Appendix C: Updated HRQL Search (Response to D4)

Identification of studies

The following databases were searched (with service providers):

- Medline (OvidSP)
- Medline In-Process & other non-indexed citations (OvidSP)
- Embase (OvidSP)
- EconLIT (OvidSP)
- NHS EED (http://onlinelibrary.wiley.com/cochranelibrary/search/

In addition, research abstracts were searched for the 2011 and/or 2012 annual meetings of the following organizations:

- European Association for the Study of the Liver (EASL)
- United European Gastroenterology (UEG)
- American Gastroenterological Association (AGA)
- American Association for the Study of Liver Diseases (AASLD)

Exact details of the search strategy are provided in Table C1.

Table C1: Search Strategy for 'Measurement and Valuation of Health Effects'

Date of search: December 17, 2012

Date span of the search:

The search in Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) encompassed all citations from 1946 through the date of the search (17 Dec 2012).

The search in EMBASE encompassed all citations from 1988 to 2012 week 49.

The search in Ovid EconLIT encompassed all citations from 1961 through the date of the search (17 Dec 2012).

The search of NHS EED encompassed all citations through the date of the search (17 Dec 2012).

Medline Search Strategy:

SEARCH #	SEARCH TEXT	HITS
1	Hepatic Encephalopathy/	8505
2	(encephalopath* adj2 (hepatic or hepatocerebral or portosystemic or portal-systemic)).tw.	5350
3	(hepatic adj1 (stupor* or coma*)).tw.	1571
4	or/1-3	11000
5	(Rifaximin-α or rifamycin or Xifaxan or refero or targaxan or tixteller or xifaxanta or redactiv or 80621-81-4 or 88747-56-2).tw,rn.	1851
6	(Lactulose or generlac or kristalose or enulose or constulose or duphalac or lactugal or normase or amivalex or 4618-18-2).tw,rn.	2760
7	(Neomycin or mycifradin or neo-fradin or neo-tab or nivemycin or fradiomycin or 11004-65-2 or 1404-04-2 or 1405-10-3 or 8026-22-0).tw,rn.	11763
8	or/5-7	16124
9	4 and 8	642

10	quality of life/	105543
11	exp questionnaires/	275658
12	exp psychology/	56870
13	exp health status/	94858
14	exp health status indicators/	178974
15	activities of daily living/	47442
16	exp health surveys/	376582
17	quality adjusted life years/	6213
18	exp Treatment outcome/	584191
19	psychometrics/	50484
20	(quality of life or QOL or health related quality of life or HRQOL or HRQL).tw.	129768
21	(quality adjusted life year* or QALY*).tw.	6173
22	(health state* or health status).tw.	36484
23	(health* year* equivalent* or HYE or HYEs).tw.	62
24	(utility or utilities).tw.	105507
25	(wellbeing or well-being).tw.	39407
26	(short form 36 or sf-36 or sf36).tw.	14154
27	(short form 12 or sf-12 or sf12).tw.	2282
28	(euroqol or eq5d or eq-5d).tw.	3211
29	(quality of wellbeing index or quality of well-being index or qwb).tw.	167
30	(health utilit* index or hui).tw.	990
31	(medical outcomes survey or mos).tw.	4776
32	(chronic liver disease questionnaire or CLDQ).tw.	62
33	(time tradeoff or time trade-off or TTO).tw.	1060
34	standard gamble.tw.	621
35	preference*.tw.	83565
36	magnitude estimation.tw.	685
37	or/10-36	1595339
38	9 and 37	136
39	letter.pt.	786831
40	editorial.pt.	323802
41	historical article.pt.	291633
42	or/39-41	1388393
43	38 not 42	126
44	animals/	5114599
45	humans/	12764478
46	44 and 45	1382805
47	44 not 46	3731794
48	43 not 47	123
49	limit 48 to English language	108

*Lines 10-37 are based on recommended HRQL search terminology from: Paisley S, Booth A, Mensinkai S. Chapter 12: health-related quality of life studies. In: Etext on Health Technology Assessment (HTA) Information Resources. [2005] (http://www.nlm.nih.gov/archive/20060905/nichsr/ehta/chapter12.html)

EMBASE Search Strategy:

SEARCH #	SEARCH TEXT	HITS
1	Hepatic Encephalopathy/	7854
2	(encephalopath* adj2 (hepatic or hepatocerebral or portosystemic or portal-systemic)).tw.	5787
3	(hepatic adj1 (stupor* or coma*)).tw.	416
4	or/1-3	9323
5	(Rifaximin-α or rifamycin or Xifaxan or refero or targaxan or tixteller or xifaxanta or redactiv or 80621-81-4 or 88747-56-2).tw,rn.	3613
6	(Lactulose or generlac or kristalose or enulose or constulose or duphalac or lactugal or normase or amivalex or 4618-18-2).tw,rn.	5371
7	(Neomycin or mycifradin or neo-fradin or neo-tab or nivemycin or fradiomycin or 11004-65-2 or 1404-04-2 or 1405-10-3 or 8026-22-0).tw,rn.	12409
8	or/5-7	20449
9	4 and 8	1169
10	exp quality of life/	219952
11	11 exp health status/	109800
12	12 exp questionnaire/	330657
13	13 health survey/	132460
14	14 exp treatment outcome/	888126
15	outcomes research/	67862
16	scoring system/	150570
17	rating scale/	75529
18	functional assessment/	42661
19	self report/	51757
20	(quality of life or QOL or health related quality of life or HRQOL or HRQL).tw.	178888
21	(quality adjusted life year* or QALY*).tw.	8734
22	(health state* or health status).tw.	40119
23	(health* year* equivalent* or HYE or HYEs).tw.	81
24	(utility or utilities).tw.	123688
25	(wellbeing or well-being).tw.	46084
26	(short form 36 or sf-36 or sf36).tw.	19088
27	(short form 12 or sf-12 or sf12).tw.	3182
28	(euroqol or eq5d or eq-5d).tw.	5037
29	(quality of wellbeing index or quality of well-being index or qwb).tw.	179
30	(health utilit* index or hui).tw.	1222
31	(medical outcomes survey or mos).tw.	6472
32	(chronic liver disease questionnaire or CLDQ).tw.	84
33	(time tradeoff or time trade-off or TTO).tw.	1337
34	standard gamble.tw.	713
35	preference*.tw.	85418
36	magnitude estimation.tw.	507
37	or/10-36	1895386

38	9 and 37	294
39	letter.pt.	677774
40	editorial.pt.	391251
41	note.pt.	539485
42	or/39-41	1608510
43	38 not 42	255
44	exp animal/	13649224
45	exp animal-experiment/	1149358
46	nonhuman/	3472863
47	(rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ti,ab,sh.	3123653
48	or/44-47	14589570
49	exp human/	11027802
50	exp human-experiment/	249370
51	or/49-50	11028477
52	48 and 51	11027983
53	48 not 52	3561587
54	43 not 53	253
55	limit 54 to English language	233

*Lines 10-37 are based on recommended HRQL search terminology from: Paisley S, Booth A, Mensinkai S. Chapter 12: health-related quality of life studies. In: Etext on Health Technology Assessment (HTA) Information Resources. [2005] (http://www.nlm.nih.gov/archive/20060905/nichsr/ehta/chapter12.html)

EconLIT Search Strategy:

SEARCH	SEARCH TEXT	HITS
1	hepatic encephalopathy [Including Limited Related Terms]	55
2	hepatocerebral encephalopathy [Including Limited Related Terms]	54
3	portosystemic encephalopathy [Including Limited Related Terms]	54
4	portal-systemic encephalopathy [Including Limited Related Terms]	54
5	hepatic stupor [Including Limited Related Terms]	4
6	hepatic coma [Including Limited Related Terms]	7
7	or/1-6	64

NHS EED Search Strategy:

SEARCH #	SEARCH TEXT	HITS
#1	MeSH descriptor: [Hepatic Encephalopathy] explode all trees	323
#2	encephalopath* and (hepatic or hepatocerebral or portosystemic or portal-systemic or portal systemic)	857
#3	hepatic and (stupor* or coma*)	205
#4	#1 or #2 or #3	987
#5	Rifaximin-α or rifamycin or Xifaxan or refero or targaxan or tixteller or xifaxanta or redactiv or 80621-81-4 or 88747-56-2	182
#6	Lactulose or generlac or kristalose or enulose or constulose or duphalac or lactugal or normase or amivalex or 4618-18-2	706
#7	Neomycin or mycifradin or neo-fradin or neo-tab or nivemycin or fradiomycin or 11004-65-2 or 1404-04-2 or 1405-10-3 or 8026-	579

