

BMJ Open Changes of individual perception in psychosocial stressors related to German reunification in 1989/1990 and cardiovascular risk factors and cardiovascular diseases in a population-based study in East Germany

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ABSTRACT

Objectives: Aim was to examine the relationship between individually perceived changes in psychosocial stressors associated with German reunification and cardiovascular effects. We hypothesised that higher levels of psychosocial stress related to German reunification were associated with an increase in cardiovascular risk factors and cardiovascular diseases (CVDs).

Design: Cross-sectional data from 2 cohort studies in East Germany were used: Cardiovascular Disease, Living and Ageing in Halle Study (CARLA), and Study of Health in Pomerania (SHIP).

Setting: 2 populations in East Germany.

Participants: CARLA study: 1779 participants, aged 45–83 years at baseline (812 women), SHIP study: 4308 participants, aged 20–79 years at baseline (2193 women).

Primary and secondary outcome measures:

Psychosocial stressors related to reunification were operationalised by the Reunification Stress Index (RSI; scale from 0 to 10). This index was composed of questions that were related to individually perceived changes in psychosocial stressors (occupational, financial and personal) after reunification. To examine the associations between the RSI and each stressor separately with cardiovascular risk factors and CVD, regression models were used.

Results: RSI was associated with CVD in women (RR=1.15, 95% CI 1.00 to 1.33). Cardiovascular risk factors were associated with RSI for both men and women, with strongest associations between RSI and diabetes in women (RR=1.10, 95% CI 1.01 to 1.20) and depressive disorders in men (RR=1.15, 95% CI 1.07 to 2.77). The change in occupational situation related to reunification was the major contributing psychosocial stressor. We observed a strong association with CVD in women who experienced occupational deterioration after reunification (RR=4.04, 95% CI 1.21 to 13.43).

Strengths and limitations of this study

- This study is the first to analyse the association of individually perceived psychosocial stressors that changed through a transition with cardiovascular outcomes on an individual basis.
- Furthermore, both studies are representative samples, and the assessment of the data are highly standardised and in agreement with other German and international studies.
- Regarding the study population, we cannot rule out the possibility of a selection bias.
- The analysis faces the usual restrictions of a cross-sectional design; to determine the causality, a longitudinal design would be required.
- Owing to the time lag between the event of reunification 1989/1990 and the interview, where the Reunification Stress Index (RSI) questionnaire was applied, recall bias may have influenced the results. However, we evaluated validity and reliability of the RSI and found no indication for recall bias.
- Additionally, we cannot exclude that outcomes like depressive disorders or hypertension already persisted before reunification. However, the exposure RSI refers to a fixed event in the past (German reunification), so we can assume a chronological order of exposure and disease outcomes for myocardial infarction and stroke.

Conclusions: Individually perceived deterioration of psychosocial stressors (occupational, financial and personal) related to German reunification was associated with cardiovascular risk factors and CVD. The associations were stronger for women than for men. An explanation for these findings could be that women were more often affected by unemployment after reunification. Morbidity and mortality follow-up of both cohorts could enhance the results.



INTRODUCTION

Mortality from cardiovascular diseases (CVDs) has decreased in the last century in European countries. However, an east-west gradient of higher mortality in central and eastern European countries is still present.^{1 2} After the epochal process of the societal transition starting in 1989/1990 in Central and Eastern Europe and the former Soviet Union, these discrepancies increased enormously.³⁻⁶ Studies have described possible causes for the increase in cardiovascular mortality after the collapse of the socialist and communistic regimes.⁷⁻⁹ Some authors have particularly emphasised the importance of psychosocial stressors on the increase in cardiovascular mortality after the social change.¹⁰⁻¹³

Assumed determinants of psychosocial stressors in this context are: occupational stressors, for example, unemployment,^{5 11} mass privatisation,⁷ job strain,¹² financial stressors,^{5 11 14 15} and personal stressors for example, social isolation^{12 15} and critical life events.¹²

It has been repeatedly shown that psychosocial stressors (eg, job strain, social isolation, depression, critical life events) can contribute to the development of CVD.¹⁶⁻²³ The political, social and economic changes in the German Democratic Republic (GDR), the so-called 'reunification', brought serious changes in requirements and fully modified the societal environment of the inhabitants. Reunification was a population-based critical life event, which entailed other critical life events.^{24 25}

The implications of psychosocial stressors during the process of a social transition as a form of social change are still unclear. As such, some researchers requested further investigations to better understand the links between social change, psychosocial stressors, health behaviour and the resulting impacts on health.^{6 11} However, specific psychosocial stressors have not been identified.¹³ We analysed individually perceived changes of occupational, financial and personal situation after the reunification as determinates of psychosocial stressors. Therefore, the aim of this study was to examine the relationship between individually perceived changes in psychosocial stressors associated with German reunification and cardiovascular effects. We hypothesised that higher levels of individually perceived psychosocial stress related to this critical life event, that is, reunification, were associated with an increase in cardiovascular risk factors and CVD.

METHODS

Study design and study population

This study was based on cross-sectional data from the baseline assessment of two cohort studies in East Germany: the Cardiovascular Disease, Living and Ageing in Halle Study (CARLA) in Saxony-Anhalt (2002–2006),²⁶ and the Study of Health in Pomerania (SHIP; 1997–2002).²⁷ We combined the cohorts for two reasons: first, these cohorts are the only ones that assessed psychosocial stressors related to reunification, and second,

to increase the sample size. Both studies drew random samples from mandatory lists. Data collection included a standardised, computer-assisted interview, questionnaires and a physical examination by trained study nurses. Written informed consent was obtained on enrolment. Both studies were approved by the local ethical committees of the associated medical schools. The response proportion was 64% for CARLA and 69% for SHIP. The CARLA study population comprised 1779 participants aged 45–83 years at baseline (812 women). The number of participants participating in the SHIP study was 4308 aged 20–79 years at baseline (2193 women). For this study, we excluded participants who had a diagnosis of myocardial infarction (MI) and/or stroke that predated 1990 (N=123), had not resided in the former GDR (N=120), were unemployed before 1990 (N=1701; mostly retired persons), who were ≤ 16 years in 1990 (N=94), or those for whom data were missing on the components of the Reunification Stress Index (RSI; N=148). In total, the study size comprised N=3901.

