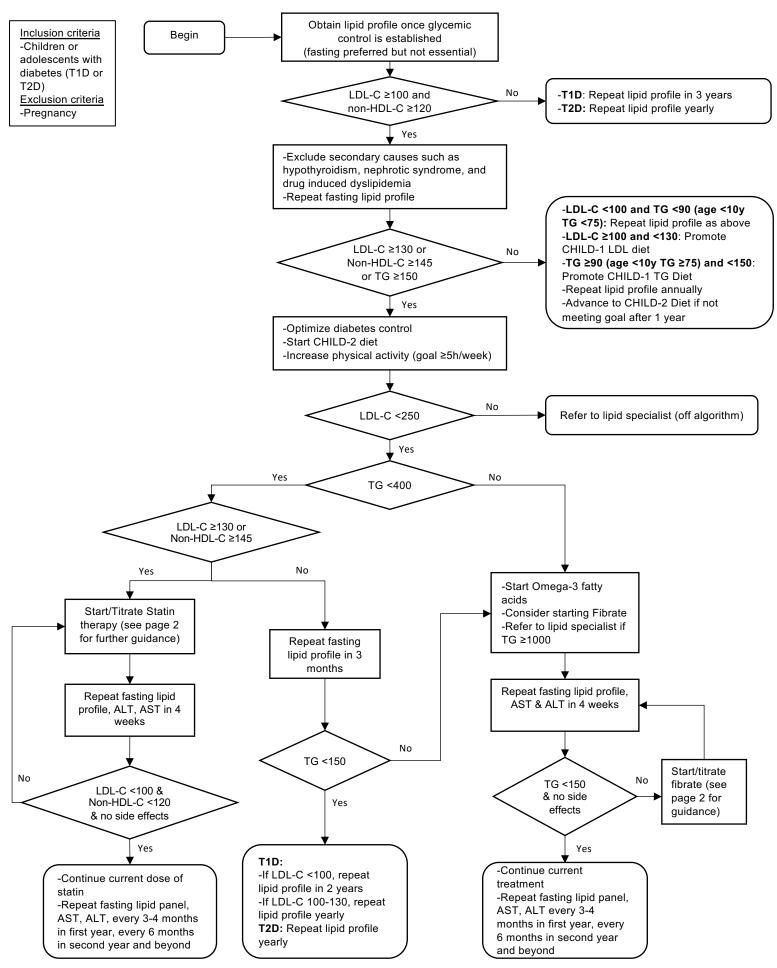
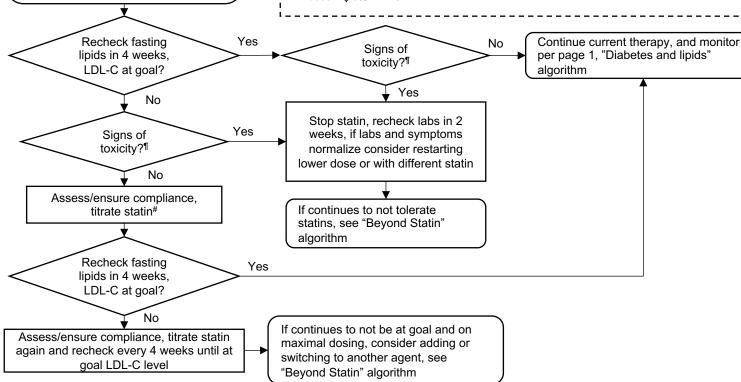
## PES Lipid SIG Diabetes and Lipids Algorithm (updated 5/2023)



# Statin initiation

- 1. Counsel about side effects,\* potential medication interactions,† contraindications,‡ adherence
- 2. Obtain baseline labs: ALT, AST, CK
- 3. Start statin (see chart below)§

- \*Side effects: muscle pain/cramp, weakness, myopathy
- †Potential medication interactions: cyclosporine, niacin, fibric acid derivative, erythromycin, azole antifungal. HIV protease inhibitor
- <sup>‡</sup>Contraindicated in pregnancy, known **teratogen**. For female patients consider contraception or gynecology referral. Also contraindicated in nursing mothers, acute liver disease, hypersensitivity to statin
- § Currently statins are approved for children starting age 7 years for HoFH and age 8 years for HeFH ¶Toxicity = AST, ALT >3x ULN, or CK >10x ULN (check CK if concern for myopathy)
- #2x dose = ↓ 6% LDL-C



