

Medical Conditions of Particular Risk for Patients with SLOS

William B. Rizzo, MD

Child Health Research Institute

University of Nebraska Medical Center

Children's Hospital & Medical Center

Omaha, Nebraska

**Child Health
Research Institute**

 University of Nebraska
Medical Center


Children's
HOSPITAL & MEDICAL CENTER

Definition of Risk

The possibility of something bad happening*

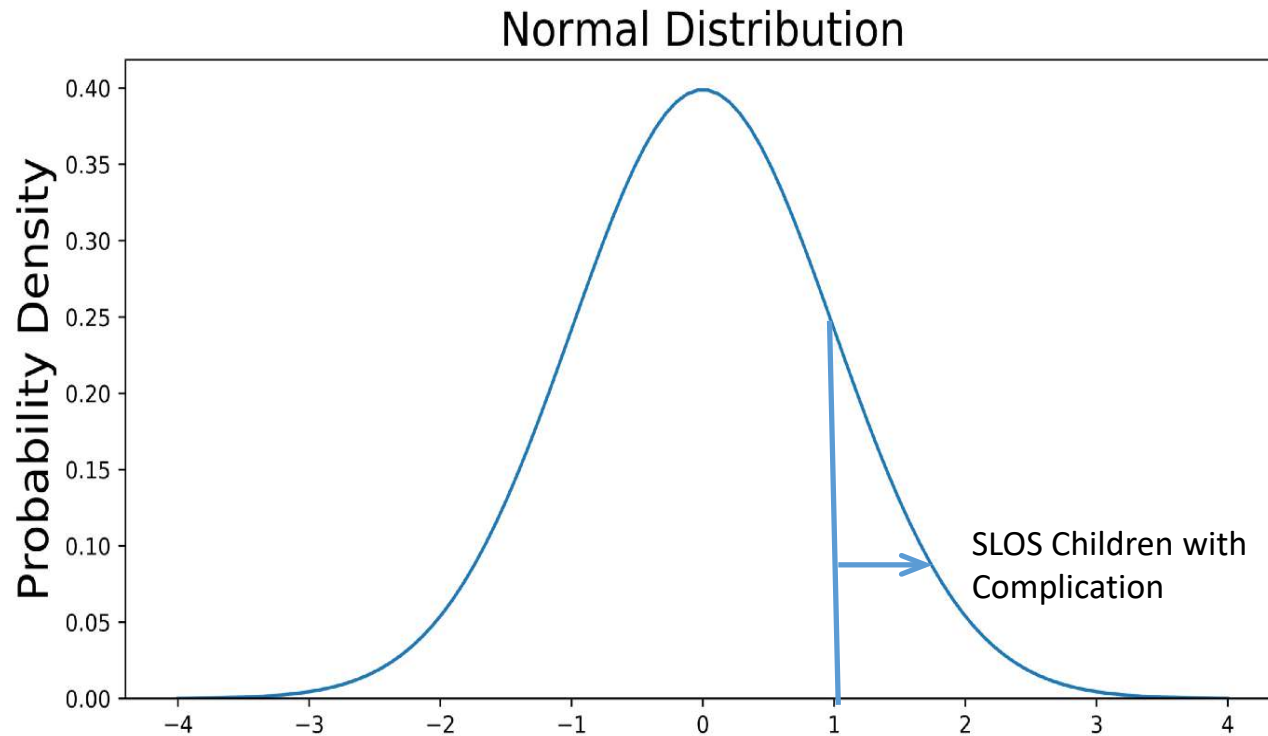
*Cambridge English Dictionary