	22-0	
#8	#5 or #6 or #7	1395
#9	#4 and #8 in Economic Evaluations	2
#10	MeSH descriptor: [Quality of Life] this term only	12121
#11	MeSH descriptor: [Questionnaires] explode all trees	13923
#12	MeSH descriptor: [Psychology] explode all trees	802
#13	MeSH descriptor: [Health Status] explode all trees	4579
#14	MeSH descriptor: [Health Status Indicators] explode all trees	13762
#15	MeSH descriptor: [Activities of Daily Living] this term only	3295
#16	MeSH descriptor: [Health Surveys] explode all trees	20840
#17	MeSH descriptor: [Quality-Adjusted Life Years] this term only	2772
#18	MeSH descriptor: [Treatment Outcome] explode all trees	78933
#19	MeSH descriptor: [Psychometrics] this term only	2081
#20	quality of life or QOL or health related quality of life or HRQOL or HRQL OR quality of life or QOL or health related quality of life or HRQOL or HRQL	34523
#21	quality adjusted life year* or QALY*quality adjusted life year* or QALY*	7466
#22	health state* or health status	59721
#23	health* year* equivalent* or HYE or HYEs or health* year* equivalent* or HYE or HYEs	3404
#24	utility or utilities	8608
#25	wellbeing or well-being or well being	83894
#26	short form 36 or sf-36 or sf36 or sf 36	7333
#27	short form 12 or sf-12 or sf12 or sf 12	8104
#28	euroqol or eq5d or eq-5d	1569
#29	quality of wellbeing index or quality of well-being index or quality of well being index or qwb	12835
#30	health utilit* index or hui	7185
#31	medical outcomes survey or mos	4323
#32	chronic liver disease questionnaire or CLDQ	458
#33	time tradeoff or time trade-off or TTO	691
#34	standard gamble	511
#35	preference*	8078
#36	magnitude estimation	517
#37	#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 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36	220979
#38	#9 and #37	68

*Lines 10-37 are based on recommended HRQL search terminology from: Paisley S, Booth A, Mensinkai S. Chapter 12: health-related quality of life studies. In: Etext on Health Technology Assessment (HTA) Information Resources. [2005] (http://www.nlm.nih.gov/archive/20060905/nichsr/ehta/chapter12.html)

The data abstraction strategy:

Data from published studies included in the review were extracted in pre-specified data extraction tables. One reviewer independently extracted the data. Another reviewer independently cross checked the extracted data for accuracy and consistency. In cases of inconsistencies, it was resolved by consensus or discussion with a third reviewer.

Study selection

Table C2 summarises the eligibility criteria for studies identified in the systematic review of HRQL studies.

Patients with HE comprised the target population, in accordance with the decision problem. Patients were not required to have had prior episodes of HE or be in remission, as HRQL data pertaining to periods of remission as well as to overt HE episodes would be valuable for the de novo model prepared as part of this submission. Patients in the identified studies were not required to be receiving treatment for HE, as HRQL associated with untreated HE may be relevant to the de novo model.

Studies were limited to English language.

To select appropriate studies, de-duplicated citations were screened at the abstract level by one reviewer. Full-text versions (if available) were retrieved for the citations that were not excluded in this initial screening, and were subsequently screened by the same reviewer. Those studies that were not excluded at the full-text level were included in the review. Two additional levels of reviewers were available for consultation if a rationale for inclusion or exclusion was not immediately identified.

