Original Article

What do we Learn from the Prevention Education Program Family Heart Study about Lifestyle change, Blood Pressure, and Lipids in Children and Parents?

Abstract

Objectives: The PEP Family Heart Study is a perspective community-based long-term project for the whole family to improve cardiovascular health aiming to assess and to amend risk factors in children and their parents by lifestyle change. Methods: A total of 48,667 subjects (24,927 adults and 23,740 children) from 3,370 families living in 94% of the elementary school districts of Nuremberg (Germany) participated in this observational study from 1993/1994 -2007/2008. The yearly surveys consisting of personal and family histories, structured interviews on leisure time physical activity and tobacco smoke exposition, physical examinations and nutritional intake as documented by seven days weighed dietary protocols and sustained healthy lifestyle counselling were mainly performed at home. Fasting blood collections for biochemical analyses in the study laboratories, cooking courses and seminars on healthy lifestyle were performed on weekends in central school buildings. Results: Here we report some of the main results demonstrating e.g., that at least one CVD risk factor in a child conferred a 2-4 fold higher risk among their parents, that obese children and adolescents had a nearly five times higher prevalence of hypertension than nonoverweight youths. Conclusions: Sustained healthy lifestyle behavior can be implemented in daily life of family members which results in amended nutritional intake and improved cardiometabolic risk factors.

Keywords: Cardiovascular disease risk factors, prospective community-based study, lifestyle change

Introduction

Since cardiovascular risk factors may result in the development of subclinical atherosclerosis and vascular changes over the course of years, it makes sense that avoidance of adverse levels of risk factors in the first place may be the most effective means for avoiding clinical events during the remaining life span. Therefore, the American Heart Association (AHA) recommends as impact Goals 2020 to improve cardiovascular health of all Americans by 20%.[1] Hence, screenings for elevated cholesterol or blood pressure (BP) in at-risk groups are key facets of cardiovascular disease (CVD) prevention guidelines, even in children and adolescents.^[2] Among others, studies from Switzerland, Australia, the USA, and Germany suggested that cardiovascular risk factors may be correlated between their parents.^[3-8] The children and Australian Busselton Population Health Studies considered the nuclear family as

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms. a point of intervention by modifying risk factors.^[4] Data on educational intervention are heterogeneous in terms of little effect on the familial aggregation of HDL- and LDL- cholesterol respectively significantly greater improvement in diet and of HDL-Cholesterol.^[5,7] In six studies, groups receiving lifestyle-based interventions offering 52 or more hours of contact showed greater improvements in BP than in control groups.^[9]

Hypothesizing that modifying CVD risk factors by healthy lifestyle should be tested in healthy families in real life, we started the Prevention Education Program (PEP) Family Heart Study 1993 in Nuremberg (Germany) among first graders and their families involving 94% of all school districts of the city.^[10] The two aims of this prospective urban family-based observational study were first to detect cardiometabolic risk factors using easily available, safe, noninvasive, and inexpensive traditional measurement procedures and second to intervene by

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regularly controlled sustained lifestyle change in terms of healthy nutritional intake, leisure-time physical activity (LTPA), and nonsmoking in young adults and their children. Here, we review some of the results from the 15 years' active phase of this long-term observational study which was mainly performed at home by specially trained professionals. Because the anthropometric and laboratory risk variables change corresponding to childhood growth and development, we had to calculate specific percentile (pctl) growth curves for this large basic sample of 23,740 children and adolescents aged 3–18 years.

Methods

Subjects

From the school years 1993/1994 to 2007/2008, a total of 48,667 volunteers living in 94% of the elementary school districts of Nuremberg were enrolled free of charge. The participants consisted of 24,927 adults (55% women) from 3370 families and 23,740 children (12,192 girls) from 3268 families without known CVD or traditional CVD risk factors. Separate analyses for adults and youths had to be performed because in children and adolescents, the anthropometric and laboratory risk variables vary by age and sex because of the natural growth in childhood from the adults respectively caregivers and adolescence.^[11] Informed written consent was obtained from the respective caregivers of all the participants that included the voluntary participation in the yearly surveys. Yearly individual health passports informed each participant about his/her actually ascertained data. Only anonymized complete data sets were scientifically evaluated by the study center. The study fulfilled the criteria of the Declaration of Helsinki and was approved by the Ethical Committee of the Medical Faculty of the Ludwig Maximilian University of Munich, the Bavarian Ministry of Science and Education, and the local authorities in Nuremberg.

Healthy lifestyle intervention

Once a year, each participant delivered complete questionnaires reporting his/her sedentary behavior, LTPA, tobacco smoke exposition, and dietary protocols recording precisely weighed on special scales, the daily nutritional intake over 7 continuous days. The sustained training for weighing dietary components correctly and completing the yearly dietary records and questionnaires together with the yearly provided individual health certificates on the actual risk profiles considerably strengthened motivation and adherence throughout the study. Beyond this health education at home, we provided further advice on healthy lifestyle including written material during blood sampling, phone calls, cooking courses, exercise sessions, special seminars, and family meetings between the visits at home. According to the AHA recommendations, we used four healthy lifestyle factors (current smoking, weight control,

LTPA, and 7 days' dietary records) to determine adherence to healthy lifestyle.^[2,6]

Measurements

Physical medical history. examinations, questionnaire-guided interviews, healthy lifestyle counseling, and 7 days' weighed dietary protocols were performed at home by specially trained physicians and certified dieticians, organized by the PEP team residing in the sanitary board of the city of Nuremberg. At each survey, weight and height were measured to the nearest 0.1 cm and 0.1 kg, using a calibrated electronic scale SECA (Vogel and Halske, Hamburg, Germany) and a Stadiometer Holtain Ltd., (Crymych, UK). Anthropometric measurements were performed as previously described^[8,10,12-15] in terms of body mass index (BMI), waist circumference (WC), circumference, waist-to-hip hip ratio (WHR), waist-to-height ratio (WHtR), triceps, and subscapular skinfold thickness (SFT) using a Holtain skinfold caliper (GPM-caliper, Zurich, Switzerland) on the left body side in triplicate to the nearest 0.1 mm calculating % BF using the age- and sex-adjusted Slaughter equations.^[14] To obviate interobserver variation during one survey, the same individuals made all anthropometric measurements. Systolic BP (SBP) and diastolic BP (DBP) were measured twice (calculating the average) in a sitting position after 5 min rest on the left arm supported, cubital fossa at heart level using a validated nonmercury ERKA-Aneroid calibrated sphygmomanometer (MTM semiannually Munich, Germany) providing four appropriate cuff sizes.^[15] Fasting blood was collected at Saturdays in November, December, and January in central school buildings. Fasting triglyceride (TG), total cholesterol (TC), LDL-C, non-HDL-C, and HDL-C were measured by enzymatic methods in the central laboratory as described previously.^[8]

