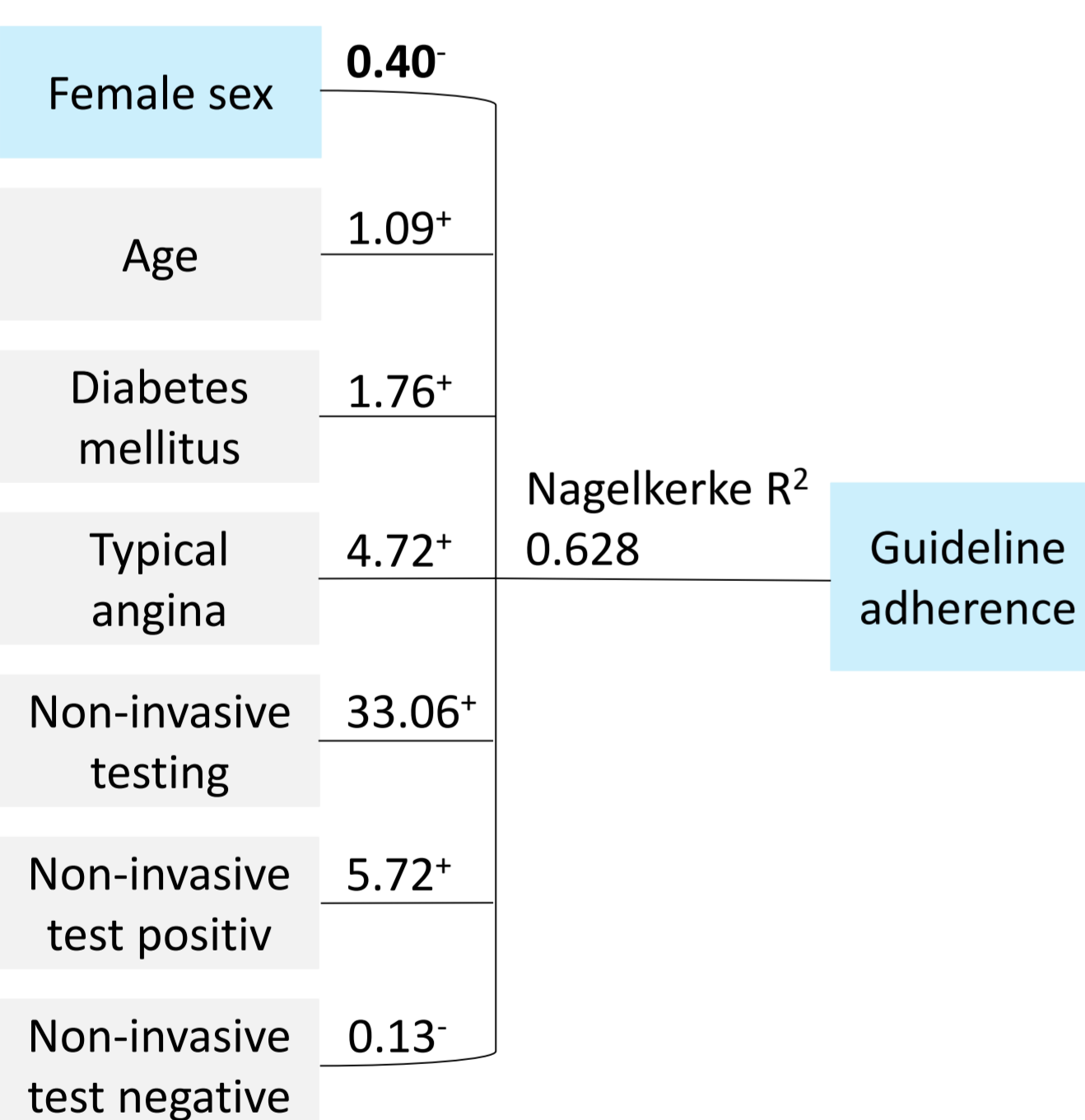
① Figure 1: Guideline adherence for CA in female and male patients



