



## BRINGING CLINICIANS TOGETHER TO DISCUSS CURRENT DRUG THERAPY

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Based on

 The following succinct analysis appeared in *Pharmacist's Letter*.

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**LIVER DISEASE**

You'll see more attention paid to the management of nonalcoholic fatty liver disease (NAFLD)...as it becomes more common.

Up to 100 million Americans have this buildup of fat in the liver...usually without any symptoms. It often goes hand in hand with obesity, dyslipidemia, insulin resistance, and diabetes.

About 20% of patients with NAFLD have nonalcoholic steatohepatitis (NASH)...the more severe form with inflammation and sometimes fibrosis.

Get used to hearing the term "NASH." It's set to be the top reason for liver transplants in the U.S. by 2020.

The tough part is that meds haven't been shown yet to decrease the risk of cirrhosis, liver transplant, or death.

Emphasize weight loss with diet and exercise.

Tell patients to aim for a 3% to 5% weight loss to reduce liver fat...and at least 7% to 10% to reduce inflammation and possibly fibrosis.

Optimize meds for dyslipidemia, diabetes, hypertension, etc.

For example, recommend statins for dyslipidemia or to lower CV risk. Reassure patients that statins can be safely used in NAFLD...even in NASH.

Continue to recommend metformin and other diabetes meds for glycemic control in NAFLD patients with diabetes.

Suggest pioglitazone up to 45 mg/day for NASH patients...with or without diabetes. It seems to reduce liver fat, inflammation, and fibrosis. But caution about edema, weight gain, heart failure, etc.

Consider suggesting vitamin E 800 IU/day for NASH patients withOUT diabetes...to possibly reduce liver fat and inflammation. But explain these high doses are linked to prostate cancer and hemorrhagic stroke.

Don't suggest vit E for patients with diabetes or milder NAFLD... due to lack of evidence. Also tell patients not to rely on milk thistle.

Listen to *PL Voices* to hear our team discuss fatty liver disease with an author of new NAFLD guidance. See our commentary, *Overview of Nonalcoholic Fatty Liver Disease*, to help manage comorbidities.

(For more on this topic, see Clinical Resource #330901 at [PharmacistsLetter.com](http://PharmacistsLetter.com).)

Primary Reference – Musso G, Cassader MC, Paschetta E, Gambino R. Thiazolidinediones and advanced liver fibrosis in nonalcoholic steatohepatitis: a meta-analysis. *JAMA Intern Med* 2017;177:633-40 [Abstract].

See LEADER NOTES for answers to discussion questions

Discussion Questions

**Overview of current therapy**

**1. What are the causes of nonalcoholic fatty liver disease? How is this disease treated?**

**Analysis of new study**

**2. What type of study was this?**

**3. What was the search strategy for identification of information?**

**4. How were studies selected for inclusion in the meta-analysis?**

**5. How were data extracted and analyzed from selected studies?**

**6. How many studies were identified? What was the patient population?**

**7. What were the results of the meta-analysis?**

**8. What were the strengths and limitations of the meta-analysis?**

**9. Were the results expressed in terms we care about and can use?**

**How should the new findings change current therapy?**

**10. Do the results change your practice? How?**

**Apply the new findings to the following case**

F.W. is a 56-year-old white male with a past medical history of morbid obesity, hypertension, and type 2 diabetes. His current medications include metformin 1000 mg BID, chlorthalidone 12.5 mg daily, and lisinopril 20mg daily.

See LEADER NOTES for answers to discussion questions

F.W. is in clinic to follow-up on labs that were drawn last week. You review his complete metabolic panel, lipid panel, and HgbA1C. All of F.W.'s labs are within normal limits except for: hemoglobin A1C 7.2%, glucose 148 mg/dL, ALT 61 units/L, and AST 55 units/L. His vitals are: BP 136/82 mmHg, heart rate 77, respiratory rate 14, and BMI 38.

**11. What are potential causes of F.W.'s mildly elevated (< 5 times the upper limit of normal) liver enzymes? How should you manage F.W. at this time?**

You obtain additional labs for F.W. and they return normal. You counsel F.W. about the importance of avoiding alcohol and focusing on weight loss, and advise him to return in 6 months for repeat labs.

F.W. returns in 6 months as advised. His A1C is 7.8%, glucose 178 mg/dL, ALT 93 units/L, and AST 72 units/L. His other liver function tests are still normal and he remains asymptomatic. He reports stopping all alcohol but did not make any other dietary or lifestyle changes, so he has gained 3 pounds. You order a right upper quadrant ultrasound, which reports hepatic steatosis. You suspect F.W. has NAFLD.

**12. What should you discuss with F.W. about treating NAFLD?**

You reinforce lifestyle modifications and increasing exercise to help F.W. lose weight. You also discuss adding pioglitazone 30 mg/day, especially since F.W.'s A1C remains elevated. Finally, you discuss starting a high-intensity statin such as atorvastatin 80 mg/day to lower F.W.'s CV risk since he has diabetes.

