



Quality of life in patients with chronic hepatitis C

Prof. Adriana Vince, MD, PhD

Croatian Reference Center for Viral Hepatitis

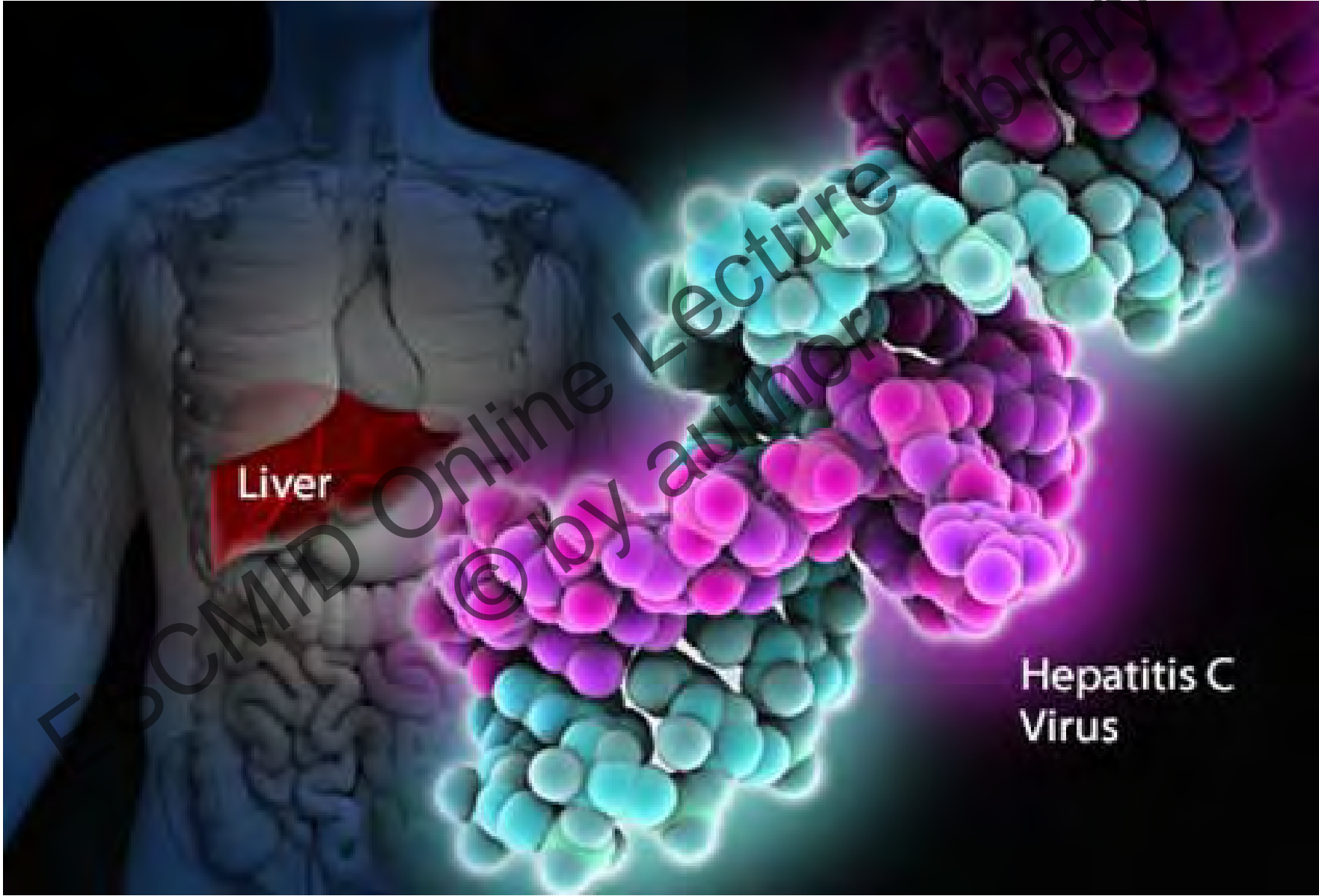
University of Zagreb School of Medicine, Zagreb, Croatia



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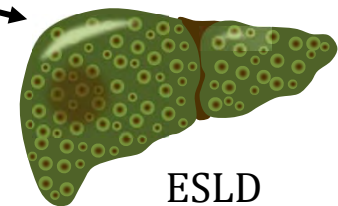
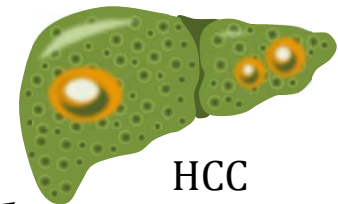
Different aspects to be considered

- Quality of life in patients with chronic hepatitis before treatment regarding different stages of fibrosis
- Quality of life-on and after treatment (Interferon/versus DAAs)
- Quality of life –as important outcome measure in evaluation of novel therapies

