

15th Residential Course on Clinical Pharmacology of Antiretrovirals

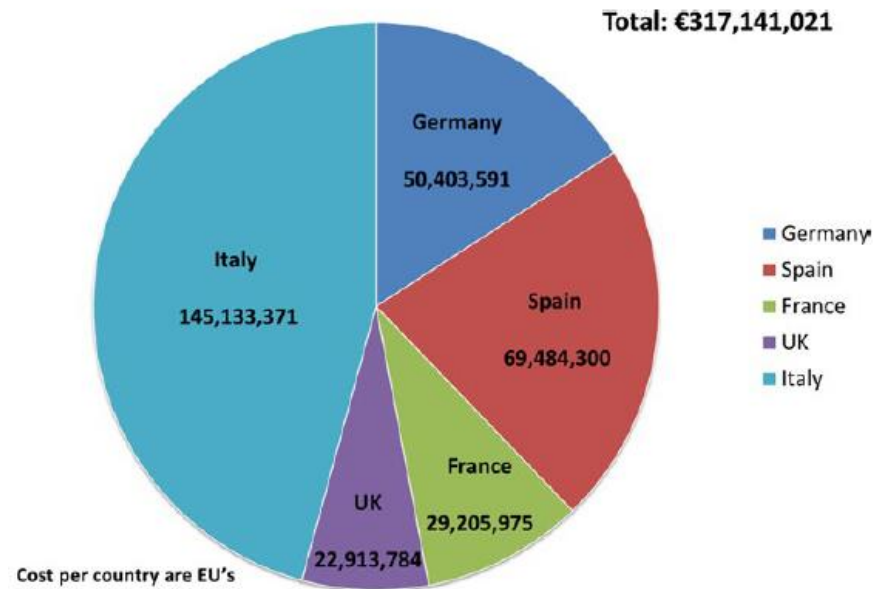
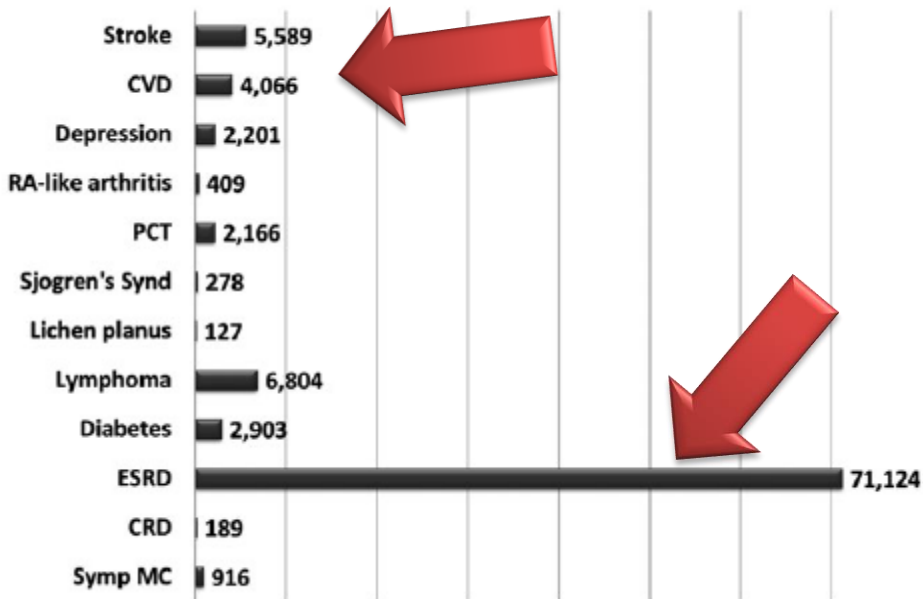
January 15-17, 2020

**Case-based discussion
on extra-hepatic manifestations beyond the cure**

Lucio Boglione

Impact of EM on the costs of care

Annual Per Person Cost of Extrahepatic Manifestations*

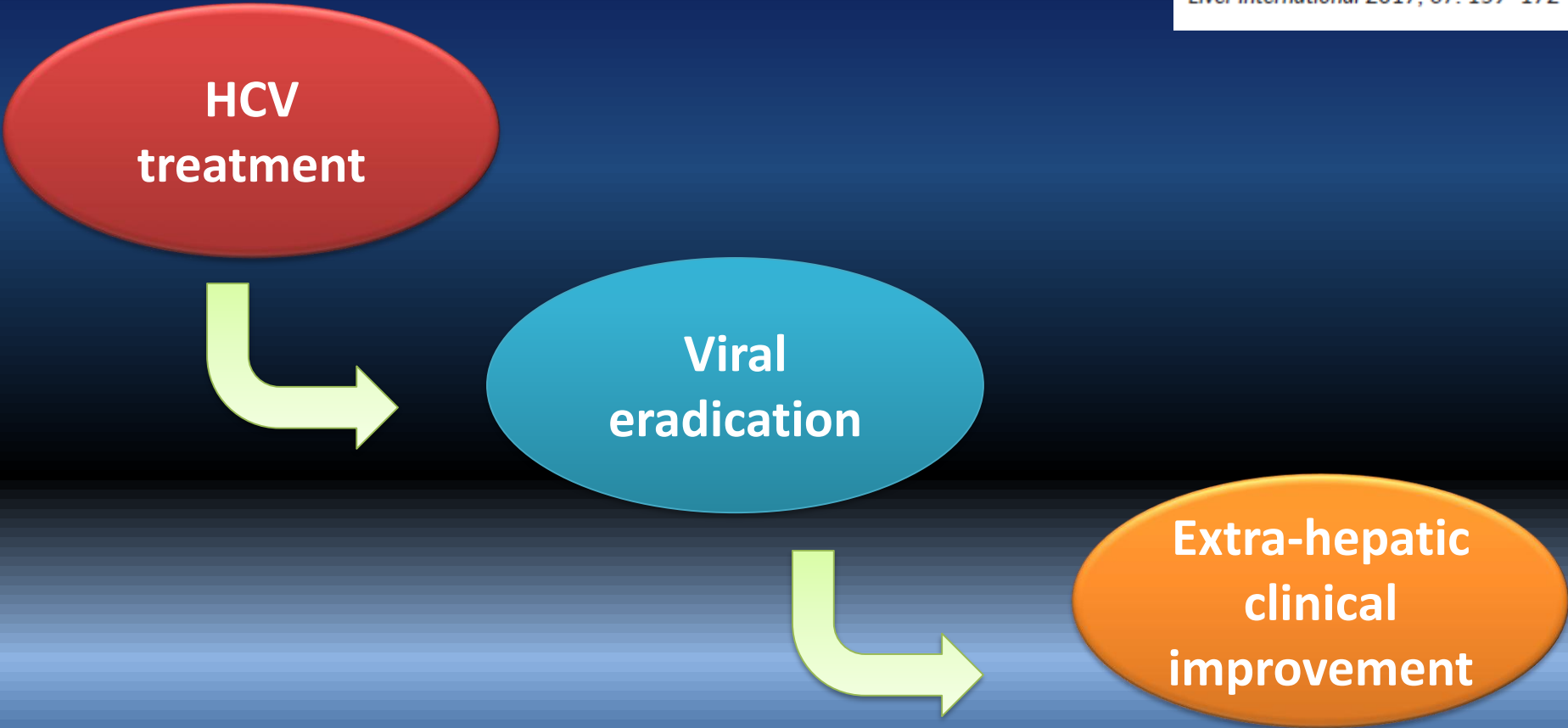


*Total annual direct costs of EHM estimated at \$1.505 bn

TABLE 1 Risk of selected EHMs in HCV infected patients compared to those without HCV³

