WHETHER COVID-19 INFECTION AFFECTS HUMAN COGNITIVE FUNCTION

A Scholarly Project

Submitted to the

Faculty of Liberty University

In partial fulfillment of

The requirements for the degree

Of Doctor of Nursing Practice

By

June Li Alsgaard

Liberty University

Lynchburg, VA

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Scholarly Project Chair Approval:

Kenneth D. Thompson, Pharm.D.

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Abstract

The COVID-19 pandemic, resulting from the SARS-CoV-2 virus, continues to impact the daily lives of individuals worldwide. Although research has been conducted on long-COVID symptoms, the underlying causes remain unclear. Notably, instances of neurological decline have been observed following SARS-CoV-2 infections. 125,573 articles regarding neurological damage and cognitive disfunction were published and can be found from major research databases. For this scholarly project, 25 peer-reviewed journal articles pertaining to long-COVID and neurologic function changes, as well as potential underlying reasons for these changes, were curated. The proposed hypotheses include the virus' ability to pass through and harm the blood-brain barrier and neuronal cells, the release of neurochemicals associated with the SARS-CoV-2 antibody spike protein, as well as vascular ischemia, hypoxia of the brain, and other organs. Urgent attention is required to conduct further research on the treatment of chronic neurologic function changes resulting from long-COVID.

Keywords: COVID-19, SARS-Cov-2, brain function, brain fog, cognitive function, brain damage, neurologic damage, hard to concentrate, memory loss, long-COVID

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SECTION ONE: INTRODUCTION

Background

COVID-19, which is caused by the novel coronavirus SARS-CoV-2, has been responsible for the ongoing pandemic (Feehan & Apostolopoulos, 2021). It is still not entirely or clearly understood what COVID-19 pathogenesis is and how it causes the damage of the human body (Paludan & Mogensen, 2022). More research has been conducted and new data have been analyzed for further understanding of COVID-19 (Paludan & Mogensen, 2022). Based on the data from the World Health Organization (WHO), as of November 18, 2022, there have been 633,601,048 confirmed cases of COVID-19 (including 6,596,542 deaths) globally and 96,752,266 confirmed COVID-19 cases in the US (including 1,064,975 deaths), that have been reported to the WHO (World health Organization [WHO], n.d.). Figure 1 and Figure 2 show more details with trends (WHO, n.d., Overview section). These numbers are likely incomplete due to US and other countries' COVID testing and treatment policies. Many sick patients are refusing to be tested for COVID-19, and the home-based rapid tests are known to produce false negative results. Even if a person receives a positive result from a home rapid test, they typically do not report it to the CDC either because they lack knowledge about how to report it or they refuse to do so. As a result, many home-based rapid test results go unreported unless people seek help from healthcare providers.

COVID-19 is becoming one of the worst pandemics in human history, without any indication of slowing down; and this is despite breakthroughs with current vaccines (Feehan & Apostolopoulos, 2021). Figure 3 shows the historical timeline of major pandemics with upper and lower estimates of deaths (Feehan & Apostolopoulos, 2021, Figure 3).

Figure 1

COVID-19 status as of November 18, 2022, from WHO (WHO, n.d., Overview section)

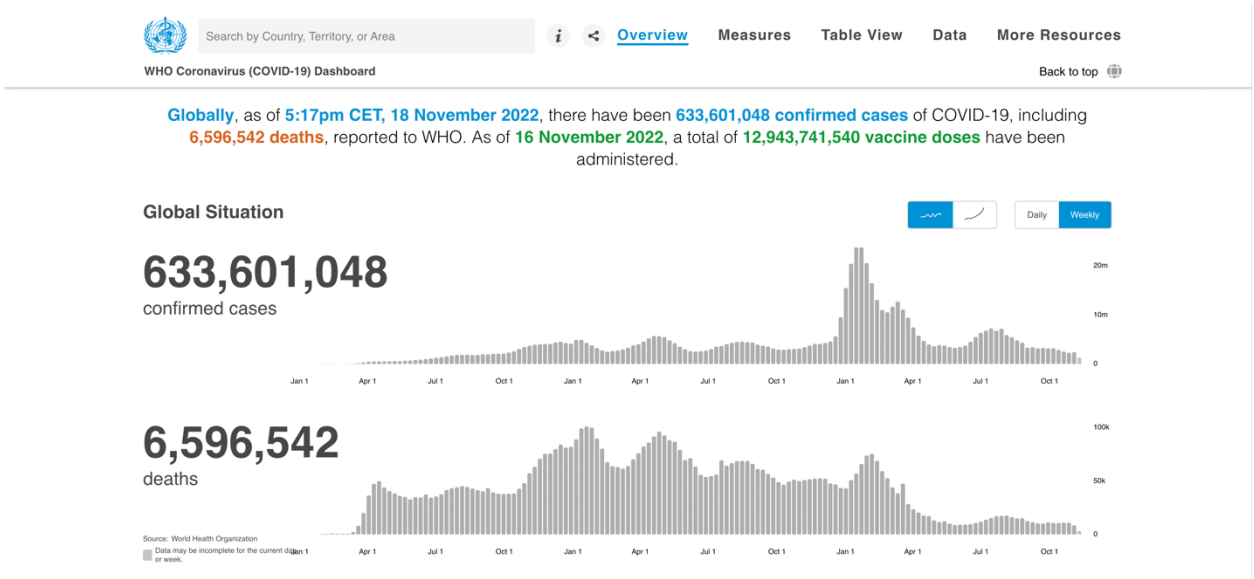


Figure 2

United States of America COVID-19 infection cases and deaths as of November 18, 2022 from WHO (WHO, n.d.)

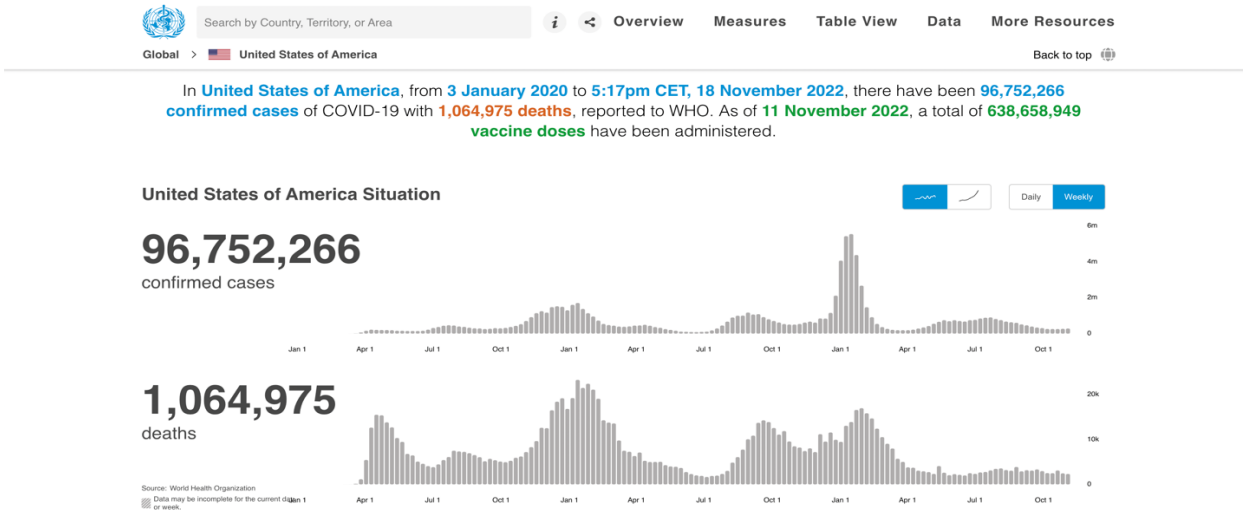
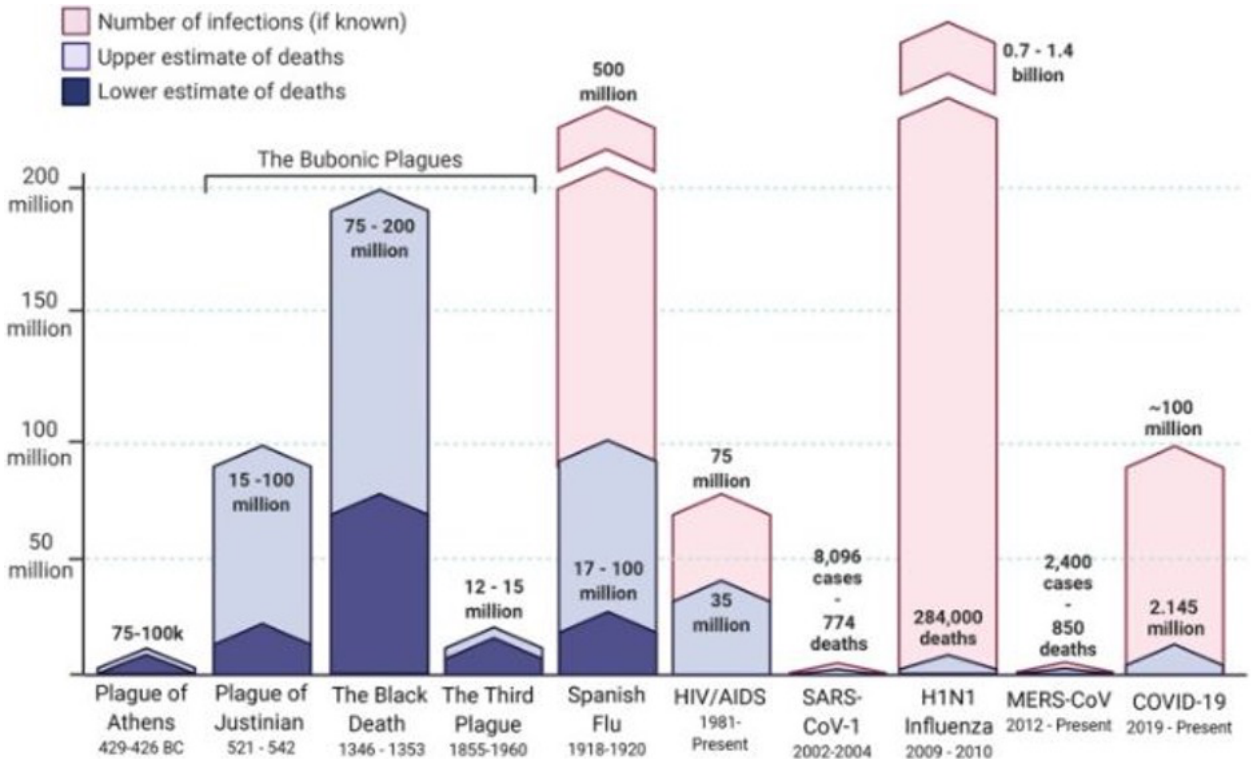