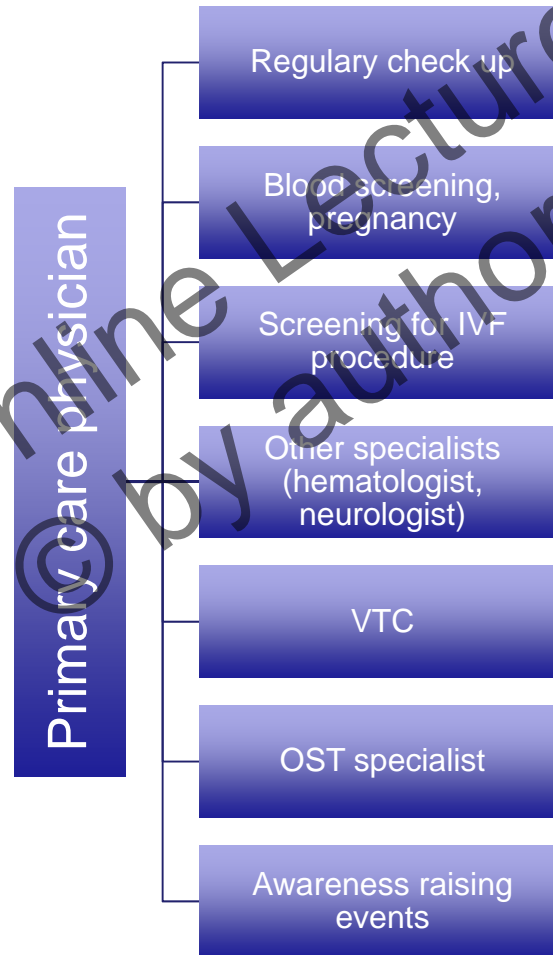
Natural History of Chronic Hepatitis C

No symptoms in 90% of patients

Not all patients have progressive disease



Referral for Specialist Care



You have a hepatitis C....



HCV-HRQOL

- Chronic hepatitis C is a chronic liver disease associated with significant deterioration of patients' HRQOL

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HRQOL

- HRQoL encompasses aspects of overall quality of life that affect health
- WHO definition of health
- “a state of complete physical, mental and social well-being and not merely absence of disease or infirmity”

HRQOL

- No standard definition for HRQoL
- **HRQoL** is a multidimensional concept which includes measures of self-estimations of physical and mental health and social life
- It focuses on the patient's subjective evaluation of well-being, individual experiences and values regarding the process of being sick-PRO

Sources:

1. Mhatre SK, Sangiry SS. Development of a conceptual model of health-related quality of life among hepatitis C patients: A systematic review of qualitative studies. *Hepatol Res* 2016;46(1):29-39.
2. Souza NP, Villar LM, Garbin AJ, Rovida TA, Garbin CA. Assessment of health-related quality of life and related factors in patients with chronic liver disease. *Braz J Infect Dis* 2015;19(6):590-5.
3. Orr JG, Homer T, Ternent L, et al. Health related quality of life in people with advanced chronic liver disease. *J Hepatol* 2014;61(5):1158-65.
4. Armstrong AR, Herrmann SE, Chassany O, et al. The International development of PROQOL-HCV: An instrument to assess the health-related quality of life of patients treated for Hepatitis C virus. *BMC Infect Dis* 2016;16(1):443.
5. Grotzinger KM, Younossi ZM, Giannini EG, et al. Health-related quality of life in thrombocytopenic patients with chronic hepatitis C with or without cirrhosis in the ENABLE-1 and ENABLE-2 studies. *Health Qual Life Outcomes* 2016;14:49.
6. Mehta G, Dusheiko G. Hepatitis C treatment and quality of life - You can't always get what you want, but you might get what you need. *J Hepatol* 2015;63(2):300-2.
7. Silva LD, Cunha CC, Cunha LR, et al. Depression rather than liver impairment reduces quality of life in patients with hepatitis C. *Rev Bras Psiquiatr.* 2015;37(1):21-30.
8. Sawamoto R, Nagano J, Kajiwara E, et al. Inhibition of emotional needs and emotional wellbeing predict disease progression of chronic hepatitis C patients: an 8-year prospective study. *Biopsychosoc Med* 2016;10:24.
9. Doyle JS, Grebely J, Spelman T, et al. Quality of Life and Social Functioning during Treatment of Recent Hepatitis C Infection: A Multi-Centre Prospective Cohort. *PLoS One* 2016;11(6):e0150655.



