Herz-Kreislauf-Gesundheit bei Frauen:

Neue Aspekte und aktuelle Herausforderungen

4. Bundeskonferenz Frauengesundheit der Bundeszentrale für gesundheitliche Aufklärung und des Bundesministeriums für Gesundheit

Bundesministerium für Gesundheit

BZgA Bundeszentrale für gesundheitliche Aufklärung

Psychosoziale Aspekte: Wie wirken sich Stress, Depressionen und Erschöpfung auf die Herz-Kreislauf-Gesundheit von Frauen aus?

Prof. Dr. Karl-Heinz Ladwig,

Klinik für Psychosomatische Medizin und Psychotherapie der TUM

DIE DEUTSCHEN UNIVERSITÄTSKLINIKA

Klinikum rechts der Isar Technische Universität München

Prolog

Männlich und weiblich ist die erste Unterscheidung, die Sie machen, wenn Sie mit einem anderen menschlichen Wesen zusammentreffen, und Sie sind gewohnt, diese Unterscheidung mit unbedenklicher Sicherheit zu machen. Die anatomische Wissenschaft teilt Ihre Sicherheit in einem Punkt und nicht weit darüber hinaus (….). Kann es vielleicht die Psychologie?

S. Freud GW XV, S. 120f

…die langen Jahre vor der Herz-Erkrankung

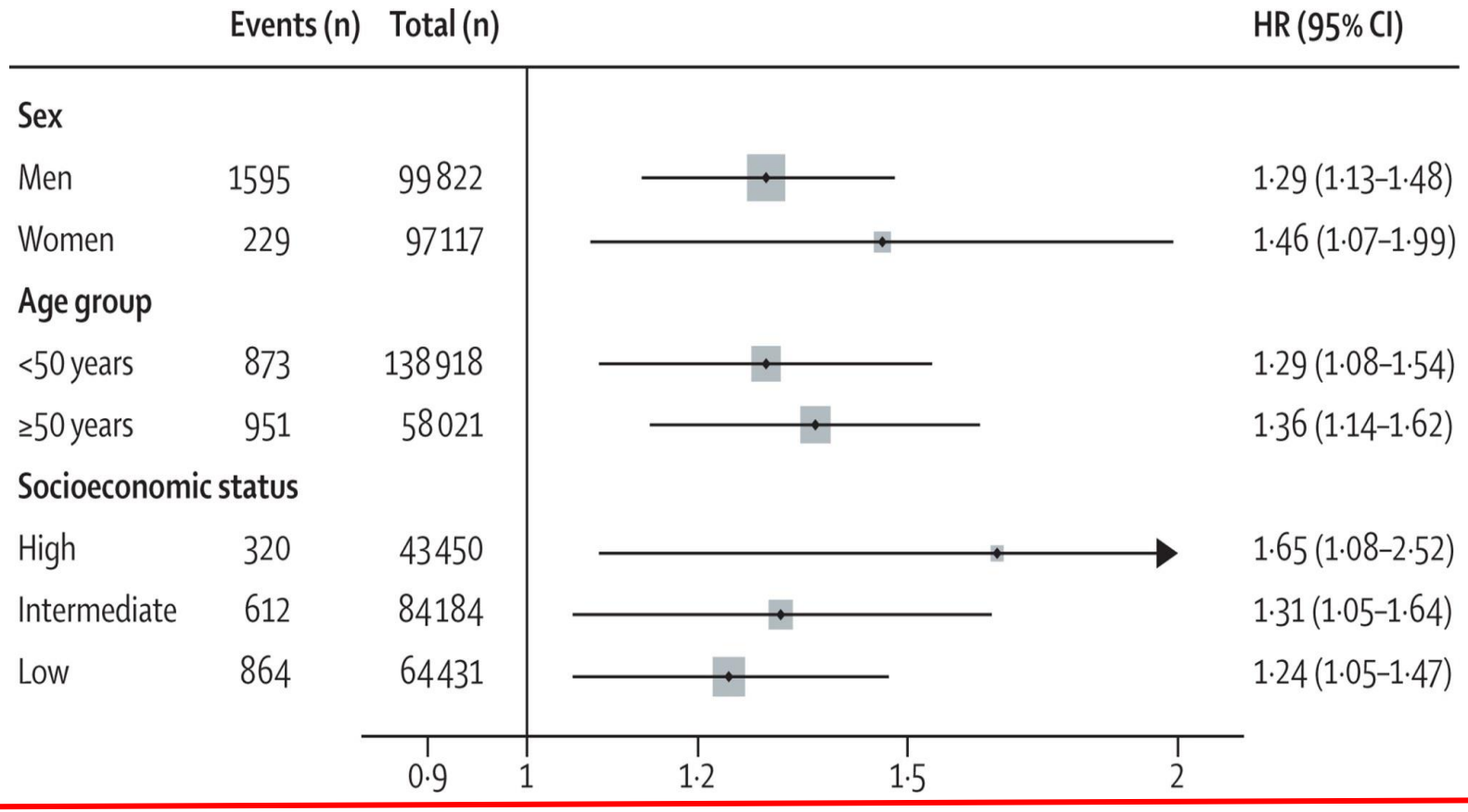
Klassifikationsschema von psychosozialen Risikofaktoren für die Entstehung einer koronaren Herzerkrankung

		1	2	3
		Chronisch langandauernde Risikokonstellationen	**Episodische Risikokonstellationen**	**Akute Stressexposition**
A	Soziale Umgebung	Aversive frühkindliche Kindheitserfahrungen, Niedriger sozialer Status (z.B. Ausbildungsjahre, Haushaltseinkommen)	Partnerschaftsstress, Arbeitsstress, Mangelnde soziale Unterstützung (soziale Isolation)	Lebensereignisse, Traumata Verlust des Arbeitsplatzes
B	Persönlichkeitsfaktoren	(Typ-A-Verhaltenstyp) Ärgerbereitschaft, Feindseligkeit, Typ-D-Verhalten		
C	Negative Affektivität	Depressivität, Ängstlichkeit	Vitale Erschöpfung, Burn-out, Depressive Episode, Hoffnungslosigkeit Posttraumatische Belastungsstörung	Akute Stressreaktion, Trauer um nahestehende Angehörige/Parnter

Job strain as a risk factor for coronary heart disease: a collaborative meta-analysis of individual participant data

Mika Kivimäki, Solja T Nyberg, G David Batty, Eleonor I Fransson, Katriina Heikkilä, Lars Alfredsson, Jakob B Bjorner, Marianne Borritz, Hermann Burr, Annalisa Casini, Els Clays, Dirk De Bacquer, Nico Dragano, Jane E Ferrie, Goedele A Geuskens, Marcel Goldberg, Mark Hamer, Wendela E Hooftman, Irene L Houtman, Matti Joensuu, Markus Jokela, France Kittel, Anders Knutsson, Markku Koskenvuo, Aki Koskinen, Anne Kouvonen, Meena Kumari, Ida E H Madsen, Michael G Marmot, Martin L Nielsen, Maria Nordin, Tuula Oksanen, Jaana Pentti, Reiner Rugulies, Paula Salo, Johannes Siegrist, Archana Singh-Manoux, Sakari B Suominen, Ari Väänänen, Jussi Vahtera, Marianna Virtanen, Peter J M Westerholm, Hugo Westerlund, Marie Zins, Andrew Steptoe, Töres Theorell, for the IPD-Work Consortium

Findings 30 214 (15%) of 197 473 participants reported job strain. In 1·49 million person-years at risk (mean follow-up 7·5 years [SD 1·7]), we recorded 2358 events of incident coronary heart disease. After adjustment for sex and age, the hazard ratio for job strain versus no job strain was 1·23 (95% CI 1·10–1·37). This effect estimate was higher in published (1·43, 1·15–1·77) than unpublished (1·16, 1·02–1·32) studies. Hazard ratios were likewise raised in analyses addressing reverse causality by exclusion of events of coronary heart disease that occurred in the first 3 years (1·31, 1·15–1·48) and 5 years (1·30, 1·13–1·50) of follow-up. We noted an association between job strain and coronary heart disease for sex, age groups, socioeconomic strata, and region, and after adjustments for socioeconomic status, and lifestyle and conventional risk factors. The population attributable risk for job strain was 3·4%.



- **197.473 Teilnehmer**
- **7,5 Jahre Nachbeobachtungszeitraum**
- **2.358 KHK Ereignisse**

Lancet 2012; 380: 1491–97

Kristina Orth-Gomér, Sarah P. Wamala, Myriam Horsten, Karin Schenck-Gustafsson, Neil Schneiderman, Murray A. Mittleman

Marital Stress Worsens Prognosis in Women With Coronary Heart Disease: The Stockholm Female Coronary Risk Study.

Table 4. Work Stress and Marital Stress in Relation to Prognosis in Women With Coronary Heart Disease

Factor	No. of Women	No. of Events	No. of Person-Years	Age-Adjusted Hazard Ratio (95% Confidence Interval)	Multivariate-Adjusted Hazard Ratio (95% Confidence Interval)*
Marital stress†					
Mild or absent	59	8	273.17	1	1
Moderate	51	17	210.28	2.68 (1.15-6.20)	2.79 (1.18-6.60)
Severe	77	27	300.08	3.02 (1.37-6.65)	2.92 (1.30-6.54)
P value				.007	.01
Work stress‡					
Mild or absent	32	7	150.88	1	1
Moderate	33	10	135.85	1.53 (0.58-4.02)	1.33 (0.43-4.10)
Severe	65	21	251.87	1.69 (0.72-3.98)	1.67 (0.64-4.32)
P value				.24	.27

*Adjusted for age, estrogen status, educational level, diagnosis at index event, symptoms of heart failure, systolic blood pressure, diabetes mellitus, smoking, triglyceride level, and high-density lipoprotein cholesterol level.
†Marital stress was defined as mild or absent (lowest quartile, scores 0-1), moderate (second quartile, scores 2-3), and severe (upper 2 quartiles, scores >3).
‡Work stress was defined as mild or absent (lowest quartile, scores 0-0.59), moderate (second quartile, scores 0.60-0.73), and severe (upper 2 quartiles, scores >0.73).

Koronar-Risiko von Frauen:

- **Bei schwerwiegendem Ehezerwürfnis: OR 2.92, 95% CI 1.30 – 6.54**
- **Bei massivem Arbeitsstress: OR 1.67, 95% CI 0.64-4.32**

JAMA , 2000; 284 (23):3008-3014.

Marital Status, Marital Strain, and Risk of Coronary Heart Disease or Total Mortality: The Framingham Offspring Study

Elaine D. Eaker, ScD, Lisa M. Sullivan, PhD, Margaret Kelly-Hayes, EdD, RN, Ralph B. D'Agostino, Sr, PhD, and Emelia J. Benjamin, MD, ScM

Objective: To determine if marriage and marital strain are related to the 10-year coronary heart disease (CHD) incidence or total mortality. Research has demonstrated associations between marital strain and prognosis of heart disease, but little research has addressed the association between specific aspects of marital strain and incident CHD. **Methods:** From 1984 to 1987, 3682 participants (mean age 48.5 ± 10.1 (standard deviation) years; 52% women) of the Framingham Offspring Study were examined; measures of marital status, marital strain, and risk factors for CHD were collected at the baseline examination. The present study describes the 10-year follow-up for incident CHD and total mortality. **Results:** After adjusting for age, systolic blood pressure, body mass index, cigarette smoking, diabetes, and total cholesterol/high density cholesterol, the married men compared with unmarried men were almost half as likely to die during follow-up (hazard ratio (HR) = 0.54; 95% confidence interval (CI): 0.34–0.83). Women who "self-silenced" during conflict with their spouse, compared with women who did not, had four times the risk of dying (HR = 4.01; 95% CI: 1.75–9.20). Men with wives who were upset by work were 2.7 times more likely to develop CHD (HR = 2.71; 95% CI: 1.22–6.03). Marital happiness, satisfaction, and disagreements were not related to the development of CHD or death in men or women. **Conclusions:** Our study suggests that marital communication, conflict, and strain are associated with health outcomes. Further research into the influence of marital stress on health is merited. **Key words:** coronary heart mortality, cohort study, marital strain, epidemiology.