Risks for Medical Complications of SLOS

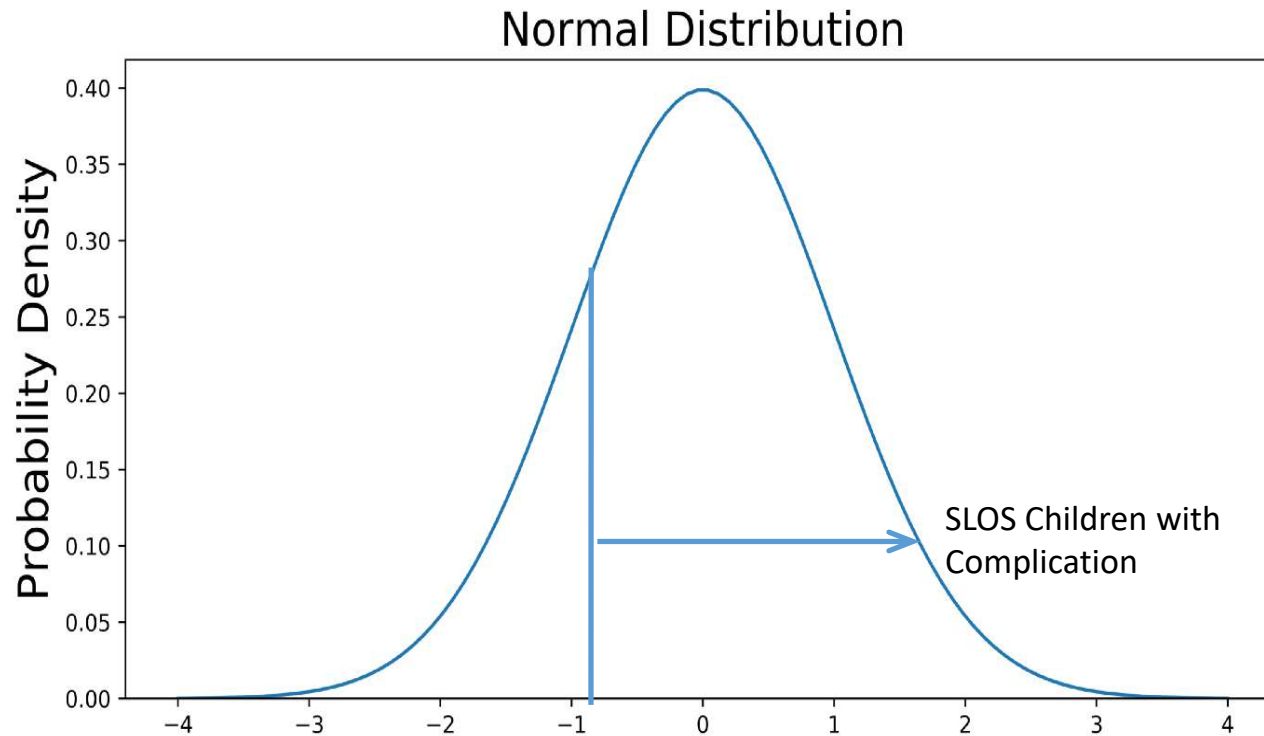
- Risks for complications are poorly defined
 - Based on anecdotal reports, limited number of rare patients, personal experience of physician, hearsay
- Probably related to “severity of mutation” and cholesterol deficiency
- Affected by seemingly random factors:
 - Other genes
 - Environment exposures
 - Independent of other medical complications:
- Risks change over time & not the same for everyone