Categorization

Nonoverweight (normal weight) is defined as BMI <85th pctl, overweight as BMI 85th to <95th pctl, obesity as BMI \geq 95th pctl, and severe obesity as \geq 120% of the 95th pctl.^[16] Prehypertension is categorized as the \geq 90th to <95th pctl or \geq 120/80 mmHg and hypertension as \geq 95th pctl on \geq 3 occasions.^[17]

Statistical analysis

All statistical analyses were performed using actual SPSS (Chicago, IL, USA). Bivariate and multivariate analyses were conducted, and multivariate regression analysis was used for age and gender adjustments. Generalized estimating equations were used to generate adjusted P values that accounted for correlation among multiple within-family observations as well as for adjustment for age and gender. Analyses were also stratified by child–parent specified between-subject gender associations by calculating estimated marginal means.^[18,19] Self-reported physical activities were calculated in metabolic equivalents

at task according to Ainsworth and Ridley using equations for adults and children as previously described.^[20,21] All variables were tested for normal distribution. Statistical tests were two-sided, and P < 0.05 was considered statistically significant, for correlations with P < 0.01 and significances for paired differences and regression coefficients, respectively, odds ratios (ORs), with P < 0.001. Smoothed age-, gender-, and height-specific pctls for children were constructed using the software package LMS Chart Maker Pro (The Institute of Child Health, London), estimating the skewness parameter *L*, the median *M*, and a measure of variation *S*.^[22]

Results

Family screening for cardiovascular disease risk factors

Since children use health-care facilities more frequently than their young parents, we examined whether we could detect silent CVD risk factors in parents by screening their children.^[8] Among the 2720 child-parent pairs, we found an age and gender adjusted 2-3 fold higher OR among parents for the same risk factors. As shown in Table 1, this was the most pronounced of the silent risk factors, i.e., dyslipidemia (e.g., for high LDL-C, OR was 2.99 and the 95% confidence interval [CI] was 2.36–3.79) and high WHtR (OR: 2.55, 95% CI: 1.80-3.62) but less for hypertension (OR: 1.3, 95%CI: 0.89-1.90). Within the same gender, the associations were even stronger, for example, if the son has low HDL-C, the risk for low HDL-C was 1.40-fold (95% CI: 0.95-2.05) in fathers and 3.32-fold (95% CI: 2.27–4.84) in mothers, respectively; in daughters with low HDL-C, the corresponding risk was 1.6-fold in fathers and 2.1-fold in mothers. If the son had hypertension, fathers had a 1.6-fold risk for hypertension while mothers had a lower risk (OR: 1.3), and if daughters were hypertensive, fathers had no higher risk, but mothers had a 1.5-fold higher risk of being hypertensive.

Our study suggests that screening elementary schoolchildren for cardiometabolic risk factors may be an efficient case-finding strategy in their parents allowing for early lifestyle intervention in parents and the whole family.

Blood pressure by age, gender, and weight in children and adolescents

Two large representative studies assessed normative pediatric BP values in German children and adolescents.^[15,24] The countrywide KiGGS study used an oscillometric design in 14,836 participants aged 3–17 years, included 17% other ethnicities, and excluded 2150 overweight and obese children and adolescents defining overweight as BMI \geq 90th pctl.^[24] The urban PEP Family Heart Study included 22,052 children and adolescents aged 3–19 years, used the international definition of overweight as BMI 85th–95th pctl and the auscultatory sphygmomanometric design precluding an interchange of

oscillometric and auscultatory BP readings, and excluded 2.6% other ethnicities.^[15-17,25]

Among the 22,051 pediatric participants of the PEP Family Heart Study, adolescets (mean age: 14.1 ± 1.9 years) had higher mean SBP values than children (mean age: 7.8 ± 2.0 years). Mean SBP was 114.5 \pm 11.4 mmHg in 3198 male adolescents and 109.9 ± 9.4 mmHg in 2817 female adolescents while 8130 boys had 104.3 ± 9.0 mmHg and 7906 girls had 103.7 ± 9.2 mmHg. However, because of the growth and development in childhood, age- and sex-specific pctls must be calculated for all children and adolescents to find individual BP values.^[15] As depicted in Figure 1, the 10 pctl curves of SBP and DBP increase from 3 to 18 years in males and females but with different gender-related slopes throughout age. Because weight is a major determinant of BP, we restricted the normative population to 18,917 nonoverweight children and adolescents which resulted in generally slightly lower pctls (by 1–2 mmHg) than in all 22,051 participants, which is consistent with the study of Rosner et al.[26]

Because BP values increase with increasing pctls^[15] in all three weight groups, we assessed BP at the 50th, 90th, and 95th pctl in 6 years and 17-year-old males and females [Table 2]. Compared with 6-year-old normal weight boys the median BP was 4/3 mmHg higher in overweight and 9/5 mmHg higher in obese boys respectively 4/4 mmHg higher in overweight and 10/7 mmHg in obese girls. Thus, compared with normal weight median BP was 7/4 mmHg higher in overweight and 12/9 mmHg higher in obese boys and 5/3 mmHg higher in overweight and 12/8 mmHg higher in obese girls at age 6-years. The corresponding differences exist in 17-year-old female and male adolescents. Because of these large BP differences between these three weight groups, we calculated separate pctls.^[15]

The prevalence of prehypertension and hypertension increased from normal weight (13.8% and 5.7%) through overweight (20.6% and 13.8%) to obesity (24.5% and 26.1%). As shown in Table 3, elevated BP was significantly associated with overweight and obesity, strongest between hypertension and obesity not only in females (OR: 5.9, 95% CI: 5.1–7.5) but also in males between prehypertension and overweight (OR: 1.6, 95% CI: 1.4-1.9). This is consistent with the US data describing for prehypertension an OR of 2.3 (95% CI 2.2-2.4) between normal weight and overweight (BMI ≥85th pctl) children.[26] In severe obesity, we found a prevalence of hypertension at $\geq 120\%$ of the 95th to <140% of the 95th pctl of 25.8% in males and 36.9% in females, and at $\geq 140\%$ of the 95th pctl the prevalence of hypertension was 59.1% in males and 56% in females [Figure 2].

