**Why Niacin?**

- Niacin (Nicotinic Acid=NA) is the first lipid lowering agent shown to reduce ASVD events and long term mortality (-11%).
- NA is the only lipid lowering agent that can improve all lipid risk factors (TC, HDL-C, LDL-C, Lp(a), TG, non-HDL-C).
- In addition to lipid improvement NA has non-lipid benefits that reduce atherosclerosis (92% of patients treated with NA).
- NA is a good compliment for use with other agents to reduce ASVD risk (meta-analysis of NA plus other agents (including statins) showed reduction of all vascular events -34% and major coronary events -25%).
- NA is the cheapest of all lipid lowering agents (@ 25 cents/day).
The Role of Niacin in the Management of Dyslipidemia
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Mechanism of Action

- Reduces LDL-C 20+%, specifically small dense LDL particles.
- Best agent to raise HDL-C, specifically Apo-A1 for reverse cholesterol transport.
- One of best agents to reduce Triglycerides.
- Only agent that can reduce Lp(a).
- Non-lipid benefits unique to NA:
  - inhibits vascular inflammation/reduces reactive oxygen species
  - reduces oxygenation of LDL-C
  - reduces intravascular adhesion molecules and monocyte chemo-attractant protein-1 (atherogenesis initiators)
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How “to do” Niacin

Patient selection:
- primary therapy in mixed dyslipidemia, (especially “Metabolic Syndrome”) if LDL-C within 20% of goal level.
- patients with elevated Lp(a).
- “add on” agent for patients with significant residual ASVD risk (e.g. on statins with persistent hypertriglyceridemia).
- patients intolerant of statins

NA agent selection:
- immediate release NA best for raising HDL-C
- extended-release better for lowering LDL, (e.g. wax-matrix NA) better tolerated (less flushing).
- caution in NA agent selection, should have demonstrated efficacy from clinical trials. e.g. wax-matrix NA, polygel NA. Avoid “no flush” NA, (Inositol Hexanicotinate) = “no benefit” NA.
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How “to do” NA continued:

• Dosing: “start low and go slow”, titrate up 250-500mg/ week to allow tolerance to develop.
• Split dose to BID or TID with meals, and take 325mg of ASA with dose to reduce flushing.
• Target dose is typically 3000mg-6000 mg/day of immediate-release or 1500-2000mg/day of extended-release as tolerated.
• Monitor LFTs, blood glucose, uric acid and homocysteine in addition to lipid parameters every 6 weeks till lipid goals or target dose reached, then every 3-6 months as maintenance.
  -if LFTs rise to 2-3 x normal limits, cut dose by 50% and emphasize methyl-donor diet (kale, berries, fish, nuts, or methionine supplement), recheck in 2 weeks (LFTS usually better and lipid benefits maintained)
  -if blood glucose elevated, just monitor at same dose, usually returns to baseline.
  -if homocysteine elevated supplement with folic acid.
  -if uric acid elevated, reduce dose or add uricosuric agent.
• Generally well tolerated: 3-8% intolerance of wax-matrix extended-release, 9% intolerance of immediate-release, and 18% polygel extended-release (when given as a single hs dose)
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Conclusion: NA Renaissance

• The dominance of statin therapy in modern lipid management has caused many providers to lose touch with how “to do” NA therapy resulting in an unnecessary incidence of NA side effects/intolerance.
• The disappointing results of 2 large statin/NA clinical trials (AIM-HIGH, and HPS-2 THRIVE), which both had serious design flaws, caused many providers to permanently discard NA as a therapeutic lipid agent.
• Despite those study’s results, multiple other studies before and after them (including statin/NA trials) have shown complementary benefits of NA with other agents.
• NA is arguably the best initiating agent in persons with mixed dyslipidemia and an LDL-C level within 20% of target level, and the only effective agent for Lp(a).
• Cardiac deaths have grown at epidemic rates with over 80% occurring in developing countries. With the cost of $37,000 per QALY for statins, and $330,000 for the alternative (PCSK-9 inhibitors). A less expensive agent is necessary = NA Renaissance.