STATIN USE FOR TREATMENT OF HYPERTENSION—AND INACCURACY OF STATIN INTOLERANCE

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Disclosures

None.

Objectives

Is there a role for statins in hypertension?

Statin side effects—how common?

Understanding statin intolerance

The Big Picture—ASCVD

- The big picture we're talking about is atherosclerotic cardiovascular disease (ASCVD).
- Two biggest components when modifying ASCVD risk are blood pressure and cholesterol.
- So we're going to talk about them!

HYPERTENSION

Hypertension accounts for more deaths in the USA than any other modifiable ASCVD risk factor.

500,000 deaths per year in USA include hypertension as a primary or contributing cause.

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease - American College of Cardiology

Facts About Hypertension | cdc.gov

Treatment Options for Hypertension

Treatment for Hypertension

Four classes considered first line treatment agents of HTN:

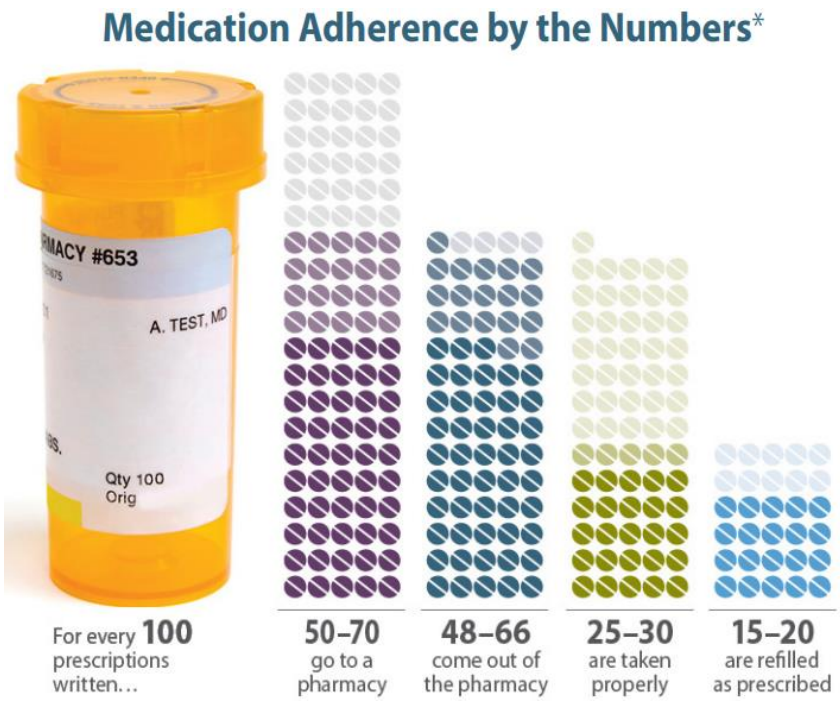
1. Thiazide diuretics
2. ACE Inhibitors
3. Angiotensin Receptor Blockers (ARBs)
4. Calcium channel blockers

Medication Adherence

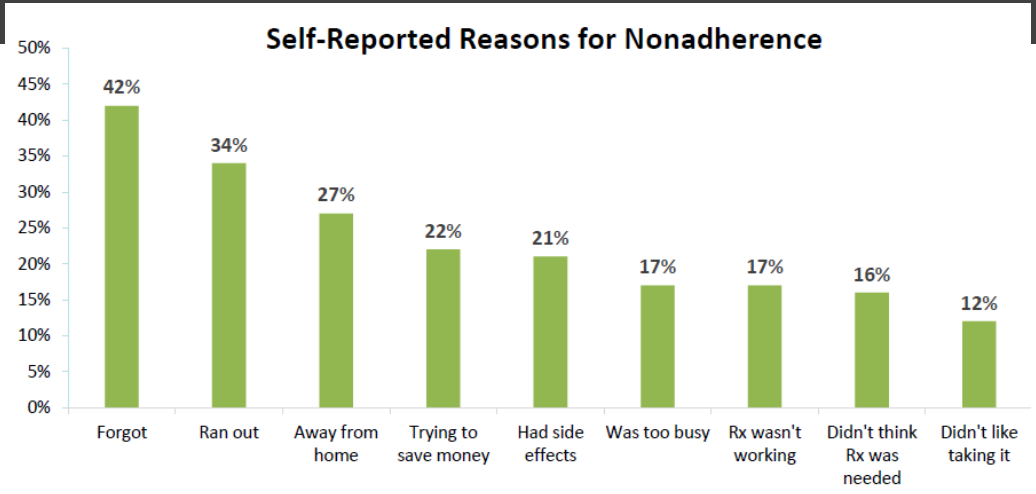
Medication adherence overall, is one of our biggest challenges in the treatment of hypertension (or any chronic disease).