Assessment of HRQOL

- Commonly used tools:
- **Generic**
 - Work Productivity and Activity Index: specific Health problem (WPAI:SHP)
 - Short Form 36
 - Sickness impact profile (SIP)
- **Disease specific**
 - Chronic Liver Disease Questionnaire (CLDC-HCV)
 - -Liver disease quality of life (LDQOL)

HRQoL tools limitations

- Difficult to conduct rigorously
- Risk of bias
- Absence of placebo controls
- Influence of comorbidities
- Concomitant psychoactive drugs or alcohol abuse

The most common symptoms before receiving the diagnosis

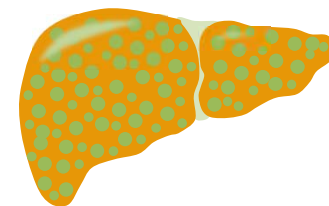
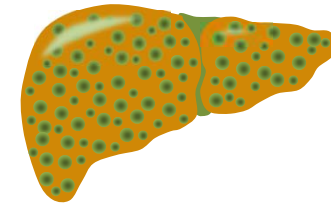
- Fatigue
- Depression
- Anxiety
- Cognitive impairment
- Muscle and joint symptoms

The impact on HRQOL after receiving the diagnosis of HCV,

- Physical health
 - Fatigue↑
 - Depression↑
 - Anxiety↑
 - Cognitive impairment
 - Muscle and joint symptoms
- Impairment of mental health and emotional status
- Impairment of social life and familiar relationships

Symptoms

- Patient with liver cirrhosis
 - Greater HRQoL impairment due to physical functioning
- Patients with chronic hepatitis
 - Equal impairment in emotional well being and mental status



HRQoL-Stage of fibrosis

- Advanced fibrosis is independently associated with the degree of HRQoL impairment and loss of work activity
- Improvement of HRQoL and work productivity after viral clearance was not associated with the stage of fibrosis

Mehta G, Dusheiko G. Hepatitis C treatment and quality of life - You can't always get what you want, but you might get what you need. J Hepatol 2015;63(2):300-2



HRQOL in people with advanced chronic liver disease

- Studies of HRQOL in liver disease usually combine a generic measure (SF-36 or SIP) with a disease-specific measure (LDQOL or CLDQ)
- HRQOL is more significantly impaired in pts with cirrhosis than in healthy controls and in patients with non-cirrhotic CLD. Impairment increases with increasing severity of cirrhosis (MELD score or CPT)
- Clinical factors which contribute to impaired HRQOL include ascites, encephalopathy and hyponatremia
- Targeting specific symptoms is likely to influence the overall HRQOL improvement

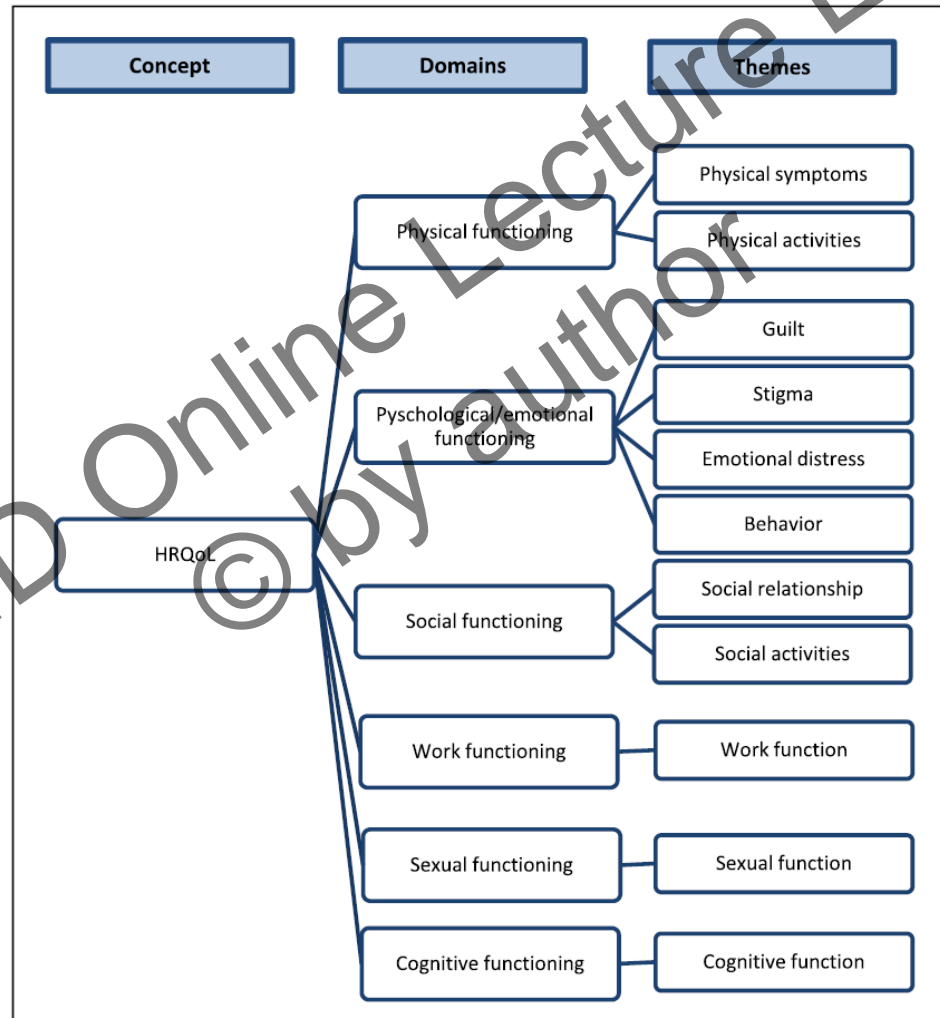
Meta-synthesis of qualitative studies

- Systematic review of 10 articles to explore the the constituent subcomponents of HRQoL in HCV patients using a qualitative study design
- Summarizes the evidence on HRQoL themes that are unique to HCV patients