Figure 3

Historical Timeline of Major Pandemics with Upper and Lower Estimates of Deaths (Feehan & Apostolopoulos, 2021)



Problem Statement

Generally speaking, it is extremely hard to avoid hysteresis and incompleteness in epidemiological data collection. As this pertains to the ongoing COVID-19 pandemic, the real number of COVID -19 infections and deaths could be much higher than the numbers we see in public publications. Despite the diligent efforts of epidemiologists and frontline healthcare professionals to ensure data accuracy, there may be numerous reasons for discrepancies. COVID-19 infection does not only pose the risk of death, as numerous research efforts and studies have highlighted potential long-term complications that can affect multiple body systems such as the heart, lungs, kidneys, skin, and brain, among others. (Center for Disease Control and

Prevention [CDC], n.d.). It has been extremely challenging for countries' top leaders to create guidelines for people to follow them globally. It may be totally different strategus using for disease control between countries, such as the U.S. and China. Today, it may still be difficult to judge which view is better or correct. The answer to these questions may be explored for many decades.

Purpose of the Project

The purpose of this evidenced-based practice (EBP) project is to identify a possible relationship between COVID-19 infection and neurologic damage which is represented by decline of cognitive function in adult population. This integrative review project started with research of databases of peer-reviewed journal articles related to COVID-19 and brain function changes.

Clinical Question

To form the clinical question in this integrative review, the PICO framework (representing patient/problem/population, intervention, comparison, and outcome) was used. As this project does not involve intervention, the focus is on COVID-19 infected patients; and specifically on the neurological damage that may occur post-infection, which can be evaluated through cognitive tests or imaging studies. The comparison will be made between cognitive function or changes in brain scans before and after infection, and the outcome will be to determine if COVID-19 causes brain damage and reduces cognitive function. Thus, the PICO statement is "Whether SARS-CoV-2 infections affect human cognitive function?"

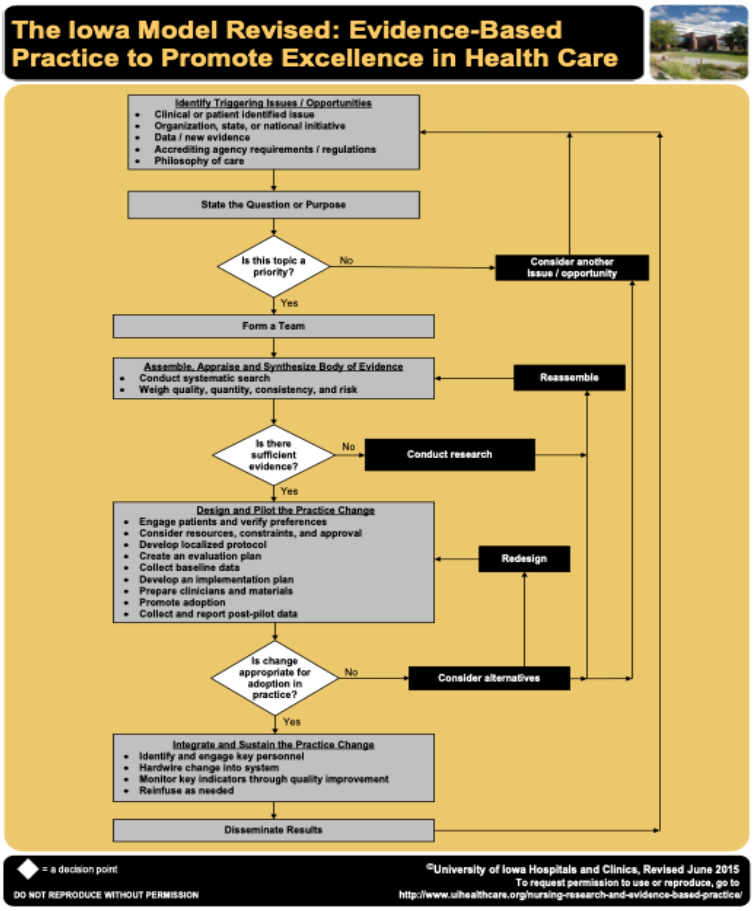
Conceptual Framework/Model

The Iowa model is a valuable tool for analyzing and implementing evidence-based practice that was used in this scholarly project. In the Iowa Model, the first step is identifying the

triggering issue and form a question or purpose of potential changes; if it is a priority, then form a team to do research for existing studies and see whether there is sufficient evidence to support the change. After completing this, the next step is to either conduct new research, or make a plan of change (Buckwalter et al., 2017). The literature review offers data to be considered for the next step. The articles listed above clearly support the relationship between SARS-CoV-2 infection and some neurologic and other long-COVID symptoms. Therefore, it could be considered enough evidence to craft a plan of a change. If there is no higher-level quantitative study or the quantitative study only proves the relationship without detailed improvement rates from a literature review, then more detailed quantitative research should be designed and conducted before planning any changes to a practice.

Figure 4

The Iowa Model



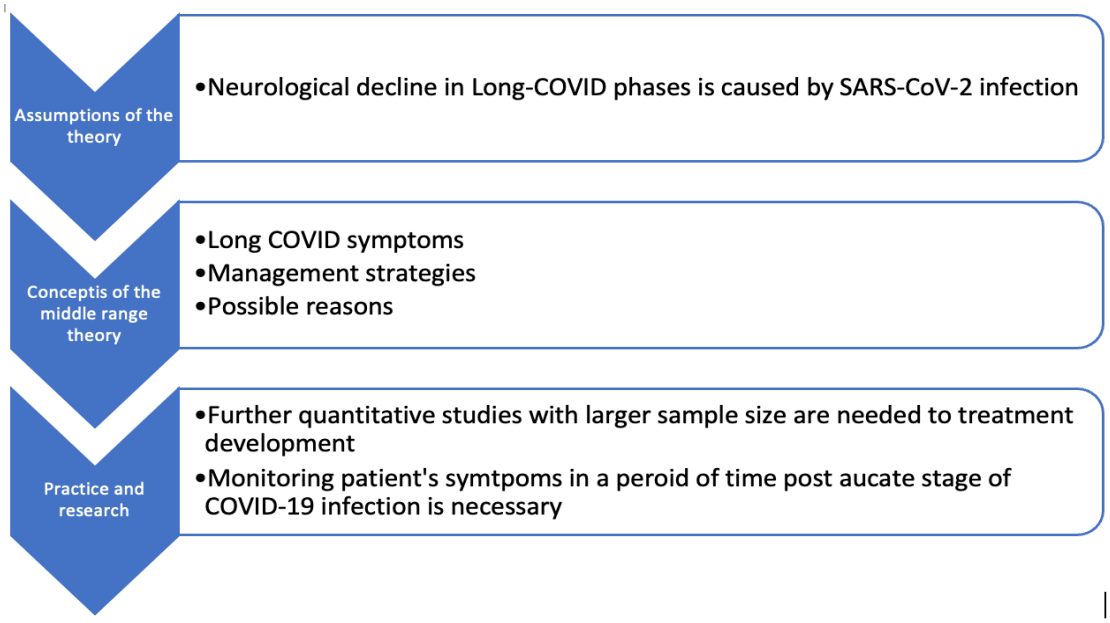
Theoretical Framework

The Symptom Management Theory was developed by a group of authors, namely Bender, Janson, Franck, and Lee, who are affiliated with the University of California, San Francisco Symptom Management Faculty Group. Based on the interactive-integrative paradigm, the theory proposes that symptom management is a result of people's interaction with their environment. It assumes that health and illness have an impact on symptom management, and that improvements in symptoms go beyond personal health. Additionally, the theory suggests that symptoms are subjective and often experienced in clusters. There are three concepts in this theory: symptom experience, symptom management strategies, and symptom status outcomes. Practice based on this theory emphasizes patient-provider communication and focused on provider understanding patient’s symptoms experience and offering effective strategies. On the

other hand, research based on this theory includes measurement of symptom-specific outcomes and contextual factors related to the symptom under study (Smith & Liehr, 2018).

Figure 5

The Symptom Management Theory



SECTION TWO: COMPREHENSIVE AND SYSTEMATIC SEARCH

Search Organization and Reporting Strategy

This study utilized Liberty University's online library to conduct systematic research. Given the focus on databases specializing in medical content, only high-quality articles from such databases were considered for the search. Ultimately, the study selected CINAHL, PsychINFO, PubMED, ProQuest, and Web of Science databases to be used. In order to choose high quality articles, only peer reviewed journal articles were selected at initial search. Time sensitivity is considered as a part of quality control for selecting articles. In this study, five-year was chosen as a time marker.

Overall, this systemic research using CINAHL, PsychINFO, PubMED, ProQuest, and the Web of Science databases, focused on peer reviewed journal articles which were published within five years.