In summary, we calculated separate BP pctls for 22,051 nonoverweight, overweight (BMI $\geq 85^{\text{th}}$ pctl), and obese (BMI $\geq 95^{\text{th}}$ pctl) urban children and adolescents and found increasing BP by weight with an increasing



Figure 1: Ten SBP and DBP percentile curves in all and in normal-weight males and females

prevalence of hypertension from 5.7% through 13.8% to 26.1%. The normative auscultatory BP pctls with and without exclusion of overweight were similar but increased by weight group, for example, from 130/83 mmHg to 148/91 mmHg in overweight and 154/95 mmHg in obese male adolescents. This increase of BP by weight as well the more than doubled prevalence of hypertension as in overweight and the 5 fold higher prevalence of hypertension in children and adolescents raised some debate on normative blood pressure values in overweight and obese vouths.^[27-30] However, different BMI-specific pctls would contradict the "decision made not to provide tables as a function of weight"[26] and would imply to ignore the higher prevalence of target organ damage in obese children and adolescents.^[27] But since we do not have adult outcome data in youths which link BP levels with CVD, we should be on the save side and continue to strongly recommend



Figure 2: Prevalence of hypertension by BMI percentiles in 11,328 males and 10,723 females, 3-18 years

weight reduction first in overweight and obese children and adolescents.

Percentiles of fasting serum lipid values in children and adolescents

The LMS curves at the 3rd, 5th, 10th, 25th, 50th, 75th, 85th, 90th, and 95th pctls for fasting serum HDL-C, LDL-C, and the ratios of LDL-C and TG/HDL-C for 5213 males and 5628 females are depicted in Figure 3. In both genders, HDL-C curves increase between the ages of 3 and 9 years and then decrease continuously in males but slightly decrease until age 13 and then re-increase again in females. While the LDL-C/HDL-C curves in both genders have similar slopes but a wider range in females (1.1-4.5) than in males (0.8-3.5), the TG/HDL-C has completely different shapes in males with decreases of all the 10 curves until the age of 9 years and then steep continuous increases reaching 2.5 in the four upper pctls in males. Table 4 compares median values (50th pctl) of serum lipids which decrease continuously for LDL-C (from 98.0 to 76.9 mg/dL in males and from 100.4 to 87.7 mg/dL in females) and for non-HDL-C (from 110.4 to 92.0 mg/dL in males and in females from 113.3 to 103.7 mg/dL) whereas TG increased from 58.6 to 71.4 mg/dL in males and from 61.9 to 72.7 mg/ dL. But from age 3 to age 18 years, HDL-C decreased by 7.3 mg/dL in males but increased by 7.0 mg/dL in females.

The comparison with the median TC, LDL-C, and HDL-C values for 6- and 14-year-old males and females



Figure 3: LMS curves at the 3rd, 5th, 10th, 25th, 50th, 75th, 85th, 90th and 95th pctl for serum lipids in 5,628 males and 5,213 females, aged 3-18 years

of the KiGGS study using the same laboratory methods demonstrates slightly higher values in adolescents but lower values in children in nonfasting serum samples from 7297 males to 6951 females aged 0–17 years collected in 167 locations all over Germany including 17% migrants.

In summary, all lipoprotein fractions containing cholesterol decrease from childhood to adolescence whereas triglyceride values increase in both genders. Norms should be based on age- and gender-specific pctl values because of strong differences.

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Anthropometric cardiovascular disease risk factors

We developed pctl curves for WC, hip circumference HC, WHtR, WHR, and SFT in 3850 German 3–11-year-old children and in 3024 German 12–18-year-old adolescents.^[31,32] Abdominal obesity is a CVD risk factor which is associated with high WC and high WHtR, and in children, increased WHtR and increased SFT are the strongest predictors for CVD risk factors. Comparison of the 90th pctl values for WC (cm) among 6–11-year-old boys and girls from 12 countries is shown in Table 5.^[13]

Table 1: Age-and gender-adjusted odds ratios in parents
based on CVD risk factors in their children

Children with	14	Odds ratio	059/ CI
	n	Ouus ratio	9370 CI
Obesity	145	2.91	1.96-4.34
High waist circumference	146	2.55	1.80-3.62
Hypertension	83	1.30	0.89-1.90
High triglycerides	96	1.38	0.92-2.07
Low HDL-Cholesterol	458	1.99	1.61-2.46
High LDL-Cholesterol	236	2.99	2.36-3.79
High non-HDL-Cholesterol	430	2.90	2.12-3.96

Table 2: Different blood pressure percentile values
in normal weight, overweight and obese 6 years old
children and 17 years old adolescents ^[12]

