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# Impact of physical and psychological factors on health-related quality of life in adult patients with liver cirrhosis: a systematic review protocol

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# Impact of physical and psychological factors on health-related quality of life in adult patients with liver cirrhosis: a systematic review protocol

## Abstract

**Review question/objective** What is the impact of physical and psychological factors on health-related quality of life in adult patients diagnosed with liver cirrhosis?

**Background** All chronic liver diseases stimulate a degree of repetitive hepatocyte injury that alters the normal liver architecture and ends in cirrhosis. Liver cirrhosis and hepatocellular carcinoma secondary to liver cirrhosis are a major public health burden, reporting increasing mortality and morbidity both in Australia and globally. The four leading causes of cirrhosis include harmful alcohol consumption, viral hepatitis B and C and metabolic syndromes related to non-alcoholic fatty liver disease and obesity. A cirrhotic liver is characterized by the presence of regenerative nodules surrounded by fibrous bands that inhibit the passing of molecules between blood and functional units of liver hepatocytes, leading to liver dysfunction. Additionally, the presence of fibrous bands disrupts the normal vascular architecture, increasing resistance within the liver sinusoids and contributing to increased portal vein pressure.

The early stages of cirrhosis are referred to as compensated liver disease with no reported symptoms or evidence of impaired liver function. However, the signs and symptoms of liver failure, as well as the mortality rate, increase as the severity of cirrhosis increases. Transition from compensated to decompensated cirrhosis is marked by one or more physiological changes. The physiological changes include increased portal vein pressure, impaired synthetic function, electrolyte imbalance and malnourishment. These physiological changes trigger the development of physical signs and symptoms and impact on the psychological wellbeing of the individual living with cirrhosis. The physical signs and symptoms include esophageal varices, ascites, hepatic encephalopathy, jaundice, irregular sleep patterns, muscle cramps, pruritus, fatigue, impaired mobility, breathlessness, abdominal discomfort, gastrointestinal symptoms, change of body image and pitting edema. Psychological symptoms include stress, depression and anxiety.

## Disciplines

Medicine and Health Sciences | Social and Behavioral Sciences

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# Impact of physical and psychological factors on health-related quality of life in adult patients with liver cirrhosis: a systematic review protocol

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## Review question/objective

What is the impact of physical and psychological factors on health-related quality of life in adult patients diagnosed with liver cirrhosis?

## Background

All chronic liver diseases stimulate a degree of repetitive hepatocyte injury that alters the normal liver architecture and ends in cirrhosis.<sup>1</sup> Liver cirrhosis and hepatocellular carcinoma secondary to liver cirrhosis are a major public health burden, reporting increasing mortality and morbidity both in Australia and globally.<sup>2-6</sup> The four leading causes of cirrhosis include harmful alcohol consumption, viral hepatitis B and C and metabolic syndromes related to non-alcoholic fatty liver disease and obesity.<sup>7-9</sup>

A cirrhotic liver is characterized by the presence of regenerative nodules surrounded by fibrous bands that inhibit the passing of molecules between blood and functional units of liver hepatocytes, leading to liver dysfunction.<sup>1,10,11</sup> Additionally, the presence of fibrous bands disrupts the normal vascular architecture, increasing resistance within the liver sinusoids and contributing to increased portal vein pressure.<sup>10,12</sup>

The early stages of cirrhosis are referred to as compensated liver disease with no reported symptoms or evidence of impaired liver function.<sup>12,13</sup> However, the signs and symptoms of liver failure, as well as the mortality rate, increase as the severity of cirrhosis increases.<sup>13</sup> Transition from compensated to decompensated cirrhosis is marked by one or more physiological changes. The physiological changes include increased portal vein pressure, impaired synthetic function, electrolyte imbalance and malnourishment.<sup>13</sup> These physiological changes trigger the development of physical signs and

symptoms and impact on the psychological wellbeing of the individual living with cirrhosis. The physical signs and symptoms include esophageal varices, ascites, hepatic encephalopathy, jaundice, irregular sleep patterns, muscle cramps, pruritus, fatigue, impaired mobility, breathlessness, abdominal discomfort, gastrointestinal symptoms, change of body image and pitting edema.<sup>14-17</sup> Psychological symptoms include stress, depression and anxiety.<sup>18,19</sup>

