Erratum to: Education and risk of coronary heart disease: assessment of mediation by behavioral risk factors using the additive hazards model

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In the article by H. Nordahl, N. H. Rod, B. L. Frederiksen, I. Andersen, T. Lange, E. Prescott, K. Overvad, M. Osler entitled “Education and risk of coronary heart disease: assessment of mediation by behavioral risk factors using the additive hazards model” (*Eur J Epidemiol* 2013;28:149–157), it has come to the authors’ attention that the study population and outcome measure (coronary heart disease (CHD) event) were inaccurately defined due to errors which have occurred during the merging of data files. We found that the correct study population comprised 239 fewer participants and 585 fewer CHD events than reported in the published article. Neither did this correction change the crude distributions of CHD events and behavioral risk factors across the three educational groups; nor did it change the overall conclusion. However, the

relative and absolute educational differences in CHD were overestimated. For example, when comparing short to long education among women, the hazards ratio for CHD changed from 1.64 (95 % CI 1.47, 1.85) to 1.30 (1.16, 1.47). Correspondingly, the total effect changed from 277 (219, 336) to 135 (80, 190) additional CHD events per 100,000 person-years. Consequently, the observed mediated effects attributable to smoking, BMI and the risk factor score were slightly overestimated in relative terms and underestimated in absolute terms. Please note this correction when referencing this article. The authors apologize for any inconvenience this error may have caused. The correct values are presented in Tables 1, 2, 3 and 4 and all numbers in the results paragraph have been corrected.

Results

A total of 7,461 (11 %) participants were diagnosed with CHD during the follow-up time: 2,854 women and 4,607

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Table 1 Descriptive statistics by sex and educational level

	Total	Women's educational level			<i>P</i> *	Men's educational level			<i>P</i> *
		Short	Medium	Long		Short	Medium	Long	
Mean age, years (5th–95th percentile)	53 (40–63)	54 (40–64)	53 (36–63)	53 (37–63)	<0.01	54 (40–63)	53 (35–63)	54 (40–63)	<0.01
CHD events, no (%)	7,461 (11)	1,348 (10)	1,159 (7)	347 (5)	<0.01	1,396 (18)	2,436 (14)	775 (10)	<0.01
Smoking status, no (%)					<0.01				<0.01
Never	23,268 (33)	4,521 (34)	7,383 (44)	3,094 (46)		1,429 (18)	4,413 (26)	2,428 (32)	
Ex-smoker	17,988 (26)	2,654 (20)	3,643 (22)	1,778 (26)		2,090 (27)	5,187 (30)	2,636 (35)	
Smoker	27,883 (40)	6,022 (46)	5,840 (35)	1,837 (27)		4,263 (55)	7,498 (44)	2,423 (32)	
Missing	135 (<1)	33 (<1)	31 (<1)	5 (<1)		22 (<1)	30 (<1)	14 (<1)	
Physical activity, no (%)					<0.01				<0.01
Sedentary	12,133 (18)	2,786 (21)	3,084 (18)	1,067 (16)		1,397 (18)	2,609 (15)	1,190 (16)	
Light activity	28,229 (41)	5,756 (44)	7,641 (45)	2,910 (43)		2,955 (38)	6,439 (38)	2,528 (34)	
Moderate activity	22,911 (33)	3,875 (29)	5,058 (30)	2,255 (34)		2,718 (35)	6,166 (36)	2,839 (38)	
High activity	5,822 (8)	773 (6)	1,081 (6)	479 (7)		686 (9)	1,871 (11)	932 (12)	
Missing	179 (<1)	40 (<1)	33 (<1)	3 (0)		48 (1)	43 (0)	12 (<1)	
Body mass index, no (%)					<0.01				<0.01
Underweight	724 (1)	231 (2)	276 (2)	110 (2)		34 (<1)	58 (<1)	15 (0.2)	
Normal weight	31,836 (46)	6,258 (47)	9,169 (54)	4,174 (62)		2,570 (33)	6,270 (37)	3,409 (45.3)	
Overweight	27,211 (39)	4,471 (34)	5,411 (32)	1,829 (27)		3,717 (48)	8,339 (49)	3,448 (45.8)	
Obese	9,401 (14)	2,244 (17)	2,017 (12)	587 (9)		1,469 (19)	2,442 (14)	653 (8.7)	
Missing	102 (<1)	26 (<1)	24 (<1)	14 (<1)		14 (<1)	19 (<1)	5 (0.1)	
Median BMI kg/m ²	26	26	25	24		27	26	25	
(5th–95th Percentile)	(20–33)	(20–35)	(20–33)	(20–32)		(21–34)	(21–33)	(21–31)	
Risk factor score, no (%)					<0.01				<0.01
Low risk	8,628 (12)	1,356 (10)	2,508 (15)	1,179 (18)		550 (7)	1,888 (11)	1,147 (15)	
1 Risk factor	28,867 (42)	5,042 (38)	7,125 (42)	3,068 (46)		2,927 (38)	7,205 (42)	3,500 (47)	
2 Risk factors	27,847 (40)	5,901 (45)	6,541 (39)	2,254 (34)		3,586 (46)	6,974 (41)	2,591 (35)	
3 Risk factors	3,570 (5)	840 (6)	645 (4)	193 (3)		669 (9)	982 (6)	241 (3)	
Missing	362 (1)	91 (1)	78 (<1)	20 (<1)		72 (1)	79 (<1)	22 (<1)	
Cohort (examination years), no (%)					<0.01				<0.01
CCHS (1981–1983)	6,876 (10)	2,107 (55)	1,324 (34)	421 (11)		1,345 (44)	1,293 (43)	386 (13)	
1936-COHORT (1981–1982)	952 (1)	220 (43)	234 (46)	55 (11)		124 (28)	262 (59)	57 (13)	
MONICA I (1982–1984)	3,544 (5)	782 (45)	766 (44)	206 (12)		515 (29)	1,038 (58)	237 (13)	
MONICA II (1986–1987)	1,325 (2)	275 (41)	293 (44)	100 (15)		203 (31)	365 (56)	89 (14)	
MONICA III (1991–1992)	1,793 (3)	357 (39)	459 (50)	97 (11)		250 (28)	502 (57)	128 (15)	
DCH (1993–1997)	49,035 (71)	8,713 (33)	12,309 (47)	5,136 (20)		4,771 (21)	12,049 (53)	6,057 (26)	
INTER99 (1999–2001)	5,749 (8)	776 (26)	1,512 (51)	699 (23)		596 (22)	1,619 (59)	547 (20)	
Total	69,274	13,290 (36)	16,897 (46)	6,714 (18)		7,804 (24)	17,128 (53)	7,501 (23)	

