NHLBI Evidence Table: RF4-RCT

PMID	First Author	Title	Year	Study Type	CVD	RF by CQ	Country	Setting	Blinding	Int Length	Total Study Duration	Main Study Objective	Total N	Target Population	Eligibility Criteria	Patient Characteristics	Int. n at Baseline (n at Follow-up)	Int. Type	Specific Intervention	Control n at Baseline (n at Follow-up)	Specific Control	Outcomes Measured	Results/CI	Significance	Safety and Adverse Events	Additional findings	Summary	Main Reported Findings by Critical Question
12700955	Trachtman H	Clinical trial of extended-release felodipine in pediatric essential hypertension	2003	RCT	None	Q5 (RF4) Q10 (RF4)	USA	Clinical	Double	3 wk	20 wk Includes 1-3 wk screening period and 14-wk open-label extension phase	Evaluate the dose-response and tolerability of the dihydropyridine calcium channel blocker, felodipine extended-release tablets (felodipine ER), given once daily to pediatric patients with essential hypertension	133	Pediatric/ Young Adults	6-16 yr SBP or DBP > 95th percentile for age, sex, and height Exclusions: SBP > 20 mmHg or DBP > 10 mmHg above the 95th percentile Evidence of secondary cause of hypertension such as coarctation of the aorta, hyperthyroidism, or a pheochromocytoma Glomerular filtration rate < 40 mL/min per 1.73 m^2 Recipients of a kidney transplant Concomitant illness such as liver disease or congestive heart failure	Mean age (SD): 12.1 yr (2.7) Males: 80 Black: 52 Non-black: 81 Non-smokers: 98%	Arm 1: 33 (NR) Arm 2: 34 (NR) Arm 3: 31 (NR)	Pharmacologic	Arm 1: Felodipine ER 2.5 mg/d Arm 2: Felodipine ER 5 mg/d Arm 3: Felodopine ER 10 mg/d Treatment was started with 2.5 mg of active drug in each arm and was titrated weekly to the target dose over a 2 or 3 wk interval in the 5 and 10 mg groups, respectively All patients were offered an option to participate in a 14-wk open-label phase designed to collect primarily safety information	35 (34)	Control Arm: Placebo All patients were offered an option to participate in a 14-wk open-label phase designed to collect primarily safety information	**Primary:** Mean change in trough sitting DBP by dose [mmHg (95% CI)] Mean change in trough supine DBP by dose [mmHg (95% CI)] Mean change in trough standing DBP by dose [mmHg (95% CI)] Mean change in trough sitting SBP by dose [mmHg (95% CI)] Mean change in trough supine SBP [mmHg (95% CI)] Mean change in trough standing SBP [mmHg (95% CI)]	**Primary:** 2.5 mg: -2.07(-6.82,2.69) 5.0 mg: -4.64(-9.18,0.09) 10 mg: 1.31(-3.56,6.11) 2.5 mg: -1.98(-6.80,2.85) 5.0 mg: -5.06(-9.68,-0.45) 10 mg: -1.73(-6.58,3.13) 2.5 mg:-1.56(-6.20,3.07) 5.0 mg:-5.09(-9.53,-0.65) 10 mg:-1.87(-6.54,2.79) No significant changes in SBP at any dose level in any position.	**NS** **S** **NS** **NS** **S** **NS** **NS** **S** **NS**	Heart racing - 1 pt D/C'd med for this complaint; headache, nausea in placebo & int. subjects.		Felodipine was ineffective in lowering SBP and only selectively effective for lowering DBP in hypertensive children and adolescents.	Q10 RF 4, Felodipine was ineffective in lowering SBP and only selectively effective for lowering DBP in hypertensive children and adolescents.
12727766	Forsyth JS	Long chain polyunsaturated fatty acid supplementation in infant formula and blood pressure in later childhood: follow up of a randomized controlled trial	2003	RCT	None	Q11 (RF4) Q13 (RF4)	Europe	Clinical	Double	4 mo	6 yr Data collection occurred when children turned age 6 yr	Determine whether supplementation of infant formula milk with long chain polyunsaturated fatty acids (LCPUFAs) influences blood pressure in later childhood	237	Pediatric/ Young adults	Children who participated in original RCT as infants	Mean age (SD): 71.0 mo (3.5) Males: 78	71 (65)	Dietary Supplements	Arm 1: Had received formula with long chain polyunsaturated fatty acids (LCPUFA) supplementation for 4 mo as infants LCPUFA source was egg yolk, with approximately 70% of LCPUFAs being esters of phospholipids	76 (71)	Control Arm: Had received formula without supplementation for 4 mo as infants 83 breastfed(BF) children were used as a reference group	**Primary: INT vs CON** Mean difference in mean BP [mmHg (95% CI)] Mean difference in DBP [mmHg (95% CI)] Mean difference in SBP [mmHg (95% CI)] **Secondary: BF vs CON*** Mean difference in DBP [mmHg (95% CI)] Mean difference in SBP [mmHg (95% CI)]	**Primary: INT vs CON at 6 y** -3.0(CI:-5.4,-0.5) -3.6(CI:-6.5,-0.6) -2.3(CI:-5.3,0.7) **Secondary:*** -3.4(CI:-6.8,-0.01) No difference. *No difference between BF and PUFA children	**S** **S** **NS** **S** **NS** **NS**	Not described	Investigators stress that mean BP is also significantly lower but MAP is 2/3 DBP.	LCPUFA supplementation in the first 4 months of life is associated with lower DBP at 6 years of age. The effect is similar to that achieved by breast feeding.	LCPUFA supplementation in formula fed babies in the first 4 months of life is associated with lower DBP at 6 years of age. The effect is similar to that achieved by breast feeding. Q11: A decrease in higher BP as a risk factor in childhood can be sustained at 6 year follow-up. Q13: Acquisition of a risk factor (RF 4 high BP) can potentially be prevented in childhood.
