## **School of Medicine**

Systematic Review Protocol & Support Template

This template is primarily intended to help you plan your review in a systematic way. Keeping a record of all the reviews will also assist in planning the work of the Centre and ensuring adequate methodological support. Not all the information will be relevant to every review and items should be adapted to fit the type of review that is being undertaken.

The template has been updated to include all the items from the PRISMA-P checklist (<http://www.prisma-statement.org/Extensions/Protocols.aspx>). All systematic reviews should be registered with PROSPERO database (<http://www.crd.york.ac.uk/PROSPERO/>) unless the review is methodological.

Please complete the form in as much detail as possible for your review and email to one of the SR Team:- Yemi (Opeyemi) Babatunde, o.babatunde@keele.ac.uk, Jo Jordan, j.jordan@keele.ac.uk, or Nadia Corp, n.corp@keele.ac.uk.

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| Title of the review | **A systematic review of international guidelines on the management of gastro oesophageal varices in acute on chronic liver failure.**  |
| **First reviewer** | Saumiya Kesavan |
| **Other reviewers (with role/contribution in the review)** | Dr Sara Muller – supervisor Dr Rajeev Desai- supervisor  |
| **Clinical Portfolio Group** |  |
| **Funding source** | Self-funded |
| **PROSPERO registration number** | Will get this done  |

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| **Amendments to the protocol** |  |

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| 1. **Background to review**

Brief introduction to the subject of the review, including rationale for undertaking the review and overall aim |
| Chronic liver disease (CLD) is a major cause of mortality in the UK. CLD can have multiple effects on various systems of the body and can lead to complications including upper gastrointestinal variceal bleeding. The management of these complications have been thoroughly studied to produce various guidelines. The aim of this is systematic review is to assess the quality of international guidelines in the management of gastro intestinal varices in acute on chronic liver disease |

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| **2.** **Specific objectives/questions the review will address** |
| Varices:  * Identify the current published guidelines for the primary and secondary prophylactic treatment for upper gastrointestinal varices.
* Identify the current published guidelines for the management of acute upper gastrointestinal variceal haemorrhage
* Critically appraise the existing clinical practical guidelines to assess their quality based on the evidence that they have used to come to those recommendations in the treatment of upper gastrointestinal varices using the AGREE II checklist
* Compare and contrast the identified guideline recommendations (for prophylaxis and haemorrhage) and relate this to the quality of evidence used in generation of the individual guidelines.

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| **3. a) Eligibility Criteria for including studies in the review** If the PICOS format does not fit the research question of interest, please split up the question into separate concepts and put one under each heading |
| * + 1. **Population, or participants and conditions of interest**
 | **Patients with acute on chronic liver disease**  |
| * + 1. **Interventions/Exposure/item of interest**
 | **Varices is the exposure. Varices are the complications that can occur in people with acute on chronic liver disease. The potential relevant search terms to pick up varices will include: varic\*, varix\*, dilated blood vessel.**  |
| * + 1. **Comparisons or control groups, if any**
 | **NA**  |
| * + 1. **Outcomes of interest**
 | **NA** |
| * + 1. **Setting**
 | **NA** |
| * + 1. **Study designs**
 | **Clinical guidelines will be used. The clinical guidelines should be evidenced-based and not opinion based. We will include studies that are backed by both systematic reviews and clinical evidence.**  |

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| **3. b) Criteria for excluding studies not covered in inclusion criteria** Any specific populations excluded, date range, language, whether abstracts or full text available, etc |
| * **Paediatric guidelines**
* **If only the abstract is available**
* **Guidelines in other languages for which the research team cannot access appropriate translation**
* **Cover only other complications of liver disease such as hepatorenal syndrome, ascites**
* **Guidelines superseded by a newer version**
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| **4. Search methods** |
| Electronic databases & websitesPlease list all databases that are to be searched and include the interface (e.g. NHS HDAS, EBSCO, OVID etc) and date ranges searched for each.**NB All search strategies should be reviewed by Jo Jordan or Nadia Corp BEFORE searching begins** | * MEDLINE via OVID
* EMBASE via OVID
* Web of Science (Science Citation Index only)
* TRIP Database for clinical guidelines.
* Epistemonikos for clinical guidelines.
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| **Other methods used for identifying relevant research** ie contacting experts and reference checking, citation tracking | * Checking the references of included papers
* Conference abstracts to ascertain whether full paper is available