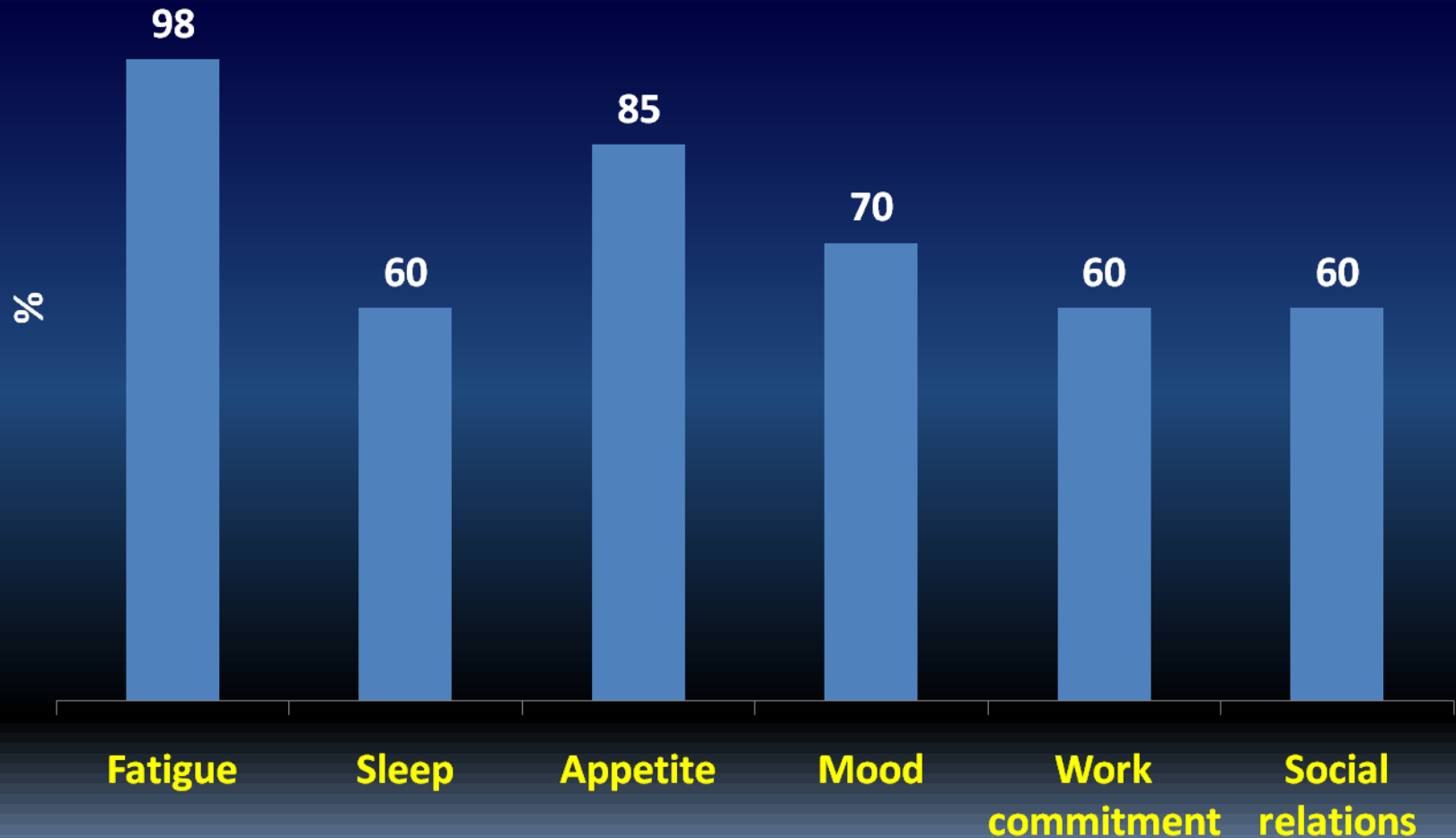
EHM	Pooled prevalence in HCV patients (95% CI)	Pooled prevalence in non-HCV populations (95% CI)	Risk of condition in HCV patients compared to non-HCV patients (95% CI)
Mixed cryoglobulinemia	30.1% (21.4%-38.9%)	1.9% (0.4%-3.4%)	OR: 11.50 (4.56-29.00) ←
Depression	24.5% (14.1%-34.9%)	17.2% (13.4%-21.0%)	OR: 2.30 (1.31-4.01) ←
Type 2 diabetes mellitus	15% (13%-18%)	10% (6%-15%)	OR: 1.58 (1.30-1.86) ←