What is Medication Adherence?

The patient's conformance with the treatment plan with respect to the timing, dosage, and frequency of medication taken during the prescribed length of time



Reasons for Not Adhering to Medications



CANDIDATES FOR STATINS

Who should get statins?

Do they actually work?

An Incomplete Picture

- Traditionally, one of the most difficult aspects of statin management was the lack of clarity.
- Competing guidelines and professional opinions are barriers.
- Diseases may change the picture for otherwise similar patients.
- The current guidelines from the American Diabetes Association and American College of Cardiology do seem to show a bit more effort to harmonize their guidelines, which is positive.

Risk Rules

- For many years we had a focus on treating to a specific number with cholesterol
- In the past decade, much more focus has been placed upon modifying ASCVD risk factors and targeting statin intensity (low, medium, high intensity doses).

Statin Intensity

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL on average by ≥50%	Daily dose lowers LDL on average by approximately 30-49%	Daily dose lowers LDL on average by <30%
Atorvastatin 40-80 mg Rosuvastatin 20-40 mg	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg BID Pitavastatin 2-4 mg	Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg

Pharmacy-Integration-Insights-graph2.png (1236×520) (uchealth-wp-uploads.s3.amazonaws.com)

American Diabetes Association Guidelines

Statin Treatment

Primary Prevention

Recommendations

10.19 For patients with diabetes aged 40–75 years without ASCVD, use moderate-intensity statin therapy in addition to lifestyle therapy. A

10.20 For patients with diabetes aged 20–39 years with additional ASCVD risk factors, it may be reasonable to initiate statin therapy in addition to lifestyle therapy. C

10.21 In patients with diabetes at higher risk, especially those with multiple ASCVD risk factors or aged 50–70 years, it is reasonable to use high-intensity statin therapy. B

10.22 In adults with diabetes and 10-year ASCVD risk of 20% or higher, it may be reasonable to add ezetimibe to maximally tolerated statin therapy to reduce LDL cholesterol levels by 50% or more. C

Secondary Prevention

Recommendations

10.23 For patients of all ages with diabetes and ASCVD, high-intensity statin therapy should be added to lifestyle therapy. A

10.24 For patients with diabetes and ASCVD considered very high risk using specific criteria, if LDL cholesterol is ≥70 mg/dL on maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor). A Ezetimibe may be preferred due to lower cost.

10.25 For patients who do not tolerate the intended intensity, the maximally tolerated statin dose should be used. E

ACC Guideline on the Primary Prevention of Cardiovascular Disease

Patients ages 20-75 years and LDL-C ≥190 mg/dl, use high-intensity statin without risk assessment.

T2DM and age 40-75 years, use moderate-intensity statin and risk estimate to consider high-intensity statins.

In those with multiple ASCVD risk factors, consider high-intensity statin with aim of lowering LDL-C by 50% or more.

- Age >75 years, clinical assessment and risk discussion.
- Age 40-75 years and LDL-C ≥70 mg/dl and <190 mg/dl without diabetes, use the risk estimator that best fits the patient and risk-enhancing factors to decide intensity of statin.
  - Risk 5% to <7.5% (borderline risk). Risk discussion: if risk-enhancing factors are present, discuss moderate-intensity statin
  - Risk ≥7.5-20% (intermediate risk). Risk discussion: use moderate-intensity statins and increase to high-intensity with risk enhancers. Risk ≥20% (high risk). Risk discussion to initiate high-intensity statin to reduce LDL-C by ≥50%.