**Lipid Lowering Dose Ranges** 

Drug	Strength	Dose	% ↓LDL-C	% 个HDL-C	% ↓Trigs	% <b>↓</b> TC
Lovastatin	10 mg	10 mg QD	22%	4%	5%	12%
	20 mg	20 mg QD	29%	7%	12%	21%
	40 mg	40 mg QD	31%	5%	2%	23%
	80 mg	80 mg QD	48%	8%	13%	36%
Atorvastatin	10 mg	10 mg QD	38%	6%	13%	28%
	20 mg	20 mg QD	46%	5%	20%	35%
	40 mg	40 mg QD	51%	5%	32%	40%
	80 mg	80 mg QD	54%	1%	25%	42%
Fluvastatin	20 mg	20 mg QD	17%	1%	5%	13%
	40 mg	40 mg QD	23%	3%	13%	19%
	80 mg XL	80 mg QD	35%	8%	11%	20%
Pravastatin	10 mg	10 mg QD	19%	10%	3%	13%
	20 mg	20 mg QD	24%	3%	15%	18%
	40 mg	40 mg QD	34%	6%	10%	24%
Rosuvastatin	5 mg	5 mg QD	45%	13%	35%	33%
	10 mg	10 mg QD	52%	14%	10%	36%
	20 mg	20 mg QD	55%	8%	23%	40%
	40 mg	40 mg QD	63%	10%	28%	46%
Simvastatin	5 mg	5 mg QD	24%	7%	12%	17%
	10 mg	10 mg QD	28%	7%	12%	21%
	20 mg	20 mg QD	35%	5%	17%	26%
	40 mg	40 mg QD	41%	10%	15%	30%
	80 mg	80 mg QD	47%	12%	36%	36%

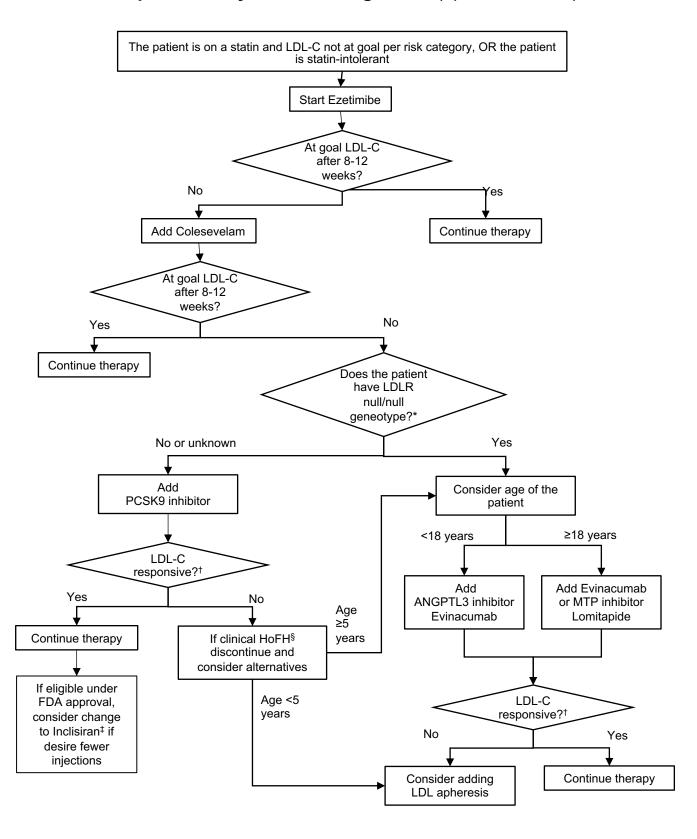
### <u>Triglyceride management (off label in pediatricsα)</u> Omega-3 fatty acids

