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Short Communication

Mapping the Literature on Nutritional Interventions in Cognitive Health: A Data-Driven Approach

Erin I. Walsh *, and Nicolas Cherbuin

Centre for Research on Ageing, Health and Wellbeing, Research School of Population Health, Australian National University; erin.walsh@anu.edu.au and Nicolas.cherbuin@anu.edu.au

* Correspondence: erin.walsh@anu.edu.au; Tel.: +61 2 6125 8291

Abstract: Manual review of the extensive literature covering nutrition-based lifestyle interventions to promote healthy cognitive ageing has proved educative, however, data-driven techniques can better account for the large size of the literature (tens of thousands of potentially relevant publications to date) and interdisciplinary nature of where relevant publications may be found. In this study we present a new way to map the literature landscape focusing on nutrition-based lifestyle interventions to promote healthy cognitive ageing. We applied a combination of citation network analysis and text mining to map out the existing literature on nutritional interventions and cognitive health. Results indicated five overarching clusters of publications, which could be further deconstructed into a total of 35 clusters. These could be broadly distinguished by focus on lifespan stages (e.g. infancy versus older age), and specificity regarding nutrition (e.g. narrow focus on iodine deficiency versus broad focus on weight gain). Rather than concentrating into a single cluster, interventions were present throughout the majority of the research. We conclude that a data-driven map of the nutritional intervention literature can benefit the design of future interventions, by highlighting topics and themes that could be synthesized across currently disconnected clusters of publications.

Keywords: citation network analysis; text mining; nutrition intervention; cognition

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The literature surrounding nutrition interventions intended to prevent cognitive decline in ageing is large, multi-faceted and heterogeneous. This reflects the heterogeneity of ageing, and the large variety of methods, participants, and intervention targets of nutrition interventions to date. Systematic reviews and meta analyses are key tools in addressing this heterogeneity and synthesizing large numbers of publications into useful formats. Systematic reviews carried out by human researchers are necessarily targeted at specific research questions, and so tend to be highly specialized. Broadly, they focus on literature with scope intentionally limited to a topic that a human reader could explore and meaningfully summarize. Examples of this are reviews focusing on intervention delivery (e.g. computer tailored promotion of adherence[1]), specific nutritional content (e.g. interventions focused on flavonoids[2], antioxidants [3], polyphenols[4], or dietary patterns such as the Mediterranean diet[5]), particular demographics (e.g. children and adolescents[6], university students[7], older adults[8], Australian adults[9]) or clinical populations (e.g. cancer patients[10]), and specific cognitive outcomes (e.g. the development of Alzheimer's Disease[11] or Dementia[12]).

From strict meta-analysis to a more narrative approach, these focused manual reviews are extremely valuable in organizing and conveying knowledge relating to any of these particular domains. Yet, they are inherently limited by any given author's or team's understanding of the existing literature, leading to the selection of topics on the basis of an incomplete picture of relevant knowledge[13]. This results in a constellation of specialized knowledge without clear synthesis or links between the topics, which does little to reveal new or underserved topics which fall beyond the a-priori scope of existing reviews. This is a reflection of the sheer breadth of available information. Even with increasingly sophisticated search and aggregation tools, it is impossible for an individual

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or team to manually identify and synthesize every relevant paper from a peer-reviewed literature which expands by over one million publications per year [14,15].

Accordingly, increasing attention is being paid to automated methods for knowledge identification, synthesis, and summary[16]. Recent advances in citation network analysis and text mining software provides new opportunities for constructing robust summaries of the literature and concepts therein by a purely data-driven approach[17,18]. Clusters formed by groups of publications connected by mutual citation can be taken as indicative of theoretical or conceptual groupings in the literature[17]. Text-mining techniques including topic models and semantic neighborhood analyses are increasingly being used to extract meaning from lengthy passages of text [19].

In this paper we present a new way to map the literature landscape focusing on nutrition-based lifestyle interventions to promote healthy cognitive ageing. We introduce a data-driven approach that draws from citation networks, abstract and title text; allows efficient synthesis of more publications than a human could manually identify and read; and demonstrate how this approach can be applied to give new insights into the themes and gaps present in the intervention literature. We conclude that a data-driven map of the nutritional intervention literature can benefit the design of future interventions, by highlighting topics and themes that could be synthesized across currently disconnected clusters of publications.

2. Materials and Methods

The citation network analysis applied here aims to map the literature space and identify citation clusters relevant to a specific topic (e.g. nutritional interventions to improve cognitive health). It involves: 1. Systematically searching the literature for pre-defined search terms and obtaining mutual citation links, full title and abstract text for this literature. 2. Conducting citation network analysis on mutual citation links to identify clusters within this literature. 3. Using text mining techniques to characterize these clusters.

2.1 Literature search and Citation Network Analysis

CiteNetExplorer[20] software is a tool for visualizing and analyzing citation networks denoted by mutual citation, including relatedness between papers as a weighted combination of year of publication and mutual citation, and identification of 'clusters' of publications. These are logical groupings of publications located near to one another in the larger citation network, established by a variant of the modularity function (described in [21]). A Web of Science Core Collection Database search was undertaken 23rd October 2018 for the terms *(((cognit* OR dementia) AND(ageing OR aging) NOT(animal)) AND (diet OR nutr*))*, with a restriction to peer-reviewed journals. Note the absence of 'nutrition' and 'diet', as the intention is to later examine the position of these terms within the revealed clusters. This yielded 6,138 citations, down to 6,045 once the search was restricted to peer-reviewed journal texts. Full records of citations and secondary articles (those citing and cited by the documents) were imported into CiteNetExplorer for cluster analysis. Cluster analysis was undertaken on the remaining 6,045 publications (minimum cluster size set to 10 publications, 10 iterations from the random seed 1337). To obtain detail, this process was repeated iteratively until larger clusters (n>500 publications) could not be further deconstructed into smaller clusters. Some citations were omitted in this process as not clearly belonging to any particular cluster, or due to missing information, resulting in a final n=4915 (see supplementary spreadsheets 01 and 02).

2.2 Text preparation

All titles and abstracts were extracted from Web Of Science search results. When unavailable from the search, titles and abstracts were reconstructed from doi, author and year via a composite of automated python script, Elsevier scopus API via 'fulltext' package in R (version 1.01) and 'roadoi' package in R (version 0.5.2; n=2372 titles and abstracts) and manual entry (n=221 titles and abstracts) referring to doi.org and Google Scholar. The resultant titles and abstracts was converted into a

Corpora (collection of natural language documents) in the tm package (version 0.6-2 [22]). Following text mining convention[23], all non-word information (stopwords, case, punctuation, case etc) was removed. Words were stemmed using Porter's stemming algorithm (e.g. "cognition", "cognitive" become "cognit"; "diet", "dietary" become "diet"). The resultant corpora was saved as spreadsheets and as term document matrices (TDM), which describe the frequency of terms (columns) occurring across the clusters (rows).

2.3 Cluster description

The simplest method of exploring a cluster is the generation of word clouds. These provide a parsimonoius visual overview of terms found within a text, with size and opacity indicating the frequency of a word within the text. Building on this, Latent Dirichlet Allocation is a Bayesian topic model which probabilistically extracts topics from terms across documents (here, manuscript titles). LDA treats each term as a finite mixture of possible underlying topics. This is expressed as beta (β), the probability of that term being generated by the topic. The log ratio of β for one topic as opposed to another, obtained by $\log(\beta_{topic1}/ \beta_{topic2})$ can be used to identify terms most distinctive to each topic, which therefore describe it best. Topic modelling was carried out on the title of each cluster using the topicmodels package for R (version 0.2-6, [24]).