Liver International 2017; 37: 159-172



Main subjective improvements after SVR

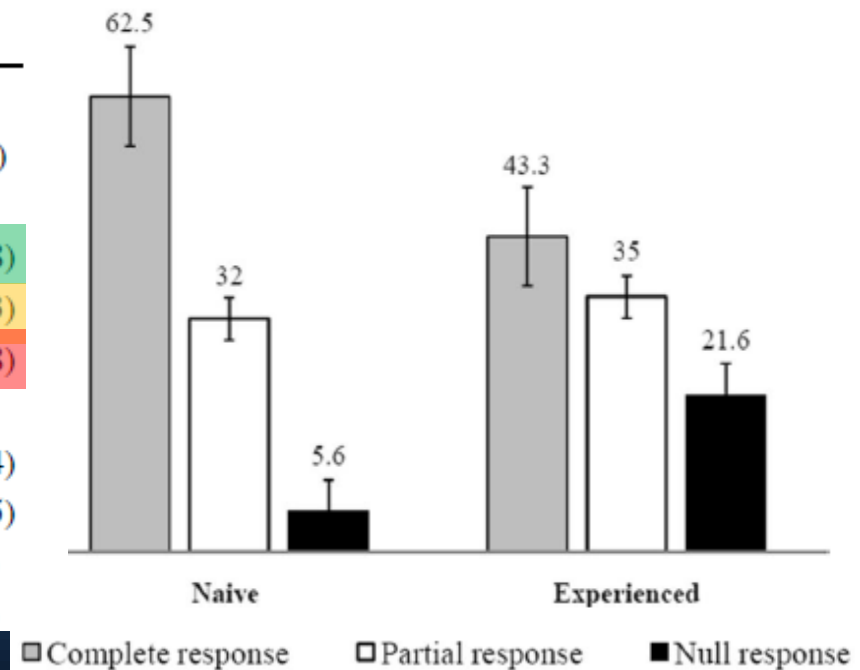
Overall improvement in quality of life



Data from treated patients Amedeo di Savoia 2015-2018

Treatment with DAA in HCV and MC+

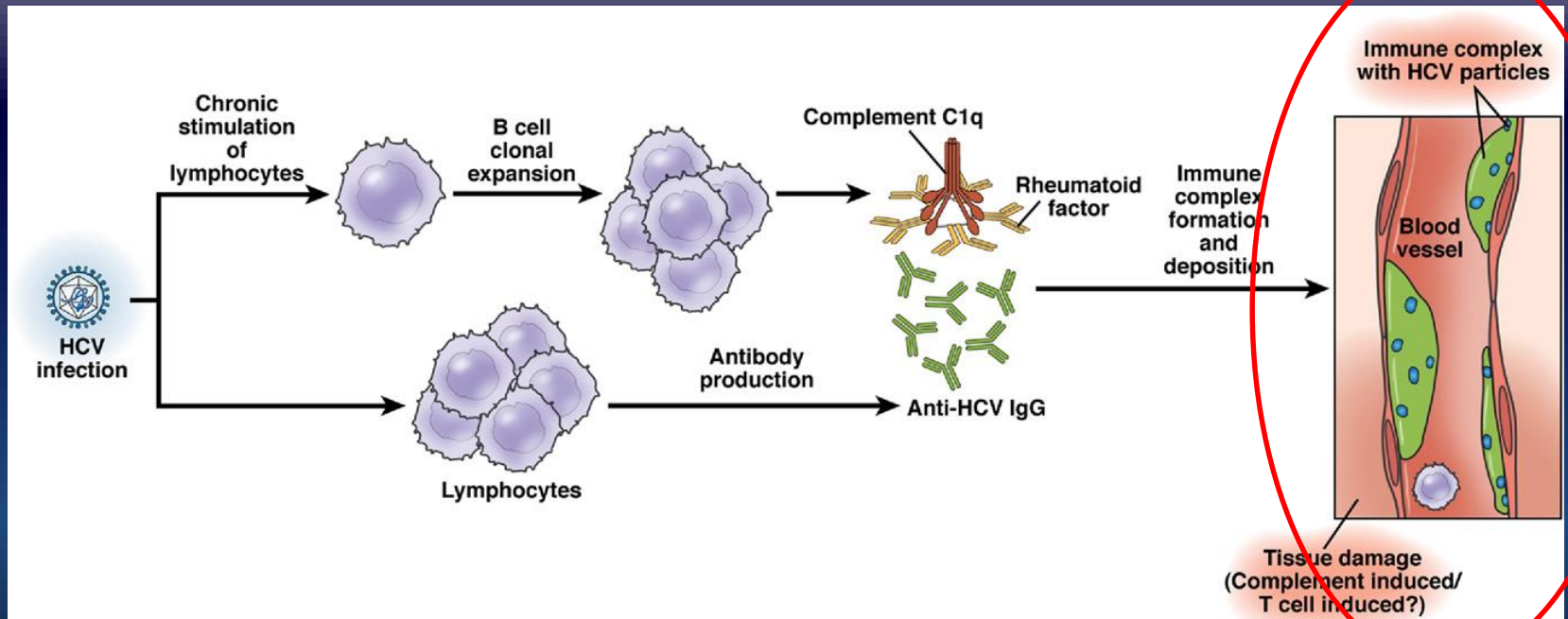
	<i>N, %</i>
Virological response	
SVR12	132 (100)
Immunological response	
Complete response	71 (53.8)
Partial response	44 (33.3)
Null response	17 (12.8)
Clinical response	
Persistence of symptoms	15 (11.4)
Improvement of symptoms	31 (23.5)
Worsening of symptoms	1 (0.8)
Resolution of symptoms	10 (7.6)



