Evidence checking process

Quality Use of Medicines in People Living with Dementia Priority Setting Partnership (PSP)

Instructions for Information Specialists

Introduction

Each evidence checker (i.e. you!) will be given a list of questions for research to check. These have come from a consultation of consumers and clinicians, so are not worded as technical research questions. As much as possible, individuals will be given questions which are within their area of interest/expertise – you may be able to say whether or not the question is 'unanswered' or not based on your existing knowledge, however, the following process still needs to be followed in order to account for and document the rationale.

"The JLA recommends that the evidence search is **pragmatic and proportionate**. A PSP should be confident that the questions it puts forward for prioritisation are broadly unanswered and should demonstrate clearly and accountably in the Question Verification Form how it came to that conclusion." (Please fill out the spreadsheet that you have been provided as the information here is used to complete the Question Verification Form.)

As a reminder: At the completion of the evidence checking process we will have a list of 'unanswered questions', i.e. questions/topics/areas where more research is needed to inform practice – another way of thinking about this is that a level of **uncertainty** still exists in this area (potentially despite some pockets of evidence). The questions that are determined to be 'answered' will be removed from the list and will not be considered in future prioritisation work.

- JLA definition of **uncertainty**: no up-to-date, reliable systematic reviews of research evidence addressing the uncertainty about the effects of the intervention/how to achieve a goal exist; or up-to-date systematic reviews of research evidence show that uncertainty exists.

Step 1

Familiarise yourself with your list of research questions (in spreadsheet). I have tried to provide people with similar questions to review – it may be possible for you to conduct the following process for more than one question at a time (i.e. your search strategy could include multiple terms for the different questions).

Additionally, I recommend you review/read the full list of research questions (this will be shared with you in a separate Word document). As you will see in Step 5 you are encouraged to document if unanswered questions are reported in the resources that you're reading (i.e. if the resource you are reading specifically states that a particular research question is unanswered/needs more research – where this is different to the question you were doing the evidence checking for).

Step 2

Begin evidence checking: searching (document that you have searched each database listed in the spreadsheet)

For each question, search the following databases/registries:

- Cochrane Database of Systematic Reviews (systematic reviews only, do not have to look at protocols, clinical trials registries or individual studies)
- NICE Guidelines
- NHMRC Guidelines registry – NB: this registry contains guidelines that have been developed/approved by NHMRC as well as those that haven't. For those that haven't, you will need to consider reliability of the guideline if you are considering assessing the research as answered.

If you feel that your question is one that wouldn't be answered in a guideline or Cochrane review, you can conduct additional searching of the following databases. (This is optional.)

- Relevant Professional associations guidance (where relevant) (e.g. search on their website, or can do a Google search for the organisation+guideline etc)
- PubMed/Medline
- https://www.epistemonikos.org/ - Combines the best of Evidence-Based Health Care, information technologies and a network of experts to provide a unique tool for people making decisions concerning clinical or health-policy questions.

You may want to login through your university library so that you can immediately look at the full text where an abstract appears to be relevant. It is up to you how you want to conduct this step – but other than Cochrane reviews possibly appearing in your PubMed search, there may not be an overlap between these – as such I suspect it will be just as quick to review the results for each database one by one rather than downloading the results into a reference manager (such as EndNote) to remove duplicates. Additionally, you do not need to look at all the citations that result from your search, it should be directed by whether you think there are likely to be relevant citations later down the list (considering that the most relevant results are returned at the top of the list).

Limits

When checking an uncertainty against a systematic review, the review needs to be relevant, up-to-date and reliable.

- The JLA recommends that an up-to-date systematic review is less than three years old **– limit searches to 2018 – onwards.** There is flexibility in relation to including sources that are older than this if you think that it shows that the question has been answered. E.g. If you are aware of an earlier guideline or systematic review (or become aware when looking at other articles).

Search terms

Search terms can be created/amended according to the question (i.e. it is up to you to decide on search terms for each question). You can use terms from the research question – however as these are in lay language you might need to convert them to appropriate terms found in research (e.g. stopping medicines: deprescribing).