There are multiple techniques available should the reader wish to go further and establish the context of a particular term (such as "intervention"). Here, we provide an example of how pairwise associations in text ('findAssocs' function of tm) and neighbourhood analysis ('neighbors' function of the LSAfun package (version 0.5.1 [9]) of abstract text within a cluster can provide this context. Using these techniquces in combination capture both physical proximity of words in the text (e.g. "Happy" next to "Child", "Joyful" next to "Adult"), and semantic proximity (e.g. "Happy" will be closer to "Joyful", while "Child" is closer to "Adult").

3. Results

Word clouds (figure 1) provide a visual overview of the 6,045 journal articles published from 1929 to 2018, relating to cognition, ageing, nutrition/diet, and interventions, grouped by cluster. In aggregate, recurrent terms throughout denote publications tend to focus on lifespan stages (with particular focus on childhood and older age), with studies focusing on 'patients' more common in older age. While some clusters reflect a very specific focus (e.g. publications surrounding phenylketonuria or iodine levels are quite distinct), there is clear overlap across the wider literature with terms such as 'develop', 'outcome' and 'function' being present throughout. Cluster descriptions revealed by topic analysis (figure 2; see supplementary tables 1-5 for more detail) demonstrates how text mining approaches can more clearly map out a large, diffuse literature such as this.

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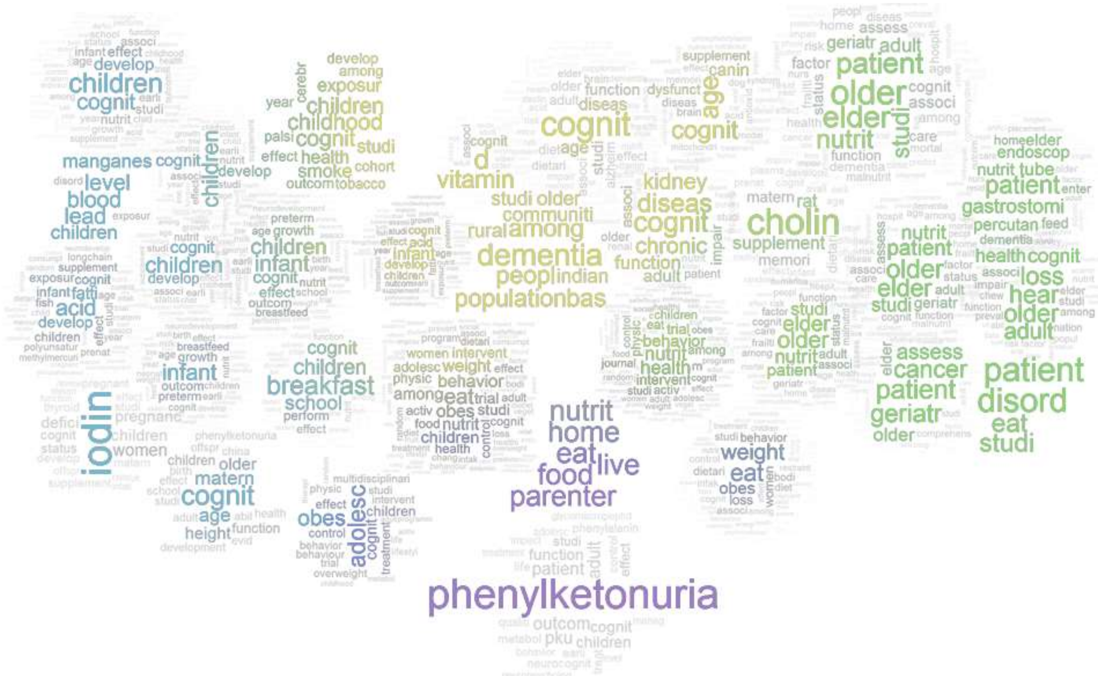

Figure 1. Visual overview of 6,045 publications.

Note. Word clouds are derived from frequency of terms within titles, grouped by clusters (described in more detail in figure 2, and supplementary tables 1-5).

Topic analysis of the five main clusters and 30 sub-clusters reveal several insights into the landscape of the literature addressing lifestyle dietary intervention to improve cognition (figure 2; supplementary tables 1-5). Broadly, clusters form around lifespan stages – two clusters focus on older age (cluster 1: the association between diet and cognitive outcomes with a focus on prediction of decline and disease; cluster 2: daily self-care and nutrition in older age), two on lifespan or midlife (cluster 4: the role of diet in overweight and obesity throughout the lifespan; cluster 5: diet and phenylketonuria), and one in childhood (cluster 3: the association between nutrition in early life and subsequent cognition). There are clear sub-literatures within larger topics, e.g. *maternal diet and breast feeding outcomes* (3ba) within *breast feeding and cognitive outcomes* (3b) within *the association between nutrition and early life and subsequent cognition* (cluster 3). Yet, the tendency for publications to cluster around time of life precludes what might be considered logical sub-cluster groupings. For example, due to conceptual similarities one might expect sub-clusters relating to antioxidants, choline, trace metals such as magnesium and iodine to fall within close proximity, however they are more specific to the adult-specific cluster 1 (antioxidants 1c; choline 1d), and child-specific cluster 3 (magnesium 3aab; iodine 3d).

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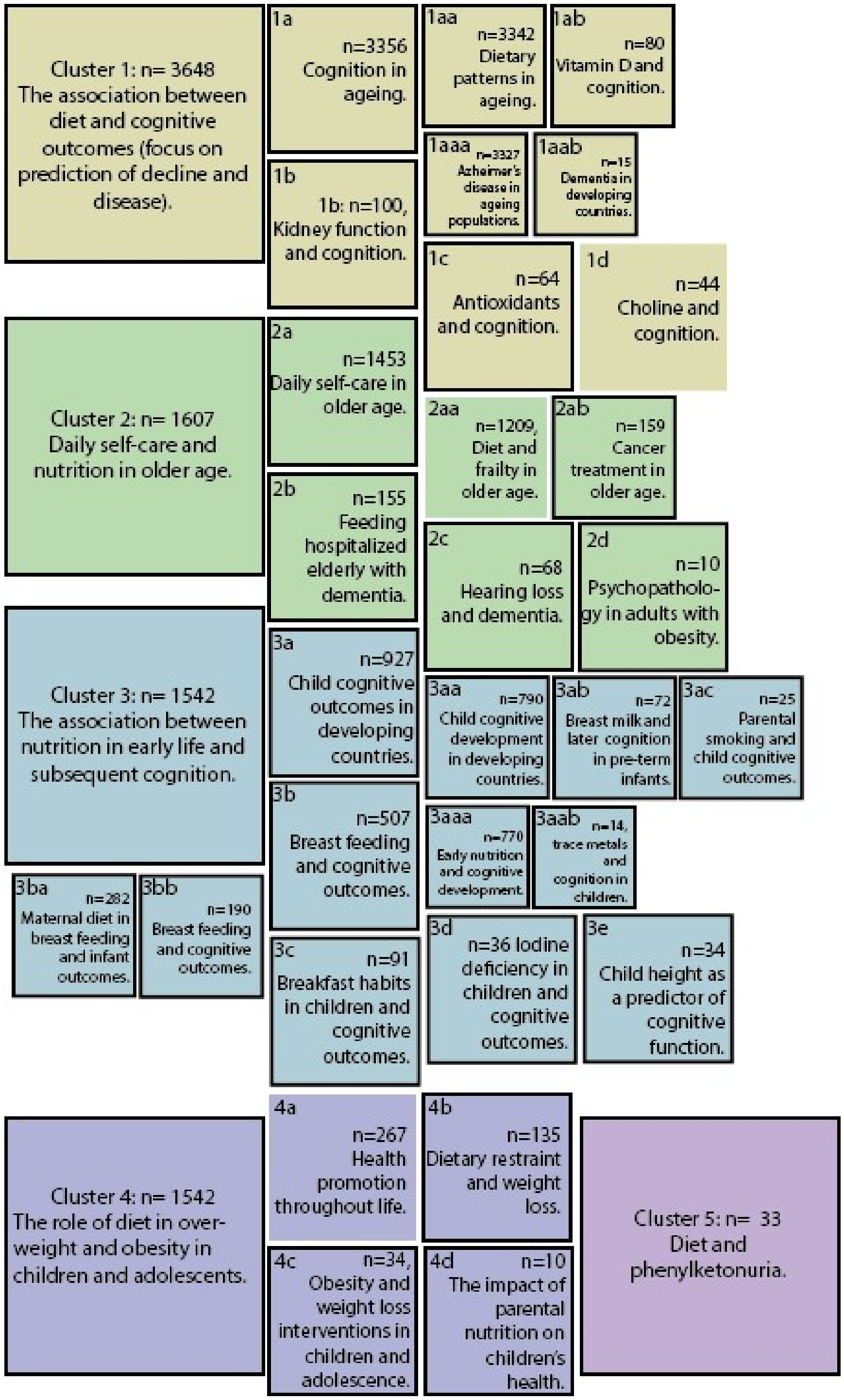