Study; location; study date; QARI score	Study aimss	Data collection: sampling method; sample size (n)	Sociodemographics	Themes
NR;Kinder M, 2009; California, USA; NR; QARI = 8	Explore and describe male patients' experiences of undergoing and completing treatment for HCV	Individual interviews; purposive sampling from support group center; n=8	Aged 18–60 years, 100% males	Physical symptoms, physical activities, emotional distress, psychological behavior, social activities, social function
Blacklaws S, 2009; Australia; 2006; QARI = 8	Explore the consequences of HCV treatment on family life	One focus group; convenient sampling using letters; n=10	100% males	Physical activities, guilt, stigma, emotional distress, psychological behavior, social relationship, work function
Sgorbini M et al., 2009; New South Wales, Australia; NR; QARI = 8	Explore the issues surrounding chronic hepatitis C, combination therapy and its impact on personal relationships	Individual interviews; recruited through liver clinics and advertisement using purposive sampling; n=5	Aged 32–54 years, 100% females living with partners	Physical symptoms, physical activities, stigma, emotional distress, psychological behavior, social relationship, social activities, social function
Dudley T et al., 2007; UK; NR; QARI = 9	Identify factors that could impact quality of life after liver transplantation for HCV infection	Individual interviews; recruited at outpatient clinics using purposive sampling; n=8	Aged 44–56 years, 25% males 75% females, Caucasians, undergone liver transplantation ≤1year	Physical activities, guilt, stigma, emotional distress, psychological behavior
Sheppard et al., 2006; Nevada, USA; NR; QARI = 10	Explore the patient's experience of undergoing combination treatment for HCV	Individual interviews; recruited through health-care provider office and HCV support group using purposive sampling; n=4	Aged 39–52 years, 25% males 75% females	Physical symptoms, emotional distress, psychological behavior, social relationship

Study; location; study date; QARI score	Study aimss	Data collection: sampling method; sample size (n)	Sociodemographics	Themes
Lang CA, 2006; Queensland, Australia; NR; QARI = 6	Identify symptoms that were attributed to HCV infection	Twenty individual interviews and 12 focus groups with 53 patients; n=73	Mean age 39 years, 66% males 34% females, 88% with some source of income, 66% with at least 12 years of education and 75% residing in MSA	Physical symptoms, emotional distress, cognitive function
Blasiole JA et al., 2006; Iowa, USA; 1998–2003; QARI = 7	Systematically examine the impact of HCV diagnosis on patients' level of social support	Individual interviews; recruited from teaching hospital; n = 342	Mean age 45 years, 63% males, 36% females, 91% Caucasians, 34% nemployed, 62% living with partners, 64% from rural areas	Physical symptoms, emotional distress, psychological behavior, social relationship, social activities, sexual function, work function
Crockett B, 2004; Melbourne, Australia; 1999–2000; QARI = 8	Report the results of a qualitative study of young women's experiences of living with HCV with a specific focus on the meaning of HCV and its impact on their lives	Individual interviews; recruited from community health center using purposive sampling; n=25	Aged 18–43 years, 100% females, 80% Anglo Celtic Australians, 80% nemployed, 50% with some education, past or current history of injecting drug use	Physical symptoms, physical activities, stigma, emotional distress, psychological behavior, social relationship, work function
Zickmund S et al., 2003; Iowa, USA; 1998–2001; QARI = 7	Test prevalence and consequences of stigmatization on the quality of life in patients with HCV	Individual interviews; recruited from liver clinic; n = 257	Mean age 45 years, 63% males, 37% females, 29% unemployed	Stigma, psychological behavior, social relationship

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Living with a virus

- **Quality assesment themes**

- Physical symptoms
- Physical activities
- Guilt
- Stigma
- Emotional distress
- Psychological behavior
- Social relationship
- Social activities
- Work function
- Sexual function
- Cognitive funcionality