Do Statins Work?

- ACC still believes in statins. With any topic, there is controversy.
- For every ~40 mg/dL LDL reduction:
  - Relative risk of major adverse cardiovascular events reduced 20-25%
  - All-cause mortality reduced by 10%

Summarizing the Current State and Evidence on Efficacy and Safety of Statin Therapy - American College of Cardiology (acc.org)

Convergence

A statin BP miracle?

STATIN REDUCTION OF BP

- Some research has led to questions if statins can independently reduce blood pressure
- Statins have been associated with increasing availability of nitric oxide, antioxidant properties, reduction of inflammation (not related to their cholesterol lowering mechanism)
- Due to these impacts on the vasculature, questions exist if statins reduce blood pressure or if this is part of their cardiovascular risk reduction
- Interesting line of study, but studies at this point are inconclusive or appear to be synergistic with anti-hypertensives rather than statin-mediated individually

Do really statins reduce blood pressure? : Journal of Hypertension (lww.com)

STATIN REDUCTION OF BP

Regardless of a statin having or not having direct impact on BP, they remain a mainstay of modifying ASCVD risk and are the focus of constant research.

Statin Side Effects

How Common?

Notable Statin Side Effects

- N/V/constipation/diarrhea, rash, weakness
- Muscle pain is the one that gets most press
- Rhabdomyolysis
- Case reports of confusion, memory impairment
- Inducing diabetes

Statin Side Effects—How Common?

- Myalgia occurs in 1-4% of patients in studies
- Observationally, some results say up to 10% -- some question if there is a heightened patient awareness factor involved with this
- Rhabdomyolysis only in 1 in 2000 or more
- Induces diabetes in less than 0.2% and relationship is unclear

Statin Side Effects—How Common?

Maybe side effects are generally similar, so it's a matter of cost, lifestyle, and degree of cholesterol improvement for many

Some believe that Fluvastatin (Lescol) and Pitavastatin (Livalo) may have fewer side effects but evidence isn't clear

Patient Statin Awareness and Suspicion

- Patient awareness of statin risks and Adverse Drug Events is very high.
- Those in the audience likely have many examples of patients who are reluctant or outright refuse statin trial.
- Patients now tend to have a very low threshold for stopping a statin and may not be willing to trial a different agent.
- As such, we are losing a great tool in our ASCVD risk reduction armory.

Statin Intolerance

What is Statin Intolerance?

- Development of side effects and unable to continue (or only at reduced dose)

A Few Risk Factors

- Elderly, frail
- Kidney or liver disease
- High grapefruit consumption

Overcoming Statin Intolerance

- Cleveland Clinic found that over 70 percent of patients thought intolerant to 2 or more statins were able to be restarted successfully.
- Methods focused on restarting the same drug at a very low dose and very slowly titrating or trying yet another different statin

CoQ-10

- The OTC supplement Coenzyme Q-10 has received some attention as perhaps being able to reduce myalgias for statin users, but current literature is inconclusive at best.

https://my.clevelandclinic.org/health/articles/17506-statin-medications--heart-disease
Coenzyme Q10 | NCCIH (nih.gov)
Effects of Coenzyme Q10 on Statin-Induced Myopathy: An Updated Meta-Analysis of Randomized Controlled Trials - PubMed (nih.gov)