Figure 2. Overview of topic analysis results.

Note. Each panel depicts a cluster as described by topic analysis undertaken on *n* manuscript title text (see supplementary tables for more detail). Size denotes nesting. Black borders indicate that pairwise word correlations with the term "intervent*" are present at r<0.5 are present with terms in that cluster's abstracts. See supplementary tables 1-5 for further detail on the topic analysis process, and characterization of each cluster and sub-cluster.

The term 'intervention' is present in the abstracts of all but 3 of the total 35 possible clusters. Text mining (supplementary tables 6 and 7) reveals that interventions are largely cluster-specific in terms

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of methods and focus. For example, in sub-cluster *breast feeding and cognitive outcomes*, 'intervention' correlates with 'baby friendly' and 'characteristic adjustment', and is semantically near terms such as 'computerized', 'instrumental' and 'intention', reflecting interventions in this cluster target breast feeding indirectly via intention (as it would be unethical to randomly assign a child who otherwise would have been breast fed to a formula condition). Conversely, in sub-cluster *dietary restraint and weight loss* (4b) 'intervention' correlates with terms 'prevent', 'trial', and 'random', and is semantically near terms such as 'wait', 'pertaining', 'targeted', reflecting interventions in this cluster directly target behaviors relating to weight gain.

4. Discussion

Nutrition interventions to prevent cognitive decline in ageing are extremely varied in terms of sample, approach, and focus. They are also highly numerous. Even if knowledge is collected and curated in the form of meta-analysis or discursive review, the sheer size of the literature makes it impossible for a single researcher or team to manually construct an overview of extant trends, syntheses, and gaps in knowledge. In this study, we demonstrated a method for efficient synthesis of a large number of publications, and produced a map of the literature surveying nutrition-based lifestyle interventions to promote healthy cognitive ageing. This map can be used to characterize the intervention literature as a whole, identify thematic overlap between work that has to date remained separate, and identify gaps requiring further study.

This approach can also be used to relatively quickly select a large number of studies which address a common topic. Based on the cluster identified in Figure 2 it is possible to retrieve all the related articles for more detailed review (supplementary file 02). This functionality can be used in its own right to survey a particular part of the literature or to supplement searches implemented in systematic reviews or meta-analyses. These approaches are complementary because the purpose of reviews and analyses is to distill concepts, which offer precision but may exclude relevant targets, while the purpose of citation network analysis is to connect concepts and uncover a broader scope of relevant targets. In particular, the inclusion of second degree connections (citations of papers included in search responses which themselves may have not been included in the original search) can uncover linkages that manual review overlooks.

Beyond accessing knowledge in clusters the mapping of the extant literature can also be used to identify hierarchical features that can provide insights on how content of interest can be better identified. In the current context, we found that the nutrition intervention literature first formed clusters on the basis of participant age (notably childhood and late life), before further subdivision into to nutritional content of the intervention. In some instances, this makes intuitive sense; prenatal nutrition (cluster 4d) is unique to very early life, while frailty (cluster 2aa) is an issue inherent in old age. However, the association between nutrition is often lifelong, and conceptual segregation based on age is not necessarily helpful. This can be seen in the topics of the clusters, for example, the theme of obesity is split into youth (*The role of diet in overweight and obesity in children and adolescents*, cluster 4) and old age (*Psychopathology in adults with obesity*, cluster 2d), and in individual publications. For example, Hamadani et al. [25] and the Supplémentation en Vitamines et Minéraux Antioxydants, Su.Vi.Max, study [26] differ in terms of size (n=168 vs n=13017 respectively), location (Bangladesh vs France), participant age and measures of cognition (3-13 month infants and the Bayley scales of infant development in vs 45-60 year-old adults and the RI-48 cued recall test respectively). They do not share a single citation in common[1], indicating that they come from disconnected portions of the literature [17]. Accordingly, they are situated in separate clusters (*Trace Metals and Cognition in Children*, aab, and *Alzheimer's Disease in Ageing populations,* 1aaa, respectively). Yet, both studies

[1] For the purposes of parsimony, the Su.Vi.Max project description is cited here; to the author's knowledge at the time of writing this statement is true for all subsequent publication of Su.Vi.Max data

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include examination of the impact of zinc supplementation on cognitive outcomes, which relies on biological processes that are relevant across the lifespan[27]. Even accounting for the possibility that there is little equivalence between these interventions beyond the inclusion of zinc supplementation, their conceptual isolation is striking.

This is not a shortcoming of the method used, but rather an insight into the genuine structure of the nutrition interventions as they currently sit within the literature. The capacity for a single citation to sit within multiple clusters indicates this is not due to single interventions including multiple targets (e.g. the Su.Vi.Max, study [26] includes both antioxidant and trace metal supplementation). Instead, it is more likely that this structure arises because of the relatively small number of interventions explicitly target a lifespan perspective[28], while the majority of studies select specific age ranges to allow clear measurement and interpretation of cognitive outcomes. This could implicitly lead to researchers consulting only age-relevant literature, particularly if their searches focus on interventions because as cross-sectional observational studies often encompass wider age ranges. The situation could be likened to the citation siloes forming on the basis of language barriers in scholarly literatures prior to widespread translation services[29]. Fortuitously, the solution to avoiding redundancy and improving knowledge synthesis in this case is simpler and more immediate. Once it is clear that the literature is organized in this way, future interventions where a nutritional factor is relevant across the lifespan can be improved by conducting searches which mindfully incorporate the whole lifespan.

