NHLBI Evidence Table: State of the Science: CV Risk Factors and the Development of Atherosclerosis in Childhood-RCT

•			Study	1000000		Int Longth Total Study			Tarnet		int not			cience: CV Risk Factors and	Control n a					Safety and Advers			Main Reported Findings by
	IID First Author 222 de Jongh S Ear	Title Ty statin therapy	Year Study CVD Type CVD 2002 RCT FMD	RF by CQ Country Q2 (RF5) Netherland		Int Length Duration 28 wk 28 wk	Main Study Objective Determine whether simvastatin	Total N 50	Target Population Pediatric/	9-18 yr	Patient Characteristics (n at Fo Mean age (SD): 28 (NR)	ollow-up)	Type rmacol 4	Specific Intervention Arm 1: Simvastatin 10-40 mg/d	Baseline (n Follow-up)	t Specific Control	Outcomes Measured Primary:	Results/CI Primary:	Significance Primary:	Events No significant	Additional finding	Summary With a significant	Critical Question Q2,10,12a. With a
129	res fun fan	y sadin tierapy de tores endothelial citos in children with ilidal ercholesterolemia	NOT PRID	Q10 (RF5) Q12 (RF5)	Onnea Oure	20 Wh	improves endothelial function in children with FH	5	Young Adults	HeFH Exclusions: Smoking Concomitant conditions (e.g., serious illness, hypertension, diabetes meilitus) Current use of any vasoactive medications	Manies: As yr (2.0) Control Arm: 14.6 yr (2.5) Males: Control Arm: 11	ogic	. (Nort) Dosage was doubled every 8 wk. from 10 to 20 to 40 mg/d		CON) 19 healthy non-FH siblings served as an additional control group (Non FH CON)	Mean change in FMD [% (SD)] FMD[%(SD)]	NTH 4.39%(4.3) vs. FH CON: +1.2%(3.9) INT: 15.5%(6.8); Non FH CON: 15.5%(5.4) Secondary; INT: 2.16(1.04) vs. FH CON: -0.05(1.17) No difference in either group INT: -2.113 (0.99) vs. FH CON: -0.05(1.08) INT: 0.19(0.37) vs. FH CON: 0.10(0.54) The absolute change of FMD was inversely correlated to change in TC and LDL(both, r=0.31)	NS	ind significant in differences in liver enzymes of CK, no adverse events were reported.		improvement in Li levels in children FH on statin thera endothelial function	OL significant improvement in LDL levels in children py, with FH on statin
1500	on	acts of diel and exercise cobesity-related vascular function in children	2004 RCT Multiple	Q 9.10.12a Hong Kong/ Australia	Clinical Single	Tyr6wk Tyr6wk	Evaluate the reversibility of obesity- related arterial dysfunction and carotiful finite-media thickening by weight change related to a dietary and/or exercise intervention program.		Family/ Caregiver	alternative cause for	Mean age: 9.9 yr 41 (41) Males: 54 54 chidren were obese (BMI>23) and 28 were overweight (BMI 21-23)) Behi	S G F C P P n f C C E ii u v v v tit E C S G E S C e v	Phase I: Delatay modification and regular supervised exercise program for 8 wk (D + EX) 8 wk (D + EX) Continued weekly exercise program or stopped exercise program or stopped exercise program but continued twice mornthly diet monitoring program but continued twice or 1 yr (No EX) CT EX) Delatary intervention included interviews with same dietician used by comparison group (twice weekly for first 6 wk and then twice monthly for 1 yl) and diet that provided 900-1200 kcall daily Diet was low in fat, high in complex carbohydrate, and sufficient in protein to support growth. Exercise training supervised by same physiotherapist team and consisted of 18 workout stations, each child did 9 stations, twice eweek for 6 wk, then once weekly for 1 yr.		