Reunification Stress Index

We operationalised the psychosocial stressors related to reunification through the RSI. The index was computed based on the answers obtained by the following three questions: 'Has your occupational situation changed since reunification (since 1990)?', 'Has your financial situation changed since reunification (since 1990)?' and 'Has your personal situation (eg, your personal contacts with friends or relatives) changed since reunification (since 1990)?'. We framed questions in a specific way so that all study persons could attribute their answers to the unique event and the consequences of reunification: 'Now we ask questions concerning reunification'. The possible answers differed between the studies: CARLA: 1=greatly improved, 2=improved, 3=no change, 4=deteriorated, 5=greatly deteriorated; SHIP: 1=improved, 2=no change, 3=deteriorated. The indicators were added into a total sum. We computed the mean of the indicators for each participant. RSI was calculated and standardised to a scale from 0 to 10 to make it comparable between the studies with the following formula: $RSI = (\text{mean} - 1) \times 10 / \text{range of the mean}$ (where mean: mean of the items of any participants; 1: minimum value of the mean; 10: chosen maximum value of the RSI; range of the mean: in CARLA=4 and in SHIP=2). Values less than 5 indicate an improvement in psychosocial factors after reunification, a value of 5 indicates no changes in psychosocial factors after reunification, and values higher than 5 indicate a deterioration in psychosocial factors after reunification. The RSI was externally validated by an independently conducted interview of 18 participants from the CARLA cohort. We validated the self-constructed RSI with our own qualitative study interviewing 18 participants from the CARLA population blindly randomly selected stratified by RSI score values. The results will be published in a separate paper. Furthermore, we also analysed the questions of the RSI

separately in order to estimate the proper effect of each psychosocial stressor (occupational, financial and personal) on the outcomes.

CVDs and cardiovascular risk factors

Prevalent MI and stroke were defined as self-reported physician's diagnoses. Coronary heart disease (CHD) was defined as the presence of MI, and/or self-reported coronary artery bypass surgery, and/or self-reported percutaneous coronary intervention. CVD was defined as CHD and/or self-reported physician-diagnosed stroke, and/or carotid surgery. Hypertension was defined as mean systolic blood pressure ≥ 140 mm Hg, and/or mean diastolic blood pressure ≥ 90 mm Hg, and/or use of antihypertensive medication according to the Anatomical Therapeutic Chemical Classification System. For high-risk drinking in men, we used a cut-off of >30 mg alcohol/day and for women, a cut-off of >20 mg alcohol/day.²⁸ Body mass index (BMI) was calculated as kg/m^2 . The definition of diabetes mellitus was based on self-reported physician's diagnosis (yes/no). Smoking behaviour was grouped as 'yes' (current smoker and ex-smoker) or 'no' (never smoker). Laboratory analyses of non-fasting venous blood samples included serum total cholesterol in mg/dL. In CARLA, the Centre for Epidemiological Studies Depression Scale (CES-D) was used to assess depressive disorders.²⁹ This 20-item scale asks respondents to evaluate how often ('rarely or never' to 'most or all of the time') in the last week they had experienced a symptom. We used a cut-off of ≥ 23 points to define depressive disorders.³⁰ The presence of psychiatric disorders in the SHIP cohort was assessed using the Composite International Diagnostic-Screener (CID-S), a 12-item self-reported questionnaire which covers psychiatric diagnoses according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV).³¹ The CID-S also covers depressive disorders. The screening questions for depressive disorders included the following two items: 'Feelings of sadness or depressed mood for a period of at least 2 weeks', and 'Lack of interest, tiredness or loss of energy for a period of at least 2 weeks'. Participants who answered positively to both questions were classified as having depressive disorders. Educational level was composed of school and vocational education, and categorised into three levels: low (no or intermediate secondary school leaving certificate without a completed vocational qualification), moderate (intermediate secondary school leaving certificate and vocational training) and high (upper secondary school leaving certificate degree and/or a completed university degree). Details of definitions of the variables are given in the respective design papers.^{26 27}

Statistical analyses

For MI and stroke, time-to-event data were available. The beginning of the time count was 1990. To examine the association between the RSI and the events MI and stroke, we estimated HRs and corresponding 95% CIs by

running proportional hazard regressions. Persons without an event were censored. The association of RSI with dichotomous outcomes, CVD, CHD and cardiovascular risk factors (hypertension, diabetes, smoking and depressive disorders), was examined by running log-binomial regression models to estimate relative risks (RRS) and corresponding 95% CIs. In case of non-convergence of the models, we used Poisson regression with robust variance. For the associations between the RSI and continuous metric outcomes (BMI, cholesterol and alcohol), linear regression models were applied to obtain the regression coefficient β and corresponding 95% CIs. To estimate the association between any single psychosocial stressor (occupational, financial and personal) and CVDs and/or cardiovascular risk factors, we used the same regression models as described above. The reference group was composed of those participants who experienced an improvement after reunification. We checked the model assumptions by visual inspection of residual plots. Model assumptions were fulfilled. We identified minimally sufficient adjustment sets (MSAS) to estimate the total effect by using causal diagrams that represent the relationships between exposure, outcome and other covariables.³² Causal diagrams resulted in a MSAS which contains sex, age, study and education. We tested interaction effects for study \times RSI, education \times RSI and age \times RSI. However, no significant interaction effects were found. We stratified all analyses by sex. All analyses were done with SAS, V.9.3. (SAS Institute, Cary, North Carolina, USA).