- 3682 Teilnehmer; 52% Frauen, 48,5 Jahre Durchschnittsalter, Bevölkerungsstudie
- 10 Jahres-Nachverfolgung
- Koronare Herzerkrankung und Gesamtmortalität Endpunkte der Untersuchung
- Kommunikation, Konfliktumgang und Anspannung mit Gesundheitsproblemen assoziiert

Women who "self-silenced" during conflict with their spouse, compared with women who did not, had four times the risk of dying (HR = 4.01; 95% CI: 1.75–9.20). Men with wives who were upset by work were 2.7 times more likely to develop CHD (HR = 2.71; 95% CI: 1.22–6.03). Marital happiness, satisfaction, and disagreements were not related to the development of CHD or death

	Coronary Heart Disease		Total Mortality	
	Men	Women	Men	Women
Event numbers/persons at risk	126/1680	47/1895	175/1769	92/1913
All participants, RR (95% CI)				
Married versus not married	0.92 (0.51–1.65)	0.85 (0.43–1.70)	0.54 (0.35,0.83)*	1.04 (0.62–1.74)
Married participants, RR (95% CI)				
Conflict with spouse (referent = always show it)				
Usually show it	0.69 (0.43–1.10)	1.16 (0.47–2.85)	0.79 (0.53–1.19)	1.77 (0.76–4.09)
Usual/Always keep to self	0.89 (0.54–1.47)	1.29 (0.48–3.50)	0.87 (0.56–1.36)	4.01 (1.75–9.20)*
Spouse show's love for you (referent = very often)	1.00 (0.58–1.72)			
Seldom	0.96 (0.54–1.71)	1.12 (0.43–2.92)	1.01 (0.62–1.63)	0.93 (0.41–2.11)
Not enough/not love		0.59 (0.18–2.01)	1.06 (0.65–1.71)	1.57 (0.83–2.96)
Married men with an employed wife, RR (95% CI)				
How is your wife's work disruptive?	2.71 (1.22–6.03)*		1.39 (0.72–2.71)	
She gets upset with work (yes versus no)				

Women, Loneliness, and Incident Coronary Heart Disease

Rebecca C. Thurston, PhD, and Laura D. Kubzansky, PhD, MPH

Objective: To examine associations between loneliness and risk of incident coronary heart disease (CHD) over a 19-year follow-up period in a community sample of men and women. Loneliness, the perceived discrepancy between actual and desired social relationships, has been linked to several adverse health outcomes. However, no previous research has prospectively examined the association between loneliness and incident CHD in a community sample of men and women. **Methods:** Hypotheses were examined using data from the First National Health and Nutrition Survey and its follow-up studies (n = 3003). Loneliness, assessed by one item from the Center for Epidemiologic Studies of Depression scale, and covariates were derived from baseline interviews. Incident CHD was derived from hospital records/death certificates over 19 years of follow-up. Hypotheses were evaluated, using Cox proportional hazards models. **Results:** Among women, high loneliness was associated with increased risk of incident CHD (high: hazard ratio = 1.76, 95% Confidence Interval = 1.17–2.63; medium: hazard ratio = 0.98, 95% Confidence Interval = 0.64–1.49; reference: low), controlling for age, race, education, income, marital status, hypertension, diabetes, cholesterol, physical activity, smoking, alcohol use, systolic and diastolic blood pressures, and body mass index. Findings persisted additionally controlling for depressive symptoms. No significant associations were observed among men. **Conclusions:** Loneliness was prospectively associated with increased risk of incident CHD, controlling for multiple confounding factors. Loneliness among women may merit clinical attention, not only due to its impact on quality of life but also its potential implications for cardiovascular health. **Key words:** coronary heart disease, cardiovascular disease, gender, women, loneliness, depression.

	Women (n = 1466)			Men (n = 1150)		
	Model 1[a] HR (95% CI)	Model 2[b] HR (95% CI)	Model 3[c] HR (95% CI)	Model 1[a] HR (95% CI)	Model 2[b] HR (95% CI)	Model 3[c] HR (95% CI)
Loneliness						
Low		—	—	—	—	—
Medium	1.06 (0.71–1.59)	0.98 (0.64–1.49)	1.01 (0.65–1.57)	0.78 (0.46–1.33)	0.85 (0.50–1.47)	0.81 (0.46–1.42)
High	2.11 (1.43–3.12)	1.76 (1.17–2.63)	1.87 (1.19–2.94)	0.98 (0.50–1.92)	0.93 (0.47–1.85)	0.88 (0.43–1.78)

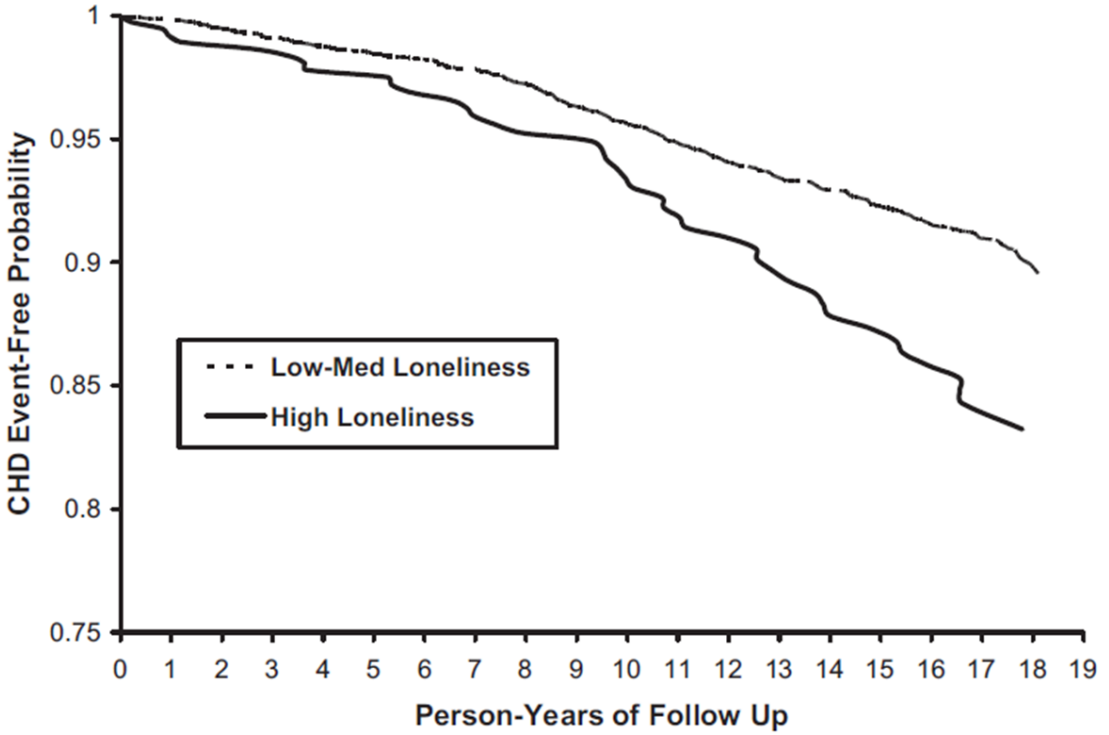


Figure 1. Loneliness and incident CHD, adjusted for age, race, and gender. CHD, coronary heart disease.

- 3.003 Teilnehmer, 1.466 Frauen; 1150 Männer;
- Fragebogenstudie
- 19 Jahre Nachverfolgungszeitraum

Wassertheil-Smoller S. et al.
Archives Internal Medicine 2004, 164: 289-298

Risikofaktor Depression

- **93,676 Frauen**
- **Follow-up von 4.1 Jahren**
- **15.8% depressive Symptome**
- **RR für KHK 1.50; RR für Gesamtmortalität 1.32**
- ***adjustiert für*: Alter, Ausbildung, Einkommen, Diabetes, Bluthochdruck, Rauchen, Cholesterin, BMI, körperliche Bewegung**

Depression and Cardiovascular Sequelae in Postmenopausal Women

The Women's Health Initiative (WHI)

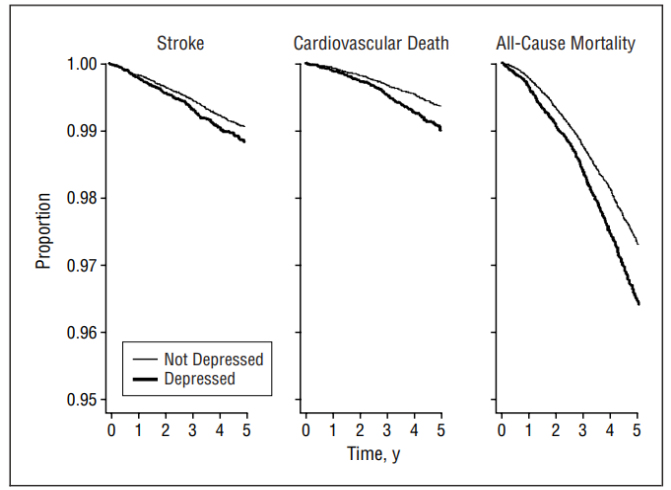
Sylvia Wassertheil-Smoller, PhD; Sally Shumaker, PhD; Judith Ockene, PhD; Greg A. Talavera, MD, MPH; Philip Greenland, MD; Barbara Cochrane, RN, PhD; John Robbins, MD; Aaron Aragaki, MS; Jacqueline Dunbar-Jacob, PhD, RN

Methods: The Women's Health Initiative Observational Study followed up 93 676 women for an average of 4.1 years. Depression was measured at baseline with a short form of the Center for Epidemiological Studies Depression Scale. Risks of cardiovascular disease (CVD) events were estimated from Cox proportional hazards models adjusting for multiple demographic, clinical, and risk factor covariates.

Results: Current depressive symptoms above the screening cutoff point were reported by 15.8% of women. Depression was significantly related to CVD risk and comorbidity (odds ratios ranging from 1.12 for hypertension to 1.60 for history of stroke or angina). Among women with no history of CVD, depression was an independent predictor of CVD death (relative risk, 1.50) and all-cause mortality (relative risk, 1.32) after adjustment for age, race, education, income, diabetes, hypertension, smoking, high cholesterol level requiring medication, body mass index, and physical activity. Taking antidepressant medications did not alter the depression-associated risks associated.

Table 3. History of CVD Events and Adjusted Odds Ratios for Current Depression

Variable	No. of Subjects	Baseline Current Depression OR*	(95% CI)
Angina ever			
No	88 863	1.00	
Yes	4372	1.57	(1.45-1.70)
Peripheral arterial disease ever			
No	91 740	1.00	
Yes	1467	1.60	(1.41-1.82)
Cardiovascular disease ever			
No	73 098	1.00	
Yes, any	18 572	1.41	(1.35-1.47)
Myocardial infarction	2306	1.45	(1.30-1.62)
Stroke	1415	1.60	(1.39-1.83)
Atrial fibrillation	4397	1.48	(1.36-1.60)
Cardiac catherterization	3837	1.41	(1.29-1.54)
Angioplasty of coronary arteries ever	1128	1.57	(1.34-1.82)
Coronary bypass surgery ever	881	1.28	(1.07-1.54)
Carotid endartarectomy/angioplasty	344	1.50	(1.13-1.99)
CHF	892	1.63	(1.38-1.93)
Aortic aneurysm	187	1.84	(1.28-2.65)
Cardiac arrest	348	1.19	(0.89-1.59)



Survival curves for those depressed and not depressed.

- 93.676 Teilnehmerinnen
- 15,8% depressive Symptome
- 4,1 Jahre Nachbeobachtung
- 18.572 Kardiovaskuläre Ereignisse
- OR 1.41, 95% CI 1.35-1.47

…die Prodromalphase und die Zeit unmittelbar vor Ausbruch der Erkrankung

Women's Early Warning Symptoms of Acute Myocardial Infarction

Jean C. McSweeney, PhD, RN; Marisue Cody, PhD, RN; Patricia O'Sullivan, EdD;
Karen Elberson, PhD, RN; Debra K. Moser, DNSc, RN; Bonnie J. Garvin, PhD, RN

Background—Data remain sparse on women's prodromal symptoms before acute myocardial infarction (AMI). This study describes prodromal and AMI symptoms in women.

Methods and Results—Participants were 515 women diagnosed with AMI from 5 sites. Using the McSweeney Acute and Prodromal Myocardial Infarction Symptom Survey, we surveyed them 4 to 6 months after discharge, asking about symptoms, comorbidities, and demographic characteristics. Women were predominantly white (93%), high school educated (54.8%), and older (mean age, 66±12), with 95% (n=489) reporting prodromal symptoms. The most frequent prodromal symptoms experienced more than 1 month before AMI were unusual fatigue (70.7%), sleep disturbance (47.8%), and shortness of breath (42.1%). Only 29.7% reported chest discomfort, a hallmark symptom in men. The most frequent acute symptoms were shortness of breath (57.9%), weakness (54.8%), and fatigue (42.9%). Acute chest pain was absent in 43%. Women had more acute (mean, 7.3±4.8; range, 0 to 29) than prodromal (mean, 5.71±4.36; range, 0 to 25) symptoms. The average prodromal score, symptom weighted by frequency and intensity, was 58.5±52.7, whereas the average acute score, symptom weighted by intensity, was 16.5±12.1. These 2 scores were correlated (r=0.61, P<0.001). Women with more prodromal symptoms experienced more acute symptoms. After controlling for risk factors, prodromal scores accounted for 33.2% of acute symptomatology.

