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LEIPZIG



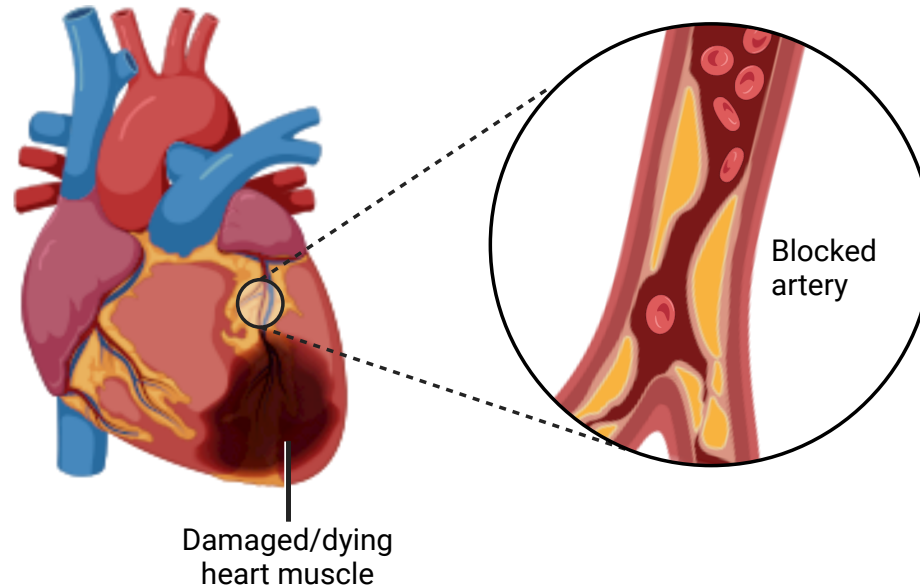
Sex Differences in Biomarker Levels Following Acute Coronary Syndrome (ACS)

Winterseminar Bled, 13.02.2025

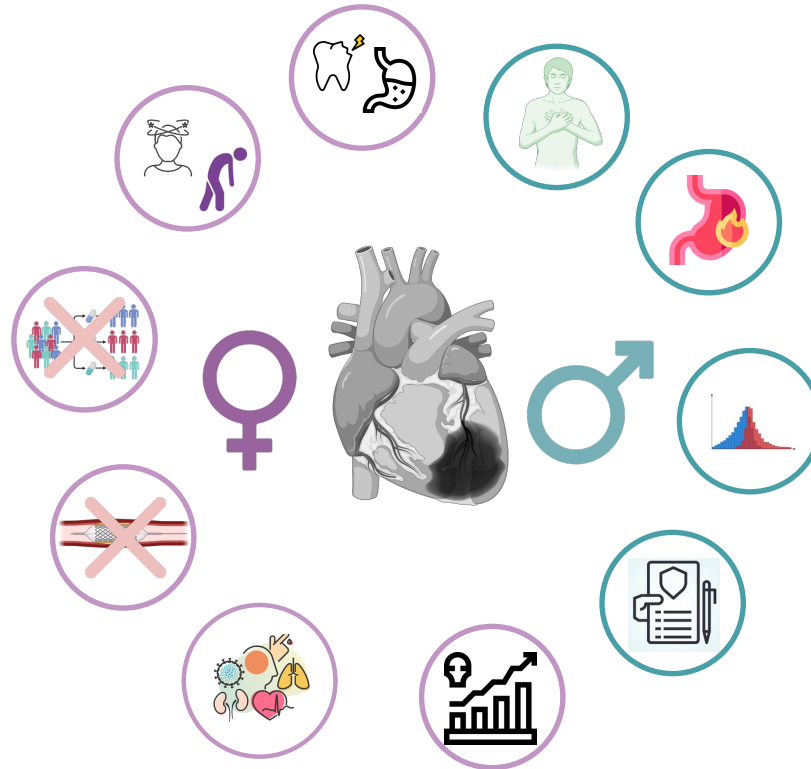
Christiane Gärtner



ACUTE CORONARY SYNDROME (ACS) - PATHOLOGY



ACUTE CORONARY SYNDROME - SEX DIFFERENCES



PHASES AFTER ACS

- **Acute phase (0-7 days):** inflammation, necrosis
- **Subacute phase (1-4 wks):** proliferative phase (resolution of inflammation, myofibroblast proliferation)
- **Chronic phase (> 4 wks):** remodelling (replacement of myocardial tissue with fibrous tissue)
- *Possible complications:* heart failure, pericarditis (autoimmune), recurrent ischemia, arrhythmias

ACUTE CORONARY SYNDROME - BIOMARKERS

Myocardial injury

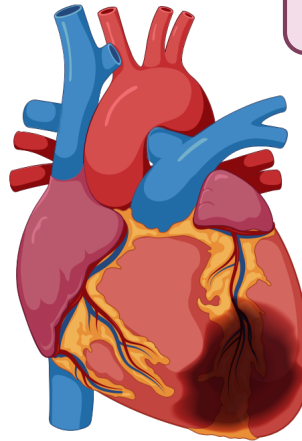
- cTnT
- cTnI

Inflammation

- CRP
- MPO
- Galectin-3

Heart failure

- NT-pro-BNP



Fibrosis

- Galectin-3
- GDF-15
- ST-2

Risk profile

- HDL
- LDL
- Cholesterol
- vWF
- Cystatin C

AIM: Can we identify sex-specific levels and trajectories of these cardiac biomarkers after an ACS?