1. Recommended dose is 4g/day DHA/EPA

#### **Fibrates**

- Counsel about side effects,<sup>β</sup> potential drug interactions,<sup>γ</sup> and contraindications<sup>δ</sup>
- 2. Prefer fenofibrate initially due to fewer side effects, better tolerated, and only once daily dosing
- Check baseline AST, ALT and again in 4 weeks to monitor on fibrate. If AST, ALT >3x ULN, stop fibrate, consider restarting at lower dose once labs normalize or refer to lipid specialist
- "Of note, TG lowering medications in adults with diabetes have shown inconsistent results with improved CVD benefit
- <sup>β</sup>Side effects: muscle toxicity, hepatotoxicity. If on fibrate and statin, higher risk of muscle toxicity
- <sup>y</sup>Drug interactions: coumarin anticoagulants, immunosuppressants, bile acid resins
- δContraindications: severe renal dysfunction, acute liver disease, gall bladder disease, hypersensitivity to fibrate, nursing mothers

### PES Lipid SIG: Beyond Statin Algorithm (updated 5/2023)



<sup>\*</sup>Genetic testing is currently not an exclusive criteria for defining familial hypercholesterolemia, and not all patients with clinical FH have identifiable mutations. Thus, the decision branch encompasses patients whose genetics are unknown

<sup>†</sup>In severe cases, initial LDL-C goal may be ≥50% reduction from baseline, and clinical judgment is required to evaluate responsiveness.

<sup>‡</sup>At this time Inclisiran is only FDA-approved for age 18 years and older

<sup>§</sup>HoFH is clinically diagnosed when a person has an untreated LDL-C level >500 mg/dL, with either the presence of cutaneous or tendinous xanthomas before the age of 10 years or documentation of untreated LDL-C levels of >250 mg/dL in both parents

# Beyond Statins – published lipid-lowering effects of medications

Medication class and drug name	Approved pediatric age range and indication	Dosage and formulation	LDL-C reduction from clinical trial	Comments	
Selective cholest	erol-absorption inh	ibitor			
Ezetimibe	Age 10-17 years and older HeFH	Pill, 10 mg daily	-28% over 12 weeks PMID: 25841542	May be used as monotherapy or add-on to statin therapy	
Bile-acid sequest	trant				
Colesevelam	Age 10-17 years and older HeFH	Powder for suspension, 3.75 gm per day	-12.5% over 8 weeks PMID: 19879596	GI side effects are common. Take at least 4 hrs after other medications.	
PCSK9 inhibitor					
Evolocumab	Age 10-17 years and older HeFH, HoFH	HeFH: 140 mg subQ injection q 2 wks, pre-filled syringe or pen device; HoFH: 420 mg subQ q 4 wks via disposable infusion device	-23.1% over 12 wks (TESLA-B) PMID: 25282520 -23.3% over 48 wks (TAUSSIG) PMID: 28215937 -44.5% over 24 wks (HAUSER-RCT)	Dependent on LDL receptor function. Not effective in LDLR null/null genotype	
ANGPTL3 inhibit	or.		PMID: 32865373		
ANGPILS IIIIIDIL	or .				
Evinacumab	Age 5-17 years and older HoFH	15 mg/kg iv infusion q 4 wks. Given in infusion center or by home health nursing.	-47.1% over 24 weeks (ELIPSE HOFH) PMID: 32813947	Teratogen counseling for females, and advised to be on effective contraception.	
FOR ADULTS ON	LY - MTP inhibitor				
Lomitapide	18 years and older HoFH	Starting dose 5 mg tabs. Titrate up to 60 mg/day. Max dose 30 mg/day if on simvastatin, atorvastatin, or lovastatin.	-50% after 26 weeks  (Phase 3 HoFH Lomitapide Study) PMID: 23122768  Rx with vitamin E and omega 3+6 supplements (see prescribing label).	Follow FDA REMS protocol for dose titration and monitoring for liver toxicity. FDA REMS provider training required. GI side effects are common.	
FOR ADULTS ON	LY – siRNA to PCSK9	mRNA			
Inclisiran	18 years and older HeFH or ASCVD	284 mg injection subQ. After initial dose, give second dose at 3 months, then every 6 months after that.	-39.7% over 15 months (ORION-9) PMID: 32197277	Not likely to be effective in LDLR null/null genotype	