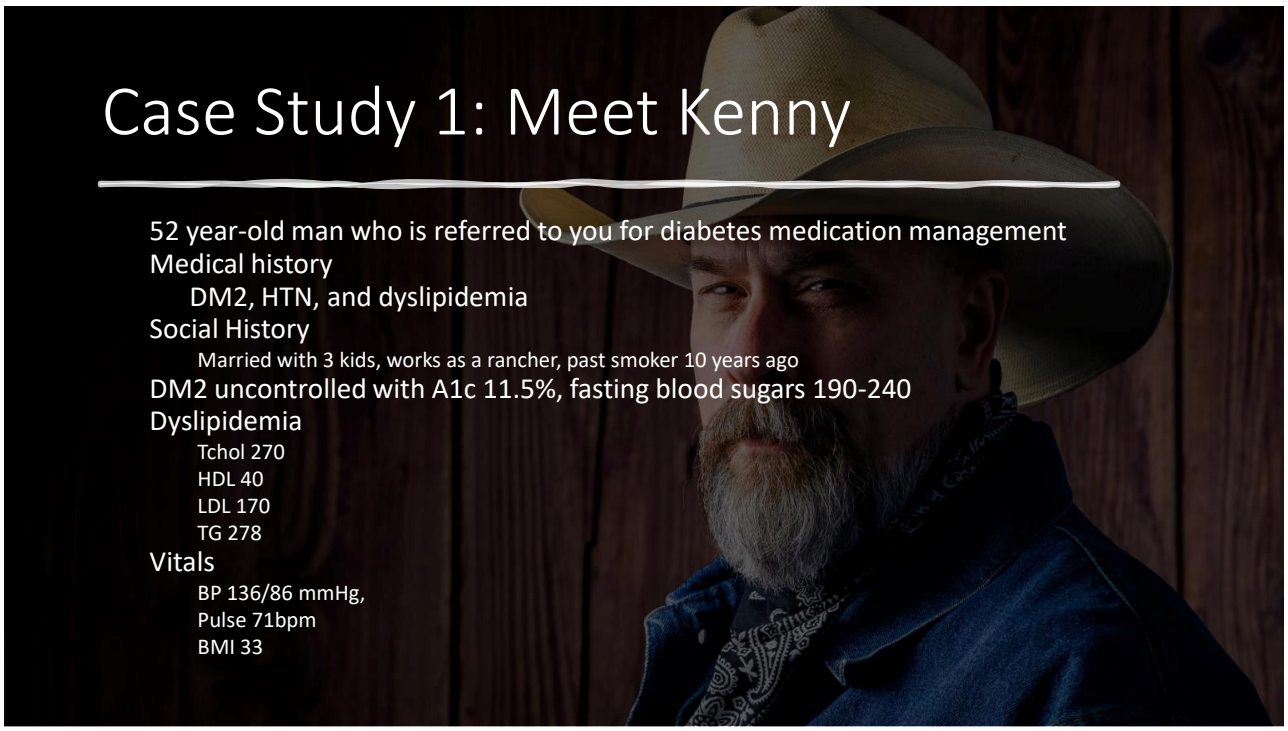
Overcoming patient resistance

- A decade ago it was all grapefruit interactions, now it's myalgias
- Patients don't FEEL different when their lipid panel is good vs uncontrolled
- Describe treating to tolerable dose up front rather than to a target
- Risks of liver and muscle damage really quite low
- Even though we're in the generic statin era, cost matters
- Remember the JAMA Cardiology study in 2019: Average NNT to prevent ASCVD event averaged 18-21 (granted, high intensity)

Provider Hesitance

- Providers hear every day the resistance of patients to statins; it wears them down
- Quite a bit of debate re: treat to tolerable dose, treat to targets, how it changes depending upon disease state
- Multidisciplinary/care team approach useful….better results anecdotally when other care members such as coordinators and pharmacists are empowered and required to attempt to get patients on statins
- Statin use is often on many quality panels in the clinic