Relatedly, the current approach can also be applied to identify gaps in the literature. It is beyond the scope of this manuscript to exhaustively identify gaps in the literature as revealed by the map, but there are some trends of note. Given the age-based structure of the literature, the most evident gap is the lack of specific clustering of interventions around mid-life, when many risk factors develop and start having a measureable impact on brain and cognitive health [30,31]. Other potential gaps may include interactive effects with genetics, social and environmental variables as well as contributions of ethnic, cultural and socio-demographic factors. There are also some gaps which are more likely to be indicative of the search terms used. This emphasizes that the choice of search terms is as important in this method as they are for reviews or meta-analyses. Interested readers will note omissions of clusters on known correlates of nutrition and cognitive outcomes, such as type 2 diabetes[32], and no clusters forming around terms such as 'neuroimaging' or 'brain'. This may be due to the choice of search terms insensitive to these topics, or possibly the reliance on titles, rather than full text, for topic analysis. This latter is likely, because the terms 'diabetes', 'neuroimaging', and 'brain' were detected as correlates of 'nutrition' when text mining was undertaken on abstracts, which by virtue of their length and purpose convey more context. This could be further investigated by conducting topic analysis on the full texts of manuscripts, though this process may prove challenging to automate due to barriers of copyright for full text access.

The data-driven approach we present here has a number of strengths. Chiefly, we have demonstrated knowledge synthesis and mapping on a scale that reflects the size of the literature rather than what is possible for a human to achieve. The map produced provides an intuitive overview of the literature, and organizes the long list of publications into a format conducive to further reading. Notably, the map we have produced is open to refinement. New more specific searches can be conducted to map a smaller part of the literature space with greater precision. However, our findings also highlight genuine avenues for improvement of the nutrition and cognition intervention literature.

5. Conclusions

We have presented a novel, data-driven combination of citation network analysis and text mining aimed at mapping the current literature surveying nutritional interventions on cognitive health. We showed a tendency for mutual citation clusters to form on the basis of age group (in particularly pertaining to children and the elderly), before topic. We also noted that interventions are an integral part (rather than a separate cluster) of the wider literature. We suggest that future interventions could benefit from researchers reading beyond their target age groups and possibly benefitting from topic-relevant insights obtained from interventions carried out at other times in life. We also recommend that researchers use this new approach to first survey the organization of the extant literature of their general field of interest using broad search terms, followed my narrower searches informed by the former to more precisely identify research closely related to their particular research focus.

Supplementary Materials: Table S1: Cluster 1: n= 3648 publications, topic of the association between diet and cognitive outcomes (focus on prediction of decline and disease), Table S2: Cluster 2: *n*= 1607 publications, topic of daily self-care and nutrition in older age, Table S3: Cluster 3: *n*= 1542 publications, topic of the association between nutrition in early life and subsequent cognition, Table S3: Cluster 4: *n*= 456 publications, topic of the role of diet in overweight and obesity in children and adolescents, Table S5: Cluster 5: *n*= 33 publications, topic of diet and phenylketonuria, Table S6: Context of the term 'intervention' within clusters: pairwise correlations, Table S7: Context of the term 'intervention' within clusters: Latent Semantic Neighbourhood Analysis.

Author Contributions: Conceptualization, E.I.W. and N.C.; methodology, E.W.; formal analysis, E.W.; resources, N.C..; data curation, E.W..; writing—original draft preparation, E.W.; writing—review and editing, N.C.; visualization, E.W.; funding acquisition, N.C.

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Conflicts of Interest: The authors declare no conflict of interest.

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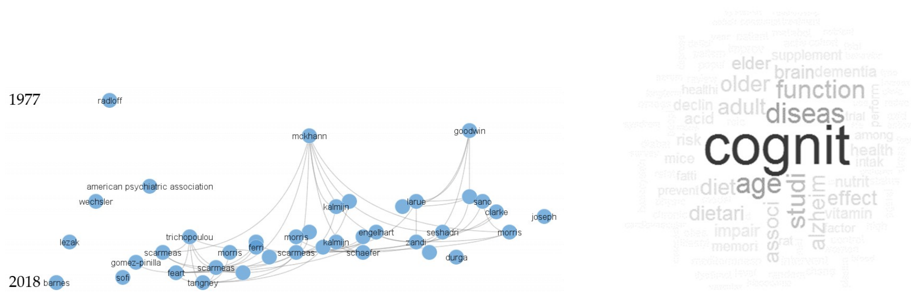
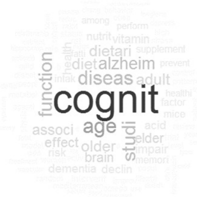
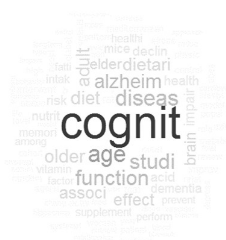
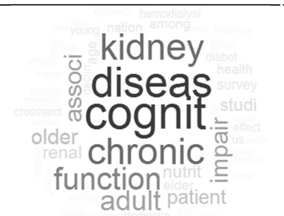
Supplementary Table 1. Cluster 1: *n*= 3648 publications, topic of the association between diet and cognitive outcomes (focus on prediction of decline and disease)

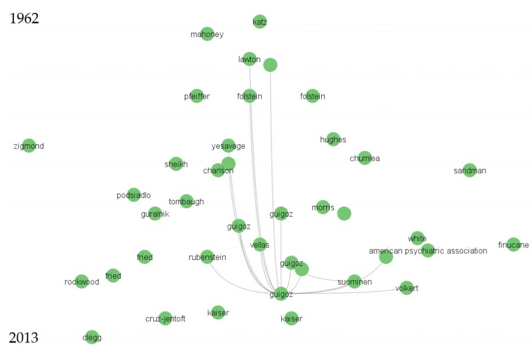


Cluster information and indicative core publication (weighted for recency)	Word cloud	Most unique topic terms (β log ratio)
1a: *n*=3356, topic of cognition in ageing. McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. M. (1984). Clinical diagnosis of Alzheimer's disease Report of the NINCDS-ADRDA Work Group* under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology, 34(7), 939-939. doi: 10.1212/WNL.34.7.939		prolifer* (8.84) disodium (8.41) nonalzheim* (8.38) rhodiola* (7.25) positron (7.02)
1aa: n=3342, topic of dietary patterns in ageing. Scarmeas, N., Stern, Y., Tang, M. X., Mayeux, R., & Luchsinger, J. A. (2006). Mediterranean diet and risk for Alzheimer's disease. Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society, 59(6), 912-921. doi: 10.1002/ana.20854		dash(9.78) scottish(8.87) initi* (8.43)
1aaa: n=3327, topic of Azheimer's disease in ageing populations. McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. M. (1984). Clinical diagnosis of Alzheimer's disease Report of the NINCDS-ADRDA Work Group* under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology, 34(7), 939-939. doi: 10.1212/WNL.34.7.939		depressivelik* (10.1) alzheimerlik* (8.81) faux(8.79)
1aab: n=15, topic of dementia in developing countries. Prince, M., Acosta, D., Chiu, H., Scazufca, M., Varghese, M., & 10/66 Dementia Research Group. (2003). Dementia diagnosis in developing countries: a cross-cultural validation study. The Lancet, 361(9361), 909-917. doi: 10.1016/S0140-6736(03)12772-9		franc* (10.94) hypometabol* (9.7) deposit* (8.95)