Key Words and Terminology

The key words for searching the articles were COVID-19, SARS-Cov-2, brain function, brain fog, cognitive function, brain damage, neurologic damage, hard to concentrate, memory loss, long-COVID.

COVID-19 refers to "a mild to severe respiratory illness that is caused by a coronavirus (Severe acute respiratory syndrome coronavirus 2 of the genus Beta-coronavirus), is transmitted chiefly by contact with infectious material (as respiratory droplets) or with contact with objects or surfaces contaminated with the causative virus, and is characterized especially by fever, cough, and shortness of breath and may progress to pneumonia and respiratory failure (Merriam-Webster, n.d.-b, section 1)".

SARS-CoV-2 refers to "the coronavirus (Severe acute respiratory syndrome coronavirus 2 of the genus Beta-coronavirus) that is the causative agent of COVID-19 (Merriam-Webster, n.d.-d, section 1)"

Brain fog refers to "a usually temporary state of diminished mental capacity marked by inability to concentrate or to think or reason clearly (Merriam-Webster, n.d.-a, section 1)"

Long-COVID refers to "a condition that is marked by the presence of symptoms (such as fatigue, cough, shortness of breath, headache, or brain fog) which persist for an extended period of time (such as weeks or months) following a person's initial recovery from COVID-19 infection : POST-COVID SYNDROME (Merriam-Webster, n.d.-c, section 1)".

SECTION THREE: MANAGING THE COLLECTED DATA

This scholarly project included a review of 125,573 results, from which twenty-five peer-reviewed journal articles were selected, encompassing various study types such as meta-analyses, cohort studies, systematic reviews of qualitative or regulatory studies. The literature review was organized according to the levels of evidence outlined by the Melnyk framework. This author had access to the full text of all selected articles. Appendix A is a literature review matrix which contains all twenty-five peer-reviewed journal articles and their key points in article title, study purpose, sampling, methods, study results, level of evidence, limitations, and whether to use as evidence to support change in practice.

SECTION FOUR: QUALITY APPRAISAL

In addition to utilizing the peer-reviewed journal article criterion and a five-year time frame, this study used the Melnyk framework as a quality control measure.

Critical Appraisal Tool

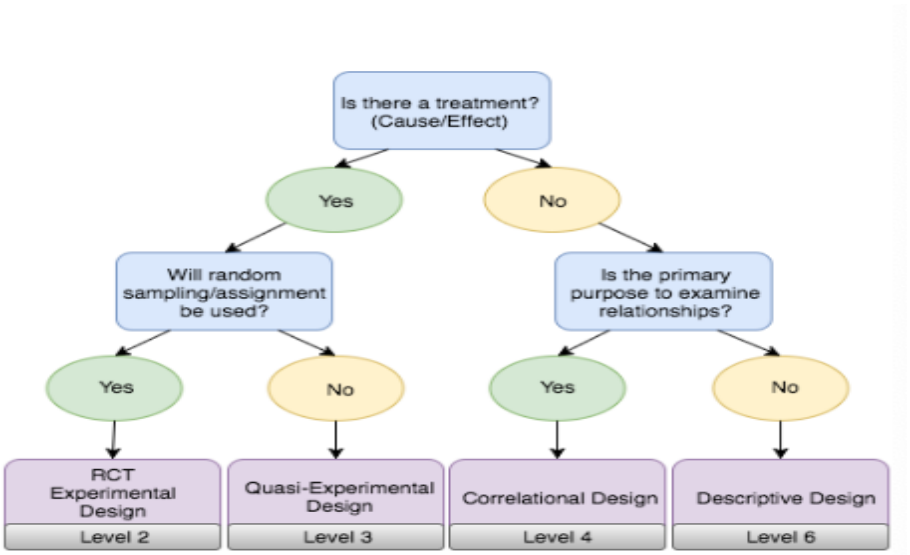
The Melnyk framework, also known as the Melnyk levels of evidence, is a tool used in evidence-based practice to evaluate the strength and quality of evidence from research studies. It consists of seven levels of evidence, each with varying degrees of reliability and rigor, and is often used to guide healthcare professionals in making clinical decisions based on the best available evidence (University of Michigan, 2022, Melnyk Levels of evidence section). Level one includes systematic review and meta-analysis of randomized controlled trials, clinical guideline based on systematic reviews or meta-analyses (University of Michigan, 2022, Melnyk levels of evidence section). Level two includes one or more randomized controlled trails (University of Michigan, 2022, Melnyk levels of evidence section). Level three includes non-

randomized sampling but controlled trial (University of Michigan, 2022, Melnyk levels of evidence section). Level four includes case-control or cohort study (University of Michigan, 2022, Melnyk levels of evidence section). Level five represents systematic review of descriptive and qualitative studies (University of Michigan, 2022, Melnyk levels of evidence section). Level six includes single descriptive or qualitative study (University of Michigan, 2022, Melnyk levels of evidence section). Level seven is for expert opinion (University of Michigan, 2022, Melnyk levels of evidence section).

A simpler way to evaluate level of evidence based on Melnyk levels of evidence is based on whether there will be a treatment. If there is a treatment involved in the study, it likely belongs to level one to level three, otherwise, the highest level will be level four.

Figure 6

Level of evidence (University of Michigan, 2022, Figure 1)



SECTION FIVE: DATA ANALYSIS AND SYNTHESIS

Data Analysis

There are five articles at Melnyk framework level one of evidence (Akbarialiabad et al., 2021; Hawke et al., 2022; Jarrott et al., 2022; Moghimi et al., 2021; Theoharides, 2022), two articles at level three (Aiello et al., 2021; Rigoni et al., 2022), fifteen articles at level four (Asadi-Pooya et al., 2021; Delgado-Alonso et al., 2022; Di Stadio et al., 2022; Douaud et al., 2022; Frontera et al., 2022; Guo et al., 2022; Hellgren et al., 2021; Hugon et al., 2021; 2021; Leta et al., 2021; Mandal et al., 2020; Salihefendic et al., 2021; Østergaard, 2021), and three articles at level five (Baig, 2021; Fernández-de-las-Peñas et al., 2021; Theoharides et al., 2021), which made total of twenty-five articles in this scholarly project. Possible relationships for certain phenomena were discovered by both quantitative studies and qualitative studies at macro level / system level and micro level/ cell and neurochemistry level. Quantitative research often offered more details and provided a higher level of evidence. However, qualitative and correlational research offered great direction or hypothesis of further quantitative research. Therefore, both types of studies can be used for supporting practice changes, and quantitative data could more likely have higher influence on decision of implementing a change. For example, the article “Comparison of serum neurodegenerative biomarkers among hospitalized covid-19 patients versus non-covid subjects with normal cognition, mild cognitive impairment, or Alzheimer's dementia. Alzheimer's & Dementia”, “Long-covid syndrome-associated brain fog and chemofog: Luteolin to the rescue” “Chronic long-covid syndrome: A protracted covid-19 illness with neurological dysfunctions ” , “Could SARS-CoV-2 spike protein be responsible for long-covid syndrome? ”, and “long covid—a hypothesis for understanding the biological basis and pharmacological treatment strategy ”, all mentioned biomarkers of neuronal and glial degeneration with patients infected by SARS-CoV-2, which could be the cause of long-COVID (Baig, 2021; Frontera et al., 2022;

Jarrott et al., 2022; Theoharides et al., 2021). All of them mentioned, further study is needed (Baig, 2021; Frontera et al., 2022; Jarrott et al., 2022; Theoharides et al., 2021).

"Long COVID—a hypothesis for understanding the biological basis and pharmacological treatment strategy" and "Could SARS-CoV-2 spike protein be responsible for long-covid syndrome?", both mentioned intracellular antioxidant, such as Luteolin, might help with preventing or treat long-COVID (Theoharides, 2022; Theoharides et al., 2021).

Quantitative research data showed that 40% to 77.9% of patients experience post-COVID symptoms or developed long-COVID syndrome (Jarrott et al., 2022; Moghimi et al., 2021). Some research showed patients' neurologic decline even getting worse after certain time (Rigoni et al., 2022), which is opposite of what general population expected.

Some studies showed possible reason of vascular ischemia of brain which may lead to hypoxia of tissues (Salihefendic et al., 2021; Theoharides, 2022; Østergaard, 2021). Even though those studies are not all quantitative, the hypothesis of hypoxia was brought to the table. We can start thinking or implementing some patient education or activates into plan of care, such as deep breathing, due to low risk of harm to patient and potential benefit of patients.

Synthesis

Numerous studies have demonstrated a clear correlation between SARS-CoV-2 infection and a decline in neurological function(Aiello et al., 2021; Asadi-Pooya et al., 2021; Baig, 2021; Delgado-Alonso et al., 2022; Di Stadio et al., 2022; Douaud et al., 2022; Fernández-de-las-Peñas et al., 2021; Frontera et al., 2022; Guo et al., 2022; Hellgren et al., 2021; Hugon et al., 2021; Leta et al., 2021; Mandal et al., 2020; Moghimi et al., 2021; Ollila et al., 2022; Rigoni et al., 2022; Salihefendic et al., 2021). Nonetheless, the underlying reasons remain uncertain, and the majority of medical professionals have not yet established or accepted any effective treatment.

The literature puts forth several hypotheses, such as inflammation-induced damage to brain or other tissue cells, vascular ischemia, hypoxia, and underlying chronic conditions (Theoharides, 2022; Theoharides et al., 2021; Østergaard, 2021). Further evaluation and higher-level studies are needed. Treatment-related experimental studies are needed urgently due to increasing cases of long-COVID syndrome (Moghimi et al., 2021).

