Appendix A. Search Strategy

Key:
/ = subject heading (including MeSH, Emtree,etc.)
MH = subject heading
ti = word in title
ab = word in abstract
adj# = adjacent within x number of words
$ = truncation
* = truncation
pt = publication type
sb = subset
kw = keyword

Databases searched:
MEDLINE
PubMed (publisher-supplied references only)
Cochrane Central Register of Controlled Trials (CENTRAL)
PsycINFO
Cumulative Index to Nursing and Allied Health (CINAHL)
EMBASE

MEDLINE via Ovid [search date: 12/2/2011]

Database(s): Ovid MEDLINE(R) without Revisions 1996 to November Week 3 2011, Ovid MEDLINE(R) Daily Update November 16, 2011, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations December 01, 2011

#	Searches	Results
1	Hepatitis C/	19947
2	Hepatitis C, chronic/	12822
3	Hepacivirus/	15764
4	hepatitis c.ti,ab.	37596
5	hcv.ti.	5683
6	1 or 2 or 3 or 4 or 5	45172
7	"Patient Acceptance of Health Care"/	18940
8	Patient Dropouts/	3594
9	Patient Compliance/	27211
10	Medication Adherence/	3080
11	Patient Participation/	10918
12	Patient Satisfaction/	43563
13	Patient Preference/	981

14	Treatment Refusal/	6511
15	"Retention (Psychology)"/	3782
16	((adhere$ or nonadhere$) adj6 (treatment$ or medication$ or therapy$ or therapies or regimen)).ti,ab.	12806
17	((compliance or comply$ or complies or complied) adj6 (treatment$ or medication$ or therapy$ or therapies or regimen)).ti,ab.	9662
18	((compliance or comply$ or complies or complied) adj3 patient$).ti,ab.	7688
19	(noncomplian$ adj6 (treatment$ or medication$ or therapy$ or therapies or regimen)).ti,ab.	946
20	(noncomplian$ adj3 patient$).ti,ab.	751
21	(persistence adj6 (treatment$ or medication$ or therapy$ or therapies or regimen)).ti,ab.	1628
22	(concordance adj6 (treatment$ or medication$ or therapy$ or therapies or regimen)).ti,ab.	399
23	patient cooperation.ti,ab.	312
24	(refusal adj3 (treatment$ or medication$ or therapy$ or therapies or regimen)).ti,ab.	449
25	(withdrawal adj3 (treatment$ or medication$ or therapy$ or therapies or regimen)).ti,ab.	3890
26	(discontinu$ adj3 (treatment$ or medication$ or therapy$ or therapies or regimen)).ti,ab.	12505
27	((dropout$ or drop$ out$) adj3 patient$).ti,ab.	1428
28	7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27	144127
29	6 and 28	1469
30	clinical trials as topic/ or controlled clinical trials as topic/ or randomized controlled trials as topic/	142687
31	(clinical trial or controlled clinical trial or meta analysis or randomized controlled trial).pt.	403700
32	control groups/ or double-blind method/ or single-blind method/	80471
33	random$.ti,ab.	440638
34	placebo$.ti,ab.	90664
35	clinical trial$.ti,ab.	133471
36	controlled trial$.ti,ab.	73483
37	case-control studies/	126566
38	retrospective studies/	304625
39	cohort studies/	111550
40	longitudinal studies/	50064
41	follow-up studies/	262459

42	prospective studies/	227185
43	cohort.ti,ab.	155175
44	longitudinal.ti,ab.	80303
45	follow up.ti,ab.	366017
46	followup.ti,ab.	10035
47	prospective$.ti,ab.	275033
48	retrospective$.ti,ab.	241307
49	comparison group$.ti,ab.	7362
50	control group$.ti,ab.	169872
51	observational.ti,ab.	48908
52	nonrandom$.ti,ab.	8674
53	30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52	1959137
54	29 and 53	886
55	limit 54 to yr="2001 -Current"	769
56	remove duplicates from 55	766
57	limit 56 to english language	700
58	56 not 57	66

PubMed [search date: 12/2/2011]

#1 "hepatitis c" AND publisher[sb] AND (adhere*[tiab] OR compliance[tiab] OR nonadhere*[tiab] OR noncomplian*[tiab] OR refusal[tiab] OR dropout*[tiab]) Limits: Publication Date from 2001 to 2013 25