Clinical response (symptoms improvement or resolution) 31%

Multivariate analysis

Years of HCV infection < 20	2.448 (1.335–6.202) $p = 0.019$
Treatment naive	2.885 (1.404–9.660) $p = 0.025$



Persistence of cellular clone

Irreversibility of tissue damage

Improvement of glicemic control in DM-II HCV+

The impact of a successful treatment of hepatitis C virus on glyco-metabolic control in diabetic patients: a systematic review and meta-analysis

Acta Diabetologica 26 November 2018

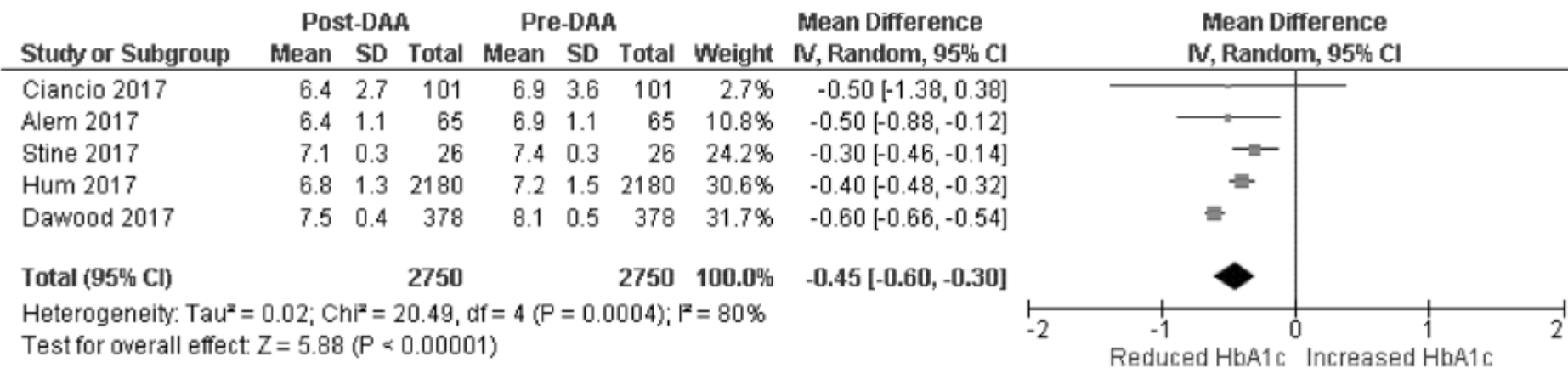
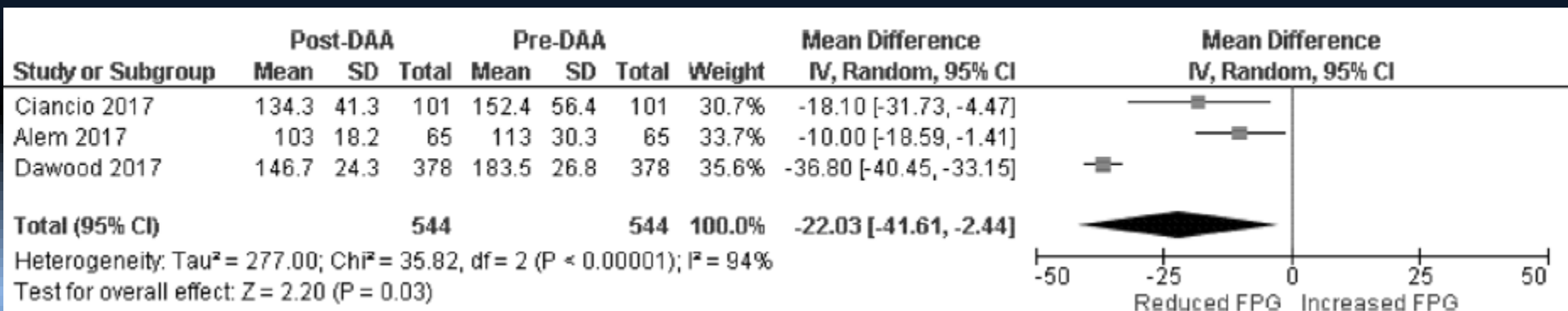
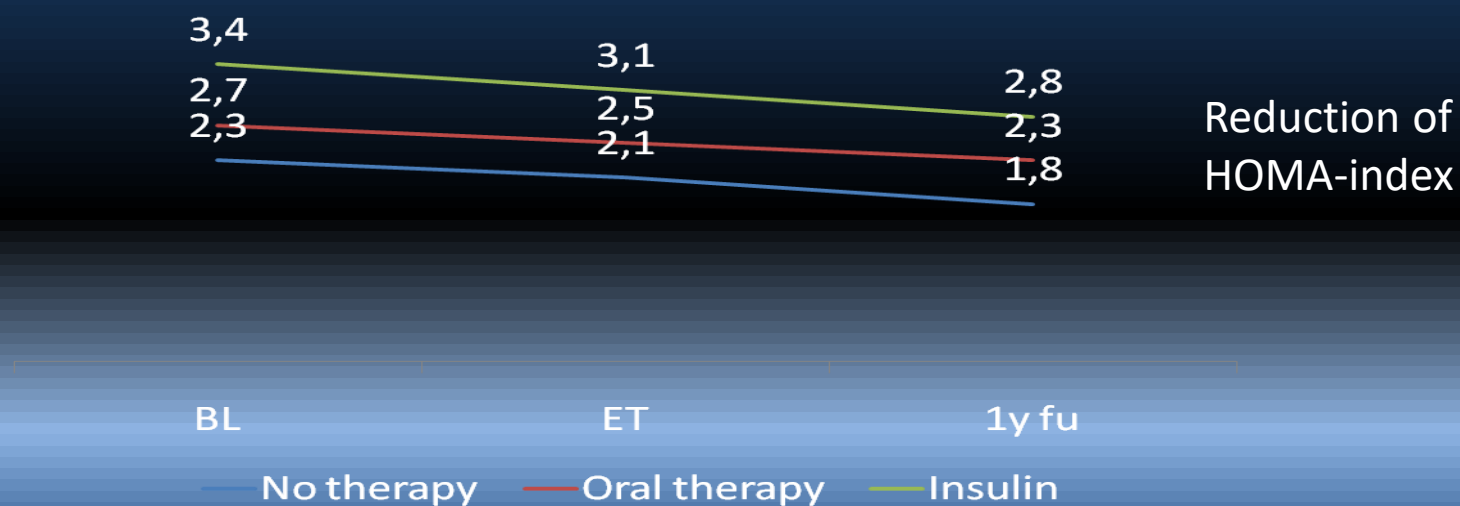
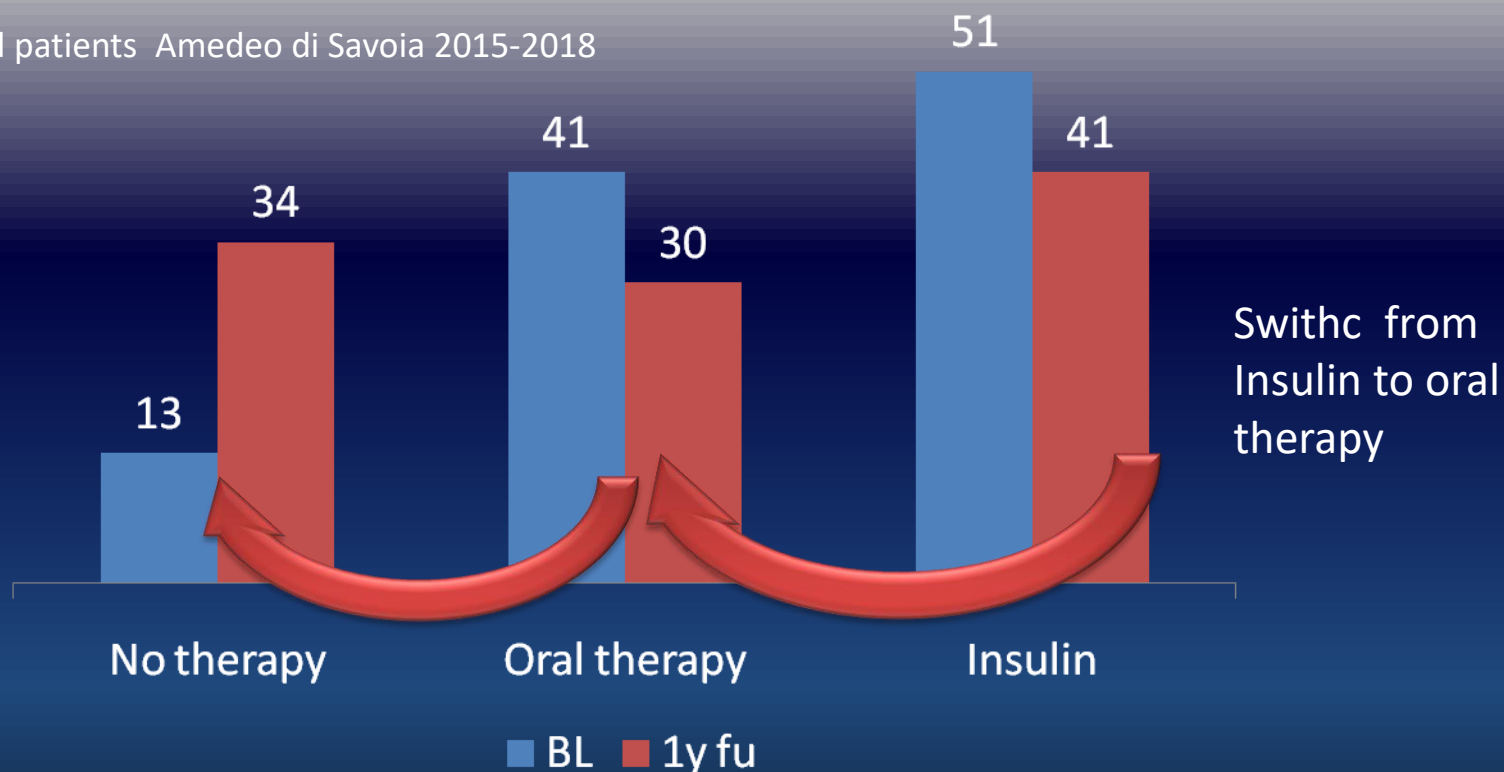