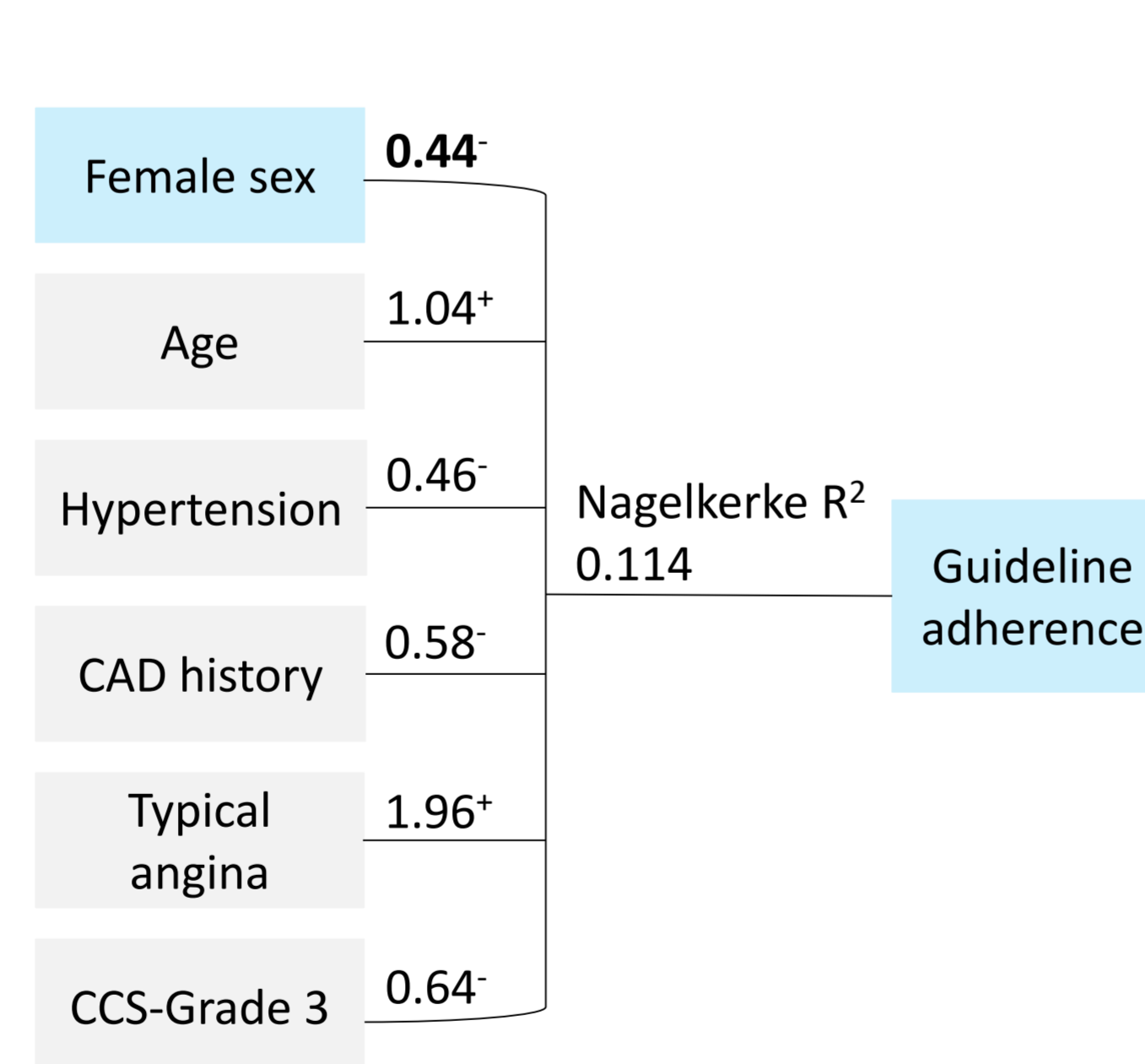
**Guideline adherence was lower in female than in male patients (Figure 1).** In addition, both regression models identified **patient sex as predictor of guideline adherence**, with female patients being less likely to receive adherent CA than male patients (Figure 2).

Figure 2: Association between patient sex and guideline adherence

(A) Results of model 1: Odds ratios\*



(B) Results of model 2: Odds ratios\*



\* All p-values were adjusted using Benjamini-Hochberg procedure. All p-values were significant (<0.05). CAD = Coronary Artery Disease, CCS = Canadian Cardiovascular Society

② **Predictors of guideline adherence differed between female and male patients (Table 1).** Non-invasive testing and its results, age and type of anginal symptoms had a significant impact on guideline adherence in male patients, whereas only a positive non-invasive test result had a significant strong impact in female patients.