Case Study 1: Meet Kenny



52 year-old man who is referred to you for diabetes medication management

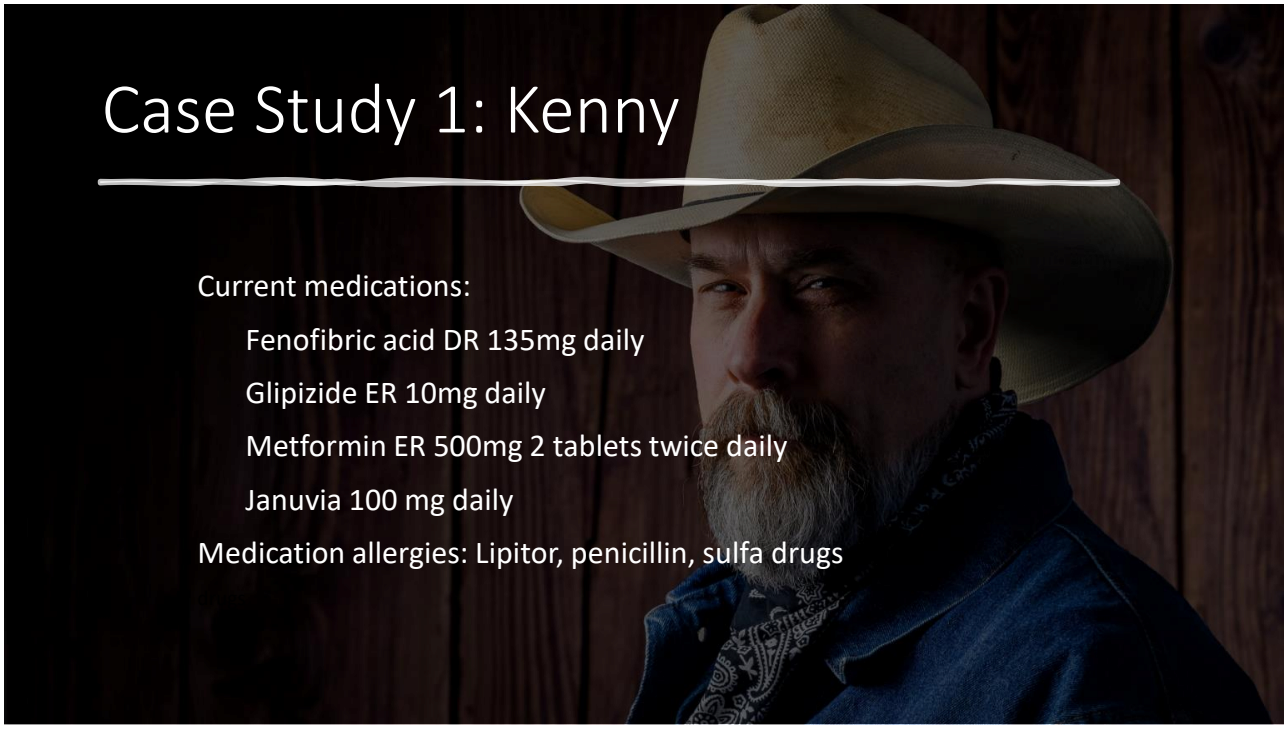
Medical history
- DM2, HTN, and dyslipidemia

Social History
- Married with 3 kids, works as a rancher, past smoker 10 years ago