14553956	Soffer B	A double-blind, placebo-controlled, dose-response study of the effectiveness and safety of lisinopril for children with hypertension	2003	RCT	None	Q10 (RF4)	USA	Clinical	Double	4 wk	5 wk Includes up to 7-d placebo washout period	Explore the dose-response relationship, safety, and tolerability of lisinopril in hypertensive children	115	Pediatric/ Young adults	6-16 yr Weight ≥ 20 kg Glomerular filtration rate ≥ 30 mL/min/1.73 m^2 Sitting DBP > 95th percentile for age, gender and height on 2 confirmatory measurements, each a mean of 3	Age: < 6-12 yr: 54 (47.0%) 13-16 yr: 61 (53.0%) Males: 75 (65.2%) White: 51 (44.3%) African American: 12 (10.4%) Asian: 1 (0.9%) Hispanic: 51 (44.3%)	115 (104)	Pharmacologic	Phase 1: Arm 1: Low dose lisinopril Patients weighing < 50 kg received 0.625 mg/d and patients weighing ≥ 50 kg received 1.25 mg/d for 2 wk Arm 2: Middle dose lisinopril Patients weighing < 50 kg received 2.5 mg/d and patients weighing ≥ 50 kg received 5 mg/d for 2 wk Arm 3: High dose lisinopril Patients weighing < 50 kg received 20 mg/d at day 3 and patients weighing ≥ 50 kg received 40 mg/d for 2 wk. Patients received a half dose for the first 2 d, then the full dose for the remaining phase Phase 2: Arm 1: Continue lisinopril at either 0.625 mg/d or 1.25 mg/d for 2 wk Control Arm 1: Placebo	NR (NR)	Refer to Specific Intervention Column	**Primary:** Mean change in trough sitting DBP [mmHg (SD,SE, 95% CI)] **Secondary:** Slope of the diastolic BP response Mean change in trough sitting SBP by dose [mmHg (SD,SE, 95% CI)] Mean change in trough sitting DBP by dose [mmHg (SD,SE, 95% CI)]	**Primary:** 6.19(1.86)mmHg **Secondary:** -0.28 mmHg per unit increase in dose low -5.4(9.9, -9.0, -1.9) mid -12.1 (9.1, -16, -8.3) high -15.2 (12.1, -18.4, -12.0) low -7.6(9.3, -10.9, -4.3) mid -9.3(8.7, -13, -5.7) high -16.4(11.7, -19.5, -13.3)	**S**** **S**** **S** **S** **S** **S** **S** **S**	Very few adverse events. Headache the most common, others included abdominal pain, nausea and diarrhea. Only one event of coughing it was not felt to be related to drug. No case on angioneurotic edema.		Lisinopril is an effective and well tolerated antihypertensive agent in children aged 6-16 yrs. Blood pressure was reduced in a dose dependent fashion. The dose response relationship was consistent across all subgroups(age, Tanner stage, ethnicity and gender)	Lisinopril is effective and well tolerated antihypertensive agent in children age 6-16 yrs. Blood pressure was reduced in a dose dependent fashion. The dose response relationship was consistent across all subgroups(age, Tanner stage, ethnicity and gender) Q10: This paper demonstrates that high BP as a RF can be reduced in children.