F.W. agrees that he needs to work to initiate weight loss, and would like to start pioglitazone and atorvastatin. He is interested in "natural" treatments and asks if there are any supplements he should try to improve his liver disease.

**13. Are there any supplements that may be beneficial for F.W.'s NAFLD?**

You discuss that evidence to support supplements for NAFLD is lacking. Vitamin E may be an option for some patients with severe NAFLD to try, but it's too soon to recommend it for patients with diabetes or less severe NAFLD.

See LEADER NOTES for answers to discussion questions

## References

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**Additional *Pharmacist's Letter* Resources** available at [PharmacistsLetter.com](http://PharmacistsLetter.com)

- Chart, Drugs for Type 2 Diabetes. *Pharmacist's Letter/Prescriber's Letter*. July 2017.
- PL Voices, Choosing Metformin Add-Ons. *Pharmacist's Letter/Prescriber's Letter*. February 2017.
- Chart, Lipid Treatment FAQs. *Pharmacist's Letter/Prescriber's Letter*. February 2017.
- Toolbox, Improving Diabetes Outcomes. *Pharmacist's Letter/Prescriber's Letter*. January 2017.
- Chart, Drugs for Weight Loss. *Pharmacist's Letter/Prescriber's Letter*. December 2016.
- Chart, Comparison of GLP-1 Agonists. *Pharmacist's Letter/Prescriber's Letter*. December 2016.
- PL Voices, Treatment of Newly-Diagnosed Type 2 Diabetes. *Pharmacist's Letter/Prescriber's Letter*. October 2016.
- Algorithm, Management of New-Onset Type 2 Diabetes. *Pharmacist's Letter/Prescriber's Letter*. October 2016.
- PL Voices, Cardiovascular Effects of Diabetes Medications. *Pharmacist's Letter/Prescriber's Letter*. August 2016.
- Chart, Diabetes Medications and Cardiovascular Impact. *Pharmacist's Letter/Prescriber's Letter*. August 2016.
- Commentary, DPP-4 Inhibitors (Gliptins) and Risk of Heart Failure. *Pharmacist's Letter/Prescribers Letter*. June 2016.
- Commentary, Clinical Use of Metformin in Special Populations. *Pharmacist's Letter/Prescriber's Letter*. June 2016.
- PL Voices, Helping Patients Stick with Metformin. *Pharmacist's Letter/Pharmacist's Letter*. December 2015.
- Algorithm, Improving Tolerability of Metformin. *Pharmacist's Letter/Pharmacist's Letter*. December 2015.
- PL Voices, Cardiovascular Outcomes with Empagliflozin (*Jardiance*). *Pharmacist's Letter/Prescriber's Letter*. November 2015.
- Commentary, Empagliflozin and Cardiovascular Disease. *Pharmacist's Letter/Prescriber's Letter*. November 2015.
- Chart, Statin Muscle Symptoms: Managing Statin Intolerance. *Pharmacist's Letter/Prescriber's Letter*. September 2015.
- PL Voices, Chronic Use of Weight Loss Drugs. *Pharmacist's Letter/Prescriber's Letter*. May 2015.
- Toolbox, Weight Loss: Helping Your Overweight and Obese Patients. *Pharmacist's Letter/Prescriber's Letter*. May 2015.
- Chart, Drugs Associated with Weight Gain. *Pharmacist's Letter/Prescriber's Letter*. March 2015.
- Patient Education Handout, Tips for Getting to a Healthy Weight. *Pharmacist's Letter/Prescriber's Letter*. June 2013.

## Welcome to PL Journal Club

PL Journal Club gives you insights and guides you to the discoveries that *Pharmacist's Letter* researchers and editors uncover. Each month we analyze many new studies and help you discover the answers to the hard questions. "What are the real advantages and disadvantages of new therapies?" "How do they compare with other options?" "What do pharmacists and prescribers need to know?" We look beyond the headlines and promotional materials to interpret the clinical studies and data. Sometimes the marketing spin doesn't stand up to scrutiny. Sometimes studies do not really prove what they are reported to prove. PL Journal Club helps guide you to the truth and how to apply new findings to patient care.

PL Journal Club builds on *Pharmacist's Letter* to provide you with background for your own journal club discussions. We won't bring up every possible question, but you can...in your own group meetings. If a question comes up, go to [PharmacistsLetter.com](http://PharmacistsLetter.com) to find more background. As a PL Journal Club participant, you get access to all of *Pharmacist's Letter*. Feel free to call or email us with suggestions or if we can be of assistance... 209-472-2240 or [PLJournalClub@pletter.com](mailto:PLJournalClub@pletter.com).

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