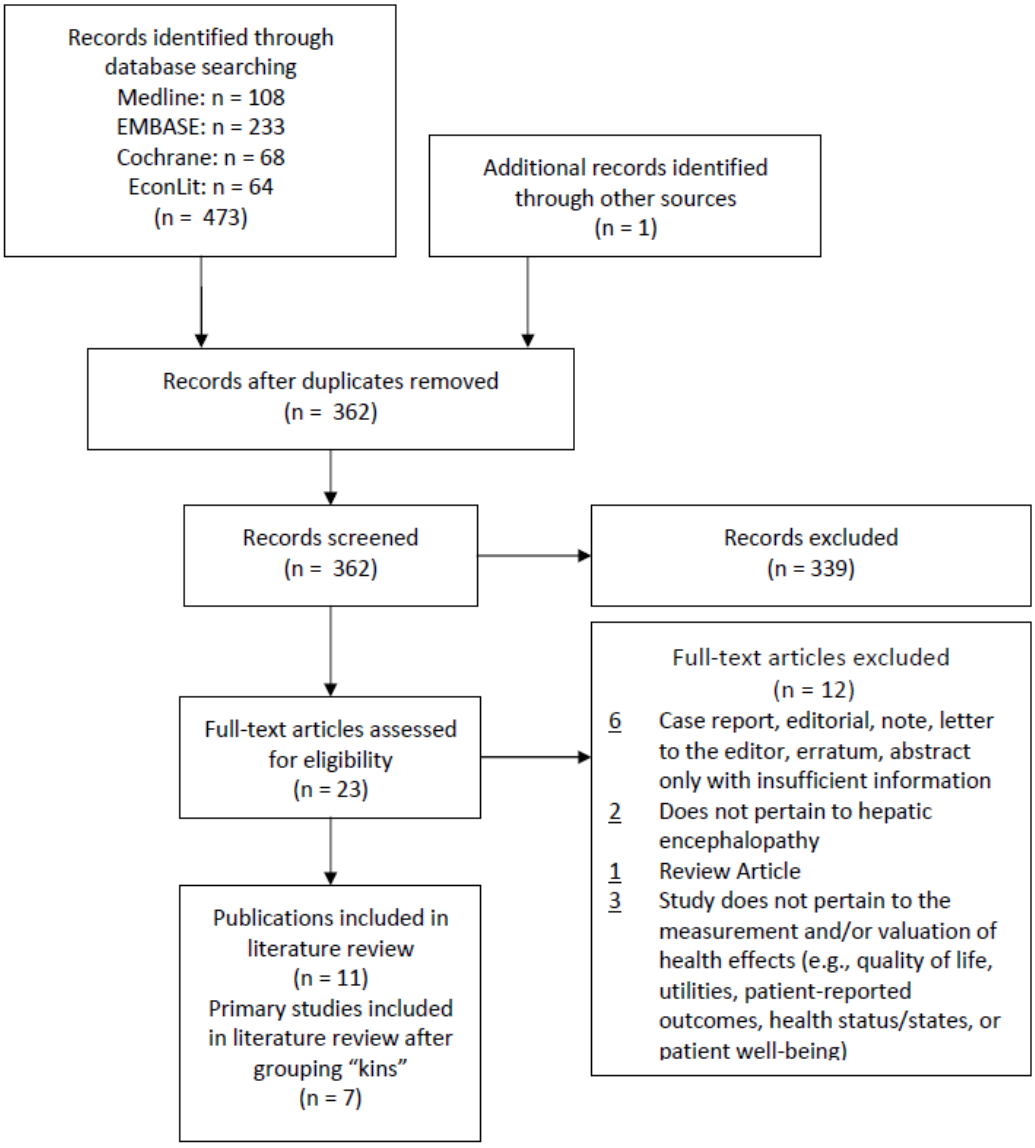
Table C2: Eligibility criteria used in search strategy

	HRQL
Inclusion criteria	Pertains to HE Adult patient population (≥ 18 years of age) Study pertains to the measurement and/or valuation of health effects (e.g., quality of life, utilities, patient-reported outcomes, health status/states, or patient well-being)
Exclusion criteria	Does not pertain to HE Case report, editorial, note, letter to the editor, erratum, or abstract only without sufficient information Review article Patient population <18 years of age Study does not pertain to the measurement and/or valuation of health effects (e.g., quality of life, utilities, patient-reported outcomes, health status/states, or patient well-being) Not in English

A PRISMA flow diagram of the systematic search and screening process is included in Fig C1

In total, 473 citations were identified in the searches of the Medline, Embase, Cochrane, and EconLit databases, with 1 additional record included from the conference abstract searches. After removal of duplicates, 362 records were screened at the abstract level. 339 records were excluded at the abstract level. Of the 23 records that advanced to full-text review, 12 were further excluded. Ultimately, 11 records fulfilled the inclusion criteria, pertaining to 7 primary studies (3 studies were represented by 2 or more records, explaining the discrepancy in total records and total primary studies).

Figure C1: PRISMA flow diagram for HRQL systematic review



A summary of the included HRQL studies as well as their associated "kins" is included in Table C3.