Multidimensional concept PROQOL-HCV

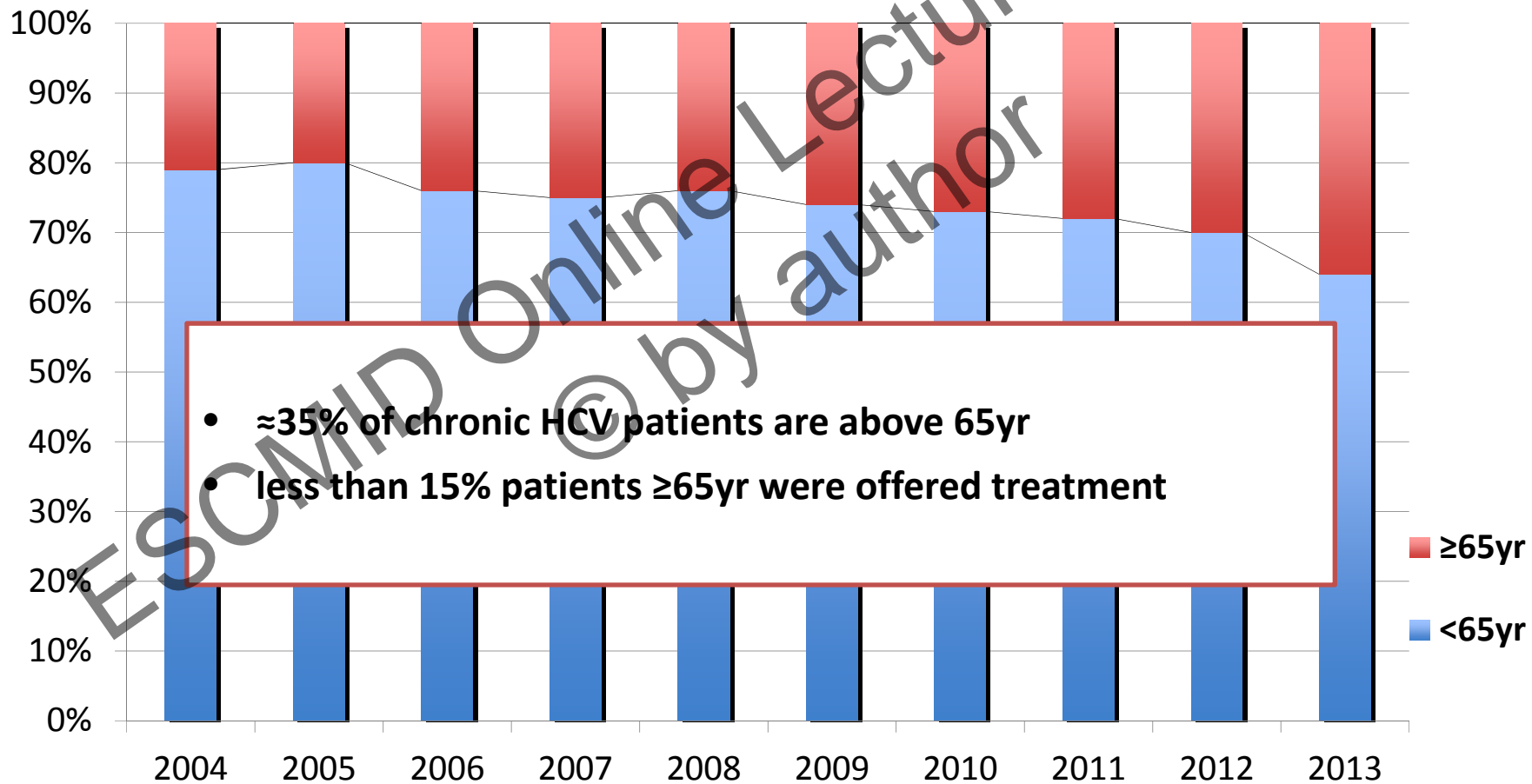
- International development in 3 languages
- Authors suggest embedding PRO in clinical care
- Includes 4 domains, Physical Health, Mental Health, Social Health and Treatment
 - Treatment adherence
 - Treatment side-effects
 - Treatment failure fear

Armstrong AR, Herrmann SE, Chassany O, et al. The International development of PROQOL-HCV: An instrument to assess the health-related quality of life of patients treated for Hepatitis C virus. BMC Infect Dis 2016;16(1):443.