1ab: n=80, topic of the vitamin D and cognition. Holick, M. F. (2007). Vitamin D deficiency. New England Journal of Medicine, 357(3), 266-281. Doi: 10.1056/NEJMra070553		fortif* (9.49) graft (9.48) demograph* (9.19)
1b: *n*=100, topic of kidney function and cognition. Cockcroft, D. W., & Gault, H. (1976). Prediction of creatinine clearance from serum creatinine. Nephron, 16(1), 31-41. doi: 10.1159/000180580		wellb* (11.22) cytokine* (8.93) occlus* (7.95) westerntyp* (7.48) systemat* (7.1)
1c: *n*=64, topic of antioxidants and cognition. Milgram, N. W., Head, E., Muggenburg, B., Holowachuk, D., Murphey, H., Estrada, J., ... & Cotman, C. W. (2002). Landmark discrimination learning in the dog: effects of age, an antioxidant fortified food, and cognitive strategy. Neuroscience & Biobehavioral Reviews, 26(6), 679-695. doi: 10.1016/S0149-7634(02)00039-8		highintens* (8.2) genderspecif* (7.87) trelong (7.84) hci (7.38) previous (7.36)
1d: *n*=44, topic of choline and cognition. Meck, W. H., & Williams, C. L. (2003). Metabolic imprinting of choline by its availability during gestation: implications for memory and attentional processing across the lifespan. Neuroscience & Biobehavioral Reviews, 27(4), 385-399. doi: 10.1016/S0149-7634(03)00069-1		fabri* (166.71) unpack (162.15) mg (162.15) odour (161.99) seroposit* (161.97)

Note. A= schematic overview of citation cluster, low citation counts omitted for readability. Colored nodes indicate core citations, lines between nodes show strong citation links. Year range indicates most frequent period of publication. B= word clouds are based on raw word frequency, with larger size and opacity indicating higher frequency. β log ratio are derived from Latent Dirichlet Allocation is a Bayesian topic models. * indicates word stem wildcard. Counts in sub-clusters may exceed total cluster count, as single publications can belong to multiple clusters.

Supplementary Table 2. Cluster 2: *n*= 1607 publications, topic of daily self-care and nutrition in older age



Cluster information and indicative core publication (weighted for recency)	Word cloud	Most unique topic terms (β log ratio)
2a: *n*=1453, topic of daily self-care in older age Lawton, M. P., & Brody, E. M. (1969). Assessment of older people: self-maintaining and instrumental activities of daily living. The gerontologist, 9(3_Part_1), 179-186. doi: 10.1093/geront/9.3_Part_1.179		dryness (352.61) geneenviron* (352.18) cpreval* (351.95) english (351.76) masticatori* (351.31)
2aa: n=1209, topic of diet and frailty in older age. Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., ... & McBurnie, M. A. (2001). Frailty in older adults: evidence for a phenotype. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 56(3), M146-M157. doi: 10.1093/gerona/56.3.M146		standard(33.12) propens* (29.47) sever* (29.24)
2ab: n=159, topic of cancer treatment in older age. Repetto, L., Fratino, L., Audisio, R. A., Venturino, A., Gianni, W., Vercelli, M., ... & Aapro, M. S. (2002). Comprehensive geriatric assessment adds information to Eastern Cooperative Oncology Group performance status in elderly cancer patients: an Italian Group for Geriatric Oncology Study. Journal of clinical oncology, 20(2), 494-502. doi: 10.1200/JCO.20.2.494		technic* (297.21) gineco* (297.12) haematology (297.09)
2b: *n*=155, topic of feeding hospitalized elderly with dementia. Finucane, T. E., Christmas, C., & Travis, K. (1999). Tube feeding in patients with advanced dementia: a review of the evidence. Jama, 282(14), 1365-1370. 10.1001/jama.282.14.1365		glycaem* (34.93) gerontopol* (34.81) mindfulnessbas* (34.62) malnutrit* (32.87) proton (32.82)

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2c: *n*=68, topic of hearing loss and dementia. Lin, F. R., Metter, E. J., O'brien, R. J., Resnick, S. M., Zonderman, A. B., & Ferrucci, L. (2011). Hearing loss and incident dementia. Archives of neurology, 68(2), 214-220. 10.1001/archneurol.2010.362		confirm (52.47) anthropometri* (50.79) disclosur* (50.56) suffoc* (50.5) pathologist (50.01)
2d: *n*=10, topic of psychopathology in adults with obesity Docet, M. F., Larranaga, A., Fernandez Sastre, J. L., & Garcia-Mayor, R. V. (2010). High rate of attention deficit hyperactivity disorder in obese adults: A case-control study. Obesity and Metabolism, 6(4), 121-124.		glp (54.55) proxim* (54.09) hyperact* (53.71) attent* (51.91) cna* (51.84)

Note. A= schematic overview of citation cluster, low citation counts omitted for readability. Colored nodes indicate core citations, lines between nodes show strong citation links. Year range indicates most frequent period of publication. B= word clouds are based on raw word frequency, with larger size and opacity indicating higher frequency. β log ratio are derived from Latent Dirichlet Allocation is a Bayesian topic models. * indicates word stem wildcard. Counts in sub-clusters may exceed total cluster count, as single publications can belong to multiple clusters.

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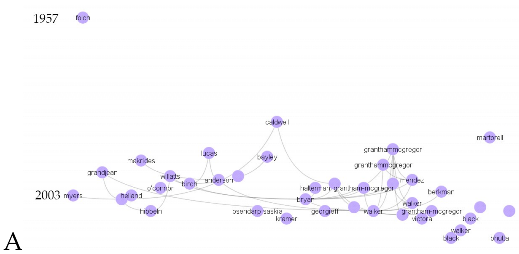
Supplementary Table 3. Cluster 3: *n*= 1542 publications, topic of the association between nutrition in early life and subsequent cognition.



A

B

Cluster information and indicative core publication (weighted for recency)	Word cloud	Most unique topic terms (β log ratio)
3a: *n*=927, topic of child cognitive outcomes in developing countries. Walker, S., Wachs, T. D., Gardner, J. M., Lozoff, B., Wasserman, G. A., Pollitt, E., & Carter, J. A. Child Development in Developing Countries 2: Child development: risk factors for adverse outcomes in development countries. Lancet 369(January), 145-157. 2007.		data (606.25) malnutrit* (606.22) beyond (105.8) anthropometr* (105.79) adopt (105.77) north (105.74)
3aa: *n*=790, topic of child cognitive development in developing countries. Grantham-McGregor, S., Cheung, Y. B., Cueto, S., Glewwe, P., Richter, L., Strupp, B., & International Child Development Steering Group. (2007). Developmental potential in the first 5 years for children in developing countries. The lancet, 369(9555), 60-70. doi: 10.1016/S0140-6736(07)60032-4		shantytown (71.57) multipl* (69.36) sinus (69.21) tanzanian (69.13)
3aaa: *n*=770, topic of early nutrition and cognitive development. Victora, C. G., Adair, L., Fall, C., Hallal, P. C., Martorell, R., Richter, L., ... & Maternal and Child Undernutrition Study Group. (2008). Maternal and child undernutrition: consequences for adult health and human capital. The lancet, 371(9609), 340-357. doi: 10.1016/S0140-6736(07)61692-4		activ* (9.21) bottlefeed (7.35) development (6.07)
3aab: *n*=14, topic of trace metals and cognition in children. Menezes-Filho, J. A., Novaes, C. D. O., Moreira, J. C., Sarcinelli, P. N., & Mergler, D. (2011). Elevated manganese and cognitive performance in school-aged children and their mothers. Environmental research, 111(1), 156-163. doi: 10.1016/j.envres.2010.09.006		sinus (9.34) mid* (8.21) face (7.03)

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3ab: *n*=72, topic of the association between breast milk and later cognition in preterm infants.

Lucas, A., Morley, R., Cole, T. J., Lister, G., & Leeson-Payne, C. (1992). Breast milk and subsequent intelligence quotient in children born preterm. The Lancet, 339(8788), 261-264. doi: 10.1016/0140-6736(92)91329-7

formulafeed (70.02)
highdos* (87.67)
lanka (84.67)
pretermbirth (83.91)
respiratori* (83.8)

3ac: *n*=25, topic of parental smoking and child cognitive outcomes.