RESULTS

The characteristics of the study participants are shown in [table 1](#). In total, 51.9% of the 3.901 study participants were male. The CARLA participants were older, and had more cardiovascular risk factors and CVDs than the SHIP participants, except for smoking, alcohol consumption, depressive disorders and education. In total, men had more CVDs and cardiovascular risk factors than women, except for BMI, education and depressive disorders. The mean value of the RSI was 4.8 (SD=2.4) for men and 4.9 (2.4) for women. The majority of the participants had an RSI less than 5 (men 46.2%, women 42.9%), and 34.6% of the men and 36.1% of the women underwent a deterioration in psychosocial stressors after reunification. The RSI was highest in the age group of 45 to <55 years for both men and women (5.3 (2.4); 5.4 (2.3)). The change in occupational situation related to reunification was the major contributing psychosocial stressor. We observed a deterioration in the occupational situation after reunification in 37.0% (men) and 38.3% (women). An improvement was reported in 31.9% of the male and 28.5% of the female participants. The majority reported an improvement in their financial situation (men: 55.7%; women: 49.4%) and no changes in the personal situation after reunification (men: 65.6%; women: 71.6%).

Table 1 Characteristics of the study participants, stratified by sex and study

	CARLA		SHIP		Total	
	Men (n=703)	Women (n=565)	Men (n=1298)	Women (n=1335)	Men (n=2001)	Women (n=1900)
Age (years)						
Mean (SD)	61.3 (8.5)	59.0 (7.0)	46.9 (12.3)	43.6 (11.1)	51.9 (13.0)	48.8 (12.1)
Age group (years)						
24 to <45 (n)	–	–	591	667	591	667
45 to <55 (n)	205	197	301	366	506	563
55 to <65 (n)	248	237	301	262	549	499
65 to <75 (n)	204	130	94	35	298	165
≥75 (n)	46	1	11	5	57	6
CVD						
MI; n (%)	42 (6.0)	7 (1.2)	30 (2.3)	5 (0.4)	72 (3.6)	12 (0.6)
Stroke; n (%)	20 (2.8)	9 (1.6)	10 (0.7)	8 (0.6)	30 (1.5)	17 (0.9)
CHD; n (%)	54 (7.7)	13 (2.3)	33 (2.5)	5 (0.4)	87 (4.3)	18 (1.0)
CVD*; n (%)	69 (9.8)	22 (3.9)	41 (3.1)	13 (1.0)	110 (5.4)	35 (1.8)
Cardiovascular risk factors						
Hypertension; n (%)	534 (76.9)	377 (66.7)	784 (60.7)	455 (34.2)	1318 (66.1)	832 (43.8)
Smoker; n (%)	512 (72.8)	205 (36.3)	1011 (77.8)	739 (55.4)	1523 (76.1)	944 (49.7)
Diabetes; n (%)	83 (11.8)	62 (11.0)	80 (6.2)	57 (4.3)	163 (8.1)	119 (6.3)
High-risk drinking†; n (%)	157 (22.3)	27(4.8)	355 (27.3)	98 (7.3)	512 (25.6)	125 (6.6)
Depressive disorders; n (%)	33 (4.9)	57 (10.3)	101 (7.8)	227 (17.1)	134 (6.8)	284 (15.1)
BMI; mean (SD)	28.2 (4.1)	28.5 (5.6)	27.8 (3.9)	26.7 (5.3)	27.9 (4.0)	27.2 (5.5)
Cholesterol; mean (SD)	208.7 (40.6)	220.6 (42.9)	227.9 (46.9)	220.2 (46.7)	220.3 (45.6)	221.2 (45.7)
Education						
Low; n (%)	22 (3.1)	49 (8.7)	77 (5.9)	100 (7.5)	99 (5.0)	149 (7.9)
Middle; n (%)	427 (60.7)	387 (68.5)	908 (70.0)	1012 (74.9)	1335 (66.8)	1382 (72.4)
High; n (%)	254 (36.1)	129 (22.8)	313 (24.1)	254 (17.9)	567 (28.3)	369 (19.4)
Exposure						
RSI; mean (SD)	4.8 (1.6)	5.0 (1.5)	4.8 (2.7)	4.9 (2.7)	4.8 (2.4)	4.9 (2.4)
<5; n (%)	331 (47.1)	235 (41.6)	593 (45.7)	580 (43.5)	924 (46.2)	815 (42.9)
5; n (%)	139 (19.8)	128 (22.7)	246 (19.0)	271 (20.3)	385 (19.2)	399 (21.0)
>5; n (%)	233 (33.1)	202 (35.8)	459 (35.4)	484 (36.3)	692 (34.6)	686 (36.1)
RSI by age group (years)						
24 to <45; mean (SD)	–	–	4.5 (2.7)	4.6 (2.7)	4.5 (2.7)	4.6 (2.7)
45 to <55; mean (SD)	5.3 (1.8)	5.4 (1.6)	5.3 (2.7)	5.4 (2.6)	5.3 (2.4)	5.4 (2.3)
55 to <65; mean (SD)	4.9 (1.6)	4.8 (1.5)	5.2 (2.6)	5.1 (2.8)	5.1 (2.2)	5.0 (2.2)
65 to <75; mean (SD)	4.4 (1.4)	4.9 (1.2)	3.8 (2.5)	3.7 (2.4)	4.2 (1.8)	4.6 (1.6)
>75; mean (SD)	4.8 (1.2)	3.3 (–)	2.4 (2.0)	2.6 (2.3)	4.3 (1.6)	2.8 (2.0)
Occupational situation						
Improvement; n (%)	211 (30.0)	143 (25.3)	411 (31.7)	398 (29.8)	622 (31.1)	541 (28.5)
No change; n (%)	264 (37.5)	230 (40.7)	375 (28.9)	402 (30.1)	639 (31.9)	632 (33.3)
Deterioration; n (%)	228 (32.4)	192 (33.9)	512 (39.5)	535 (40.1)	740 (37.0)	727 (38.3)