Ethical Consideration

Ethical consideration is a set of principles that guide researchers and scientists during the stages of research design and practices. It is an important part of consideration during research. However, it could be different internationally. Some countries do not require ethical approval for clinical research, but others may have very straight restrictions. For example, in article "Long-COVID symptoms and duration in SARS-CoV-2 positive children-a nationwide cohort study", the authors pointed out that ethical approval was not requested by Danish law (Borch et al., 2022, Materials and methods section). Marta Rigoni and the team clearly stated in the article "Long-COVID results after hospitalization for SARS-CoV-2 infection" that their study was approved by the ethic committee of the Autonomous Province of Trento and followed the Declaration of Helsinki Ethical Principles for Medical Research Involving Human subjects (Jarrott et al., 2022, Ethics statement section).

In the total of twenty-five articles, there are eight articles were approved by their local government or hospital ethical committee(Aiello et al., 2021; Delgado-Alonso et al., 2022; Di Stadio et al., 2022; Douaud et al., 2022; Guo et al., 2022; Hawke et al., 2022; Hellgren et al., 2021; Ollila et al., 2022; Rigoni et al., 2022), four of them clearly stated that they did not have ethical approval based on the nature of the study (Akbarialiabad et al., 2021; Borch et al., 2022; Jarrott et al., 2022; Theoharides, 2022), and thirteen of them did not mention ethical

consideration in the research paper which includes systemic reviews (Asadi-Pooya et al., 2021; Baig, 2021; Fernández-de-las-Peñas et al., 2021; Frontera et al., 2022; Hawke et al., 2022; Hugon et al., 2021; 2021; Leta et al., 2021; Mandal et al., 2020; Moghimi et al., 2021; Salihefendic et al., 2021; Theoharides et al., 2021; Østergaard, 2021).

Ethical approval

The study does not require ethical approval, because the systematic review is based on already published reports and the original data are anonymous. All of the patient information was deidentified.

SECTION SIX: DISCUSSION

Significance and implications for Practice

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, is still ongoing. While the number of daily infections may decrease for various reasons, the number of patients suffering from long-COVID continues to rise (Theoharides et al., 2021). Quantitative research data showed from 40% to 77.9% of patients experience post-COVID symptoms or developed long-COVID syndrome (Jarrott et al., 2022; Moghimi et al., 2021). The reasons behind long-COVID remain unclear. SARS-CoV-2 infection causes brain change which is represented by cognitive functions declining was observed clinically and brain changes in certain area has been proved by image studies (Di Stadio et al., 2022; Douaud et al., 2022; Salihefendic et al., 2021). From 8.7 % to 46.7% patients reported mental clouding/brain fog after COVID-19 infection from variety studies (Aiello et al., 2021; Asadi-Pooya et al., 2021; Di Stadio et al., 2022; Guo et al., 2022; Hugon et al., 2021).

This evidence-based project has significance and relevance related to patient care in daily practice. It summarized data from high quality published articles with real symptoms observed

clinically. While pulmonary changes received extensive coverage and public attention, the topic of brain changes and declining cognitive functions did not garner the same level of prominence. Consequently, it was more susceptible to being overlooked or ignored. Nevertheless, it is important to recognize that brain cell damage resulting from cognitive decline can potentially have lasting effects on individuals' lives. It goes without saying that those experiencing a decline in cognitive function also suffer noticeable decrease in their overall quality of life. The best way to avoid this is prevention from infection of the virus. This project brought awareness to both patients and clinicians. It offers evidence-based data to prove that brain damage is not as people expected that the symptoms improve over time, but get worse (Rigoni et al., 2022). It supports the importance of wearing a high-quality mask and warning patients that even though they might not suffer from severe symptoms during acute stage of SARS-CoV-2 virus infection, there still could be a significant consequence from the infection. Asymptomatic infection should not be an excuse for lowering the level of prevention.

Another implication for practice is the need of cognitive function evaluation after COVID-19 infection. For patients who already showed symptoms of cognitive function decline, COVID-19 infection should be considered as a risk factor. The importance of prevention of COVID-19 infection should be on going in patients' education at daily practice. The brain damage should be mentioned as potential consequence to increase the public understanding and awareness. More people should be aware of the long-term consequence.

Several hypotheses have been discovered and discussed by healthcare professionals, including biomarkers of neuronal and glial degeneration with patients infected by SARS-CoV-2, which could be the cause of long-COVID (Baig, 2021; Frontera et al., 2022; Jarrott et al., 2022; Theoharides et al., 2021), vascular ischemia of brain which may lead to hypoxia of tissues

(Salihefendic et al., 2021; Theoharides, 2022; Østergaard, 2021), and COVID-19 spike protein may passing and damaging BBB and neuron (Theoharides, 2022). Some studies even showed patients' neurologic decline even getting worse after certain time (Rigoni et al., 2022), which is opposite of what general population expected. Unfortunately, no effective treatment has been discovered yet, which could be an urgent need in the current situation. Therefore, it has become imperative to expedite higher-level quantitative experimental research to address these concerns. Given the global battle against the SARS-CoV-2 virus, international cooperation may be crucial in the current situation.

Sustainability

The COVID-19 global pandemic, precipitated by the SARS-CoV-2 virus, may eventually reach an official conclusion. Nevertheless, the virus persists and continues to exert its impact on afflicted individuals on a daily basis. While the mortality rate has decreased to a level that signifies progress in curbing the global pandemic, it is crucial to acknowledge the enduring long-term repercussions stemming from infection. Early detection and intervention still play an important role to keep death rate low. They may also help with long-COVID symptoms. More research of discover the relationship between early intervention or vaccine and long-COVID symptoms, especially brain damage is urgently needed in the future. No published article related to this topic was found in this project. Continuing education of the importance of prevention, such as wearing masks in medical settings, should become one of the daily practice protocols. For diseases which may cause long-term and potentially permanent damage, such as SARS-CoV-2 virus infection done to the brain, should be clearly conveyed to patients. Healthcare providers should stay updated and educated in fast changing situations, making a realistic plan

for patients to follow, and emphasizing the effective way and importance of preventing disease, not only COVID-19, but also other contiguous disease as well.

Dissemination plan

The dissemination plan for this project will be multi-faceted and include multiple levels of focus. The first level involves a focus on sharing the research results with healthcare professionals. Inside of this author's practice and organizations that the author joins, discussing results from this evidence-based project could be done at weekly or monthly meetings. Outside of the author's practice or at organizations with direct connections, discussing the results from this project can be done at lunch meetings or other official or non-official meetings. For healthcare providers who do not have direct connection with the author, this author plan to publish the article and give presentation in healthcare conference to share the results from this evidence-based project with other healthcare professionals to spread out the words.

The second level focuses on sharing the research results with patients. Patient education of COVID-19 prevention will be added to the daily practice protocol where this author works. Patient education hand-outs regarding signs and symptoms of brain damage which are represented by cognitive function decline will be given to patients who have or potentially have COVID-19 infection, especially during high sickness seasons, such as winter. It will be recommended that patients who had COVID-19 infections in the past do a comprehensive cognitive evaluation, and this will be added to the daily practice at this author's practice. Early referral to a neurologist to slow down or stop the symptoms getting worse will be discussed with patients as needed.

The third level is focusing on sharing the research data with the public. A short educational video could be beneficial to the public. Putting the video on the practice's website

and social media platforms like Facebook or YouTube in parallel with hosting some public webinars could be ways to reach the goal.

Conclusion

The COVID-19 pandemic, stemming from the SARS-CoV-2 virus, continues to profoundly impact daily life for individuals worldwide. While studies have been conducted on the phenomenon of long-COVID symptoms, the precise underlying causes remain elusive. Remarkably, observations of neurological decline subsequent to SARS-CoV-2 infection have been documented. The scientific community has responded with great interest, resulting in the publication of a significant number of articles—approximately 125,573—within major research databases, exploring the subject of neurological damage and cognitive dysfunction. To contribute to this body of knowledge, this scholarly project focuses on curating 25 peer-reviewed journal articles specifically related to long-COVID and its association with changes in neurologic function, as well as potential etiological factors contributing to such changes.

Among the proposed hypotheses examined in the curated articles are the virus's ability to breach the blood-brain barrier and inflict damage upon neuronal cells, the release of neurochemicals linked to the SARS-CoV-2 antibody spike protein, as well as the occurrence of vascular ischemia, brain hypoxia, and other organ-related manifestations. Urgent attention must be directed towards further research into the treatment of chronic neurologic function alterations stemming from long-COVID, emphasizing the significance of preventive measures against COVID-19 infection in everyday practice.

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Appendix A

Literature review matrix

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
[1] Guo, P., Benito Ballesteros, A., Yeung, S. P., Liu, R., Saha, A., Curtis, L., Kaser, M., Haggard, M. P., & Cheke, L. G. (2022). Covcog 2: Cognitive and memory deficits in long covid: A second publication from the covid and cognition study. Frontiers in Aging Neuroscience, 14. https://doi.org/10.3389/fnagi.2022.804937	This second paper from an ongoing study sets out to prove if there is a link between COVID-19 infection and later cognitive decline ("brain fog"). It also sought	A total of 421 participants over 18 years old were recruited via word of mouth and social media advertisements. Most of the participants were from	Six cognitive tasks were given to the participants, including a word list recognition memory test, a pictorial associative memory test, a category fluency test, a mental rotation test, a cart sorting test, and a number	A consistent and clear correlation was found between COVID-19 infections and decreases in cognitive ability as demonstrated with poorer performance	Level 4: Correlational Design (cohort study)	Some participants in the study indicated they were unsure if they had COVID-19, and it was not proven with laboratory tests if they had been infected. In	Yes. The study itself says the conclusion of this study, and others like it, should convince policy-makers to rethink relaxing safety protocols for COVID-19. The