14553956	Soffer B	A double-blind, placebo-controlled, dose-response study of the effectiveness and safety of lisinopril for children with hypertension	2003																Arm 2: Continue lisinopril at either 2.5 mg/d or 5 mg/d for 2 wk Control Arm 2: Placebo Arm 3: Continue lisinopril at either 20 mg/d or 40 mg/d for 2 wk Control Arm 3: Placebo								
15062892	Barnes VA	Impact of transcendental meditation on ambulatory blood pressure in African-American adolescents	2004	RCT	None	Q10 (RF4) Q13 (RF8, RF11)	USA	Mult settings	None/NR	4 mo	4 yr (8 school semesters) Study was conducted as 2 4-mo interventions per semester After each 4 mo intervention, students were followed for 4 mo	Determine the impact of stress reduction on BP in adolescents by the Transcendental Meditation program	156	Pediatric/ Young Adults	African-American Adolescents Inner-city high schools Resting SBP in the ≥ 85th and ≤ 95th percentile for age, sex and height on 3 consecutive occasions	Mean age (SD): Arm 1: 16.0 yr (1.3) Control Arm: 16.3 yr (1.4) Males: Arm 1: 32 Control Arm: 31 Single mother head of household: Arm 1: 63% Control Arm: 60% Mean Hollingshead Four Factor Social Status Index (SD): Arm 1: 35.7 (13.0) Arm 2: 34.8 (12.7) Patient characteristics pertain only to the 100 subjects with complete data at follow-up	NR (50)	Behavioral	Arm 1: Transcendental Meditation(TM) 15-min sessions at home and at school each school d and 15-min twice daily individual home practice on weekends for 4 mo	NR (50)	Control Arm: Lifestyle education sessions (CON) 15-min sessions each school d Lifestyle education sessions were based in part on National Institutes of Health guidelines on lowering BP through weight management, diet and physical activity	**Primary:** LS mean daytime SBP [mmHg (SE)] LS mean daytime DBP [mmHg (SE)] LS mean daytime HR [bpm (SE)] LS mean nighttime SBP [mmHg (SE)] LS mean nighttime DBP [mmHg (SE)] LS mean nighttime HR [bpm (SE)]	**B/L #4(F/U)** **TM:** 129.2(1.1) 125.3(1.2) **CON:** 130.6(1.1 129.7(1.2) **TM:** 75.3(0.9) 72.9(1.2) **CON:** 75.8(0.9) 75.7(1.2) No significant differences for any other measure. * For all subjects, there was a significant effect for time with SBP & DBP decreasing across all 4 visits.	**S** **NS** **p=.06** **NS**	None	None	There is a beneficial impact of TM on BP in African-American adolescents with pre-hypertension	There is a beneficial impact of TM on BP in African-American adolescents with pre-hypertension. Q10 RF4: BP can be decreased by TM.
15262902	Li JS	Is the extrapolated adult dose of fosinopril safe and effective in treating hypertensive children?	2004	RCT	None	Q10 (RF4)	USA Russia Israel	Clinical	Double	58 wk Includes a 4-wk dose-response phase, a placebo withdrawal phase of 2 wk, a 52 wk open label period	59 wk, 3 d Includes a lead-in period of up to 10 d., a 4-wk dose-response phase, a placebo withdrawal phase of 2 wk, and a 52-wk open-label safety phase	Evaluate the efficacy, safety, and dose-response relationship of fosinopril in children aged 6 to 16 years with hypertension or high-normal blood pressure with an associated medical condition requiring treatment	253	Pediatric/ Young adults	6-16 yr 3 sequential SBP or DBP > 95th percentile for gender, age, and height SBP or DBP > 90th but ≤ 95th percentile Associated medical condition such as diabetes	Mean age (SD): 12.1 yr (2.6) Males: 166 White: 152 Black: 52 Asian: 5 Hispanic: 35 Native American: 1 Other race/ethnicity: 8	253 (209)	Pharmacologic	Phase 1: 10 d screening + fosinopril 0.1 mg/kg test dose Phase 2: Arm 1: Low dose fosinopril 0.1 mg/kg for 4 wk Arm 2: Medium dose fosinopril 0.3 mg/kg for 4 wk Start at 0.1 mg/kg and titrate to 0.3 mg/kg Arm 3: High dose fosinopril 0.6 mg/kg for 4 wk Start at 0.3 mg/kg and titrate to 0.6 mg/kg Phase 3: Arm 1: Withdrawal phase for 2 wk Control Arm 1: Placebo Arm 2: Withdrawal phase for 2 wk Control Arm 2: Placebo	NR (115)	Refer to Specific Intervention Column	**Primary:** Mean change in trough SBP from baseline to wk 4 [mmHg (SE, 95% CI)] **Secondary:** Mean change in trough DBP from baseline to wk4 [mmHg (SE, 95% CI)] Mean change in trough SBP during withdrawal phase [mmHg (SE, 95% CI)] Mean change in trough DBP during withdrawal phase [mmHg (SE, 95% CI)] Safety % pt with both S & DBP <90% end wk 4	**Primary:** Low: -10.9(1.2)(-13.2,-8.6) Med: -11.3(1.1)(-13.4,-9.1) High: -11.9(1.1)(-14.2,-9.7) **Secondary:** Low: -4.5(0.8)(-6.0,-3.0) Med: -4.2(0.7)(-5.7,-2.8) High: -5.1(0.7)(-6.6,-3.6) Any fosiniopril vs placebo: -3.7(-6.6,-0.8) Any fosiniopril vs placebo: -1.6(-3.5,0.3) Well tolerated (any dose) 45%, 47%,42% reached goal for low, mid, high dose (4 wk)	**S** **S** **S** **S** **S** **S** **S** **NS** **Unspecified** **NS difference b/t doses**	Well described, minor AE.		Fosinopril decreases BP with the effect significant for SBP & DBP but there is no dose response effect. Fosinopril in even a low dose was effective.	Q10: There is evidence that Fosinopril can be used to treat high BP as a RF in childhood.