Continued

Table 1 Continued

	CARLA		SHIP		Total	
	Men (n=703)	Women (n=565)	Men (n=1298)	Women (n=1335)	Men (n=2001)	Women (n=1900)
Financial situation						
Improvement; n (%)	394 (56.1)	273 (48.3)	720 (55.5)	666 (49.9)	1114 (55.7)	939 (49.4)
No change; n (%)	183 (26.0)	163 (28.9)	336 (25.9)	341 (25.5)	519 (25.9)	504 (26.5)
Deterioration; n (%)	126 (17.9)	129 (22.8)	242 (18.6)	328 (24.6)	368 (18.4)	457 (24.1)
Personal situation						
Improvement; n (%)	46 (6.5)	23 (4.1)	131 (10.1)	139 (10.4)	177 (8.9)	162 (8.5)
No change; n (%)	488 (69.4)	422 (74.7)	825 (63.6)	938 (70.3)	1313 (65.6)	1360 (71.6)
Deterioration; n (%)	169 (24.0)	120 (21.2)	342 (26.4)	258 (19.3)	511 (25.5)	378 (19.9)

*Multiple responses possible.

†High-risk drinking: >30 g alcohol per day for men, >20 g alcohol per day for women.

BMI, body mass index; CARLA, Cardiovascular Disease, Living and Ageing in Halle Study; CHD, coronary heart disease; CVD, cardiovascular disease; cholesterol in mg/dL, alcohol in g/day; MI, myocardial infarction; RSI, Reunification Stress Index; SHIP, Study of Health in Pomerania.

RSI and CVDs and cardiovascular risk factors

In men, no association was found between the RSI and CVDs. In women, a positive association was found between the RSI and MI (HR=1.22, 95% CI 0.92 to 1.63), stroke (HR=1.17, 95% CI 0.93 to 1.47) and CVD (RR=1.15, 95% CI 1.00 to 1.33). The RSI was associated with all cardiovascular risk factors for both men and women (except high-risk drinking), for example, per unit increase in RSI, the risk of diabetes in women increased by 10% (RR 1.10, 95% CI 1.01 to 1.20). The strongest association was seen in men between RSI and depressive disorders (RR=1.15, 95% CI 1.07 to 1.24). However, the associations between the RSI and cardiovascular risk factors were stronger in women than in men (table 2).

Psychosocial stressors and CVD

We observed a strong association of CVD in women who reported a deterioration or no change in their occupational situation after reunification compared with women who reported an occupational improvement (RR=4.04, 95% CI 1.21 to 13.43 and RR=3.76, 95% CI 1.03 to 13.72, respectively; table 3). We found no associations between other CVDs and occupational, financial, and personal changes.

Occupational situation and cardiovascular risk factors

Deterioration in the occupational situation was considerably associated with cardiovascular risk factors for both men and women. The strongest associations were observed for diabetes in women, for depressive disorders in men, and for cholesterol in both men and women. The RR for diabetes in women who reported an occupational deterioration after reunification compared with women who had an occupational improvement after reunification was 1.66 (95% CI 1.05 to 2.63). For an occupational deterioration associated with depressive disorders in men, the corresponding RR was 1.85 (95% CI 1.24 to 2.77). In men who underwent occupational deterioration after reunification, total cholesterol increased by about 7.65 mg/dL (95% CI 2.70 to 12.61) compared with men who had an occupational improvement after reunification. No relevant association was observed for high-risk drinking.

Financial situation and cardiovascular risk factors

Deterioration in the financial situation was considerably associated with cardiovascular risk factors in both men and women, particularly in women. The strongest associations were observed for smoking in women (RR=1.24, 95% CI 1.12 to 1.38), for diabetes in both men and women (RR=1.45, 95% CI 1.01 to 2.11; RR=1.98, 95% CI 1.30 to 2.99, respectively), for depressive disorders in men (RR=1.83, 95% CI 1.24 to 2.89), and for total cholesterol in men (β =8.93 mg/dL, 95% CI 3.52 to 14.35). No relevant association was observed for high-risk drinking (table 4).

Table 2 Associations of RSI with cardiovascular diseases and cardiovascular risk factors for men and women

	Men		Women	
	Crude HR (95% CI)	Adjusted HR (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI)
Cardiovascular diseases				
MI	0.98 (0.88 to 1.08)	1.01 (0.90 to 1.13)	1.21 (0.92 to 1.57)	1.22 (0.92 to 1.63)
Stroke	0.90 (0.76 to 1.06)	0.94 (0.78 to 1.15)	1.17 (0.94 to 1.46)	1.17 (0.93 to 1.47)
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
CVD	0.94 (0.88 to 1.01)	0.96 (0.87 to 1.06)	1.10 (1.00 to 1.22)	1.15 (1.00 to 1.33)
CHD	0.95 (0.88 to 1.04)	0.97 (0.87 to 1.09)	1.07 (0.93 to 1.24)	1.13 (0.89 to 1.43)
Cardiovascular risk factors				
Hypertension	1.02 (1.002 to 1.03)	1.02 (1.002 to 1.03)	1.04 (1.02 to 1.06)	1.04 (1.02 to 1.06)
Smoking	1.02 (1.01 to 1.02)	1.01 (1.004 to 1.02)	1.03 (1.01 to 1.05)	1.03 (1.01 to 1.04)
Diabetes	1.03 (0.98 to 1.10)	1.05 (0.98 to 1.13)	1.07 (1.01 to 1.13)	1.10 (1.01 to 1.20)
High-risk drinking	0.98 (0.95 to 1.02)	0.99 (0.95 to 1.02)	0.97 (0.90 to 1.05)	0.99 (0.92 to 1.06)
Depressive disorders	1.15 (1.06 to 1.24)	1.15 (1.07 to 1.24)	1.07 (1.01 to 1.12)	1.07 (1.02 to 1.11)
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
BMI	0.17 (0.09 to 0.24)	0.16 (0.08 to 0.24)	0.32 (0.22 to 0.42)	0.25 (0.16 to 0.55)
Cholesterol	1.44 (0.60 to 2.28)	1.47 (0.64 to 2.43)	1.70 (0.85 to 2.55)	1.40 (0.59 to 2.20)

Adjusted by education, study, age.