#2 "hepatitis c" AND publisher[sb] AND (adhere*[tiab] OR compliance[tiab] OR nonadhere*[tiab] OR noncomplian*[tiab] OR refusal[tiab] OR dropout*[tiab]) Limits: English, Publication Date from 2001 to 2013 24

#3 #14 NOT #15 1

EMBASE via Ovid [search date: 11/28/2011]

Database(s): Embase 1996 to 2011 Week 46 via Ovid

#	Searches	Results
1	hepatitis C/	49960
2	Hepatitis C virus/	30192
3	1 or 2	61667

4	patient attitude/	32594
5	patient compliance/	65391
6	patient participation/	10418
7	patient preference/	947
8	patient satisfaction/	61564
9	refusal to participate/	586
10	treatment refusal/	6852
11	or/4-10	165624
12	3 and 11	1271
13	randomized controlled trial/	244592
14	clinical trial/ or clinical study/	686750
15	controlled clinical trial/	166321
16	meta analysis/	53262
17	randomization/	45268
18	double blind procedure/	75164
19	single blind procedure/	13023
20	placebo/	140037
21	"systematic review"/	45174
22	case control study/	50896
23	population based case control study/	3688
24	retrospective study/	208153
25	cohort analysis/	99458
26	longitudinal study/	39417
27	follow up/	463440
28	prospective study/	152369
29	control group/	27599
30	observational study/	24075
31	or/13-30	1592663
32	12 and 31	645
33	limit 32 to yr="2001 -Current"	637

34 limit 33 to english language 596

35 33 not 34 41

PsycINFO via APA PsycNET [search date: 11/29/2011]

((KEYWORDS:adhere* OR ab:adhere*) OR (KEYWORDS:nonadhere* OR ab:nonadhere*) OR (KEYWORDS:compliance OR ab:compliance) OR (KEYWORDS:noncomplian* OR ab:noncomplian*)) OR((IndexTermsFilt:("Client Attitudes" OR "Client Participation" OR "Client Satisfaction" OR "Treatment Barriers" OR "Treatment Compliance" OR "Treatment Dropouts" OR "Treatment Refusal"))
AND
(KEYWORDS:"hepatitis c") OR (ab:"hepatitis c")
AND
[2001 TO 2011]:PublicationYear = 114

english:Language= 109
non-english = 5

CINAHL via EBSCOhost [search date: 11/29/2011]

S1 ((MH "Hepatitis C, Chronic") OR (MH "Hepatitis C")) OR TX "hepatitis c"
S2 ((MH "Medication Compliance") OR (MH "Patient Compliance")) OR ((MH "Patient Dropouts") OR (MH "Patient Satisfaction")) OR (MH "Treatment Refusal")
S3 TX (adhere* OR nonadhere*) OR TX (compliance OR noncomplian*)
S4 S2 or S3
S5 S1 and S4
S6 (MH "Case Control Studies") OR (MH "Matched Case Control") OR (MH "Population-Based Case Control") OR (MH "Prospective Studies") OR (MH "Concurrent Prospective Studies") OR (MH "Nonconcurrent Prospective Studies")
S7 (MH "Correlational Studies") OR TX cohort OR TX observational
S8 (MH "Randomized Controlled Trials") OR (MH "Clinical Trials") OR (MH "Random Assignment") OR (MH "Single-Blind Studies") OR (MH "Double-Blind Studies") OR (MH "Triple-Blind Studies") OR TX clinical n1 trial* OR TX controlled n1 trial* OR PT Clinical trial OR PT randomized controlled trial
S9 S6 or S7 or S8
S10 S5 and S9 Limiters - Published Date from: 20010101-20111231 = 80

Cochrane Central Register of Controlled Trails via Wiley, issue 4 of 4, Oct. 2011 [search date: 12/2/2011]

#1	"hepatitis c":ti,ab,kw, from 2001 to 2011 in Clinical Trials	1779
#2	adhere*:ti,ab,kw OR nonadhere*:ti,ab,kw OR compliance:ti,ab,kw OR noncomplian*:ti,ab,kw, from 2001 to 2011 in Clinical Trials	9853
#3	"patient acceptance":ti,ab,kw OR refusal:ti,ab,kw OR dropout*:ti,ab,kw, from 2001 to 2011 in Clinical Trials	2606
#4	(#2 OR #3), from 2001 to 2011	11922
#5	(#1 AND #4), from 2001 to 2011	112