15262902	Li JS	Is the extrapolated adult dose of fosinopril safe and effective in treating hypertensive children?	2004																Arm 3: Withdrawal phase for 2 wk Control Arm 3: Placebo Phase 4: 52 wk open label safety phase Fosinopril could be titrated from 1 mg/kg to 0.6 mg /kg to achieve target BP control of < 90th percentile for age, gender, height The maximum dose permitted during all phases was 40 mg								

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PMID	First Author	Title	Year	Study Type	CVD	RF by CQ	Country	Setting	Blinding	Int Length	Total Study Duration	Main Study Objective	Total N	Target Population	Eligibility Criteria	Patient Characteristics	Int. n at Baseline (n at Follow-up)	Int. Type	Specific Intervention	Control n at Baseline (n at Follow-up)	Specific Control	Outcomes Measured	Results/CI	Significance	Safety and Adverse Events	Additional findings	Summary	Main Reported Findings by Critical Question
15343191	Flynn JT	A randomized, placebo-controlled trial of amlodipine in children with hypertension	2004	RCT	None	Q10 (RF4)	United States Canada Argentina Brazil	Clinical	Double	8 wk	> 8 wk Includes wash out period of least 5 half-lives of the relevant drug taken prior to intervention by subjects receiving antihypertensive therapy at enrollment; for those subjects receiving amoldipine, the washout period was 8 d	Evaluate the efficacy and safety of amlodipine in hypertensive children	268 (49 centers)	Pediatric/ Young adults	6-16 yr Seated SBP ≥ 95th percentile for age, sex and height on 3 occasions Exclusions: Transient, malignant, or accelerated hypertension Residual aortic coarctation with an upper -to- lower extremity BP gradient of > 30 mmHg Unstable chronic renal, hepatic, hematologic, endocrine, or neurologic disease History of prior or ongoing treatment with > 2.5 mg amlodipine per d	Mean age (SD): 12.1yr (3.3) Boys: 177 (66.0%) Family history of hypertension: 172 (64.2%)	268 (256)	Pharmacologic	Phase 1: Arm 1: Amlodipine 2.5 mg qd for 4 wk Arm 2: Amlodipine 2.5 mg qd for 2 wk then titrated to 5.0 mg qd for 2 wk Phase 2: Arm 1: Continued amlodipine 2.5 mg qd for 4 wk Control Arm: Placebo Arm 2: Continued amlodipine 5.0 mg qd for 4 wk Control Arm: Placebo Subjects seen weekly throughout the study for BP measurements, study drug dispensing, and assessment of adverse effects. Adjustments to the dose of study drug were not made unless symptomatic hypotension developed.	N/A	Refer to Specific Intervention Column	**Primary:** Effect of amlodipine on systolic blood pressure **Secondary:** Mean change in DBP [mmHg (SD)] Effect of amlodipine as a function of dose and body size Effect of amlodipine as a function of sex Effect of amlodipine as a function of race.	**Primary:** -8.7(13.3) at 5 mg -6.9(12.5) at 2.5 mg -3.6(12.7) placebo **Secondary:** -4.4(10.2) at 5 mg -4.2(10.7) at 2.5 mg -0.4(11) for placebo Greater change in SBP & DBP with higher dose Greater reduction in systolic and diastolic BP amoung females No difference for SBP or DBP by race or underlying casue of hypertension.	**S* vs placebo** **S vs placebo** **NS** **NS** **S for SBP & DBP** **S*** **NS**	6 subjects withdrawn, 3 because of worsening hypertension, 1 facial edema, l edema of fingers and rash, and 1 with PVCs. Most common AEs were headache, aesthenia, dizziness, abdominal pain, vasodilatation, and epistaxis.	64% of all subjects had a (+) family hx of hypertension.	Amlodipine effectively lowers systolic BP in a dose-dependent manner and this effect is greater in females than males. No difference in efficacy of amlodipine between races. Amlodipine was well tolerated with just 6 children withdrawn because of drug related adverse events. Q10: This paper does demonstrate that RF (BP = RF 4) can be decreased in children.	Amlodipine effectively lowers systolic BP in a dose-dependent manner and this effect is greater in females than males. No difference in efficacy of amlodipine between races. Amlodipine was well tolerated with just 6 children withdrawn because of drug related adverse events. Q10: This paper does demonstrate that RF (BP = RF 4) can be decreased in children.
15343191	Flynn JT	A randomized, placebo-controlled trial of amlodipine in children with hypertension	2004																Total of 4 BP measurements taken 24 hr after the last dose of study drug at each study visit; the mean of the last 3 readings was calculated and recorded as the subject's BP.									