14/12/21: We may ask experts for their opinion regarding the inclusion of some of the papers. They may also have an idea what papers should be included that may necessarily not have been part of the search.  I will check websites of relevant professional organisations and include guidelines written in English : * European association for the study of the liver (EASL)
* National institute of clinical excellence (NICE)
* American association for the study of liver disease (AASLD)
* Asian pacific association for the study of the liver (APASL)
* Armenian hepatological forum (AHF)
* Austrian society of gastroenterology and hepatology (OEGGH)
* Azerbaijan Gastroenterologists and Hepatologists association (AGHA)
* Byelorussian Gastroenterology association
* Belgian Association for the Study of the Liver (BASL)
* Association of Gastroenterologists and Hepatologists in Bosnia and Herzegovina
* Bulgarian society of gastroenterology
* Croatian Society of gastroenterology
* Czech Society of Hepatology (CSH)
* Danish gastroenterology and hepatology association (DSGH)
* Eesti Gastroenteroloogide Selts, Estonian Socity of Gastroneterology
* Finish Society of Gastroenterology
* Association Fracaise Pour l’Etude du Foie (AFEF)
* Georgian Hepatology Association
* German Association for the study of the liver (GASL)
* Hullenic Association for the study of the liver (HASL)
* Hungarian Liver Research society
* Irish society of Gastroenterology (ISG)
* Israel Association for the study of the liver diseases
* Associazione Italiana per lo Studio del Fegato (AISF)
* GastroHepato TransplantGroup Astana
* Latvian Association of Infectologists and Hepatologists
* Lithuanina Society of Gastroenterology
* Polish Association for the study of the liver (PASL)
* Associacao Poruguesa para o Estudo do Figado (APEF)
* Romanian Association for the study of the liver (ARSF)
* Russian Scientific Liver Society (RSLS)
* Hepatology section of the Serbian Medical Society
* Slovak Society of Hepatology
* Slovenian Society for Gastroenterology and Hepatology
* Asociacion Espanola para el Estudio del Higado (AEEH)
* Svensk Gastroenterologisk Förening (SGF)
* Swiss Association for the Study of the Liver (SASL)
* Nederlandse Vereniging voor Hepatologie Duth Society for Hepatology
* Turkish Association for the Study of the Liver (TASL)
* Ukraninan Association for the study of the liver disease (UASL)
* The British Association for the study of the liver (BASL)
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| Journals hand searchedIf any are to be hand searched, please list which journals and date searched from, including a rationale.  |  NA |