DATASET - BIOMARCS COHORT

= **BIOM**arker study to identify the **Acute** risk of a **Coronary S**yndrome

INCLUSION CRITERIA:

- Patients with ACS
- > 40yrs
- + at least 1 risk factor

PRIMARY ENDPOINTS:

- Death due to cardiac condition
- Re-infarction

➡ 844 patients included

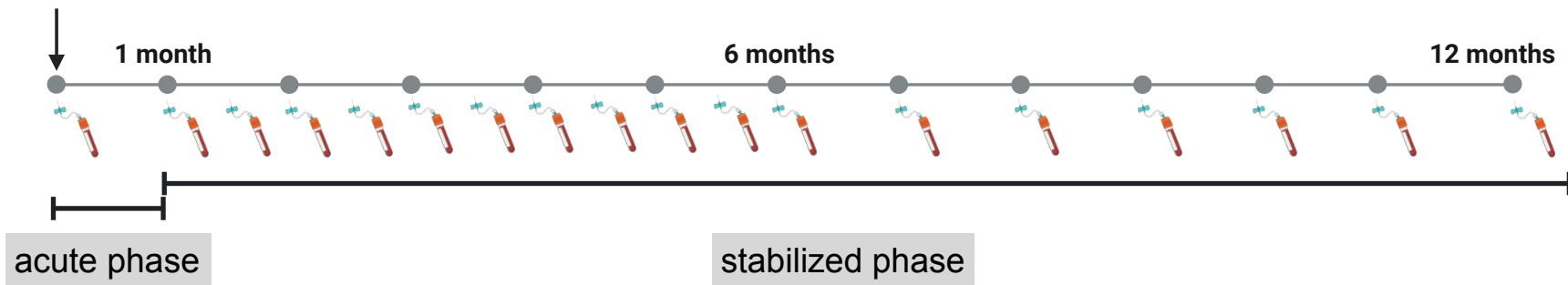


DATASET - BIOMARCS COHORT

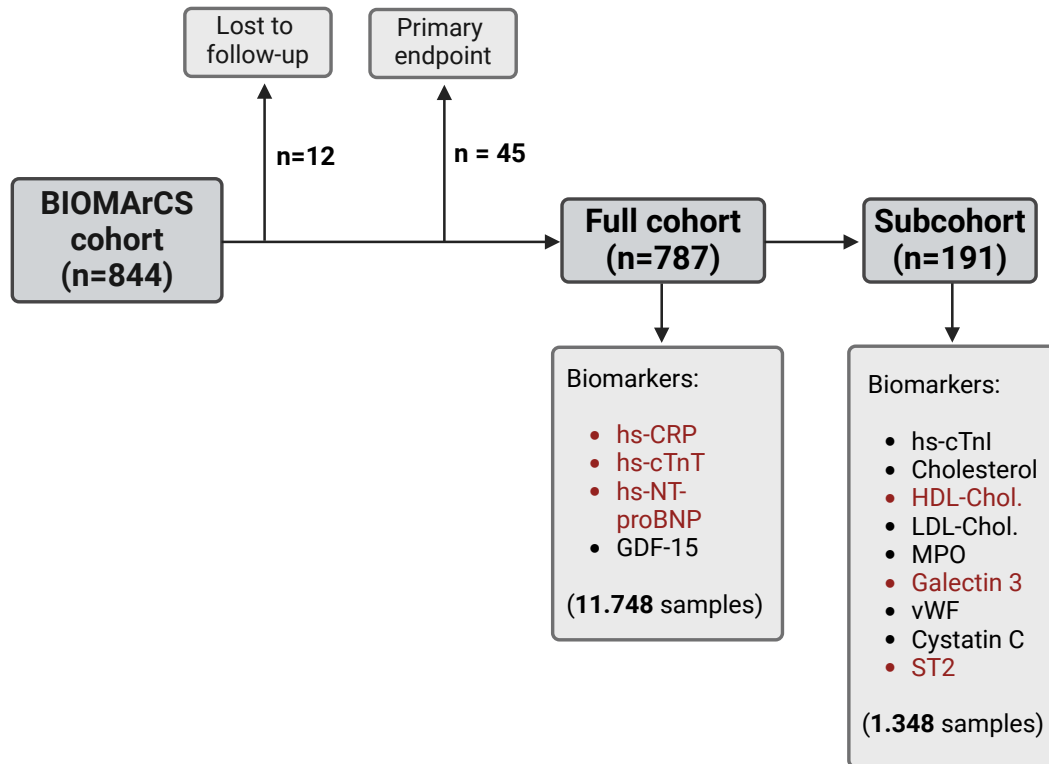
Blood sampling protocol:



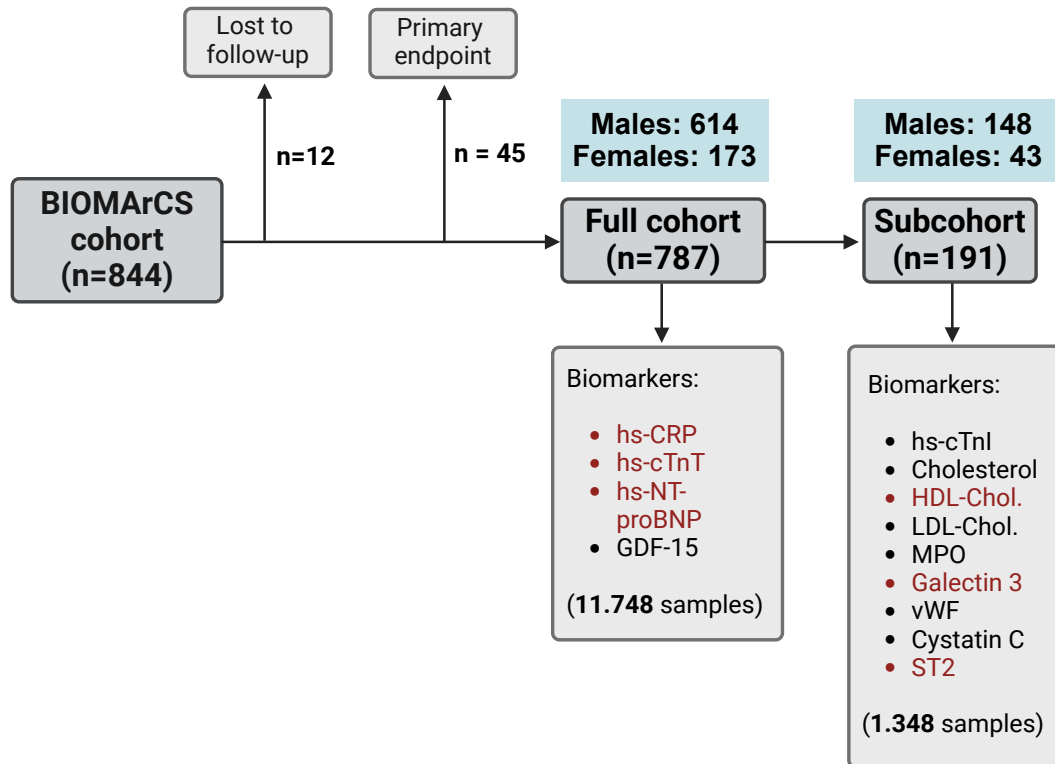
Myocardial
infarction (ACS)