15752945	Shahinfar S	A double-blind, dose-response study of losartan in hypertensive children	2005	RCT	None	Q10 (RF4)	USA Africa Europe North America South America	Clinical	Double	5 wk	6 wk Includes a 2-7 d placebo washout period	Determine the dose-response relationship for losartan and assess the safety and tolerability of losartan over a wide dose range in hypertensive children	175	Pediatric/ Young Adults	6-16 yr Body weight ≥ 20 kg Mean sitting DBP above the 95th percentile based on gender, height, and age Glomerular filtration rate ≥ 30 mL/min/1.73 m^2	Mean age (SD): 12.0 yr (3.1) Males: 99 (56%) Ethnicity: White: 98 (55%) Hispanic: 38 (21%) African American: 20 (11%) Other: 21 (12%)	175 (164)	Pharmacologic	Phase 1: Arm 1: Low dose losartan 2.5 mg or 5.0 mg for 2 wk Patients weighing < 50 kg received 2.5 mg qd and patients weighing ≥ 50 kg received 5.0 mg qd Arm 2: Middle dose losartan 25 mg or 50 mg for 2 wk Patients weighing < 50 kg received 25 mg qd and patients weighing ≥ 50 kg received 50 mg Arm 3: High dose losartan 25 mg-50 mg or 50 mg-100 mg for 2 wk Patients weighing < 50 kg received 25 mg and were titrated to 100 mg at day 3 and patients weighing ≥ 50 kg received 50 mg and were titrated to 100 mg at day 3	N/A	Refer to Specific Intervention Column	**Primary:** Mean change in sitting DBP by dose [mmHg (SE, 95% CI)] Mean change in sitting SBP by dose [mmHg (SE, 95% CI)]	**Phase 1, Baseline to day 21.** Low -6.0 (-7.8, -4.2) Mid -11.7 (-14.6, -8.8) High -12.2 (-14.4, -10.0) Low -4.4 (-6.2, -2.6) Mid -10.0 (-12.9, -7.1) High - 8.6 (-11.0, -6.3) **Phase 2 is placebo withdrawal. There was no change for those continuing the dose. For those withdrawing to placebo:** DBP: Low 3.3(7.5) Mid 9.4(9.5) High 7.9(11.2) SBP: Low 0.7(9.3) Mid 7.0(8.0) High 8.1(12.5)	**S** **S** **S** **S** **S** **S** **NS** **S** **S** **NS** **NS** **S**	1 episode of hypotension	None	In children age 6-16 years, high BP can be safely and effectively reduced by Losartan.	In children age 6-16 years, high BP can be safely and effectively reduced by Losartan. Q10 RF 4: Study provides evidence that high BP as a RF can be reduced by losartan
15752945	Shahinfar S	A double-blind, dose-response study of losartan in hypertensive children	2005																Phase 2: Arm 1: Continued low dose losartan 2.5/5.0 mg for 2 wk Control Arm 1: Placebo Arm 2: Continued middle dose losaratan 25/50 mg for 2 wk Control Arm 2: Placebo Arm 3: Continued high dose losartan 50/100 mg for 2 wk Control Arm 3: Placebo									
16702318	Larnkjaer A	Maternal fish oil supplementation during lactation does not affect blood pressure, pulse wave velocity, or heart rate variability in 2.5-y-old children	2006	RCT	Distensibility	Q13 (RF4, RF9, RF11)	Denmark	Clinical	Double	4 mo	2.5 yr	Investigate whether fish oil supplementation of lactating mothers could modify BP, pulse wave velocity, and heart rate variability in their children after 2 yr	122	Pediatric/ Young Adults	Healthy pregnant women with singleton deliveries and fish intake below the population median [< 0.4 g (n-3) LC-PUFA/d]	Mean age of children at follow-up (SD): Arm 1: 31.67 mo (0.86) Arm 2: 31.82 mo (0.80) Boys: Arm 1: 66.7% Arm 2: 58.6% Patient characteristics pertain only to children born to mothers participating in the study who were still available at 2.5 yr follow-up	Arm 1: 62 (42) Arm 2: 60 (30)	Dietary Supplements	Arm 1: Fish oil supplement 4.5 g/d Arm 2: Olive oil supplement 4.5 g/d	N/A	53 mothers with naturally high fish intake of > 75th percentile [> 0.82 g (n-3) LC-PUFA/d] served as a reference group	**Primary:** Mean MAP[mmHg (SD)] Mean SBP [mmHg (SD)] Mean DBP [mmHg (SD)] PWV HRV measures Mean HR [bpm (SD)] **Secondary:** Mean child (n-3) PUFA intake [g/d (SD)] Mean BP by (n-3) PUFA intake in children	**Primary:** No significant difference between groups for any measure. **Secondary:** Increased (4 mo, 2.5 yrs) Negative correlation - 0.5 g/d higher (n-3) PUFA intake corresponded to a 4 mmHg lower mean BP	**NS for all measures.** **S** **S**	Not reported.		Fish oil supplement to lactating moms did not lower BP or improve arterial stiffness or autonomic tone in infants assessed at 2.5 y of age.	Q13: Fish oil supplement to lactating moms did not lower BP or improve arterial stiffness or autonomic tone in infants assessed at 2.5 y of age.