Conclusions—Most women have prodromal symptoms before AMI. It remains unknown whether prodromal symptoms are predictive of future events. **(*Circulation*. 2003;108:2619-2623.)**

TABLE 1. Frequency of Prodromal and Acute Symptoms (n=515)

Symptom	Prodromal Frequency, n (%)	Acute Frequency, n (%)
Discomfort/pain		
General chest	67 (13.0)	102 (19.8)
Centered high in chest	74 (14.4)	157 (30.5)
Left breast	48 (9.3)	76 (14.8)
Neck/throat	38 (7.4)	84 (16.3)
Jaw/teeth	23 (4.5)	49 (9.5)
Back/between or under shoulder blades	67 (13.0)	109 (21.2)
Top of shoulders	26 (5.0)	52 (10.1)
Both arms	28 (5.4)	63 (12.2)
Left arm/shoulder	61 (11.8)	112 (21.7)
Right arm/shoulder	12 (2.3)	24 (4.7)
Leg(s)	18 (3.5)	7 (1.4)
General symptoms		
Cold sweat*	...	201 (39.0)
Hot/flushed*	...	167 (32.4)
Anxious†	183 (35.5)	...
Sleep disturbance†	246 (47.8)	...
Unusual fatigue	364 (70.7)	221 (42.9)
Weakness*	...	282 (54.8)
Cough	95 (18.4)	54 (10.5)
Heart racing	141 (27.4)	118 (22.9)
Shortness of breath	217 (42.1)	298 (57.9)
Difficulty breathing at night†	99 (19.2)	...

In der Prodromalzeit (> 1 Monat vor dem AMI):
70,7% ungewöhnliche Erschöpfung; 47,8% Schlafstörungen;
42,1 % Kurzatmigkeit

Burn-out, Neurasthenie….ICD-9/10 F 48.0

Burn-out (Neurasthenie)

erschöpft, ausgebrannt, Rückzug;
Konzentrationsschwäche;
Vergesslichkeit, erreicht mit immer mehr Energie nur noch selten den Status quo….

Compassion fatigue

Unfähigkeit, den Patienten als Person wahrzunehmen, mitfühlend zu reagieren…

European Heart Journal (2015) **36**, 1385–1393
doi:10.1093/eurheartj/ehv027

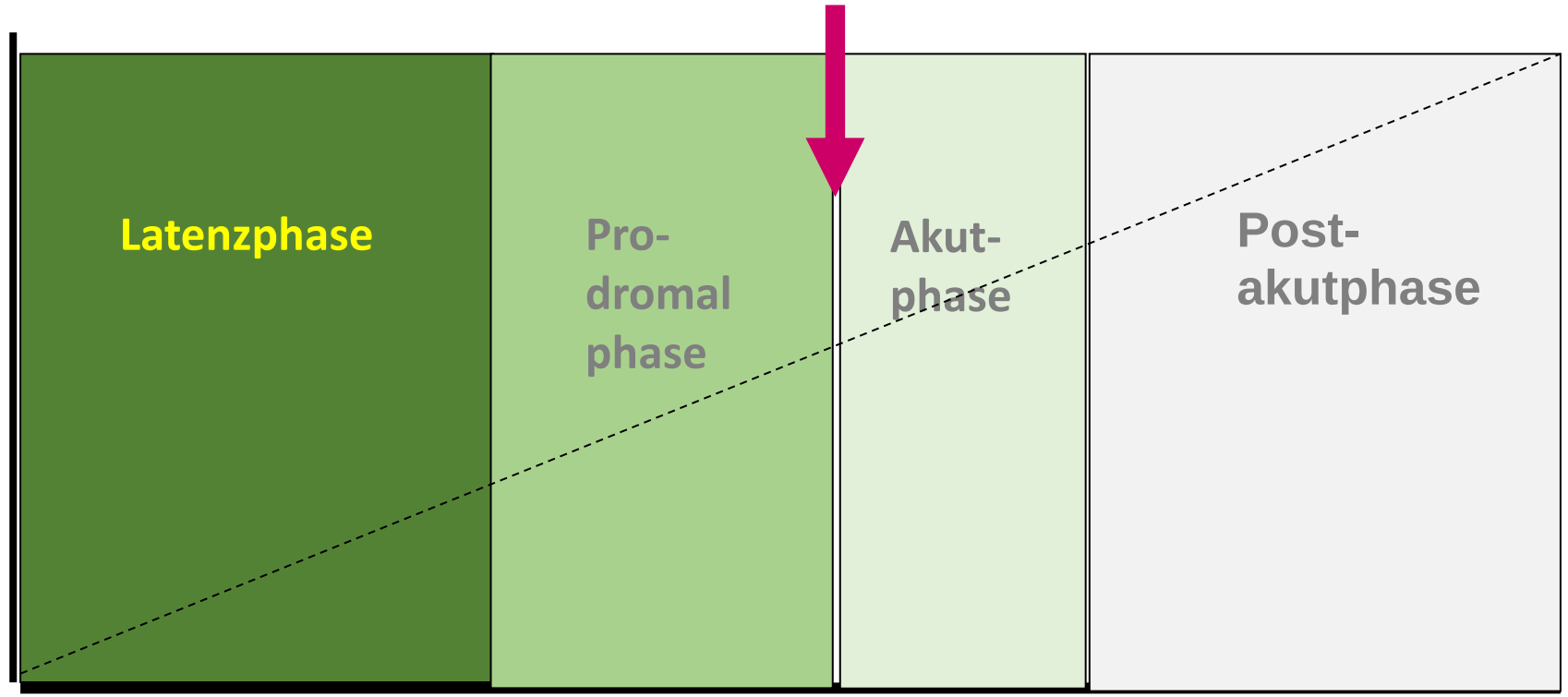
Ranking of psychosocial and traditional risk factors by importance for coronary heart disease: the Copenhagen City Heart Study

Peter Schnohr[1]*, Jacob L. Marott[1], Tage S. Kristensen[1], Finn Gyntelberg[1], Morten Grønbæk[1,2], Peter Lange[1,3], Magnus T. Jensen[1], Gorm B. Jensen[1,4], and Eva Prescott[1,5]

Methods and results

The Copenhagen City Heart Study is a prospective cardiovascular population study randomly selected in 1976. The third examination was carried out from 1991 to 1994, and 8882 men and women free of cardiovascular diseases were included in this study. Events were assessed until April 2013. Forward selection, population attributable fraction, and gradient boosting machine were used for determining ranks. The importance of vital exhaustion for risk prediction was investigated by C-statistics and net reclassification improvement. During the follow-up, 1731 non-fatal and fatal coronary events were registered. In men, the highest ranking risk factors for coronary heart disease were vital exhaustion [high vs. low; hazard ratio (HR) 2.36; 95% confidence interval (CI), 1.70–3.26; $P < 0.001$] and systolic blood pressure (≥160 mmHg or blood pressure medication vs. <120 mmHg; HR 2.07; 95% CI, 1.48–2.88; $P < 0.001$). In women, smoking was of highest importance (≥15 g tobacco/day vs. never smoker; HR 1.74; 95% CI, 1.43–2.11; $P < 0.001$), followed by vital exhaustion (high vs. low; HR 2.07; 95% CI, 1.61–2.68; $P < 0.001$). Vital exhaustion ranked first in women and fourth in men by population attributable fraction of 27.7% (95% CI, 18.6–36.7%; $P < 0.001$) and 21.1% (95% CI, 13.0–29.2%; $P < 0.001$), respectively. Finally, vital exhaustion significantly improved risk prediction.

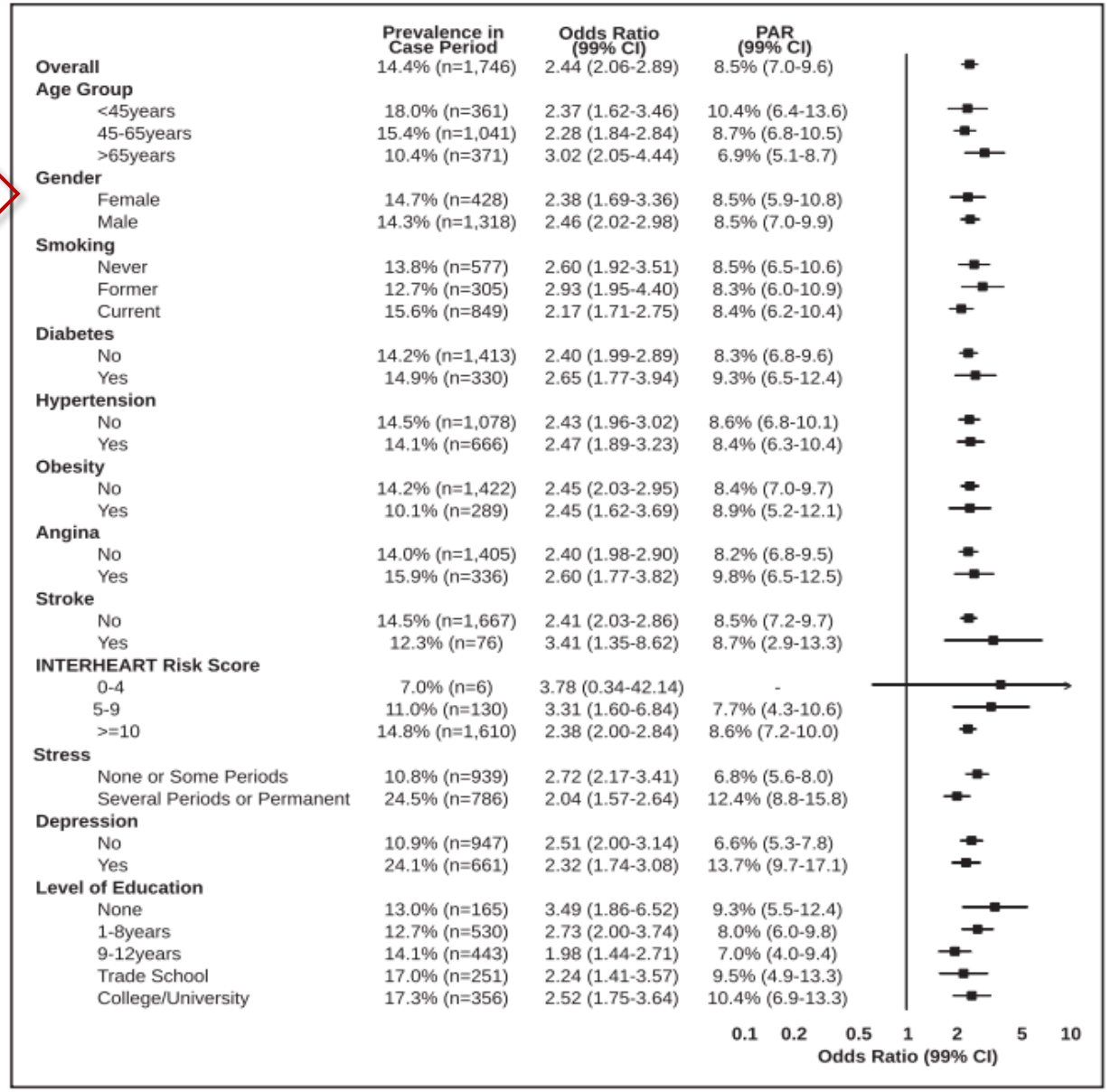
Phasenablauf der koronaren Herzerkrankung



Physical Activity and Anger or Emotional Upset as Triggers of Acute Myocardial Infarction

The INTERHEART Study

RESULTS: Of 12461 cases of AMI 13.6% (n=1650) engaged in physical activity and 14.4% (n=1752) were angry or emotionally upset in the case period (1 hour before symptom onset). Physical activity in the case period was associated with increased odds of AMI (odds ratio, 2.31; 99% confidence interval [CI], 1.96–2.72) with a population-attributable risk of 7.7% (99% CI, 6.3–8.8). Anger or emotional upset in the case period was associated with an increased odds of AMI (odds ratio, 2.44; 99% CI, 2.06–2.89) with a population-attributable risk of 8.5% (99% CI, 7.0–9.6). There was no effect modification by geographical region, prior cardiovascular disease, cardiovascular risk factor burden, cardiovascular prevention medications, or time of day or day of onset of AMI. Both physical activity and anger or emotional upset in the case period were associated with a further increase in the odds of AMI (odds ratio, 3.05; 99% CI, 2.29–4.07; *P* for interaction <0.001).