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
	to establish a relationship between the severity of cognitive decline and the severity of the COVID-19 infection.	English-speaking countries (US, Canada, Australia, etc.). Of these, 181 (130 women) had been infected with COVID-19, and 185 (118 women) had not been infected	counting test. Speed and accuracy were measured with the tests. Test results were first sorted into COVID and non-COVID groups. Next, various statistical analyses were performed.	on cognitive assessments.		addition to this, participants in the control group may have had mild COVID-19 infections without reporting it in the study.	long-term societal impacts of allowing COVID-19 to spread unchecked could be disastrous.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
		by COVID-19.					
[2] Hugon, J., Msika, E.-F., Queneau, M., Farid, K., & Paquet, C. (2021). Long covid: Cognitive complaints (brain fog) and dysfunction of the cingulate cortex. Journal of Neurology, 269(1), 44–46. https://doi.org/10.1007/s00415-021-10655-x	The purpose of this study is to show brain scans of two patients who suffered cognitive decline ("brain fog") as a result of COVID-19 infections.	Two patients (one 45-year-old male and one 43-year-old female) who both reported cognitive decline after COVID-19 infections. Neither	Myriad health screenings and brain scans were conducted on both patients to attempt to determine the cause of their reported cognitive declinations. Both MRI scans were reported as being "normal", but	Ultimately, this study found abnormalities with Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET) scan results in both patients, though the scan results	Level 4: Cohort study	This study was severely limited by its population size of only two individuals, but these were unique in that doctors conducted a very thorough	Yes, this study underscores how little we still know or understand about the cognitive decline associated with long COVID.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
		patient had any risk factors like obesity, diabetes, or hypertension.	symptoms persisted for the patients.	had differences from each other.		series of tests and scans on both patients to attempt to identify the root cause of their cognitive dysfunctions.	
Douaud, G., Lee, S., Alfaro-Almagro, F., Arthofer, C., Wang, C., McCarthy, P., Lange, F., Andersson, J. R., Griffanti, L., Duff, E., Jbabdi, S., Taschler, B., Keating, P., Winkler, A. M., Collins, R., Matthews, P. M., Allen, N.,	The goal of this study is to determine if brain-related abnormalities from	A total of 785 participants of UK Biobank between 51 and 81 years old	Before COVID-19 began, a UK Biobank MRI imaging study had already been underway.	This study identified significant negative effects related to SARS-CoV-2 infections.	Level 4: Cohort-based quantitative imaging study with	The process for ruling out the effects of pneumonia and influenza	Yes, this study contains direct quantitative evidence of the negative effect

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Miller, K. L., Nichols, T. E., & Smith, S. M. (2022). Sars-cov-2 is associated with changes in brain structure in uk biobank. Nature, 604(7907), 697–707. https://doi.org/10.1038/s41586-022-04569-5	COVID-19 infections can be detected in milder cases, with the subsequent goal of determining the exact mechanisms that contribute to brain pathology with COVID-19 infections.	were imaged twice using MRI scans. 401 patients had tested positive for COVID-19 between their two MRI scans, while 384 did not test positive for COVID-	Researchers were able to use these scans and then compare them with scans of the same individuals after they had been infected with COVID-19 (proven primarily via antigen tests). The control group (individuals who had never had COVID-19) were then	The primary effect was atrophy and increased tissue damage in cortical areas connected to the olfactory cortex. Another effect was a measurable decrease of brain and cerebrospinal fluid volume in patients with COVID-19	correlational design.	on this study's results were somewhat weakened by a small comparative sample size (only 5 patients were reported to have influenza in between their MRI scans). This is likely due	COVID-19 has on the brain.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
		19 between their scans (the control group).	selected and retested for COVID-19 with antigen tests. Image-derived phenotypes (IDPs) were used to model compounding effects and estimate the longitudinal changes between each person's two MRI scans.	infections. Significant loss of gray matter was also observed in areas of the brain with high connectivity to the olfactory system.		to healthcare organizations not focusing on influenza during the COVID-19 pandemic.	
Aiello, E., Fiabane, E., Manera, M., Radici, A., Grossi, F., Ottonello, M., Pain,	This study aims to determine	The study used a sample of	The severity of the COVID-19 infections was	Both screeners (tests) were	Level 3: Retroactive	This study used a relatively	Yes, but not directly. This study

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
D., & Pistarini, C. (2021). Screening for cognitive sequelae of sars-cov-2 infection: A comparison between the mini-mental state examination (mmse) and the montreal cognitive assessment (moca). Neurological Sciences, 43(1), 81–84. https://doi.org/10.1007/s10072-021-05630-3	which cognitive assessment (the Mini-Mental State Examination (MMSE) or the Montreal Cognitive Assessment (MoCA)) is best suited for detecting cognitive deficits in patients who have	100 individuals from northern Italy who had recovered from COVID-19 infections between May 2020 and 2021.	categorized as “asymptomatic”, “mildly symptomatic”, “mild-to-moderate (oxygen, but no ventilation), and “moderate to severe” (requiring ventilation or ICU treatment). Data from the MMSE or MoCA tests that had been administered to the patients	to detect severe cognitive deficits in patients, but the MoCA test performed better in detecting sub-clinical cognitive changes. The MoCA test was also better at differentiating between diverse levels of	statistical analysis study using data from psychological screenings within a set time period.	small sample size in one region of the world (northern Italy).	demonstrates which type of cognitive test is best used in determining whether a patient is experiencing cognitive deficits after recovering from COVID-19.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
	recovered from COVID-19 infections.		were retroactively collected and analyzed for this study.	mental efficiencies in patients.			
Hawke, L. D., Nguyen, A. P., Ski, C. F., Thompson, D. R., Ma, C., & Castle, D. (2022). Interventions for mental health, cognition, and psychological wellbeing in long covid: A systematic review of registered trials. Psychological Medicine, 1–15. https://doi.org/10.1017/s0033291722002203	The goal of this study is to synthesize the results of large registered trials related to cognitive decline in patients with long COVID so that mental	This study reviewed 42 registered trials, with a total sample size of 5,814 participants.	The standard systematic review guidelines were followed, with trials selected from large-trial registries between 2020 and May 2022.	Generally speaking, there are mixed results from the studies reviewed; and this is especially true regarding the outcomes of the physiotherapy and natural	Level 1: Systematic Review	Given the wide variety of the studies reviewed, it is difficult to provide specific recommendations for interventional treatments for patients	Yes, but the change might be more on the type of studies being funded and conducted in the future related to cognitive decline with

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
	health interventions can be more readily understood and implemented.			supplement intervention trials.		with long COVID. This weakness is shared across many current and ongoing studies, as it seems to be difficult to pinpoint specific causes of some cognitive symptoms related to	long COVID.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
						long COVID.	
Di Stadio, A., Brenner, M. J., De Luca, P., Albanese, M., D'Ascanio, L., Ralli, M., Roccamatisi, D., Cingolani, C., Vitelli, F., Camaioni, A., Di Girolamo, S., & Bernitsas, E. (2022). Olfactory dysfunction, headache, and mental clouding in adults with long-covid-19: What is the link between cognition and olfaction? a cross-sectional study. Brain Sciences, 12(2), 154. https://doi.org/10.3390/brainsci12020154	This study focuses on the correlation between loss of smell (olfactory dysfunction) and brain fog associated with long COVID, and the study aims to prove there is a	The study included 152 adult patients in Italy (102 females and 50 males) in their late 30's and 40's who self-reported a loss of smell associated with their COVID-	The inclusion criteria for patients included smell alteration after a COVID-19 infection that persisted over six months after testing negative via swab tests, between 18-65 years old, without any severe visual or hearing issues, and	None of the 152 patients had been hospitalized for COVID-19. Smell alteration (loss of smell) was present for an average of about 10 months (9.8 +/- 2.8) after testing negative for COVID-19. 76 patients	Level 4: Cohort study	This study did not include a population of people with long COVID and no olfactory dysfunction, and the scale to measure mental clouding is not perfect. The study population	Yes, but the usefulness of this study might be limited as it is more focused on the link between loss of smell and cognitive dysfunction.

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	direct correlation between the two.	19 infection.	consent to participate in the study. Exclusion criteria included chronic small alteration, headache, or memory problems prior to COVID-19. Cognitive function was assessed using the Mini Mental State Examination (MMSE) test, and headaches	(50%) reported persistent headache, and 71 (46.7%) reported mental clouding. There appears to be a statistically significant link between olfactory dysfunction and other cognitive dysfunction in patients		was skewed more toward women who had milder cases of COVID-19, and smell alterations appear to be more common with patients experiencing mild cases of	

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
			were evaluated using the Wong-Baker FACES Pain Rating Scale. Statistical analysis was conducted with the Odds Radio (OR) looking at the single neurological symptom (brain fog or headache).	with long COVID.		COVID-19.	
Frontera, J. A., Boutajangout, A., Masurkar, A. V., Betensky, R. A., Ge, Y., Vedvyas, A., Debure, L., Moreira, A., Lewis, A., Huang, J., Thawani,	The main goal for this study was to determine a	A total of 251 patients at the New York	Using a total of 4,491 patients who had enrolled in the SNaP study,	This study identified significant elevations in biomarkers	Level 4: Retrospective Analysis Patient	Due to a limited sample population (a lot of	Yes, this study provides direct evidence of

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
S., Balcer, L., Galetta, S., & Wisniewski, T. (2022). Comparison of serum neurodegenerative biomarkers among hospitalized covid-19 patients versus non-covid subjects with normal cognition, mild cognitive impairment, or alzheimer's dementia. Alzheimer's & Dementia, 18(5), 899–910. https://doi.org/10.1002/alz.12556	correlation between patients who were hospitalized for COVID-19 and elevated neurodegenerative biomarkers (t-tau, p-tau181, GFAP, NfL, UCHL1, and Aβ40,42).	University (NYU) Center for Biospecimen Research and Development who had been hospitalized were retrospectively analyzed using biospecimen collected and	researchers for this study narrowed down their sample to those who were hospitalized, had laboratory-confirmed cases of COVID-19, and had consented to store biospecimen samples at NYU. A control population of non-infected	of neuronal and glial degeneration with patients who had been hospitalized for COVID-19 with signs of neurological injury. The most significant difference was with that of the biomarker TME. This study also	Cohort Study	samples had to be excluded for various reasons), the number of patients tested for each of the individual biomarkers varied more than researchers had hoped.	a significant elevation of neurodegenerative biomarkers in patients who have been hospitalized for COVID-19.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
		banked during their hospitalization for COVID-19. These patients had voluntarily enrolled in the Study of Neurologic and Psychiatric Events in Acute COVID-19 (SNaP	people was formed using blood samples banked prior to the onset of COVID-19 in New York (prior to January 1, 2020) from the NYU Alzheimer's Disease Research Center (ARDC) Clinical Core cohort. Samples were thawed once in	found strong correlations between neurodegenerative biomarkers and the inflammatory marker D-dimer, which might yield clues as to how COVID-19 causes cognitive degeneration during and after infection.			