	50 th	pctl	90 th	pctl	95 th pctl		
	Boys	Girls	Boys	Girls	Boys	Girls	
Normal weight							
6 years	102/66	101/65	112/76	112/76	115/79	115/79	
17 years	120/75	111/71	135/85	122/80	140/88	125/83	
Overweight							
6 years	106/69	105/69	118/80	117/79	122/83	120/82	
17 years	126/76	116/75	140/86	128/85	143/88	132/88	
Obese							
6 years	109/71	111/72	122/84	123/84	127/88	127/87	
17 years	130/83	120/79	148/91	136/91	154/95	124/95	
	Boys	Girls	Boys	Girls	Boys	Girls	
Normal weight							
6 years	102/66	101/65	112/76	112/76	115/79	115/79	
17 years	120/75	111/71	135/85	122/80	140/88	125/83	
Overweight							
6 years	106/69	105/69	118/80	117/79	122/83	120/82	
17 years	126/76	116/75	140/86	128/85	143/88	132/88	
Obese							
6 years	109/71	111/72	122/84	123/84	127/88	127/87	
17 years	130/83	120/79	148/91	136/91	154/95	124/95	

Because the cutoff as a measure of abdominal adiposity is controversially discussed, we calculated 10 pctls for 22,113 urban 3–18-year-old youth.^[33] Opposite to the impressive slogan "Keep your WC to less than half of your height" for all ages and both genders,^[34] we found substantially different age- and gender-specific pctls in children and adolescents: in 7-year-old children, WHtR at the 50th pctl was 0.45 in both genders; in 15-year-old adolescents, WHtR at the 85th pctl was 0.45, while the ratios were 0.48 for both genders, and WHtR at the 95th pctl was 0.53 in males and females.

Silent CVD risk factors such as dyslipidemia and elevated BP can be detected in adolescents by anthropometric measures in adolescents.^[12] Among 412 adolescents with abdominal obesity, age-adjusted risk factor clustering was 3-4 times higher than in 2626 adolescents without abdominal adiposity [Table 6]. We found significant associations with dyslipidemia in terms of hypertriglyceridemia (OR: 4.9), elevated LDL-C (OR: 2.0), low HDL-C (OR: 1.6), and fasting blood glucose (OR: 1.3) and a 2.5 times higher risk of hypertension. At or above the 90th pctl, the sum of SFT $(SFT_{biceps}, SFT_{triceps}, and SFT_{subscapular})$ was 56.4% in boys and 26.7% in girls, whereas the sum was similar in adolescents with (3.5%) and without (3.1%) abdominal adiposity. We calculated percentage body fat (%BF) based on SFT estimations using the Slaughter equations^[35] in 22,113 urban children and adolescents, demonstrating that the median %BF is considerably higher in females than in males and urban percentage body fat values seem to be lower than the national values irrespective of the country.

Because joint international pediatric studies on the metabolic syndrome are rare, we compared youths with different ethnicities living in three different continents.^[36] This study included 4473 children and 6800 adolescents from Brazil, Iran, and Germany (BIG study) and found very similar prevalences of abdominal adiposity in these three countries. However, the prevalence of dyslipidemia was considerably higher in Brazil and Iran than in German. BP was lower in Iranian but similar in Brazilian and German children and adolescents. Furthermore, we compared anthropometric and lipid pctls between Iranian and German youths,^[37] assessed the effects of smoking on body fat, dyslipidemia, and BP in Germans and Turks,^[38] and compared central obesity in Polish and German youths.^[39]

	Table 3: Associations (odds ratios) between weight groups and blood pressure levels										
	Prehype	rtension				Нуре	rtension				
OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	Weight group			
0.5	(0.4-0.6)	0.4	(0.4-0.5)	0.3	(0.2-0.3)	0.2	(0.2-0.2)	Non overweight			
1.6	(1.4-1.9)	1.8	(1.6-2.2)	2.1	(1.7-2.6)	2.7	(2.2-3.3)	Overweight			
2.4	(1.9-2.9)	3.3	(2.7-4.1)	4.3	(3.5-5.2)	5.9	(5.1-7.5)	Obese			
Bovs		Girls		Boys Girls			Girls				

	-	(mg/dL) in 3-18 years	old children and adolesce	nts	
		a. 5,	213 males		
Age	Total cholesterol	LDL-Cholesterol	HDL-Cholesterol	Non HDL-C	Triglycerides
3	165.46	97.97	54.22	110.36	58.60
4	166.58	98.24	55.23	110.30	57.27
5	167.62	98.34	56.31	110.14	56.05
6	168.56	98.23	57.47	109.87	55.05
7	169.27	97.90	58.52	109.50	54.36
8	169.69	97.44	59.32	109.09	53.92
9	169.46	96.67	59.69	108.46	53.91
10	167.96	95.28	59.38	107.28	54.42
11	164.92	93.16	58.25	105.36	55.37
12	160.54	90.49	56.37	102.85	56.77
13	155.32	87.39	54.08	99.89	58.52
14	150.08	84.11	51.86	96.82	60.52
15	145.79	81.20	50.07	94.29	62.77
16	142.94	79.07	48.77	92.71	65.34
17	141.36	77.73	47.80	92.07	68.28
18	140.47	76.88	46.96	92.00	71.44
		b. 5,6	28 females		
Age	Total cholesterol	LDL-Cholesterol	HDL-Cholesterol	Non HDL-C	Triglycerides
3	164.49	100.40	50.06	113.27	61.90
4	167.78	101.92	51.84	114.83	61.61
5	170.68	103.13	53.51	116.03	61.34
6	172.82	103.74	54.97	116.65	61.18
7	173.69	103.48	55.99	116.47	61.32
8	173.11	102.30	56.37	115.59	61.98
9	171.32	100.28	56.10	114.11	63.19
10	168.74	97.74	55.40	112.20	64.60
11	165.59	94.90	54.48	109.92	65.94
12	162.36	92.30	53.66	107.51	66.99
13	159.85	90.35	53.25	105.46	67.78
14	158.42	88.98	53.38	103.99	68.50
15	158.20	88.19	53.99	103.27	69.34
16	158.85	87.80	54.92	103.12	70.36
17	159.96	87.68	55.97	103.32	71.49
18	161.27	87.69	57.05	103.67	72.68

Table 4a and b: Median percentiles (59th pctl) of total Cholesterol, LDL-C, HDL-C, Non HDL-C and Triglycerides

Table 5: Comparison of 90th percentile values for WC (cm) among 6-11-year-old boys and girls from 12 countries^[13]