Likelihood of Medical Risk



Likelihood of Medical Risk

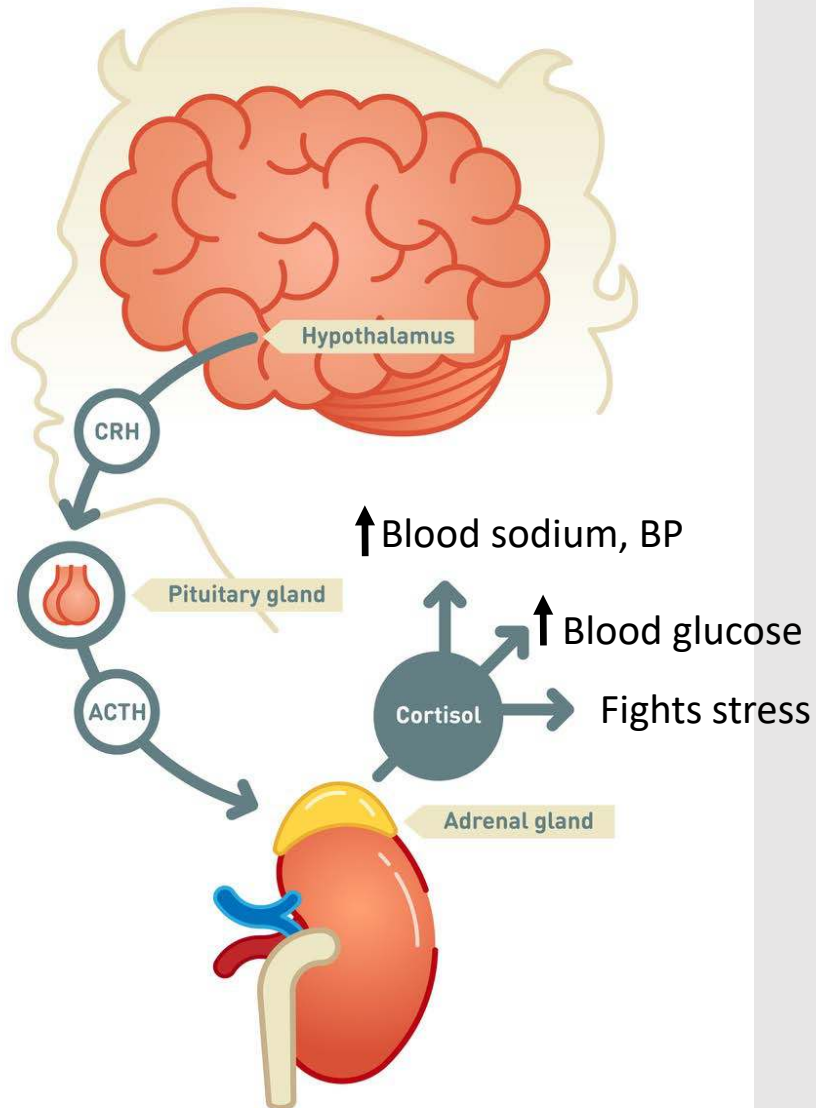


Medical Risks for SLOS

- High risks
 - Adrenal insufficiency
- Moderate risks?
 - Immune dysfunction
 - Pneumonia
 - Electrolyte disturbances
- Lower risks?
 - Hypothyroidism



Adrenal Insufficiency in SLOS



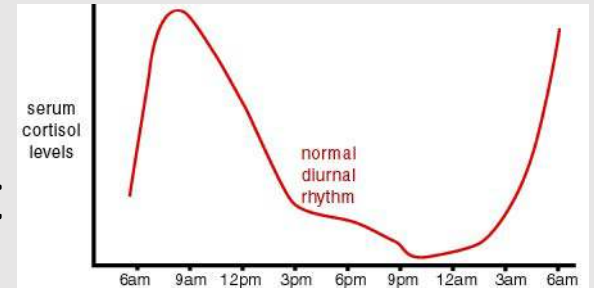
Cortisol and related hormones are made from cholesterol

Symptoms of Low Cortisol

- Low blood pressure → light-headedness, headache, fainting
- Low sodium → vomiting, irritability, headache, seizures
- Hypoglycemia → fatigue, sweating, confusion
- Poor stress response to fever, serious infections, anesthesia complications
- Hyperpigmentation due to high ACTH

Adrenal Insufficiency in SLOS

- Diagnosis
 - 8 am cortisol and ACTH levels
 - Adrenal (ACTH) stimulation test
- Treatment
 - Hydrocortisone liquid/tabs (\pm fludrocortisone tabs) – given 2-3 times/day
 - Extra “stress doses” with fevers, serious infections or surgery



Electrolyte Disturbances & Complications

- Low blood sodium (hyponatremia)
 - Nausea & vomiting
 - Irritability, confusion, headache
 - Muscle weakness, cramps
 - Seizures, coma
- Low blood calcium (hypocalcemia)
 - Numbness, tingling in hands, feet and lips
 - Muscle cramps in hands and feet (tetany)
 - Facial twitching
 - Slow heartbeat



Electrolyte Treatment

- Diagnosis requires blood tests (electrolytes, calcium)
 - Check for adrenal insufficiency
- Hyponatremia
 - Supplemental sodium chloride (salt)
 - IV fluids and/or oral salt
- Hypocalcemia
 - IV calcium for serious symptoms
 - Oral calcium supplements
 - ± Vitamin D (improves calcium absorption from diet)