Ogden, C. L., Kuczmarski, R. J., Flegal, K. M., Mei, Z., Guo, S., Wei, R., ... & Johnson, C. L. (2002). Centers for Disease Control and Prevention 2000 growth charts for the United States: improvements to the 1977 National Center for Health Statistics version. Pediatrics, 109(1), 45-60. doi: 10.1542/peds.109.1.45

reliabl* (70.8)
protest (70.41)
secular (70.18)

3b: *n*=507, topic of breast feeding and cognitive outcomes.

Anderson, J. W., Johnstone, B. M., & Remley, D. T. (1999). Breast-feeding and cognitive development: a meta-analysis–. The American journal of clinical nutrition, 70(4), 525-535. doi: 10.1093/ajcn/70.4.525

stunt (72.77)
programm* (72.71)
extern* (37.97)
protect (37.32)
folat* (36.5)

3ba: *n*=282, topic of maternal diet in breast feeding and infant outcomes.

Hibbeln, J. R., Davis, J. M., Steer, C., Emmett, P., Rogers, I., Williams, C., & Golding, J. (2007). Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): an observational cohort study. The Lancet, 369(9561), 578-585. doi: 10.1016/s0140-6736(07)60277-3

dummi* (102.06)
lowincom* (101.21)
entranc* (100.02)

3bb: *n*=190, topic of breast feeding and cognitive outcomes.

Kramer, M. S., Aboud, F., Mironova, E., Vanilovich, I., Platt, R. W., Matush, L., ... & Collet, J. P. (2008). Breastfeeding and child cognitive development: new evidence from a large randomized trial. Archives of general psychiatry, 65(5), 578-584. doi: 10.1001/archpsyc.65.5.578

folat* (92.99)
male (91.68)
formulafeed (91.65)

3c: *n*=91, topic of breakfast habits in children and cognitive outcomes.

Rampersaud, G. C., Pereira, M. A., Girard, B. L., Adams, J., & Metzl, J. D. (2005). Breakfast habits, nutritional status, body weight, and academic performance in children and adolescents. Journal of the American Dietetic Association, 105(5), 743-760. doi:10.1016/j.jada.2005.02.007

monnieri (42.49)
mediterranean (42.1)
nonlinear (40.08)
limit (39.48)
oil (39.09)

doi:10.20944/preprints201811.0527.v1

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3d: *n*=36, topic of iodine deficiency in children and cognitive outcomes. Bleichrodt, N., & Born, M. P. (1994). A meta-analysis of research on iodine and its relationship to cognitive development. The damaged brain of iodine deficiency, 1994, 195-200.		iodiz* (614.52) perchlor* (614.52) urinari* (614.52) iodin* (613.71) decad* (613.52)
3e: *n*=34, topic of child height as a predictor of cognitive function. Abbott, R. D., White, L. R., Ross, G. W., Petrovitch, H., Masaki, K. H., Snowdon, D. A., & Curb, J. D. (1998). Height as a marker of childhood development and late-life cognitive function: the Honolulu–Asia Aging Study. Pediatrics, 102(3), 602-609.10.1542/peds.102.3.602		anaem* (73.76) arithmet* (73.76) aspart* (73.76) aspartam* (73.76) atkin (73.76)

Note. A= schematic overview of citation cluster, low citation counts omitted for readability. Colored nodes indicate core citations, lines between nodes show strong citation links. Year range indicates most frequent period of publication. B= word clouds are based on raw word frequency, with larger size and opacity indicating higher frequency. β log ratio are derived from Latent Dirichlet Allocation is a Bayesian topic models. * indicates word stem wildcard. Counts in sub-clusters may exceed total cluster count, as single publications can belong to multiple clusters.

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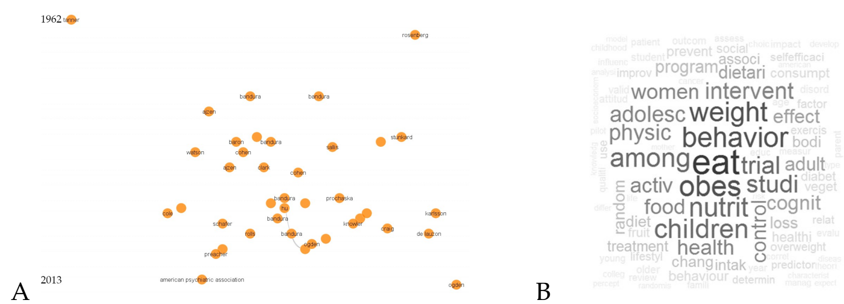
Supplementary Table 4. Cluster 4: *n*= 456 publications, topic of the role of diet in overweight and obesity in children and adolescents.



Cluster information and indicative core publication (weighted for recency)	Word cloud	Most unique topic terms (β log ratio)
4a: *n*=267, topic of health promotion throughout life. Bandura, A. (2004). Health promotion by social cognitive means. Health education & behavior, 31(2), 143-164. doi:10.1177/1090198104263660		al* (331.77) socialcognit* (331.73) start (330.35) media (330.02) mf* (329.92)
4b: *n*=153, topic of dietary restraint and weight loss. Stunkard, A. J., & Messick, S. (1985). The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. Journal of psychosomatic research, 29(1), 71-83. doi:10.1016/0022-3999(85)90010-8		evasion (617.14) fluid (617.14) cardiometabol* (616.14) chimpanzee (616.14) computertailor*(616.14)
4c: *n*=34, topic of obesity and weight loss interventions in children and adolescence. Cole, T. J., Bellizzi, M. C., Flegal, K. M., & Dietz, W. H. (2000). Establishing a standard definition for child overweight and obesity worldwide: international survey. Bmj, 320(7244), 1240. doi:10.1136/bmj.320.7244.1240		energi* (611.14) characterist* (327.36) student (326.27) loss (325.92) predict (325.88)
4d: *n*=10, topic of the impact of parental nutrition on children's health. Wilburn, J., McKenna, S. P., Heaney, A., Rouse, M., Taylor, M., Culkin, A., ... & Lal, S. (2018). Development and validation of the Parenteral Nutrition Impact Questionnaire (PNIQ), a patient-centric outcome measure for Home Parenteral Nutrition. Clinical Nutrition, 37(3), 978-983.		parenter* (521.87) inuit* (521.29) addict* (520.29) arctic (520.29) cdetermin* (520.29)

Note. A= schematic overview of citation cluster, low citation counts omitted for readability. Colored nodes indicate core citations, lines between nodes show strong citation links. Year range indicates most frequent period of publication. B= word clouds are based on raw word frequency, with larger size and opacity indicating higher frequency. β log ratio are derived from Latent Dirichlet Allocation is a Bayesian topic models. * indicates word stem wildcard. Counts in sub-clusters may exceed total cluster count, as single publications can belong to multiple clusters.