Fig. 2 Forest plot of pre- and post-SVR HbA1c values in diabetic patients

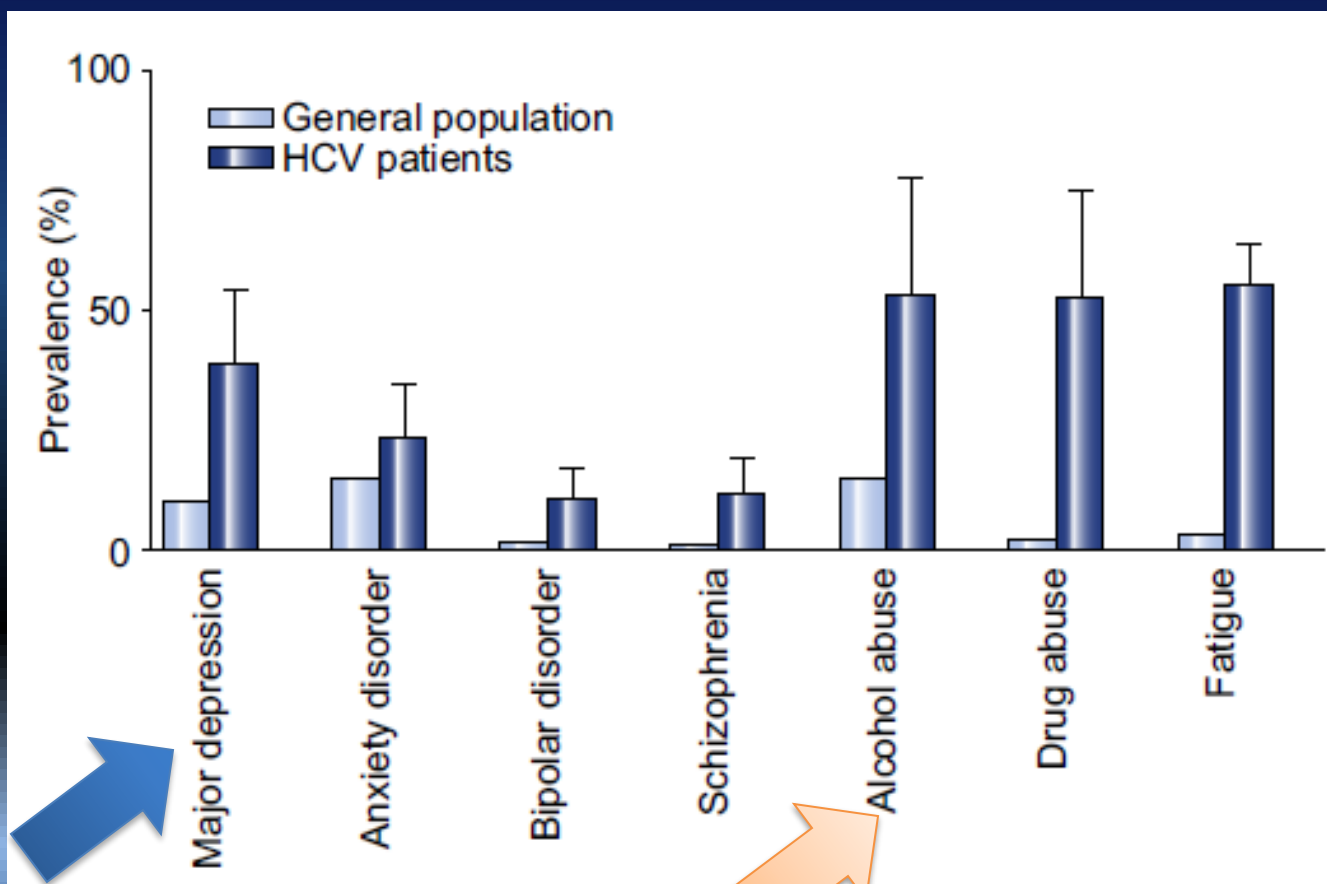


Data from treated patients Amedeo di Savoia 2015-2018



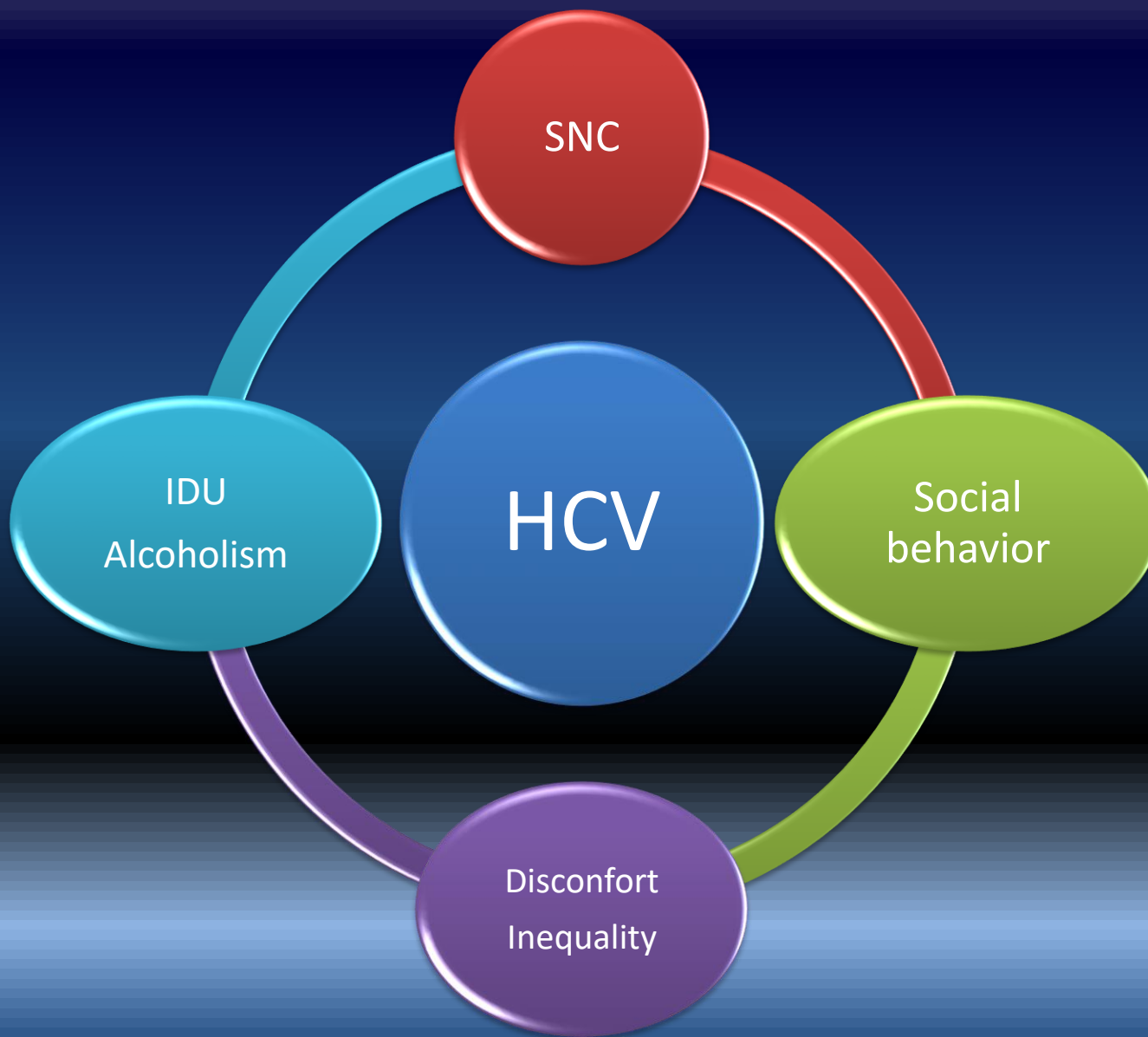
Hepatitis C infection, antiviral treatment and mental health: A European expert consensus statement

Martin Schaefer^{1,2,*}, Lucile Capuron³, Astrid Friebe⁴, Crisanto Diez-Quevedo⁵, Geert Robaey⁶, Sergio Neri⁷, Graham R. Foster⁸, Achim Kautz⁹, Daniel Forton¹⁰, Carmine M. Pariante¹¹



Hepatitis C virus and neurological damage

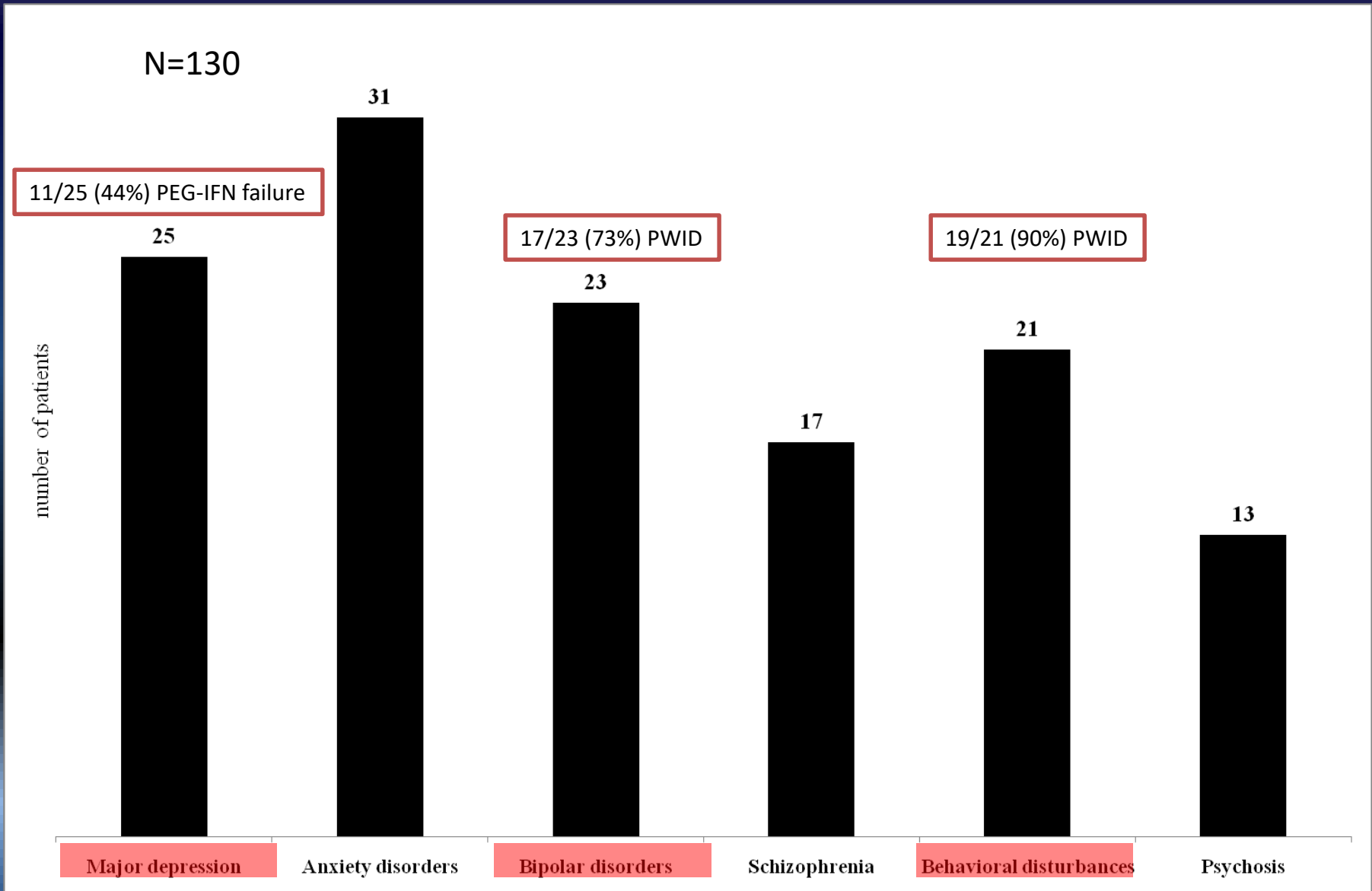
World J Hepatol 2016 April 28; 8(12): 545-556
ISSN 1948-5182 (online)