	Bo	oys		Girls				
6 years	cm	11 years	cm	6 years	cm	11 years	cm	
Japan	55.0	UK	67.9	Japan	56.0	UK	65.4	
UK	57.1	Japan	70.0	UK	57.0	Japan	66.0	
China	60.0	Australia	71.3	China	58.0	Turkey	68.4	
Turkey	61.3	Canada	71.7	Turkey	60.1	Canada	68.7	
Australia	61.9	Turkey	72.5	Germany	61.8	China	69.0	
Germany	52.6	China	75.0	Australia	62.7	Australia	70.4	
USA	64.2	IRAN	77.1	Iran	63.5	Germany	74.7	
Cyprus	65.0	Germany	78.4	USA	64.0	Iran	75.0	
Italy	65.6	Cyprus	81.1	Cyprus	65.9	Mexico	75.2	
Mexico	67.4	USA		Mexico	68.0	Cyprus	76.6	

Healthy lifestyle and cardiovascular disease risk factors

The association between energy consumption and overweight was significant, and calorie intake was associated with clustering of ≥ 3 cardiovascular risk factors (OR: 4.72; 95% CI: 1.22-18.33) in four age groups of females.^[40] In 575 parents and 411 children, we implemented a healthy diet according to the recommendations of the Nutrition Societies of Germany, Austria, and Switzerland (D-A-CH).[41] Table 7 depicts acceptance and healthy changes over 1 year in parents and their children in terms of an increased ratio of polyunsaturated fat to saturated fat, reduction of total fat calories, and fiber alcohol. Only in parents, the consumption of saturated fat and cholesterol decreased. The effects of sustained healthy lifestyle counseling consisting of healthy

thickness (SFT) in 3,038 adolescents										
All (<i>n</i> =3,038)	WC	BMI	WHtR	WHR	Skinfoldsum	Central Obesity				
LDL-C≥130mg/dL			3.0 (1.7-5.3)			2.8 (1.4-2.9)				
HDL-C ≤40mg/dL	1.7 (1.1-2.8)					1.6 (1.1-2.2)				
TG≥150mg/dL				2.3(.2-4.4)	2.3 (1.2-4.4)	4.9 (3.1-7.7)				
TG/HDL-C ≥3.5	6.1 (1.9-19.8)				3.9 (1.2-13.9)	7.2 (2.9-17.9)				
NonHDL-C ≥ 123 mg/dL			2.7 (1.8-4.0)			2.1 (1.7-2.7)				
$FFG \ge 100 mg/dL$		1.8 (1.2-2.7)				1.3 (1.0-1.6)				
Hypertension		4.9 (2.8-8.4)	2.7 (1.9-4.8)			2.5 (1.8-3.5)				
\geq 3 nonanthrop risk factors					1.9 (1.1-3.4)	3.8 (2.6-5.5)				

Table 6: Age- and gender-adjusted significant (*P*<0.001) associations (OR; (95% CI) of the CVD risk factors lyslipidemia, hypertriglyceridemia and hypertension with WC, BMI, WHtR, waist-to-hip-ratio (WHR) and slinfold thickness (SFT) in 3.038 adolescents

Legend: Central adiposity was defined as WC ≥90th percentile and/or WHtR ≥0.5

Table 7	Table 7: Two-year follow up of energy intake and consumption of macronutrients (based on complete 7 d weighed											
	Men (/	dietary r n=254)	ecords) of 575 Women	parents and 4 $(n=321)$	11 children; r Boys ($\frac{\text{nean} (\text{SD})^{[42]}}{n=195}$	Girls (n=216)				
	vear 1	vear2	vear1	vear2	vear1	vear2	vear1	vear2				
Kcal/d	2470.8	2424.6	1892.8	1820.6	1599.5	1704.0	1454.8	1523.0				
	(468.4)	(492.6)	(403.2)*	(398.3)	(342.1)	(314.1)*	(269.9)	(288.6)*				
Fata	101.6	99.5	80.6	75.3	63.1	65.1	57.8	59.3				
	(25.0)	(26.1)	(22.3)*	(21.5)	(17.1)	(15.6)	(13.2)	(14.6)				
%kcal	38.2*	36.9	39.4*	37.1	36.5*	34.4	36.91*	35.0				
PUFAa	14.8 (4.7)	15.6 (5.2)*	11.8 (3.9)	11.9 (4.2)	8.3 (2.9)	9.5 (3.3)*	7.9 (2.8)	8.7 (3.2)*				
%kcal	5.6	6.0*	5.8	6.1	4.8	5.2*	5.0	5.3*				
%fat	14.7	15.9*	14.8	15.9*	13.1	14.7*	13.7	14.8*				
MUFAa	36.8 (9.5)	36.0 (10.3)	28.2 (8,5)*	26.5 (7.9)	22.0 (6.5	22.3 (6.2)	19.9 (5.0)	20.3 (5.4)				
%kcal	13.9	13.8	13.8*	13.4	12.7*	12.1	12.7	12.4				
%fat	36.2	36.1	34.9	35.1	34.8	34.2	34.3	34.1				
SAFAa	43.1 (12.2)*	41.2 (12.2)	35.1 (10.7)*	31.8 (10.4)	28.5 (8.2)	28.7 (7.1)	26.0 (6.3)	26.1 (7.0)				
%kcal	16.2*	15.7	17.1*	16.1	16.5*	15.6	16.6*	15.9				
%fat	42.2*	41.2	43.4*	42.0	45.2*	44.1	45.0*	44.0				
p/s	0.36	0.40	0.35	0.39	0.30	0.34	0.31	0.35				
Cholb	380.4	352.8	300.9	268.6	237.6	240.1	222.9	219.2				
	(114.2)*	(110.2)	(95.5)*	88.2	70.4	(73.9)*	(74.4)*	(70.8)				
Carboha	255.5	255.7	208.0	203.9	201.9	218.8	182.8	193.5				
	(60.5)	(64.5)	(51.5)	(49.5)	(46.4)	(42.9)*	(38.3)	(41.3)*				
%kcal	42.4	43.0	45.0	45.7*	51.9	52.4	51.5	51.8				
Fiber	21.0 (6.8)	21.7 (7.1)	18.6 (5.3)	18.6 (5.4)	14.7 (4.1)	16.0 (4.5)*	13.7 (4.0)	14.8 (4.4)*				
Protein	88.2	87.6	65.2	64.0	50.7	54.8	46.2	48.6				
	(19.3)	(18.1)	(14.4)	(14.6)	(12.3)	(11.8)*	(10.3)	(11.0)*				
%kcal	14.7	14.9	14.3	14.5	13.0	13.1	13.0	13.1				
Alcohola	23.0 (21.4)*	19.2 (17.8)	8.1 (8.9)	7.4 (9.2)	0.4 (0.5)	0.3 (0.4)	0.3 (0.5)	0.(0.3)				
	6.6*	5.3	3.0*	2.7	0.2*	0.1	0.1*	0.0				