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
		Acute COVID) study.	ice, centrifuged 5 minutes at 10,000 g before being manually diluted 1:4 in 96-well plates. Each sample was run in duplicate and the average value of both runs was used for the study.8				
Delgado-Alonso, C., Valles-Salgado, M., Delgado-Álvarez, A., Yus, M., Gómez-Ruiz, N., Jorquera, M., Polidura, C., Gil, M., Marcos, A., Matías-Guiu, J., & Matías-Guiu, J. A.	This study seeks to determine and understand the	This study included 50 Spanish-speaking patients	A cross-sectional study was conducted with patients who were recruited from	Patients who had been infected by COVID-19 had the worst scores	Level 4: Cross-sectional cohort study.	The population size for this study is relatively	Yes, this study includes one of the more comprehensive

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(2022). Cognitive dysfunction associated with covid-19: A comprehensive neuropsychological study. Journal of Psychiatric Research, 150, 40–46. https://doi.org/10.1016/j.jpsychires.2022.03.033	characteristics of cognitive dysfunction in patients who reported cognitive complaints after they were infected with COVID-19. Furthermore, this study aims to evaluate the correlation between	who had been infected with COVID-19 and who later reported cognitive complaints at least three months after the onset of their disease. The population included	patients consulting due to cognitive issues after COVID-19. As with similar studies, patients with existing cognitive disabilities were excluded. The acceptance rate for the study was 94.3%. Neuropsychological protocol included paper and pencil tests	in the recall and recognition trials. The frequency of impairment was at least three times more frequent with COVID-19 patients than with the control group in Cognitive testing.		small. The patients who were enrolled in the study were not screened for other issues that may have contributed to cognitive impairments (e.g., prior brain injuries).	neuropsychological tests of patients with complaints of post-COVID-19 cognitive impairment.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
	anxiety, depression, sleep, and olfactory function with cognitive dysfunction.	37 women and 13 men around 50 years of age.	that were administered by trained psychologists. Protocol also included a forward and backward digit span, Corsi block-tapping test, Symbol Digit Modalities Test, Boston Naming Test (BNT), Judgment Line Orientation (JLO), among others.				

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Ollila, H., Pihlaja, R., Koskinen, S., Tuulio-Henriksson, A., Salmela, V., Tiainen, M., Hokkanen, L., & Hästbacka, J. (2022). Long-term cognitive functioning is impaired in icu-treated covid-19 patients: A comprehensive controlled neuropsychological study. Critical Care, 26(1). https://doi.org/10.1186/s13054-022-04092-z	The main goal of this study is to determine a link between severe COVID-19 infections (those requiring ICU care) and severe cognitive impairment as a result of long COVID.	A total of 213 participants at Helsinki University Hospital and the University of Helsinki in Finland volunteered to fill out questionnaires six months after the acute	Medical and demographic data were gathered from electronic medical records (with consent) and through interviews conducted four months after the acute phase of COVID-19 infections.	Patients who required treatment in an ICU showed more severe long-term cognitive impairment compared to those who did not. Interestingly, with patients who had more than a decade of education, cognitive impairment	Level 4: Prospective controlled cohort study.	The largest weakness is with the lack of laboratory testing to confirm the control group of non-infected patients had, indeed, never been infected by COVID-19. The authors of the study	Yes, this study provides direct evidence that early treatment and intervention in severe COVID-19 infections can help reduce or prevent later cognitive impairment.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
		phase of their COVID-19 infections. 72 patients were in the ICU, 49 were ward-treated, 44 isolated at home (no hospitalization), and 48 represented the control group		was primarily in the area of attention for men, and of executive functions in general.		could, therefore, not rule out a subclinical infection during the study.	

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
		without any acute infection of COVID-19.					
Hellgren, L., Birberg Thornberg, U., Samuelsson, K., Levi, R., Divanoglou, A., & Blystad, I. (2021). Brain mri and neuropsychological findings at long-term follow-up after covid-19 hospitalisation: An observational cohort study. BMJ Open, 11(10), e055164. https://doi.org/10.1136/bmjopen-2021-055164	This study reports findings on brain MRI scans and neurocognitive function after long-term follow-ups with patients who had been	A total of 734 patients who were hospitalized for COVID-19 (lab confirmed) in Sweden between March 1, 2020 and May 31,	The reporting for this study was guided by the Strengthening the Reporting of Observational Studies in Epidemiology statement for cohort studies. The study excluded	This study found 25 out of 35 patients had abnormal MRI scan results, with white matter lesions being the most common finding. 26 patients reported	Level 4: Ambi-directional observational cohort study.	There was no control group in this study.	Yes, the findings from the study support evidence that further research needs to be done on COVID-19 patients and how to limit long

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
	hospitalized with COVID-19 in the spring of 2020. The goal is to determine a correlation between COVID-19 infection and subsequent reduced cognitive ability.	2020 were included in this observational study. Of the 734 patients, 35 reported cognitive issues and volunteered to undergo brain MRI scans.	patients with existing cognitive conditions that would make it harder to determine the effect of COVID on their cognitive abilities (e.g., patients who already had dementia).	clinically-significant fatigue. Patients with abnormal MRI results had lower Visuospatial Index scores (p=0.031) compared to those with normal MRI scan results.			COVID symptoms like brain fog.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Asadi-Pooya, A. A., Akbari, A., Emami, A., Lotfi, M., Rostamihosseinkhani, M., Nemati, H., Barzegar, Z., Kabiri, M., Zeraatpisheh, Z., Farjoud-Kouhanjani, M., Jafari, A., Sasannia, S., Ashrafi, S., Nazeri, M., Nasiri, S., & Shahisavandi, M. (2021). Long covid syndrome-associated brain fog. Journal of Medical Virology, 94(3), 979–984. https://doi.org/10.1002/jmv.27404	Investigate the frequency of brain fog in confirmed COVID-19 adult patients	A total number of 2696 confirmed COVID-19 adult patients (age 18-55) who admitted to the healthcare facilities (55 centers) in the south of Iran from February 19, 2020	Data collected by ER physicians. Total number of 13,165 patients admitted during the study period; 1,694 died and 11,471 as target population. Choose every other patient randomly, 5,735 patients selected, finally 2,696 participated	1680 (62.3%) patients reported chronic symptoms (Long COVID syndrome-LCS): intolerance of exercise (619, 23%), fatigue (781, 29%), dyspnea (554, 20.5%), muscle pain (44`,	Level 4: Cohort study	This study is based on phone consultation, without clinical, psychological or biological evaluations. There was no control group in this study. There is no treatment involved in this study	Yes. This study has large sample which may be able to represent general population. Random selection and controlled design helps with accuracy and reliability of the result.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
		to November 20, 2020 participated for this study. All patients had positive COVID-19 PCR test.	successfully. Phone call used for contacting patients. A specifically designed questionnaire used for data collection.Kolmogorov-smirov normality test used for statistical analyses.	16.4%), loss of smell (129, 4.8%), cough (234, 8.7%), brain fog (194, 7.2%), chest pain (130, 14.5%), sleep difficulty (392, 14.5%). Chronic post-COVID brain fog is significant associated with sex of female,		to make it a higher level.	

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				respiratory symptoms at the onset, and ICU admission			
Hugon, J., Msika, E.-F., Queneau, M., Farid, K., & Paquet, C. (2021). Long covid: Cognitive complaints (brain fog) and dysfunction of the cingulate cortex. Journal of Neurology, 269(1), 44–46. https://doi.org/10.1007/s00415-021-10655-x	Report two cases of patients (no risk factors) developed neurocognitive disorders which involved cingulate cortex change after	Two patients	FDG PET scan used for this study.	Hypometabolic regions of the cingulate cortex was found by FDG PET scan, from both patients, after COVID-19 infection. MRI showed normal of	Level 4: cohort study	Sample size is too small to represent general population, but very valuable due to limited study in this field.	Yes, objective data with image showed clearly change in brain activities.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
	COVID-19 infection			both patients. Patient 1 developped cognitive disorders combining memory problems, slowness of ideation, general fatigue, anxiety and depression without anosmia after COVID-19			

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				infection in March 2020. Patient 2: Patient infected in May 2020. After several months, fatigue, walking and memory problems and speech deficit occurred.			
Theoharides, T. C., Cholevas, C., Polyzoidis, K., & Politis, A. (2021). Long-covid syndrome-associated brain fog	Compare Long-covid syndrome with	No sampling	Analyze the symptoms experienced by long-COVID	There are no clinically effective interventions	Level 5--Systematic	Not experimental design. No	No. There are theories

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
and chemofog: Luteolin to the rescue. BioFactors, 47(2), 232–241. https://doi.org/10.1002/biof.1726	multisystem inflammation syndrome (MIA-A/MIA-C), myalgic encephalomyelitis (ME), chronic fatigue syndrome (CFS), mast cell activation syndrome (MCAS), and	in this article	syndrome patients and ME/CFS, MCAS, SM. Try to associate possible reasons and brain change with symptoms.	for long-COVID syndrome or brain fog associated with either chemobrain, ME/CFS. Or MCAS. The number of COVID-19 cases may become fewer, but the number of patients with long-COVID syndrome	review of descriptive & qualitative studies	compare group to support the hypothesis of using luteolin formulations to prevent or reduce brain fog.	with medical knowledge behind this study, but lack of experimental research to support. Further study needed.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
	systemic mastocytosis (SM)			may increase. The brain fog associated with long-COVID syndrome and use of chemo therapy may be prevented/reduced with appropriated using luteolin formulations.			