To help with your search you can use as appropriate the following search strategies (in Pubmed format below). But – this is quite an extensive search and can be reduced/edited as you feel appropriate.

Dementia:

((((dementia[Title/Abstract]) OR (cognitive impairment[Title/Abstract])) OR ("dementia"[MeSH Major Topic])) OR ("dementia"[MeSH Terms])) OR ("dementia/drug therapy"[MeSH Terms])

Systematic reviews and guidelines:

((((((((((((((guid*[Title/Abstract]) OR (clinical protocol[Title/Abstract])) OR (polic*[Title/Abstract])) OR ("guideline adherence"[MeSH Major Topic])) OR ("guidelines as topic"[MeSH Major Topic])) OR ("practice guidelines as topic"[MeSH Major Topic])) OR ("clinical protocols"[MeSH Major Topic])) OR (guideline[MeSH Terms])) OR (clinical practice guideline[MeSH Terms])) OR (adherence, guideline[MeSH Terms])) OR (guideline adherence[MeSH Terms])) OR (review, systematic[MeSH Terms])) OR ("systematic reviews as topic"[MeSH Major Topic])) OR ("review literature as topic"[MeSH Major Topic])) OR ("systematic review"[Title/Abstract])

Date limit:

(("2018/01/01"[Date - Publication] : "3000"[Date - Publication]))

Combine the above with AND and keywords for your question. Suggest sticking to MeSH and use of keywords in Title/Abstract.

Here is it in total:

(("2018/01/01"[Date - Publication] : "3000"[Date - Publication])) AND ((((((dementia[Title/Abstract]) OR (cognitive impairment[Title/Abstract])) OR ("dementia"[MeSH Major Topic])) OR ("dementia"[MeSH Terms])) OR ("dementia/drug therapy"[MeSH Terms])) AND (((((((((((((guid*[Title/Abstract]) OR (clinical protocol[Title/Abstract])) OR (polic*[Title/Abstract])) OR ("guideline adherence"[MeSH Major Topic])) OR ("guidelines as topic"[MeSH Major Topic])) OR ("practice guidelines as topic"[MeSH Major Topic])) OR ("clinical protocols"[MeSH Major Topic])) OR (guideline[MeSH Terms])) OR (clinical practice guideline[MeSH Terms])) OR (adherence, guideline[MeSH Terms])) OR (guideline adherence[MeSH Terms])) OR (review, systematic[MeSH Terms])) OR ("systematic reviews as topic"[MeSH Major Topic])) OR ("review literature as topic"[MeSH Major Topic])) OR ("systematic review"[Title/Abstract])))

A reminder: This search and review process IS NOT the same as what would be expected in a systematic review/overview of reviews. For example, you do not need to conduct title/abstract and full text screening in two separate stages. You DO NOT need to record how many results you get for each question/from each database.

If you try a few search terms without getting relevant results – edit your search terms as necessary. As we need a high level of evidence to provide certainty that the question has been 'answered' we probably need guidelines and systematic reviews that are on that research question. E.g. a guideline on heart failure probably doesn't give any information/recommendations about how to manage polypharmacy in people with dementia (even though the terms memory/cognitive and the terms polypharmacy/medications/medication burden/medication review may well appear in this guideline).

Additionally, if there are multiple similar reviews, you can jump straight to the most recent review.

Step 3

Assess whether the research question is answered or unanswered.

This will be informed by the following:

- For the majority of research questions, the minimum level of evidence that is required to certify that a question is 'answered' is a systematic review (so you will be looking for systematic reviews, overviews of systematic reviews and evidence-based guidelines).
- A single study of high quality which directly answers the research question may be accepted to assess a question as 'answered' in rare cases based on the expertise/experience of the evidence checker. (But this doesn't mean that you have to search for all original research on the topic, just that if you are aware of one, or if one comes up in your search you can make an argument that the question is answered.)
- Guidelines are a great source of determining whether a research question is answered or unanswered as they will often provide conclusions about whether further research is needed (may be described as saying that future research may change recommendations, or through description of the level of evidence). Look for the section on future updates if you cannot see any information about this.
- Just because there is a guideline recommendation/systematic review on the research question this does NOT mean that the question is answered. (I'm sure we all have had the experience of conducting a systematic review and concluding that more research is needed.)
- When deciding that the research question is answered/unanswered – ask yourself whether there is a need for more research/if more research could add important information to inform treatment decisions/how care is structured.
- We are not providing any specific rules for what is 'answered' (e.g. we could say that if there is evidence/a recommendation that is assessed as 'high quality' according to GRADE then it is answered – but I think that there is so much grey area around this that such specific rules would probably create more confusion).
- If there is research that answers part of the research question (as some of the questions are relatively broad) you can make recommendations for changing the research question so that it only covers the unanswered part. I.e. we would be splitting the research question into two and assessing one of those as answered and the other as unanswered. But if it isn't really clear cut/easy to split then you can still assess it as unanswered as a whole. (e.g. there might be really good evidence in a specific population like those with diabetes, attending a memory clinic, with access to specific services – but to reword the question to exclude this group but keep all other groups might cause more confusion.) Where helpful, you can use the quotes to help guide this. For example, if the only nutritional supplement mentioned in the quotes is Souvenaid, and the question about Souvenaid has been answered then we can remove 'nutritional supplements' from the question.
- Reliability of the source: The above databases, excluding PubMed, can be assumed to be reliable and meet methodological standards (although see note about NHMRC above). (i.e. no further consideration of the reliability of the source is needed if it is a Cochrane review.) When reviewing systematic reviews from the PubMed search, use your knowledge and consider: if the authors follow a published methodology for undertaking the review, and if the methodology has made provision for managing bias. When looking at guidelines, the

author needs to have made efforts to identify all relevant and reliable trials or systematic reviews. Reliability can be further ascertained from the confidence intervals around the main outcomes, enabling an informed reader to make an informed decision about the result. Narrative reviews, which do not give details or numerical results, may fail the requirements of relevance and reliability. Considering reliability is most important when you find a systematic review/guideline that indicates that the reference is answered – if this is the case, but you think that the review/guideline has serious limitations/methodological flaws then you can still assess this as unanswered. You do not have to document assessing the quality of every review/guideline that you look at/include – but if you are including a SR that concludes that the question is 'answered', but you feel that the quality is lacking and so would assess the question as 'unanswered' then it would be good to make a few brief notes about this.

- If you are unsure – make clear notes and ask for others to comment (i.e. when you send your assessments back to me). (although as much as possible, please make the assessment yourself – if you are finding that you are unsure on lots of them, send me an email and we can organise a time to chat about the process.) All questions that are unsure will be reviewed by ER (to allow for some consistency across reviewers) – but this is only required if you are unsure, it does not need to be conducted for every question. (If ER is unsure this will be checked with another member of the team).

- Given the lack of good data/research including people living with dementia – I am expecting that MOST of the research questions will be assessed as UNANSWERED. (But don't be afraid to assess something as answered!) This process is as much about finding systematic reviews/guidelines that demonstrate that there is uncertainty (and recording this, or indeed recording that there aren't any) as it is about finding systematic reviews/guidelines that answer the questions.

- When considering research where it is health services research (e.g. how should medication reviews be done/used) – as a minimum, at least one of the studies in the systematic review needs to have been done in Australia (preferably more and in different settings where the research question isn't limited to a single setting), and while we don't need high quality implementation research, some consideration of feasibility is important and relevant to knowing whether this research question is 'answered'. (e.g. there might be a high quality systematic review that pharmacist in home medication reviews are effective at reducing polypharmacy in people with dementia – but consider how much heterogeneity there was in the studies in regards to the setting/country/process of med review and whether significant further research would be required for this 'service' to be implemented in Australia to the same standard as conducted in the included articles.)

- This whole project is focused on people living with dementia – I expect that in almost all cases, we want a systematic review that is focused/exclusively on people with dementia. We may consider systematic reviews/guidelines are aren't exclusive to people with dementia, but there at least needs to be clear evidence/recommendations for people with dementia. E.g. if there is a high quality systematic review on treating depression in older adults and it mentioned/includes people with dementia – please consider how many participants in the studies had dementia and if sub-group analysis was done etc.

