Author’s response to reviews

Title: Cognitive medicine - a new approach in health care science

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Editor Comments:
The premise of cognitive medicine is an important one, and this review has the potential to make a useful contribution to the literature. However in order to do this the structure of this paper requires some work. The arguments posed require strengthening and the authors should review the structure of the paper.

Response from authors: Please regard the responses to the Reviewers. The structure of the paper has been modified and the argumentation has been strengthened.
Helen Macpherson (Reviewer 1):

Reviewer 1: This perspective article covers an important topic, that a cognitive medicine approach is needed to help understand how to maintain and optimise cognitive health. The structure of this perspective piece is not effective and the main points of the article, which are important, are not easily identifiable. The concept of cognitive medicine is not introduced until page 10 and this article would be more cohesive if this concept was introduced at the beginning, with the rest of the article supporting the importance of the premise.

Response from authors: We agree. Please regard our responses to the following comments from Reviewer 1.

Reviewer 1: Major suggestions:
Restructure the article so that the article begins with 'cognitive medicine - an emerging field'. This may require integrating some of the content from the earlier sections. The dot points included in the 'Conclusions' section should become the main focus of the paper with relevant evidence used to describe both the problem raised and potential solutions.

Response from authors: As suggested by Reviewer 1, the manuscript now starts with 'Cognitive medicine - an emerging field'. A summary of the dot points in the 'Conclusions' section has been incorporated at the end of the new version of 'Cognitive medicine - an emerging field'. The remaining part of the manuscript has been re-written so that the dot points previously included in the 'Conclusions' section are the main focus of the manuscript.

Reviewer 1: This paper lacks concrete evidence which would help to provide a stronger argument. How many people are affected, by which conditions? What is the size of the problem? Without evidence this perspective is superficial and potentially valuable points are weaker than they could be.

Response from authors: A new section has been included in the manuscript with the title 'Prevalence of cognitive dysfunction and health economy'. In this section, the prevalence of
dementia and mild cognitive impairment is discussed as well as the need for more prevalence studies and health economy evaluations.

Reviewer 1: Additional suggestions:
Cognitive function: would be better integrated with the section on 'Cognitive function throughout the lifespan'. The 'Cognitive functions' section is not effective in its current form. Which domains change with age and which are affected in other pathological conditions? Which cognitive domains may be most relevant to the concept of cognitive medicine?

Response from authors: As suggested by Reviewer 1: the 'Cognitive functions' section has been moved to the section 'Cognitive function throughout the lifespan'. The term cognition in cognition medicine is broadly used, but with a special emphasis on cognitive functions that typically decline in advancing age. This has now been clarified in the text. In addition, the text on age-related preservation and decline of cognitive function have been expanded. Under the heading ‘Basic research perspective' examples of cognitive profiles in pathological conditions are presented

Reviewer 1: Cognitive function throughout the lifespan: is lacking references and is very superficial. The focus should include both decline as well as development

Response from authors: The reference list is now updated with 10 new references. The decline and development issue - please see the previous response from authors.

Reviewer 1: Disability: is lacking references and is very superficial. Given that disability due to mental illness versus physical illness may have markedly different impacts on cognition, this should be explored.

Response from authors: The text about disability has been expanded and references added.

Reviewer 1: Patient and disease perspective: The first paragraph does not meaningfully contribute to the paper.
Response from authors: We agree. The first paragraph of this section has been deleted. The remaining parts of this section has been re-written and the heading of the section is now 'Basic research perspective'.

Reviewer 1: Global Issue perspective: it would seem relevant here to mention the population ageing that is taking place even in developing countries and the impact this will have on number of people affected by dementia in the future.

Response from authors: In 'Global perspective', first sentence, it is now stated that the number of elderly individuals is increasing also in developing countries, which will result in a marked increase in the prevalence of age-related brain diseases including dementia. Furthermore, in the new section 'Prevalence of cognitive dysfunction and health economy', first sentence, the prevalence of dementia worldwide and the expected increase in dementia prevalence are described.

Reviewer 1: Can the authors discuss how cognitive medicine could be integrated with existing medical care practices and how it could complement existing mental health services?

Response from authors: Thanks for raising this question. Before 'Conclusion' we have inserted a new paragraph 'Integration with existing medical care practice' with the following text 'Memory clinics or similar health care units deal mainly with AD and related dementia disorders. The responsibilities of such units may be expanded to include also investigation of various somatic and psychiatric disorders usually not classified as dementia disorders, but which may exhibit cognitive impairment as an essential component that worsen rehabilitation and return to work. The overall aim of such health care units, in addition its traditional task, would be to identify and evaluate severity, profile and consequences of cognitive impairment for treatment of the somatic and psychiatric disorders. Furthermore, competence in cognitive medicine can be increased by introducing 6-12 months practice at these units for doctors trained in neurology, psychiatry, rehabilitation medicine or general practice. Nurses and psychologists can increase their competence in cognitive medicine in a similar way.'
Reviewer 1: Generally this paper is lacking references.
Response from authors: The number of references have been increased from 17 to 27.