BMI, body mass index; CHD, coronary heart disease; CVD, cardiovascular disease, cholesterol in mg/dL, alcohol in g/day, high-risk drinking: >30 g alcohol per day for men, >20 g alcohol per day for women; MI, myocardial infarction.

Personal situation and cardiovascular risk factors

We observed no association between changes in personal situation and cardiovascular risk factors, except in women for depressive disorders. The RR for depressive disorders in women who had a deterioration in personal situation after reunification was 1.67 (95% CI 1.08 to 2.59; [table 4](#)).

DISCUSSION

To our knowledge, this study is the first to analyse psychosocial stressors that changed for individuals through a transition, with direct reference to cardiovascular

outcomes on an individual basis. We analysed the consequences of the reunification for changes in psychosocial stressors (occupational, financial and personal). Reunification was a fixed event in the past which entailed changes of these factors. We investigated if different reflections of German reunification on the psychosocial level may be associated with different levels of risk factors or frequencies of occurrence of disease. We observed an increase in CVD morbidity in women with a higher RSI. Furthermore, we found that the RSI was weakly but consistently associated with cardiovascular risk factors for both men and women. Deterioration in

Table 3 Associations of the changes in occupational, financial and personal situation after reunification with CVD in men and women

	Men		Women	
	Crude RR (95% CI)	Adjusted RR (95% CI)	Crude RR (95% CI)	Adjusted RR (95% CI)
Occupational situation				
Improvement	1	1	1	1
No change	0.97 (0.63 to 1.49)	0.71 (0.46 to 1.08)	4.56 (1.33 to 15.54)	3.76 (1.03 to 13.72)
Deterioration	0.68 (0.43 to 1.08)	0.79 (0.50 to 1.26)	3.96 (1.16 to 13.55)	4.04 (1.21 to 13.43)
Financial situation				
Improvement	1	1	1	1
No change	0.99 (0.65 to 1.50)	0.91 (0.60 to 1.36)	3.45 (0.47 to 2.51)	3.10 (0.45 to 2.14)
Deterioration	0.69 (0.40 to 1.20)	0.90 (0.52 to 1.58)	2.10 (0.25 to 1.81)	2.63 (0.29 to 2.37)
Personal situation				
Improvement	1	1	1	1
No change	0.67 (0.38 to 1.17)	0.77 (0.45 to 1.31)	3.45 (0.47 to 2.51)	3.10 (0.45 to 2.14)
Deterioration	0.64 (0.34 to 1.20)	0.87 (0.48 to 1.59)	2.10 (0.25 to 1.81)	2.63 (0.29 to 2.37)

Adjusted by education, study, age, 'improvement'=reference group.

CVD, cardiovascular disease; RR, relative risk.

Table 4 Associations of the changes in the occupational, financial and personal situation after the reunification with cardiovascular risk factors in men and women