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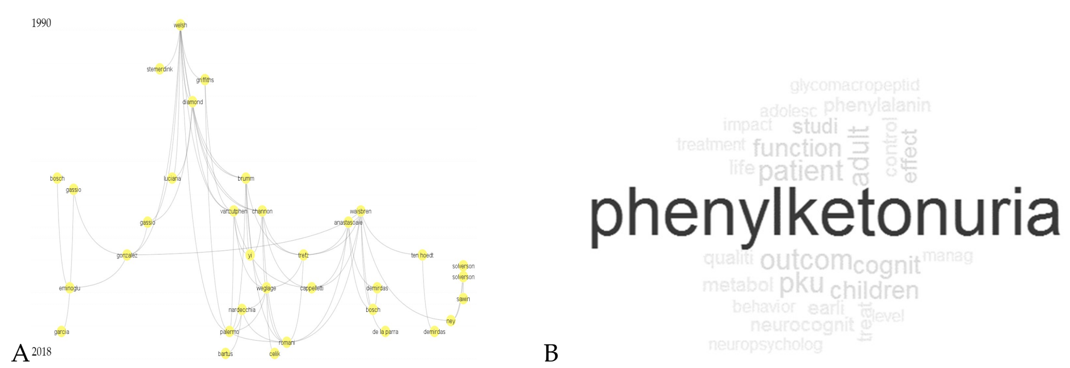
Supplementary Table 5. Cluster 5: *n*= 33 publications, topic of diet and phenylketonuria



Five indicative publications	Most unique topic terms (β log ratio)
Waisbren, S. E., Noel, K., Fahrbach, K., Cella, C., Frame, D., Dorenbaum, A., & Levy, H. (2007). Phenylalanine blood levels and clinical outcomes in phenylketonuria: a systematic literature review and meta-analysis. Molecular genetics and metabolism, 92(1), 63-70. doi:10.1016/j.ymgme.2007.05.006	cohort (4.212)
Welsh, M. C., Pennington, B. F., Ozonoff, S., Rouse, B., & McCabe, E. R. (1990). Neuropsychology of early-treated phenylketonuria: Specific executive function deficits. Child development, 61(6), 1697-1713. doi:10.2307/1130832	femal (3.703)
Brumm, V. L., Azen, C., Moats, R. A., Stern, A. M., Broomand, C., Nelson, M. D., & Koch, R. (2004). Neuropsychological outcome of subjects participating in the PKU adult collaborative study: a preliminary review. Journal of inherited metabolic disease, 27(5), 549-566. doi:10.1023/b:boli.0000042985.02049.ff	age (3.622)
Channon, S., Goodman, G., Zlotowitz, S., Mockler, C., & Lee, P. J. (2007). Effects of dietary management of phenylketonuria on long-term cognitive outcome. Archives of Disease in Childhood, 92(3), 213-218. doi:10.1136/adc.2006.104786	long* (3.425)
Anastasoaie, V., Kurzius, L., Forbes, P., & Waisbren, S. (2008). Stability of blood phenylalanine levels and IQ in children with phenylketonuria. Molecular genetics and metabolism, 95(1), 17-20. doi:10.1016/j.ymgme.2008.06.014	studi* (3.106)

Note. A= schematic overview of citation cluster, low citation counts omitted for readability. Colored nodes indicate core citations, lines between nodes show strong citation links. Year range indicates most frequent period of publication, rather than full time period in which any publications were generated. Upper right is a word cloud based on raw word frequency, with larger size and opacity indicating higher frequency. β and β log ratio are derived from Latent Dirichlet Allocation is a Bayesian topic models. Top 5 citations reported omit repeated mention of multiple editions of the DSM. * indicates word stem wildcard.

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Supplementary table 6. Context of the term 'intervention' within clusters: pairwise correlations

Cluster 1: the association between diet and cognitive outcomes (focus on prediction of decline and disease)

1aaa:	**1aab**	**1ab**
multidomain (0.46)	advanc* (r=0.99)	independentliv* (0.99)
trial (0.42)	combin* (r=0.99)	overweight (0.99)
	dearth* (r=0.99)	program (0.99)
	design* (r=0.99)	cognitivebehavior (0.97)
	elder* (r=0.99)	highdens* (0.97)

1b	**1c**
program (0.83)	singl* (0.77)
fast (0.79)	concurr* (0.73)
irisin* (0.79)	nutritionalbas* (0.73)
japanes* (0.79)	proprietari* (0.73)
kinet* (0.79)	prove (0.73)

Cluster 2: daily self-care and nutrition in older age

2aa	**2ab**	**2b**
trial (0.47)	conven* (0.64)	adapt* (0.64)
	advoc* (0.57)	adher* (0.64)
	attende* (0.57)	array (0.64)
	conjunct (0.57)	categor* (0.64)
	dissemin* (0.57)	handl* (0.64)

2c	**2d**
basi* (0.64)	ah* (0.99)
futur* (0.53)	ascertain (0.99)
concurr* (0.49)	bing (0.99)
critic* (0.49)	blood (0.99)
environ* (0.49)	bmi (0.99)

Cluster 3: the association between nutrition in early life and subsequent cognition.

3aaa	**3ab**	**3ac**
lay* (0.54)	antihelminth (0.55)	school (0.79)
visitor (0.53)	divid* (0.53)	econom* (0.68)
parentchild (0.52)	biscuit (0.48)	endogen* (0.68)
advocaci* (0.51)	coupl* (0.48)	equat* (0.68)
africanamerican (0.51)	fortif* (0.48)	link (0.68)

3ba	**3bb**	**3c**
finsteen (0.49)	iv (0.67)	alloc (0.66)
studiesteen (0.49)	babyfriend* (0.65)	coeduc (0.66)
meat (0.44)	characteristicadjust* (0.65)	dine (0.66)
	cluster* (0.65)	

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mix (0.44)		disengag (0.66)
bergen (0.43)		england (0.66)
3d	**3e**	
demograph (0.86)	context (0.99)	
resourc* (0.86)	normal(0.99)	
anem* (0.81)	adapt* (0.89)	
assist* (0.81)	environ* (0.84)	
capsul* (0.81)	absolut* (0.80)	
Cluster 4: the role of diet in overweight and obesity throughout the lifespan.		
4b	**4c**	**4d**
prevent (0.66)	effect (0.81)	improv* (0.99)
trial (0.58)	background (0.75)	ad* (0.94)
random (0.54)	lifestyl* (0.71)	among (0.94)
lifespan (0.53)	glucos* (0.69)	arctic (0.94)
deliv* (0.48)	insulin (0.69)	avail* (0.94)
Cluster 5: diet and phenylketonuria.	percent (0.8)	
	achenbach (0.7)	
	adapt (0.7)	
	allow (0.7)	
	begun (0.7)	

Note. Figure in bracket is Pearson pairwise *r*, describing the relationship between the term "intervention" and the word reported in the table. When context within sub-clusters were identical (e.g. 'multidomain' had an identical 0.46 correlation for 1a, 1aa, and 1aaa), only the most specific cluster is reported. Where no pairwise correlation >0.5 was present, that cluster is omitted. * indicates word stem truncation. Correlations obtained via the findAssocs' function of tm version 0.6-2.

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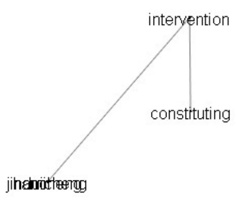
Supplementary table 7. Context of the term 'intervention' within clusters: Latent Semantic Neighbourhood Analysis.