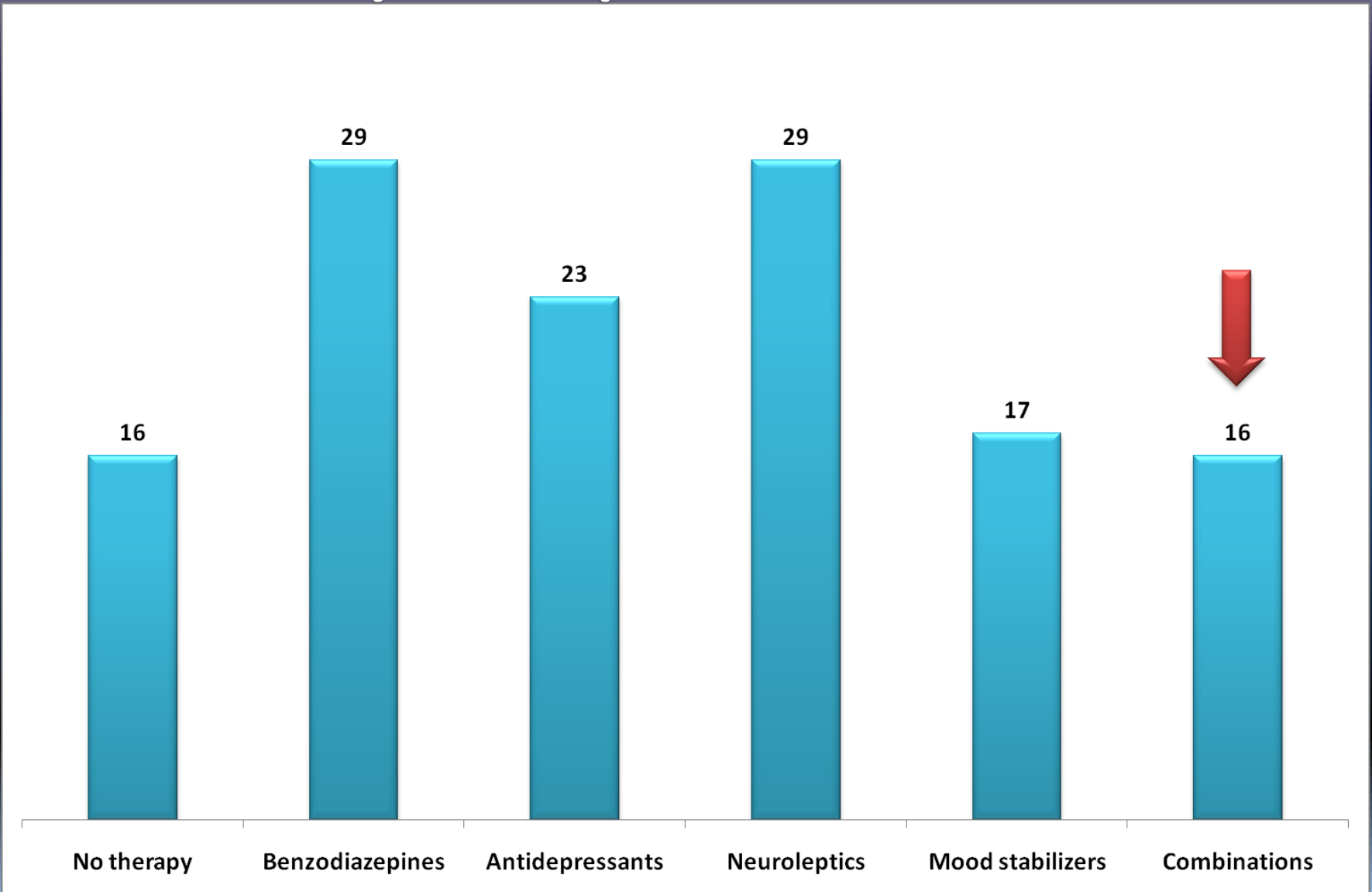


Efficacy and safety of interferon-free regimens in patients affected by chronic hepatitis C and psychiatric disorders[☆]

L. Boglione et al. / J Infect Chemother 26 (2020) 18–22



Psychotropic medications



Flunitrazepam

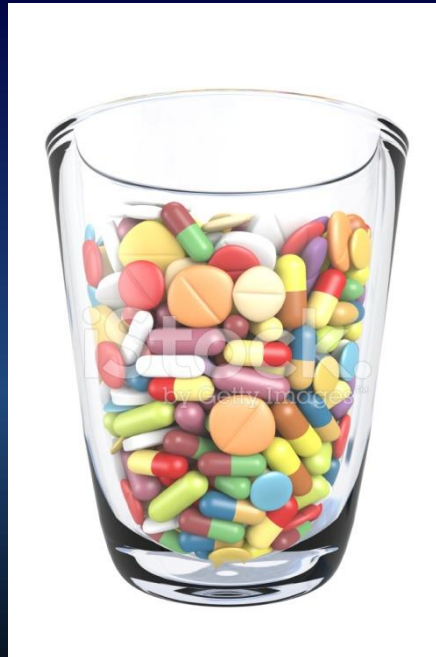
Aripiprazole

Risperidone

Mirtazapine

Escitalopram

Psychosis
Paranoid schizophrenia



Brotizolam

Quetiapine

Carbamazepine

Sertraline

Buspirone

Bipolar disorder
Maniacal psychosis

Liver Illness and Psychiatric Patients

Paul Carrier,^{1,2,*} Marilyne Debette-Gratien,^{1,2} Murielle Girard,³ Jérémie Jacques,¹ Philippe Nubukpo,⁴

Medications and drugs	Potential Toxicity	Type of Injury	In Hepatic Insufficiency
Benzodiazepines	Rare	Cytolytic or cholestatic	Induce or aggravate encephalopathy
Mood stabilizers			
Valprate	+	Steatosis, mitochondrial toxicity	Contra-indicated Careful prescription
Carbamazepine	Rare	Idiosyncratic	
Lithium	Rare	Hyperbilirubinemia	Can aggravate liver function
Anti-depressants			
Tricyclics	+	Idiosyncratic, more rarely hypersensitivity	Change of dose or interruption in the majority of treatments
SSRI	+	Generally cytolytic injury	
SNRI	+		
Bupropion	Rare	Essentially risk of steatosis (clozapine, olanzapine ++)	Generally contra- indicated in patients with decompensated cirrhosis
Neuroleptics			
Phenothiazines	++		
Butyrophenones	+		
Clozapine	+		
Olanzapine	+		
Quetiapine	Rare		
Risperidone	Rare		

Table 4D. Drug-drug interactions between HCV DAAs and central nervous system drugs.