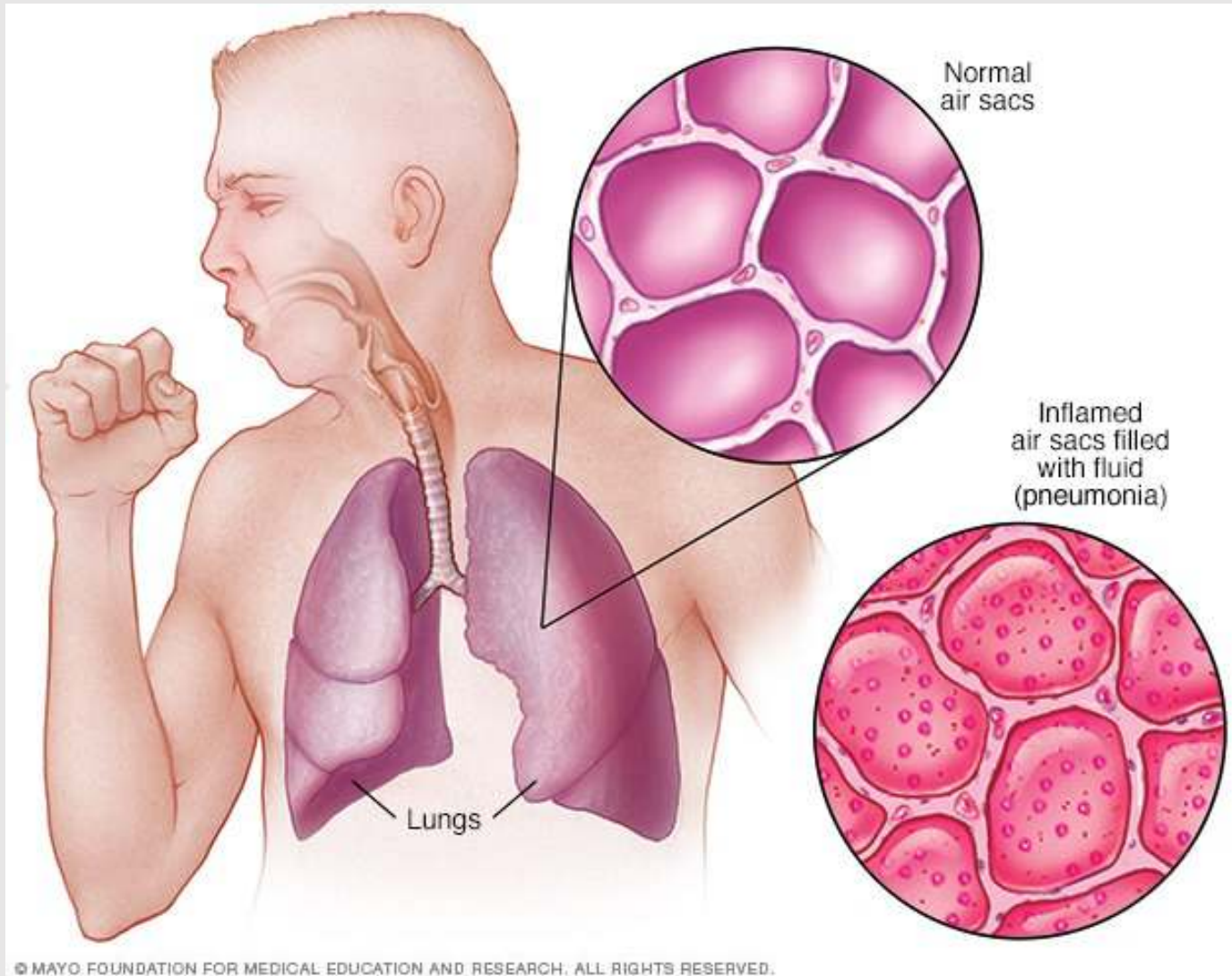
Immune Dysfunction & Infections

- **Antibody immune deficiency** (Babovic-Vuksanovic et al, J Inherit Metab Dis, 2005)
 - Recurrent respiratory infections
 - Absent immune response to Pneumovax, Hepatitis B vaccine
 - Low immunoglobins (antibodies)
- **Fatal adenovirus infection** (Beby-Defaux et al, J Med Virol, 2001)
- **Recurrent or fatal infections in SLOS** (Donoghue et al, 2018)
 - 3 of 14 SLOS children died of sepsis and 2 had recurrent infections
 - Thymus hypoplasia was seen