Gary Christopher (Reviewer 2):

Abstract
Reviewer 2: I do not feel this is the best summary of the paper. It could be a little more focused and definite in its message.

Response from authors: The Abstract has been re-written in order to describe the aims of cognitive medicine more clearly.

Main body
Reviewer 2: As with the Abstract, the opening paragraph could be more attention grabbing. What exactly is 'cognitive medicine'?

Response from authors: In response to a comments from Reviewer 1, the section 'Cognitive medicine - an emerging field' has been moved to the start of the manuscript. This section has also been partly re-written in order to introduce the concept of cognitive medicine and to be more attention grabbing.

Reviewer 2: The statement, "working-memory system, which is one of several components of executive functioning," is not particularly accurate.

Response from authors: This has been corrected.

Reviewer 2: This section seems to flit all over the place. One minute the focus is briefly on attention, then working memory, then long-term memory. It is a little difficult to follow. There needs to be a stronger overall logic here.
Response from authors: The section has been rewritten – see response to reviewer 1 and new text in ms.

Reviewer 2: p.7 ln.1, "Cognitive impairment is known to be a major denominator of disability": Should this read "determinant" rather than "denominator"?

Response from authors: In response to one of the comments from Reviewer 1, this paragraph has been removed. Thus, this statement has been deleted.

Reviewer 2: There is an occasional lack of an evidence base (e.g., However, cognitive impairment is related to many other diseases and thus often represents a silent and underreported condition.). Need to provide appropriate references.

Response from authors: In response to one of the comments from Reviewer 1, this paragraph has been removed. Thus, this statement has been deleted.

Reviewer 2: What is meant by, "Under the umbrella of cognitive medicine fragmentized (methodological) knowledge about cognition and its relationship to the whole spectrum of medical conditions are integrated over the life course." This is not at all clear.

Response from authors: We agree that this sentence was unclear. This sentence has therefore been re-written (Cognitive medicine – an emerging field, second paragraph, second sentence): "Cognitive medicine could be an umbrella for knowledge of how to prevent, diagnose and handle cognitive decline in a wide spectrum of medical conditions over the life course (Figure 1)."

Reviewer 2: Many of the statements are not fully qualified (e.g., "The new classification system for mental disorders, The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [17], is well in agreement with the cognitive medicine perspective, in that categories such as "dementia disorders" have been substituted by the term "neurocognitive disorders.") More of an explanation is needed to make the necessary leap.
Response from authors: We agree that this statement was indistinct. This has been shortened to (Cognitive medicine – an emerging field, second paragraph, second last sentence): "In the new classification system for mental disorders, The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), there is a focus on both mild and pronounced degrees of cognitive dysfunctions and categories such as “dementia disorders” have been substituted by “neurocognitive disorders”.

Reviewer 2: "In short, cognitive medicine fills the gap between (cognitive) neuropsychology and medicine which, with some exceptions, has an oversimplified approach to cognition and cognition-related disability." In what way is it over-simplified?

Response from authors: We agree that this statement was unclear. In the new version of the manuscript, this statement has been shortened and been incorporated into another sentence. The new sentence is as follows (Cognitive medicine – an emerging field, second paragraph, last sentence): "However, cognitive medicine is broader than only neurocognitive disorders and could be a bridge between (cognitive) neuropsychology and medicine."

Reviewer 2: "Cognitive medicine is aiming at obtaining specific knowledge about the relationships between disease processes, cognitive functions and disabilities in a broader medical context than is represented by the current memory clinic approach focused on Alzheimer's disease and related disorders." Not clear what is meant by this.

Response from authors: Thanks for noticing unclear sentences. The last part of the sentence has been deleted, i.e., “…in a broader medical context than is represented by the current memory clinic approach focused on Alzheimer's disease and related disorders.” has been deleted.

Reviewer 2: "Under the umbrella of cognitive medicine, the most urgent need is to establish valid and reliable tools for identification of cognitive impairment in various medical conditions." Is this entirely accurate?
Response from authors: We agree. This has been changed to (Conclusions, second sentence): "There is a need to establish new tools for identification of cognitive impairment in various medical conditions."

Reviewer 2: Overall, phrasing could be a little clearer (e.g., p.4 ln.54).

Response from authors: The sentence referring to has been deleted.

Reviewer 2: On the whole, there are too many holes in the argument. There needs to be more evidence of a consistent, sold argument underlying the structure. Some points need to be elaborated upon in order to make a stronger case. The level of detail is a little sporadic. A more transparent evidence base is required.

Response from authors: Please regard our responses to previous comments from the Reviewers. We believe that the argumentation now is more detailed and more complete. A condensed version of the take home message, “Cognitive medicine – an emerging field”, is now situated very early in the ms, which hopefully increases the readability of the paper. Furthermore, we believe that the text about cognition, disability, basic research and health economy are more comprehensive. The role memory clinics is specified. The list of references is extended.

Reviewer 2: I feel this is a good idea. However, a stronger argument is needed to justify it.

Response from authors: Many thanks for this comment. Please regard our responses to other comments from the Reviewers. We believe that the argumentation now is considerably stronger.