Table 1: Multiple binary logistic regression analysis for guideline adherence in female and male patients

Variable	Female patients		Male patients			
	OR <sup>†</sup>	95% CI	Nagelkerke R <sup>2</sup>	OR <sup>†</sup>	95% CI	Nagelkerke R <sup>2</sup>
<b>Model 1<sup>a</sup></b>			0.634			0.613
Age				1.11**	1.07-1.15	
Diabetes mellitus	3.68*	1.33-10.21				
Respiratory disease	3.13*	1.06-9.23				
Smoking				0.48	0.25-0.92	
Typical angina				8.46**	4.02-17.79	
Non-invasive testing				14.19**	5.49-36.71	
Non-invasive test positive	173.27**	50.02-600.18		7.94**	2.97-21.22	
Non-invasive test negative				0.22	0.05-0.97	
CCS-Grade 4	4.40*	1.23-15.71				
CAD history	0.23	0.08-0.68				
<b>Model 2<sup>b</sup></b>			0.066			0.260
Overweight	0.42	0.22-0.81				
Age				1.07**	1.04-1.10	
Smoking				0.55	0.34-0.90	
Typical angina				3.58**	2.15-5.97	
Hypertension				0.30*	0.17-0.56	
CAD history	0.48	0.25-0.93		0.52	0.31-0.86	
CCS-Grade 3				0.51	0.30-0.89	

<sup>†</sup> All p-values were adjusted using Benjamini-Hochberg procedure. All p-values were significant (<0.05); \* P-value <0.001  
<sup>a</sup> Male patients: Final model:  $\chi^2$  218.580, p<0.001; Female patients: Final model:  $\chi^2$  138.094, p<0.001; <sup>b</sup> Male patients: Final model:  $\chi^2$  78.062, p<0.001; Female patients: Final model:  $\chi^2$  11.467, p=0.003  
 CAD = Coronary Artery Disease, CCS = Canadian Cardiovascular Society, CI = Confidence Interval, OR = Odds Ratio

<sup>†</sup> OR > 1: Variable is associated with a **higher probability** of guideline adherence  
<sup>†</sup> OR < 1: Variable is associated with a **lower probability** of guideline adherence

## Conclusion

- » In the ENLIGHT-KHK trial population, **women with suspected CAD were less likely to receive guideline-adherent CA** than men.
- » Differences in predictors of guideline adherence between female and male patients suggest that **non-invasive testing and its results, age and type of anginal symptoms have less impact** on the diagnostic work-up using CA in women than in men.
- » These results **add to the known lower guideline-adherence in the management of ACS** and may reflect limited awareness and knowledge of chronic CAD in women.
- » Generating and **disseminating sex-specific evidence on CAD** could potentially reduce sex differences in guideline adherence for the diagnosis of chronic CAD.

**Funding**  
 The Innovation Committee at the Federal Joint Committee [grant number 01VSF17011]

**References**  
<sup>1</sup>Discharge Trial Group; Maurovich-Horvat P, Bossert M, Kofoed KF, et al. CT or Invasive Coronary Angiography in Stable Chest Pain. N Engl J Med 2022;386:1591-1602; <sup>2</sup>Arzneimittelkommission Der Deutschen Ärzteschaft (AkdÄ), Deutsche Gesellschaft Für Allgemeinmedizin Und Familienmedizin (DEGAM), Deutsche Gesellschaft Ernährungsmedizin (DGEM), et al. Nationale VersorgungsLeitlinie Chronische KHK - Langfassung, 5. Auflage. Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF); 2019; <sup>3</sup>Pagidipati NJ, Coles A, Hemal K, et al. Sex differences in management and outcomes of patients with stable symptoms suggestive of coronary artery disease: Insights from the PROMISE trial. Am Heart J. 2019;208:28-36; <sup>4</sup>Madan N, Gajo E, Sanghani RM, Volgman AS. Sex-Based Considerations in the Evaluation of Chest Pain and Management of Obstructive Coronary Artery Disease. Curr Atheroscler Rep. 2020;22(8):39; <sup>5</sup>Wilkinson C, Bebb O, Dondo TB, et al. Sex differences in quality indicator attainment for myocardial infarction: a nationwide cohort study. Heart. 2019;105(7):516-523; <sup>6</sup>Daly C, Clemens F, Lopez Sendon JL, et al. Gender Differences in the Management and Clinical Outcome of Stable Angina. Circulation. 2006;113(4):490-498; <sup>7</sup>Seleznova Y, Wein B, Mueller D, et al. Evaluation of guideline adherence for cardiac catheterization in patients with presumed obstructive coronary artery disease in Germany (ENLIGHT-KHK) - A multicentre, prospective, observational study. Cardiovascular Revascularization Medicine. 2020; 31:19-25