Respiratory Infections

- Pneumonia (lower respiratory infection)
 - Cough, high fever, rapid breathing, chest pain, lethargy, pallor
 - “Really sick looking”, not eating, rapid progression of symptoms possible
 - Caused by bacteria or viruses (including influenza)
 - “Bacterial sepsis” and stress
- Upper respiratory infections
 - Runny nose, cough, sore throat, \pm low fever
 - Sometimes other symptoms (diarrhea, rash)
 - Usually caused by viruses

Pneumonia



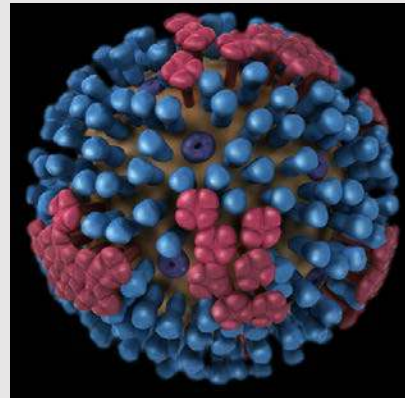
Diagnosis and Treatment of Pneumonia

- Physical exam
 - Vital signs – resp rate, heart rate, temp, BP
 - Lung sounds
 - Look for other areas of infections i.e ears
- Diagnostic tests
 - Chest X-ray
 - Blood studies: Complete Blood Count
 - Bacterial: elevated white blood cells (particularly neutrophils)
 - Viral: Normal WBC, elevated lymphocytes
- Treatment
 - Bacterial: antibiotic therapy
 - Viral: supportive therapy, anti-viral drugs
 - Stress doses of adrenal hormones for SLOS with adrenal insufficiency