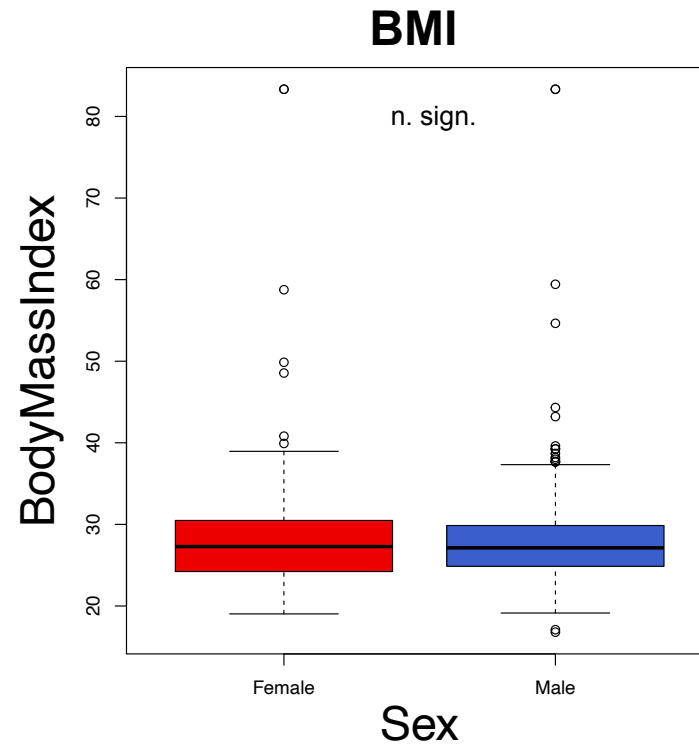
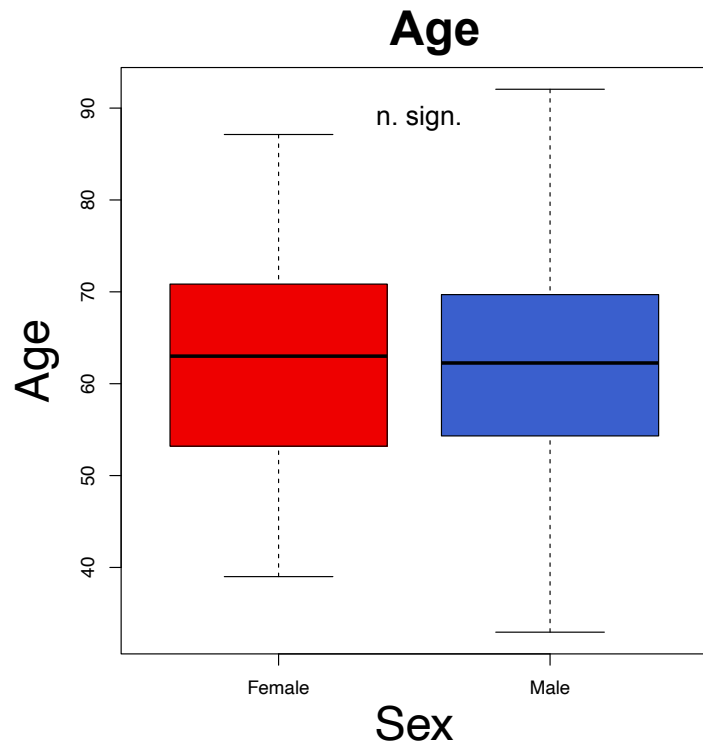
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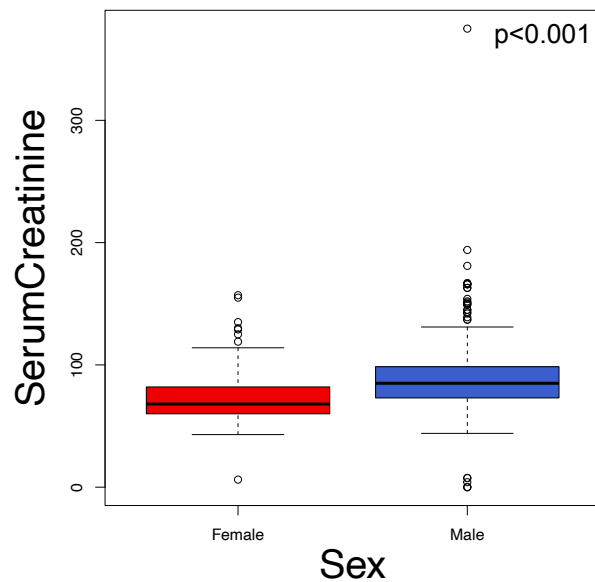