Table C3: Summary of citations included in the review of HRQL studies

	Citations Included in HRQL Review
Primary data sources	• Mittal et al. 2011 • Poo et al. 2006 • Prasad et al. 2007 • Sanyal et al. 2011 • Sidhu et al. 2011 • Takuma et al. 2010 • Zeng et al. 2006
Secondary ("kin") data sources identified in the systematic review	• Mittal et al. 2009 (kin to Mittal et al. 2011) • Sanyal et al. 2010 (kin to Sanyal et al. 2011) • Sidhu et al. 2010 (kin to Sidhu et al. 2011) • Younossi et al. 2011 (kin to Sanyal et al. 2011)

A summary of each the 7 HRQL studies identified in the systematic review described in section can be found in table C4.

Table C4: Summary list of HRQL data identified in systematic review:

Study	Population (including location)	Recruitment	Intervention/ Comparators (if applicable)	Sample Size and Response Rates	Health States Valued	Elicitation Method	Valuation Method	Mapping	Results (including measures of uncertainty)
Mittal et al. 2011	Hospitalised cirrhotic patients with MHE. Location: India	HRQL assessment was conducted as part of a RCT.	No Treatment (i.e. standard cirrhosis treatment) Lactulose 30-60 ml/d in divided dose for a stool frequency of 2-3 semisolid stools Probiotics (110 billion colony forming units twice daily) LOLA 6g 3 times per day	Randomised total: N= 160 Analysed: No Treatment: n=31 Lactulose: n=35 Probiotics: n=40 LOLA: n=40 [Response rates NR]	HRQL was assessed at baseline and at 3 months	Questionnaire in both English and Hindi translations	SIP	NA	After intervention, there was a statistically significant decrease in total SIP scores (ΔSIP score) in groups treated with Lactulose, Probiotics, and LOLA compared with No Treatment. Comparing Lactulose with Probiotics (P=0.573), Lactulose with LOLA (P=0.492), and Probiotics with LOLA (P=0.254) there was no significant improvement in SIP score. Δ SIP (P < 0.001): No Treatment: 1.05 ± 2.6 Lactulose: 6.98 ± 4.1 Probiotics: 6.24 ± 3.4 LOLA: 7.33 ± 3.8
Poo et al. 2006	Patients with hepatic cirrhosis, regardless of aetiology with chronic persistent	HRQL assessment was conducted as part of a RCT.	Lactulose monotherapy at 30mL/day for 2 weeks, which could be adjusted to a max of	Randomised: N=20 Lactulose: n=10 LOLA: n=10 [Response rates NR]	HRQL was assessed at baseline and at study end (i.e., 2 weeks from	Questionnaire	SF-36 EuroQoL VAS	NA	Baseline SF-36: Lactulose: 42.0 ± 19.5 LOLA: 47.0 ± 22.0 Final SF-36: Lactulose: 41.0 ± 15.3 LOLA: 54.0± 21.0

	grade I or II overt HE in the last 6 months and a fasting plasma ammonia > 60µg/dL Location: Mexico		60mL/day in accordance with researcher's opinion LOLA at 5g sachet formation containing granules at 9g/day for 2 weeks, which could be adjusted to a max of 18g/day in accordance with researcher's opinion		baseline)				Baseline Euro-QoL VAS: Lactulose: 51.1 24.1 LOLA: 56.5 24.5 Final Euro-QoL VAS (P<0.05): Lactulose: 61.5 ± 15.8 LOLA:70.0 ± 19.4
Prasad et al. 2007	All patients diagnosed as having cirrhosis Location: India	HRQL assessment was conducted as part of a Randomised un-blinded trial.	NMHE: Patients without MHE MHE-NL: Patients with MHE, not receiving lactulose MHE-L: Patients with MHE receiving	NMHE: n=29 Randomised: n=61 MHE-NL: n=30 MHE-L: n=31	HRQL was assessed at baseline and after 3 months of treatment	Questionnaire	SIP	NA	Total SIP at 0 months: NMHE: 1.73 (95%CI 1.40-2.07) MHE-NL: 10.36 (95%CI 8.98- 11.73) MHE-L: 10.39 (95%CI 9.36-11.43) (P<0.001 for MHE-NL and MHE-L comparisons to NMHE) Total SIP at 3 months: NMHE: 1.52 (95%CI 1.18-1.85) MHE-NL: 10.39 (95%CI 8.36-12.42) MHE-L: 3.77 (95%CI 2.52-5.02) (P<0.002 for MHE-L compared to MHE-NL)