	Occupational situation				Financial situation				Personal situation			
	Men		Women		Men		Women		Men		Women	
	Crude RR (95% CI)	Adjusted RR (95% CI)	Crude RR (95% CI)	Adjusted RR (95% CI)	Crude RR (95% CI)	Adjusted RR (95% CI)	Crude RR (95% CI)	Adjusted RR (95% CI)	Crude RR (95% CI)	Adjusted RR (95% CI)	Crude RR (95% CI)	Adjusted RR (95% CI)
Hypertension												
Improvement	1	1	1	1	1	1	1	1	1	1	1	1
No change	1.06 (0.98 to 1.15)	0.99 (0.92 to 1.07)	1.06 (0.98 to 1.15)	0.99 (0.92 to 1.07)	1.10 (1.02 to 1.18)	1.08 (1.06 to 1.16)	1.12 (0.99 to 1.27)	1.08 (0.97 to 1.20)	1.04 (0.93 to 1.18)	1.06 (0.94 to 1.19)	1.12 (0.91 to 1.36)	1.02 (0.85 to 1.21)
Deterioration	1.08 (1.003 to 1.17)	1.06 (0.98 to 1.14)	1.08 (1.003 to 1.17)	1.06 (0.98 to 1.14)	1.07 (0.99 to 1.16)	1.11 (1.02 to 1.20)	1.16 (1.01 to 1.29)	1.19 (1.06 to 1.34)	1.02 (0.89 to 1.16)	1.06 (0.94 to 1.21)	1.12 (0.91 to 1.40)	1.08 (0.87 to 1.33)
Smoking												
Improvement	1	1	1	1	1	1	1	1	1	1	1	1
No change	1.01 (0.94 to 1.08)	0.99 (0.93 to 1.06)	1.01 (0.94 to 1.08)	0.99 (0.93 to 1.06)	1.09 (1.03 to 1.15)	1.05 (0.99 to 1.12)	1.12 (1.00 to 1.24)	1.11 (1.01 to 1.24)	0.98 (0.90 to 1.07)	0.98 (0.90 to 1.07)	0.92 (0.79 to 1.08)	1.01 (0.86 to 1.17)
Deterioration	1.11 (1.05 to 1.18)	1.09 (1.03 to 1.16)	1.11 (1.05 to 1.18)	1.09 (1.03 to 1.16)	1.15 (1.08 to 1.22)	1.11 (1.04 to 1.18)	1.27 (1.14 to 1.41)	1.24 (1.12 to 1.38)	0.97 (0.89 to 1.07)	0.96 (0.88 to 1.06)	0.98 (0.82 to 1.17)	1.02 (0.86 to 1.21)
Diabetes												
Improvement	1	1	1	1	1	1	1	1	1	1	1	1
No change	1.23 (0.84 to 1.80)	1.02 (0.70 to 1.49)	1.23 (0.84 to 1.80)	1.02 (0.70 to 1.49)	1.09 (0.77 to 1.56)	1.06 (0.75 to 1.51)	1.12 (1.00 to 1.24)	1.11 (1.01 to 1.24)	0.85 (0.51 to 1.42)	0.90 (0.55 to 1.48)	0.76 (0.43 to 1.33)	0.82 (0.47 to 1.45)
Deterioration	1.20 (0.83 to 1.74)	1.20 (0.83 to 1.73)	1.20 (0.83 to 1.74)	1.20 (0.83 to 1.73)	1.29 (0.89 to 1.88)	1.45 (1.01 to 2.11)	1.27 (1.14 to 1.41)	1.24 (1.12 to 1.38)	0.97 (0.56 to 1.67)	1.12 (0.65 to 1.94)	0.75 (0.39 to 1.45)	0.81 (0.32 to 1.16)
High-risk drinking												
Improvement	1	1	1	1	1	1	1	1	1	1	1	1
No change	1.01 (0.84 to 1.21)	1.06 (0.88 to 1.28)	0.90 (0.85 to 1.40)	0.95 (0.61 to 1.48)	1.05 (0.88 to 1.25)	1.06 (0.89 to 1.27)	0.65 0.42 to 1.02	0.72 (0.45 to 1.13)	0.84 (0.66 to 10.7)	0.84 0.66 to 1.07	0.66 0.39 to 1.12	0.69 (0.41 to 1.18)
Deterioration	0.96 (0.80 to 1.15)	0.97 (0.81 to 1.17)	1.05 (0.69 to 1.59)	1.17 0.76 to 1.81	1.08 (0.88 to 1.31)	1.04 (0.85 to 1.27)	0.83 (0.55 to 1.27)	0.90 (0.59 to 1.38)	0.83 (0.63 to 7.08)	0.79 0.60 to 1.03	0.74 0.40 to 1.36	0.79 (0.43 to 1.46)
Depressive disorders												
Improvement	1	1	1	1	1	1	1	1	1	1	1	1
No change	0.69 (0.42 to 1.15)	0.73 (0.44 to 1.21)	0.89 (0.66 to 1.19)	0.97 (0.72 to 1.29)	0.84 (0.54 to 1.30)	0.89 (0.56 to 1.42)	1.02 (0.77 to 1.32)	1.02 (0.78 to 1.35)	0.67 (0.37 to 1.18)	0.71 (0.40 to 1.25)	0.93 (0.62 to 1.41)	1.02 (0.67 to 1.56)
Deterioration	1.77 (1.20 to 2.61)	1.85 (1.24 to 2.77)	1.19 (0.92 to 1.55)	1.23 (0.94 to 1.60)	1.85 (1.27 to 2.68)	1.83 (1.24 to 2.89)	1.29 (1.01 to 1.67)	1.32 (1.02 to 1.70)	1.52 (0.85 to 2.72)	1.51 (0.85 to 2.56)	1.65 (1.07 to 2.54)	1.67 (1.08 to 2.59)
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
BMI												
Improvement	0	0	0	0	0	0	0	0	0	0	0	0
No change	0.51 (0.0 to 0.92)	0.30 (-0.10 to 0.71)	0.43 (-0.17 to 0.71)	-0.03 (-0.61 to 0.53)	0.28 (-0.11 to 0.68)	0.18 (-0.21 to 0.58)	0.87 (0.32 to 1.43)	0.61 (0.09 to 1.14)	0.20 (-0.41 to 0.82)	0.24 (-0.36 to 0.86)	0.63 (-0.24 to 1.51)	0.39 (-0.43 to 1.22)
Deterioration	1.18 (0.74 to 1.62)	1.02 (0.58 to 1.45)	1.63 (1.02 to 2.24)	1.17 (0.58 to 1.76)	0.73 (0.25 to 1.20)	0.75 (0.28 to 1.23)	1.55 (0.93 to 2.16)	1.34 (0.74 to 1.94)	0.31 (-0.40 to 1.03)	0.50 (-0.20 to 1.21)	1.00 (-0.03 to 2.05)	0.81 (-0.17 to 1.80)
Cholesterol mg/dL												
Improvement	0	0	0	0	0	0	0	0	0	0	0	0
No change	3.34 (-1.43 to 8.11)	3.65 (-1.05 to 8.3)	0.44 (-0.70 to 964)	1.82 (-3.08 to 6.74)	5.60 (1.00 to 10.20)	5.24 (0.68 to 9.79)	2.52 (-2.40 to 7.45)	1.81 (-2.88 to 6.51)	2.69 (-4.36 to 9.75)	5.62 (-1.26 to 12.52)	2.09 (-5.37 to 9.57)	2.34 (-4.63 to 9.31)
Deterioration	8.96 (3.94 to 13.99)	7.65 (2.70 to 12.61)	11.25 (6.21 to 16.2)	7.83 (3.06 to 12.60)	8.62 (3.18 to 14.05)	8.93 (3.52 to 14.35)	7.19 (2.11 to 12.26)	6.88 (2.02 to 11.74)	5.24 (-2.9 to 13.46)	7.74 (-0.44 to 15.93)	1.32 (-6.98 to 9.64)	1.18 (-6.89 to 9.26)

Adjusted by education, study, age; 'improvement'=reference group.

High-risk drinking: >30 g alcohol per day for men, >20 g alcohol per day for women.

BMI, body mass index.

the occupational and financial situation after reunification was considerably associated with diabetes, depressive disorders, cholesterol and smoking. In general, the associations were stronger for women than for men, with the exception of depressive disorders.