Appendix B. Studies Pending Assessment

Study Reference	Design	Aim	Location	Number of Participants	Intervention Description	Relevant Outcomes	2012 Status
Bruce 2008 [101]	RCT	Investigate whether integrating HCV treatment into methadone and buprenorphine improves HCV outcomes	US	125	Integrated substance abuse and HCV treatment with DOT	1. HCV viral load 2. Adherence 3. Drug treatment outcomes	Protocol
Klein 2008 [102]	RCT	Investigate whether antidepressant prophylaxis can increase successful completion of HCV therapy	Canada	NR	Administration of citalopram to prevent neuro-psychiatric symptoms	1. Proportion of prescribed pegIFN and ribavirin doses taken per month 2. Development of depression	Protocol
Litwin 2011[103]	RCT	Investigate whether enhanced DOT (PEG/RBV-DOT) is associated with increased adherence and SVR compared to standard DOT (PEG-DOT)	US	80	Provide adults with directly observed daily ribavirin plus provider-administered weekly IFN	1. Self-reported and pill count adherence 2. End to treatment response or SVR	Protocol; Currently recruiting
North 2008[104]	RCT	Investigate whether family-responsive psychoeducation can increase eligibility and adherence to HCV treatment	US	400	PsychoEducation Response to Families (PERF)	1. Treatment readiness and adherence to HCV treatment 2. Quality of life	Protocol
Shun 2012[105]	RCT	Investigate whether exercise can improve health related fitness, quality of life and adherence to HCV therapy	Taiwan	300	Personalized Physical Activity and Psych-Education (PPAPE) Program	1. Health related physical fitness 2. Quality of life 3. Adherence	Protocol; Currently recruiting
Sulkowski 2011[106]	RCT	Determine extent of HCV disease and treatment in IDU; evaluate if behavioral reinforcement	US	800	Contingent Voucher Incentive (CVI) provided based on clinic visits and HCV treatment adherence	1. Treatment eligibility 2. Liver disease staging 3. Treatment	Protocol; Currently recruiting

		interventions increase adherence				incentives 4. Liver stiffness 5. BMI 6. Serum markers	
Weiss 2011[107]	RCT	Investigate whether patients undergoing HCV treatment receiving Armodafinil have fewer missed doses, dose reductions, treatment discontinuation.	US	130	Administration of Armodafinil (FDA approved stimulant)	7. Adherence to medications 8. Fatigue Severity Scale (FSS)	Currently recruiting

Abbreviations: DOT: directly observed treatment; FDA: Food and Drug Administration; HCV: hepatitis C virus; IDU: intravenous drug users; IFN: interferon; PEG: pegylated; RBV: ribavirin; RCT: randomized controlled trial; SVR: sustained viral response; US: United States

Appendix C. List of Excluded Studies

1. Alavian SM, Aalaei-Andabili SH. Education by a Nurse Increases the Adherence to Therapy in Chronic Hepatitis C Patients. Clin Gastroenterol Hepatol 2012;10(2):203. **KQ1E5, KQ3E5, KQ4E5.**

2. Arase Y, Suzuki F, Suzuki Y, et al. Side effects of combination therapy of peginterferon and ribavirin for chronic hepatitis-C. Internal Medicine 2007;46(22):1827-32. PMID: 18025763. **KQ2E1.**

3. Baran RW, Bhor M, Dietz B, et al. Poor adherence to treatment with pegylated interferon/ribavirin in patients with chronic hepatitis C infection is associated with detrimental health outcomes. Hepatology. 60th Annual Meeting of the American Association for the Study of Liver Diseases: The Liver Meeting 2009 Boston, MA; 2009. p. 653A. PMID: 70074157. **KQ2E2.**

4. Bertino G, Ardiri A, Boemi PM, et al. Epoetin alpha improves the response to antiviral treatment in HCV-related chronic hepatitis. European Journal of Clinical Pharmacology 2010 Oct;66(10):1055-63. PMID: 20652232. **KQ3E2.**

5. Bonkovsky HL, Tice AD, Yapp RG, et al. Efficacy and safety of peginterferon alfa-2a/ribavirin in methadone maintenance patients: randomized comparison of direct observed therapy and self-administration. American Journal of Gastroenterology 2008 Nov;103(11):2757-65. PMID: 18684176. **KQ3E2, KQ4E2.**

6. Brau N, Bini EJ, Currie S, et al. Black patients with chronic hepatitis C have a lower sustained viral response rate than non-Blacks with genotype 1, but the same with genotypes 2/3, and this is not explained by more frequent dose reductions of interferon and ribavirin*. Journal of Viral Hepatitis 2006 Apr;13(4):242-49. PMID: 16611190. **KQ2E4a.**