Living with liver cirrhosis has a marked impact on the quality of life of the individual. Health-related quality of life (HRQOL) is the individual's perception of their physical, cognitive, emotional and social functioning.<sup>20</sup> Studies report that physical and psychological factors affect the quality of life of patients with cirrhosis which can be problematic and debilitating.<sup>18,21-28</sup> There is strong evidence which indicates that disease severity is associated with an impairment of the patient's HRQOL.<sup>15,18,22,24-26,29</sup> For example, gross ascites causes abdominal discomfort, breathlessness, increased stress and anxiety related to body image, immobility and an increased likelihood of falls. In addition, the management of ascites involves frequent invasive procedures, an increase in pill burden and implementation of dietary restrictions, all of which impact on HRQOL.<sup>26</sup>

Despite the clear relationship between HRQOL and severity of disease, there has been no systematic review undertaken to determine the physical, psychological and physiological factors that affect the HRQOL of patients with liver cirrhosis. This systematic review will therefore identify the best available evidence related to the impact of physical, psychological and physiological factors on the health-related quality of life of adult patients with liver cirrhosis. The results of the review will increase clinicians' knowledge and highlight areas of clinical management that may require additional strategies and treatment plans to improve symptom relief and HRQOL.

## **Keywords**

Cirrhosis; health related quality of life; encephalopathy

## **Inclusion criteria**

### ***Types of participants***

This review will consider studies that include adult patients aged 18 years and over who have been clinically diagnosed with compensated or decompensated liver cirrhosis. Studies investigating non-liver disease-related cirrhosis, the use of herbal medications, pre- and post-liver transplant and/or hepatocellular carcinoma patients, include non-cirrhotic patients, inpatient data, non-liver-related comorbidities, patients undergoing interferon therapies and clinical trial studies investigating the use of medications or alternate interventions on HRQOL will be excluded.

### ***Types of intervention(s)/phenomena of interest***

Studies will be included if they have assessed the impact of the following physical and psychological factors on the HRQOL of patients. The physical factors will include but not limited to esophageal varices, ascites, hepatic encephalopathy, jaundice, irregular sleep patterns, muscle cramps, pruritus, fatigue, impaired mobility, breathlessness, abdominal discomfort, gastrointestinal symptoms, muscle wasting and pitting edema. The psychological factors include stress, depression and anxiety.

**Types of outcomes**

Studies will be included if they have objectively measured HRQOL including measuring any of the following domains: physical, social and family wellbeing; and emotional, psychological and functional wellbeing.

Studies will be included if quality of life has been measured using objective scales including but not limited to Liver Disease Quality of Life 1.0 (LDQOL), Short Form 36 Profile (SF-36), Chronic Liver Disease Questionnaire (CLDQ), Liver disease symptom index 2.0 (LDSI 2.0), Hepatitis Quality of Life Questionnaire.

**Types of studies**

This review will consider experimental study designs including prospective and retrospective cohort studies and descriptive studies for inclusion.

**Search strategy**

The search strategy aims to find both published and unpublished studies. A three-step search strategy will be utilized in this review. An initial limited search of the Cochrane Library, MEDLINE and CINAHL will be undertaken, followed by analysis of the text words contained in the titles and abstracts, and of the index terms used to describe the articles. A second search using all identified keywords and index terms will then be undertaken across all included databases. Thirdly, the reference lists of all identified reports and articles will be searched for additional studies. Studies published in the English language will be considered for inclusion in this review due to limited resources. Studies published from 1999 will be considered for inclusion in the review as this is when HRQOL data specific to chronic liver disease and excluding chronic hepatitis C were first reported.<sup>30-32</sup>

The databases to be searched include: Medline, CINAHL, Embase, Cochrane Central Register of Controlled Trials (CENTRAL) and Scopus

The search for unpublished studies will include: ProQuest Dissertation & Theses and MedNar

Initial key words to be used will be:

Cirrhosis

Quality of life

Health related quality of life

Encephalopathy

Ascites

Portal hypertension

Esophageal varices

Muscle cramps

Cognitive impairment

Sleep disturbance

Pitting edema  
Depression  
Pruritus  
Health distress  
Activity  
Memory  
Hypo-natremia  
Hypo-albuminemia  
Anxiety  
Alexithymia  
Abdominal bloating  
Abdominal pain  
Diarrhea  
Fecal incontinence.