	Prevalence in Case Period	Odds Ratio (99% CI)	PAR (99% CI)
Overall	14.4% (n=1,746)	2.44 (2.06-2.89)	8.5% (7.0-9.6)
Age Group			
<45years	18.0% (n=361)	2.37 (1.62-3.46)	10.4% (6.4-13.6)
45-65years	15.4% (n=1,041)	2.28 (1.84-2.84)	8.7% (6.8-10.5)
>65years	10.4% (n=371)	3.02 (2.05-4.44)	6.9% (5.1-8.7)
Gender			
Female	14.7% (n=428)	2.38 (1.69-3.36)	8.5% (5.9-10.8)
Male	14.3% (n=1,318)	2.46 (2.02-2.98)	8.5% (7.0-9.9)
Smoking			
Never	13.8% (n=577)	2.60 (1.92-3.51)	8.5% (6.5-10.6)
Former	12.7% (n=305)	2.93 (1.95-4.40)	8.3% (6.0-10.9)
Current	15.6% (n=849)	2.17 (1.71-2.75)	8.4% (6.2-10.4)
Diabetes			
No	14.2% (n=1,413)	2.40 (1.99-2.89)	8.3% (6.8-9.6)
Yes	14.9% (n=330)	2.65 (1.77-3.94)	9.3% (6.5-12.4)
Hypertension			
No	14.5% (n=1,078)	2.43 (1.96-3.02)	8.6% (6.8-10.1)
Yes	14.1% (n=666)	2.47 (1.89-3.23)	8.4% (6.3-10.4)
Obesity			
No	14.2% (n=1,422)	2.45 (2.03-2.95)	8.4% (7.0-9.7)
Yes	10.1% (n=289)	2.45 (1.62-3.69)	8.9% (5.2-12.1)
Angina			
No	14.0% (n=1,405)	2.40 (1.98-2.90)	8.2% (6.8-9.5)
Yes	15.9% (n=336)	2.60 (1.77-3.82)	9.8% (6.5-12.5)
Stroke			
No	14.5% (n=1,667)	2.41 (2.03-2.86)	8.5% (7.2-9.7)
Yes	12.3% (n=76)	3.41 (1.35-8.62)	8.7% (2.9-13.3)
INTERHEART Risk Score			
0-4	7.0% (n=6)	3.78 (0.34-42.14)	-
5-9	11.0% (n=130)	3.31 (1.60-6.84)	7.7% (4.3-10.6)
>=10	14.8% (n=1,610)	2.38 (2.00-2.84)	8.6% (7.2-10.0)
Stress			
None or Some Periods	10.8% (n=939)	2.72 (2.17-3.41)	6.8% (5.6-8.0)
Several Periods or Permanent	24.5% (n=786)	2.04 (1.57-2.64)	12.4% (8.8-15.8)
Depression			
No	10.9% (n=947)	2.51 (2.00-3.14)	6.6% (5.3-7.8)
Yes	24.1% (n=661)	2.32 (1.74-3.08)	13.7% (9.7-17.1)
Level of Education			
None	13.0% (n=165)	3.49 (1.86-6.52)	9.3% (5.5-12.4)
1-8years	12.7% (n=530)	2.73 (2.00-3.74)	8.0% (6.0-9.8)
9-12years	14.1% (n=443)	1.98 (1.44-2.71)	7.0% (4.0-9.4)
Trade School	17.0% (n=251)	2.24 (1.41-3.57)	9.5% (4.9-13.3)
College/University	17.3% (n=356)	2.52 (1.75-3.64)	10.4% (6.9-13.3)

Figure 2. Anger or emotional upset as a trigger of acute myocardial infarction.
No significant subgroup effects (all *P* for interaction >0.01). CI indicates confidence interval; and PAR, population-attributable risk.

Circulation. 2016;134:1059–1067. DOI: 10.1161/CIRCULATIONAHA.116.023142

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Zeit ist Myokard. Zeit ist Leben. Verzögerungszeit.

Pre-hospital treatment of STEMI patients. A scientific statement of the Working Group Acute Cardiac Care of the European Society of Cardiology

Acute Coronary Syndromes
DOI:
10.3109/17482941.2011.581292

M. Tubaro[*a], N. Danchin[b], P. Goldstein[c], G. Filippatos[d], Y. Hasin[e], M. Heras[f], P. Jansky[g], T. M. Norekval[h], E. Swahn[i], K. Thygesen[j], C. Vrints[k], D. Zahger[l], H. R. Arntz[m], A. Bellou[n], J. E. de La Coussaye[o], L. de Luca[p], K. Huber[q], Y. Lambert[r], M. Lettino[s], B. Lindahl[t], S. McLean[u], L. Nibbe[v], W. F. Peacock[w], S. Price[x], T. Quinn[y], C. Spaulding[z], G. Tatu-Chitoiu[aa] & F. van de Werf

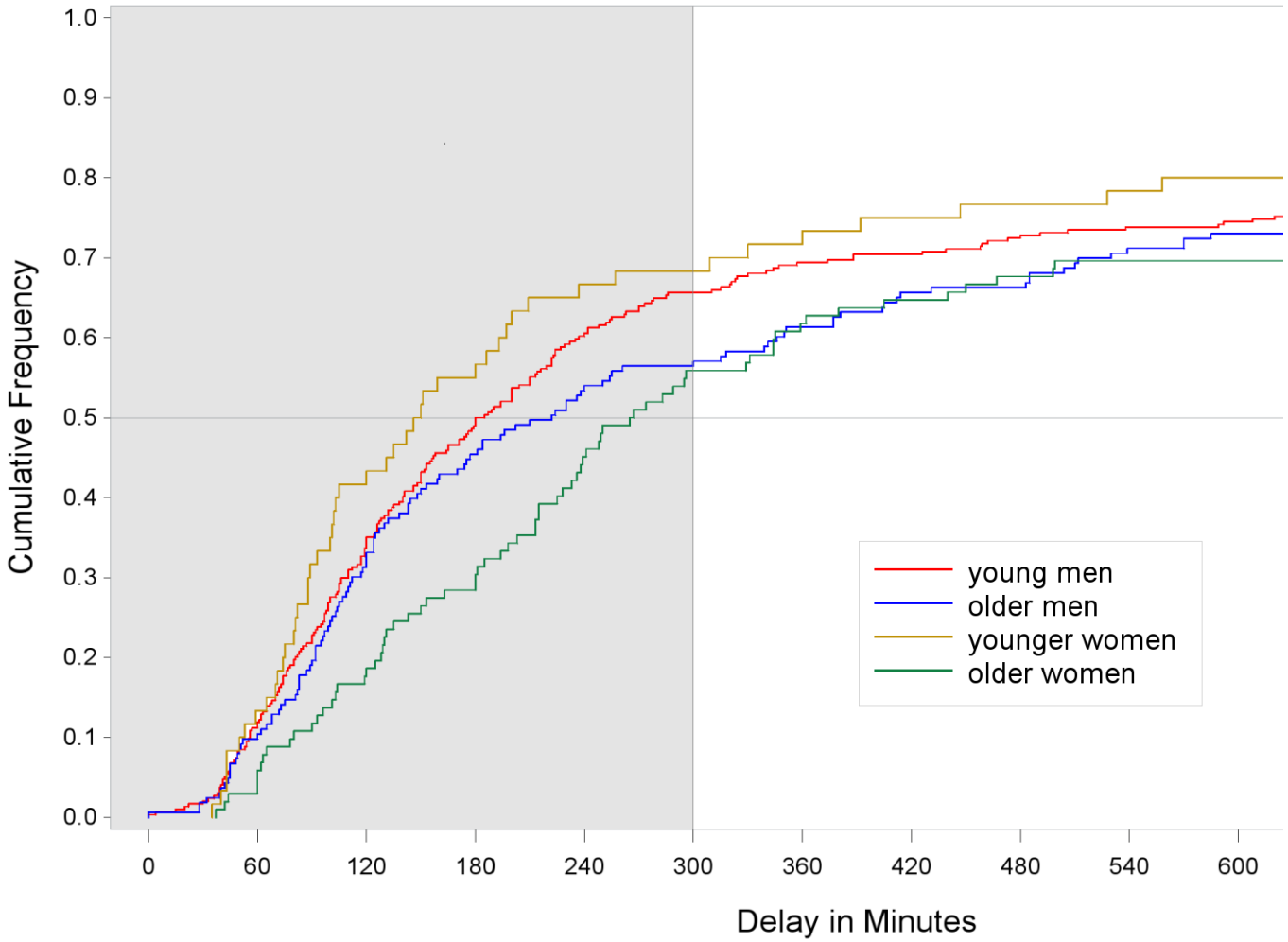
Acute Cardiac Care 2011

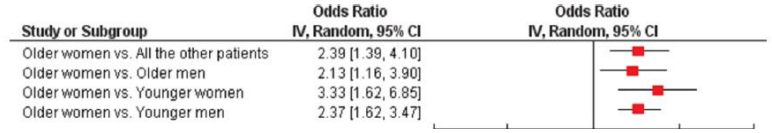
Indeed, recent guidelines of the European Society of Cardiology[9] identified the prehospital phase as the most critical in reducing mortality and reiterated that efforts must be made to reduce patient delay. In particular, people with existing coronary heart disease (CHD) are a population most at risk of experiencing an episode of ACS[10] and therefore a very important group in which to ensure prompt help-seeking.

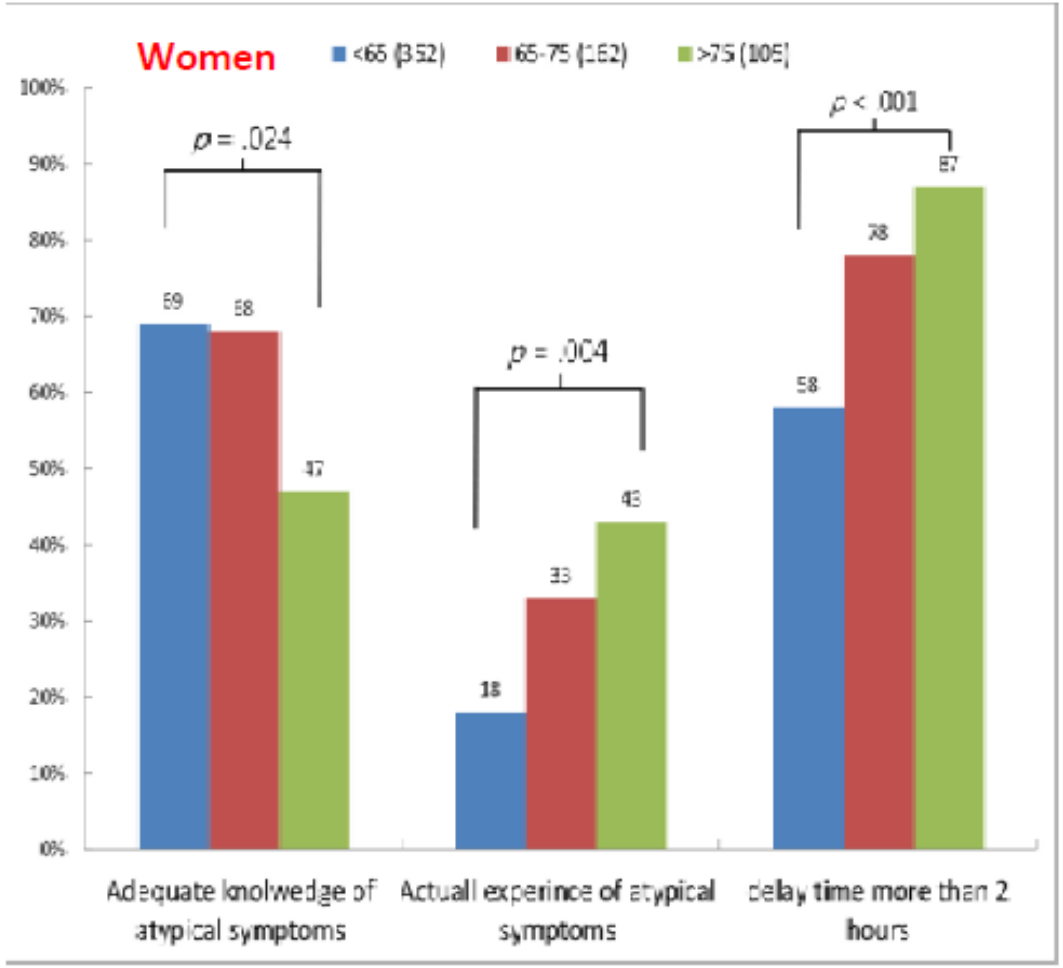
De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. Circulation 2004; 109: 1223-5

"…the risk of one-year mortality is increased by 7.5% for each 30 minutes of delay!"