			30-60ml of lactulose in 2 or 3 divided doses						ΔSIP: NMHE: 0.22 (95%CI -0.13-0.57) MHE-NL: 0.17 (95%CI -0.29-0.63) MHE-L: 6.81 (95%CI 5.24-8.37) (NMHE compared to MHE-NL, P=0.998; NMHE compared to MHE-L, P<0.001; MHE-NL compared to MHE-L, P<0.001)
Sanyal et al. 2011	≥18 yr., ≥2 episodes of overt HE (Conn score ≥ 2) associated with cirrhosis during the previous 6 months, remission (Conn score 0/1) at enrolment, and a score of ≤ 25 on the MELD Location: United States and Canada	HRQL assessment was conducted as a part of the RCT by Bass et al., 2010.	Rifaximin-α: 550mg twice daily Placebo	Randomised N= 219 Placebo: n= 118 Rifaximin-α: n=101	HRQL was assessed at baseline and days: 28, 56, 84, 112, 140, 168	Questionnaire	CLDQ	NA	Baseline mean (SD) overall CLDQ score: Rifaximin-α: 4.2 (1.2) Placebo: 4.1 (1.2) Patients who experienced overt breakthrough HE had a significantly lower time weighted average of the CLDQ score than patients who maintained remission from overt HE in all aspects of their HRQL as measured by CLDQ, irrespective of treatment with rifaximin-α or placebo. Spearmen correlation coefficient for overall CLDQ and breakthrough HE= -0.5830 (95% CI: -0.67, -0.49) Time-weighted averages for overall CLDQ score and individual domains score were significantly higher in rifaximin-α group than in placebo group for between-group differences in favour of rifaximin-α (P< 0.05)

									Significant improvement in responses to 26 individual items within CLDQ domains observed in those receiving rifaximin-α compared to placebo
Sidhu et al. 2011	Cirrhotic patients Location: India	HRQL assessment was conducted as part of a RCT.	Placebo Rifaximin-α: 200mg, two tablets 3 times a day for 8 weeks	Placebo: n=45 Rifaximin-α: n=49	HRQL was assessed at baseline and end of study (i.e. 8 weeks)	Questionnaire with both English and Hindi translations	SIP	NA	Baseline total SIP score: Placebo: 9.86 (95%CI 8.66-11.06) Rifaximin-α: 11.67 (95%CI 10.31-13.03) MHE negative: 2.12 (95%CI 1.96-2.28) MHE total (inclusive of Placebo and Rifaximin-α): 10.71 (95%CI 9.80-11.61) 8 weeks total SIP score: Placebo: 8.51 (95%CI 7.35-9.67) Rifaximin-α: 6.45 (95%CI 5.59-7.30) (P=0.000) ΔSIP score from 0-8 weeks (P=0.00): Placebo: 0.88 (95%CI 0.47-1.29) Rifaximin-α: 4.61 (95%CI 3.76-5.46)
Takuma et al. 2010	Cirrhotic patients with grade 1/ 2 recurrent episodic HE unresponsive to standard therapies	HRQL assessment was conducted as part of a RCT	Zinc: Polaprezinc 225mg in addition to ongoing standard therapies of protein-restricted diet including BCAA and lactulose	Analysed: Zinc: n=39 Control: n=40	HRQL was assessed at baseline and at 6 months	Questionnaire	SF-36	NA	RP and PCS in the zinc group significantly improved after 6 months (p=0.04 and P=0.02, respectively). There was no significant change in the control group. Significant improvements in PF, RP, and PCS in the zinc group were found compared to the control group (P=0.04, P<0.01, and P=0.04, respectively).