CCHS Copenhagen City Heart Study, DCH Diet Cancer and Health Study

* *P* value for comparison of between educational levels obtained from one-way ANOVA F-test (continuous data) and Pearson χ^2 -test (categorical data)

Table 2 Hazard ratios (HRs) and 95 % confidence intervals for CHD using Cox proportional hazards model, by educational level

	Women’s educational level						% Excess risk*	Men’s educational level					% Excess risk*
	Short		Medium		Long	% Excess risk*		Short		Medium		Long	
	HR	CI 95 %	HR	CI 95 %	(REF.)			HR	CI 95 %	HR	CI 95 %	(REF.)	
Baseline model	1.30	1.16, 1.47	1.16	1.02, 1.31	1.00			1.36	1.24, 1.48	1.27	1.17, 1.38	1.00	
<i>Plus adjustments for</i>													
Tobacco: Smokers and ex-smokers	1.28	1.13, 1.44	1.15	1.02, 1.30	1.00	−2		1.33	1.22, 1.45	1.26	1.16, 1.37	1.00	−2
Physical activity: Sedentary-light activity	1.30	1.15, 1.47	1.16	1.03, 1.31	1.00	0		1.35	1.23, 1.48	1.27	1.17, 1.38	1.00	−1
BMI (5-unit increase)	1.24	1.10, 1.40	1.14	1.01, 1.29	1.00	−5		1.26	1.15, 1.38	1.21	1.12, 1.32	1.00	−7
Risk factor score (1-unit increase)	1.26	1.11, 1.41	1.14	1.01, 1.29	1.00	−3		1.30	1.19, 1.42	1.25	1.15, 1.35	1.00	−4

All estimates are adjusted for cohort

* HR comparing short versus long educational level

Table 3 Direct effects (DE), indirect effects (IE), and total effects (TE) of educational level on CHD for each risk factor derived from linear regression parameter estimates and the additive hazards model (WOMEN)

Potential mediators	Educational level	DE $\times 10^{-5}$	95 % CI	IE $\times 10^{-5}$	95 % CI	IE/TE %	95 % CI
Tobacco:	Long $\rightarrow$ short	120	66, 175	17	12, 22	12	8, 21
Smokers and ex-smokers	Long $\rightarrow$ medium	63	14, 112	3	1, 6	5	1, 17
Physical activity:	Long $\rightarrow$ short	134	80, 189	1	−1, 3	0	0, 2
Sedentary and light activity	Long $\rightarrow$ medium	66	16, 115	1	−1, 2	1	−1, 6
BMI	Long $\rightarrow$ short	106	51, 161	25	17, 33	19	11, 35
(5-Unit increase)	Long $\rightarrow$ medium	54	5, 104	12	8, 16	18	9, 65
Risk factor score	Long $\rightarrow$ short	108	54, 164	27	20, 33	19	13, 34
(1-Unit increase)	Long $\rightarrow$ medium	56	7, 105	10	7, 14	16	8, 56

All estimates are adjusted for cohort

Total effect (95 % CI) $\times 10^{-5}$: Long $\rightarrow$ short: 135 (95 % CI 80, 190) and long $\rightarrow$ medium: 66 (95 % CI 17, 115)

men. Baseline levels of behavioral risk factors differed between the three educational levels (Table 1). Women and men with short education were more likely to be current smokers, have a sedentary leisure time, have a higher BMI, and have a less favorable risk factor score than those with long education.