COHORT - BASELINE

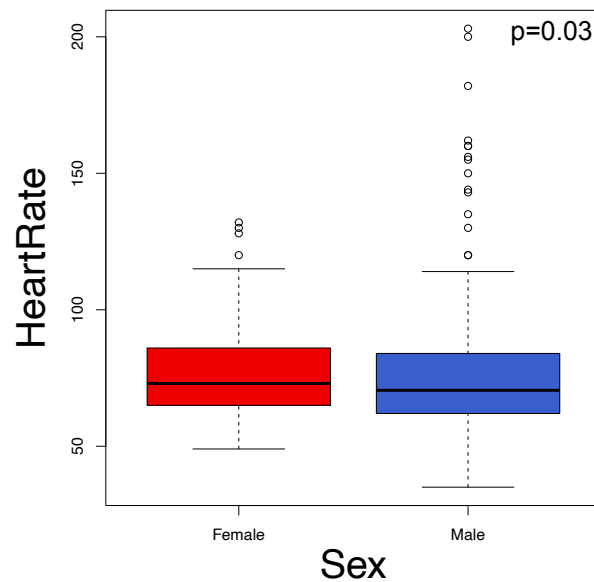


COHORT - BASELINE

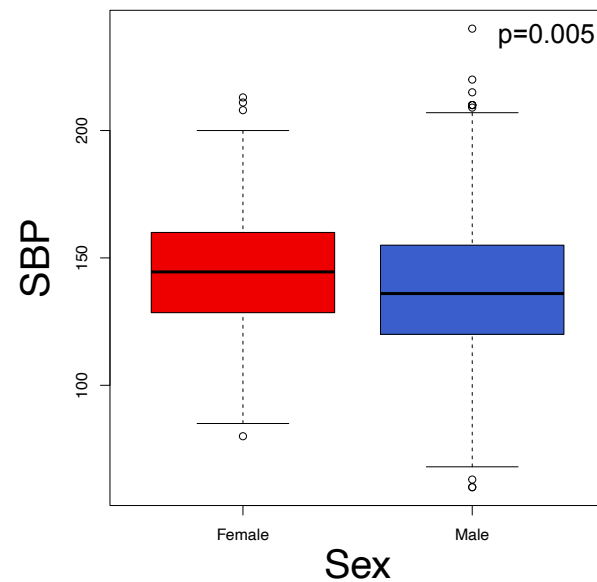
Creatinine



Heart Rate

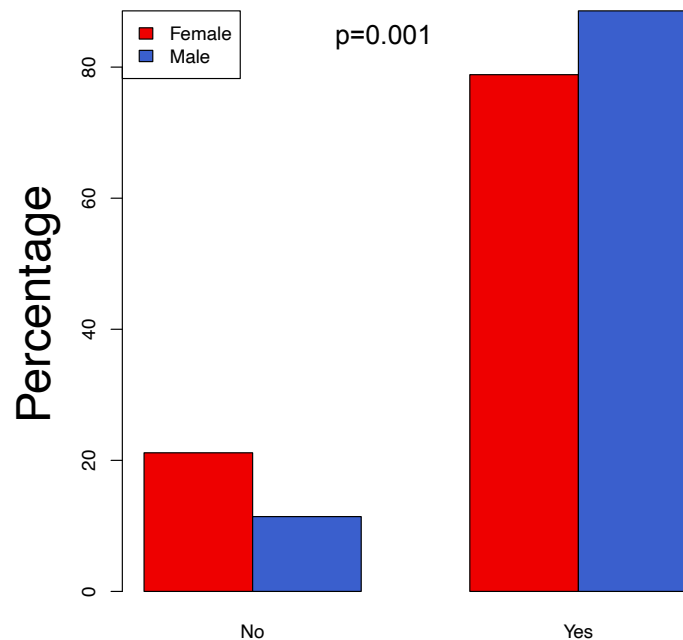


Systolic blood pressure

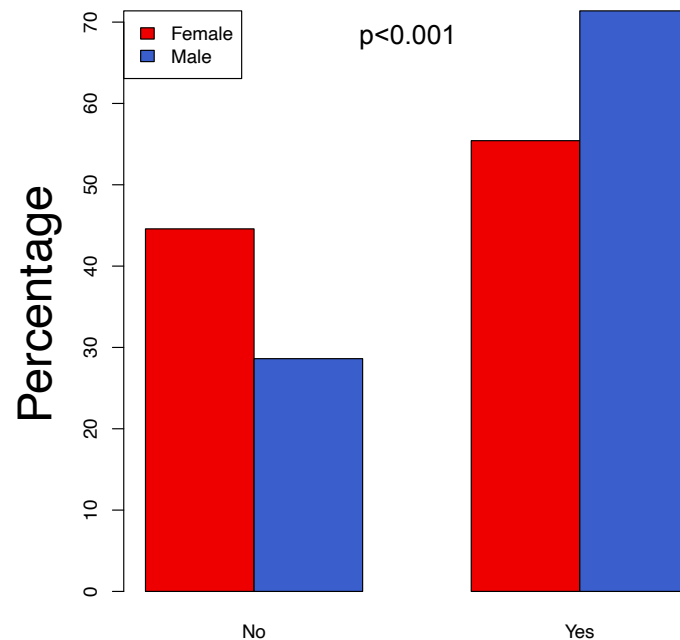


COHORT - BASELINE

PCI performed



ACEi discharge medication



METHODS - LINEAR MIXED-EFFECTS MODELS (LMM)

- Extension of linear regression to account for longitudinal measurements
- Fixed effects = explanatory variables, assumed to be constant across all groups or individuals

The diagram illustrates the components of a Linear Mixed-Effects Model (LMM) equation. The equation is displayed as:

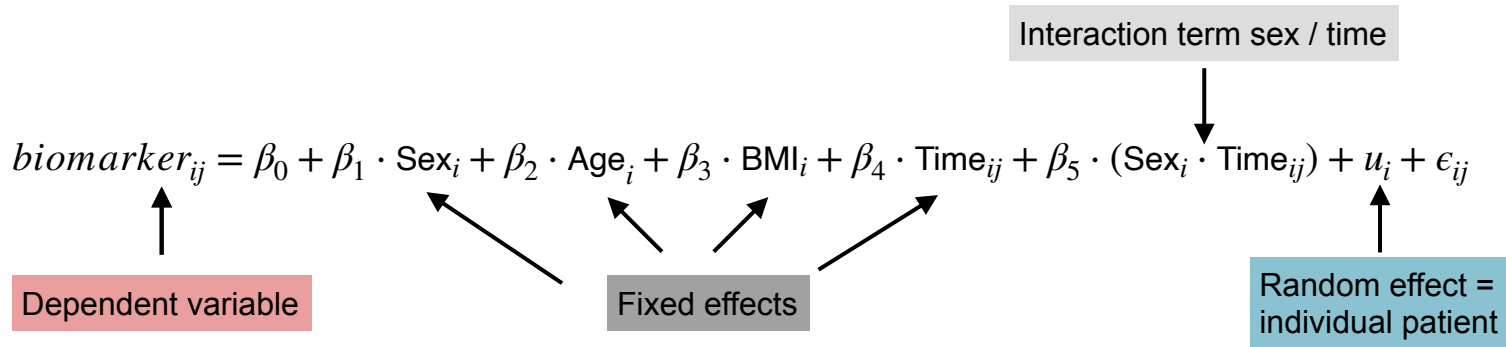
$$biomarker_{ij} = \beta_0 + \beta_1 \cdot Sex_i + \beta_2 \cdot Age_i + \beta_3 \cdot BMI_i + \beta_4 \cdot Time_{ij} + \beta_5 \cdot (Sex_i \cdot Time_{ij}) + u_i + \epsilon_{ij}$$