DM2 uncontrolled with A1c 11.5%, fasting blood sugars 190-240

Dyslipidemia
- Tchol 270
- HDL 40
- LDL 170
- TG 278

Vitals
- BP 136/86 mmHg,
- Pulse 71bpm
- BMI 33

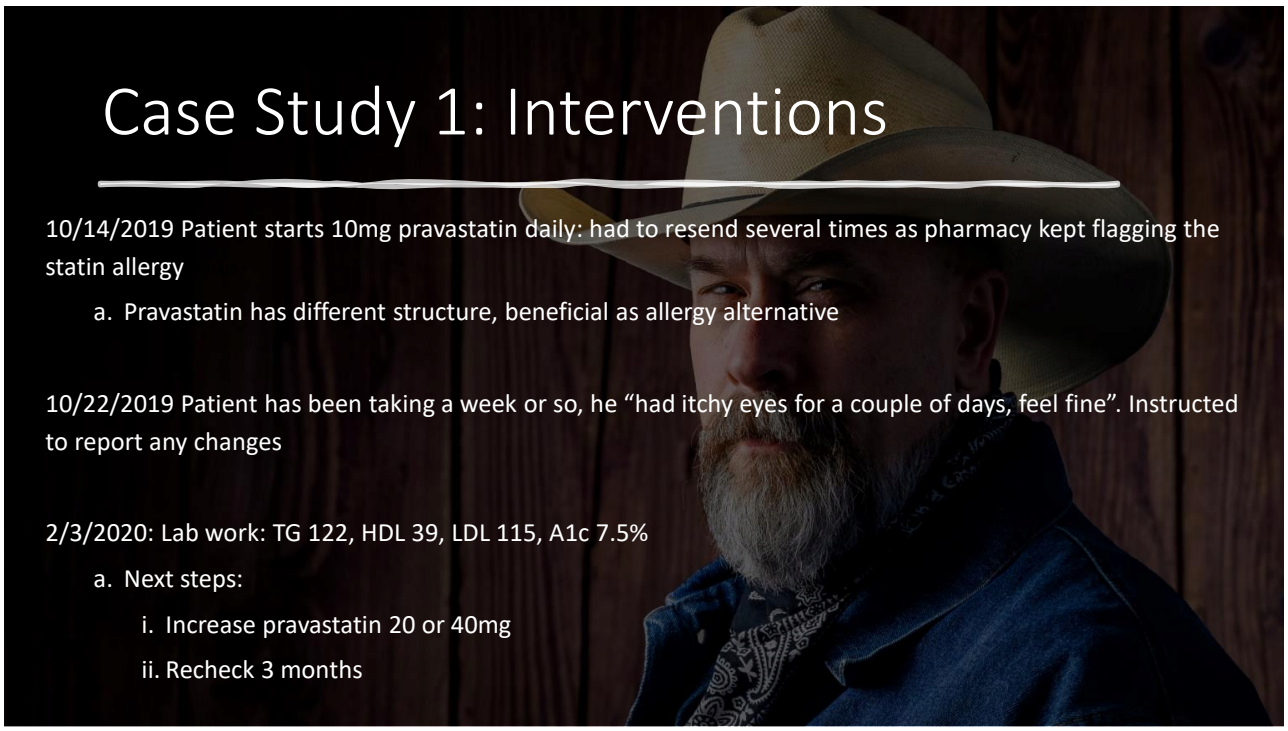


Case Study 1: Kenny

Current medications:

- Fenofibric acid DR 135mg daily
- Glipizide ER 10mg daily
- Metformin ER 500mg 2 tablets twice daily
- Januvia 100 mg daily

Medication allergies: Lipitor, penicillin, sulfa drugs



Case Study 1: Interventions

10/14/2019 Patient starts 10mg pravastatin daily: had to resend several times as pharmacy kept flagging the statin allergy

a. Pravastatin has different structure, beneficial as allergy alternative

10/22/2019 Patient has been taking a week or so, he "had itchy eyes for a couple of days, feel fine". Instructed to report any changes

2/3/2020: Lab work: TG 122, HDL 39, LDL 115, A1c 7.5%

a. Next steps:
   i. Increase pravastatin 20 or 40mg
   ii. Recheck 3 months

Case Study 2: Meet Sandy

Case Study 2: Sandy

75 year-old woman presents to ER with severe muscle pain and "rusty" colored urine