7. Cacoub P, Ouzan D, Melin P, et al. Patient education improves adherence to peg-interferon and ribavirin in chronic genotype 2 or 3 hepatitis C virus infection: a prospective, real-life, observational study. World Journal of Gastroenterology 2008 Oct 28;14(40):6195-203. PMID: 18985810. **KQ4E2.**

8. Chainuvati S, Khalid SK, Kancir S, et al. Comparison of hepatitis C treatment patterns in patients with and without psychiatric and/or substance use disorders. Journal of Viral Hepatitis 2006 Apr;13(4):235-41. PMID: 16611189. **KQ2E4a.**

9. Chen T-M, Huang P-T, Wen C-F, et al. Reappraisal of the importance of mutations in the NS5A-PKR-binding domain of hepatitis C-1b virus in the era of optimally individualized therapy. Journal of Viral Hepatitis 2011;18(2):119-28. PMID: 20236237. **KQ2E8.**

10. Chun DS. An assessment of support group participation on depression and adherence in veterans with hepatitis C. 63 ed. US: ProQuest Information & Learning; 2002. **KQ3E4a.**

11. Costiniuk CT, Mills E, Cooper CL. Evaluation of oral cannabinoid-containing medications for the management of interferon and ribavirin-induced anorexia, nausea and weight loss in patients treated for chronic hepatitis C virus. Canadian Journal of Gastroenterology 2008;22(4):376-80. PMID: 18414712. **KQ3E4a, KQ4E4a.**

12. Curcio F, Di MF, Capraro C, et al. Together ... to take care: multidisciplinary management of hepatitis C virus treatment in randomly selected drug users with chronic hepatitis. Journal of Addiction Medicine 2010 Dec;4(4):223-32. PMID: 21769040. **KQ4E2.**

13. De Careaga BO. Predictive factors for response to treatment of chronic hepatitis C. Annals of Hepatology 2006;5(Suppl 1):S24-S28. **KQ2E1.**

14. Delgado JS, Baumfeld Y, Novack V, et al. Efficacy of combined pegylated interferon and ribavirin therapy in Jewish patients of Israel suffering from chronic hepatitis C. Hepatol Int 2011 May 8 PMID: 21553307. **KQ2E8.**

15. Dore GJ, Hellard M, Matthews GV, et al. Effective treatment of injecting drug users with recently acquired hepatitis C virus infection.

Gastroenterology 2010 Jan;138(1):123-35. PMID: 19782085. **KQ2E4.**

16. Ebner N, Wanner C, Winklbaur B, et al. Retention rate and side effects in a prospective trial on hepatitis C treatment with pegylated interferon alpha-2a and ribavirin in opioid-dependent patients. Addiction Biology 2009 Apr;14(2):227-37. PMID: 19291011. **KQ1E1, KQ2E1, KQ3E1, KQ4E1.**

17. El Makhzangy H, Esmat G, Said M, et al. Response to pegylated interferon alfa-2a and ribavirin in chronic hepatitis C genotype 4. J Med Virol 2009 Sep;81(9):1576-83. PMID: 19626613. **KQ2E8.**

18. Evon DM, Esserman DA, Ramcharran D, et al. Social support and clinical outcomes during antiviral therapy for chronic hepatitis C. Journal of Psychosomatic Research 2011 Nov;71(5):349-56. PMID: 21999979. **KQ2E2.**

19. Fumaz CR, Munoz-Moreno JA, Ballesteros AL, et al. Influence of the type of pegylated interferon on the onset of depressive and neuropsychiatric symptoms in HIV-HCV coinfected patients. AIDS Care 2007 Jan;19(1):138-45. PMID: 17129869. **KQ2E2.**

20. Gardenier D, Wisnivesky J, McGinn LK, et al. Hepatitis C treatment completion in individuals with psychiatric comorbidity and depression. Gastroenterol Nurs 2011 Mar;34(2):102-06. PMID: 21455042. **KQ3E1.**

21. Gazdag G, Horvath G, Szabo O, et al. Difficulties with interferon treatment in former intravenous drug users. Brazilian Journal of Infectious Diseases 2011 Apr;15(2):163-66. PMID: 21503405. **KQ2E2.**

22. Gleason OC, Yates WR, Isbell MD, et al. An open-label trial of citalopram for major depression in patients with hepatitis C. J Clin Psychiatry 2002 Mar;63(3):194-98. PMID: 11926717. **KQ3E1.**