Step 4

Provide reference(s) and short summary

Whether the assessment is answered or unanswered – include a reference(s):

- The reference(s) should usually be a systematic review or guideline
- If no relevant systematic reviews or guidelines you can mark to say no relevant SRs/guidelines, or can provide recent original research that say there is still uncertainty in this field (if this came up in your search/your existing knowledge).
- If you have assessed it as unanswered because there are really no systematic reviews/guidelines that focused on this, then you don't have to provide a reference (but please make a note of this in the summary section, e.g. "No guideline or SR found")
- A single reference can be sufficient – you can include up to two additional references if appropriate. (If you think more need to be included, e.g. because the question is broad, then that is fine – this recommendation is to highlight that you don't need to include every article that you looked at or commented that further research is needed.)

If your assessment is that the question is <u>answered</u>: provide a brief summary, e.g. *High quality guideline (which will be provided in the reference column), with recommendations on use/not to use Souvenaid for dementia (quality of evidence: high). (this is just an example that I made up)*

You do not need to document all the details about what the answer is!

If your assessment is that the question is <u>unanswered</u>: provide a brief summary. E.g. *No recent systematic review, recent original research study highlights that more evidence is needed. OR While a guideline exists, authors of guidelines say further research is needed that focuses on people with dementia/includes important outcomes etc. OR Recent systematic review was not able to make strong conclusions as there is a significant amount of uncertainty. OR studies only observational/small sample sizes etc OR there are some discussion/commentary style papers but no clear evidence addressing this problem.*

 This summary is necessary for informing later stages of this work and for publishing – for an example of a completed PSP click here: https://www.jla.nihr.ac.uk/priority-setting-partnerships/occupational-therapy/top-10-priorities.htm - click on any of the questions (in blue) and see the information that is provided in 'Evidence' row.

Step 5

Document any notes or if you found studies/review/guideline in progress

An example of a note would be if a guideline/review you read highlighted a different unanswered research question. Please record this (and the reference if different to the one provided for that question) – they will then be added to the list of questions for prioritisation (if this question was not already on our list of questions). You do not have to provide notes for every question/reference.

Another example might be to reword the question, split the research question and/or join two research questions together. We do not want to make significant/a large amount of changes to the questions at this stage as they have been derived from the survey responses and reviewed by our Steering Group – but it is possible that in your expertise/your reading of the articles there is something that we didn't consider in this process – e.g. you might realise that two questions should

be joined as the type of research (i.e. the study that would be done) that would be done to answer one of the questions may result in also answering the other. Or rewording the question would ensure that research is focused on the correct aspect: e.g.

> "Which medicines increase the risk of falls in people living with dementia?" – you may find evidence of a list of medicines, but find that authors of these articles highlight that the relative effect/burden of each of these medicines and what to do with this list in practice is unclear. Therefore you may recommend that the question should be more focused on prediction/prevention – e.g. "How can medicine-induced falls be predicted/prevented in people living with dementia" If you are making such a recommendation you can also review the quotes that informed this question to make sure that we are still staying true to this.

Note: Ongoing trials and studies

It has been decided for this PSP that we are not searching for/considering ongoing trials and studies in relation to deciding whether a question is 'answered'. If you identify a protocol for a systematic review what would seemingly answer the question then you can include a note about this in the notes section (with, if possible, an anticipated completion/publication date), however, it will not affect your assessment of answered/unanswered.

- An ongoing study (or even systematic review) may not mean that an uncertainty will be resolved and is therefore not worth prioritising.
- However, identifying ongoing studies/reviews may help to avoid waste in research at a later stage by demonstrating that a priority may not need immediate action until a trial is complete and has reported its results.
- Prior to the workshop, (when analysing the results of the second survey and deciding the interim priorities for the final workshop) we will refer to our spreadsheet and check if any of those that are going through to the next round are one of the ones with an ongoing study/systematic review. Where the study/review is now published this will be reviewed by two members of the research team to decide if this should be removed and now marked as 'answered'. This decision will then be reviewed by the Steering Group.

Step 6

Send completed spreadsheet back to me!