### **Assessment of methodological quality**

Quantitative papers selected for retrieval will be assessed by two independent reviewers for methodological validity prior to inclusion in the review using standardized critical appraisal instruments from the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) (Appendix I). Any disagreements that arise between the reviewers will be resolved through discussion, or with a third reviewer.

### **Data collection**

Quantitative data will be extracted for papers included in the review using the standardized data extraction tool from JBI-MAStARI (Appendix II). The data will be extracted independently by one author and checked by a second author. The data extracted will include specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives. Authors of primary studies will be contacted for missing information or to clarify unclear data.

### **Data synthesis**

Quantitative papers will, where possible, be pooled in statistical meta-analysis using JBI-MAStARI. All results will be subject to double data entry. Effect sizes expressed as odds ratios (for categorical data) and weighted mean differences (for continuous data) and their 95% confidence intervals will be calculated for analysis. Heterogeneity will be assessed statistically using the standard chi-square and also explored using sub-group analyses based on different quantitative study designs included in this review. Where statistical pooling is not possible, the findings will be presented in narrative form including tables and figures to aid in data presentation where appropriate.

### **Conflicts of interest**

No conflicts of interest can be identified or foreseen in relation to this proposed systematic review.

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## Appendix I: Appraisal instruments

### MAStARI appraisal instrument

#### JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial

Reviewer ..... Date .....

Author ..... Year ..... Record Number .....

	Yes	No	Unclear	Not Applicable
1. Was the assignment to treatment groups truly random?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were participants blinded to treatment allocation?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Was allocation to treatment groups concealed from the allocator?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Were the outcomes of people who withdrew described and included in the analysis?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Were those assessing outcomes blind to the treatment allocation?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Were the control and treatment groups comparable at entry?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were groups treated identically other than for the named interventions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Were outcomes measured in the same way for all groups?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Were outcomes measured in a reliable way?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Was appropriate statistical analysis used?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal:    Include                   Exclude                   Seek further info.

Comments (Including reason for exclusion)

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**JBI Critical Appraisal Checklist for Descriptive / Case Series**

Reviewer ..... Date .....

Author ..... Year ..... Record Number .....

	Yes	No	Unclear	Not Applicable
1. Was study based on a random or pseudo-random sample?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were the criteria for inclusion in the sample clearly defined?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Were confounding factors identified and strategies to deal with them stated?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Were outcomes assessed using objective criteria?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. If comparisons are being made, was there sufficient descriptions of the groups?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Was follow up carried out over a sufficient time period?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were the outcomes of people who withdrew described and included in the analysis?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Were outcomes measured in a reliable way?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Was appropriate statistical analysis used?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal:      Include                   Exclude                   Seek further info

Comments (Including reason for exclusion)

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**JBI Critical Appraisal Checklist for Comparable Cohort/ Case Control**

Reviewer ..... Date .....

Author ..... Year ..... Record Number .....

	Yes	No	Unclear	Not Applicable
1. Is sample representative of patients in the population as a whole?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Are the patients at a similar point in the course of their condition/illness?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Has bias been minimised in relation to selection of cases and of controls?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Are confounding factors identified and strategies to deal with them stated?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Are outcomes assessed using objective criteria?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Was follow up carried out over a sufficient time period?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were the outcomes of people who withdrew described and included in the analysis?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Were outcomes measured in a reliable way?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Was appropriate statistical analysis used?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal:    Include                     Exclude                     Seek further info.

Comments (Including reason for exclusion)

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**Appendix II: Data extraction instruments**

**MAStARI data extraction instrument**

**JBI Data Extraction Form for  
Experimental / Observational Studies**

Reviewer ..... Date .....

Author ..... Year .....

Journal ..... Record Number .....

**Study Method**

RCT                       Quasi-RCT                       Longitudinal   
 Retrospective                       Observational                       Other

**Participants**

Setting \_\_\_\_\_

Population \_\_\_\_\_

**Sample size**

Group A \_\_\_\_\_ Group B \_\_\_\_\_

**Interventions**

Intervention A \_\_\_\_\_

Intervention B \_\_\_\_\_

Authors Conclusions:

\_\_\_\_\_  
 \_\_\_\_\_

Reviewers Conclusions:

\_\_\_\_\_  
 \_\_\_\_\_

**Study results**

**Dichotomous data**

Outcome	Intervention ( ) number / total number	Intervention ( ) number / total number

**Continuous data**

Outcome	Intervention ( ) number / total number	Intervention ( ) number / total number