23. Gonzalez SA. Consensus interferon: tailored therapy and the impact of adherence. Digestive Diseases & Sciences 2011 Mar;56(3):631-34. PMID: 21259073. **KQ1E4, KQ2E4, KQ3E4, KQ4E4.**

24. Grebely J, Matthews GV, Hellard M, et al. Adherence to treatment for recently acquired hepatitis C virus (HCV) infection among injecting drug users. Journal of Hepatology 2011;55(1):76-85. PMID: 21145855. **KQ2E4.**

25. Huang JF, Yu ML, Huang CF, et al. The efficacy and safety of pegylated interferon plus ribavirin combination therapy in chronic hepatitis c patients with hepatocellular carcinoma post curative therapies - a multicenter prospective trial. Journal of Hepatology 2011 Feb;54(2):219-26. PMID: 21056500. **KQ2E8.**

26. Huckans MS, Loftis JM, Blackwell AD, et al. Interferon alpha therapy for hepatitis C: treatment completion and response rates among patients with substance use disorders. Substance Abuse Treatment, Prevention, & Policy 2007;2:4. PMID: 17222348. **KQ2E4a.**

27. Jeong SW, Kim JD, Woo HY, et al. Impact of adherence to peginterferon-ribavirin combination therapy in chronic hepatitis C patients on achieving a sustained virologic response. Korean Journal of Hepatology 2009 Sep;15(3):338-49. PMID: 19783883. **KQ2E7.**

28. Kawaguchi Y, Mizuta T, Takahashi K, et al. High-dose vitamins E and C supplementation prevents ribavirin-induced hemolytic anemia in patients with chronic hepatitis C. Hepatology Research 2007 May;37(5):317-24. PMID: 17441803. **KQ1E4a, KQ2E4a, KQ3E4a, KQ4E4a.**

29. Kevans D, Farrell G, Hopkins S, et al. Haematological support during peg-interferon therapy for HCV-infected haemophiliacs improves virological outcomes. Haemophilia 2007 Sep;13(5):593-98. PMID: 17880449. **KQ2E1.**

30. Kogure T, Ueno Y, Fukushima K, et al. Pegylated interferon plus ribavirin for genotype Ib chronic hepatitis C in Japan. World Journal of Gastroenterology 2008;14(47):7225-30. PMID: 19084938. **KQ2E8.**

31. Krook AL, Stokka D, Heger B, et al. Hepatitis C treatment of opioid dependants receiving maintenance treatment: results of a Norwegian pilot study. Eur Addict Res 2007;13(4):216-21. PMID: 17851243. **KQ1E1, KQ4E1.**

32. Larrey D, Salsé A, Pageaux G, et al. Effects of systematic nurse-provided therapeutic education on adherence and efficiency of PEG-Interferon-a2a (Pegasys®)-ribavirin treatment in chronic hepatitis C (Pegobs Protocol). Hepatology 2007;46(4):377A-8A. **KQ1E2, KQ2E2, KQ3E2, KQ4E2.**

33. Larrey D, Salse A, Pageaux GP, et al. Effects of systematic nurse-provided therapeutic education on adherence and efficiency of PEG-interferon-ALPHA2A (PEGASYS®)ribavirin treatment in chronic hepatitis C (PEGOBS protocol). Journal of Hepatology 2008;48(Suppl 1):S300. **KQ1E2, KQ3E2, KQ4E2.**

34. Larrey D, Salse A, Ribard D, et al. Education by a Nurse Increases Response of Patients With Chronic Hepatitis C to Therapy With Peginterferon-alpha2a and Ribavirin. Clinical Gastroenterology and Hepatology 2011;9(9):781-85. PMID: 21683161. **KQ4E2.**

35. Lebray P, Nalpas B, Vallet-Pichard A, et al. The impact of haematopoietic growth factors on the management and efficacy of antiviral treatment in patients with hepatitis C virus. Antiviral Therapy 2005;10(6):769-76. PMID: 16218177. **KQ1E7, KQ3E7.**

36. Mak C, Heft SM, Amkraut H, et al. Compliance as an explanatory variable in Hepatitis-C. Drug Information Journal 2001;35(4):1351-61. **KQ2E1.**

37. Malaguarnera M, Vacante M, Bertino G, et al. The supplementation of acetyl-L-carnitine decreases fatigue and increases quality of life in patients with hepatitis C treated with pegylated interferon-alpha 2b plus ribavirin. Journal of Interferon and Cytokine Research 2011;31(9):653-59. PMID: 21923249. **KQ1E2.**