16875928	Menon S	Racial differences are seen in blood pressure response to fosinopril in hypertensive children	2006	RCT	None	Q5 (RF4) Q10 (RF4)	USA Russia Israel	Clinical	Double	59 wk, 3 d	59 wk, 3 d	Assess the efficacy of fosinopril in children with hypertension and determine whether response to fosinopril varies by race	253 at randomization (Phase 2)	Pediatric/ Young Adults	6-16 yr Hypertension (defined as 3 sequential SBP or DBP measurements > 95th percentile for sex, age, and height) or high-normal BP (defined as SBP or DBP > 90th percentile but ≤ 95th percentile) with an associated medical condition requiring antihypertensive therapy	Mean age (SD): Arm 1: White: 11.9 yr (2.8) Black: 11.6 yr (2.6) Arm 2: White: 11.6 yr (2.6) Black: 13.1 yr (2.1) Arm 3: White: 12.5 yr (2.3) Black: 12.4 yr (2.5) Male: Arm 1: White: 34 Black: 4 Arm 2: White: 37 Black: 15 Arm 3: White: 34 Black: 13 White: 152 Black: 52 Hispanic: 35 Asian: 5 Native American: 1	253 (NR)	Pharmacologic	Phase 1: 10 d screening + fosinopril 0.1 mg/kg test dose Phase 2: Arm 1: Low dose fosinopril 0.1 mg/kg for 4 wk Arm 2: Medium dose fosinopril 0.3 mg/kg for 4 wk Patients were started at a dose of 0.1 mg/kg and titrated to 0.3 mg/kg Arm 3: High dose fosinopril 0.6 mg/kg for 4 wk Patients were started at a dose of 0.3 mg/kg and titrated to 0.6 mg/kg Phase 3: Arm 1: Continue fosinopril 0.1 mg/kg for 2 wk Control Arm 1: Placebo Arm 2: Continue fosinopril 0.3 mg/kg for 2 wk	N/A	Refer to Specific Intervention column	**Primary:** Change in SBP from baseline in both populations Change in trough SBP with increasing dose in white population [mmHg (SE, 95% CI)] Change in trough DBP with increasing dose in white population [mmHg (SE, 95% CI)] Change in trough SBP with increasing dose in black population [mmHg (SE, 95% CI)] Change in trough DBP with increasing dose in black population [mmHg (SE, 95% CI)]	**Primary:** White -11.2 (1.4) Black -12.8(1.9) -11.5(1.5) low -13(1.3) med -11.2(1.4) high -4.5(1.1) low -4.4(0.9) med -5.5(1.0) high -4.7(2.9) low -11.0(2.0) med -12.8(1.9) high -0.4(2.3) low -3.5(1.6) med -2.3(1.5) high	**S but unspecified in both blacks and whites.** **NS,comparing low to high.** **NS, comparing low to high.** **S, comparing low to high** **NS, comparing low to high**	none reported		Fosinopril was effective in treating hypertension but black children required a higher dose per weight in order to achieve adequate control.	Fosinopril was effective in treating hypertension but black children required a higher dose per weight in order to achieve adequate control. Q5: This paper does answer the Q that Race/ethnicity influences BP risk status in children and adolescents. Q10: This does demonstrate that BP in children can be decreased.
16875928	Menon S	Racial differences are seen in blood pressure response to fosinopril in hypertensive children	2006													Other or mixed race: 8 Patient characteristics pertain only to those 253 patients who entered Phase 2 of the study; age and sex are reported only for white and black patients within this group			Control Arm 2: Placebo Arm 3: Continue fosinopril 0.6 mg/kg for 2 wk Control Arm 3: Placebo Phase 4: 52 wk open-label safety phase During Phase 4, fosinopril could be titrated from 0.1 mg/kg to 0.6 mg/kg to achieve target BP control (defined by SBP and DBP < 90th percentile for age, sex, and height) The maximum dose permitted during all phases was 40 mg Subjects weighing > 60 kg were given 10, 20, or 40 mg daily in the low-, medium- and high-dose groups, respectively									

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PMID	First Author	Title	Year	Study Type	CVD	RF by CQ	Country	Setting	Blinding	Int Length	Total Study Duration	Main Study Objective	Total N	Target Population	Eligibility Criteria	Patient Characteristics	Int. n at Baseline (n at Follow-up)	Int. Type	Specific Intervention	Control n at Baseline (n at Follow-up)	Specific Control	Outcomes Measured	Results/CI	Significance	Safety and Adverse Events	Additional findings	Summary	Main Reported Findings by Critical Question