Annotations and arrows:

- A red box labeled "Dependent variable" has an arrow pointing up to $biomarker_{ij}$.
- A grey box labeled "Fixed effects" has four arrows pointing to the fixed effect terms: $\beta_1 \cdot Sex_i$, $\beta_2 \cdot Age_i$, $\beta_3 \cdot BMI_i$, and $\beta_4 \cdot Time_{ij}$.
- A grey box labeled "Interaction term sex / time" has an arrow pointing down to the interaction term $\beta_5 \cdot (Sex_i \cdot Time_{ij})$.

METHODS - LINEAR MIXED-EFFECTS MODELS (LMM)

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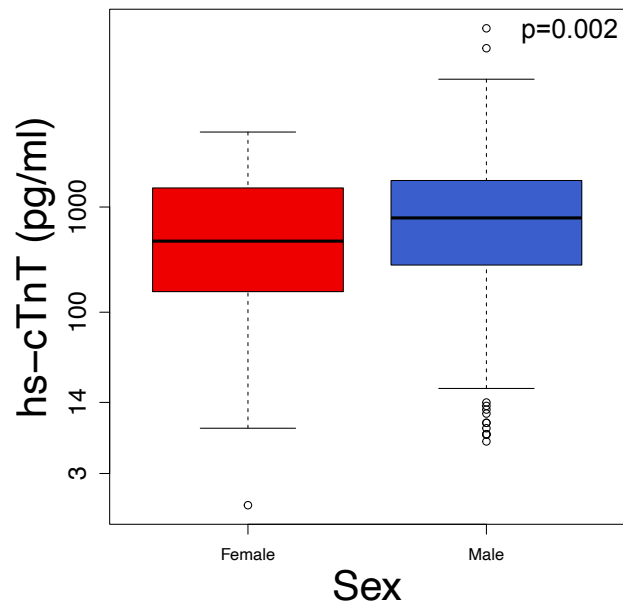
Annotations with arrows point to specific parts of the equation:

- Dependent variable** (red box) points to $biomarker_{ij}$.
- Fixed effects** (grey box) points to the fixed effect terms: $\beta_1 \cdot Sex_i$, $\beta_2 \cdot Age_i$, $\beta_3 \cdot BMI_i$, $\beta_4 \cdot Time_{ij}$, and $\beta_5 \cdot (Sex_i \cdot Time_{ij})$.
- Interaction term sex / time** (grey box) points to the interaction term $(Sex_i \cdot Time_{ij})$.
- Random effect = individual patient** (blue box) points to the random effect term u_i .