Phase I: Dietary modification (D) Phase II: Continued twice monthly diet monitoring program for 1 yr Dietary intervention included interviews with same dietician used by comparison group (twice weekly for first 0 st was (twice weekly for first 0 st was and cited that provided 900-1200 kcal daily. Diet was low in fat, high in complex carbohydrate, and sufficient in protein to support growth.	Body fat percent [%(SD)] If Waist-hip ratio[SD]	Primary: At 6 weeks: D + EX: 6.8(2.0) to 8.0(1.8); D: 6.9(2.0) to 7.5(1.9) D + EX: 6.8(2.0) to 8.0(1.8); D: 6.9(2.0) to 7.5(1.9) D + EX: 6.7(0.4) to 0.46(0.04); D: 0.47(0.05) to 0.47(0.04) Secondary: At 6 weeks: D + EX: 5.4(4.1) to 25.3(3.2); D:24.5(2.9) to 24.1(2.7) D + EX: 5.4(4.1) to 25.3(3.2); D:24.5(2.9) to 24.1(2.7) D + EX: 37.9(3.6) to 37.3(4.0); D:37.3(3.8) to 37.0(3.5) D + EX: 0.88(0.05) to 0.85(0.09); D: 0.89(0.07) to 0.86(0.05) D + EX: 4.8(0.9) to 4.5(0.8); D:2.9(0.9) to 4.5(0.8) D + EX: 2.9(0.9) to 2.6(0.8); D:2.9(0.9) to 2.7(0.7) No change No change No change No EX: 6.7(2.3) to 7.4(2.5); CT EX:6.9(1.5) to 8.6(1.8); D: 4.9(0.9); D: 4.7(0.05) to 0.45(0.04) No EX: 6.7(2.0) to 7.1(1.5) No EX: 0.7(7.005) to 0.46(0.03); CT EX: 0.48(0.04) to 0.46(0.03); D:0.47(0.05) to 0.45(0.04) No EX: 26.1(4.0) to 26.1(4.2); CT EX: 25.3(2.4) to 25.4(2.4); D: 24.7(3.1); 24.5(3.3)	S**, S*, S* between grps NS; NS; NS between grps NS; NS; NS between grps NS; NS; NS between grps S*, S; NS between grps S*, S; NS between grps S*, NS; NS between grps NS	None		improvement in E the continued exe	and exercise decrease some measures of obesity, improve lipid results and improve consists and improve consists and improve consists and improve exercise in a second consists and improvement in vascular function and control consists and improvement in vascular function and control consists and improvement in vascular function and control consists and control contr
151:	on	ects of exercise training 2 vascular function in see children	RCT FMD (crosso ver)	Q10 (RF8) Australia Q12a (RF11) Q13 (RF4, RF5, RF14)	Clinical None/NR		Characterize the impact of obesity on vascular function in young children and determine whether an exercise program research abnormalities in vascular function	14	Pediatric/ Young Adults		Mean age (SD): 8.9 yr 14 (14) (1.6) Boys: 6 White: 13 Asian descent: 1 Exclusions: Cigarette smokers) Beha	E 1	intervention: Exercise training Exercise regimen consisted of 3 1-Hr sessions of whole body exercise each wk	14 (14)	Control: No training 7 lean subjects matched for age and physical activity levels served as a reference group		Primary: OB: Bit. 6.00%(0.69) to POST: 7.35%(0.99) Secondary: No significant changes in any secondary outcome.	S	Not addressed	obese subjects w compared with lea	an a small number of obese children sh a significant improvement in Fl after 8 wks of train	se in crossover trial of supervised exercise in a owed small number of obese children showed a significant improvement in FMD after 8 wks of training