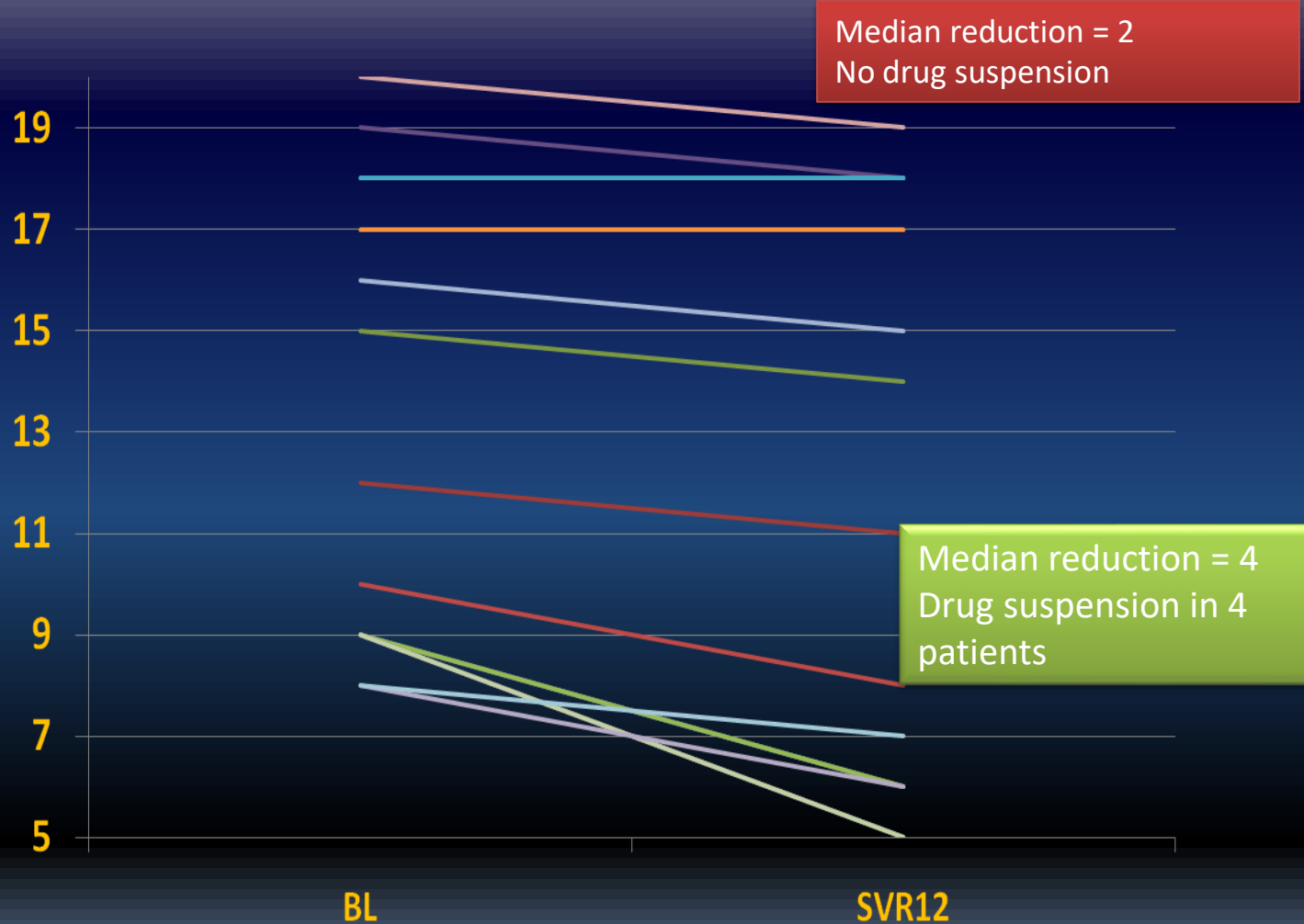
		SOF	SOF/ LDV	SOF/ VEL	OBV/ PTV/r + DSV	GZR/ EBR	SOF/ VEL/ VOX	GLE/ PIB
Anti-depressants	Amitriptyline	◆	◆	◆	■	◆	◆	◆
	Citalopram	◆	◆	◆	◆	◆	◆	◆
	Duloxetine	◆	◆	◆	◆	◆	◆	◆
	Escitalopram	◆	◆	◆	◆	◆	◆	◆
	Fluoxetine	◆	◆	◆	◆	◆	◆	◆
	Paroxetine	◆	◆	◆	◆	◆	◆	◆
	Sertraline	◆	◆	◆	■	◆	◆	◆
	Trazodone	◆	◆	◆	■	◆	◆	◆
	Venlafaxine	◆	◆	◆	■	◆	◆	◆
Anti-psychotics	Amisulpiride	◆	◆	◆	◆	◆	◆	◆
	Aripiprazole	◆	◆	◆	■	■	◆	■
	Chlorpromazine	◆	◆	◆	■	◆	◆	◆
	Clozapine	◆	◆	◆	■	◆	◆	■
	Flupentixol	◆	◆	◆	■	◆	◆	◆
	Haloperidol	◆	◆	◆	■	◆	◆	◆
	Olanzapine	◆	◆	◆	■	◆	◆	◆
	Paliperidone	◆	■	◆	◆	◆	■	■
	Quetiapine	◆	◆	◆	●	■	◆	■
	Risperidone	◆	◆	◆	■	◆	◆	◆
	Zuclopentixol	◆	◆	◆	■	◆	◆	◆

The effect of SVR on psychiatric disorders

- **Theoretically**, the HCV resolution could improve the psychiatric diseases
- This effect could be probably observed only in mild-moderate diseases such as anxiety or sleep disorders (with chance of drug suspension).
- In severe psychiatric diseases remains difficult the treatment suspension/reduction and the effect of HCV eradication is not easily demonstrable

