

## Extrahepatic manifestation of HCV infection: Does HCV cause fatigue?

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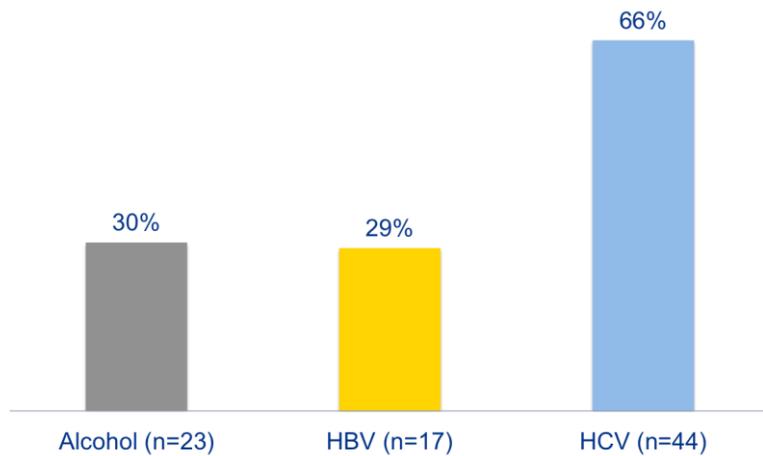
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### My disclosures

- Research grants: Merck, Gilead, abbvie, and Medivir
- Advisory board: Merck, Gilead, and abbvie

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## Excessive fatigue in liver disease



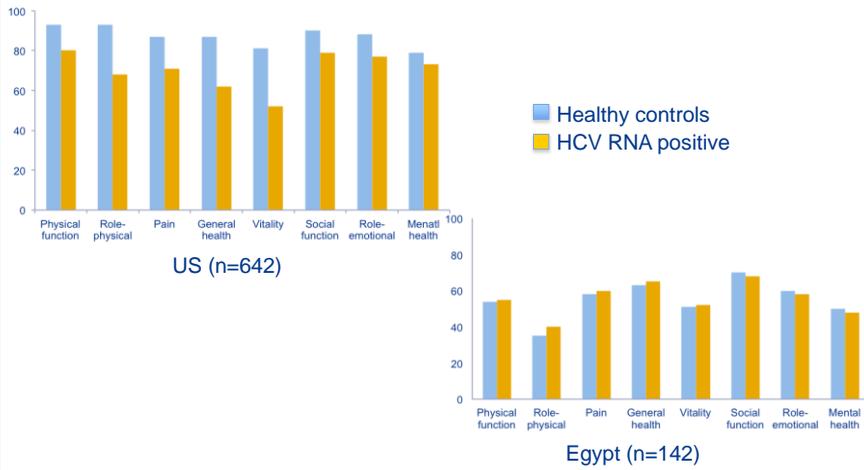
Barkhuizen. Am J Gastroenterol 1999

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## Suggested mechanisms for increased fatigue in HCV patients

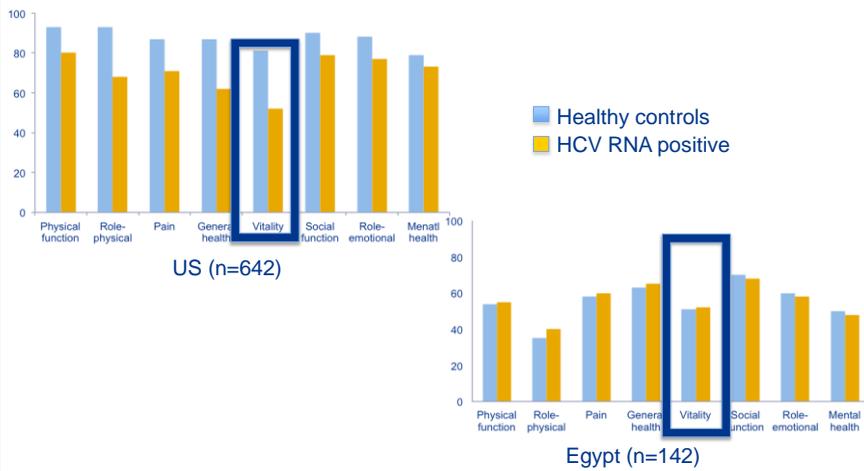
- Biological effect
  - Inflammation
    - Systemic
    - Cerebral
  - Liver function
- Psychological effect
- Confounding effect
  - Comorbidities

### Confounding effect?



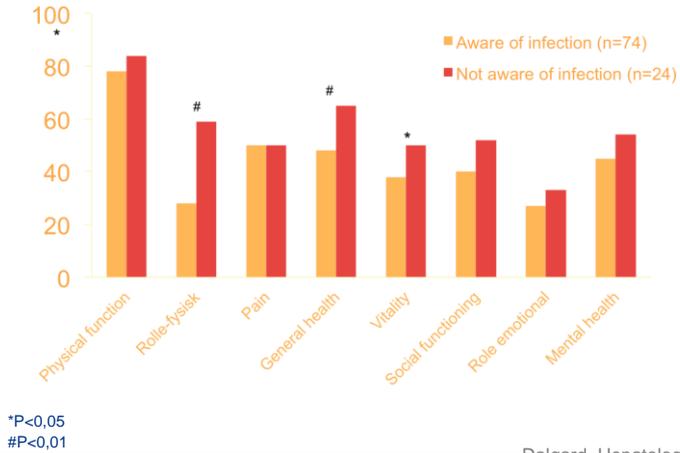
<sup>1</sup>Bonkovsky. Hepatology 1999 and Schwarzinger. Hepatology 2004.