38. Mangia A, Dalgard O, Minerva N, et al. Ribavirin dosage in patients with HCV genotypes 2 and 3 who completed short therapy with peg-interferon alpha-2b and ribavirin. Alimentary Pharmacology & Therapeutics 2010 Jun;31(12):1346-53. PMID: 20222909. **KQ2E1.**

39. Manolakopoulos S, Deutsch MJ, Anagnostou O, et al. Substitution treatment or active intravenous drug use should not be contraindications forantiviral treatment in drug userswith chronic hepatitis C. Liver International 2010;30(10):1454-60. **KQ1E4a, KQ2E4a.**

40. Marino EL, Alvarez-Rubio L, Miro S, et al. Pharmacist intervention in treatment of patients with genotype 1 chronic hepatitis C. Journal of Managed Care Pharmacy 2009 Mar;15(2):147-50. PMID: 19236128. **KQ1E2, KQ3E2, KQ4E2.**

41. McHutchison JG, Manns M, Patel K, et al. Adherence to combination therapy enhances sustained response in genotype-1-infected patients with chronic hepatitis C. Gastroenterology 2002 Oct;123(4):1061-69. PMID: 12360468. **KQ1E2, KQ2E2.**

42. Missiha S, Heathcote J, Arenovich T, et al. Impact of asian race on response to combination therapy with peginterferon alfa-2a and ribavirin in chronic hepatitis C. American Journal of Gastroenterology 2007 Oct;102(10):2181-88. PMID: 17640318. **KQ2E4a.**

43. Morasco BJ, Rifai MA, Loftis JM, et al. A randomized trial of paroxetine to prevent interferon-alpha-induced depression in patients with hepatitis C.[Erratum appears in J Affect Disord. 2009 Feb;113(1-2):201]. Journal of Affective Disorders 2007 Nov;103(1-3):83-90. PMID: 17292481. **KQ1E4a, KQ3E4a, KQ4E2.**

44. Nudo CG, Wong P, Hilzenrat N, et al. Elderly patients are at greater risk of cytopenia during antiviral therapy for hepatitis C. Canadian Journal of Gastroenterology 2006 Sep;20(9):589-92. PMID: 17001400. **KQ3E4a.**

45. Ramsey SE, Engler PA, Stein MD, et al. Effect of CBT on Depressive Symptoms in Methadone Maintenance Patients Undergoing Treatment for Hepatitis C. J Addict Res Ther 2011 May 13;2(2):2-10. PMID: 21743837. **KQ1E2, KQ4E2.**

46. Raptopoulou-Gigi M, Tsantoulas D, Vafiadi I, et al. The effect of adherence to therapy on sustained response in daily or three times a week interferon alpha-2b plus ribavirin treatment of naive and nonresponder chronic hepatitis C patients. Journal of Viral Hepatitis 2005;12(1):91-95. PMID: 15655054. **KQ2E4a.**

47. Ridruejo E, Adrover R, Cocozzella D, et al. Efficacy, tolerability and safety in the treatment of chronic hepatitis C with combination of PEG-Interferon - Ribavirin in daily practice. Annals of Hepatology 2010 Jan;9(1):46-51. PMID: 20308722. **KQ2E8.**

48. Robaeys G, Van VH, Mathei C, et al. Similar compliance and effect of treatment in chronic hepatitis C resulting from intravenous drug use in comparison with other infection causes. European Journal of Gastroenterology & Hepatology 2006 Feb;18(2):159-66. PMID: 16394797. **KQ2E4a.**

49. Rodis JL, Kibbe P. Evaluation of medication adherence and quality of life in patients with hepatitis C virus receiving combination therapy. Gastroenterol Nurs 2010 Sep;33(5):368-73. PMID: 20890160. **KQ3E2.**

50. Saab S. Academic perspectives on hepatitis C treatment adherence. Gastroenterology and Hepatology 2009;5(3 Suppl 9):6-7. **KQ4E5.**

51. Saito H, Tada S, Ebinuma H, et al. Role of erythrocytes as a reservoir for ribavirin and relationship with adverse reactions in the early phase of interferon combination therapy for chronic hepatitis C virus infections. Journal of Clinical Microbiology 2006 Oct;44(10):3562-68. PMID: 17021083. **KQ2E4a.**

52. Satapathy SK, Lingisetty CS, Proper S, et al. Equally poor outcomes to pegylated interferon-based therapy in African Americans and Hispanics with chronic hepatitis C infection. J Clin Gastroenterol 2010 Feb;44(2):140-45. PMID: 19826275. **KQ2E2.**