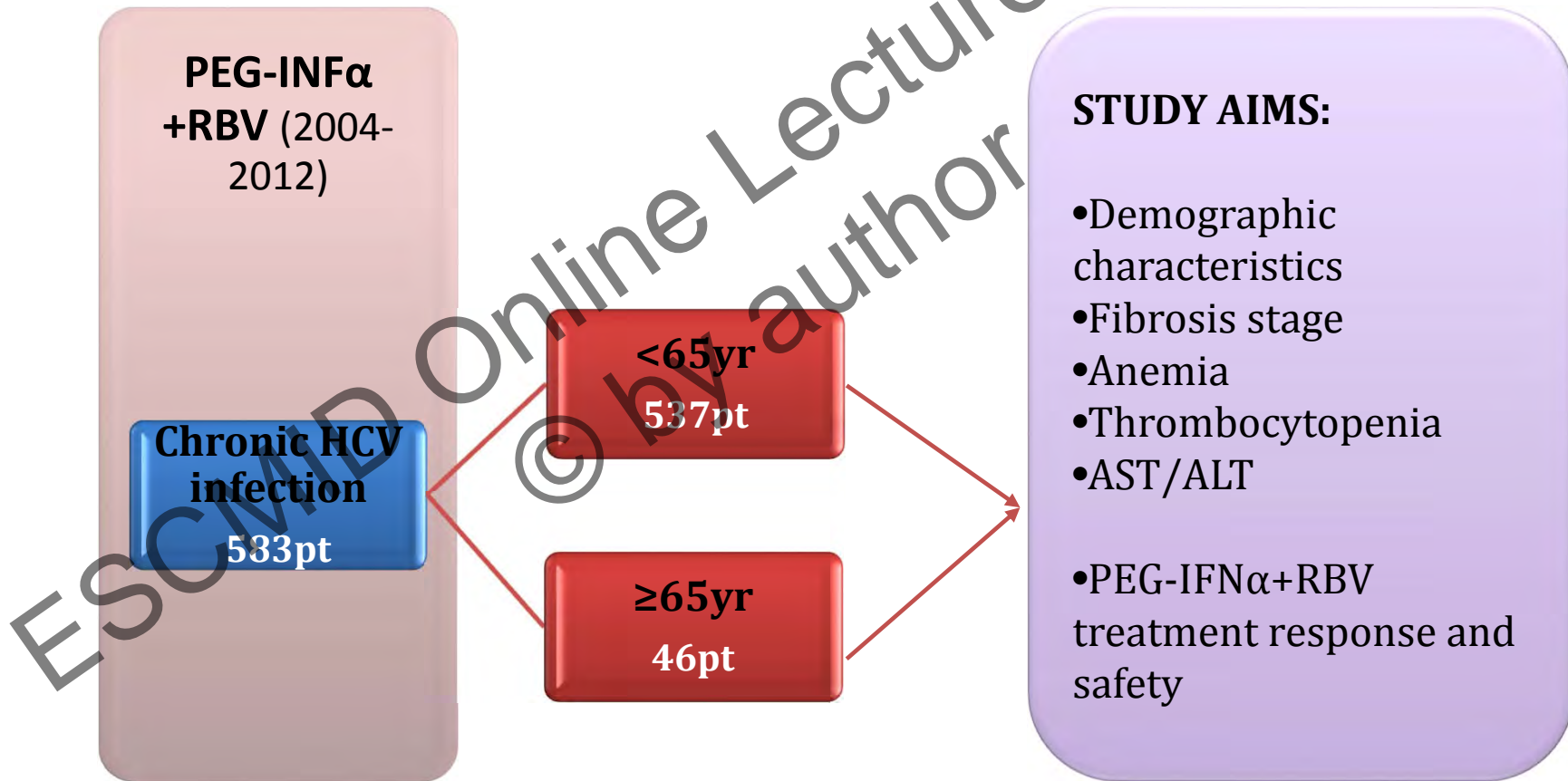
Chronic hepatitis C at UHID, Croatia

Chronic hepatitis C visits in UHID outpatient Clinic,
by age (2004-2013)



PEG-IFN α +RBV treatment response and safety

Study outline



PEG-IFN α +RBV treatment side-effects

	<65yr (n=537)	≥65yr (n=46)	P- value*
Anemia	183 (34%)	32 (69%)	<0.001
Neutropenia	64 (12%)	16 (34%)	<0.001
Thrombocytopenia	48 (9%)	21 (45%)	<0.001
Arthralgiae/mialgiae	70 (13%)	12 (26%)	0.024
Dermatological (including dermatitis, rash, pruritus)	113 (21%)	9 (19%)	1.000
Hipo/hiperthyreosis	21 (4%)	1 (3%)	1.000
Flu-like symptoms	242 (45%)	18 (39%)	0.537
Respiratory symptoms	48 (9%)	6 (12%)	0.422
Anxiety	75 (14%)	9 (19%)	0.279
Depression	16 (3%)	2 (5%)	0.645
Insomnia	27 (5%)	6 (14%)	0.037