Comparison of Delay Times Between Symptom Onset of an Acute ST-elevation Myocardial Infarction and Hospital Arrival in Men and Women <65 Years Versus ≥65 Years of Age.







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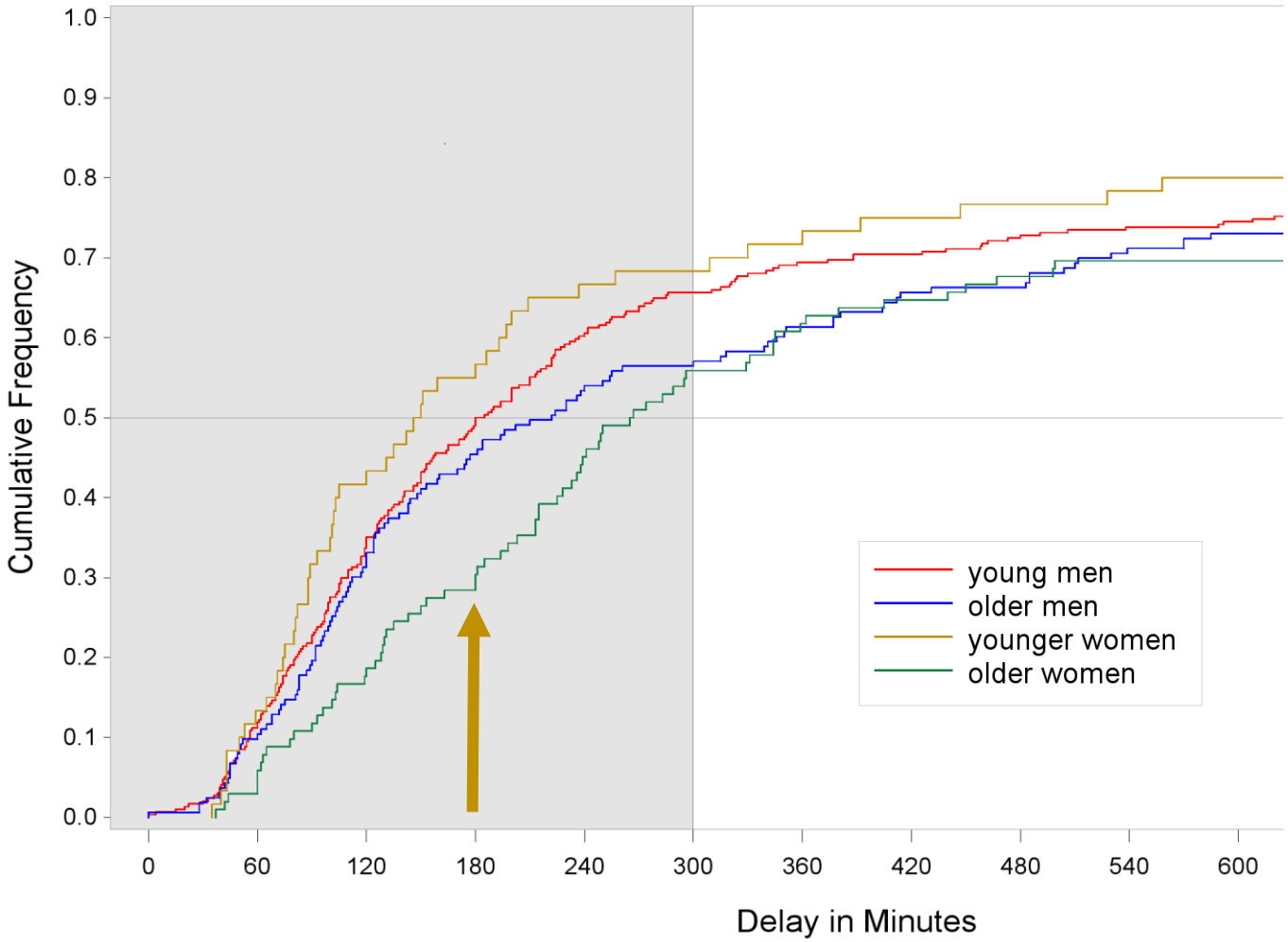
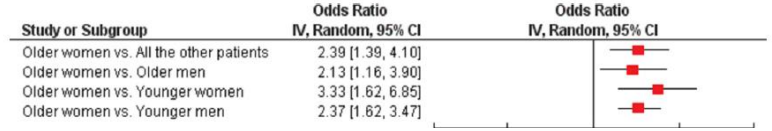
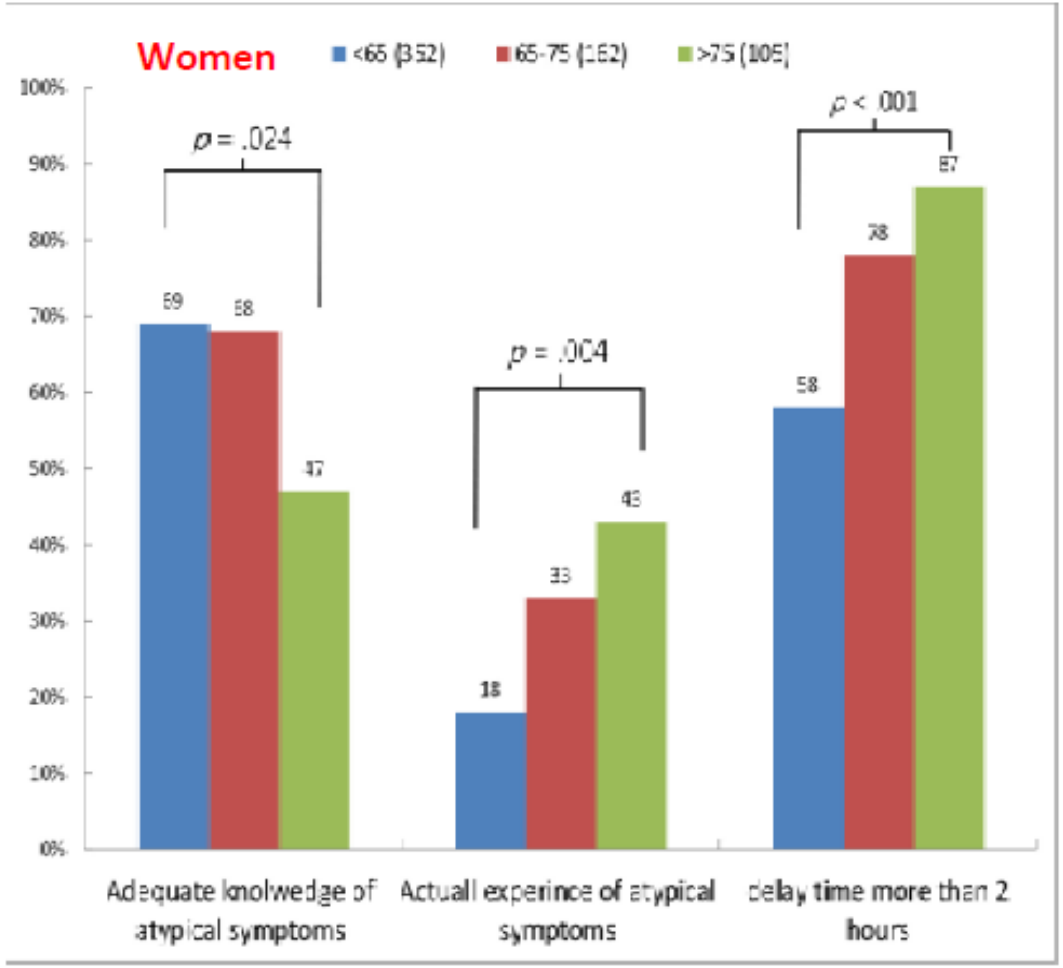
Comparison of Delay Times Between Symptom Onset of an Acute ST-elevation Myocardial Infarction and Hospital Arrival in Men and Women <65 Years Versus ≥65 Years of Age.







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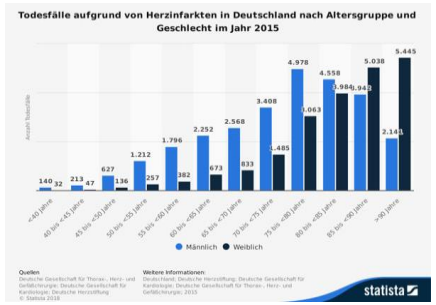
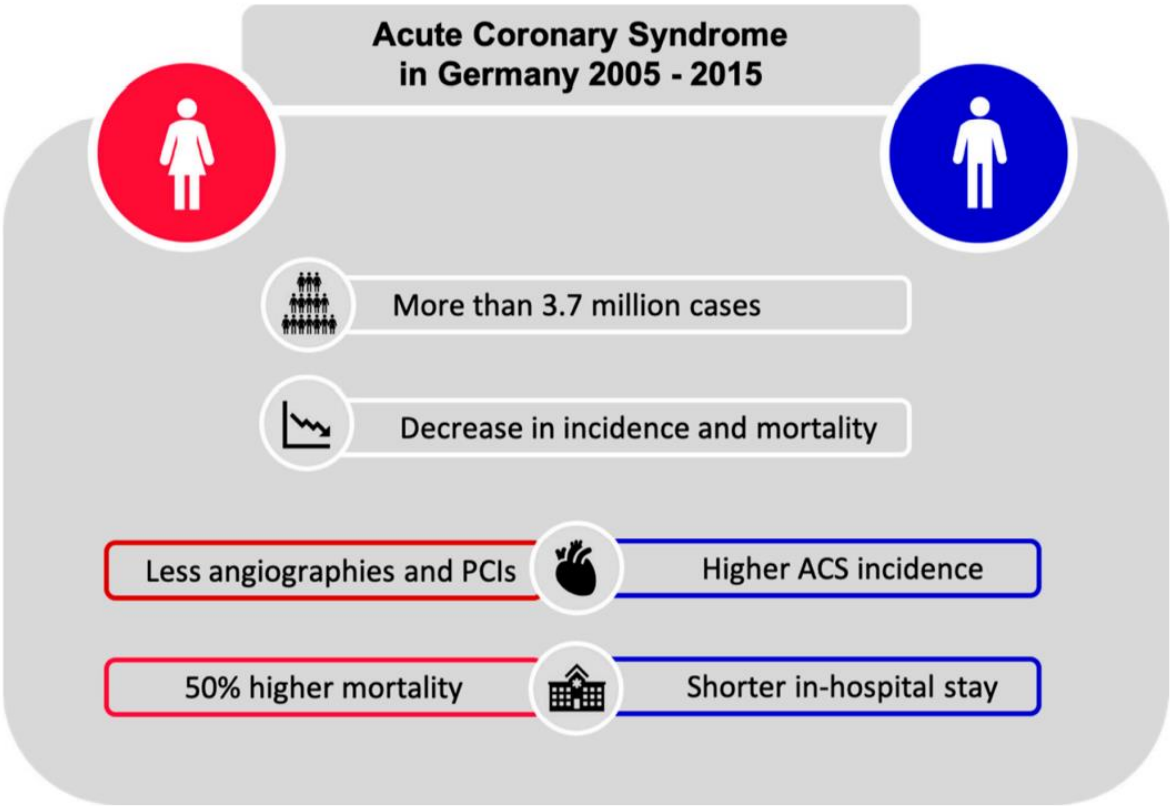
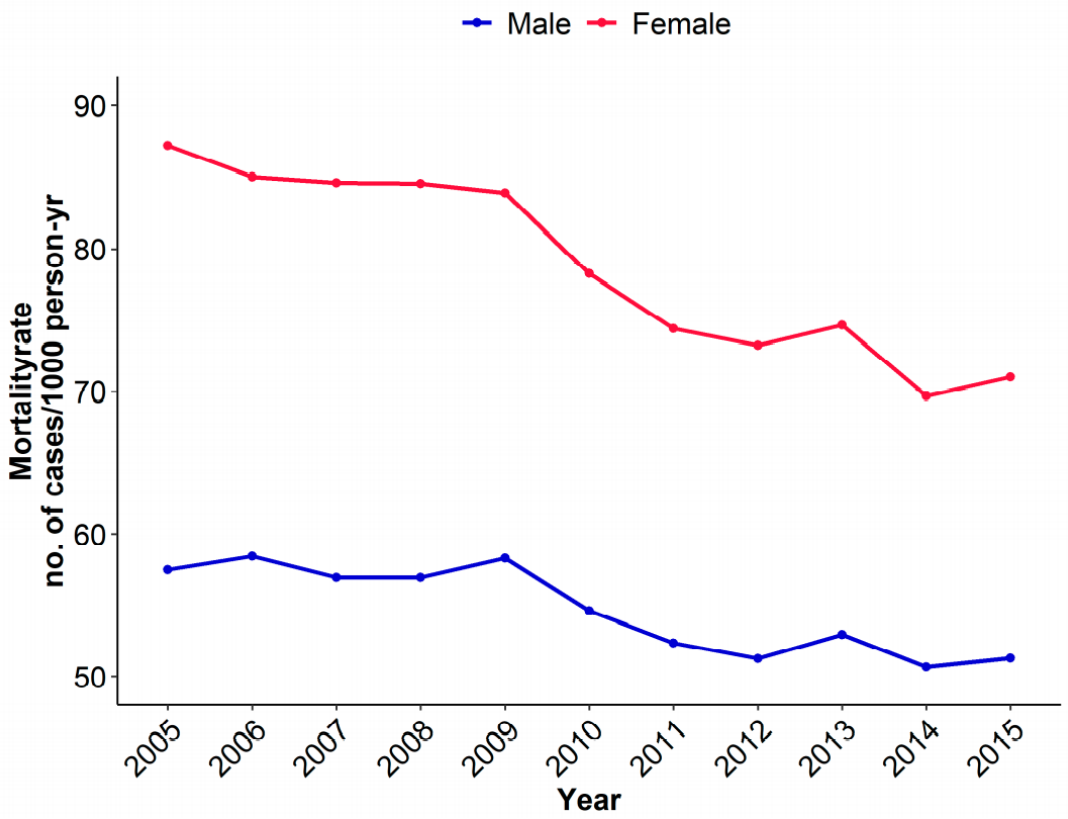
…nach Manifestwerden der Erkrankung