a) g/day, b) mg/day. *Significant changes between year-1 and year-2 (P<0.05)

diet, LTPA, and nonsmoking in 687 biological child-parent pairs are shown in Table 8, demonstrating improvements of the risk factor profiles of parents and children. After 1 year sustained lifestyle counseling, elevated SBP decreased in fathers by 3.2% and in mothers by 1.9%, in sons by 1.5%, in daughters by 5.5% and elevated DBP decreased in fathers by 5.1%, in mothers by 4.0%, in sons by 1.1%, and in daughters by 6.5%. The prevalence of hypertension decreased by 6.2% in fathers, by 4.4% in mothers, and by 12.2% in daughters but did not change in sons. Elevated fasting plasma glucose decreased in fathers by 16.9%, in sons by 15.9%, and in daughters by 7.8% whereas the serum lipid concentrations did not change. However, the percentage of tobacco smoke exposition decreased throughout 1 year, most strongly in daughters. In growing children, we found no relevant changes of fat patterning while abdominal adiposity in terms of elevated WC and WHtR slightly decreased among parents.

	counseling; mean (SD), * <i>P</i> <0.05 between baseline and year 2 ^[42]										
	Fathers	(<i>n</i> =254)	Mothers	(<i>n</i> =321)	Sons (n=195)	Daughter	rs (n=216)			
	Year 1	Year 2	Year1	Year2	year1	year2	year1	year2			
BMIb	25.3 (3.2)	25.3 (3.0)	23.7 (3.7)	3.9 (3.7)*	15.9 (2.0)	16.2 (2.1)*	15.8 (2.0)	16.3 (2.5)*			
%high	8.7	9.4	6.9	6.2	2.6	2.6	2.8	2.3			
WC (cm)	91.7 (9.1)	91.5 (8.9)	77.2().5)	77.2 (9.3)	77.2 (5.8)	58.8 (6.4)*	56.3 (5.8)	57.6 (7.1)*			
%high	13.4	11.4	17.1	13.4	1.0	9.2	3.7	2.8			
WHtR	0.51 (0.05)	0.51 (0.05)	0.47 (0.06)	0.47 (0.06)	0.46 (0.03)*	0.45 (0.04)	0.45 (0.04)*	0.44 (0.04)			
%high	55.1	51.2	24.6	22.4	6.7	7.2	9.3	5.1			
% fat	21.6 (6.2)	21.2 (5,7)	26.0 (6.9)	26.5 (7.)	21.3 (3.0)	20.4 (3.6)	22.8 (3.4)	22.0 (3.8)			
SBP	130.6 (13.6)	129.3) 13.8)	118.6 (12.6)*	117.0 (11.9)	102.7 (8.5)	104.7 (8.6)*	103.4 (9.7)	103.5 (8.5)			
%high	46.9	43.7	15.0	13.1	5.1	3.6	8.3	2.8			
DBP	84.7 (9.5)	84.1 (10.1)	77.2 (9.7)*	76.1 (9.3)	67.2 (8.1)	68.0 (8.1)	67.7 (8.5)	67.3 (7.7)			
%high	47.2	42.1	19.6	15.6	10.3	9.2	16.7	10.2			
Glucosea	103.0 (14.7)	103.1 (12.7)	97.5 (10.5)	97.2 (9.7)	96.1 (10.5)*	93.5 (9.8)	95.5 (9.3)*	92.6 (9.8)			
%high	27.5	10.6	2.5	5.0	22.6	6.7	15.7	7.9			
TGa	110.6 (131.6)	108.4 (65.3)	73.7 (33.8)	73.1 (32.9)	59.8 (24.6)*	55.2 (17.3)	67.6 (23.9)	65.0 (24.3)			
%high	14.2	16.1	4.4	2.2	3.1	1.0	5.6	3.7			
ТСа	202.8 (39.8)	201.1 (36.3)	191.5 (34.1)	191.4 (32.6)	171.7 (29.6)	172.6 (29.7)	175.5 (26.9)	173.6 (28.2)			
%high	48.0	51.6	34.3	33.3	15.4	14.4	16.2	13.4			
HDL-Ca	48.8 (11.9)	49.5 (12.4)	62.9 (14.7)	62.8 (13.0)	57.7 (12.4)	57.6 (11.9)	55.5 (15.0)	55.4 (11.8)			
%low	21.3	20.9	20.2	15.9	5.6	2.6	10.6	5.1			
LDL-Ca	132.3 (33.0)	130.3 (32.9)	113.8 (30.7)	113,9 (31.2)	102.0 (26.6)	104.0 (26.9)	106.5 (24.1)	105.5 (25.1)			
%high	49.2	48.8	24.6	28.0	33.3	33.8	44.0	31.5			
NonHDL-Ca	154.0 (40.7)	151.7 (36.0)	128.5 (32.8)	128.6 (33.2)	114.0 (27.5)	115.0 (27,8)	102.0 (24.5)	118.4 (31.9)			
%high	44.5	43.3	17.8	17.8	32.8	33.8	44.0	31.0			
LDL-C/HDL-C	2.86 (0.98)	2.79 (0.97)	1.92 (0.74)	1.92 (0.78)	1.86 (0.70)	1.88 (0.65)	2.10 (0.81)	1.99 (0.64)			
%high	37.8	34.6	8.1	7.8	4.6	5.6	12.5	4.2			
Tse	26.0	21.3	13.7	11.8	17.4	15.2	19.0	13.0			