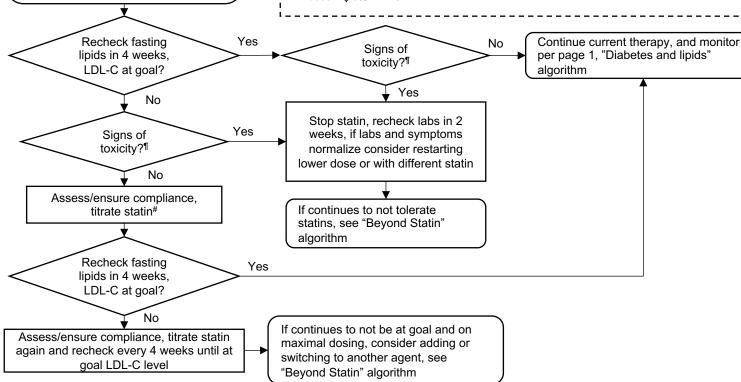
#### PES Lipid SIG LDL-C Algorithm- updated 5/2023 LDL-C ≥130mg/dL in the absence of other conditions i.e. hypothyroidism, cholestatic liver disease, nephrotic syndrome. medications High risk Moderate risk At risk -HoFH -Severe obesity (BMI >120th of 95%tile, -Obesity -T2D or >35 kg/m2) -Insulin resistance with comorbidities -T1D -HeFH (dyslipidemia, NAFLD, PCOS) -Confirmed hypertension -ESRD -White coat hypertension -Kawasaki with persistent aneurysm -Coarctation -Cardiomyopathies -Solid organ transplant vasculopathy -Pulmonary hypertension -Elevated Lp(a) -Childhood cancer survivor (stem cell -Predialysis chronic kidney disease -Chronic inflammatory conditions (JIA, recipient) -Aortic stenosis SLE. IBD. HIV) -Childhood cancer survivor (chest -S/p coronary artery translocation for radiation) anomalous coronary arteries or transposition of great arteries -Childhood cancer (cardiotoxic chemotherapy only) -Kawasaki with regressed aneurysm Reassign risk: if ≥2 additional comorbidities advance to next higher risk category Smoking history present Family history of early CAD in 1<sup>st</sup> degree relative (M age ≤55 years, F ≤65 vears) present BP (3 separate occasions) ≥90%tile for age/sex or 120/70, whichever is lower BMI ≥95%tile Fasting glucose ≥100 mg/dL Physical activity history <5 h/week <u>At risk</u> Moderate risk High risk Threshold to treat LDL-C ≥130 mg/dL Threshold to treat LDL-C ≥160mg/dL Threshold to treat LDL-C ≥160 mg/dl Continue screening every 6-12 months with non-fasting non-HDL, LDL-C meets No followed by fasting lipid profile if threshold to treat? initial TC >200. HDL-C <45. or non-Yes HDL-C >145 mg/dL At risk High risk Moderate Risk Start CHILD-2 LDL diet\* and increase Start CHILD-2 LDL diet\* and increase Start CHILD-2 LDL diet\* and increase physical activity activity (goal >5h/week) physical activity activity (goal >5h/week) physical activity (goal >5h/week) AND x 6mo Start statin simultaneously (as per Fig x 3mo 1, page 2) Goal LDL-C <100 mg/dL Goal LDL-C <130 mg/dL Goal LDL-C <130 mg/dL Yes Repeat LDL-C, Continue current therapy, meets goal? monitor/reassess periodically No Moderate risk At risk High risk Consider statin and titrate to goal as Consider statin and titrate to goal as Titrate statin to goal as above above, intensify lifestyle above, intensify lifestyle