Sex-Specific Outcomes in Patients with Acute Coronary Syndrome

Johannes T. Neumann [1,2,3,*], Alina Goßling [1], Nils A. Sörensen [1,2], Stefan Blankenberg, Christina Magnussen [1,2] and Dirk Westermann [1,2]







J. Clin. Med. 2020, 9(7), 2124;
https://doi.org/10.3390/jcm9072124

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Technische Universität München

Depressive Symptoms After Acute Myocardial Infarction

Evidence for Highest Rates in Younger Women

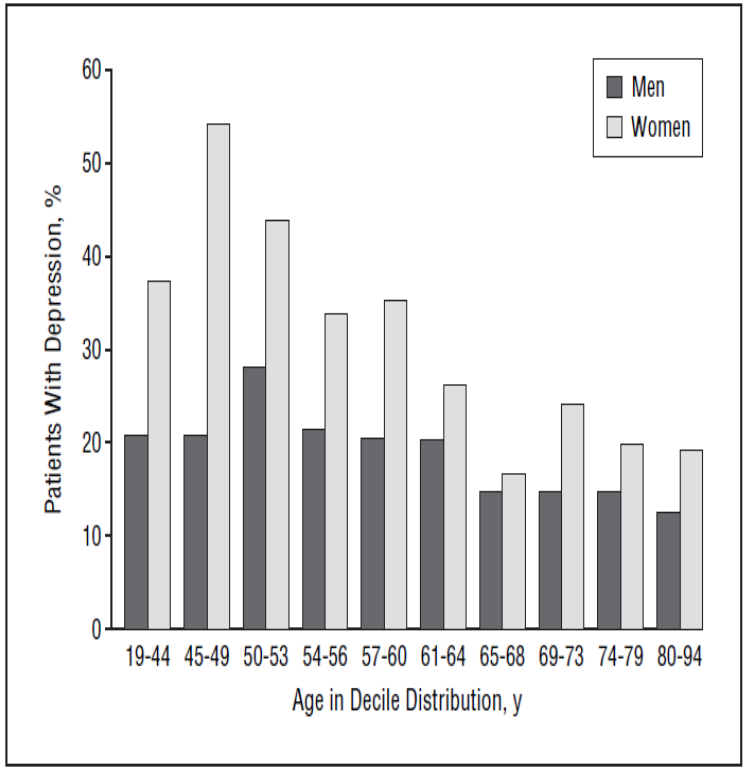


Figure 3. Distribution of depression rate by age in decile distribution (10% of data in each age range) and sex.

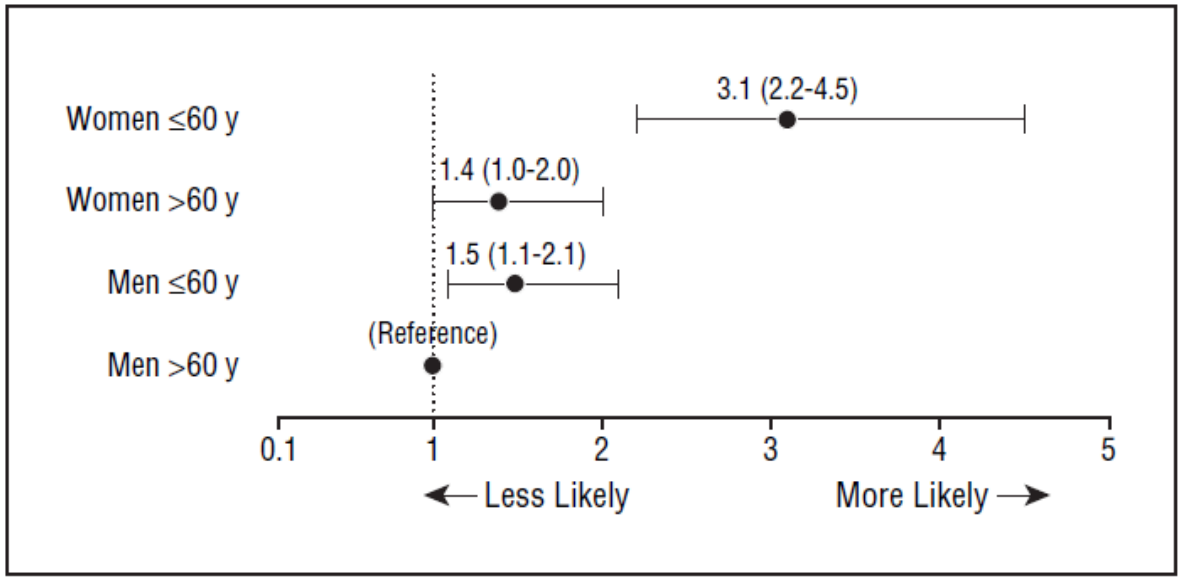


Figure 4. Odds ratio (95% confidence intervals) plot for multivariable logistic regression modeling Primary Care Evaluation of Mental Disorders Brief Patient Health Questionnaire depression score of 10 or higher. Age-sex effect controlling for site, demographic factors (race, marital status, and level of education), patients' perceived economic burden, history of smoking, medical history (diabetes, hypertension, hypercholesterolemia, cerebrovascular accidents, angina, myocardial infarction, coronary artery bypass grafting, percutaneous coronary intervention, peripheral vascular disease, lung disease), and clinical status on admission (congestive heart failure, systolic blood pressure, renal failure).

Cardiac Rehabilitation for Women: A Systematic Review of Barriers and Solutions

Marta Supervía, MD, MSc; Jose R. Medina-Inojosa, MD, MSc; Colin Yeung, MD; Francisco Lopez-Jimenez, MD, MSc; Ray W. Squires, PhD; Carmen M. Pérez-Terzic, MD, PhD; LaPrincess C. Brewer, MD, MPH; Shawn E. Leth, MEd; and Randal J. Thomas, MD, MS

ARTICLE HIGHLIGHTS

- Fewer women than men participate in cardiac rehabilitation because of a complex and unique array of demographic, socioeconomic, medical, and societal challenges faced by women.
- Systematic approaches to cardiac rehabilitation referral, enrollment, and participation have been shown to improve cardiac rehabilitation participation and are recommended to help overcome the gender gap in cardiac rehabilitation participation.
- Further research is warranted on the impact of novel cardiac rehabilitation delivery models, such as home-based cardiac rehabilitation, on the gender gap in cardiac rehabilitation participation.

Colella TJ, Gravely S, Marzolini S, Grace SL, Francis JA, Oh P, Scott LB.
Sex bias in referral of women to outpatient cardiac rehabilitation? A meta-analysis.
Eur J Prev Cardiol . 2015 Apr;22(4):423-41

Results: Of 623 screened articles, 19 observational studies reporting data for 241,613 participants (80,505 women) met the inclusion criteria. In the pooled analysis, women (39.6%) were significantly less likely to be referred to CR compared to men (49.4%; odds ratio 0.68, 95% confidence interval 0.62-0.74). Heterogeneity was considered significant (I (2)= 90%). There was no change in significant findings when subgroup analyses were conducted, examining fee for service vs. no fee, high-quality studies vs. others, or studies pooled by different study methodologies.
Conclusions: CR referral remains low for all patients, but is significantly lower for women than men. Evidence-based interventions to increase referral for all patients, including women, need to be instituted. It is time to ensure broader implementation of these strategies.

Mayo Clin Proc. ■ April 2017;92(4):565-577 ■ http://dx.doi.org/10.1016/j.mayocp.2017.01.002
www.mayoclinicproceedings.org ■ © 2017 Mayo Foundation for Medical Education and Research

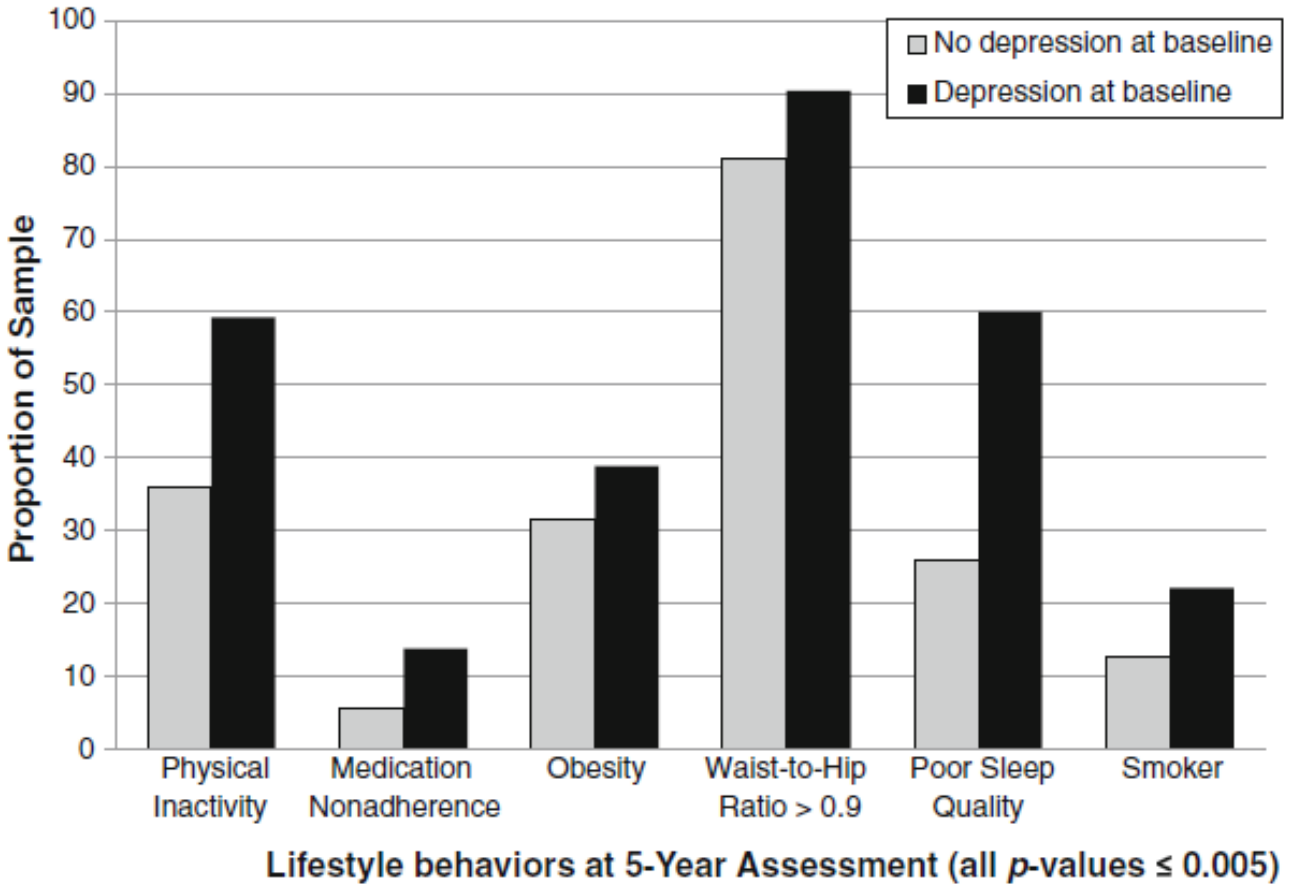
…Mechanismen ?