Table 8: CVD risk factors in 575 parents and 411 children at baseline and after one year of sustained healthy lifestyle

a) mg/dL, b) kg/m²; Tse=Tobacco smoke exposure

In six studies, groups receiving lifestyle-based interventions offering 52 or more hours of contact showed greater improvements in BP than in control groups in terms of -6.4 mmHg (95% CI: -8.6 to -4.2) for SBP and -4.0 mmHg (95% CI: -5.6 to -2.5) for diastolic BP.[9] A dietary intervention study in children describes a greater self-reported reduction of dietary fat intake and greater decrease of calculated LDL-C (-4.8 mg/dL in year 1) in 663 participants aged 8-10 years.^[42]

Strength and limitations

The results of this community-based 15 years' observational study cannot be generalized because nearly all voluntarily participating family members lived in the same household residing in 94% of the elementary school districts of Nuremberg (Germany). The continuous contact among the participating families did strongly support adherence to the study design including sustained counseling and contacts with the large staff located in the health department of the city. The regularly trained dieticians, medical assistants, and physicians used home-based uncomplicated, noninvasive procedures which were important for sustained lifestyle implementation and correct assessment of nutritional intake by 7-day weighed dietary protocols. Anthropometric

measurements in children and adolescents adopted normal growth and maturation constructing age- and gender-adjusted LMS-pctls. This as well as not using dietary recalls and not assessing yet food patterns might limit comparisons with other studies. Furthermore, we have no valid CVD history of the parents and only incomplete data on CVD endpoints.

Discussion

In 1947, the first director of the Framingham Heart Study applied for support from the US Public Health Service "to study the expression of coronary artery disease in a 'normal' or unselected population and to determine the factors predisposing to the development of the disease through clinical and laboratory exam and long term follow-up."^[23] With this in mind, in 1993, we started the pilot project of the PEP Family Heart Study in typical elementary schools in two socially different school districts in the city of Nuremberg (Germany) for the assessment and prevention by lifestyle change of CVD risk factors in the first graders, their siblings, and parents.^[10] From the school years 1993/1994 to 2007/2008 we enrolled 48,667 subjects (24,927 adults and 23,740 children) without known CVD or traditional CVD risk factors.

Conclusions

This report on CVD risk factors in 39 years old parents and their 3-18 year-old children at baseline and the 14 years' follow-up of healthy lifestyle change is encouraging and a strong support and follow-up throughout 15 years' healthy lifestyle change is encouraging and a strong support for the AHA goal 2020 that "healthy diet, LTPA and non-smoking can be implemented in daily life."^[1]

What is new in this community-based lifestyle-intervention 14 years' observational family study?

- 1. Cardiovascular risk screening of children as a case-finding strategy for their young parents including the chance for early family-based prevention
- 2. Providing the first urban pediatric fat patterning in terms of age- and gender-adjusted pctls for BMI, WC, WHtR, SFT, and auscultatory BP pctls in nonoverweight, overweight, and obese children and adolescents
- 3. Sustained healthy lifestyle can be implemented in health-conscious families improving the cardiovascular risk factor profile under daily life conditions in parents and their children.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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References

- 1. Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, *et al.* Defining and setting national goals for cardiovascular health promotion and disease reduction: The American Heart Association's Strategic Impact Goal through 2020 and beyond. Circulation 2010;121:586-613.
- Kavey RE, Daniels SR, Lauer RM, Atkins DL, Hayman LL, Taubert K, *et al.* American Heart Association guidelines for primary prevention of atherosclerotic cardiovascular disease beginning in childhood. Circulation 2003;107:1562-6.
- Staehelin HB, Bruppacher R. The influence of the family on risk factors in children and adolescents – The Basle family study. In: Cardiovascular Risk Factors in Children and Adolescents. Bern, Switzerland: Verlag Hans Huber; 1984. p. 88-149.
- Knuiman MW, Divitini ML, Welborn TA, Bartholomew HC. Familial correlations, cohabitation effects, and heritability for cardiovascular risk factors. Ann Epidemiol 1996;6:188-94.
- Ellison RC, Myers RH, Zhang Y, Djoussé L, Knox S, Williams RR, *et al.* Effects of similarities in lifestyle habits on familial aggregation of high density lipoprotein and low density lipoprotein cholesterol: The NHLBI Family Heart Study. Am J Epidemiol 1999;150:910-8.
- Reis EC, Kip KE, Marroquin OC, Kiesau M, Hipps L Jr., Peters RE, *et al.* Screening children to identify families at increased risk for cardiovascular disease. Pediatrics 2006;118:e1789-97.
- 7. Mosca L, Mochari H, Liao M, Christian AH, Edelman DJ, Aggarwal B, *et al.* A novel family-based intervention trial to improve heart health: FIT heart: Results of a randomized controlled trial. Circ Cardiovasc Qual Outcomes 2008;1:98-106.
- Schwandt P, Bischoff-Ferrari HA, Staehelin HB, Haas GM. Cardiovascular risk screening in school children predicts risk in parents. Atherosclerosis 2009;205:626-31.
- 9. O'Connor EA, Evans CV, Burda BU, Walsh ES, Eder M, Lozano P, *et al.* Screening for obesity and intervention for weight management in children and adolescents: Evidence report and systematic review for the US Preventive Services Task Force. JAMA 2017;317:2427-44.
- Schwandt P, Geiss HC, Ritter MM, Ublacker C, Parhofer KG, Otto C, *et al.* The Prevention Education Program (PEP). A prospective study of the efficacy of family-oriented life style modification in the reduction of cardiovascular risk and disease: Design and baseline data. J Clin Epidemiol 1999;52:791-800.
- de Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J, *et al.* Development of a WHO growth reference for school-aged children and adolescents. Bull World Health Organ 2007;85:660-7.
- 12. Schwandt P, Bertsch T, Haas GM. Anthropometric screening for silent cardiovascular risk factors in adolescents: The PEP Family Heart Study. Atherosclerosis 2010;211:667-71.
- Schwandt P, Haas GM. Reference curves of waist circumference in children and adolescents 2012, Part 13. In: Preedy VR, editor. Handbook of Anthropometry. London, UK: Springer Science Business Media, LLC; 2012. p. 1405-12.
- Schwandt P, von Eckardstein A, Haas GM. Percentiles of percentage body fat in German children and adolescents: An international comparison. Int J Prev Med 2012;3:846-52.
- Schwandt P, Scholze JE, Bertsch T, Liepold E, Haas GM. Blood pressure percentiles in 22,051 German children and adolescents: The PEP Family Heart Study. Am J Hypertens 2015;28:672-9.
- Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011-2012. JAMA 2014;311:806-14.
- 17. National High Blood Pressure Education Program Working