* Fisher's exact test



PEG-IFN α +RBV treatment modifications

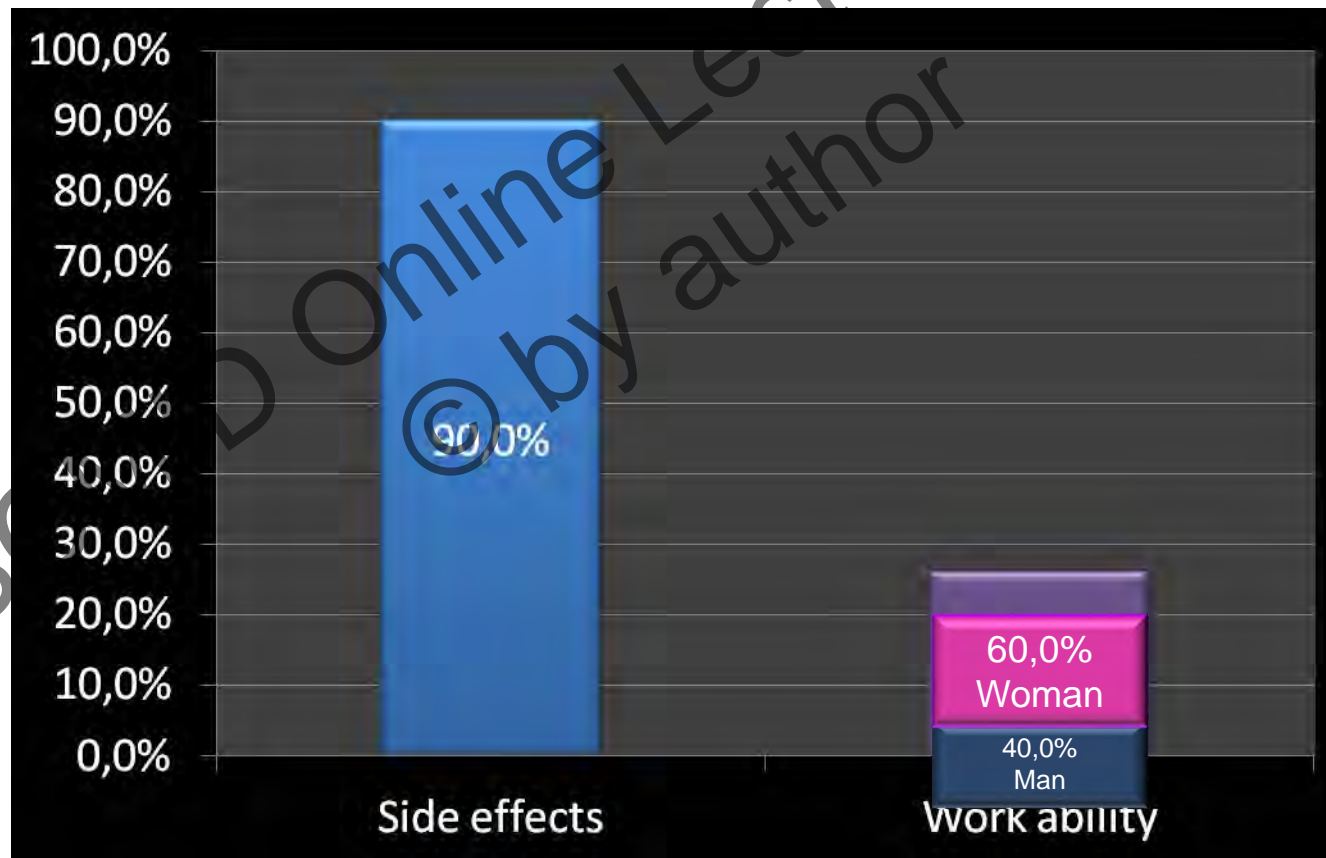
	<65yr (n=537)	\geq 65yr (n=46)	P- value*
PEG-IFN α reduction	31 (5.6%)	5 (9.8%)	0.191
Ribavirin reduction	38 (7%)	9 (19%)	0.007
PEG-IFN α + RBV reduction	11 (2.1%)	2 (4%)	0.237
Therapy discontinuation	38 (7%)	8 (17%)	0.021

* Fisher's exact test



Work ability in patients treated with PEG+RIBA

- 632 patients treated with PEG+RBV (UHID, Zagreb 2004-2015)