<sup>\*</sup>See reference for more information on CHILD-2 LDL lowering diet (Williams, L, Wilson, D. Nutritional management of pediatric dyslipidemia. Endotext. 2020) LDL-C low density lipoprotein cholesterol, HoFH Homozygous familial hypercholesterolemia, T2D type 2 diabetes mellitus, T1D type 1 diabetes mellitus, ESRD end stage renal disease, BMI body mass index, HeFH Heterozygous familial hypercholesterolemia, Lp(a) lipoprotein (a), NAFLD nonalcoholic fatty liver disease, PCOS polycystic ovary syndrome, JIA Juvenile idiopathic arthritis, SLE systemic lupus erythematosus, IBD inflammatory bowel disease, HIV human immunodeficiency virus, CAD coronary artery disease, M male, F female, BP blood pressure, h hours, non-HDL non high density lipoprotein, TC total cholesterol, HDL-C high density lipoprotein, CHILD-2 LDL Cardiovascular Health Integrated Lifestyle- 2 low density lipoprotein diet

# Statin initiation

- 1. Counsel about side effects,\* potential medication interactions,† contraindications,‡ adherence
- 2. Obtain baseline labs: ALT, AST, CK
- 3. Start statin (see chart below)§

- \*Side effects: muscle pain/cramp, weakness, myopathy
- †Potential medication interactions: cyclosporine, niacin, fibric acid derivative, erythromycin, azole antifungal. HIV protease inhibitor
- <sup>‡</sup>Contraindicated in pregnancy, known **teratogen**. For female patients consider contraception or gynecology referral. Also contraindicated in nursing mothers, acute liver disease, hypersensitivity to statin
- § Currently statins are approved for children starting age 7 years for HoFH and age 8 years for HeFH ¶Toxicity = AST, ALT >3x ULN, or CK >10x ULN (check CK if concern for myopathy)
- #2x dose = ↓ 6% LDL-C



**Lipid Lowering Dose Ranges** 

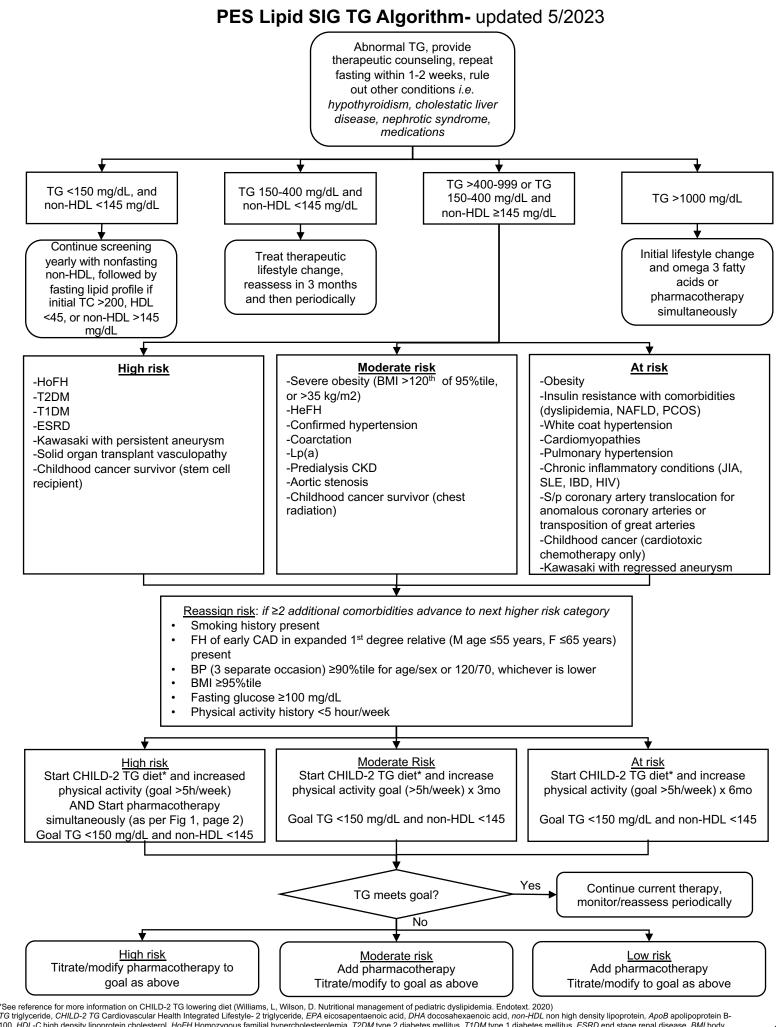
Drug	Strength	Dose	% ↓LDL-C	% 个HDL-C	% ↓Trigs	% <b>↓</b> TC
Lovastatin	10 mg	10 mg QD	22%	4%	5%	12%
	20 mg	20 mg QD	29%	7%	12%	21%
	40 mg	40 mg QD	31%	5%	2%	23%
	80 mg	80 mg QD	48%	8%	13%	36%
Atorvastatin	10 mg	10 mg QD	38%	6%	13%	28%
	20 mg	20 mg QD	46%	5%	20%	35%
	40 mg	40 mg QD	51%	5%	32%	40%
	80 mg	80 mg QD	54%	1%	25%	42%
Fluvastatin	20 mg	20 mg QD	17%	1%	5%	13%
	40 mg	40 mg QD	23%	3%	13%	19%
	80 mg XL	80 mg QD	35%	8%	11%	20%
Pravastatin	10 mg	10 mg QD	19%	10%	3%	13%
	20 mg	20 mg QD	24%	3%	15%	18%
	40 mg	40 mg QD	34%	6%	10%	24%
Rosuvastatin	5 mg	5 mg QD	45%	13%	35%	33%
	10 mg	10 mg QD	52%	14%	10%	36%
	20 mg	20 mg QD	55%	8%	23%	40%
	40 mg	40 mg QD	63%	10%	28%	46%
Simvastatin	5 mg	5 mg QD	24%	7%	12%	17%
	10 mg	10 mg QD	28%	7%	12%	21%
	20 mg	20 mg QD	35%	5%	17%	26%
	40 mg	40 mg QD	41%	10%	15%	30%
	80 mg	80 mg QD	47%	12%	36%	36%