17179023	Singhal A	Promotion of faster weight gain in infants born small for gestational age: is there an adverse effect on later blood pressure?	2007	RCT	None	Q6 (RF2, RF4, RF8) Q13 (RF4)	United Kingdom	Clinical	Double	9 mo	8 yr	Investigate the role of early nutrition and weight gain on later CVD risk in small for gestational age (SGA) infants	299	Pediatric/ Young Adults	≥ 37 weeks of gestation Birth weight < 10th percentile for gestation and sex according to UK growth charts Free of congenital abnormalities	Mean age (SD): 4 d Baseline characteristics among children followed up at 6-8 yr: Male: 68 Social class: 20% nonmanual Maternal qualifications: None: 46 Degree or higher: 5	152 (70)	Dietary Supplements	Arm 1: Nutrient-enriched formula Formula containinig 28% more protein than standard formula and larger amounts of minerals, trace elements, and vitamins	147 (83)	Control Arm: Standard formula 175 breast-fed infants of similar age and weight were included as a reference group	**Primary:** Mean arterial pressure (MAP) [mmHg(SD)] Mean DBP [mmHg (SD)] **Secondary:** Mean SBP [mmHg (SD)] Adjusted mean difference in DBP [mmHg (95% CI)] Adjuste mean difference in MAP [mmHg(95%CI)] Adjusted mean difference in SBP [mmHg (95% CI)]	**Primary:** STD: 76.9(8.3) vs Enriched: 79.5(7.8) STD: 61.3(8.2) vs Enriched: 64.5(8.3) **Secondary:** STD: 100.5(10.2) vs Enriched: 102.2(9.8) -3.5(-6.2, -0.7) -3.0 (-5.6,-0.3) -2.0 (-5.3, 1.3) * SGA infants fed the enriched formula did increase ht and wt significantly more rapidly than those fed the std formula by 9 mos of age - differences in growth did not persits on F/U at 18 mos and 6 - 8 yrs.	**p=0.06** **S** **NS** **S*** **S** **NS**	None	Breast fed SGA infants who gained weight faster had higher SBP, DBP, and MAP than those who did not.	In SGA babies, a nutrient-enriched diet in infancy promoted more rapid wt gain in infancy and this was associated with higher mean and diastolic BPs 6 - 8 yrs later. These findings suggest that faster growth in infancy may have adverse later effects on BP.	Q13. In SGA babies, a nutrient-enriched diet in infancy promoted more rapid wt gain in infancy and this was associated with higher mean and diastolic BPs 6 - 8 yrs later. These findings suggest that faster growth in infancy may have adverse later effects on BP.
17236889	Batisky DL	Efficacy and safety of extended release metoprolol succinate in hypertensive children 6 to 16 years of age: a clinical trial experience	2007	RCT	None	Q10 (RF4)	USA	Clinical	Double	4 wk	58 wk Includes 1-to 2-wk run-in period to discontinue anti-hypertensive medication and a 52-wk open-label treatment protocol to collect safety and tolerability information	Evaluate the efficacy, tolerability, and BP lowering effect of extended release metoprolol succinate in children 6 to 16 yr with established hypertension	140	Pediatric/ Young Adults	6-16 yr Persistent sitting SBP and/or sitting DBP ≥ 95th percentile adjusted for age, sex and height Not to exceed > 20 mmHg SBP and/or <10 mmHg DBP above the 95th percentile for height-adjusted charts for age and sex Targeted enrollment required a mixture of African-American and non-African-American children Exclusions: Asthma or other contraindications to beta-blocker therapy Secondary hypertension Type I diabetes mellitus Impaired liver function	Mean age (SD): 12.5 yr (2.8) Males: 98 African-American: 36 Non-African-American: 104 Previously treated for hypertension: 32	Arm 1: 45 (45) Arm 2: 23 (23) Arm 3: 49 (49)	Pharmacologic	Arm 1: 0.2 mg/kg extended release metoprolol succinate Arm 2: 1.0 mg/kg extended release metoprolol succinate 0.5 mg/kg qd for 1 wk and, if tolerated, 1.0 mg/kg for 3 wk Arm 3: 2.0 mg/kg extended release metoprolol succinate 0.5 mg/kg qd for 1 wk, 1.0 mg/kg for 1 wk, then 2.0 mg/kg for remaining 2 wk	23 (23)	Control Arm: Placebo	Mean change in sitting SBP [mmHg (95% CI)] Mean change in sitting DBP [mmHg (95% CI)] SBP & DBP < 95th%ile (% of subjects)	**AT 4 weeks: SBP** PLACEBO: -1.9 (-5.5,1.8) 0.2 mg/kg: -5.2(-7.7,-2.6) 1.0 mg/kg: -7.7 (-11.3,-4.0) 2.0 mg/kg: -6.3 (-8.7,-3.8) **AT 4 weeks: DBP** PLACEBO: -21. (-5.7,1.5) 0.2 mg/kg: -3.1 (-5.7,-0.5) 1.0 mg/kg: -4.9 (-8.6,-1.3) 2.0 mg/kg: -7.5 (-10.0,-5.0) **AT ONE YEAR:** Mean dose=112+/-69 mg 64% of pts classified as "responders" with both SBP & DBP < 95th%ile	**NS** **S** **S** **NS** **NS** **S**	Mean HR slowed by -6.5 bpm. Only 1 pt in each dose level reported fatigue during the 4 wk study. 5 pts (of 105) in the 52 wk study D/C'd treatment because of a serious adverse event	No dose titration effect for SBP but this was demonstrated for DBP. SBP response was less in obese pts than in non-obese pts.	ER metoprolol significantly lowered SBP and DBP in this pediatric population with moderate hypertension. No dose response for SBP but this was seen for DBP. During 1 yr open label F/U, 64% of pts had SBP & DBP below the 95th%ile.	Q10. ER metoprolol significantly lowered SBP and DBP in this pediatric population with moderate hypertension. No dose response for SBP but this was seen for DBP. During 1 yr F/U, 64% of pts had SBP & DBP below the 95th%ile.