Pain in mostly in arms and thighs

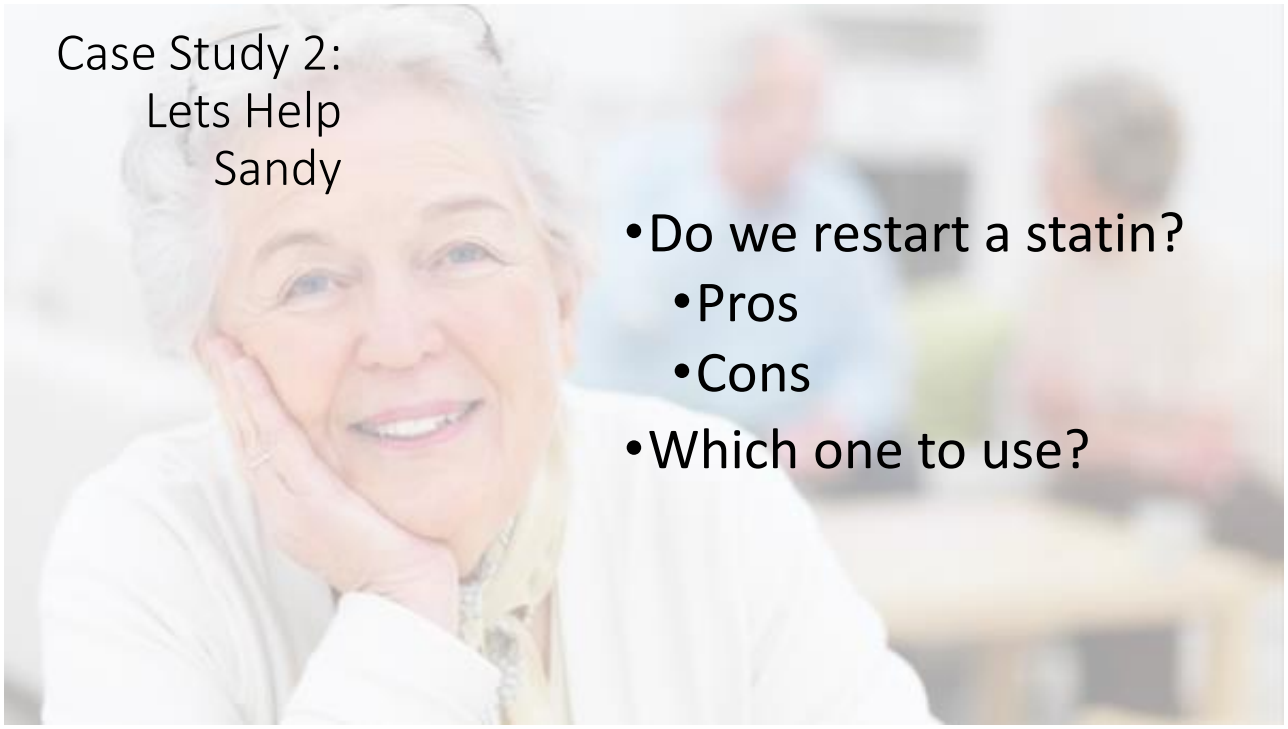
Appears acutely ill

Afebrile

- **Findings:**
  - BP 98/60mmHg
  - HR 52 bpm
  - WBC 12,100
  - TChol 198
  - TG 200
  - HDL 32
  - LDL 154
  - Troponin 0.01
  - CK 12,000
  - Urine positive for myoglobin

Case Study 2: Sandy

- Patient was hospitalized 3 weeks ago for Afib and discharged with additional H. Pylori and high cholesterol dx.
- Previous medications: diltiazem 240mg and omeprazole 40mg.
- Discharge medications:
  - Diltiazem 180mg
  - Amiodarone 200mg
  - Simvastatin 40mg
  - Metronidazole 500mg daily



Case Study 2: Lets Help Sandy

- Do we restart a statin?
  - Pros
  - Cons
- Which one to use?

Case Study 2: Sandy

In this case, provider did not re-challenge statin due to age and comorbid conditions

- New Rx for ezetimibe 10mg at 3mos

Options

Pravastatin and rosuvastatin not 3A4

- Start low and titrate
- Intermittent dosing
- **Non-statin based therapy**
  - Ezetimibe
  - Bile acid sequestrant
  - Niacin
  - Fibrates
  - PCSK9 inhibitors
  - **Nonpharmacological Tx**

Questions?

Thank you!

- https://my.clevelandclinic.org/health/articles/17506-statin-medications--heart-disease
- UpToDate-Statin Side effects and Administration
- https://www.heart.org/en/news/2018/12/10/safety-of-statins-emphasized-in-new-report
- https://professional.heart.org/professional/ScienceNews/UCM_503181_AHAs-Statement-on-the-Safety-Profile-of-Statins-Big-Benefit-with-Low-Risk.jsp