➡ Modeling for each biomarker for acute and stabilized phase

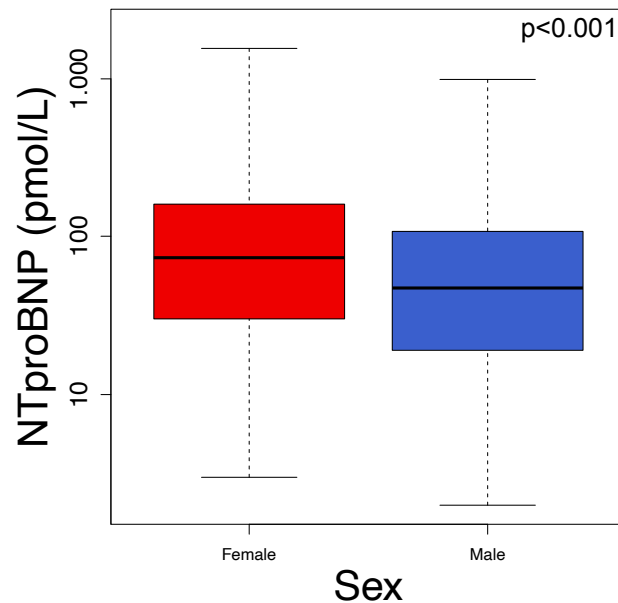
RESULTS - ACUTE PHASE - FULL COHORT

Troponin T



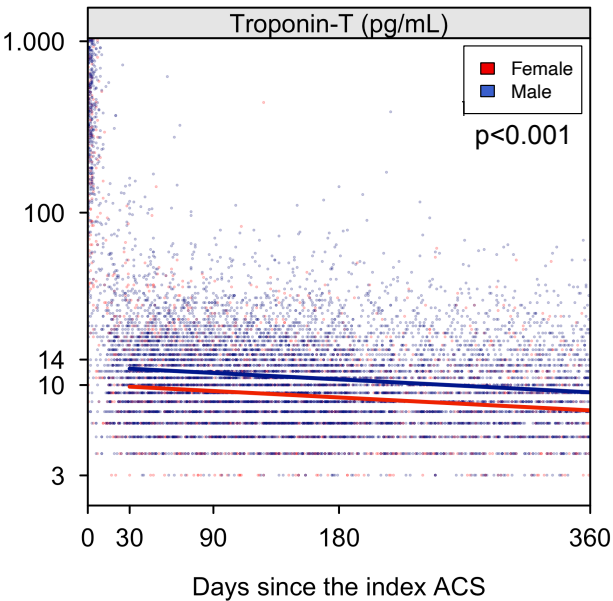
cardiac damage

NT-proBNP



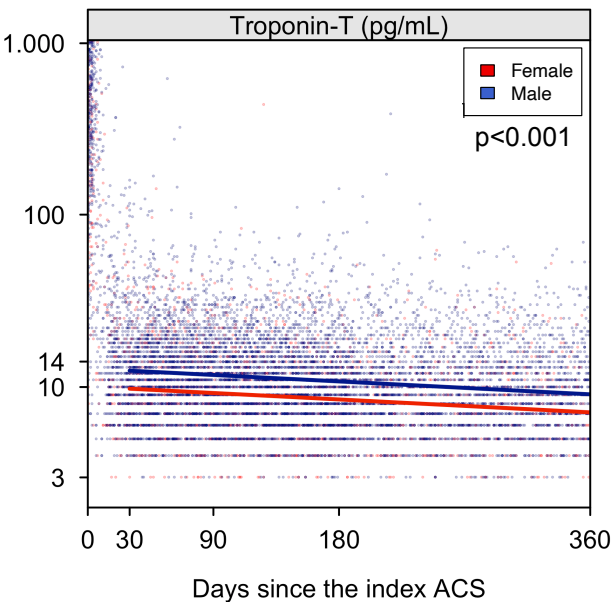
heart failure

RESULTS - STABILIZED PHASE - FULL COHORT

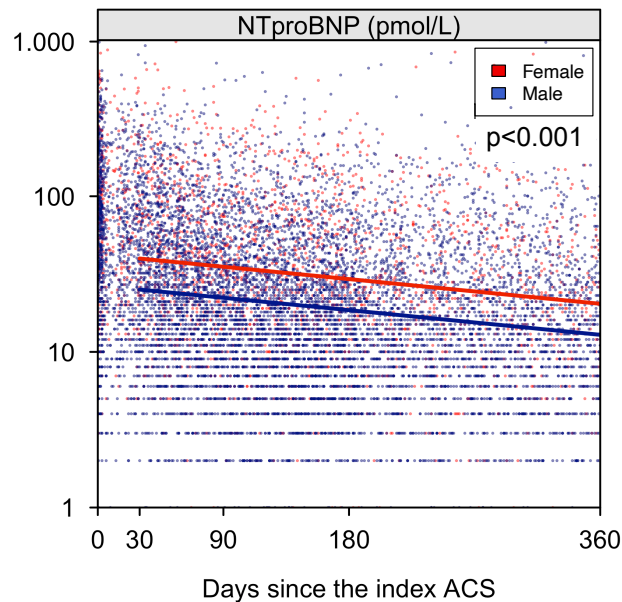


cardiac damage

RESULTS - STABILIZED PHASE - FULL COHORT

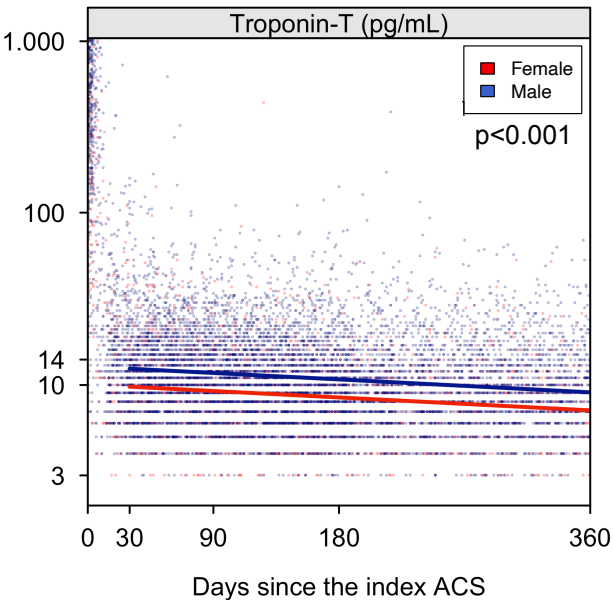


cardiac damage

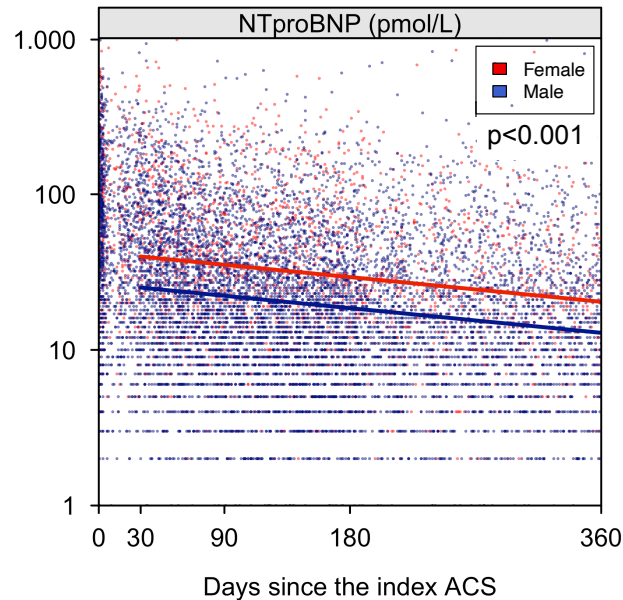


heart failure

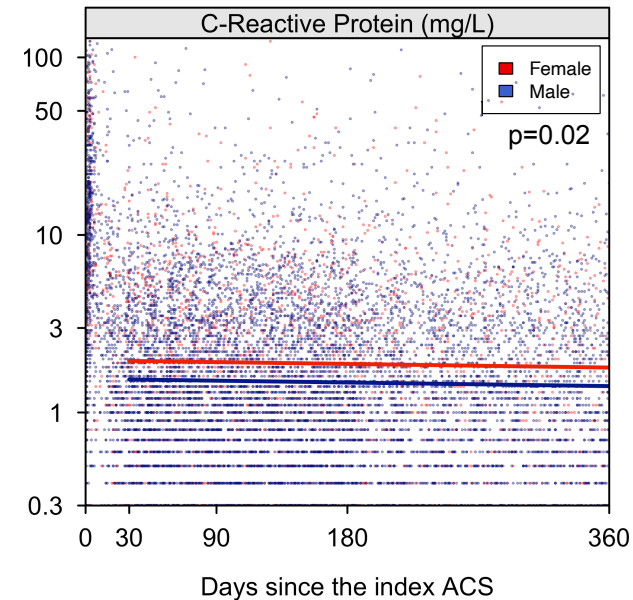
RESULTS - STABILIZED PHASE - FULL COHORT



cardiac damage



heart failure



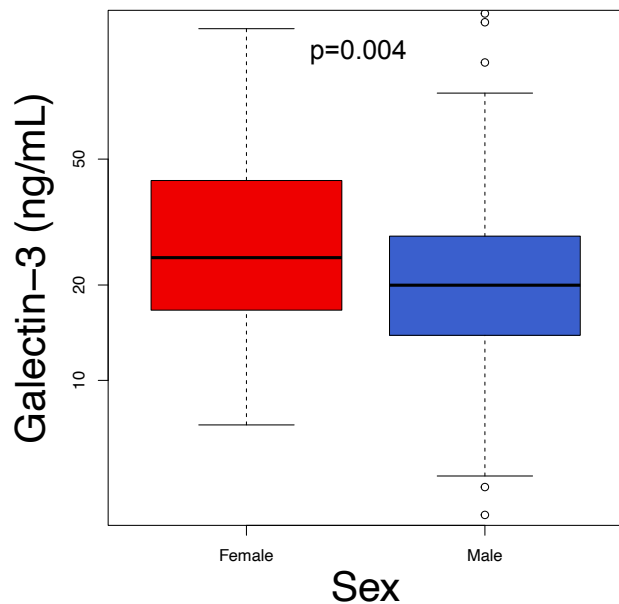
inflammation

FULL COHORT - OTHER TRENDS

- **Age:**
 - positive correlation with **NT-proBNP**, **TnT**, **GDF-15** (acute and stabilized phases)
- **BMI:**
 - positive correlation with **TnT**, **GDF-15**, **CRP** (stabilized phase)