Durch welche Bedingungen wird Depressivität zu einer potenziell letalen Expositionsvariablen? Geschlechtsspezifische Besonderheiten?

- **Selbstschädigende Verhaltensweisen (*life style patterns*) wie körperliche Inaktivität, Rauchen, neg. Ernährungsgewohnheiten**
- **Pathomechanismen, die direkt auf das Herz- und Gefäßsystem wirken**

Direction of Association Between Depressive Symptoms and Lifestyle Behaviors in Patients with Coronary Heart Disease: the Heart and Soul Study

Nancy L. Sin, PhD [1,2] · Anupama D. Kumar, BA [3] · Anil K. Gehi, MD [4] · Mary A. Whooley, MD [5,6,7]



Methods Depressive symptoms and lifestyle behaviors (physical activity, medication adherence, body mass index, waist to hip ratio, sleep quality, and smoking status) were assessed at baseline and 5 years later among a prospective cohort of 667 patients with stable coronary heart disease.

Results Greater depressive symptoms at baseline predicted poorer lifestyle behaviors 5 years later (less physical activity, lower medication adherence, higher body mass index, higher waist to hip ratio, worse sleep quality, and smoking). After adjustment for demographics, cardiac disease severity, comorbidity, and baseline lifestyle behaviors, depressive symptom severity remained predictive of subsequent worsening of physical activity (beta = −0.08; 95 % confidence interval (CI) = −0.16, −0.01; $p = 0.03$), medication adherence (beta = −0.16; 95 % CI = −0.24, −0.08; $p < 0.001$), and sleep quality (beta = −0.19; 95 % CI = −0.27, −0.11; $p < 0.001$). Baseline lifestyle behaviors also predicted 5-year change in depressive symptoms, although the associations were attenuated after adjustment for baseline depressive symptoms and covariates.

Durch welche Bedingungen wird Depressivität zu einer potenziell letalen Expositionsvariablen? Geschlechtsspezifische Besonderheiten?

- Psychobiologische Pathomechanismen, die direkt auf das Herz- und Gefäßsystem wirken

Autonome Dysbalance

Endokrine Dysfunktion

Immunreaktionen (chronische Entzündung)

Sex differences in brain activation patterns with mental stress in patients with coronary artery disease

Nicole Kasher[1], Matthew T. Wittbrodt[2], Zuhayr S. Alam[2], Bruno B. Lima[1,3], Jonathon A. Nye[4], Carolina Campanella[2], Stacy Ladd[2], Muhammad Hammadah[3], Amit J. Shah[1,3,5], Paolo Raggi[6], Arshed A. Quyyumi[3], Viola Vaccarino[1,3] and J. Douglas Bremner[2,4,5*]

Methods: We investigated sex differences in neural correlates of mental stress in a sample of 53 female and 112 male participants ($N = 165$) with CAD, with and without mental stress-induced myocardial ischemia (MSI), during exposure to mental arithmetic tasks and public speaking stress tasks using high-resolution positron emission tomography (HR-PET) and radiolabeled water imaging of the brain.

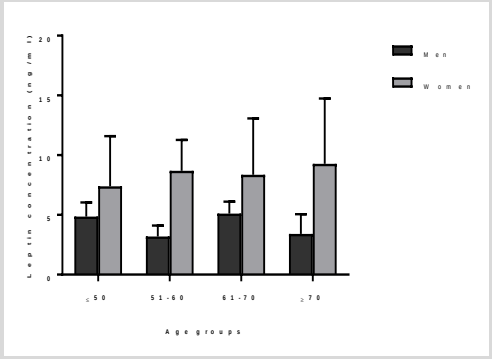
Results: Women compared to men had significantly greater activation with stress in the right frontal (BA 9, 44), right parietal lobe (Area 3, 6, 40), right posterior cingulate gyrus (BA 31), bilateral cerebellum, and left temporal/fusiform gyrus (BA 37) and greater deactivation in bilateral anterior cingulate gyrus (BA 24, 32), bilateral medial frontal gyrus (BA 6, 8, 9, 10), right parahippocampal gyrus, and right middle temporal gyrus (BA 21). Women with MSI (but not those without MSI) showed significantly greater activation than men in the right posterior cingulate gyrus (BA 31) and greater deactivation in several frontal and temporal lobe areas.

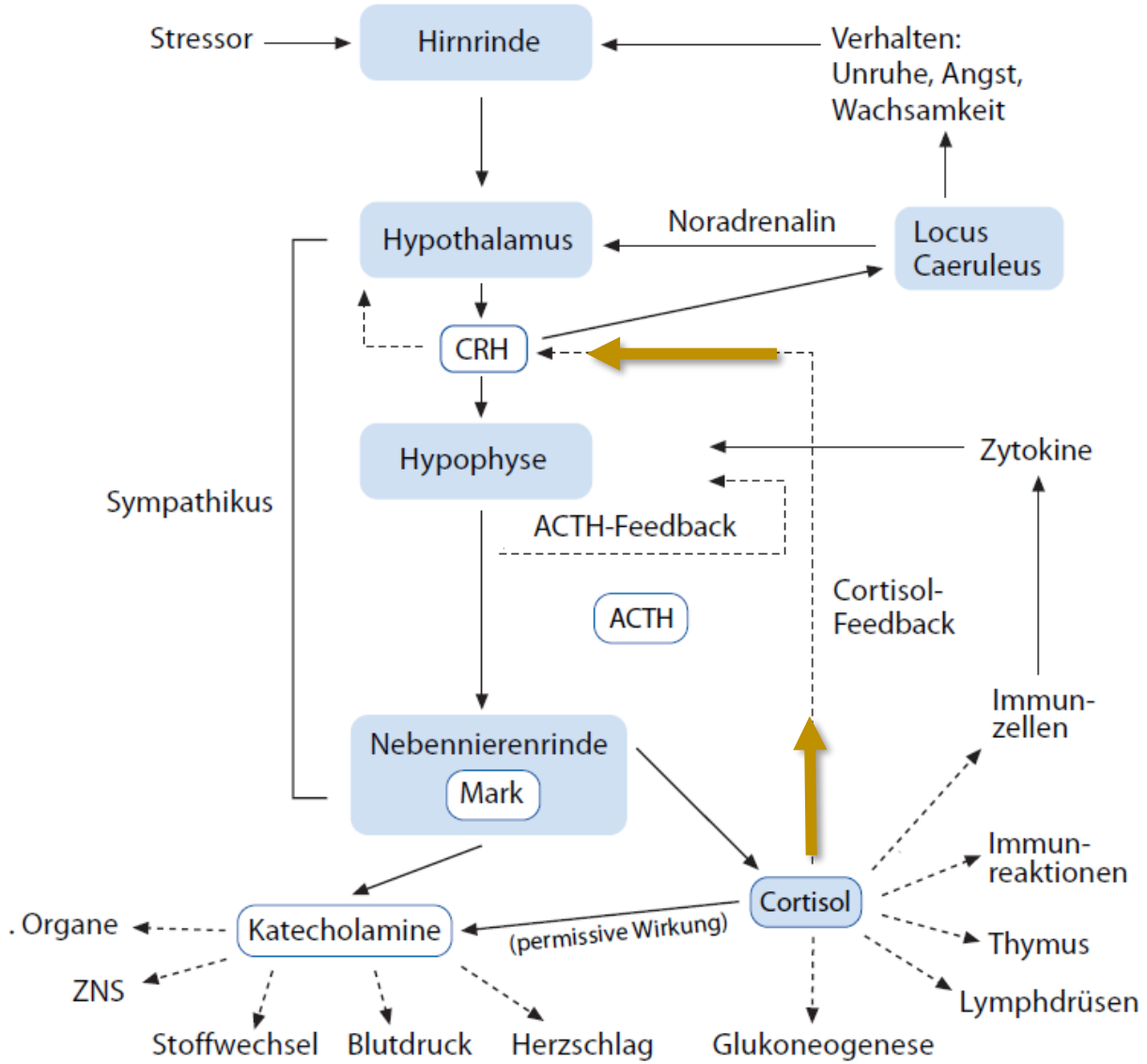
Conclusion: Men and women with CAD show differences in responses to stress in brain limbic areas that regulate emotion, and these functional responses differ by MSI status. Our results suggest that the cingulate gyrus may be involved in sex differences in MSI.

Fig. 3 Sagittal brain slices representing greater ($p < 0.005$) cerebral blood flow increases (activation; red) and decreases (deactivation; blue) during mental stress compared to control tasks in women ($n = 9$) versus men ($n = 35$) with coronary artery disease and mental stress induced myocardial ischemia using [^{15}O]H_2O positron emission tomography. Values below brain denote Talairach x-coordinates, where positive and negative values correspond to the right and left hemisphere, respectively. Color bars indicate Z values of activation or deactivation

Endokrine Dysfunktion

- HPA Achsenaktivierung
- Cortisol Dysregulation
- Überexpression pleiotroper (Stress) Hormone wie Leptin





Autonome Dysfunktion

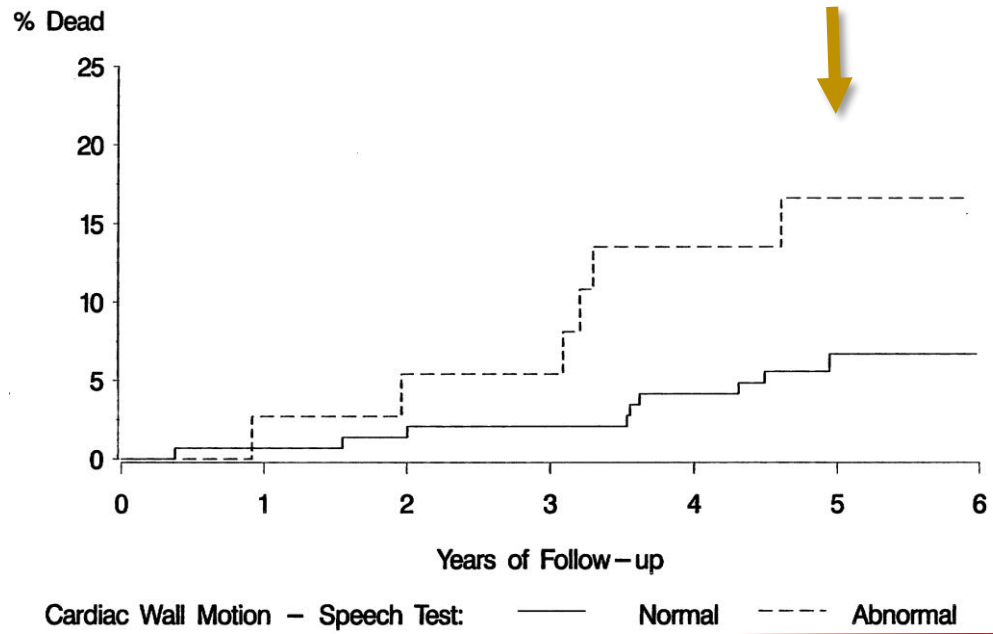
- Parasympathische Hyperaktivierung:
  - Akute Abnahme der Herzfrequenz
  - Vasodilatorische Reaktionen in der Skelettmuskulatur
  - Abnahme des arteriellen Drucks und des Herzzeitvolumens
- Hypersympathikotone Regulation:
  - Anstieg der Herzfrequenz/Herzarbeit
  - Steigerung der Erregungsleitung
  - Auftreten supraventrikulärer oder ventrikulärer Extrasystolen
- Sympathikotone-parasympathikotone Dysbalance
  - Einschränkung der Herzfrequenzvariabilität
  - Elektrische Instabilität des Myokards mit der Gefahr der Entwicklung von ventrikulären Tachykardien