All three behavioral risk factors and the risk factor score were found to be associated with risk of CHD (data not shown). Being a smoker or ex-smoker was associated with a higher risk of CHD in women (hazard ratio (HR) = 1.36, 95 % confidence interval (CI) 1.26, 1.47) and men (HR = 1.32, 95 % CI 1.23, 1.43). A 5-unit increment in BMI was also associated with a higher risk of CHD in women (HR = 1.16, 95 % CI 1.11, 1.21) and men (HR = 1.31, 95 % CI 1.26, 1.36). The risk factor score was linearly related to the risk of CHD and for one risk factor increment at baseline, the hazard ratio for women was 1.24

(95 % CI 1.18, 1.30), and for men 1.25 (95 % CI 1.20, 1.30). Being low physically active was associated with a higher risk of CHD among men (HR = 1.11, 95 % CI 1.04, 1.18) but statistically insignificant among women (HR = 1.05, 95 % CI 0.97, 1.14).

Table 2 shows the results of the proportional hazards model, with the hazard ratios of CHD by educational level before and after adjustments for the behavioral risk factors (potential mediators). The educational gradient in CHD was skewed, since short education was associated with a higher risk of CHD. In the baseline model among women, those with short education (HR = 1.30, 95 % CI 1.16, 1.47) and medium education (HR = 1.16, 95 % CI 1.02, 1.31) were at higher risk of CHD compared to women with long education. Correspondingly, among men a higher risk of CHD was observed in those with short (HR = 1.36, 95 % CI 1.24, 1.48) and medium (HR = 1.27, 95 % CI 1.17, 1.38) education

Table 4 Direct effects (DE), indirect effects (IE), and total effects (TE) of educational level on CHD for each risk factor derived from linear regression parameter estimates and the additive hazards model (MEN)

Potential Mediators	Educational level	DE $\times 10^{-5}$	95 % CI	IE $\times 10^{-5}$	95 % CI	IE/TE %	95 % CI
Tobacco:	Long $\rightarrow$ short	271	183, 357	27	19, 35	9	6, 14
Smokers and ex-smokers	Long $\rightarrow$ medium	212	143, 281	14	10, 19	6	4, 10
Physical activity:	Long $\rightarrow$ short	294	207, 380	2	1, 5	1	0, 1
Sedentary and light activity	Long $\rightarrow$ medium	224	155, 293	1	-1, 2	0	0, 1
BMI	Long $\rightarrow$ short	219	131, 307	71	57, 85	24	17, 36
(5-Unit increase)	Long $\rightarrow$ medium	180	110, 249	44	35, 54	20	14, 30
Risk factors score	Long $\rightarrow$ short	247	160, 335	50	39, 61	17	12, 25
(1-Unit increase)	Long $\rightarrow$ medium	202	133, 271	25	19, 32	11	8, 17

All estimates are adjusted for cohort

Total effect (95 % CI) $\times 10^{-5}$: Long $\rightarrow$ short: 296 (95 % CI 209, 383) and long $\rightarrow$ medium: 224 (95 % CI 156, 293)

compared to long education. Adjustment for a 5-unit increment in BMI reduced the hazard ratio of both women (HR = 1.24, 95 % CI 1.10, 1.40) and men (HR = 1.26, 95 % CI 1.15, 1.38) with short education accounting for 5 % and 7 % of the excess risk of CHD, while adjustment for smoking reduced it by 2 % (HR_{women} = 1.28, 95 % CI 1.13, 1.44 and HR_{Men} = 1.33, 95 % CI 1.22, 1.45). Low physical activity had no noticeable influence on the relative difference in CHD. Adjusting for the risk factor score reduced the relative difference between short and long education in risk of CHD by 3 % among women, and 4 % in men.

The results derived from the additive hazards model estimating direct, indirect, and total effects of educational level on CHD are presented in Table 3 (women) and Table 4 (men). The direct and indirect effects were expressed as a single number since no indication of time dependent effects for either the exposure or mediators was observed. Parallel to the results in Table 2, the incidence of CHD was lowest among women and men with long education. Being in the short educational level compared with

long educational level was associated with 135 (95 % CI 80, 190) additional cases of CHD per 100,000 person-years at risk among women. Of these additional cases, 17 (95 % CI 12, 22) cases or 12 % (95 % CI 8, 21) could be attributed to the pathway through smoking (Table 3). Furthermore, 25 (95 % CI 17, 33) cases or 19 % (95 % CI 11, 35) could be attributed to the pathway through a 5-unit increment in BMI. Among men, being in the short educational level compared with long educational level was associated with 296 (95 % CI 209, 383) extra cases per 100,000 person-years at risk, of which 27 (95 % CI 19, 35) cases per 100,000 person years or 9 % (95 % CI 6, 14) and 71 (95 % CI 57, 85) cases or 24 % (95 % CI 17, 36) could be attributed to the pathway through smoking and BMI, respectively (Table 4). The effect of low physical activity was negligible both among women and men. A 1-unit increment in the risk factor score seemed to be attributable to 27 (95 % CI 20, 33) and 50 (95 % CI 39, 61) additional cases per 100,000 person years of the social gradient in CHD among women and men, respectively.