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| **5. Methods of review** |
| How will search results be managed & documented?ie which reference management software, how duplicates dealt with | * Zotero can be used as a web-based bibliography. This will also be able to delete the duplicates/ near close matches. This will be then exported into Rayyan, a free software, that will help with the screening process- titles and abstract.
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| Selection processNumber of reviewers, how agreements to be reached and disagreements dealt with, etc. | The current selection criteria:* Saumiya Kesavan will screen the titles initially by herself.
* There will be two reviewers past the title screening stage- Saumiya Kesavan and either Sara Muller or Rajeev Desai.
* At the abstract screening stage, any paper included by either reviewer will be retained.
* At the full text screening stage, any disagreements will be resolved through discussion. If agreement in not possible, the third reviewer will arbitrate
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| Quality assessmentTools or checklists used with references or URLs, was this piloted? Is it to be carried out at same time as data extraction? | AGREE II – this is a quality appraisal tool that has been used extensively to appraise the quality of guidelines. The AGREE 2 checklist contains 6 domains. As the appraiser, we are allowed to prioritise the domains and assess their scores. This will be done at the same time as data extraction. AGREE II developers suggest the use of a score of 70% or more on the most important domain (as defined by the review team) to take the guidelines forward for assessment of the other domains. This process will be modified slightly. First, a three-stage process will be adopted. 1) Domain 1 (scope and purpose) will be used to ensure the guideline is relevant to the question posed, 2) Domain 3 (rigour of development) will be used to ensure only high quality, evidence-based guidelines are included in the final review. 3) Domains, 2, 4, 5,6 will be assessed in the remaining guidelines. Second, scores will be used to help inform decisions and discussion between reviewers, but not as the sole basis on which to reject a guideline. Choices as to inclusion or exclusion of a guideline from the review based on Domain 1 and Domain 3 will be based on this discussion, which will be documented, and not only on a score over 70%. However, it is expected that the majority of included guidelines will score ≥70% on these domains and those excluded will score <70%. Where this is not the case, a detailed argument will be given. AGREE II Domain 1 (scope and purpose) will be used to confirm the eligibility of the study for the review. Any guideline that does not clearly address the management of varices in liver disease will not be taken forward.Domain 3 (rigour of development) will be used to further screen out low quality guidelines that were not based on a sufficiently rigorous review of the evidence and or on poor quality evidence. Domains 2, 4, 5 and 6 will be completed for those guidelines remaining in the review after assessment against Domains 1 and 3. These will be used to enable the remaining reviews to be compared and contrasted more holistically in terms of quality. This will allow the review to feed into another objective of the MPhil project of which this systematic review is the first part – the highest quality guideline(s) will be used as an audit standard against which to compare local data. The use of this checklist and associated data extraction, will be piloted by Saumiya Kesavan and Sara Muller against the British Gastroenterology Society (BSG) guidelines. |
| **How is data to be extracted?**What information is to be collected on each included study? If databases or forms on Word or Excel are used, were these piloted and how is this recorded and by how many reviewers? | * A pilot of the data extraction will be carried out using the BSG guidelines. The data extraction will be done by two reviewers: Saumiya Kesavan and either Sara Muller or Rajeev Desai.
* For the data extracted, see appended document.
* Alongside of this, the quality appraisal will also be done using the AGREE 2 checklist.
* Data extraction will be done on the guidelines in accordance to the appended document which will have the header on them.
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| **Outcomes to be extracted & hierarchy/priority of measures**ie which measure is preferred and if that is not available which is next in order of preference? | The focus of this review is on quality and identifying guidelines based on high quality evidence. However, for all guidelines retained after applying AGREE II Domain 1 (scope and purpose), the recommendations in the guidelines will be compared between those scoring highly on Domain 3 (and therefore retained for the other domains) and those scoring less highly and not assessed using the remaining AGREE II domains. Guidelines that are assessed against Domains 2, 4, 5 and 6 and scoring highly (using ≥70% as a guide, but at the discretion of the review team, with documenting of reasoning) will be compared in terms of their content against those guidelines scoring less highly on these domains.  |
| Narrative synthesisDetails of what methods, how synthesis will be done and by whom. Is the Narrative Synthesis Framework to be used? | The narrative synthesis will be done by Saumiya Kesavan. The data will be **tabulated** so that comparisons can be made between the different clinical practice guidelines, based on factors such as: similarities, differences, strength of the data, and quality appraisal scores using the AGREE 2 checklist. Although we will not look at subgroups of patients, we will break down the results by recommendations, and see what the overall popular recommendations are. With these recommendations, we will see which guidelines support this view and what their quality appraisal score is (AGREE 2). We will also be doing the same for the recommendations that are not as prominent, and see which guidelines support this and what their quality appraisal score is.  |
| **Meta-analysis** Details of what and how analysis and testing will be done. If no meta-analysis is to be conducted, please give reason. | NA |
| Will the overall strength of evidence be assessed? If so, how? ie GRADE? | We will present the scores over the 6 domains in the AGREE 2 checklist for the guidelines that are included in the review.  |

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| **6. Presentation of results** |
| Outputs from review Papers and target journals, conference presentations, reports, etc | MPhil thesisPublication and conference attendance: * Midland Gastroenterology Society conference November 2022 (abstract in for summer of 2022).
* British Society of Gastroenterology annual conference (20-23 June 2022)
* United European Gastroenterology Week 2022 (October 8-11 2022)
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| **7. Timeline for review – when do you aim to complete each stage of the review** |
| **Protocol**  | 30/09/2021 |
| **Literature searching** | 8/10/2021 (will do this alongside the protocol development)  |
| **Screening search results** | 22/10/2021 |
| **Quality appraisal** | 31/01/2022 |
| **Data extraction** | 31/01/2022 |
| **Synthesis** | 31/03/2022 |
| **Writing up** | This should be done alongside the review |

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| **Support** – please state if advice/training or personnel required at each stage |
| **SR overview** | Advice/ training required |
| **Protocol development** | Advice/ training required |
| **Literature searching** | Advice/ training required |
| **Screening (Titles & abstracts and full text)** | Advice/ training required |
| **Quality appraisal** | Advice/ training required |
| **Data Extraction** | Advice/ training required |
| **Synthesis** | Advice/ training required |
| **Writing up** | Advice/ training required |

Please send your completed protocol to Opeyemi, Nadia or Jo (see email below) so we can give you advice on your review.

The systematic review team are available to answer any queries or give advice on completing your review. Systematic review workshops are run at least once a year or can be arranged on an ad hoc basis if needed by a group.

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Jo Jordan – j.jordan@keele.ac.uk