Reunification was a critical life event that no one was able to escape. The rapid transition from communism or socialism to capitalism has been called 'shock therapy'.⁷ This led, at the level of the labour market, to a precarious employment relationship and mass unemployment.³³ Within a few years, millions of people lost their jobs due to the rapid de-industrialisation in most of the transition countries. Between 1989 and 1991, more than 2.5 million people in the former GDR became unemployed. Fifty per cent of East Germans changed their place of work during 1990/1991, and more than 60% of industrial workers became unemployed.³⁴ Many studies have shown a negative impact of unemployment on health.³⁵ The unemployment rate in East Germany rose rapidly after reunification. Although unemployment affected both men and women, this increased dramatically for women. The rate of unemployment in 1994 in East Germany was 22% in women and 11% in men.³⁴ This could also explain the stronger associations of stressors with CVD and cardiovascular risk factors for women in this study. Additionally, in a prospective study on the changes in perceived stress as a result of the 2008 economic crisis in Iceland, it was shown that the perceived stress of women after the economic crisis was significantly higher than before the crisis, especially for women who were unemployed. These changes were much stronger for women than for men.³⁶ This is in line with our findings. During the economic crisis in Iceland, the use of cardiac emergency rooms increased for women. This was explained by a state of uncertainty and anxiety about the future.³⁷

Our study showed a strong association between RSI and occupational changes and depressive disorders for men. In Romania and Hungary, depression and affective disorders increased sharply after the collapse of the communist regime, especially in men.^{38 39} Kopp *et al*³⁹ explained this with the loss of social rank. Men are less able to compensate for this than women.⁴⁰ Cockerham assumed that unhealthy lifestyles are the principal social determinant of increased mortality in Russia and selected Eastern European countries. Our data suggest rather that the deterioration in psychosocial factors after reunification was associated with an unhealthier lifestyle like smoking habits.¹³ The MONICA survey in East German study sites found a slight increase in smoking for women between 1988 and 1992. This is in line with our findings.

We found an association between personal change and depressive disorders in women. The MONICA survey in East Germany found an increased number of women who felt 'very isolated' after reunification, particularly the unemployed women.²⁴ Unemployment and

the changes in the labour market may explain the decrease in social support. The working environment played a central role in the GDR. The workplace ensured social care (eg, child care, medical care, recreational facility, and sporting and cultural activities). With the loss of their workplace or with a change in structural labour market conditions, a lot of people lost their social contacts. It could be that social isolation explains the increase of depressive disorders in women who experienced deterioration in their personal situation after reunification.

There are some factors that limit our study. First, this analysis faces the usual restrictions of a cross-sectional design; to determine the causality, a longitudinal design would be required. Additionally, we cannot exclude that outcomes like depressive disorders or hypertension already persisted before reunification. However, the exposure RSI refers to a fixed event in the past (German reunification); therefore, we can assume a chronological order of exposure, and disease outcomes MI and stroke. Second, the basic surveys were undertaken from 1998 to 2006, that is, 8–16 years after reunification. Given this time lag, recall bias may have influenced the results. However, we evaluated validity and reliability of the RSI and found no severe indication for recall bias. We argue that after this time delay, answering questions concerning personal impact of reunification will give a more steady reflection of the personal state. Furthermore, participants were not told the specific study hypotheses and therefore, would not have been aware of the potential link between reunification-related stress and CVD. Consequently, if there is a kind of recall error regarding reunification-related stressors, participants with and without relevant outcomes should be equally affected. This kind of non-differential misclassification could result in an underestimation of effects. Third, we assume that we lost potential participants because of illness or death due to factors associated to reunification. Furthermore, it is well known that healthy women and men were more likely to migrate after reunification to the western part of Germany. We thus cannot exclude a selection bias, which could change our results in both directions. Fourth, some questionnaires are different between the studies, for example, for depressive disorders. However, in analyses stratified by study the effects were similar. However, we have been cautious with regard to the interpretation of the effects because a depressive disorder exists for a long period; therefore, it is possible that depressed persons answer in a negative way due to the depressive disorder. Fifth, potentially we did not cover all psychosocial stressors due to a transition. However, we decided to analyse psychosocial stressors in terms of occupation, financial and personal stressors as in the appropriate literature these factors seem to be the most relevant.

In summary, our findings show that an individually perceived deterioration of psychosocial stressors in terms

of occupational, financial and personal stressors related to German reunification was associated with cardiovascular risk factors and CVD. An explanation for these findings could be that women were more often affected by unemployment after reunification. Our findings support the established hypothesis that psychosocial stressors favour cardiovascular risk factors and CVD after social change. Morbidity and mortality follow-up examination of both cohorts could enhance the results.