Mental Stress–Induced Ischemia and All-Cause Mortality in Patients With Coronary Artery Disease

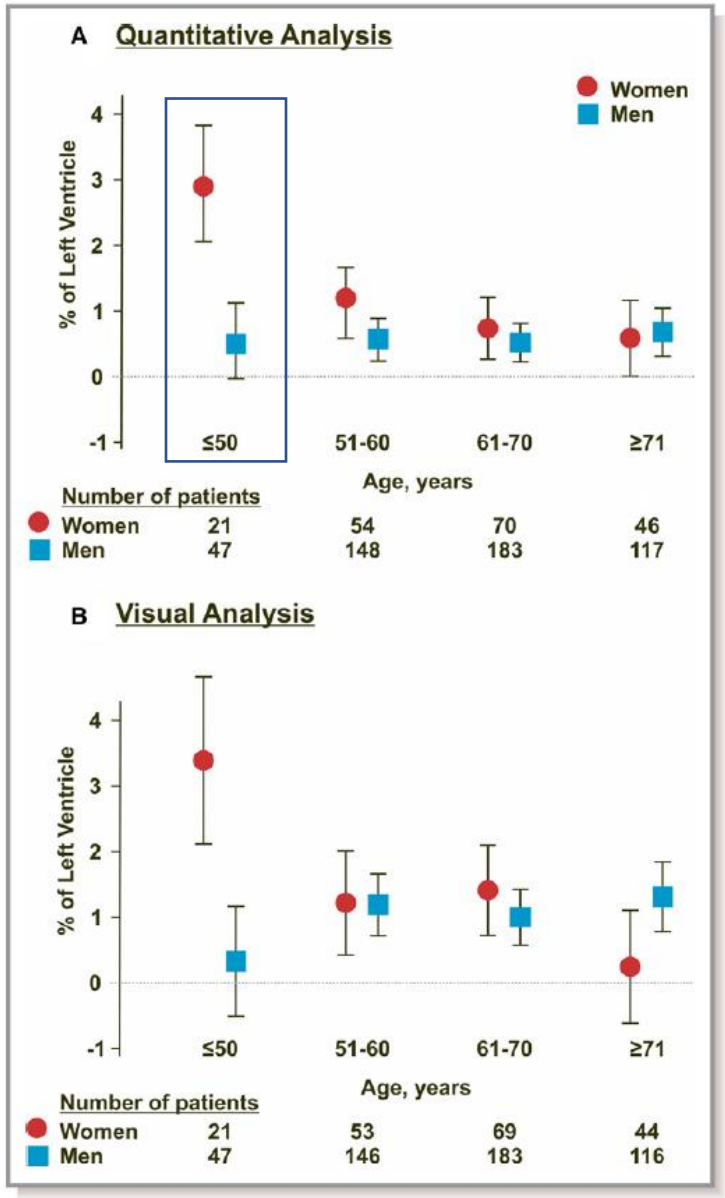
Results From the Psychophysiological Investigations of Myocardial Ischemia Study

David S. Sheps, MD; Robert P. McMahon, PhD; Lewis Becker, MD; Robert M. Carney, PhD; Kenneth E. Freedland, PhD; Jerome D. Cohen, MD; David Sheffield, PhD; A. David Goldberg, MD; Mark W. Ketterer, PhD; Carl J. Pepine, MD; James M. Raczynski, PhD; Kathleen Light, PhD; David S. Krantz, PhD; Peter H. Stone, MD; Genell L. Knatterud, PhD; Peter G. Kaufmann, PhD

- 196 Patienten mit AMI und belastungsabhängige Ischämie
- Psychologischer Stresstest mit nuklearmedizinischem Verfahren
- 5, 2 Jahre Nichtverfolgungszeitraum



Sheps, D. S. et al. Circulation 2002;105:1780-1784



Sex Differences in Mental Stress-Induced Myocardial Ischemia in Patients With Coronary Heart Disease

Viola Vaccarino, MD, PhD, FAHA; Kobina Wilmot, MD; Ibhar Al Mheid, MD; Ronnie Ramadan, MD; Pratik Pimple, MBBS, MPH; Amit J. Shah, MD, MSCR; Ernest V. Garcia, PhD; Jonathon Nye, PhD; Laura Ward, MPH; Muhammad Hammadah, MD; Michael Kutner, PhD; Qi Long, PhD; J. Douglas Bremner, MD; Fabio Esteves, MD; Paolo Raggi, MD, FAHA, FACC; Arshed A. Quyyumi, MD, FACC

Background—Emerging data suggest that young women with coronary heart disease (CHD) are disproportionally vulnerable to the adverse cardiovascular effects of psychological stress. We hypothesized that younger, but not older, women with stable CHD are more likely than their male peers to develop mental stress-induced myocardial ischemia (MSIMI).

Methods and Results—We studied 686 patients (191 women) with stable coronary heart disease (CHD). Patients underwent ^{99m}Tc-sestamibi myocardial perfusion imaging at rest and with both mental (speech task) and conventional (exercise/pharmacological) stress testing. We compared quantitative (by automated software) and visual parameters of inducible ischemia between women and men and assessed age as an effect modifier. Women had a more-adverse psychosocial profile than men whereas there were few differences in medical history and CHD risk factors. Both quantitative and visual indicators of ischemia with mental stress were disproportionally larger in younger women. For each 10 years of decreasing age, the total reversibility severity score with mental stress was 9.6 incremental points higher (interaction, $P<0.001$) and the incidence of MSIMI was 82.6% higher (interaction, $P=0.004$) in women than in men. Incidence of MSIMI in women ≤50 years was almost 4-fold higher than in men of similar age and older patients. These results persisted when adjusting for sociodemographic and medical risk factors, psychosocial factors, and medications. There were no significant sex differences in inducible ischemia with conventional stress.

Conclusions—Young women with stable CHD are susceptible to MSIMI, which could play a role in the prognosis of this group.
(*J Am Heart Assoc*. 2016;5:e003630 doi: 10.1161/JAHA.116.003630)

Figure 3. Inducible myocardial ischemia with mental stress according to sex and age group. Young women (≤50 years) showed more ischemia with mental stress than any of the other groups. Ischemia was expressed as percent of ischemic myocardium and was derived with 2 separate methods: automated quantitative analysis (A) and visual analysis (B). In both analyses, the interaction between sex and age was highly significant ($P<0.001$), and the comparison between women and men in the group ≤50 was also highly significant ($P<0.0001$). Error bars indicate confidence intervals.

Women, but not men, have prolonged QT interval if depressed after an acute coronary syndrome

William Whang[1]*, Howard M. Julien[1], Laura Higginbotham[1], Ana V. Soto[1], Nisha Broodie[1], J. Thomas Bigger[2], Hasan Garan[2], Matthew M. Burg[1,3], and Karina W. Davidson[1]

EUROPEAN SOCIETY OF CARDIOLOGY®

Europace (2012) **14**, 267–271
doi:10.1093/europace/eur246

Table 1 Demographic and clinical characteristics of acute coronary syndrome patients by depressive symptom status

	BDI < 5 (*n* = 200), %	BDI ≥ 10 (*n* = 182), %	*P* value
Age > 65	36.0	34.6	0.83
Female	27.0	46.7	<0.01
Non-White	25.0	44.0	<0.01
BMI ≥ 25 kg/m^2	64.5	58.2	0.25
Hypertension	63.0	69.2	0.23
Diabetes	26.0	33.0	0.15
QT-prolonging medication	9.5	11.5	0.61
Non-STEMI	33.0	34.1	0.83
LVEF <0.40	8.5	6.0	0.43

Table 2 Baseline electrocardiographic characteristics of acute coronary syndrome patients according to depressive symptoms by Beck Depression Inventory score

	BDI < 5	BDI ≥ 10	*P* value
Women (*n* = 139)			
Heart rate (bpm)	68.0 (11.2)	70.2 (12.0)	0.29
PR interval (ms)	168.0 (23.7)	160.8 (18.8)	0.06
QTcF (ms)	408.6 (24.3)	435.4 (26.6)	<0.01
QT_{Nc} (ms)	410.0 (23.3)	434.4 (28.9)	<0.01
ECG-LVH	7.7 %	23.8 %	0.02
Q waves	14.8 %	18.8 %	0.65
ST depression ≥1 mm	11.1 %	16.5 %	0.46
Men (*n* = 243)			
Heart rate (bpm)	68.9 (13.7)	66.5 (12.4)	0.15
PR interval (ms)	171.8 (33.1)	172.0 (29.1)	0.97
QTcF (ms)	412.0 (25.8)	415.4 (23.6)	0.29
QT_{Nc} (ms)	414.0 (25.6)	417.2 (29.0)	0.38
ECG-LVH	11.0 %	13.5 %	0.55
Q waves	23.3 %	15.5 %	0.15
ST depression ≥1 mm	11.6 %	14.4 %	0.56

Table 3 Multivariable linear regression analyses of QT interval in milliseconds, with correction for heart rate by two different methods

	QTcF		QT_{Nc}	
	Beta coefficient (95% CI)	*P* value	Beta coefficient (95% CI)	*P* value
BDI ≥ 10	3.3 (−3.1, 9.6)	0.31	2.5 (−4.2, 9.2)	0.47
Female	−3.4 (−11.1, 4.4)	0.39	−4.1 (−12.2, 4.1)	0.33
Female × BDI ≥ 10	22.9 (12.3, 33.5)	<0.001	20.9 (9.8, 32.0)	<0.001

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Zusammenfassung (I)

1. Partnerschaftsstress hat für Frauen messbar fatalere gesundheitliche Folgen als für Männer, insbesondere bei maligner Konfliktkommunikation („self silencing“).

2. Einsamkeit ist ein bedeutsamer KHK Risikofaktor für Frauen. Die gesellschaftliche Bedeutung wird zunehmen.

3. Depressivität im mittleren Lebensalter ist ein signifikanter aetiologischer KHK Risikofaktor. Mit dem Näherrücken des Krankheitsausbruches („*die letzten 180 Tage vor dem Infarkt*“) gewinnt die vitale Erschöpfung als zentrales Kernsymptom bei Frauen eine hohe klinische Bedeutung.

4. Die subjektive Verzögerungszeit, die Rettungskette in der akuten Infarktsituation zu aktivieren, ist bei älteren Frauen (>65 Jahre) extrem verlängert. Drei Stunden nach Infarkteintritt haben weniger als die Hälfte dieser Risikogruppe akutmedizinische Hilfe in Anspruch genommen.

5. Frauen haben ein höheres Post Infarkt Mortalitätsrisiko (insbesondere „*in-hospital mortality*“ bei jüngeren Frauen). Depressivität ist ein signifikanter prognostischer RF.

6. Das Risiko, eine Postinfarkt-Depression zu erleiden, ist bei jüngeren Frauen (< 60 J) mehr als dreimal so hoch verglichen mit älteren Männern (> 60 J).

7. Trotzdem zeigt sich europaweit eine Unterversorgung von weiblichen Postinfarktpatientinnen in Bezug auf eine kardiologische Rehabilitation.

Zusammenfassung (II)

1. Als Antwort auf (psychosoziale) Stress Stimuli zeigen Frauen und Männer in Untersuchungen mit bildgebenden Verfahren bedeutsame Unterschiede in den Hirnregionen, die die Emotionen regulieren (limbisches System, Cingulate Gyrus).

2. Die psycho-neuro-biologischen Vermittlungswege zwischen Herz und Psyche basieren bedeutsam auf drei Achsen: das autonome, das hormonelle und das immunologische System.

3. Bedingt durch die hormonellen Unterschiede zwischen den Geschlechtern, liegt es nahe, Unterschiede in endokrinen Sekretionmustern zu erforschen. (Hyperkortisolismus, Leptinüberproduktion etc.)

4. Gegenwärtig sieht es so aus, dass stressinduzierte Störungen in der autonomen Regulation des Herzen besonders bedeutsame Unterschiede zwischen den Geschlechtern erkennen lassen: QT Zeitverlängerung bei depressiven Postinfarktpatientinnen; mental stress induced Ischemia.

5. All dies: Die geschlechtsspezifischen Unterschiede in der psychosozialen Stressverarbeitung im alltäglichen Leben, deren psychobiologischen Folgen; die Unterschiede in der Symptomwahrnehmung mit den fatalen Konsequenzen und die nach wie vor erheblich höheren Mortalitäts-Risiken von Frauen nach Eintritt der KHK zeigen sehr deutlich, dass die Berücksichtigung von Geschlecht und Gender ein selbstverständlicher Teil der Forschung und Versorgung der KHK Risikogruppen sein muß.