170	vas car in c six-	provement of early cutal rounds and diovascular rhanges and diovascular risk factors bese children after a month exercise gram	RCT Multiple	Q10 (RF8) Germany Q12a (RF4, RF5, RF7, RF8, RF11, RF14)	Clinical None/NR	6 mo 6 mo	Assess effect of a 6 me exercise program in obese children on FMD, IMT, and cardiovascular risk factors		Young Adults	Obese (BMI > 97th percentile for the German pediatric population) Exclusions: Smoking Active participation in any exercise activity ≥ 30 min more than once/wk Participation in organized diet programs Diabetes, heart, renal, or liver disease	Mean age (SD: 14.2 50 (33) yr (1.9) Boys: 47) Beha	n E a g E irr t c o o	Arm 1: Exercise 3xWk + nuntritional consultation (INT) Exercise included swimming, aqua aerobic training, sports games and walking Exercise was progressively internsified as individually olderated Children in both groups received one consultation with a nutritionist to enhance knowledge about healthy nutrition	46 (34)	Control Arm: Nutritional consultation (CON) Instructed to maintain current levels of physical activity Children in both groups received one consultation with a nutritionist to enhance knowledge about healthy nutrition A separate non-randomized lean control group was compared only at baseline	Primary: Flow mediated dilation [%] ciMT [mm] Mean iMT: mean common carotid artery [mm (SD)] Mean iMT: mean carotid bifurcation [mm (SD)] Mean iMT: mean carotid bifurcation [mm (SD)] Mean iMT: maximum carotid bifurcation [mm (SD)] Secondary: Mean BMI (SD) Mean BMI (SD) Mean BF [% (SD)] Mean insulin [cmol/L (SD)] Mean insulin resistance (SD) Mean HbAtc (SD) Mean TG [mmol/L (SD)]	Primary: INT: 4.09(1.76) to 7.71(2.53).CON: 5.49 to 4.33(SD NR) INT: 4.09(1.76) to 0.74(.08); CON:0.47(.06) to 0.45(.06) INT: 0.53(.08) to 0.48(.08); CON:0.51(.07) to 0.50(.06) INT: 0.53(.06) to 0.46(.08); CON:0.51(.06) to 0.47(.05) INT: 0.58(.07) to 0.51(.09); CON:0.56(.07) to .57(.06) Secondary: INT: 2.8 (5.63 to 27.2(4.8); CON:31.0(4.42) to 31.3(4.21) Decreased Decreased but NS from B/L for both groups INT: 13.8(5.2) to 11.16(4.61); CON:No change INT: 3.94(1.75) to 3.12(1.38); CON:No change INT: 1.41(1.14) to 1.04(0.48); CON:No change	S** for INT S** for INT; NS for CON S* for INT; NS for CON S** NS for both S* for INT; NS for CON S for INT; NS for CON	None	At baseline, both obses groups differed significan from lean controls in all parameters. At 6 mos, obese CON differed significantly from obese INT in all parameters.	atly decreased BMI, improved CV risk	A 6 m trial of regular exercise decreased BMI, improved CV risk profile, improved enthothelial function MT and decreased clMT in
170	vas car in c six-	provement of early cular changes and diovascular risk factors bese children after a month exercise gram	RCT														Mean LDL-C [mmol/L (SD)] Mean HDL-C [mmol/L (SD)] Mean CRP [mg/L (SD)] Mean SBP [mmHg (SD)] Mean exercise SBP [mmHg (SD)] Mean LV mass index [g/m² (SD)] Mean maximum work capacity at exercise [W/kg (SD)] Mean maximum work capacity at exercise [% normal value (SD)] Mean sport activity [hr/wk]	INT: 2.71(70) to 2.57(.68); CON: No change No change in either group INT: 4.84(6.31) to 2.05(2.44); CON: No change INT:128(15.7) to 120(13.3); CON: No change INT:128(15.7) to 120(13.3); CON: No change No change in INT: increased in CON No change in either group INT: 2.14(.37) to 2.46(.62); CON: No change INT: 8.4.9(14.3) to 76.9(20.9); CON: No change Not reported With regression analysis, FMD change correlated best with change in hrs of sports/wk(r=0.537,p=S**) but also with change in BMI, W/H,Dody fat & INS.	S for INT, NS for CON NS for both groups S for INT, NS for CON S NS for both groups NS for both groups S** for INT, NS for CON S** for INT, NS for CON				