### Confounding effect?



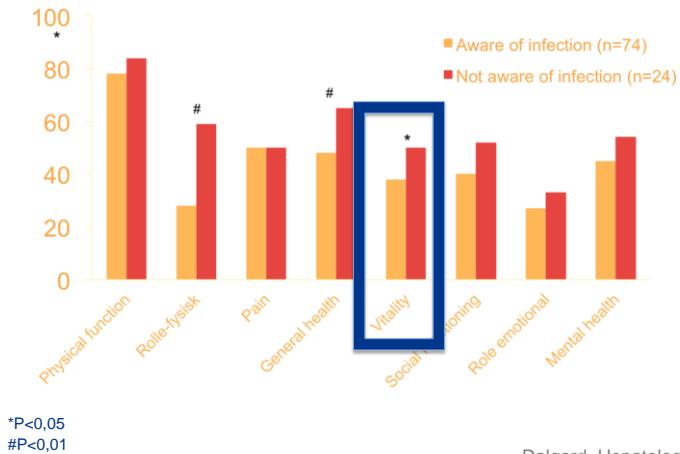
<sup>1</sup>Bonkovsky. Hepatology 1999 and Schwarzinger. Hepatology 2004.

### Psychological effect?



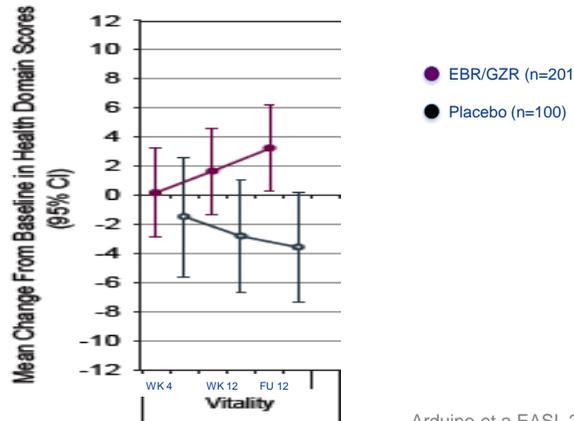
Dalgard. Hepatology 2004

### Psychological effect?



Dalgard. Hepatology 2004

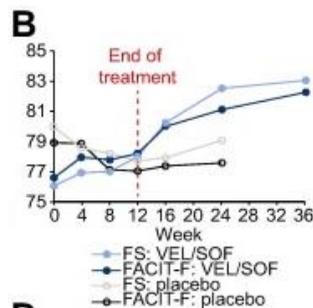
## Treatment of HCV infection (EBR/GZR) reduces fatigue in patients on OST.



Arduino et al EASL 2016

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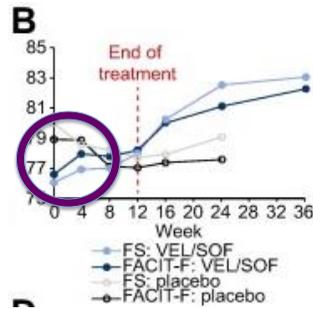
## Treatment of HCV infection (SOF/VEL) reduces fatigue.



Younossi ZM J Hepatol 2016

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## Treatment of HCV infection (SOF/VEL) reduces fatigue.

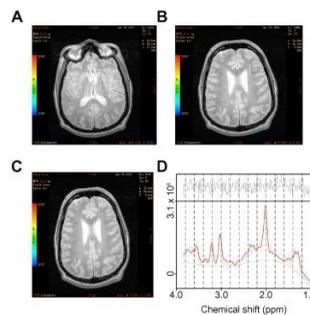


Younossi ZM J Hepatol 2016

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## Cerebral abnormalities?

- Postmortem detection of HCV sequences in brain tissue
- Proton MR spectroscopy
  - Metabolic abnormalities, which are also seen in HIV but not in HBV infection.
    - Suggest cerebral inflammation.
    - Correlate with cognitive changes
    - Association with fatigue not studied



Forton. Hepatology 2000; Forton. Lancet 2001 and Byrnes J Hepatol 2012

## Defining clinically minimal important difference (MCID)

- Consensus: “A change in SF 36 vitality score of 4.2 may be used as MCID”.
- SOF/VEL
  - Change from baseline to FW 24: +6
- EBR/GZR
  - Change from baseline to FW 12: +3.2

Spiegel Hepatology 2005

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## Conclusion

- HCV infection is associated with fatigue.
- There is no significant change in fatigue during successful HCV treatment but six months after there is a significant reduction in fatigue
  - The change may be clinically important
- There is evidence both for psychological and biological mechanism behind the improvement
- This finding support the notion that all patients with HCV infection should receive HCV treatment

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