18346503	Couch SC	The Efficacy of a Clinic-Based Behavioral Nutrition Intervention Emphasizing a DASH-Type Diet for Adolescents with Elevated Blood Pressure	2008	RCT	None	Q10 (RF4, RF9)	USA	Clinical	None	3 mo	6 mo	Examine the efficacy of 3-month clinic-based behavioral intervention emphasizing a diet high in fruits, vegetables, and low fat dairy (DASH intervention) versus routine outpatient hospital-based nutrition care (RC) on diet and blood pressure (BP) in adolescents with elevated BP.	99	Pediatric/ Young Adults	Adolescents with elevated BP		29 (18)	Behavioral	Slighlty modified version of DASH diet for adults to meet nutritional needs of adolescents. Intervention included 60-minute face-to-face counseling session with dietician, adolescent, and parent; 8 weekly and 2 biweekly phone calls by trained interventionists; biweekly mailings; and recording of food intake for 5 of 7 days each week. DASH-style Diet: 8 servings/d of F&V 3 servings/d of low fat dairy foods < 30% of calories from fat	28 (18)	Routine care (RC) intervention provided nutrition counseling that is routinely given to patients at the Cincinnati Children's Hypertension Center (CCHC). The intervention included 60-minute face-to-face counseling session with adolescent and parent and booklet entitled "Eat Right to Lower Blood Pressure." Adolesents were encouraged to implement recommended behavior changes themselves with the help of their families.	**Primary:** Mean SBP [mmHg(SD)] Mean DBP [mmHg(SD)] Fruit consumption [# /day(SD)] Total fat intake [%kcal(SD)] Vegetable consumption [# /day(SD)] Saturated fat intake [%kcal(SD)] Calcium intake [mg/day(SD)] Mean sodium intake [mg/day(SD)]	**Primary: Post-treatment:** DASH:131.3(8.9) to 120.9(10.4) RC:125(6.5) to 123.1(9.9) **3 m F/U:** DASH:129.4(7.2) to 120.1(10.5) RC: 124.3(5.8) to 120(10.8) **Post treatment:** DASH:79.5(6.8) to 72.7(9.6) RC: 82.3(7.2) to 75.9(9.7) **3 m F/U:** DASH: 80.4(7.2) to 75.2(8.9) RC: 81.7(6.3) to 76.4(12.7) **Post treatment:** DASH: 1(1.2) to 2.9(2.6) RC: 0.7(0.8) to 0.6(0.6) **3 m F/U:** DASH: 0.8(1) to 1.4(1.6) RC: 0.7(0.8) to 0.7(0.9) **Post treatment:** DASH: 11.1(2.3) to 9.3(2.7) RC: 11.8(1.8) to 11.6(2) **3 m F/U:** DASH: 10.8(2.3) to 10.9(3.1) RC: 11.7(1.7) to 11.7(2.7) No difference from B/L for either group post treatment or at 3 m for any of these variables.	**S*** **NS** **p<.1** **NS** **NS** **NS** **S**** **NS** **NS** **NS** **p<.1** **NS** **NS** **NS**	None reported	By post-Rx, 50% of the DASH group achieved BP normalization vs 36% of the RC group. (p=15) By 3m F/U, 61% of the DASH group achieved BP normalization vs 44% of the RC group. (p=.36) DASH group received multiple supportive diet reminders vs none for the RC group.	A DASH-style diet was acceptable and efficacious in the short term in improving diet quality and lowering BP in adolescents with HTN & pre-HTN.	Q10. A DASH-style diet was acceptable and efficacious in the short term in improving diet quality and lowering BP in adolescents with HTN & pre-HTN.
18346503	Couch SC	The Efficacy of a Clinic-Based Behavioral Nutrition Intervention Emphasizing a DASH-Type Diet for Adolescents with Elevated Blood Pressure	2008																			Mean BMI [kg/m2(SD)] Mean potassium intake [mg/day(SD)] Mean sodium intake [mg/day(SD)] Potassium intake [mg/day(SD)] BMI[kg/m2(SD)]	**Post treatment:** DASH:1943(675) to 2764(1163) RC: 1951(1083) to 2022(772) No difference from B/L at 3 m F/U for either group. **Post treatment:** DASH:29.2(6.3) to 28.7(6.4) RC: 28.9(6.1) to 28.8(6.3) 3 m F/U: DASH: 29.1(6.2) to 30(6.2) RC: 29.5(5.5) to 28.9(5.8)	**S**** **NS** **NS** **NS** **S** **NS**				