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Borch, L., Holm, M., Knudsen, M., Ellermann-Eriksen, S., & Hagstroem, S. (2022). Long covid symptoms and duration in sars-cov-2 positive children — a nationwide cohort study. European Journal of Pediatrics, 181(4), 1597–1607. https://doi.org/10.1007/s00431-021-04345-z	To evaluate long-COVID symptoms in children.	37,522 patients aged 0-17 with SARS-CoV-2 infection, confirmed by RT-PCR test were recruited in testing group. 78,037 randomly selected children who had not been	An electronic questionnaire (REDCap) was sent to both experimental group and control group from March 24th until May 9th, 2021. Patients aged 15 and above received the questionnaire themselves, and others by parents. The children were divided into two	A total of 16, 836 (44.9% of 37,522 children) SARS-CoV-2 infected children completed this study, 16,620 (21.3% of 78,037 children) completed this study in control group. SARS-CoV-2 infected	Level 4: Correlational design	This study does not identify clearly what viral infection in control group. It could affect the result due to the nature of different virus infection.	Yes. This is a nation-wide study with a large number of children involved. The data is good to represent general pediatric population.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
		tested positive for SARS-CoV-2 were in control group. This study was approved by the Danish Health Data Authority and registered at the Central	groups: pre-school (0-5 years old) and school age (6-17 years old). Risk differences were estimated. StataMP 17 was used for statistical analysis. Unpaired two-sample t test was used to determine whether a significant difference between two	children complained more of fatigue, loss of smell, loss of taste, muscle weakness in pre-school group, loss of smell and taste, fatigue, were more in school age group. Control group, pre-school age (0-5)			

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
		Denmark region. Control group children were picked from five municipalities public school or day-care in Denmark (Aalborg, Herning, Aarhus, Randers and	groups. Person Chisquare test was used to test independence of two categorical variables.	children experienced significant more cough, fever, concentration difficulties and diarrhea than experimental group same age group children; school age children in control group were suffering more in concentratio			

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
		Frederiksberg)		n difficulties, headaches, nausea, muscle and join pain, cough, diarrhea and fever than SARS-CoV-2 infected same age group children. Depends on the age, symptoms resolved in a minimum of 54-75% of			

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				children within 1-5 months.			
Rigoni, M., Torri, E., Nollo, G., Donne, L., Rizzardo, S., Lenzi, L., Falzone, A., & Cozzio, S. (2022). "long covid" results after hospitalization for sars-cov-2 infection. Scientific Reports, 12(1). https://doi.org/10.1038/s41598-022-13077-5	To evaluate COVID-19 outcomes at six and twelve months after hospitalization.	471 hospitalized SARS-CoV-2 infected patients were considered initially, but 58 died before discharge. 413 were enrolled for study.	Follow up with patients after discharge, at 6 months and 12 months point. Telephone consultation or ambulatory visit used for evaluating symptoms.	At 6 months mark, within 355 patients, 30.3% had any symptoms, 18.0% dyspnea, 6.2% neurological symptoms, 52 out of 105 had major damages of lung confirmed	Level 3-Quasi-experimental design	There is limited availability of resources to be used in this study. Not randomly sampling used which is lower the level of evidence.	Yes. This study was follow up for 12 months. Majority of patients joined at both 6-month checkup and 12-month checkup. The data is limited affecting of

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				by image study. Patient who received ventilation has a higher probability of having symptoms. At 12 months mark, within 344 patients, 25.3% reported any symptoms, 12.2% dyspnea, 101% neurological			individual difference.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				symptoms, 37 out of 47 were present with severe interstitial lesions. Patients who had respiratory support (both non-invasive ventilation or invasive mechanical ventilation) had higher probability of experiencing			

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				symptoms, including neurological symptoms. The neurocognitive symptoms increased from 6.2% to 10.1% from 6-month to the 12-month time mark.			
Mandal, S., Barnett, J., Brill, S. E., Brown, J. S., Denneny, E. K., Hare, S. S., Heightman, M., Hillman, T. E., Jacob, J., Jarvis, H. C., Lipman, M. I.,	To study symptoms among patients after	384 patients from three large hospitals	Blood test and image study done at discharge. Patients who	Among 384 patients who enrolled for this study, majority of	Level 4— correlati	This study only enrolled patients who tested	Yes. This study has limitations

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Naidu, S. B., Nair, A., Porter, J. C., Tomlinson, G. S., & Hurst, J. R. (2020). 'long-covid': A cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for covid-19. Thorax, 76(4), 396–398. https://doi.org/10.1136/thoraxjnl-2020-215818	discharged from hospital.	in London, were enrolled in this study.	tested abnormal at discharge were invited back for follow up and repeat testing after discharge. All patients were tested positive for SARS-CoV-2 infection. Follow up was done by phone or in-person visit at four-to-six weeks after discharge.	them blood test returned to normal level at follow up, 7.3% of 247 patients had persisting lymphopaenia, 30.1% of 229 patients had elevated d-dimer, 9.5% of 190 patients had elevated CRP. 333 patients out of 384 had a chest	onal design	positive for SARS-CoV-2 infection, and patients requiring prolonged ICU and inpatient stay. Not all symptoms were included in this study. Not all patients are willing to follow up	but using objective data (blood test and image study) to evaluate the situation. It is more trusted with objective data, comparing with subjective feeling reported by patients only.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				radiograph. 49 (15%) were normal, 188 (56%) were typical of COVID-19 infection, 96 (29%) were unlikely related to COVID-19 change. 244 of 384 patients had follow up image study done. 151 (62%) showed		and being part of interview.	

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				normal, 66 (27%) showed significant improvement, 4 (2%) were unchanged, 23 (9%) showed significant deterioration. Among 23 patients who demonstrated worsening at follow up, 2 of them (9%) had normal result			

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				previously, 10 of them(43%) showed typical COVID-19 infection previously, 11 of them (43%) were unlikely linked the change to COVID-19 in the past.			
Baig, A. (2021). Chronic long-covid syndrome: A protracted covid-19 illness with neurological dysfunctions. CNS Neuroscience &	To discuss possible reason and neurological change	No Sampling	Literature review	Neurological damage after SARS-CoV-2 infection may be	Level 5—systematic review	Further experimental study is needed, or image	Yes. This study is offered possible

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Therapeutics, 27(12), 1433–1436. https://doi.org/10.1111/cns.13737	after SARS-CoV-2 infection.			difference because of viral load, infected location of brain, immune system responds, and inflammation process. The inability of the neurons to regenerate following damage maybe the cause of	of descriptive & qualitative studies	study is needed with larger patient population to increase reliability of the result.	reasons of long-COVID, especially neurological change after COVID -19 infection. It is a good start to guide further studies.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				long-COVID symptoms. In-depth research is needed to further evaluate whether vaccination could help with long-COVID.			
Fernández-de-las-Peñas, C., Palacios-Ceña, D., Gómez-Mayordomo, V., Cuadrado, M. L., & Florencio, L. L. (2021). Defining post-covid symptoms (post-acute covid, long covid, persistent post-covid): An integrative classification.	To clearly defining Post-COVID symptoms and establish the time	No sampling	Data review and literature review.	There are four phases were defined for Post-COVID symptoms: Transition Phase:	Level 5—systematic review of descripti ve &	No sampling involved in this study.	Yes. It offered a good definition of post-COVID symptoms

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
International Journal of Environmental Research and Public Health, 18(5), 2621. https://doi.org/10.3390/ijerph18052621	reference points after COVID-19 infection.			symptoms potentially associated with acute COVID-19, up to 4-5 weeks; Phase 1: Acute post-COVID symptoms: symptoms from week 5 to week 12; Phase 2: Symptoms from week 12 to week 24; Phase 3: symptoms	qualitative studies		with timeline. It is good for further evaluation and offer guidance for long-COVID studies in the future.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				lasting more than 24 weeks (persistent post-COVID symptoms).			
Moghimi, N., Di Napoli, M., Biller, J., Siegler, J. E., Shekhar, R., McCullough, L. D., Harkins, M. S., Hong, E., Alaouieh, D. A., Mansueto, G., & Divani, A. A. (2021). The neurological manifestations of post-acute sequelae of sars-cov-2 infection. Current Neurology and Neuroscience Reports, 21(9). https://doi.org/10.1007/s11910-021-01130-1	To summarize the possible pathophysiology, risk factors, incidence, and proposed management of neurological clinical	No sampling for this article, but over thousands of patients were studied from literatures that used	Literature review	PASC is a multi-organ disorder which lasting for weeks or even longer following recovery from initial SARS-CoV-2 infection. The growing numbers of	Level 1—systematic review; clinical guideline based on systematic reviews	More studies could be available in the future. Current data may be still limited due to timing.	Yes. It is a high level evidence related to post-COVID study, especially related neuro-PASC.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
	symptoms of post-acute stage of SARS-CoV-2 infection (PASC) or neuro-PASC, from current published literatures.	in this article.		COVID-19 patients who developed neuro-PASC should be recognized. One study done after seven months of infection with 3762 patients enrolled , showed 77.9% of post-COVID patients, reported persistent	or meta-analyses		