### <u>Triglyceride management (off label in pediatricsα)</u> Omega-3 fatty acids

1. Recommended dose is 4g/day DHA/EPA

#### **Fibrates**

- Counsel about side effects,<sup>β</sup> potential drug interactions,<sup>γ</sup> and contraindications<sup>δ</sup>
- 2. Prefer fenofibrate initially due to fewer side effects, better tolerated, and only once daily dosing
- Check baseline AST, ALT and again in 4 weeks to monitor on fibrate. If AST, ALT >3x ULN, stop fibrate, consider restarting at lower dose once labs normalize or refer to lipid specialist
- "Of note, TG lowering medications in adults with diabetes have shown inconsistent results with improved CVD benefit
- <sup>β</sup>Side effects: muscle toxicity, hepatotoxicity. If on fibrate and statin, higher risk of muscle toxicity
- <sup>y</sup>Drug interactions: coumarin anticoagulants, immunosuppressants, bile acid resins
- δContraindications: severe renal dysfunction, acute liver disease, gall bladder disease, hypersensitivity to fibrate, nursing mothers

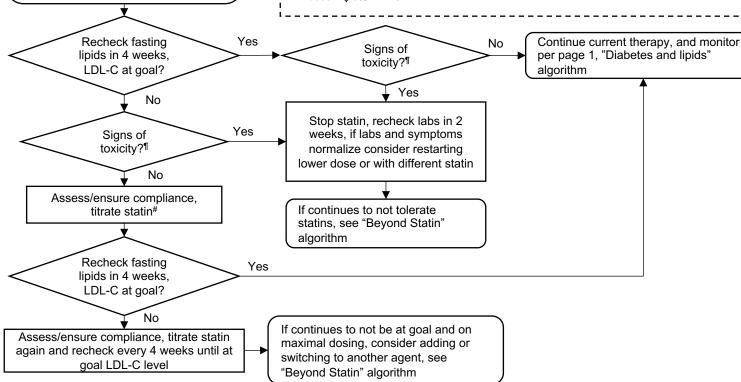


Te triglyceride, CHILD-2 TG Cardiovascular Health Integrated Lifestyle-2 triglyceride, EPA eicosapentaenoic acid, DHA docosahexaenoic acid, non-HDL non high density lipoprotein, ApoB apolipoprotein B-100, HDL-C high density lipoprotein cholesterol, HoFH Homozygous familial hypercholesterolemia, T2DM type 2 diabetes mellitus, T1DM type 1 diabetes mellitus, ESRD end stage renal disease, BMI body mass index, HeFH Heterozygous familial hypercholesterolemia, Lp(a) lipoprotein (a), CKD chronic kidney disease, NAFLD nonalcoholic fatty liver disease, PCOS polycystic ovary syndrome, JIA juvenile idiopathic arthritis, SLE systemic lupus erythematosus, IBD inflammatory bowel disease, HIV human immunodeficiency virus, CAD coronary artery disease, M male, F female, BP blood pressure