Group on High Blood Pressure in Children and Adolescents. The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. Pediatrics 2004;114:555-76.

- 18. Liang KY, Zeger SL. Longitudinal analysis by using generalised linear models. Biometrika 1986;73:13-22.
- 19. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. Biometrics 1986;42:121-30.
- Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett DR Jr., Tudor-Locke C, *et al.* 2011 compendium of physical activities: A second update of codes and MET values. Med Sci Sports Exerc 2011;43:1575-81.
- Ridley K, Ainsworth BE, Olds TS. Development of a compendium of energy expenditures for youth. Int J Behav Nutr Phys Act 2008;5:45.
- Cole TJ. The LMS method for constructing normalized growth standards. Eur J Clin Nutr 1990;44:45-60.
- Meadors GF. Justification for the Budget Estimate for the Sub-Project "Epidemiology". Rockville, MD: United States Public Health Service. Framingham, MA: Framingham Heart Study Archives; July 19, 1947.
- Neuhauser HK, Thamm M, Ellert U, Hense HW, Rosario AS. Blood pressure percentiles by age and height from nonoverweight children and adolescents in Germany. Pediatrics 2011;127:e978-88.
- 25. Lurbe E, Cifkova R, Cruickshank JK, Dillon MJ, Ferreira I, Invitti C, *et al.* Management of high blood pressure in children and adolescents: Recommendations of the European Society of Hypertension. J Hypertens 2009;27:1719-42.
- Rosner B, Cook N, Portman R, Daniels S, Falkner B. Determination of blood pressure percentiles in normal-weight children: Some methodological issues. Am J Epidemiol 2008;167:653-66.
- Urbina EM, Falkner B. Right analysis-wrong conclusion: Obese youth with higher BP are at risk for target organ damage. Am J Hypertens 2015;28:570-1.
- Schwandt P, Scholze JE, Bertsch T, Ecotroph EL, Haas GM. Response to "Right analysis-wrong conclusion: Obese youth with higher BP are at risk for target organ damage". Am J Hypertens 2015;28:1072-3.
- Genovesi S, Giussani M. Blood pressure reference values for normal-weight children: Are they necessary? Int J Obes (Lond) 2015;39:1174.
- 30. Schwandt P, Haas GM. Why stigmatize overweight young people as hypertensive by using normative percentiles from

non-overweight youth? Int J Obes (Lond) 2015;39:1508.

- 31. Haas GM, Liepold E, Schwandt P. Predicting cardiovascular risk factors by different body fat patterns in 3850 German children: The PEP Family Heart Study. Int J Prev Med 2011;2:15-9.
- 32. Haas GM, Liepold E, Schwandt P. Percentile curves for fat pattering in German adolescents. World J Pediatr 2011;7:16-23.
- 33. Schwandt P, Haas GM. Is the ratio waist circumference to height (WHtR) of 0.5 a universal measure for abdominal adiposity in children and adolescents? Int J Obes (Lond) 2016;40:1141-2.
- 34. McCarthy HD, Ashwell M. A study of central fatness using waist-to-height ratios in UK children and adolescents over two decades supports the simple message-'keep your waist circumference to less than half your height'. Int J Obes (Lond) 2006;30:988-92.
- 35. Slaughter MH, Lohman TG, Boileau RA, Horswill CA, Stillman RJ, Van Loan MD, *et al.* Skinfold equations for estimation of body fatness in children and youth. Hum Biol 1988;60:709-23.
- Schwandt P, Kelishadi R, Ribeiro RQ, Haas GM, Poursafa P. A three-country study on the components of the metabolic syndrome in youths: The BIG study. Int J Pediatr Obes 2010;5:334-41.
- Kelishadi R, Schwandt P, Haas GM, Hosseini M, Mirmoghtadaee P. Reference curves of anthropometric indices and serum lipid profiles in representative samples of Asian and European children. Arch Med Sci 2008;4:329-35.
- 38. Can G, Schwandt P, Onat A, Hergenc G, Haas GM. Body fat, dyslipidemia, blood pressure and the effects of smoking in Germans and Turks. Turk J Med Sci 2009;39:579-89.
- 39. Nawarycz T, Haas GM, Krzyżaniak A, Schwandt P, Ostrowska-Nawarycz L. Waist circumference and waist-to-height ratio distributions in polish and German schoolchildren: Comparative analysis. Int J Prev Med 2013;4:786-96.
- 40. Schwandt P, Haas GM, Bertsch T. Nutrition and cardiovascular risk factors in four age groups of female individuals: The PEP Family Heart Study. Int J Prev Med 2010;1:103-9.
- 41. Schwandt P, Bertsch T, Haas GM. Sustained lifestyle advice and cardiovascular risk factors in 687 biological child-parent pairs: The PEP Family Heart Study. Atherosclerosis 2011;219:937-45.
- 42. Obarzanek E, Kimm SY, Barton BA, Van Horn LL, Kwiterovich PO Jr., Simons-Morton DG, *et al.* Long-term safety and efficacy of a cholesterol-lowering diet in children with elevated low-density lipoprotein cholesterol: Seven-year results of the dietary intervention study in children (DISC). Pediatrics 2001;107:256-64.