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				fatigue, 71.2% of them reported post-exertional malaise, 56.8% and 67.5% of them reported cognitive dysfunctions. Another study with 1733 confirmed SARS-CoV-2 infection			

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				by lab testing, showed 76% of them complained at least one following symptoms: fatigue/muscle weakness (63%), difficulty sleeping (26%), hair loss (22%), loss of smell (11%), loss of taste (9%), trouble with			

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				mobility (7%). Chronic fatigue (CFS/ME) have been reported with other virus infection as well. About 800,000 and 3.4 million Americans suffering from CFS. 1 in 4 post-COVID patients still can be			

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				diagnosed with CFS after one year of infection. The appropriate and efficient treatments and early diagnosis are needed urgently.			
Theoharides, T. C. (2022). Could sars-cov-2 spike protein be responsible for long-covid syndrome? Molecular Neurobiology, 59(3), 1850–1861.	To explore whether SARS-CoV-2 spike protein is	No sampling	Literature reviews	Spike protein of. SARS-CoV-2 might pass or damage the blood-	Level 1—systematic review	Risk of bias	Yes. This article summarized possible reasons for

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
https://doi.org/10.1007/s12035-021-02696-0	the cause of long-COVID.			brain barrier (BBB) cause brain perivascular inflammation. SARS-CoV-2 could entry into the brain from gustatory-olfactory trigeminal pathway and pass BBB has been reported in deer mice infected with	& meta-analysis		brain damage after COVID-19 infection, offer hypotheses for further study.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				SARS-CoV-2. From autopsy report of patients died from COVID-19, including infant, evidence of severe neuronal loss was founded.			
Jarrott, B., Head, R., Pringle, K. G., Lumbers, E. R., & Martin, J. H. (2022). “long covid”—a hypothesis for	To summarize current literatures	No Sampling	Literature review	About 60% of patients who infected with SARS-	Level 1-systemat	Risk of bias.	No. This article offered a

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
understanding the biological basis and pharmacological treatment strategy. Pharmacology Research & Perspectives, 10(1). https://doi.org/10.1002/prp2.911	and studies, offering a hypothesis for understanding the biological reasons of SARS-CoV-2 infection and Long COVID and possible treatment strategy.	in this article	Both human and animal study data were considered.	CoV-2 virus have eliminated the virus after 28 days, but about 40% of them developed Long COVID syndrome. The virus binding to the ACE-2 protein which leads the blood vessels inflammatio	ic review	Further study is needed to prove the hypothesis that brought up in this study.	good hypothesis to further study. However, no evidenced based practice solution clearly stated. It may be able to support adjusting of current education and treatment for COVID-

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				n may be one of the causes of Long COVID. Theoretically, intracellular antioxidant might help with the symptoms, which bring a hypothesis to be proved in the future study, such as melatonin usage in Long			19 infected patient. Further study is needed.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				COVID prevention or treatment.			
Østergaard, L. (2021). Sars cov-2 related microvascular damage and symptoms during and after covid-19: Consequences of capillary transit-time changes, tissue hypoxia and inflammation. Physiological Reports, 9(3). https://doi.org/10.14814/phy2.14726	To explore the damage caused by SARS-CoV-2 infection and possible reason of clinical symptoms.	No sampling	Literature review	COVID and Long COVID symptoms may be caused by cell damage, organ inflammation which leads to hypoxemia of tissue.	Level 4—systematic review of descriptive & qualitative studies	Need further study to prove the hypothesis.	Yes. There is no harm to help patient stay with a good oxygen level. Early education of ways of keep good oxygen level, such as increasing deep breathing

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
							will not harm patients.
Leta, V., Rodríguez-Violante, M., Abundes, A., Rukavina, K., Teo, J. T., Falup-Pecurariu, C., Irincu, L., Rota, S., Bhidayasiri, R., Storch, A., Odin, P., Antonini, A., & Ray Chaudhuri, K. (2021). Parkinson's disease and post–covid-19 syndrome: The parkinson's long-covid spectrum. Movement Disorders, 36(6), 1287–1289. https://doi.org/10.1002/mds.28622	To post-COVID syndrome in Parkinson's disease (PD) patients.	27 patients who had PD and infected by COVID-19. Patients were selected from several centers in UK, Italy, Romania, and Mexico	Monitoring post-COVID symptoms in PD patients and dosage of levodopa.	23 (85.2%) patients with PD developed post-COVID 19 symptoms. 51.9% patient presented worsening motor function, 48.2% PD patients increased daily	Level 4-cohort study	Sample size was small, may not represent general population.	Yes. Good data even with small sample size.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
		from beginning of March 2020 to April 2021.		levodopa dosage requirement, 40.7% developed fatigue, 22.2% developed cognitive disturbances (including brain fog, loss of concentration and memory deficits), 22.2% reported			

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				sleep disturbance.			
Akbarialiabad, H., Taghrir, M., Abdollahi, A., Ghahramani, N., Kumar, M., Paydar, S., Razani, B., Mwangi, J., Asadi-Pooya, A. A., Malekmakan, L., & Bastani, B. (2021). Long covid, a comprehensive systematic scoping review. Infection, 49(6), 1163–1186. https://doi.org/10.1007/s15010-021-01666-x	To summarize current understanding of Long COVID from reviewing literatures until January 30, 2021	No sampling for this article, but randomized clinical trials and non-randomized clinical trials were included in this study.	Literature review 120 papers were selected for this study, including one randomized clinical trial, 22 cohort, 28 cross-sectional studies.	As of 120 papers, 49.1% focus on signs and symptoms, 23.3% on management, and 10.8% on pathophysiology. 10 of 120 focus on imaging studies. The predominant symptoms	Level 1—systematic review of randomized and non-randomized clinical trials	Very limited number of randomized clinical trials included in this study.	Yes. High level evidence represent from this article.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				include fatigue, arthralgia, sleep disorder, breathlessness, and chest pain. The risk of long-term issue with cutaneous, respiratory, cardiovascular, musculoskeletal, mental health, neurologic, and renal			

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				involvement within patient population who survive the acute phase of the infection.			
Salihefendic, N., Zildzic, M., & Huseinagic, H. (2021). Ischemic vasculitis as a cause of brain disorder's in patients with long covid: Case report. Medical Archives, 75(6), 471. https://doi.org/10.5455/medarh.2021.75.471-474	To describe two young adult patients with neuropsychiatric symptoms of long COVID-19 syndrome.	2 younger females who diagnosed with COVID-19 infection without respiratory	Data collection based on 2 selected patients.	Both patients developed the brain disorder which CT scan showed signs of ischemic vasculitis after 1-2 months of	Level 4— Cohort study	Sample size is small, not randomly selected. The result may be not able to represent general population.	Yes. Even the sample size is small, but the detailed data was measured.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
		complications.		COVID-19 infection.			

Appendix B

DEVELOPING A CLINICAL QUESTION

Patient/Problem/Population:

neurological damage in adult COVID-19 infected patients

Intervention:

No intervention

Comparison: (if applicable)

Compare cognitive function with testing group and data base of the same age group people before COVID 19 pandemic

Outcome:

COVID-19 infection decreases cognitive function

I. Based on the content above, write out your question in sentence format:

In adult patients infected with COVID 19, does COVID 19 infection decrease patient's cognitive function in three months?

II. Based on your work above, make a list of possible search terms that may be used in the literature search:

COVID 19	long-COVID	SARS-CoV-2
Long COVID	Neurological damage	Brain function
Brain damage	hard to concentrate	memory loss

Appendix C

CITI Certificate

CITI PROGRAM

Completion Date 13-Dec-2022
Expiration Date 13-Dec-2025
Record ID 52972994

This is to certify that:

June Alsgaard

Not valid for renewal of certification through CME.

Has completed the following CITI Program course:

Biomedical Research - Basic/Refresher
(Curriculum Group)
Biomedical & Health Science Researchers
(Course Learner Group)
1 - Basic Course
(Stage)

Under requirements set by:

Liberty University

CITI
Collaborative Institutional Training Initiative

Verify at www.citiprogram.org/verify/?wf49ba30c-ebdc-47b7-8033-d4c7dba720d1-52972994

Appendix D

Permission to use IOWA Model

Sunday, October 30, 2022 at 22:28:24 Eastern Daylight Time

Subject: Permission to Use and/or Reproduce The Iowa Model (1998)
Date: Thursday, October 27, 2022 at 10:04:33 PM Eastern Daylight Time
From: Kimberly Jordan - University of Iowa Hospitals and Clinics
To: June Alsgaard

You have permission, as requested today, to review and/or reproduce *The Iowa Model of Evidence-Based Practice to Promote Quality Care (Revised 1998).* Click the link below to open.

The Iowa Model of Evidence-Based Practice to Promote Quality Care (Revised 1998)

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Reference: Titler, M. G., Kleiber, C., Steelman, V. J., Rakel, B.A., Budreau, G., Everett, L. Q., ...Goode, C. J. (2001). The Iowa model of evidence-based practice to promote quality care. *Critical Care Nursing Clinics of North America, 13*(4), 497-509.

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Please contact UIHCNursingResearchandEBP@uiowa.edu or 319-384-9098 with questions.

Appendix E

IRB approval letter

Date: 3-30-2023

IRB #: IRB-FY22-23-1150
Title: Whether COVID-19 Infection Affects Human Cognitive Function: An Integrative Review
Creation Date: 2-22-2023
End Date:
Status: Approved
Principal Investigator: June Alsgaard
Review Board: Research Ethics Office
Sponsor:

Study History

Submission Type Initial	**Review Type** Exempt	**Decision** No Human Subjects Research

Key Study Contacts

Member June Alsgaard	**Role** Principal Investigator	[redacted]
Member June Alsgaard	**Role** Primary Contact	
Member Kenneth Thompson	**Role** Co-Principal Investigator	