# Statin initiation

- 1. Counsel about side effects,\* potential medication interactions,† contraindications,‡ adherence
- 2. Obtain baseline labs: ALT, AST, CK
- 3. Start statin (see chart below)§

- \*Side effects: muscle pain/cramp, weakness, myopathy
- †Potential medication interactions: cyclosporine, niacin, fibric acid derivative, erythromycin, azole antifungal. HIV protease inhibitor
- <sup>‡</sup>Contraindicated in pregnancy, known **teratogen**. For female patients consider contraception or gynecology referral. Also contraindicated in nursing mothers, acute liver disease, hypersensitivity to statin
- § Currently statins are approved for children starting age 7 years for HoFH and age 8 years for HeFH ¶Toxicity = AST, ALT >3x ULN, or CK >10x ULN (check CK if concern for myopathy)
- #2x dose = ↓ 6% LDL-C



**Lipid Lowering Dose Ranges** 

Drug	Strength	Dose	% ↓LDL-C	% 个HDL-C	% ↓Trigs	% <b>↓</b> TC
Lovastatin	10 mg	10 mg QD	22%	4%	5%	12%
	20 mg	20 mg QD	29%	7%	12%	21%
	40 mg	40 mg QD	31%	5%	2%	23%
	80 mg	80 mg QD	48%	8%	13%	36%
Atorvastatin	10 mg	10 mg QD	38%	6%	13%	28%
	20 mg	20 mg QD	46%	5%	20%	35%
	40 mg	40 mg QD	51%	5%	32%	40%
	80 mg	80 mg QD	54%	1%	25%	42%
Fluvastatin	20 mg	20 mg QD	17%	1%	5%	13%
	40 mg	40 mg QD	23%	3%	13%	19%
	80 mg XL	80 mg QD	35%	8%	11%	20%
Pravastatin	10 mg	10 mg QD	19%	10%	3%	13%
	20 mg	20 mg QD	24%	3%	15%	18%
	40 mg	40 mg QD	34%	6%	10%	24%
Rosuvastatin	5 mg	5 mg QD	45%	13%	35%	33%
	10 mg	10 mg QD	52%	14%	10%	36%
	20 mg	20 mg QD	55%	8%	23%	40%
	40 mg	40 mg QD	63%	10%	28%	46%
Simvastatin	5 mg	5 mg QD	24%	7%	12%	17%
	10 mg	10 mg QD	28%	7%	12%	21%
	20 mg	20 mg QD	35%	5%	17%	26%
	40 mg	40 mg QD	41%	10%	15%	30%
	80 mg	80 mg QD	47%	12%	36%	36%

### <u>Triglyceride management (off label in pediatricsα)</u> Omega-3 fatty acids

1. Recommended dose is 4g/day DHA/EPA

#### **Fibrates**

- Counsel about side effects,<sup>β</sup> potential drug interactions,<sup>γ</sup> and contraindications<sup>δ</sup>
- 2. Prefer fenofibrate initially due to fewer side effects, better tolerated, and only once daily dosing
- Check baseline AST, ALT and again in 4 weeks to monitor on fibrate. If AST, ALT >3x ULN, stop fibrate, consider restarting at lower dose once labs normalize or refer to lipid specialist
- "Of note, TG lowering medications in adults with diabetes have shown inconsistent results with improved CVD benefit
- <sup>β</sup>Side effects: muscle toxicity, hepatotoxicity. If on fibrate and statin, higher risk of muscle toxicity
- <sup>y</sup>Drug interactions: coumarin anticoagulants, immunosuppressants, bile acid resins
- δContraindications: severe renal dysfunction, acute liver disease, gall bladder disease, hypersensitivity to fibrate, nursing mothers