

Are we ready to recommend  
pharmacologic therapy to patients  
with NAFLD?

Unfortunately,  
  
NO

The scope of the problem

75 million adults in the U.S. with NAFLD

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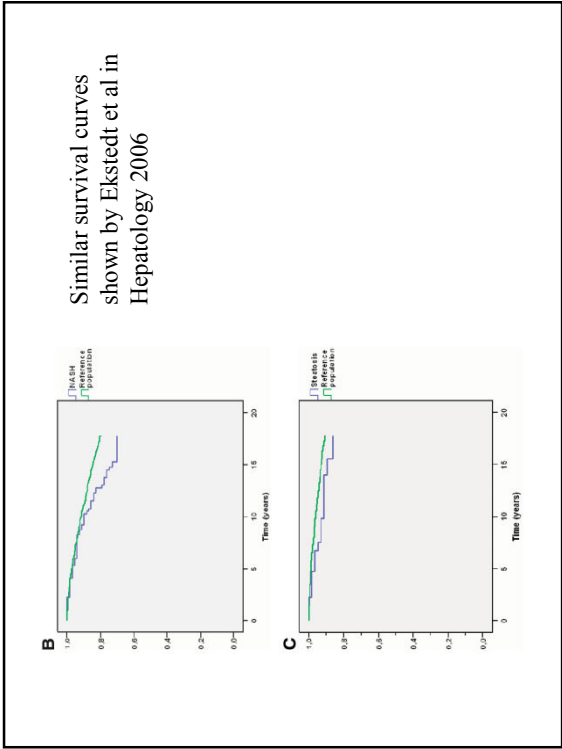
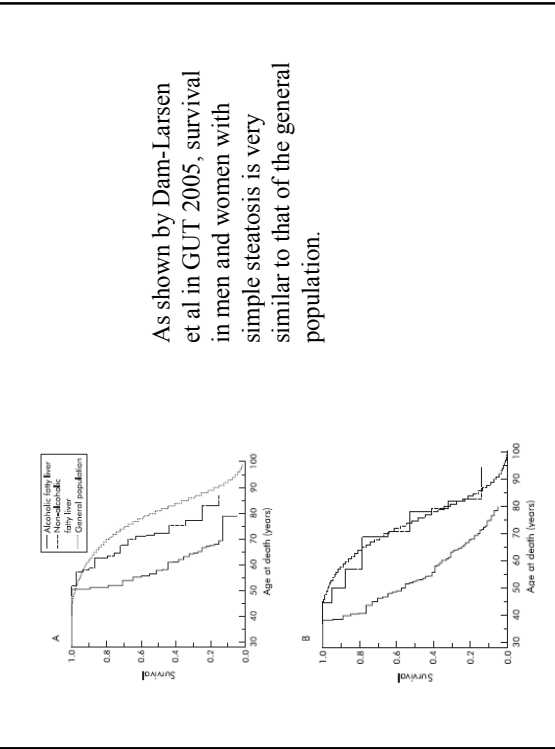
7.5 million of these may have NASH

**The scope of the problem**

75 million adults in the U.S. with NAFLD

7.5 million of these may have NASH

1.5 million of these may progress to cirrhosis



**Treatment**

Those patients identified with NASH are the ones that treatment should be focused on.

Our current understanding:

- Insulin resistance
- Oxidative stress

We know that diet/exercise help.

All treatment trials have focused on attacking these 2 entities.

## Metformin

5 studies with a total of 160 patients  
 Biopsies done uniformly in the smallest study only (10 patients) and no improvement was shown  
 Longest duration → 12 months  
 Largest study (110 patients) only had biopsy data in 17 of 55 patients receiving metformin.

## Thiazolidinediones

5 studies with a total of 64 patients  
 Histologic and biochemical improvement was seen but returned to baseline levels after treatment was stopped.  
 No placebo groups  
 Longest duration was 12 months  
 2 patients were withdrawn because of hepatotoxicity.

## Vitamin E

6 trials with a total of 142 patients  
 ALT improved in some, not in others  
 In available biopsy specimens, no histologic improvement was seen  
 Recent evidence suggests that vitamin E is not harmless after all

## Ursodeoxycholic Acid

4 trials with a total of 238 patients  
 The largest trial (166 patients in a placebo-controlled RCT) showed no benefit

### Betaine

1 study with 10 patients  
Some promising results, but only 10 patients were evaluated.

### Probuco

Withdrawn from the market because of pro-arrhythmic potential

### Pentoxifylline

2 studies with a total of 38 patients  
ALT improved but no biopsy data were available

### Losartan

1 study with 7 patients  
ALT improved, but histology did not

### HMG-CoA Reductase Inhibitors

3 studies with a total of 60 patients  
Improvement in ALT was seen but biopsy data was only available in 5 patients  
Concerns remain for statins in liver disease

### Fenofibrates

2 studies with a total of 62 patients  
Improvement seen in one of the studies but the duration was only 1 month

### Conclusion

A grand total of 828 patients have been studied with 13 different medications  
There are some promising results but:  
Studies are almost all pilot studies  
Small sample sizes which also hurts assessment of adverse reactions  
Scant biopsy data

### Conclusion

NAFLD is now considered to be the most common liver “disease” in the western world  
Given this are we going to begin treating this massive number of patients based on the available data?

No, this would be irresponsible and certainly lead to many adverse reactions.

A common theme in these trials in which improvement was seen was that the improvement disappeared with cessation of medication.

## Conclusion

Larger randomized, double-blind, placebo-controlled trials are underway studying:

Pioglitazone  
Metformin  
Vitamin E  
Betaine  
Silymarin

We owe it to our patients to wait for these results to guide any therapy.

## Conclusion