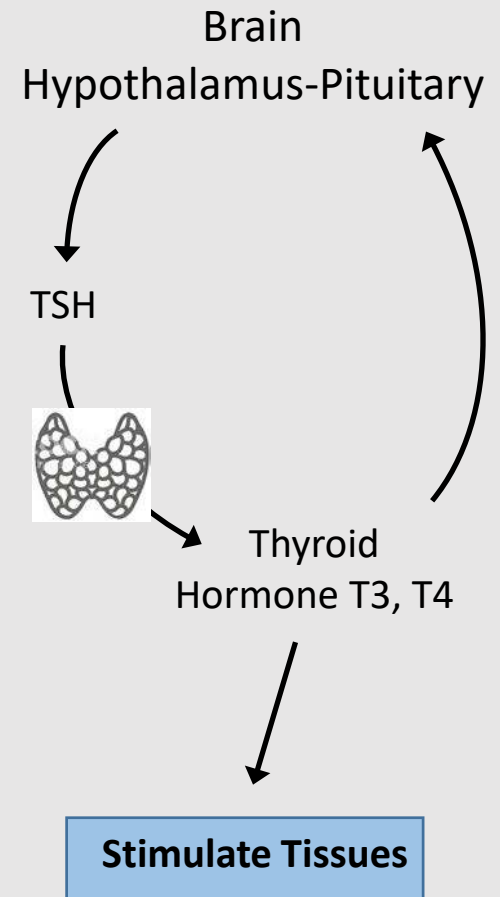
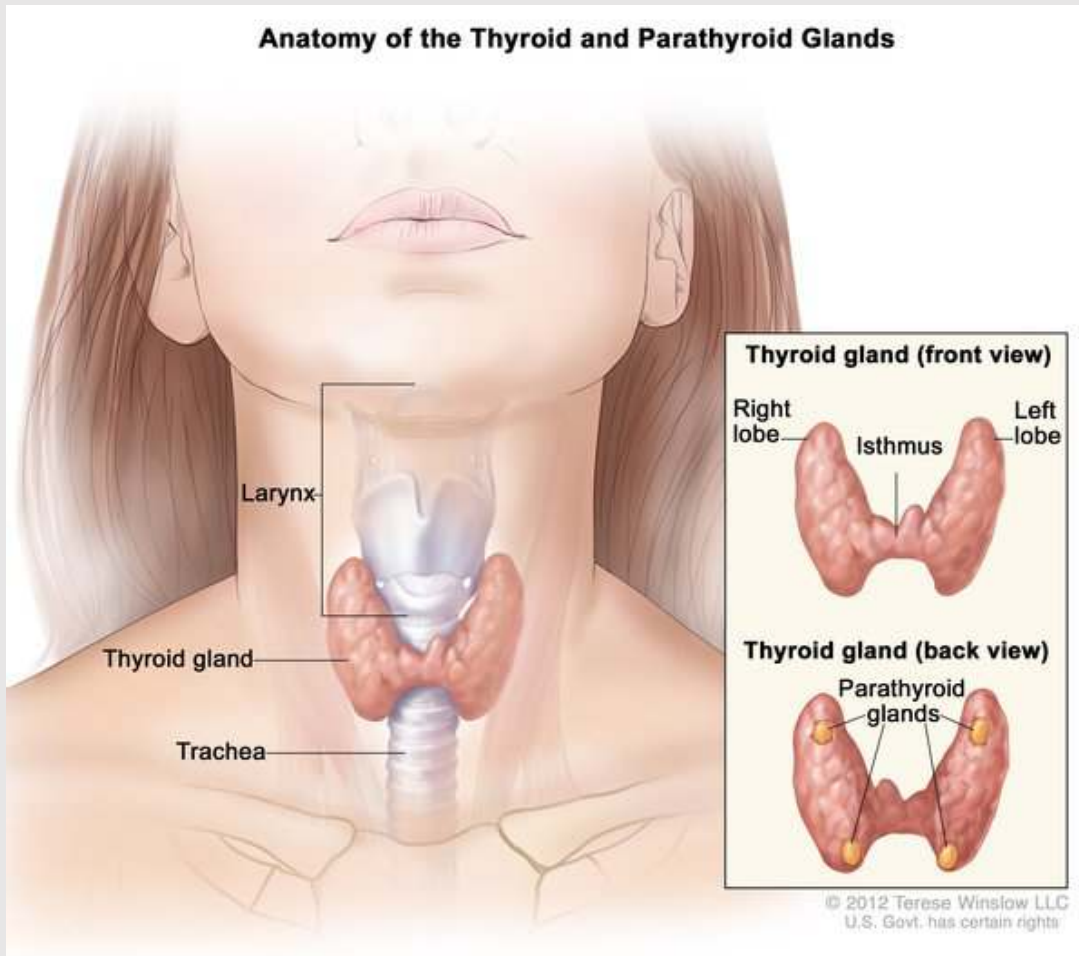


Immunizations Prevent Infectious Disease Risks

- Immunizations are effective and do save lives
- Complications of immunizations are overblown
 - No proven association with autism
- Influenza immunizations
 - Needed yearly
 - Variable efficacy
 - In children: decreased flu-related death 51%
 - Milder course



Hypothyroidism



Hypothyroid Symptoms

- Younger children
 - Lethargy, fatigue, growth failure, developmental delay, constipation, course facial features, thick skin.
- Older children
 - Fatigue, exercise intolerance, weight gain, cold intolerance, sparse dry hair, hoarse voice, droopy eyelids, slow speech



Hypothyroidism Diagnosis and Treatment

- Diagnosis:
 - Blood TSH and free T4 levels
- Treatment:
 - Thyroid hormone supplementation
- Outcome:
 - Depends on age of onset and elapsed time before treatment is started

Conclusions

- Serious and sometime life-threatening complications occur in SLOS
- Some complications are easily diagnosed and treated or prevented
- More research is needed to:
 - Define the true incidence and risks for SLOS children
 - Understand immune dysfunction and infections
 - Determine if cholesterol supplementation or other medications can prevent complications

Questions?