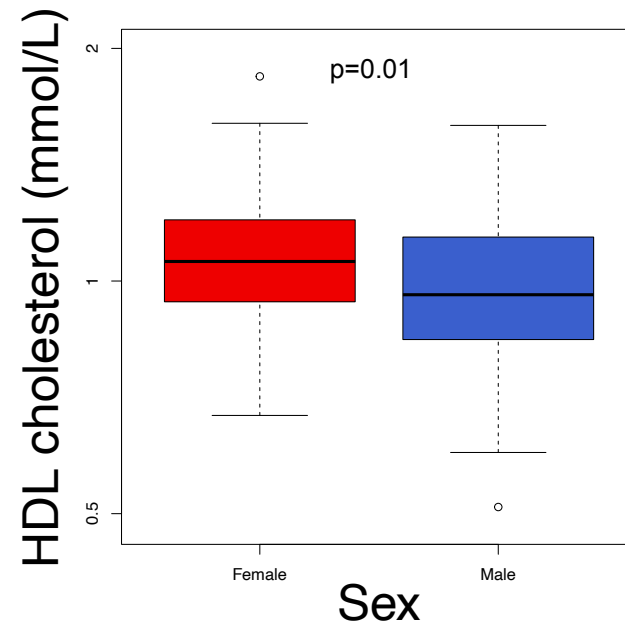
RESULTS - ACUTE PHASE - SUBCOHORT

Galectin-3



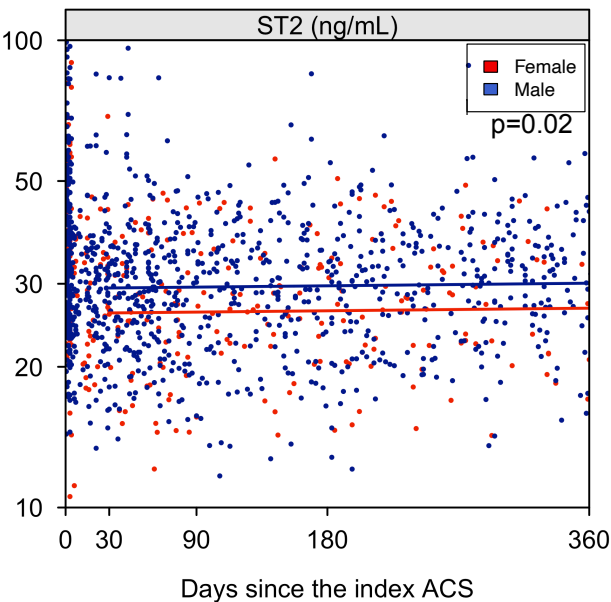
fibrosis risk & inflammation

HDL Cholesterol



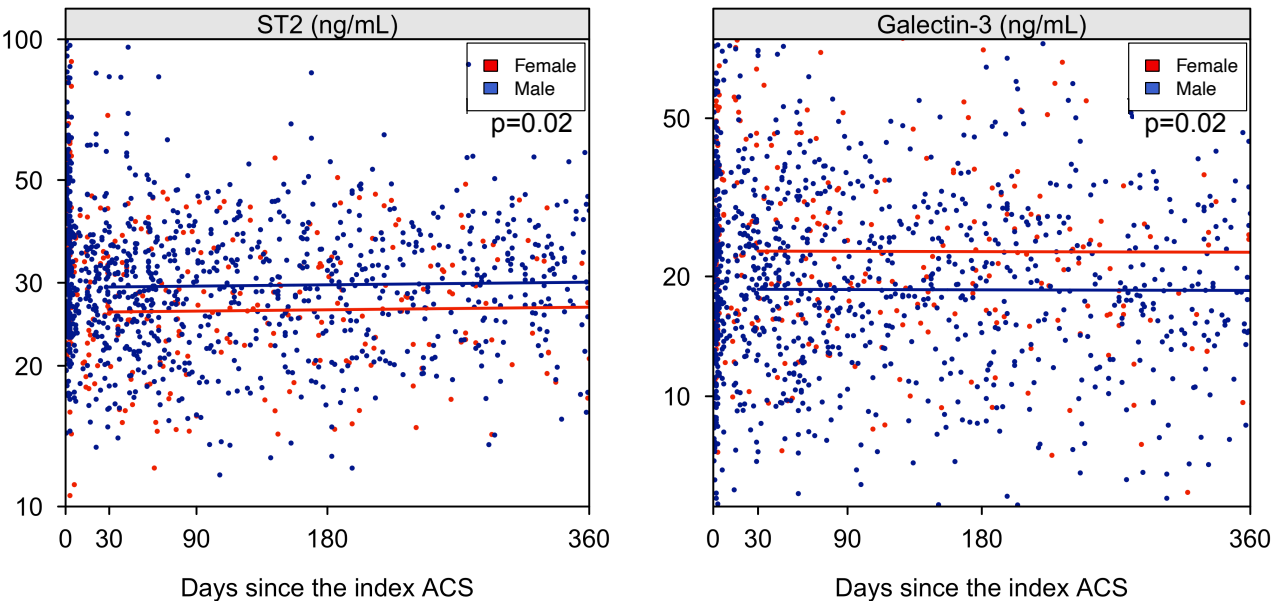
risk profile

RESULTS - STABILIZED PHASE - SUB COHORT



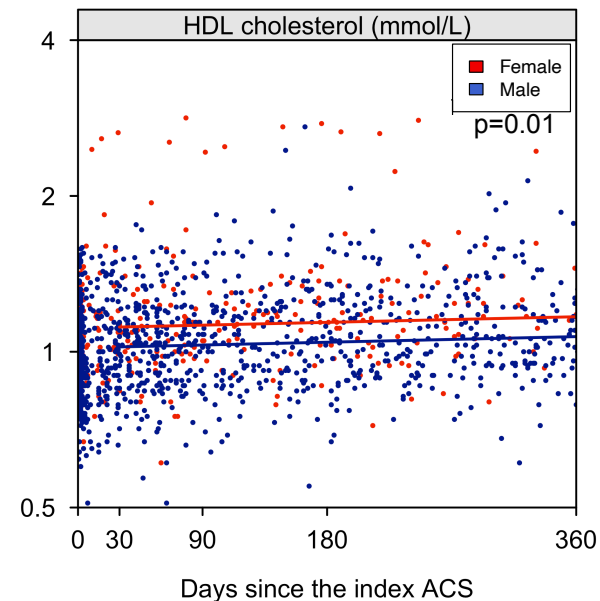
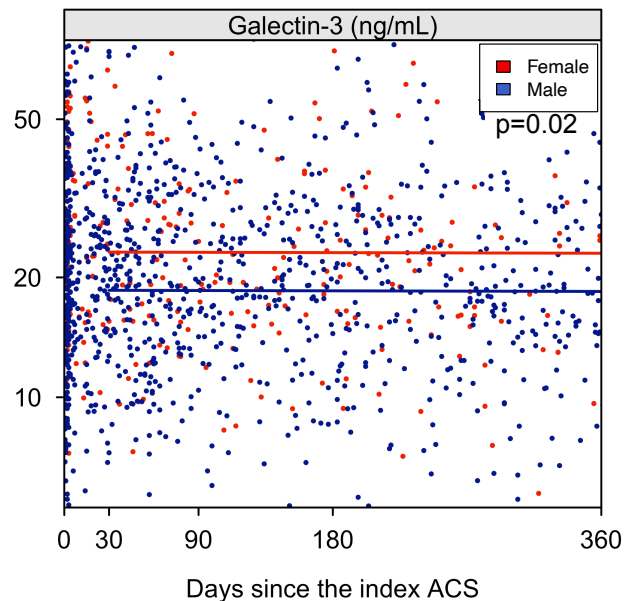
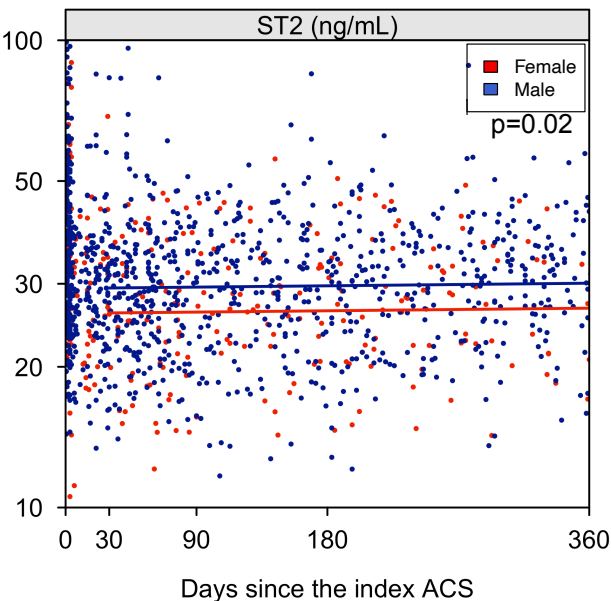
fibrosis risk & inflammation

RESULTS - STABILIZED PHASE - SUB COHORT



fibrosis risk & inflammation

RESULTS - STABILIZED PHASE - SUB COHORT



fibrosis risk & inflammation

risk profile

SUBCOHORT - OTHER TRENDS

- **BMI**: pos. correlated with **Gal-3**
- **Age**: pos. correlated with **TnI**, **ST2**, **HDL**
- **Kidney function** (eGFR): pos. correlated with **LDL**, **HDL**, **Cholesterol**

SUMMARY & OUTLOOK

- Biomarker trajectories after ACS differ only slightly by sex
- Sex differences in biomarker levels reflecting
 - cardiac damage (troponin),
 - heart failure risk (NT-proBNP),
 - fibrosis (ST-2, Gal-3),
 - inflammation (CRP, Gal-3)

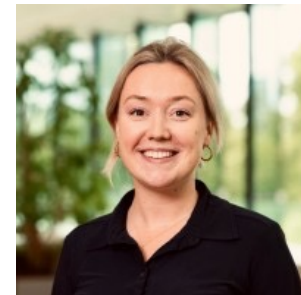
SUMMARY & OUTLOOK

- Biomarker trajectories after ACS differ only slightly by sex
- Sex differences in biomarker levels reflecting
 - cardiac damage (troponin),
 - heart failure risk (NT-proBNP),
 - fibrosis (ST-2, Gal-3),
 - inflammation (CRP, Gal-3)
- ➔ sex differences in repair and development of complications after myocardial infarction
- ➔ sex-specific therapy and follow-up regimens in order to prevent complications and improve outcomes

ACKNOWLEDGMENTS

Epidemiology & Cardiology Group Erasmus MC

- Jeanine Roeters van Lennep
- Eric Boersma
- Marte van der Bijl



Bioinformatics Group, Leipzig

- Peter F. Stadler
- Stephan H. Bernhart





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THANK YOU!



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