53. Schaefer M, Hinzpeter A, Mohmand A, et al. Hepatitis C treatment in "difficult-to-treat" psychiatric patients with pegylated interferon-alpha and ribavirin: response and psychiatric side effects. Hepatology 2007;46:991-98. PMID: 17668880. **KQ2E2.**

54. Sezaki H, Suzuki F, Kawamura Y, et al. Poor response to pegylated interferon and ribavirin in older women infected with hepatitis C virus of genotype 1b in high viral loads. Digestive Diseases & Sciences 2009 Jun;54(6):1317-24. PMID: 18958621. **KQ2E8.**

55. Sharvadze L, Tsertsvadze T, Gochitashvili N, et al. Ifn/Rbv treatment induced anemia and its correction with epoetin alpha in patients with hepatitis C. Georgian Medical News 2006;8(137):62-65. PMID: 16980747. **KQ3E2, KQ4E2.**

56. Shehab TM, Fontana RJ, Oberhelman K, et al. Effectiveness of interferon alpha-2b and ribavirin combination therapy in the treatment of naive chronic hepatitis C patients in clinical practice. Clinical Gastroenterology & Hepatology 2004 May;2(5):425-31. PMID: 15118982. **KQ2E4a.**

57. Shin SR, Sinn DH, Gwak G-Y, et al. Risk factors for relapse in chronic hepatitis C patients who have achieved end of treatment response. Journal of gastroenterology and hepatology 2010;25(5):957-63. PMID: 20546450. **KQ2E2.**

58. Sola R, Galeras JA, Montoliu S, et al. Poor response to hepatitis C virus (HCV) therapy in HIV- and HCV-coinfected patients is not due to lower adherence to treatment. AIDS Research & Human Retroviruses 2006 May;22(5):393-400. PMID: 16706615. **KQ2E4a.**

59. Soriano V, Miralles C, Berdun MA, et al. Premature treatment discontinuation in HIV/HCV-coinfected patients receiving pegylated interferon plus weight-based ribavirin. Antiviral Therapy 2007;12(4):469-76. PMID: 17668555. **KQ2E2.**

60. Stainbrook TR. Maximizing hepatitis C treatment adherence in the community setting. Gastroenterology and Hepatology 2009;5(3 Suppl 9):8-10. **KQ1E5, KQ3E5, KQ4E5.**

61. Sylvestre DL, Clements BJ, Malibu Y. Cannabis use improves retention and virological outcomes in patients treated for hepatitis C. European Journal of Gastroenterology & Hepatology 2006 Oct;18(10):1057-63. PMID: 16957511. **KQ1E4a, KQ2E4a, KQ3E4a, KQ4E4a.**

62. Sylvestre DL, Clements BJ. Adherence to hepatitis C treatment in recovering heroin users maintained on methadone. European Journal of Gastroenterology & Hepatology 2007 Sep;19(9):741-47. PMID: 17700258. **KQ2E4a.**

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Appendix D. Quality of Included Randomized Controlled Trials

Study, Year	Valid Random Assign-ment?	Allocation Concealed ?	Groups Similar at Baseline?	Measure-ments: Equal, Reliable, Valid	Blind-ing of Patients	Blinding of Outcome Assessors	Completeness of Followup	Intervent-ion Fidelity?	Adequate Compliance to Intervention ?	ITT Analy-sis	Overall Quality
Bertino 2010[56]	NR	NR	NR	Likely	No	NR	Week 72 Total: 134/134 = 100% IG: 100% CG: 100%	NR	NR	ITT	Poor
Bonkov-sky 2008[60]	NR	NR	Yes	Likely	No	NR	Total (28/48=58%) IG: 16/42=63% CG: 12/24=50%	NR	NR	ITT	Poor
Larrey, 2011[91]	NR	NR	Yes	NR	No	NR	Total (244/250=97.6 %) IG: 123/123=100% CG: 121/127=95.3%	Likely	NR	ITT	Poor
Mora-sco, 2010[93]	Uncertain	NR	Yes	NR	Yes	NR	NR	Likely	NR	NR	Poor
Ram-sey, 2011[94]	Yes	Yes	No	Likely	NR	NR	Total 82.5% at 48 weeks for DNA data IG: 10/14=71% CG: 14/15=93%	Likely	IG completed mean of 5.93 (out of 8) sessions; 9 of 14 participants completed 6 or more sessions	ITT	Fair