Effect of SVR on the sleep disorders

Insomnia score
ISI index
0-7 normal
8-14 mild
15-21 moderate
>21 severe

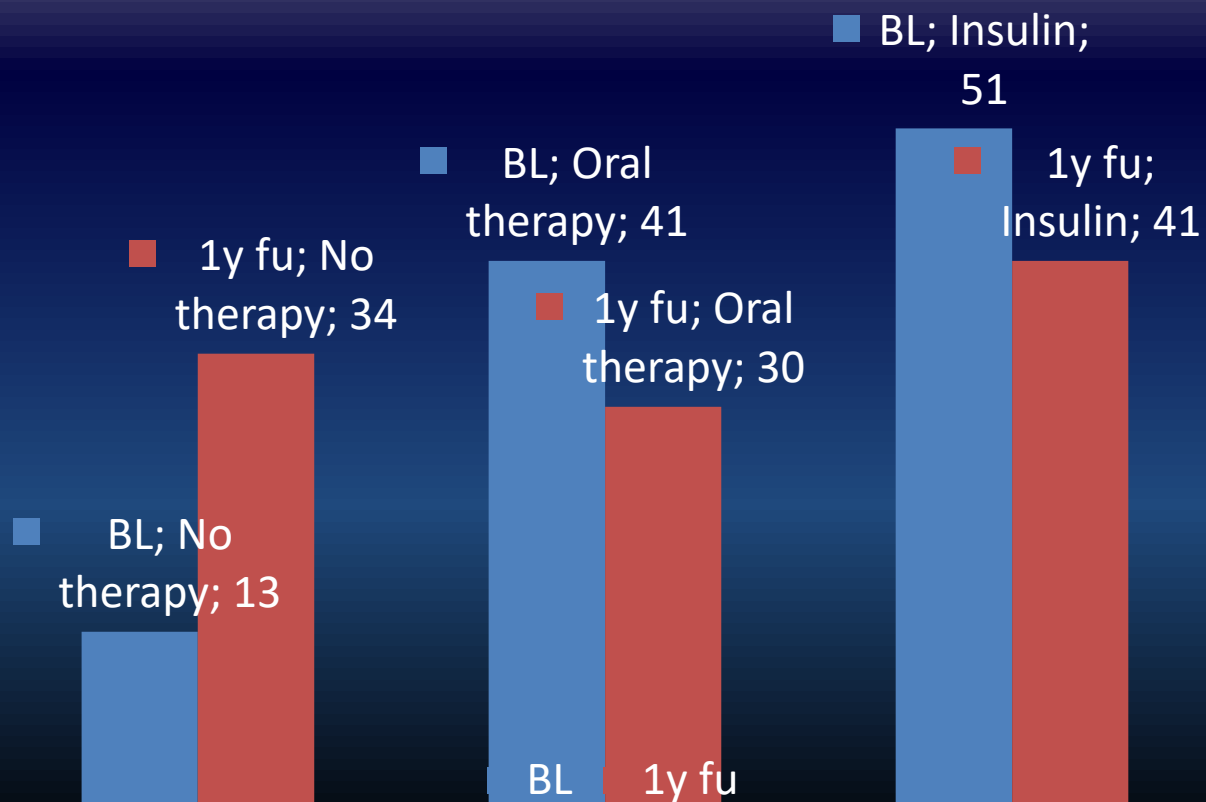


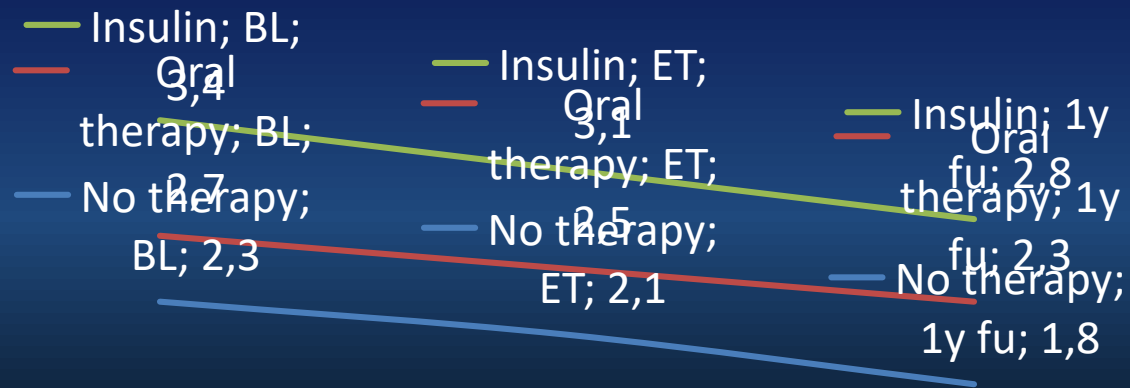
SUMMARY

- Extra-hepatic manifestations have a great impact on the quality of life and costs in HCV+
- Viral eradication generally leads to improvement of symptoms related to extra-hepatic morbidities
- Major benefit were observed in glicemic control and mixed cryoglobulinemia
- Not fully demonstrable this effect on more severe psychiatric disorders

Thanks for your Time

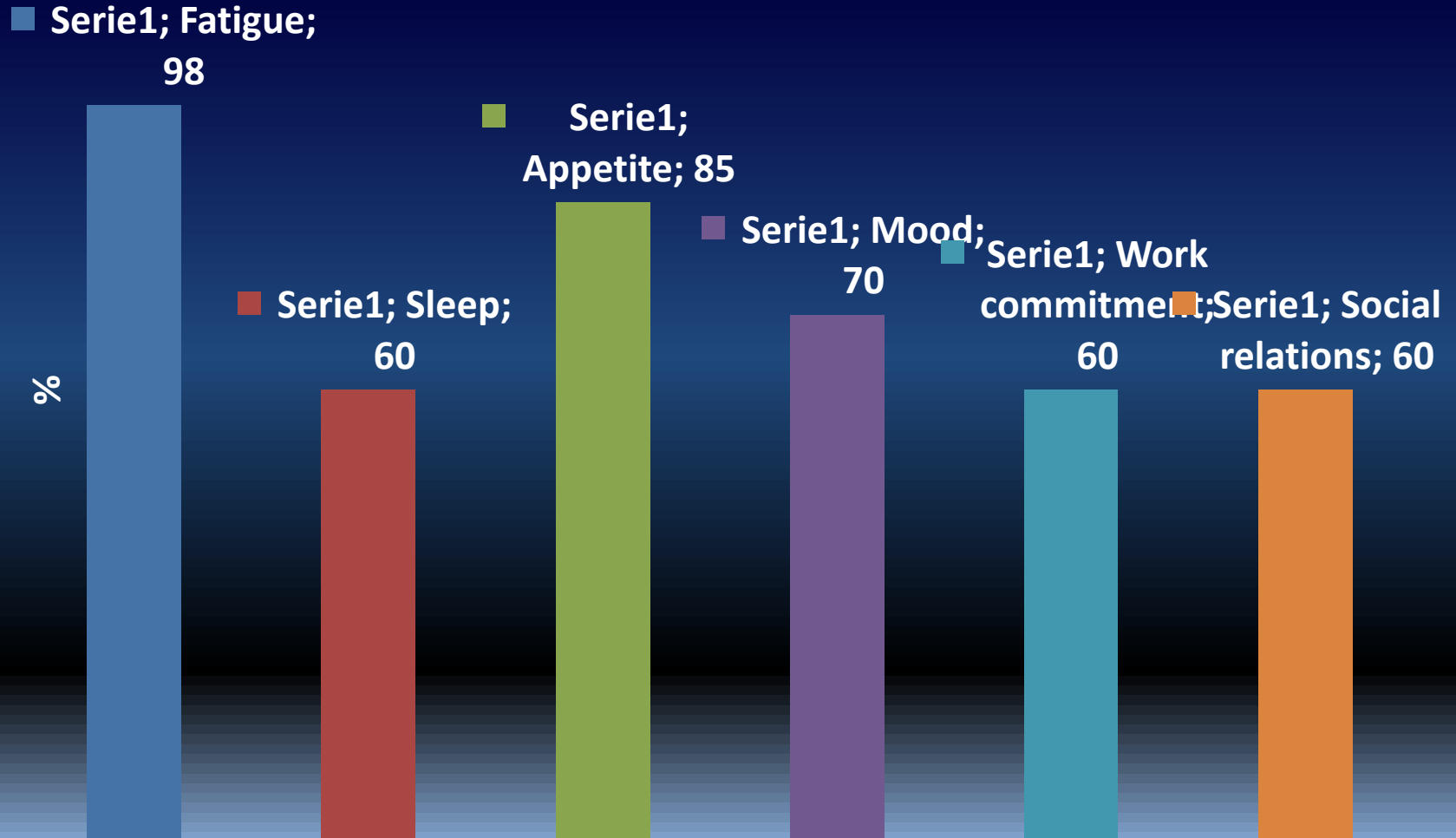






— No therapy — Oral therapy — Insulin

Main subjective improvements after SVR No!!



Boglione et al. 2018 personal data