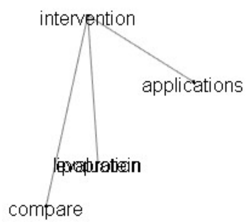
Cluster 1: the association between diet and cognitive outcomes (focus on prediction of decline and disease)

1aaa:



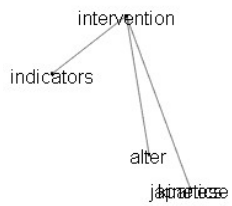
constituting (0.37)
hancheng (0.35)
jinduicheng (0.35)

1ab:



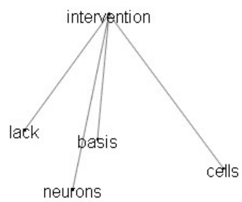
applications (0.99)
compare (0.99)
evaluation (0.99)
lipoprotein (0.99)

1b:



alter (0.95)
indicators (0.95)
japanese (0.95)
kinetics (0.95)

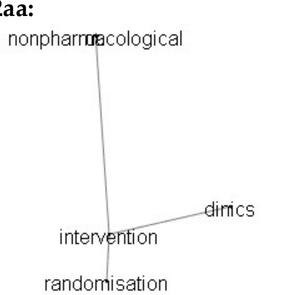
1c:



basis (0.89)
lack (0.89)
cells (0.87)
neurons (0.84)

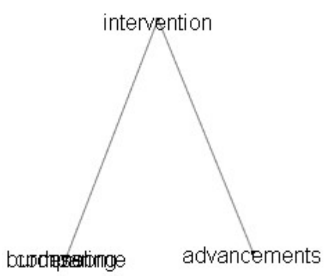
Cluster 2: daily self-care and nutrition in older age

2aa:



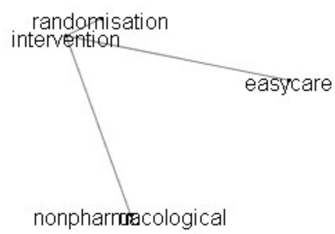
randomisation (0.58)
nonpharmacological (0.42)
uc (0.42)
dinics* (0.4)

2ab:



advancements (0.75)
burdensome (0.75)
comparing (0.75)
counseling (0.75)

2b:



assessed (0.89)
controlled (0.87)
cochrane (0.87)
diagnostic (0.87)

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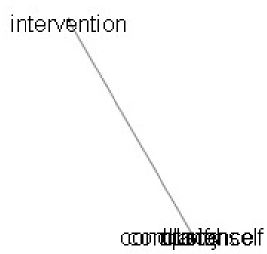
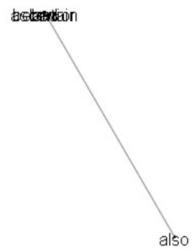
2c:



blood (0.79)
clarify (0.79)
competence (0.79)
self (0.79)

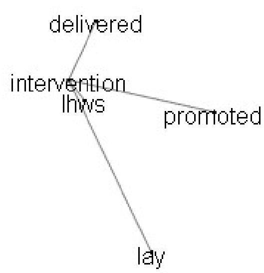
2d:



also (1)
am (1)
ascertain (1)
bed (1)
behavior (1)

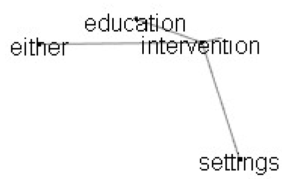
Cluster 3: the association between nutrition in early life and subsequent cognition.

3aaa:



delivered (0.48)
lhws (0.41)
lay (0.37)
promoted (0.37)

3ab:

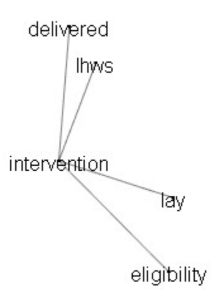


either (0.79)
education (0.78)
settings (0.75)

3ac:

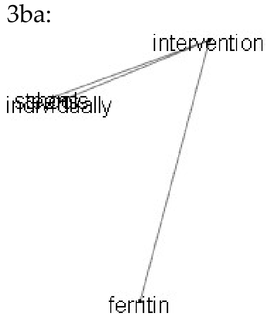
access (1)
adapted (1)
adversity (1)
already (1)
attending (1)

3a:



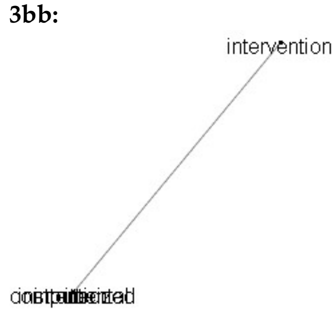
delivered (0.46)
lhws (0.41)
lay (0.37)
eligibility (0.37)

3ba:



individually (0.82)
ferritin (0.81)
schools (0.8)
teens (0.8)

3bb:



computerized (0.83)
instrumental (0.83)
intention (0.83)
itt (0.83)

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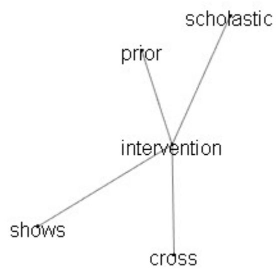
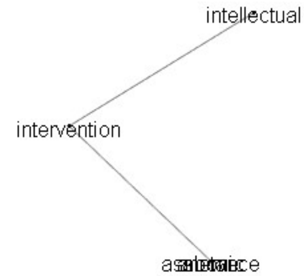
3b:



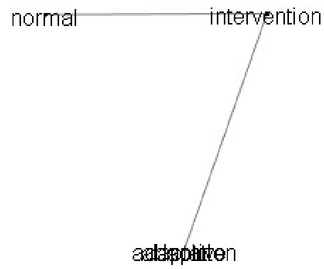
prior (0.76)
cross (0.73)
shows (0.7)
scholastic (0.68)

3d:



intellectual (0.96)
above (0.94)
anemic (0.94)
assistance (0.94)

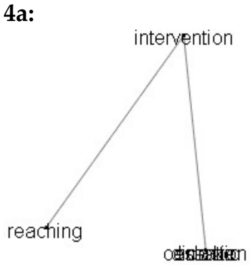
3e:



normal (1)
absolute (0.91)
adaptation (0.91)
adaptive (0.91)

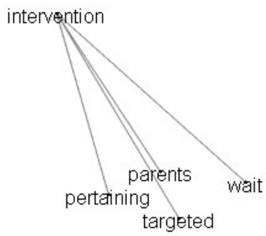
Cluster 4: the role of diet in overweight and obesity in childhood and adolescence.

4a:



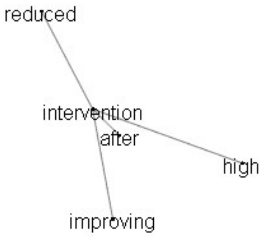
reaching (0.52)
cessation (0.49)
smoke (0.49)
didactic (0.49)

4b:



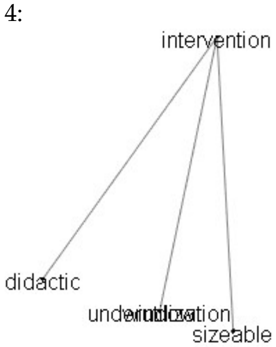
parents (0.82)
wait (0.81)
pertaining (0.76)
targeted (0.75)

4c:



after (0.98)
high (0.84)
improving (0.8)
reduced (0.78)

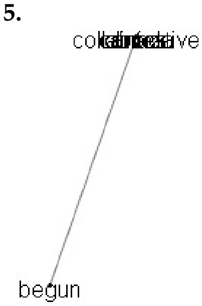
4:



didactic (0.46)
sizeable (0.46)
underutilization (0.46)
window (0.46)

Cluster 5: diet and phenylketonuria.

5.



begun (1)
canada (1)
clinics (1)
collaborative (1)
context (1)

Note. Figure in bracket is distance in semantic space (as pictured in the figures) between the term "intervention" and the word reported in the table. This is obtained by neighborhood analysis, a method of latent semantic analysis which takes into account the larger semantic context of the term, as derived from the text (here, corpora formed by abstracts within each cluster). Neighbourhood analysis was carried using the 'neighbors' function of the LSAfun package (version 0.5.1). When

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Peer-reviewed version available at *Nutrients* **2018**, *11*, 38; doi:10.3390/nu11010038

context within sub-clusters were identical, only the most specific cluster is reported. When there was insufficient proximity between "intervention" and other terms in the cluster for neighbourhood analysis to converge, that cluster is omitted.