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REFERENCES

- Tunstall-Pedoe H, Kuulasmaa K, Mähönen M, *et al.* Contribution of trends in survival and coronary-event rates to changes in coronary heart disease mortality: 10-year results from 37 WHO MONICA Project populations. *Lancet* 1999;353:1547–57.
- Bobak M, Marmot M. East-West mortality divide and its potential explanations: proposed research agenda. *BMJ* 1996;312:421–5.
- McKee M, Fister K. Post-communist transition and health in Europe. *BMJ* 2004;329:1355–6.
- Nolte E, Shkolnikov V, McKee M. Changing mortality patterns in East and West Germany and Poland. II: short-term trends during transition and in the 1990s. *J Epidemiol Community Health* 2000;54:899–906.
- Walberg P, McKee M, Shkolnikov V, *et al.* Economic change, crime, and mortality crisis in Russia: regional analysis. *BMJ* 1998;317:312–18.
- Landsbergis P, Klumbiene J. Coronary heart disease mortality in Russia and Eastern Europe. *Am J Public Health* 2003;93:1793.
- Stuckler D, King L, McKee M. Mass privatisation and the post-communist mortality crisis: a cross-national analysis. *Lancet* 2009;373:399–407.
- Kuulasmaa K, Tunstall-Pedoe H, Dobson A, *et al.* Estimation of contribution of changes in classic risk factors to trends in coronary-event rates across the WHO MONICA Project populations. *Lancet* 2000;355:675–87.
- Leon DA, Chenet L, Shkolnikov VM, *et al.* Huge variation in Russian mortality rates 1984–94: artefact, alcohol, or what? *Lancet* 1997;350:383–8.
- Laaksonen M, McAlister AL, Laatikainen T, *et al.* Do health behaviour and psychosocial risk factors explain the European East-West gap in health status? *Eur J Public Health* 2001;11:65–73.
- Leon DA, Shkolnikov VM. Social stress and the Russian mortality crisis. *JAMA* 1998;279:790–1.
- Barth W, Claßen E, Heinemann L, *et al.* Development of the cardiovascular morbidity and mortality in East Germany after the political change. *Z Gesundheitswiss* 1998;6:120–36.
- Cockerham WC. The social determinants of the decline of life expectancy in Russia and Eastern Europe: a lifestyle explanation. *J Health Soc Behav* 1997;38:117–30.
- Kopp M, Skrabski A, Szántó Z, *et al.* Psychosocial determinants of premature cardiovascular mortality differences within Hungary. *J Epidemiol Community Health* 2006;60:782–8.
- Kozielec S, Lopuszańska M, Szklarska A, *et al.* The negative health consequences of unemployment: the case of Poland. *Econ Hum Biol* 2010;8:255–60.
- Rosengren A, Hawken S, Ounpuu S, *et al.* Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;364:953–62.
- Eller NH, Netterstrøm B, Gyntelberg F, *et al.* Work-related psychosocial factors and the development of ischemic heart disease: a systematic review. *Cardiol Rev* 2009;17:83–97.
- Kivimäki M, Nyberg ST, Batty GD, *et al.* Job strain as a risk factor for coronary heart disease: a collaborative meta-analysis of individual participant data. *Lancet* 2012;380:1491–7.
- Zellweger MJ, Osterwalder RH, Langewitz W, *et al.* Coronary artery disease and depression. *Eur Heart J* 2004;25:3–9.
- Knox SS, Uvnäs-Moberg K. Social isolation and cardiovascular disease: an atherosclerotic pathway? *Psychoneuroendocrinology* 1998;23:877–90.
- Theorell T. Critical life changes. A review of research. *Psychother Psychosom* 1992;57:108–17.
- Dittmann K, Rittner K, Weber I, *et al.* Premature myocardial infarct and social stress. *MMW Munch Med Wochenschr* 1981;123:1841–2.
- Justice B. Critical life events and the onset of illness. *Compr Ther* 1994;20:232–8.
- Ergebnisse des MONICA-Projektes Ostdeutschland 1984–1993. *Abschlussforschungsbericht an das Bundesministerium für Bildung, Wissenschaft, Forschung und Technologie*, 1997.
- Filipp SH, Aymanns P. *Kritische Lebensereignisse und Lebenskrisen*. Stuttgart: Kohlhammer, 2010.
- Greiser KH, Kluttig A, Schumann B, *et al.* Cardiovascular disease, risk factors and heart rate variability in the elderly general population: design and objectives of the CARDiovascular disease, Living and Ageing in Halle (CARLA) Study. *BMC Cardiovasc Disord* 2005;5:33.
- John U, Greiner B, Hensel E, *et al.* Study of Health in Pomerania (SHIP): a health examination survey in an East German region: objectives and design. *Soz Präventivmed* 2001;46:186–94.
- Bühringer G, Augustin R, Bergmann E, *et al.* (Hrsg) (2000) Alkoholkonsum und alkoholbezogene Störungen in Deutschland. Schriftenreihe des Bundesministeriums für Gesundheit. Bd128, Nomos Baden-Baden.
- Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas* 1977;1:385–401.
- Milette K, Hudson M, Baron M, *et al.*, Canadian Scleroderma Research Group. Comparison of the PHQ-9 and CES-D depression scales in systemic sclerosis: internal consistency reliability, convergent validity and clinical correlates. *Rheumatology (Oxford)* 2010;49:789–96.



31. Wittchen HU, Höfler M, Gander F, *et al.* Screening for mental disorders: performance of the Composite International Diagnostic— Screener (CID-S). *Int J Methods Psychiatr Res* 1999;8:59–70.
32. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. *Epidemiology* 1999;10:37–48.
33. Stuckler D, Basu S, Suhrcke M, *et al.* The health implications of financial crisis: a review of the evidence. *Ulster Med J* 2009;78:142–5.
34. Rosenzweig B. Deutschland Ost-Deutschland West. Opfer, Verliererinnen, ungleiche Schwestern? *Der Bürger Staat* 2000;4:225–30.
35. Roelfs DJ, Shor E, Davidson KW, *et al.* Losing life and livelihood: a systematic review and meta-analysis of unemployment and all-cause mortality. *Soc Sci Med* 2011;72:840–54.
36. Hauksdóttir A, McClure C, Jonsson SH, *et al.* Increased stress among women following an economic collapse—a prospective cohort study. *Am J Epidemiol* 2013;177:979–88.
37. Guðjónsdóttir GR, Kristjánsson M, Ólafsson Ó, *et al.* Immediate surge in female visits to the cardiac emergency department following the economic collapse in Iceland: an observational study. *Emerg Med J* 2012;29:694–8.
38. Ionescu I. Depression in post-communist Romania. *Lancet* 2005;365:645–6.
39. Kopp MS, Skrabski A, Székely A, *et al.* Chronic stress and social changes: socioeconomic determination of chronic stress. *Ann N Y Acad Sci* 2007;1113:325–38.
40. Rethelyi JM, Kopp MS. Hierarchy disruption: women and men. *Behav Brain Sci* 2004;27:305–7.

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