	Location: Japan		Control: Only standard therapies						Baseline SF-36: Control: PF: 65.4 ±26.3 RP: 50.5 ± 33.9 BP: 65.4 ± 23.2 GH: 41.9 ± 18.5 VT: 50.9 ± 24.5 SF: 66.9 ± 28.2 RE: 54.4 ± 33.3 MH: 63.3 ± 24.2 PCS: 35.9 ± 13.2 MCS: 43.3 ± 12.7 NCT-A (s): 72.6 ± 30.5 NCT-A (abnormal/ normal): 23/17 NCT-B(s): 141.6 ± 31.3 NCT-B (abnormal/normal): 31/9 DST (points): 10.9 ± 3.8 DST (abnormal/normal): 31/9 Mean #s abnormal NP tests: 2.1 ± 1.0 Zinc: PF: 64.9 ±24.6 RP: 57.4 ± 31.3 BP: 56.7 ± 24.4 GH: 41.4 ± 20.1 VT: 48.7 ± 20.0 SF: 71.5 ± 23.3 RE: 62.8 ± 31.2 MH: 67.1 ± 20.2 PCS: 34.5 ± 13.3 MCS: 46.5 ± 10.4 NCT-A (s): 78.8 ± 27.0 NCT-A (abnormal/ normal): 30/9 NCT-B(s): 145.8 ± 30.4 NCT-B (abnormal/normal): 32/7

									DST (points): 9.8 ± 2.4 DST (abnormal/normal): 31/8 Mean #s abnormal NP tests: 2.4 ± 1.0
Zeng et al. 2006	Cirrhotic patients. Location: China	HRQL assessment was conducted as part of a case-control observational study.	Control: vitamin B for 24 weeks, 2 tablets for each 3 times a day Short-term: lactulose 15-90mL per day. Dosage adjusted according to times of stool every day (2 or 3 times) for 8 weeks Long-term: same as short term, but for 24 weeks	HRQL analysis: Control: n=19 Short-term: n=19 Long-term: n=18	HRQL was assessed at weeks 0, 8, 16, and 24	Questionnaire if the patient was literate. If the patient was illiterate, professional interviewers were available.	WHOQOL-BREF	NA	Before treatment: Physiological: Control: 42.9 ± 17.2 Short: 49.6 ± 17.4 Long: 47.0 ± 22.9 Before treatment: Psychological: Control: 55.2 ± 12.1 Short: 57.5 ± 17.7 Long: 52.3 ± 17.1 Before treatment: Social: Control: 51.7 ± 17.6 Short: 55.0 ± 18.2 Long: 56.2 ± 21.3 Before treatment: Environmental: Control: 55.3 ± 16.0 Short: 54.7 ± 14.7 Long: 52.7 ± 13.1 8 weeks: Physiological: Control: 36.6 ± 15.5 Short: 61.8 ± 13.0 Long: 61.2 ± 17.6 8 weeks: Psychological: Control: 47.3 ± 14.1 Short: 67.9 ± 12.7 Long: 65.6 ± 15.2

									8 weeks: Social: Control: 45.9 ± 14.7 Short: 64.2 ± 17.1 Long: 67.9 ± 16.3 8 weeks: Environmental: Control: 53.1 ± 15.3 Short: 56.6 ± 12.4 Long: 55.0 ± 14.2 16 weeks: Physiological: Control: 33.2 ± 18.0 Short: 42.9 ± 17.1 Long: 60.2 ± 21.6 16 weeks: Psychological: Control: 43.8 ± 13.1 Short: 51.0 ± 13.7 Long: 64.4 ± 17.4 16 weeks: Social: Control: 38.6 ± 15.2 Short: 46.5 ± 5.4 Long: 65.4 ± 16.5 16 weeks: Environmental: Control: 52.8 ± 15.8 Short: 52.8 ± 15.4 Long: 51.7 ± 14.6 24 weeks: Physiological:

									Control: 28.4 ± 18.7 Short: 37.2 ± 18.0 Long: 54.0 ± 18.9 24 weeks: Psychological: Control: 41.5 ± 13.9 Short: 44.3 ± 14.9 Long: 58.3 ± 14.9 24 weeks: Social: Control: 37.5 ± 15.5 Short: 42.0 ± 15.34 Long: 59.7 ± 17.4 24 weeks: Environmental: Control: 51.2 ± 17.8 Short: 53.1 ± 15.0 Long: 50.7 ± 12.9

Abbreviations: BP = bodily pain; DST = digital symbol test; GH = general health; LOLA = L-ornithine L-aspartate; MELD = Model for End Stage Liver Disease; MHE = minimal hepatic encephalopathy; MCS = mental component scale; MH = mental health; NCT = number connection test; NP = neuropsychometric; OHE = overt hepatic encephalopathy; PCS = physical component scale; PF = physical functioning; RE = role emotional; RP = role playing; SF-36 = short-form-36 v2; SF = social functioning; SIP = sickness impact profile; VAS = visual analogue scale; VT = vitality