Abbreviations: CG: control group; IG: intervention group; ITT: intention to treat; NR: not reported

Appendix E. Quality of Included Cohort Studies

Study, Year	Study Type	Selection of the Nonexposed Cohort	Method of Ascertaining Exposure	Measurements: Equal, Reliable, Valid	Blinding of Outcome Assessors	Completeness of Followup	Adjustment/Matching for Potential Confounders	Overall Quality
Alam, 2010[87]	Prospective cohort study	Appropriate	Patient registry data	Likely	NR	24 weeks Total: 450/503=89.5% E: 311/346=89.9% NE: 139/157=88.5%	Unadjusted	Fair
Cacoub, 2008[88]	Prospective cohort study	Appropriate	Patient self-report of therapeutic education by a third party including distribution of support documents	Likely	NR	Total (646/674=96%) Loss to followup not presented by exposure	Adjusted for all important factors that could be obtained	Good
Cohen, 2009[61]	Retrospective cohort study	Appropriate	Patient charts; Pharmacy reports of being a "specialty" versus "standard" pharmacy added to patient chart	Likely	NR	NR (all patients included in analyses)	Adjusted for a limited number of important factors in SVR analyses, but not in adherence analyses	Fair
Curcio, 2010[89]	Prospective cohort study	Inappropriate	Exposure is the TTTC group (adequate exposure)	Uncertain	Uncertain	Total (100/100=100%)	Inadequate matching	Poor
Hussein, 2010[90]	Retrospective cohort study	Appropriate	Enrollment in BIC program recorded in claims database	Likely	NR	Retrospective cohort - but missing data at 24 and 48 weeks 24 weeks: E: 638/780=81.8% NE: 7014/8572=81.8%	Used propensity score matching technique, included several factors in generating propensity score	Good

Study, Year	Study Type	Selection of the Nonexposed Cohort	Method of Ascertaining Exposure	Measurements: Equal, Reliable, Valid	Blinding of Outcome Assessors	Completeness of Followup	Adjustment/Matching for Potential Confounders	Overall Quality
						48 weeks: E: 333/780=42.7% NE: 4071/8572=47.5%		
Liu, 2010[92]	Retrospective cohort study	Appropriate	Chart review of antidepressant use	Likely	NR	Total (100/100=100%)	Unadjusted	Poor

Abbreviations: BIC: Be in Charge; E: exposed group; NE: nonexposed group; NR: not reported; SVR: sustained viral response; TTTC: Together to Take Care

Appendix F. Quality of Life Outcomes

Study, Year Quality	Study Design	Comparison	Group	Sample Size (N)	Quality of Life Measure	Followup	Quality of Life Score, Mean (SD)	P-value for Difference Between Groups at Followup
Bertino, 2010[56] Fair	RCT	HCV Patients on epoetin vs. usual care	IG	67	Energy Score Change*	36 weeks	18 ± 17.3	Energy Score Change: p<0.05 Activity Score Change: p<0.01
					Activity Score Change*		20 ± 18.5	
			CG	67	Energy Score Change*		12.2 ± 21.6	
					Activity Score Change*		7 ± 18.7	
Bonkovsky, 2008[60] Poor	RCT	Supervised treatment vs. self-administered treatment in methadone clinic users	IG	24	Hepatitis specific limitations	Baseline	74.5 (6.0)	NR
						End of Treatment	59.1 (7.4)	
						End of Followup (72 weeks)	84.2 (5.6)	
					Hepatitis specific health distress	Baseline	63.8 (5.5)	
						End of Treatment	58.7 (8.2)	
						End of Followup (72 weeks)	81.6 (6.0)	
			CG	24	Hepatitis specific limitations	Baseline	76.8 (6.1)	
						End of Treatment	40.0 (8.7)	
						End of Followup (72 weeks)	68.9 (9.6)	
					Hepatitis specific health distress	Baseline	69.8 (5.7)	
						End of Treatment	50.4 (7.4)	

Study, Year Quality	Study Design	Comparison	Group	Sample Size (N)	Quality of Life Measure	Followup	Quality of Life Score, Mean (SD)	P-value for Difference Between Groups at Followup
						End of Followup (72 weeks)	67.3 (7.3)	

*Linear Analogue Self-Assessment (LASA) Scale

Abbreviations: CG: control group; HCV: hepatitis C virus; IG: intervention group; NR: not reported; RCT: randomized controlled trial; SD: standard deviation; Vs: versus