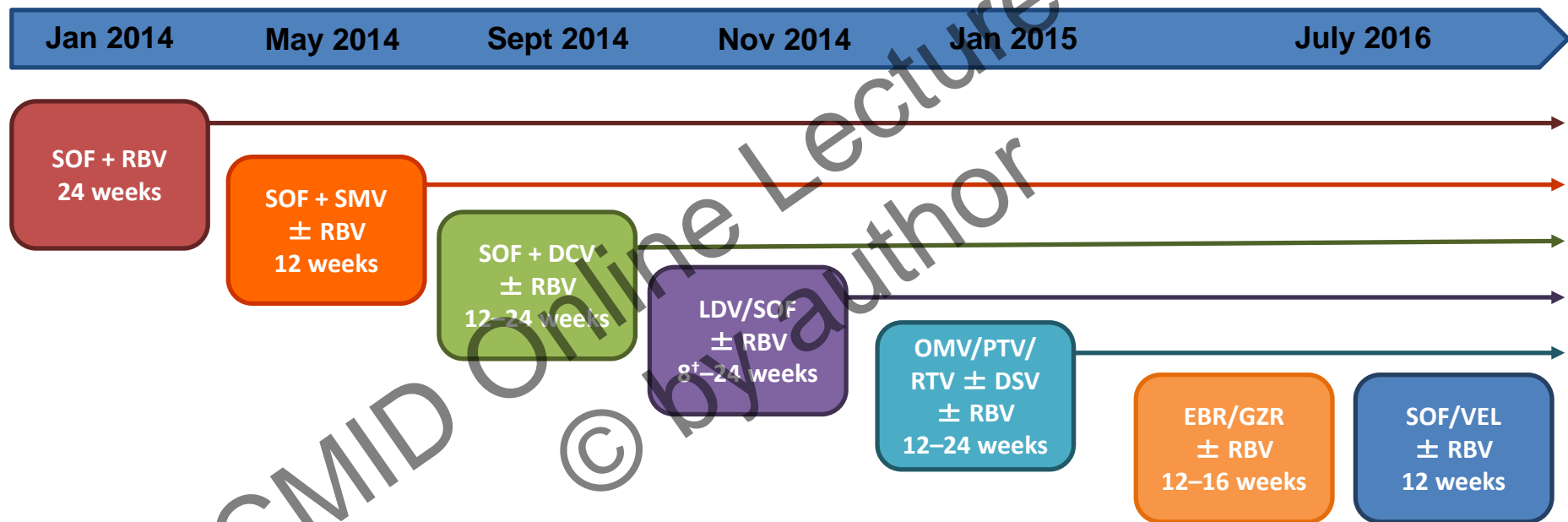
Reasons to continue working

- Men
 - Former PWID, low level of education, afraid of loosing their “new” job
- Women
 - High education, Having a constant jobs, stigma, did not want anybody in the office to know

PRO and interferon-ribavirin treatment

- IFN/RIBA treatment led to significant impairment of HRQoL and work ability,
- PRO and work ability returned after treatment end, and people with SVR showed additional improvements in HRQoL and work ability.

DAAs available in Europe to treat chronic HCV in adults



Janssen-Cilag Ltd. OLYSIO▼ (simeprevir) SmPC, June 2016;
 Bristol-Myers Squibb Pharma EEIG. DAKLINZA▼ (daclatasvir) SmPC, June 2016;
 Gilead Sciences Europe Ltd. SOVALDI▼ (sofosbuvir) SmPC, March 2016;
 Gilead Sciences Europe Ltd. HARVONI▼ (ledipasvir/sofosbuvir) SmPC, July 2016;
 AbbVie Ltd. VIEKIRAX▼ (ombitasvir/paritaprevir/ritonavir) SmPC, May 2016;
 AbbVie Ltd. EXVIERA▼ (dasabuvir) SmPC, May 2016;
 Gilead Sciences Europe Ltd. EPCLUSA▼ (velpatasvir/sofosbuvir) SmPC, July 2016
 Merck Sharp & Dohme Corp ZEPATIER▼ (elbasvir/grazoprevir) SmPC, July 2016

DAA: direct-acting antiviral agent; DCV: daclatasvir; DSV: dasabuvir; EBR: elbasvir;
 GZR: grazoprevir; IFN: interferon; LDV: ledipasvir; OMV: ombitasvir; PI: protease
 inhibitor; PTV: paritaprevir; RBV: ribavirin; RTV: ritonavir; SMV: simeprevir; SOF:
 sofosbuvir; STR: single tablet regimen;
 TN: treatment-naïve; VEL: velpatasvir

DAAs were well-tolerated clinical trials with HIV/HCV co-infected patients

Table 1. Adverse events in clinical trials of DAAs in HIV/HCV co-infected patients

	ALLY-2 DCV + SOF N=203	ION-4 LDV/SOF N=335	TURQUOISE-I OMV/PTV/R TV + DSV + RBV N=63	C-EDGE CO- INFECTION EBR/GZR N=218	ASTRAL-5 SOF/VEL N=106
Fatigue	17%	21%	48%	13%	25%
Headache	11%	25%	16%	12%	13%
Diarrhea	7%	11%	8%	7%	8%
Nausea	13%	10%	17%	9%	7%
D/C due to AE	0	0	0	0	2 (2%)

Wyles D, et al. N Engl J Med 2015;373:714–25; Sulkowski MS, et al. JAMA 2015;313:1223–31; Naggie S, et al. N Engl J Med 2015;373:705–13; Rockstroh JK, et al. Lancet HIV 2015;2(8):e319-27; Brau N, et al. IAS, Durban, 2016: abstract #XX

AE: adverse events; D/C discontinuation

PRO-DAAAs

- Improvement of health-related quality of life and work productivity in chronic hepatitis C patients with early and advanced fibrosis treated with ledipasvir and sofosbuvir
- No negative impact on HRQoL during treatment
- Eradication of virus with sofosbuvir + ledipasvir leads to improvement of HRQoL independently of fibrosis stage.

(*Younossiet al, 2015*)



PRO-DAAs

- **Ribavirin-Free Regimen With Sofosbuvir and Velpatasvir: Results From Astral-2 and 3 Clinical Trials**
- Patients on SOF/VEL without ribavirin had significantly better PRO results during treatment in comparison with ribavirin+regimen.
- Treatment regimen SOF/VEL bez without ribavirin resulted in quick improvement of PRO in patients with genotype 2 i 3 during treatment as well after achieving of SVR12.

(Younossiet al, 2016)



Conclusion

- Majority of patients with chronic hepatitis C are unaware of the infection, except for symptomatic patients with cirrhosis or extrahepatic manifestations
- Impairment of HQRoL when receiving the diagnosis in different aspects of emotional and social themes
- Treatment with Interferon and ribavirin have the negative impact on HQRoL during treatment
- DAAs improve HRQoL during therapy and afterwards

Conclusion

- Diagnosing patient with HCV in the non-cirrhotic phase of the chronic infection and not offering a chance for cure is disputable in terms of HRQoL

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